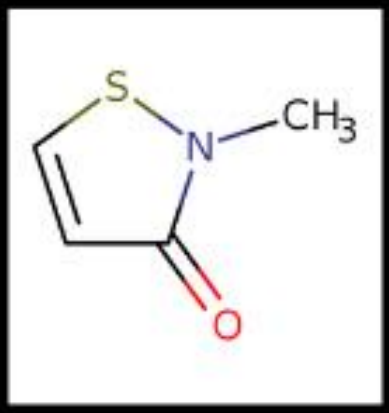
Monographs of Cosmetic Allergens

UPDATE 2017-2025

Anton de Groot





MONOGRAPHS OF COSMETIC ALLERGENS

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FOREWORD

Nearly 8 years have passed since I finished writing the book Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics. Since then, I have seen many published reports of allergic contact dermatitis from cosmetics caused by new, previously unpublished allergens passing by, especially in the journal *Contact Dermatitis*. Also, a large number of additional cases of cosmetic allergy from known, but rare or infrequent allergens, have been published. So, a couple of month ago I decided it was time for an update.

Right at that moment I decided that I would rather publish an update myself and not ask the publishers of the 'mother book' if they were willing to publish it. The reason for this is that I would like as many dermatologists as possible – and thereby their patients – to benefit from my work. And I am specifically addressing the American Contact Dermatitis Society (ACDS) , the European Society of Contact Dermatitis (ESCD) and their members, to whom I am so much indebted for the honour and kindness they have shown me. The book, I decided, had to be made available to all of them free of charge.

I turned it into an e-book. That wasn't too difficult, because I had already written and completely formatted all 4 books in the Monographs in Contact Allergy series in Word previously. To produce them, the publisher only had to turn on the printer, so to speak. An e-book also has the advantage that there are no additional production costs, it doesn't have to be sent by post and you can add all kinds of handy tricks to it, such as links to external websites, files and links in the book itself. In this book, for example, you are redirected from the contents with 1 click directly to the monograph that you want to open. That took some research, but it was fun to do and I was helped a lot by my friend ChatGPT, with whom I have built up a solid friendship in a short time.

This update presents literature data on 39 new non-fragrance contact allergens in cosmetics and updated information on 74 already known allergens that have caused allergic contact dermatitis due to their presence in cosmetic products. The book is mainly about cosmetic allergy, but I have included all non-cosmetic literature that I came across during the screening of *Contact Dermatitis* and *Dermatitis* between September 2017 and March 2025 in the chapters, albeit mostly (very) briefly.

I intend to place the file of the book on my website www.antondegroot.com, where you can download it free of charge. I will kindly ask the secretaries of the ACDS, the ESCD and the Dutch Society of Dermatology and Venereology to send notifications of the book's availability in their Newsletters. Please feel free to send any feedback / comments you have to antondegroot@planet.nl. Much appreciated!

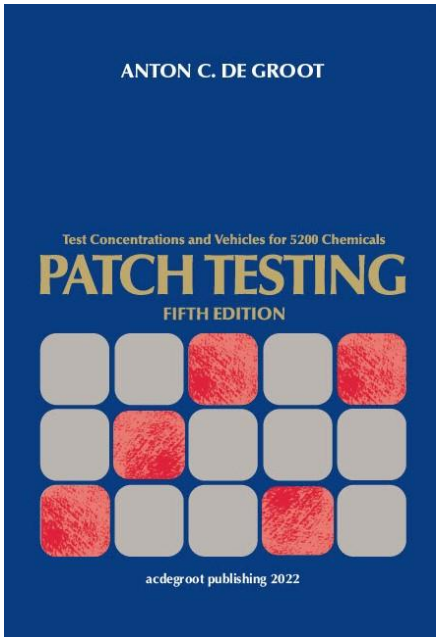
Anton de Groot, MD PhD
Wapserveen, The Netherlands, April 2025

ABOUT THE AUTHOR

Anton C. de Groot, MD PhD (1951) received his medical and specialist training at the University of Groningen, The Netherlands. In 1980, he started his career as dermatologist in private practice in 's-Hertogenbosch. At that time, he had already become interested in contact allergy and in side effects of drugs by writing the chapter Drugs used on the skin with his mentor prof. Johan Nater, for the famous Meyler's Side Effects of Drugs series. Soon, the subject of this chapter in new editions and the yearly Side Effects of Drugs Annuals would be expanded to include cosmetics and oral drugs used in dermatology (1980-2000). Contact allergy to cosmetics would become de Groot's main area of interest and expertise and in 1988, he received a PhD degree on his Thesis entitled Adverse Reactions to Cosmetics, supervised by prof. Nater.

Frustrated by the lack of easily accessible information on the ingredients of cosmetic products, and convinced that compulsory ingredient labeling of cosmetics (which at that time was already implemented in the USA) would benefit both consumers and allergic patients and would lead to only slight and temporary disadvantages to the cosmetics industry, De Groot approached the newly founded European Society of Contact Dermatitis and became Chairman of the Working Party European Community Affairs. The European Commission and its committees, elected legislators, national trade, health departments and the cosmetics industries were extensively lobbied by the members of this group. This resulted in new legislation by the Commission of the European Communities in 1991, making ingredient labeling mandatory for all cosmetic products sold in EC Member States by December 31, 1997.

Anton has been the chairman of the 'Contact Dermatitis Group' of the Dutch Society for Dermatology and Venereology from 1984 to 1998. In 1990, he was one of the founders of the Nederlands Tijdschrift voor Dermatologie en Venereologie (Dutch Journal of Dermatology and Venereology) and was Editor of this scientific journal for 20 years, of which he served 10 years as Editor-in-chief. De Groot has authored 21 book titles, twelve of which – all co-authored by Johan Toonstra MD PhD – are general dermatology books in Dutch for medical students, general practitioners, and paramedical professionals. Anton has written eight (including this e-book) international books, of which one has had three Editions: Unwanted Effects of Cosmetics and Drugs used in Dermatology (first Edition 1983, second 1985, third 1994).



Of his best known book Patch Testing, 5 editions have been published (first Edition 1986, second 1994, third 2008, fourth 2018, 5th 2022). Anton has donated the files of the most recent edition to the American Contact Dermatitis Society and the European Society of Contact Dermatitis, after which it was placed on the websites of these societies, where the book can be accessed online by their members.

After writing a book entitled Essential Oils: Contact Allergy and Chemical Composition with Erich Schmidt, which appeared in 2016, he started working on a series of Monographs in Contact Allergy books. The first Volume discussing 'Non-fragrance allergens in cosmetics', to which book this is an update, was released in 2018, followed by 'Fragrances and essential oils' in 2019, 'Topical drugs' in 2020, and 'Systemic drugs' in 2022. In addition to these books, Anton has written over 70 book chapters (mostly in international books), over 150 articles in international journals (the great majority in *Contact Dermatitis*) and some 235 articles in Dutch medical and paramedical journals. He served as board member of several journals including Dermatosen and is currently member of the Editorial Advisory Board of the Journal *Dermatitis*.

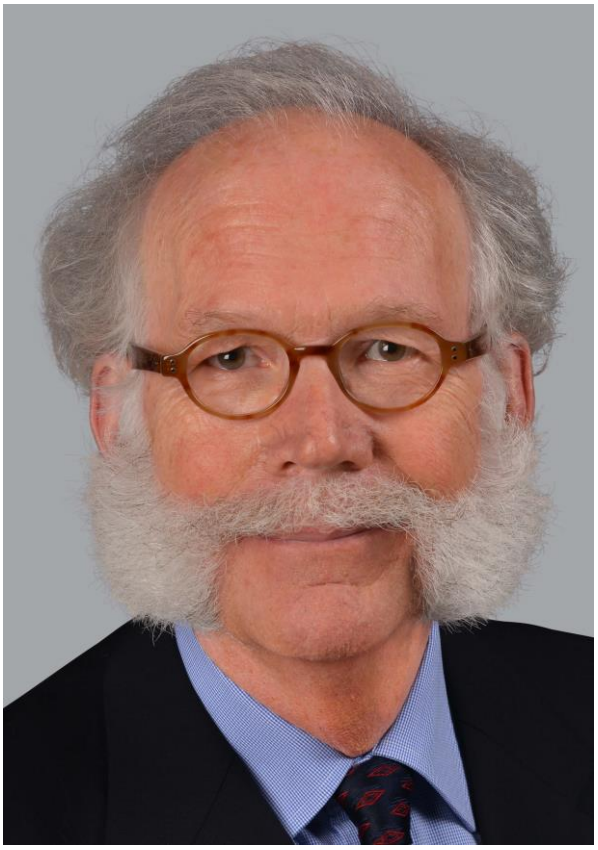
In 2019, the author received the American Contact Dermatitis Society Honorary Membership status for his 'vast contributions to contact dermatitis'. In 2022, Anton also received the Honorary Membership of the

European Society of Contact Dermatitis ‘for his contributions to the European legislation on cosmetic ingredient labelling, his book Patch Testing and his many other scholarly books and review articles’.

From 2008 to 2020, De Groot has had an unpaid, informal (no staff membership of the Department of Dermatology), part-time position at the University Medical Centre Groningen for regularly teaching general dermatology to junior doctors. This gave him access to the university library through a proxy-account which enabled him to write his articles, chapters and books. The corona pandemic with the inherent health threat to people his age (he was 69 at that time) made him decide not to pursue continuation of this position.

Since June 2023 he has a guest position at the Department of Dermatoallergology (head: prof. dr. dr. Thomas Rustemeyer) of Amsterdam University Medical Centers, where he is currently the daily supervisor of a PhD candidate.

Anton has been married since 1980, he and his wife Janny have two daughters, both lawyers, and three grandchildren.



Anton de Groot in 2016.

Picture taken by a professional photographer for the book *Essential oils. Contact allergy and chemical composition* (2016).

Since then, the author has hardly aged …… in his books.

Acknowledgements

I am very grateful to CRC press Taylor and Francis for allowing me to reproduce the **IDENTIFICATION** sections of the updated chapters and some other material from the book to which this is an update, Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, (Part 1 and Part 2). Boca Raton, Fl, USA: CRC Press Taylor and Francis Group, 2018 (ISBN 978-1-138-57325-3 and 9781138573383)

CONTENTS

CHAPTER 1 INTRODUCTION

1.1 AN UPDATE TO 'MONOGRAPHS IN CONTACT ALLERGY, VOLUME 1. NON-FRAGRANCE ALLERGENS IN COSMETICS'

Seven years ago the author's book Monographs in Contact Allergy, Volume 1. Non-fragrance allergens in cosmetics was published. The two-part book with 1430 pages presented 497 monographs on chemicals and substances that had caused allergic contact dermatitis from their presence in cosmetics, i.e., causing allergic cosmetic dermatitis. Each monograph also fully reviewed the literature on contact allergy to the allergens/haptens from non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and much more relevant information up to September 2017.
Since then, many newly identified cosmetic allergens have been described in literature and new reports have appeared presenting additional cases of cosmetic allergy, especially to rare or infrequent allergens. Enough material to write an update to the book! This is not a 'second edition', the material previously published is not shown here, with the exception of the (adapted) Identification sections and selected literature references. Only new material is presented, thereby providing updates to the book. Although information on non-cosmetic aspects of the allergens, published in *Contact Dermatitis* and *Dermatitis*, is included, the emphasis is clearly on allergic cosmetic dermatitis.
This book is published as e-book, which has given the opportunity to include links to websites, webpages, (nearly) all cited articles (DOI-links), and, last but hopefully not least, to the author.

1.2 DATA PROVIDED IN THIS BOOK

SCOPE AND DATA COLLECTING
This book provides monographs on chemicals/substances that have caused allergic contact dermatitis, immediate contact reactions (contact urticaria) or photoallergic contact dermatitis from their presence in cosmetic products reported in publications from October, 2017 through March, 2025. The literature up to September 2017 was presented in the author's book Monographs in Contact Allergy, Volume 1. Non-fragrance allergens in cosmetics, so the current publication is an Update to this book.

The main sources of information are the journals *Contact Dermatitis* and *Dermatitis*. All issues of *Contact Dermatitis* were fully screened for relevant articles from Volume 77, issue 4 (October 2017) to and including Volume 92, issue 5 (May 2025), as were the articles of 'Early view', the Online version of records before inclusion in an issue (accessed April 10, 2025). All issues of *Dermatitis* were fully screened for relevant articles from Volume 28, issue 5 (September - October 2017) to and including Volume 36, issue 2 (March-April 2025), as were the articles of 'Online now', the Online publications Ahead of print (accessed April 10, 2025). The journal *Cosmetics* (not indexed in PubMed) was also screened for this time frame. Literature lists of journal publications thus identified and used for this book were searched for other relevant articles. In addition, a PubMed search was conducted with single search terms 'cosmetic allergy' and 'cosmetic dermatitis', and using search terms 'dermatitis' OR 'contact dermatitis' OR 'eczema' combined with (AND) 'cosmetics'. Finally, all chemicals for which a monographs was written were used as search term combined with (AND) 'contact allergy' OR 'allergic contact dermatitis' AND 'cosmetics' OR 'cosmetic allergy' (performed mid-December 2024). These searches resulted in only a few hits in journals other than *Contact Dermatitis* and *Dermatitis*.

CRITERIA FOR INCLUSION
Included in this book are chemicals/substances that, between October 2018 through March 2025, were reported to have caused allergic contact dermatitis, immediate contact reactions (contact urticaria), photoallergic contact dermatitis, or a combination of these side effects, *from their presence in cosmetic products*. Only these cosmetic ingredients are presented in monographs, either new cosmetic allergens/ haptens (not previously reported) (Chapter 2), or allergens already included in the Monographs Volume 1

('Updates', Chapter 3). Allergens that were already discussed in the Monographs Volume 1 for which updated information was found but only *unrelated to cosmetic products* are *not* included here.

SEARCH RESULTS

The search has resulted in the identification of 39 new cosmetic allergens. Two of these also caused immediate-type reactions (contact urticaria) from their presence in cosmetic products. Their monographs are presented in Chapter 2. Cosmetic allergy was also found for 74 allergens which were already present in the Monographs book. The updates to the previous chapters are presented in Chapter 3. Nine of these have also caused immediate contact reactions, one photoallergic contact dermatitis and 2 photoaggravation of allergic contact dermatitis. Finally, there were nine reports of (only) contact urticaria to ingredient in cosmetics, which are presented in Chapter 4.

DATA PROVIDED IN THE MONOGRAPHS

The data provided in the monographs – when available and relevant – are shown in table 1.1. The sections in yellow apply to the updated monographs in Chapter 3 only. In the section 'Previous cases of allergic cosmetic dermatitis', such publications discussed in the Monographs book are listed in the Literature section; they are not discussed. When there were a few previous reports only, they are typically mentioned all. In the case of a larger number (usually 7 or more), only a few recent ones are shown, and the reader is referred for more information to the corresponding chapter in the Monographs book.
In the section 'Other publications', information on the allergen is presented that was found during the screening of *Contact Dermatitis* and *Dermatitis* from October 2017 through March 2025 which is not directly related to cosmetic products. Examples of data that is – briefly – discussed there include (occupational) allergic contact dermatitis or contact urticaria from the allergen in non-cosmetic products, cross-reactivity, results of patch testing with different concentrations or materials, review articles, routine testing with the allergen (only when the article is entirely about the allergen, *not* results of testing multiple allergens in routine series such as the NACDG screening series or the European baseline series), market surveys of allergens in products, risk assessment studies and chemical analyses for identification of allergens in products.

Table 1.1. Information provided (when available) in each monograph

INCI NAME OF ALLERGEN	
IDENTIFICATION	**Previous chapter to which this is an update**
Description/definition	
Classification	**CONTACT ALLERGY**
INCI name USA	**Case series**
IUPAC name	**Case reports**
Other names	**Previous cases of allergic cosmetic dermatitis**
CAS registry number	
EC number	**IMMEDIATE-TYPE REACTIONS**
CIR reports	**Case reports**
SCCS opinions	**Previous cases of immediate-type reactions**
Wikipedia	
Functions in cosmetics (EU, USA)	**Presence in cosmetic products**
EU cosmetic restrictions	
Patch testing	**OTHER PUBLICATIONS**
Molecular formula	
Structural formula	**LITERATURE**

IDENTIFICATION

In the section **IDENTIFICATION** the chemicals are identified by INCI name (EU name; USA name is mentioned only when different from the EU name), IUPAC name (International Union of Pure and Applied Chemistry; https://iupac.org/), other names (synonyms), CAS registry number (Chemical Abstract Service;

www.cas.org), EC number (European Community) (formerly: EINECS [European Inventory of Existing Commercial Chemical Substances]), and their molecular and structural formulas (where applicable and available). Also, a general description/definition of the compounds is provided, the chemical class(es) to which they belong, and whether and where more information can be found in reports and monographs published by CIR (Cosmetic Ingredient Review), and Wikipedia. Reference is made to any published Opinions of the European Union SCCS (Scientific Committee on Consumer Safety), and EU cosmetic restrictions. The functions of the chemicals in cosmetics, both in the EU and the USA are mentioned and data on how the chemical or substance can best be patch tested is provided in each Monograph.
The CAS numbers shown in this book have not been verified by the Chemical Abstract Service (www.cas.org). However, most are from CAS Common Chemistry (https://commonchemistry.cas.org/) and are therefore reliable.

The sources of data provided in the sections **IDENTIFICATION** and **Presence in cosmetic products** are shown below.

IDENTIFICATION	**Sources**
Description/definition	1,2
Classification	1,3
INCI name USA	1
IUPAC name	3
Other names	3
CAS registry number	4, 3
EC number	5
CIR reports	6
SCCS opinions	7
Wikipedia	8
Functions in cosmetics (EU, USA)	1,2
EU cosmetic restrictions	2
Patch testing	9
Molecular formula	1,3,5
Structural formula	10, 11, 1, and websites (chemical databases, suppliers of chemicals) found on the internet showing structural formulas
Presence in cosmetic products	
FDA's Voluntary Cosmetic Registration Program	1
EWG's Skin Deep Cosmetics Database	12

SOURCES OF INFORMATION

1 INCIpedia, the Personal Care Products Council (formerly Cosmetic, Toiletry and Fragrance Association) continuously updated web-based compendium of information related to INCI names and regulatory information. https://incipedia.personalcarecouncil.org/. Choose Government, Ingredient Search (subscription only, accessible to members of the American Contact Dermatitis Society).
2 The European Commission database with information on cosmetic substances and ingredients CosIng. https://ec.europa.eu/growth/tools-databases/cosing/.
3 NIH National Library of Medicine, PubChem. https://pubchem.ncbi.nlm.nih.gov/.
4 Cas Common Chemistry. https://commonchemistry.cas.org/.
5 ECHA European Chemicals Agency, EC Inventory. https://echa.europa.eu/information-on-chemicals/ec-inventory.
6 Cosmetic Ingredient Review: http://www.cir-safety.org/.

7 European Commission, Public Health. Scientific Committee on Consumer Safety (SCCS). SCCS – Opinions. https://health.ec.europa.eu/scientific-committees/scientific-committee-consumer-safety-sccs/sccs-opinions_en.
8 Wikipedia, the free encyclopedia. https://en.wikipedia.org/wiki/Main_Page.
9 Providers of patch test allergens: Chemotechnique Diagnostics (www.chemotechnique.se), SmartPractice (www.smartpracticecanada.com, www.smartpracticeeurope.com). If not available from these suppliers, the test concentration(s) as used in the publication(s) is/are usually mentioned.
10 Sigma-Aldrich (Merck). www.sigmaaldrich.com.
11 SAAPEDIA. https://www.surfactant.top/en/.
12 EWG's Skin Deep Cosmetics Database. https://www.ewg.org/skindeep/.

CHAPTER 2 MONOGRAPHS OF NEW COSMETIC ALLERGENS 2017-2025

2.1 INTRODUCTION

By screening all issues of the journal *Contact Dermatitis*, *Dermatitis*, and *Cosmetics* between September/October 2017 and March 2025 and with a PubMed search as described in Chapter 1.2, the author found 39 single ingredients or substances that had caused allergic contact dermatitis by their presence in cosmetic products (i.e., causing allergic cosmetic dermatitis) and that had not previously been described as allergens/haptens in cosmetics. These 'new' allergens, which were not yet included in the 2018 Monographs in Contact Allergy, Volume 1, to which this publication is an update, are shown in Table 2.1 and are all discussed in separate monographs in this chapter.

By far, most publications were found in *Contact Dermatitis*. In some cases, the diagnostic process had been rather simple: the patient was patch tested with her of his suspected cosmetic products, which resulted in one or more positive reactions. The dermatologist then contacted the manufacturer of the product and requested samples of its ingredients. When these were obtained, they were tested in a new patch test session on the patient and one or more of the ingredients of the product would react positively. Sometimes it was immediately known which allergen was involved, sometimes the test materials were coded and the manufacturer had to be contacted again to request the name of the substance. Usually, if sufficient material was available, a number of unexposed control patients ('volunteers') were also patch tested with the substance to rule out that the 'positive' allergic reaction was actually a false-positive irritant response.

Yet, it was not always that easy, some researchers had to conduct a real quest to find out whether the patient was indeed allergic and, if so, to which product and which ingredient. Diagnostic procedures included use tests, repeated open application tests, repeated patch tests, patch tests with a longer than usual application time, and patch testing with other concentrations, other vehicles or a dilution series. Unfortunately, it is not always possible to identify the allergen in patients with allergic cosmetic dermatitis, for example when manufacturers refuse to supply ingredients or do not respond to (repeated) requests from dermatologists. Such an uncooperative attitude was rule rather than exception 40 years ago when the author did research on cosmetic allergy for his Thesis Adverse reactions to cosmetics (1988), but apparently even today an unwilling manufacturer is not an exception……

Table 2.1 New cosmetic allergens presented in monographs in this chapter

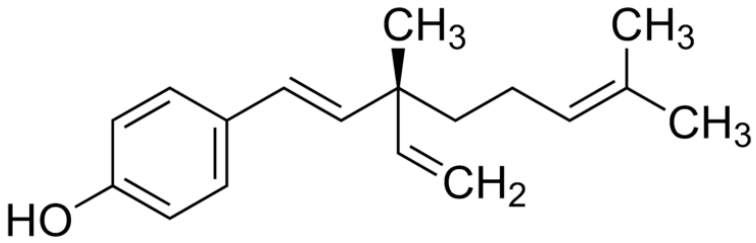
Bakuchiol	Luffa cylindrica seed oil [a]
4-Butylresorcinol	Menthyl anthranilate
Calcium pantothenate	Methoxypropylamino cyclohexenylidene ethoxyethylcyanoacetate
Capryloyl glycine	1-Naphthol
Caprylyl glycol [a]	Nigella sativa seed oil
Cetyl PEG/PPG-10/1 dimethicone	Oleoyl tyrosine
Chitosan	PEG-45 dodecyl glycol copolymer
Di-C12-13 alkyl malate	Phloretin
Glyceryl ascorbate	Polyacrylamide/C13-14 isoparaffin/laureth-7 mix
Helianthus annuus seed oil	Salvadora Persica bark/root extract
HEMA (2-Hydroxyethyl methacrylate)	Sodium cetearyl sulfate
Hydroxyacetophenone	Sodium lauroyl methylaminopropionate
C12-14 Hydroxyalkyl hydroxyethyl sarcosine	Sodium stearoyl glutamate
10-Hydroxydecenoic acid	Sorbitan caprylate
2-Hydroxyphenyl propamidobenzoic acid	Stannous chloride
Indigo	Sucrose distearate
Iris Germanica root oil	Sucrose polystearate
Isobutylamido thiazolyl resorcinol	Sucrose stearate
Isopropyl lauroyl sarcosinate	Tetrahexyl ascorbate
Lauryl PCA	

[a] Also caused an immediate-type reaction

2.2 BAKUCHIOL

IDENTIFICATION

Description/definition : Bakuchiol is the meroterpenoid (a chemical compound having a partial terpenoid structure) that conforms to the structural formula shown below
Classification : Phenols - terpenophenols
IUPAC name : 4-[(1*E*,3*S*)-3-Ethenyl-3,7-dimethylocta-1,6-dienyl]phenol
CAS registry number : 10309-37-2
EC number : 685-515-4
Wikipedia : https://en.wikipedia.org/wiki/Bakuchiol
Functions in cosmetics : EU: antimicrobial; antioxidant; skin conditioning – emollient; skin conditioning. USA: antioxidants; cosmetic biocides; skin-conditioning agents - emollient
Patch testing : 0.1% pet. (1,2); 1% pet. (2; five controls were negative)
Molecular formula : $C_{18}H_{24}O$



GENERAL

Bakuchiol is a chemical extracted from *Psoralea corylifolia* seeds. *P. corylifolia* (Babchi) is a leguminous plant used in Ayurveda and Chinese traditional medicine. Its extracts contain numerous phytochemicals, including flavonoids, coumarins, and meroterpenes (bakuchiol and 3-hydroxybakuchiol) (2). In *in vitro* experimental models, bakuchiol has shown various biological properties, including anticancer, antioxidant, oestrogen-like, antimicrobial, antifungal, liver-protective, antidiabetic and immunosuppressive activity (1). In addition, it has been found to have retinol-like effects *in vitro*, stimulating collagen synthesis in mature fibroblasts and upregulating genes involved in extracellular matrix and dermoepidermal junction maintenance (2). *In vivo*, it may reduce wrinkles and hyperpigmentation without the irritating effects of retinol. Accordingly, bakuchiol is often presented as a 'natural' alternative to retinol, being more photostable and less irritant than the latter molecule, and is widely used in anti-acne and anti-aging cosmetics (2).
More general information on bakuchiol can be found here.

The authors of ref. 1 mention 17015-60-0 as the CAS number, but CAS common chemistry, PubChem, Wikipedia and the European Chemical Agency list is as 10309-37-2.

CONTACT ALLERGY (cosmetics)

Case reports

A 33-year-old female patient presented with a 1-year history of erythematous and itchy plaques on both eyelids, the perioral area, and the neck. She associated her symptoms with food, spices and coffee, but not with cosmetics, as she stated that she used only 'hypoallergenic cosmetic products for sensitive skin'. Patch tests with the European baseline series, a cosmetic series and her own cosmetic products were positive to a cosmetic cream (+++), drometrizole, propyl gallate, dodecyl gallate, and 3-(dimethylamino)-1-propylamine (all + reactions). The latter 4 were not clinically relevant. Patch testing with the ingredients of the cream, provided by its manufacturer, showed a +++ positive reaction to bakuchiol 0.1% pet. at D3. Ten controls were negative (1). This was the first reported case of allergic contact dermatitis from bakuchiol.

A 23-year-old woman was investigated for recurrent facial eczema. She reported repeated flares of erythematous and oedematous itchy lesions strictly localized to her face and more specifically on the eyelids after applying an anti-ageing eye cream. Patch tests with the European baseline series, an additional routine series, a cosmetic series, and the suspected cream 'as is' were negative. However, a repeated open application test (ROAT) with the eye cream was already positive on D1 with a follicular pattern. Testing with the ingredients obtained from the manufacturer were positive to bakuchiol 1% pet. (++ on D2 and D4), which was the concentration of bakuchiol in the cream. Later, the patient also reacted to bakuchiol 0.1% pet. (+ on D2, ++ on D4). Five controls were negative to bakuchiol 1% pet. (2).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 17/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 336/123,000.

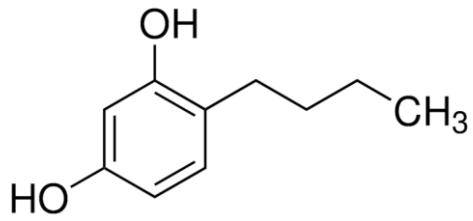
LITERATURE

1 Malinauskiene L, Linauskiene K, Černiauskas K, Chomičiene A. Bakuchiol - A new allergen in cosmetics. Contact Dermatitis. 2019;80(6):398-399. doi: 10.1111/cod.13211.
2 Raison-Peyron N, Dereure O. A new case of contact dermatitis to bakuchiol in a cosmetic cream. Contact Dermatitis. 2020;82(1):61-62. doi: 10.1111/cod.13387.

2.3 4-BUTYLRESORCINOL

IDENTIFICATION

Description/definition : 4-Butylresorcinol is the resorcinol-derivative that conforms to the structural formula shown below
Classification : Resorcinols
IUPAC name : 4-Butylbenzene-1,3-diol
Other names : 3-Dihydroxy-4-*n*-butyl benzene; rucinol
CAS registry number : 18979-61-8
EC number : 606-191-2
Wikipedia : https://en.wikipedia.org/wiki/4-Butylresorcinol
Functions in cosmetics : EU: antioxidant. USA: antioxidants
Patch testing : 0.5% pet. (1)
Molecular formula : $C_{10}H_{14}O_2$



GENERAL

4-Butylresorcinol is a derivative of resorcinol, which is used as an antioxidant and skin depigmentation agent in a variety of cosmetics. By inhibiting human tyrosinase, it reduces melanin production and hyperpigmentation (1).

CONTACT ALLERGY (cosmetics)

Case report

A 50-year-old woman had suffered severe recurrent eczema on the face, neck, and chest for 6 months. The use of strong topical corticosteroids had not resulted in improvement. The patient ascribed the eczema to the use of a new night cream. Fifteen years ago she had developed allergic contact dermatitis following the use of hair dyeing products, and patch tests had been positive for nickel and *p*-phenylenediamine (PPD). Patch tests with the extended European baseline series (without PPD), a pharmaceutical series, a cosmetic series, a hairdressers series, a textile series, and the patient's own cosmetics showed positive reactions to potassium dichromate, nickel sulfate, textile dye mix, toluene-2,5-diamine sulfate, *m*-aminophenol, 4-aminoazobenzene, disperse orange 3, and the night cream (++). In a second test session, patch tests with the 27 separate ingredients of the cream yielded a positive reaction on D2 and D4 to 4-butylresorcinol 0.5% pet. (++). After cessation of the use of the cream and avoiding all other allergens, the eczema disappeared. In this patient, there was no cross-reactivity between 4-butylresorcinol and resorcinol (1).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 9/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 4/123,000.

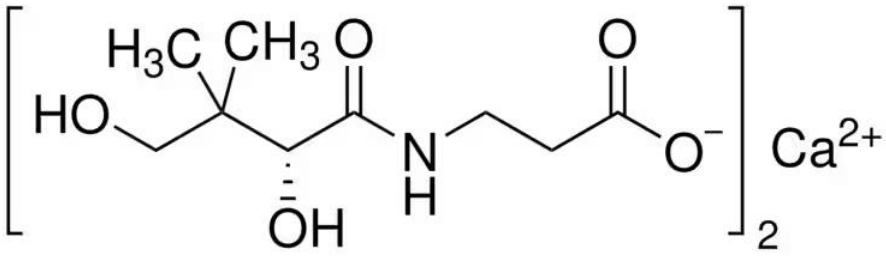
LITERATURE

1 Lapeere H, de Keyser E. Allergic contact dermatitis caused by 4-*n*-butylresorcinol present in a night cream for skin hyperpigmentation. Contact Dermatitis. 2020;83(2):134-135. doi: 10.1111/cod.13543.

2.4 CALCIUM PANTOTHENATE

IDENTIFICATION

Description/definition : Calcium pantothenate is the calcium salt of pantothenic acid that conforms to the structural formula shown below
Classification : Vitamins
IUPAC name : Calcium;3-[[(2*R*)-2,4-dihydroxy-3,3-dimethylbutanoyl]amino]propanoate
Other names : Vitamin B5, calcium salt; (+)-pantothenic acid, calcium salt; Calcium *N*-(2,4-dihydroxy-3,3-dimethyl-1-oxobutyl-β-alanine
CAS registry number : 137-08-6
EC number : Not available
CIR reviews : Int J Toxicol 2022;41(Suppl.3):77-128
Functions in cosmetics : EU: hair conditioning; skin conditioning - miscellaneous. USA: hair conditioning agents; skin conditioning agents - miscellaneous
Patch testing : 5% pet. (1). Possibly, a higher concentration may be more suitable
Molecular formula : $C_{18}H_{32}CaN_2O_{10}$



GENERAL

Calcium pantothenate is the calcium salt of pantothenic acid; it is used in cosmetics for its antistatic and hair- and skin-conditioning properties (1).

CONTACT ALLERGY (cosmetics)

Case report

A 59-year-old female nurse's aide had suffered from intermittent eczematous lesions on the eyelids and the face since 6 years. Two patch test sessions showed contact allergy to nickel, but no positive reactions to her cosmetic products. These were nevertheless replaced and the skin lesions fully cleared. Three months later new facial lesions developed following the re-application of a cleansing milk and facial tonic, products that had been patch tested previously with negative results. Repeated open application tests (ROAT) with the products were also negative. However when the patient was patch tested with the 2 cosmetics' individual ingredients, provided by the manufacturer, a ?+ reaction was observed on D3 to calcium pantothenate 5% pet., which was present in both products. The following week, the patient agreed to be patch tested again and now a stronger result was noted (+ on D5), interpreted as a booster effect. Twenty controls were negative. There was no reaction to panthenol 5%, which was also present in the products. After exposure avoidance, no further lesions were observed in a 5-year follow-up period (1).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (January, 2020): 2/unknown (approx. 32,000?).
EWG's Skin Deep Cosmetics Database (February 2025): 406/123,000.

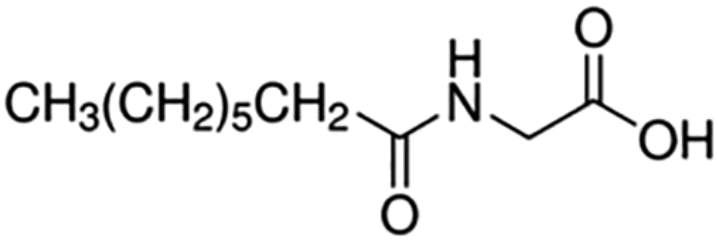
LITERATURE

1 Pastor-Nieto MA, Gatica-Ortega ME, Sánchez-Herreros C, Jiménez-Blázquez E, Martín-Fuentes A, Checa-Recio I, et al. Calcium pantothenate is present in cosmetics and may cause allergic contact dermatitis. Contact Dermatitis.2021;84(3):201-203. doi: 10.1111/cod.13709.

2.5 CAPRYLOYL GLYCINE

IDENTIFICATION

Description/definition : Capryloyl glycine is the acylation product of glycine with caprylic acid chloride, that conforms to the formula shown below
Classification : Fatty amides; amino acid alkyl amides
IUPAC name : 2-(Octanoylamino)acetic acid
Other names : *N*-Octanoylglycine; caprylyl glycine
CAS registry number : 14246-53-8
EC number : 238-122-3
CIR reviews : Int J Toxicol 2017;36(Suppl.1):17-56
Functions in cosmetics : EU: anti-seborrheic; antimicrobial; anti-sebum; deodorant; hair conditioning; surfactant - cleansing. USA: antiacne agents; antidandruff agents; deodorant agents; hair conditioning agents; preservatives; surfactants - cleansing agents
Patch testing : 1% in 50 water/50 alcohol (1); a higher test concentration may be necessary, and petrolatum may be preferably as vehicle (1)
Molecular formula : $C_{10}H_{19}NO_3$



GENERAL

Capryloyl glycine (CG) is a polyfunctional ingredient in cosmetic leave-on and rinse-off products and in household detergents. In cosmetics, besides being a skin- and hair-conditioning agent, it is a surfactant and has antimicrobial properties. CG inhibits the proliferation of *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Propionibacterium acnes*, and *Pityrosporum ovale*, and is thus included in products marketed for the treatment of acne-prone skin and dandruff. Yet, capryloyl glycine it is not considered to be a full-fledged preservative. It is often used together with other preservative agents to obtain a synergistic preservative effect (1).

CONTACT ALLERGY (cosmetics)

Case reports

A 50-year-old man who had recently been diagnosed with contact allergy to methylisothiazolinone (MI), MCI/MI, Myroxylon pereirae resin, fragrance mix II and ricinus oil, developed an itchy, papular skin eruption on his arms and legs after the application of a body lotion. He had also suffered from a similar skin eruption after the use of two sunscreens, but none of these products contained any of his known contact allergens. Patch tests were performed with the three suspected products, tested 'as is', the separate ingredients of the body lotion provided by the manufacturer, a photopatch test series and ingredients of the sunscreens that were commercially available as patch test preparations.
Positive reactions were observed to the body lotion (++), and to its ingredient capryloyl glycine 1% in 50% water/50% ethanol (+). A repeated patch test was again positive (+), but a patch test with capryloyl glycine (CG) 1% water obtained from a different cosmetic company gave only a doubtful reaction (?+). Twenty control patients were negative to both CG 1% water and CG 1% in 50% water/50% ethanol. The patient also had positive reactions to the two sunscreens (+) and to benzophenone-10 (which was not present in the sunscreens). The authors had previously seen five other patients who had developed dermatitis following the use of the same body lotion. All had reacted to patch tests with the body lotion 'as is' (+ to ++). Some of them had also previously been tested with the separate ingredients, but none had reacted positively to capryloyl glycine 1% in 50% water/50% ethanol (1).

A 40-year-old atopic female nurse had suffered two episodes of acute allergic contact dermatitis (ACD) from two different cosmetic products. The first episode occurred 1 day following the application of a body lotion and the dermatitis was localized on the face, trunk, legs and arms, at the application sites of the body lotion. Three months later, 1 day following the application of an after-sun, a similarly severe ACD occurred over the décolleté and arms. Patch tests with the European baseline series, a cosmetic series, and both creams 'as is' (also tested semi-open) showed ++ on D3 and D4 to the two cosmetic products (semi-open and patch tests). The ingredients common to both products were glycerin, sodium stearoyl glutamate, linalool and geraniol. Three months later, the ingredients of the after-sun, obtained from the manufacturer, were tested which revealed positive reactions to sodium stearoyl glutamate 1% water (D3/4 ++), and to capryloyl glycine 1% water (D3/4 +). The authors suggested possible cross-reactivity between sodium stearoyl glutamate and capryloyl glycine (2).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 94/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 316/123,000.

LITERATURE

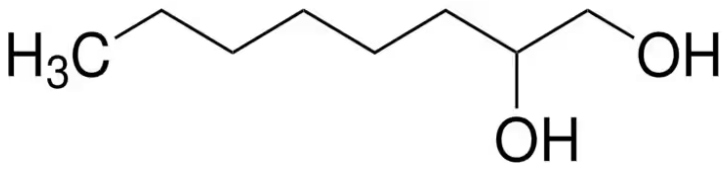
1 Mangodt EA, Dendooven E, De Fré C, Lambert J, Aerts O. Capryloyl glycine: A polyfunctional cosmetic ingredient and potential skin sensitizer. Contact Dermatitis. 2019;80(6):400-402. doi: 10.1111/cod.13215.

2 Pralong P, Dendooven E, Aerts O. Sodium stearoyl glutamate: Another amino acid alkyl amide sensitizer in cosmetics. Contact Dermatitis 2022;87(5):453-454. doi: 10.1111/cod.14184.

2.6 CAPRYLYL GLYCOL

IDENTIFICATION

Description/definition : Caprylyl glycol is the fatty alcohol that conforms to the structural formula shown below
Classification : Alcohols; 1,2-glycols
IUPAC name : Octane-1,2-diol
Other names : 1,2-Dihydroxyoctane; 1,2-octanediol; 1,2-octylene glycol; capryl glycol
CAS registry number : 1117-86-8
EC number : 214-254-7
CIR reviews : Int J Toxicol 2012;31(Suppl.2):147-168
Wikipedia : https://en.wikipedia.org/wiki/1,2-Octanediol
Functions in cosmetics : EU: deodorant; skin conditioning – emollient; hair conditioning; skin conditioning. USA: deodorant agents; hair conditioning agents; preservatives; skin-conditioning agents - emollient
Patch testing : 1% pet. (2)
Molecular formula : $C_8H_{18}O_2$



GENERAL

The fatty alcohol caprylyl glycol is widely used in cosmetics for its hair- and skin-conditioning, deodorant, preservative (antimicrobial) and emollient properties. In cosmetic formulations, it is found in concentrations of 0.00003% to 5%, typically in the 0.5-1% range in leave-on cosmetics (1).

CONTACT ALLERGY (cosmetics)

Case report

A 37-year-old woman presented with a 6-month history of eyelid dermatitis. She had suffered intermittent facial dermatitis 3 years previously, which was attributed to her nail varnish, as it improved with avoidance. The patient was patch tested with the hospital baseline series, a face series, an artificial nails series, relevant parts of the hair dressing series, and her own products appropriately diluted. There were positive reactions to caprylyl glycol 1% white soft petrolatum prepared in the hospital pharmacy from neat material (+), phthalic anhydride 5% pet. (+), adipic acid 5% pet. (+), and two of the patient's own nail varnishes on D2 and D4. A second test confirmed the positive reaction to caprylyl glycol (+) on D2. This chemical was present in a blusher and long-lasting foundation the patient used. The eyelid dermatitis cleared with avoidance. The nail varnish allergies were considered to be of past relevance (2).
Caprylyl glycol had been part of the authors' hospital extended facial series for over 2 years with no previous positive reactions in over 1000 patients. Somewhat surprisingly, they did not comment on the relevance of the positive patch test reactions to phthalic anhydride and adipic acid (2).

IMMEDIATE CONTACT REACTIONS (CONTACT URTICARIA)

A 60-year-old woman presented with a 6-month history of oedema and pruritus of the face after use of a 'specific cosmetic' (identity not disclosed by the authors). Application of this product to the skin in a chamber 8 mm in diameter resulted in an urticarial reaction within 5 minutes. Successive patch tests were carried out with various cosmetics with different combinations of substances, and the appearance of the urticarial skin lesions was observed only with cosmetics that contained caprylyl glycol (CG). The same tests

performed with CG 0.5% water and caprylic acid resulted in an urticarial reaction to CG after 8 minutes. Late readings of this test on D2 and D4 identified no eczematous reaction. Three controls were negative. The patient was requested not to use products containing CG anymore and there was no recurrence of urticaria after 8 months of follow-up (1).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 4559/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 21,604/123,000.

LITERATURE

1 Coelho EQ, Wu SLC, Nunes RS, Reis VMS. Contact urticaria following the use of a cosmetic containing caprylyl glycol: A case report. Contact Dermatitis. 2019;81(4):308-309. doi: 10.1111/cod.13299.
2 Kreeshan FC, Williams JDL. Allergic contact dermatitis to caprylyl glycol: A novel "para-preservative" allergen. Contact Dermatitis. 2020;83(5):418-419. doi: 10.1111/cod.13628.

2.7 CETYL PEG/PPG-10/1 DIMETHICONE

IDENTIFICATION

Description/definition : Cetyl PEG/PPG-10/1 dimethicone is a siloxane polymer prepared by reacting hydrogen dimethicone (q.v.) with hexadecene (q.v.) and the allyl ether of PEG/PPG-10/1.
Classification : Siloxanes and silanes; alkoxy polysiloxane copolymers
IUPAC name : 1-[2-[[[Simethyl(trimethylsilyloxy)silyl]oxy-hexadecyl-methylsilyl]oxy-dimethylsilyl]oxyethoxy]propan-2-ol
CAS registry number : 142321-71-9
EC number : 965-961-9
CIR reviews : Final report, December 09, 2014
Functions in cosmetics : EU: surfactant – emulsifying; skin conditioning; surfactant - cleansing. USA: skin-conditioning agents – miscellaneous; surfactants - emulsifying agents
Patch testing : 5% and 30% pet. (1)
Molecular formula : $C_{29}H_{68}O_6Si_4$ (PubChem)

GENERAL

Cetyl PEG/PPG-10/1 dimethicone, a skin conditioner, emulsifier, and surfactant, is the copolymer of cetyl dimethicone and an alkoxylated derivative of dimethicone, containing an average of 10 mol of ethylene oxide and 1 mol of propylene oxide (1). In Italy, in 2015, 310 patients were patch tested with an emulsifier series including cetyl PEG/PPG-10/1 dimethicone 30% pet., but there were no positive reactions (2). The CIR (Cosmetic Ingredient Review), in their Safety assessment of polyoxyalkylene siloxane copolymers, alkyl-polyoxyalkylene siloxane copolymers, and related ingredients as used in cosmetics, reported that cetyl PEG/PPG-10/1 dimethicone was not sensitizing to humans or guinea-pigs in maximization tests (data available here).

CONTACT ALLERGY (cosmetics)

Case report

A 47-year-old male patient, working as an ambulance driver, developed a symmetric erythematous rash involving his armpits and the lateral trunk. He related the reaction to a fireproof jacket that he had starting wearing at work a few weeks before that made him sweat profusely. Patch tests with the European baseline series, textile series, pieces of clothing including the fireproof jacket and a polo shirt (moistened with water), and personal products gave a positive reaction to nickel sulfate and a deodorant 'as is'. The patient mentioned applying this deodorant repeatedly to reduce his sweating. The manufacturer provided combinations of ingredients for further patch testing, and only the combination of cetyl PEG/PPG-10/1 dimethicone and pentaerythrityl tetra-di-*t*-butyl hydroxyhydrocinnamate gave a positive result. The latter was negative when tested as single chemical. However, patch tests with a sunscreen lotion containing cetyl PEG/PPG-10/1 dimethicone and with cetyl PEG/PPG-10/1 dimethicone 5% and 30% pet., prepared in-house, were positive on D4. Five controls were negative (1).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 344/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 4,600/123,000.

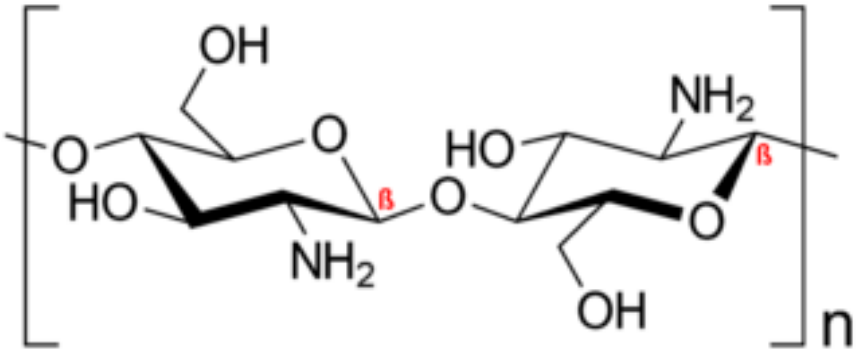
LITERATURE

1 Pastor-Nieto MA, Gatica-Ortega ME, Alcántara-Nicolás FD, Pérez-Mesonero R, Gil-Redondo R, Martín-Alcalde E, et al. Allergic contact dermatitis resulting from cetyl PEG/PPG-10/1 dimethicone in a deodorant cream. Contact Dermatitis. 2018;78(3):236-239. doi: 10.1111/cod.12922.
2 Corazza M, Virgili A, Ricci M, Bianchi A, Borghi A. Contact sensitization to emulsifying agents. An underrated issue? Dermatitis. 2016;27(5):276-281. doi: 10.1097/DER.0000000000000209.

2.8 CHITOSAN

IDENTIFICATION

Description/definition : Chitosan is deacetylated chitin. Chitin is a polysaccharide found in the exoskeleton of various crustaceans, in insects, and the cell walls of various fungi. It consists chiefly of *N*-acetyl-glucosamine residues
Classification : Biological polymers and derivatives
Other names : Deacetylchitin; chitin, *N*-deacetyl-
CAS registry number : 9012-76-4
EC number : 618-480-0
Wikipedia : https://en.wikipedia.org/wiki/Chitosan
Functions in cosmetics : EU: film forming; hair fixing. USA: film formers; hair fixatives
Patch testing : Unspecified (2)
Molecular formula : $C_{56}H_{103}N_9O_{39}$ (PubChem)



Chitosan is a linear polysaccharide composed of D-glucosamine and *N*-acetyl-D-glucosamine units, which are linked by β-(1–4) glycosidic linkage (1).

GENERAL

Chitosan is an amino polysaccharide obtained by deacetylation of chitin and is the second most commonly used natural polymer. Chitosan shows several biological activities like antimicrobial, antifungal, antitumor, anticancer, anti-diabetic, wound healing, and antioxidant. Due to all these activities, chitosan is widely used in biomedical applications and drug delivery such as oral, nasal, ocular, pulmonary, mucosal, gene delivery, and vaccine delivery. Chitosan's application is limited in many sectors since it is insoluble in water and some organic solvents. To avoid this hurdle, chitosan is often chemically modified (1). In cosmetics, chitosan is used as film former and hair fixative.

CONTACT ALLERGY (cosmetics)

Case report

A 39-year-old female patient had allergic contact dermatitis from a deodorant. Patch tests with the European baseline series with Belgian extension, a cosmetic and a pharmaceutical series were positive to nickel sulfate, linalool hydroperoxides and decyl glucoside. The deodorant itself was not tested, but patch tests with its ingredients, obtained from the manufacturer, were positive (+) to sorbitan caprylate 1% pet. and chitosan (test concentration not mentioned) (2).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 44/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 119/123,000.

LITERATURE

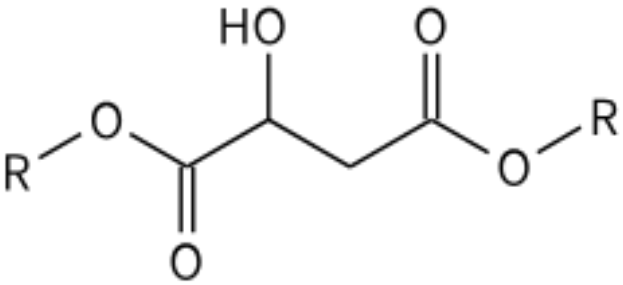
1 Anuja Harugade A, Sherje AP, Pethe A. Chitosan: A review on properties, biological activities and recent progress in biomedical applications. Reactive and Functional Polymers 2023;191:105634. doi. 10.1016/j.reactfunctpolym.2023.105634

2 Vandeweghe J, Decoster E, Lapeere H. First report of allergic contact dermatitis caused by sorbitan caprylate. Contact Dermatitis. 2018;78(2):162-164. doi: 10.1111/cod.12876.

2.9 DI-C12-13 ALKYL MALATE

IDENTIFICATION

Description/definition : Di-C12-13 alkyl malate is the C12-13-diester of malic acid, that conforms to the formula shown below
Classification : Alkyl malates
IUPAC name : 1,4-bis(2-Methyldodecyl) 2-hydroxybutanedioate
Other names : Bis(C12-C13)alkyl-2-hydroxybutandioate; butanedioic acid, hydroxy-, bis-(C12-13-alkyl) esters; hydroxybutanedioic acid, di-C12-13 alkyl esters; Cosmacol EMI ®
CAS registry number : 149144-85-4
EC number : 413-390-6
CIR reviews : Int J Toxicol 2015;34(Suppl.1):5-17
Functions in cosmetics : EU: skin conditioning – emollient; skin conditioning. USA: skin-conditioning agents - emollient
Patch testing : 10% pet. and 'as is' (probably 'as supplied'; 5 controls were negative) (1)
Molecular formula : $C_{28}H_{54}O_5$ - $C_{30}H_{58}O_5$



R represents the C12-13 alkyl group.

GENERAL

Di-C12-13 alkyl malate is chemically a mixture of different, synthetically produced di-esters of C12-13 aliphatic alcohols and malic acid. It belongs to the family of dialkyl malates which are used in cosmetic products such as emollients, skin conditioners, and keratolytic agents. All dialkyl malates have a similar chemical structure and similar physicochemical properties (1). Experimental data from CIR (Cosmetic ingredient review) have shown that these malic acid esters are generally safe for use in cosmetics (2).

CONTACT ALLERGY (cosmetics)

Case report

A 41-year-old woman had suffered an episode of acute facial eruption which occurred one day after the application of two cosmetic products: a cleansing gel and a skin care product. The symptoms improved quickly after topical application of a corticosteroid. Patch tests were performed with the European baseline series, a cosmetic series and the 2 cosmetics 'as is' and in a 10% aqueous solution; these were also tested semi-open. There was a positive reaction to the skin care product only. A repeated open application test with this cosmetic was positive on D2. In a second session, its ingredients were patch tested, resulting in positive reactions to di-C12-13 alkyl malate 10% pet. and 'as is' (both ++ on D2 and D4). Five controls were negative to the undiluted test material (1).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 14/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 18/123,000.

LITERATURE

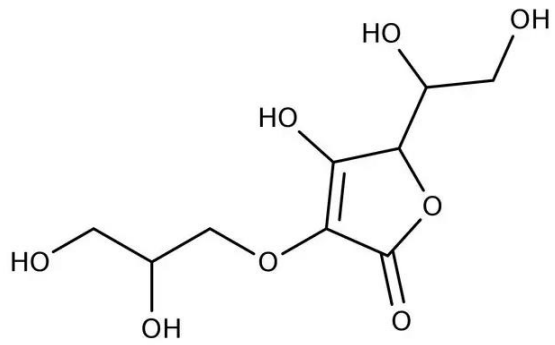
1 Prost A, Leleu C, Jordan M, Pasteur J, Collet E. First case of contact dermatitis caused by C12-13 alkyl malate used in a skin care product for acne. Contact Dermatitis. 2019;81(6):465-466. doi: 10.1111/cod.13369.

2 Becker LC, Bergfeld WF, Belsito DV, Hill RA, Klaassen CD, Liebler DC, et al. Safety assessment of dialkyl malates as used in cosmetics. Int J Toxicol. 2015;34(Suppl.1):5S-17S. doi: 10.1177/1091581815584625.

2.10 3-GLYCERYL ASCORBATE

IDENTIFICATION

Description/definition : 3-Glyceryl ascorbate is the organic ascorbic acid-derivative that conforms to the structural formula shown below
Classification : Ethers; polyols; vitamin C derivatives
IUPAC name : (2*R*)-2-[(1*S*)-1,2-Dihydroxyethyl]-4-(2,3-dihydroxypropoxy)-3-hydroxy-2*H*-furan-5-one
Other names : 2-*o*-Glyceryl ascorbic acid
CAS registry number : 120360-13-5
EC number : Not available
Functions in cosmetics : EU: antioxidant; humectant. USA: antioxidants; humectants
Patch testing : 10% water (1)
Molecular formula : $C_9H_{14}O_8$



GENERAL

Ascorbic acid (vitamin C) exerts multifunctional effects on skin integrity by inhibiting melanogenesis and increasing collagen synthesis. However, it has poor stability in cosmetic formulations (1). The compound 3-glyceryl ascorbate is a novel derivative of ascorbic acid developed by introducing a glycerol group into the C-3 position of ascorbic acid. It has high stability in cosmetic formulations and easily penetrates the stratum corneum. It is used as antioxidant, humectant and skin-lightening agent (1).

CONTACT ALLERGY (cosmetics)

Case report

A 44-year-old woman presented with a 2-month history of a recurring itchy eruption on her face. She had started applying a new skin-lightening lotion on her face 5 months earlier. The skin lesions had improved with topical corticosteroids and cessation of all cosmetics; however, the eruption recurred after resuming their use. Physical examination revealed facial erythema with prominent swelling of the eyelids. Patch testing with all her cosmetics applied 'as is' showed a strong positive reaction to the skin-lightening lotion (D2++; D3++; D7++). Subsequent patch testing with the ingredients of this lotion, at the concentrations used in the product, provided by the manufacturer, yielded a strong positive reaction to 3-glyceryl ascorbate 10% water (D2++; D3++; D7+), whereas the other ingredients, such as glycerol and trisodium ascorbyl palmitate phosphate, were negative. Three controls were negative. Discontinuation of the use of the skin-lightening lotion led to complete healing of the dermatitis without any relapses (1).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (January 2020): 1/32,000.
EWG's Skin Deep Cosmetics Database (February 2025): 9/123,000.

LITERATURE

1 Kawakami Y, Umayahara T, Hirai Y, Morizane S. A case of allergic contact dermatitis due to 3-glyceryl ascorbate in a skin-lightening lotion. Contact Dermatitis. 2021;85(2):245-246. doi: 10.1111/cod.13820.

2.11 HELIANTHUS ANNUUS SEED OIL

IDENTIFICATION

Description/definition	: Helianthus annuus (sunflower) seed oil is the fixed oil expressed from the seeds of the sunflower, *Helianthus annuus*
Classification	: Fats and oils
INCI name USA	: Helianthus annuus (sunflower) seed oil
Other names	: Sunflower seed oil
CAS registry number	: 8001-21-6
EC number	: 232-273-9
CIR reports	: Int J Toxicol 2017;36(Suppl.3):51-129
Wikipedia	: https://en.wikipedia.org/wiki/Sunflower_oil (sunflower oil)
Functions in cosmetics	: EU: skin conditioning – emollient; solvent; skin conditioning – miscellaneous; skin conditioning - occlusive. USA: skin-conditioning agents – emollient; skin-conditioning agents – miscellaneous; skin-conditioning agents – occlusive; viscosity increasing agents - nonaqueous
Patch testing	: 10% pet. (1)

GENERAL

Helianthus annuus (sunflower) seed oil is the fixed oil expressed from the seeds of the sunflower, *Helianthus annuus*. It is widely used in cosmetics for its skin-conditioning and emollient properties.

CONTACT ALLERGY (cosmetics)

Case report

A 32-year-old atopic female patient suffered severe cheilitis lasting a few months, together with a longer standing mild dermatitis of the face and hand. Initially, she had developed dry cracked lips, diagnosed as atopic cheilitis, for which she had tried 6 different lip balms. Clinical examination showed a severe lip dermatitis complicated by bacterial superinfection. The patient was advised to use unscented toothpaste and petrolatum jelly as lip balm, and the cheilitis and infection were treated with oral antibiotics, topical compresses and a topical corticosteroid. After full healing, patch tests with a baseline, cosmetic, fragrance and bakery series together with four of six suspected lip balms showed + to ++ reactions to the four lip balms, and to several haptens (all +): fragrances (fragrance mix I, limonene and linalool hydroperoxides), fragrance indicators (Myroxylon pereirae resin, colophonium, propolis), octylisothiazolinone, HEMA and sorbitan sesquioleate (SSO). Although contact allergy to SSO potentially explained the positive patch tests to M. pereirae resin, the fragrance mix and HEMA, the patient also reacted to limonene hydroperoxides, which was considered relevant for the cheilitis and the facial and hand dermatitis, as limonene was present in several cosmetics, including her toothpaste. Only one of four tested lip balms was effectively scented, and therefore, ingredient patch testing was performed with preparations obtained from cosmetic manufacturers. Now, positive reactions were observed to Helianthus annuus seed oil 10% pet., Butyrospermum parkii (shea) butter 30% pet., cera alba (beeswax) 30% pet., and candelilla cera 41% pet., which were present in 1/6, 4/6, 5/6, and 1/6 of the previously used lip balms, respectively. Twenty controls were negative to all four test materials. Using cosmetics free from all demonstrated allergens led to complete resolution of the cheilitis, and significant improvement of the hand and face dermatitis (1).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 2463/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 14,303/123,000.

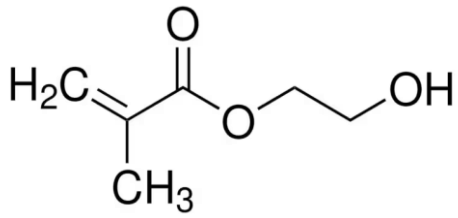
LITERATURE

1 Aerts O, Pyl J, Mangodt E, Dendooven E. Severe contact cheilitis from cera alba and other cosmetic oils, fats and waxes in lip balms. Contact Dermatitis 2023;88(4):322-323. doi: 10.1111/cod.14272.

2.12 HEMA (2-HYDROXYETHYL METHACRYLATE)

IDENTIFICATION

Description/definition	: HEMA is the hydroxyethyl ester of methacrylic acid, that conforms to the structural formula shown below
Classification	: Methacrylates
IUPAC name	: 2-Hydroxyethyl 2-methylprop-2-enoate
Other names	: Glycol methacrylate
CAS registry number	: 868-77-9
EC number	: 212-782-2
CIR reviews	: Int J Toxicol 2005;24(Suppl. 5):53-100; Int J Toxicol 2023;42(Suppl. 3):61-73
SCCS opinions	: SCCS/1592/17
Wikipedia	: https://en.wikipedia.org/wiki/(Hydroxyethyl)methacrylate
Functions in cosmetics	: EU: nail sculpting. USA: artificial nail builders
EU cosmetic restrictions	: The use of HEMA and di-HEMA TMHDC in nail cosmetics is permitted only in products for professional use. The warnings 'for professional use only' and 'can cause an allergic reaction' must be stated on the package of nail products containing HEMA, di-HEMA TMHDC or both (3)
Patch testing	: 2% pet. (Chemotechnique, Smartpractice); 1% pet. (Smartpractice); TEST ADVICE: 2% pet. (4)
Molecular formula	: $C_6H_{10}O_3$



GENERAL

In recent years, 2-hydroxyethyl methacrylate (HEMA) has caused an epidemic of allergic contact dermatitis from its presence in modern nail cosmetics. The literature up to mid-2023 has been fully reviewed in 2 articles written by the author and co-author Thomas Rustemeyer, which were published OPEN ACCESS in *Contact Dermatitis* in December 2023 (part 1 [1]) and January 2024 (part 2 [2]). In this chapter, only the recent literature on HEMA not included in these reviews is presented briefly.

CONTACT ALLERGY (cosmetics)

Investigations in groups of patients with allergic contact dermatitis from nail cosmetics

In the Amsterdam University Medical Centers a retrospective study was performed between January 2015 and August 2023 among patients diagnosed with allergic contact dermatitis (ACD) from acrylate-containing nail cosmetics. Sixty-seven patients, all women, were identified, representing 1.6% of all individuals and 2.3% of all women patch tested in this period. Sixty-five of sixty-seven (97%) subjects had a positive patch test to 2-hydroxyethyl methacrylate (HEMA). Forty-nine patients (73%) were consumers and 18 (27%) were professional nail stylists. The sites most frequently affected with dermatitis were the fingers (79%), hands (40%) and the head and/or neck. Avoidance of contact with acrylate-containing products resulted in complete clearing of dermatitis in 80% of patients. It was concluded that ACD from acrylate-containing nail cosmetics is frequent in women patch tested in Amsterdam. Nearly all were identified by a positive patch test to HEMA in the (meth)acrylate series or the European baseline series (5).

In a university clinic in Athens, Greece, 30 patients (15 nail technicians, 15 consumers) with allergic contact dermatitis from nail cosmetics were investigated. Extensive clinical data were provided, including patch test results, localisation of dermatitis, symptoms of ACD and even height, weight, body mass index, BMI class, smoking habits and Fitzpatrick skin type. The author fails to see the relationship with allergy to nail cosmetics of the latter data. The most common allergens were: 2-hydroxyethyl methacrylate (HEMA), 2-hydroxypropyl methacrylate (HPMA) and ethyleneglycol dimethacrylate (EGDMA), which tested positive in all 30 patients. Nail technicians exhibited extensive skin lesions. Three of them (20%) had to discontinue their work. In the case of users, 12/15 (80%) stopped completely their exposure to nail enhancement procedures after diagnosing ACD from acrylates (6).

Prognosis and sequelae of sensitization

An investigation by telephone survey from Spain evaluated the prognosis, work performance impairment and sequelae of a cohort of beauticians and manicure consumers with allergic contact dermatitis from (meth)acrylic monomers sensitized from the exposure to manicure products. One hundred and six patients were evaluated, including 75 beauticians and 31 consumers; all were women. Thirty-seven of 75 beauticians (49%) continued to work. Twenty-seven of 106 (26%) patients continued to use manicure products with (meth)acrylates regularly. Seventeen of 51 (33%) patients who discontinued the exposure described ongoing nail/periungual changes. Nine of 58 (16%) patients who required dental restoration, orthodontic or occlusal splint materials recalled reactions from them; and, 25 of 96 (26%) who used sanitary napkins recalled intolerance to them starting after the diagnosis of allergic contact dermatitis from (meth)acrylic monomers (7).

Testing HEMA in the European baseline series

In a retrospective study among patients with positive patch tests to HEMA investigated between June 2019 and August 2023 in Amsterdam, of 2927 consecutive patients, 88 (79 women and 9 men; 3.0%) had a positive reaction to HEMA. The prevalence in women was 3.9%, in men 1.0%. Forty-three (49%) reactions were judged to be of current clinical relevance and 21 (24%) of past relevance. In this group of 64 patients with relevant reactions, 18 (28%) had occupational contact with (meth)acrylate-containing products, of who 11 (61%) were nail stylists. In 46 patients with non-occupational allergic contact dermatitis, 31 (67%) had allergic reactions to nail cosmetics (8).

From January 2019 to December 2022, HEMA 2% pet. was prospectively patch tested in 24 REIDAC (Spanish Allergic Contact Dermatitis Registry) centres. 6,134 patients were investigated and 265/6134 (4.3%) were positive to HEMA. Relevance of positive patch test reactions was considered to be current in 184/265 (69.4%), past in 25/265 (9.4%), and unknown in 56/265 (21.1%). The variable ‘occupational’ was found to be significantly associated with a higher risk for relevant positive reactions to 2-HEMA (OR: 10.9; 95% CI: 8.1–14.9). Quite curiously, the culprit products were not mentioned (9).

Between 2020 and 2023, in a tertiary center in Tel Aviv, Israel, 1671 consecutive patients were patch tested with HEMA in the European baseline series and there were 135 patients (8.1%) with positive reactions, of who 130 were women. The prevalence in women (11.0%) was significantly higher compared to men (1.0%). The highest frequency of HEMA sensitivity (16.7%) was seen among women younger than 30 years of age, with odds ratio of 2.3 compared to older women. There was an increase in frequency among women between the years 2022 and 2023 compared to 2020–2021. 111 positive reactions to HEMA (84%) were judged to be of clinical relevance and nail cosmetics were responsible for 95% of these. Of 111 patients with relevant reactions (110 females, 1 male), 20 (18%) had occupational contact dermatitis (18 nail stylists, 2 dentists). Other culprit products included sanitary pads (n=4), medical adhesives (n=3), and paints (n=2) (10).

Impact of EU legislation on contact allergy to methacrylate-containing nail products

Due to EU legislation, the use of HEMA and di-HEMA TMHDC in nail cosmetics since 2020 is permitted only

in products for professional use. The warnings 'for professional use only' and 'can cause an allergic reaction' must be stated on the package of nail products containing HEMA, di-HEMA TMHDC or both (3). From 3 June 2021 on, products not complying to these regulations cannot be placed on the Union market. The European Environmental Contact Dermatitis Research Group (EECDRG) has performed a study to determine the effectiveness of the EU Commission Regulation in the 2 full years following its implementation in 2021 compared to a baseline prior to this, by comparing patch test results. A total of 26,297 patients were tested to HEMA in the baseline series between 2016 and 2023 in 7 European centres. The prevalence of contact allergy to HEMA from all sources amongst females was 2.82% compared to 0.34% amongst males. The prevalence of nail-related contact allergy rose from 0.91% in 2016 (2 centres) to 0.99% in 2017 (3 centres), 1.24% in 2018 (5 centres), 1.23% in 2019 (6 centres), 1.36% in 2020 (7 centres), 1.30% in 2021 (7 centres), 1.52% in 2022 (7 centres) and 1.98% in 2023 (7 centres). It was concluded that EU legislation appears not to have had the intended impact on controlling allergic contact dermatitis from methacrylates in nail cosmetics (11).

Presence of HEMA and other (meth)acrylates in nail cosmetics

In The Netherlands, an online market survey was conducted to investigate: 1. the frequency in which HEMA and di-HEMA trimethylhexyl dicarbamate are present in nail cosmetics; 2. whether nail cosmetics comply with EU regulations; and 3. which other (meth)acrylates are present in nail cosmetics and how often. HEMA was present in nearly 60% of 394 cosmetic nail products and di-HEMA trimethylhexyl dicarbamate in 34%. Mandatory warnings on the packages of products containing HEMA were absent in 35% ('For professional use only') resp. 55% ('Can cause an allergic reaction'). Forty-five other (meth)acrylates were identified, of which the most frequent were hydroxypropyl methacrylate (25%), isobornyl methacrylate (16%) and trimethylolpropane triacrylate (12%). Some ingredient lists mentioned non-INCI names or non-specific names. It was concluded that HEMA was by far the most common ingredient of nail cosmetics, being present in nearly 60% of the products. Violations of EU legislation occurred in >30% (mandatory warnings missing) resp. 10% (mislabelling) of nail cosmetics (12).

In Finland, a study was initiated to analyse (meth)acrylates in gel nail and acrylic nail products and to compare the results with the information in the product labels. Also, penetration of artificial nail materials through selected disposable gloves was investigated. 31 gel nail products and 6 acrylic nail products were analyzed by gas chromatography–mass spectrometry (GC–MS). Penetration of two nail products through three disposable gloves: nitrile rubber, neoprene rubber and polyvinyl chloride (PVC) was studied. 32/37 products contained (meth)acrylates. In all of them, there was discrepancy between the listed (meth)-acrylates and those discovered in the analysis. The commonest (meth)acrylates were HEMA (20/37 samples) and hydroxypropyl methacrylate (9/37 samples), but many of the product packages failed to declare them. Isobornyl acrylate (IBA) was discovered in nine gel nail products. The neoprene glove could withstand nail gel for 20 minutes and thin nitrile glove and PVC glove for 5 minutes. Acrylic nail liquid penetrated through disposable gloves quickly. It was concluded that labelling of artificial nail products was notably incorrect on most products. Disposable gloves can probably be used short-term in gel nail work, whereas disposable gloves do not protect the user from acrylic nail liquids (13).

Case reports

A case of an 8-year-old child with allergic contact dermatitis from a nail lacquer was reported. She had strong patch test reactions to HEMA and various other methacrylates, but it was not verified that the culprit products actually contained HEMA (14).

A woman had become sensitized to several methacrylates including HEMA from an artificial nail application. It was not ascertained that the product actually contained HEMA. However, a special feature was that she had an extensive pustular eruption with erythema and mild edema of the eyelids and periorbital skin. The patient also had erythema and squamous lesions of the hands with a few pustules. The authors diagnosed 'pustular allergic contact dermatitis', but it was not mentioned whether swabs for bacterial cultures had been collected (15).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 170/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 103/123,000.

LITERATURE

1 De Groot AC, Rustemeyer T. 2-Hydroxyethyl methacrylate (HEMA): A clinical review of contact allergy and allergic contact dermatitis—Part 1. Introduction, epidemiology, case series and case reports. Contact Dermatitis. 2023;89(6):401-433. doi:10.1111/cod.14405.

2 De Groot AC, Rustemeyer T. 2-Hydroxyethyl methacrylate (HEMA): A clinical review of contact allergy and allergic contact dermatitis. Part 2. Cross-and co-sensitization, other skin reactions to HEMA, position of HEMA among (meth)acrylates, sensitivity as screening agent, presence of HEMA in commercial products and practical information on patch test procedures. Contact Dermatitis. 2024;90(1):1-16. doi:10.1111/cod.14430.

3 Commission regulation (EU) 2020/1682 of November 12, 2020 amending annex III to regulation (EC) No 1223/2009 of the European Parliament and of the council on cosmetic products. 2020 Official J Eur Union. 379:31–33.

4 Kocabas G, Ipenburg NA, de Groot AC, Rustemeyer T. 2-Hydroxyethyl methacrylate (HEMA) 1% versus 2%. Contact Dermatitis. 2024;91(2):171-172. doi:10.1111/cod.14571.

5 Steunebrink IM, de Groot A, Rustemeyer T. Contact allergy to acrylate-containing nail cosmetics: A retrospective 8-year study. Contact Dermatitis. 2024;90(3):262-265. doi:10.1111/cod.14475.

6 Gkousiaki M, Karalis VD, Kyritsi A, Almpani C, Geronikolou S, Stratigoset A et al. Contact allergy caused by acrylates in nail cosmetics: A pilot study from Greece. Contact Dermatitis. 2024;90(3):273-279. doi:10.1111/cod.14485.

7 Gatica-Ortega ME, Rodríguez-Lago L, Beneyto P, Pastor-Nieto MA, Borrego L. Prognosis and sequelae of meth(acrylate) sensitization in beauticians and consumers of manicure materials. Contact Dermatitis. 2023;89(6):471-479. doi:10.1111/cod.14408.

8 Kocabas G, Steunebrink IM, de Groot A, Rustemeyer T. Results of patch testing 2-hydroxyethyl methacrylate (HEMA) in the European baseline series: A 4-year retrospective study. Contact Dermatitis. 2024;90(5):466-469. doi:10.1111/cod.14488.

9 Gatica-Ortega ME, Pastor-Nieto MA, Giménez-Arnau AM, Mercader-García P, Sanz-Sánchez T, Carrascosa-Carrillo JM, et al. 2-Hydroxyethyl methacrylate (2-HEMA) sensitization, a global epidemic at its peak in Spain? Contact Dermatitis. 2024;90(5):507-513. doi:10.1111/cod.14520.

10 Hilewitz D, Trattner A, Reiter O, Uvaidov V, Noyman Y, Solomon Cohen E, et al. Pandemic of sensitivity to acrylate containing nail cosmetic among young Israeli women? Result of patch testing 2-hydroxyethyl methacrylate in the European baseline series. Contact Dermatitis. 2024;91(6):485-490. doi:10.1111/cod.14683.

11 Wilkinson SM, Aerts O, Agner T, Bruze M, Brans R, Foti C, et al. Contact allergy to methacrylate containing nail products: lack of impact of eu legislation. An audit on behalf of the European Environmental Contact Dermatitis Research Group (EECDRG). Contact Dermatitis. 2024 Dec 25. doi: 10.1111/cod.14745.

12 Steunebrink IM, de Groot A, Rustemeyer T. Presence of 2-hydroxyethyl methacrylate (HEMA) and other (meth)acrylates in nail cosmetics, and compliance with EU legislation: An online market survey. Contact Dermatitis. 2024;90(1):60-65. doi:10.1111/cod.14441.

13 Suuronen K, Ylinen K, Heikkilä J, Mäkelä E, Vastapuu R, Aalto-Korte K, et al. Acrylates in artificial nails—Results of product analyses and glove penetration studies. Contact Dermatitis. 2024;90(3):266-272. doi:10.1111/cod.14474.

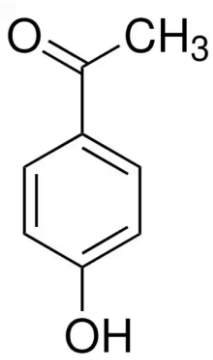
14 Coco-Viloin M, Giordano F. Severe bullous hand eczema from nail (meth)acrylates in an 8-year-old child. Contact Dermatitis. 2024;91(3):240-243. doi:10.1111/cod.14577.

15 Menanteau M, Bensefa-Colas L, Crepy M-N. First case of pustular eyelid allergic contact dermatitis to methacrylates in artificial nails. Contact Dermatitis. 2025;92(3):241-243. doi:10.1111/cod.14717.

2.13 HYDROXYACETOPHENONE

IDENTIFICATION

Description/definition : Hydroxyacetophenone is the acetophenone that conforms to the structural formula shown below
Classifications : Ketones; phenols
IUPAC name : 1-Phenylethanone
Other names : *p*-Hydroxyacetophenone; phenyl methyl ketone; methyl phenyl ketone; piceol
CAS registry number : 99-93-4
EC number : 202-802-8
CIR reviews : Final report, September 27, 2022
Wikipedia : https://en.wikipedia.org/wiki/Piceol
Functions in cosmetics : EU: antioxidant. USA: antioxidants; skin-conditioning agents - miscellaneous
Patch testing : 0.6% water (1,2)
Molecular formula : $C_8H_8O_2$



GENERAL

Hydroxyacetophenone is used as an antioxidant in cosmetics such as shampoos, conditioners, creams, and lotions and as a flavoring agent in food (1,2). It can be obtained from extracts of plants such as *Ficus recta* var. *beecheyana* or *Artemisia ordosica* (2). According to Wikipedia, hydroxyacetophenone (piceol) can be found in the needles and in mycorrhizal roots of Norway spruces (*Picea abies*) and it is used in the synthesis of several pharmaceutical drugs including octopamine, sotalol, bamethan, and dyclonine.

CONTACT ALLERGY (cosmetics)

Case reports

A 79-year-old man had recurrent dermatitis for 7 months, involving the upper and lower eyelids, predominantly on the right side. He had been using several brands of eyedrops for ocular hypertension and also applied his wife's face cream from time to time. Patch tests with the Spanish baseline series, all previously used eye drops, and his wife's face cream 'as is', only yielded a ?+ reaction to the cosmetic cream at D4. A repeated open application test (ROAT) on the upper arm with this cream showed erythema, infiltration, and papules. Testing all ingredients of the face cream, supplied by the manufacturer, resulted in a positive reaction to hydroxyacetophenone 0.6% water (D2 +, D4 ++). Ten controls were negative. The dermatitis cleared within 5 days with the use of topical tacrolimus, and no recurrence was seen after withdrawal of the face cream (1).

A 55-year-old woman presented with a history of four episodes of pruritic eczema involving the eyelids, nasolabial folds and anterior neck. Patch tests with the Spanish baseline series, an additional series of frequent allergens and 32 personal cosmetic products were negative on D2, D4 and D7. Repeated open application tests (ROATs) were sequentially performed, at the inner side of the forearm, with three cosmetics most suspected by the patient. A cosmetic anti-wrinkle serum triggered a positive reaction at

the ROAT site on D7, accompanied by a flare-up reaction involving the neck. In a next session, ingredient patch testing showed a ?+ reaction to hydroxyacetophenone 0.6% water on D2 and D4. Re-patch testing on D5 with occlusion time of 72 hours resulted in a + booster reaction after 2 days, along with a feeling of discomfort at the face and neck. On D7 a ROAT with hydroxyacetophenone 0.6% water was performed on the inner forearm, which 2 days later led to another flare-up reaction involving her eyelids and neck, but without any reaction at the ROAT site itself. A second ROAT gave the same result. Patch tests with hydroxyacetophenone 0.6% water were negative in 20 controls (2).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 791/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 2350/123,000.

LITERATURE

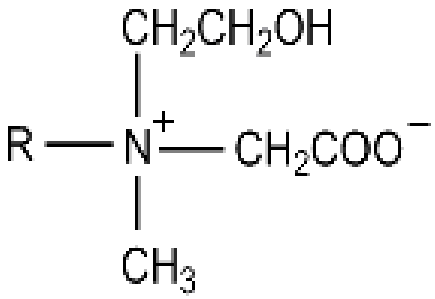
1 Sanz-Sánchez T, Valverde Garrido R, Maldonado Cid P, Díaz-Díaz RM. Allergic contact dermatitis caused by hydroxyacetophenone in a face cream. Contact Dermatitis. 2018;78(2):174-175. doi: 10.1111/cod.12900.

2 Gatica-Ortega ME, Sanz-Sánchez T, Pastor-Nieto MA. Allergic contact dermatitis from hydroxyacetophenone in an anti-wrinkle facial serum with flare-up reactions triggered by the repeated open application test. Contact Dermatitis. 2023;88(5):407-409. doi: 10.1111/cod.14284.

2.14 C12-14 HYDROXYALKYL HYDROXYETHYL SARCOSINE

IDENTIFICATION

Description/definition : C12-14 Hydroxyalkyl hydroxyethyl sarcosine is an alkyl betaine type amphoteric surfactant; it conforms to the structural formula shown below
Classification : Hydroxy linear alkyl betaines
Chemical/IUPAC name : Carboxylatomethyl(hydroxy-C12-14-alkyl)(2-hydroxyethyl)methylammonium
Other names : Softazoline™ LMEB
CAS registry number : 941296-64-6
EC number : Not available
Functions in cosmetics : EU: cleansing; surfactant - foam boosting; hair conditioning; viscosity controlling. USA: hair conditioning agents; surfactants – cleansing agents; surfactants – foam boosters; viscosity increasing agents - aqueous
Patch testing : 0.3% water (1)
Molecular formula : $C_{17}H_{35}NO_4$ - $C_{19}H_{39}NO_4$; $C_{17}H_{35}N_1O_4$ - $C_{19}H_{39}N_1O_4$



R represents the C12-14 hydroxyalkyl group.

GENERAL

C12–14 hydroxyalkyl hydroxyethyl sarcosine (C12–14 HHS) is an ampholytic surfactant used in soaps and shampoos. In hair colour shampoos, the addition of C12–14 HHS is expected to increase the intensity of the dyeing process.

CONTACT ALLERGY (cosmetics)

Case report

A 54-year-old man was investigated for a 4-month history of itchy eruptions on the entire body. Physical examination showed pruritic erythema with thick scales on the scalp, face, and upper trunk. A skin biopsy specimen from a papule on the neck showed lymphocytic infiltration with marked spongiosis. A hair colour shampoo that the patient had used for one year was suspected to be the culprit. Patch testing with this shampoo (1% water) showed positive reactions on D2, D3, and D7 (all +). Later, the ingredients of the product, provided by the manufacturer, were tested which yielded positive reactions to C12–14 hydroxyalkyl hydroxyethyl sarcosine 0.3% water (+/+/+), basic blue 99 0.5% pet. (++/++/++), lauramide DEA 0.5% pet. (++/++/+) and *N*-methyl-*N*-(1-oxododecyl)-β-alaninate 0.3% water (+/+/+). Two controls were negative at D2, D3 and D7. In addition, a lymphocyte transformation test (LTT) with the patient's lymphocytes using the four components showed positive reactions in the patient, but were negative in 5 healthy volunteers. Topical steroids were administered, and the patient was advised to stop using the shampoo. In just 10 days, the lesions had completely resolved, and no recurrence has been observed for 6 months (1).

Quite curiously, the authors did not mention that contact allergy to '*N*-methyl-*N*-(1-oxododecyl)-β-alaninate' had apparently not previously been reported. They did mention that its chemical structure is

similar to that of lauramide DEA, but they did not present identification markers for this chemical such as the CAS registry number. I have been unable to find any reference to this chemical.

The authors probably meant sodium lauroyl methylaminopropionate, with synonym sodium *N*-methyl-*N*-(1-oxododecyl)-β-alaninate (PubChem). Allergy to this chemical is presented in chapter 2.33 Sodium lauroyl methylaminopropionate.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 0/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 0/123,000.

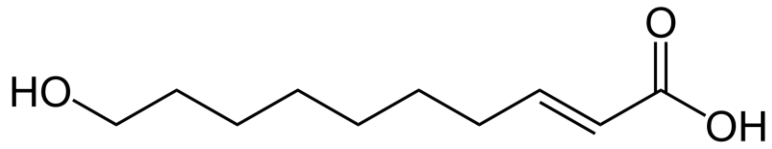
LITERATURE

1 Kosumi H, Yanagi T, Izumi K, Ito T, Shimizu H. Hair colour shampoo dermatitis. Contact Dermatitis. 2017;77(6):419-421. doi: 10.1111/cod.12851.

2.15 10-HYDROXYDECENOIC ACID

IDENTIFICATION

Description/definition : 10-Hydroxydecenoic acid is the straight-chain fatty acid that conforms to the structural formula shown below
Classification : Carboxylic acids; hydroxy fatty acids
IUPAC name : (*E*)-10-Hydroxydec-2-enoic acid
Other names : Royal jelly acid; queen bee acid
CAS registry number : 765-01-5
EC number : 808-119-7
Wikipedia : https://en.wikipedia.org/wiki/Queen_bee_acid (Queen bee acid)
Functions in cosmetics : EU: skin conditioning. USA: skin-conditioning agents - miscellaneous
Patch testing : 0.01% pet. (1); the concentration can likely be increased to 1% pet. or higher
Molecular formula : $C_{10}H_{18}O_2$



GENERAL

10-Hydroxydecenoic acid is a hydroxy fatty acid that is also called 'royal jelly acid'. It is the dominant (10% of the dry mass) and quite specific lipid component present in royal jelly, which is a substance secreted by the pharyngeal glands of honeybees. Several biological and pharmacological properties have been ascribed to 10-hydroxydecenoic acid, including antitumour, antibacterial, immunomodulatory, pro-oestrogenic and pro-neurogenic activities (1). In cosmetics, it is used as a skin-conditioning agent. More generally, unsaturated hydroxy fatty acids are frequently included in topical pharmaceutical or cosmetic ointments because of their (alleged) anti-collagenase, lipolytic or anti-acne properties (1).

CONTACT ALLERGY (cosmetics)

Case report

A 21-year-old atopic man had pompholyx-type hand dermatitis of 3 years' duration. The eruption worsened after application of a moisturizing cream for the treatment of dry skin. In contrast, avoidance of this cream resulted in complete clearance. Patch tests with the European baseline series and the patient's personal products resulted in a positive reaction (D2 ?+, D4 ++) to the cream tested 'as is'. In a second session, all its ingredients, provided by the manufacturer, were individually tested. Among the 13 tested ingredients, a positive result was found only for 10-hydroxydecenoic acid (0.01% pet). Later, a twice-daily repeated open application test (ROAT) was carried out with this material on the volar aspect of the patient's forearm, resulting in a follicular dermatitis at D4. Five controls were patch tested with 10-hydroxydecenoic acid 0.01% pet. with negative results (1).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): unknown/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 7/123,000.

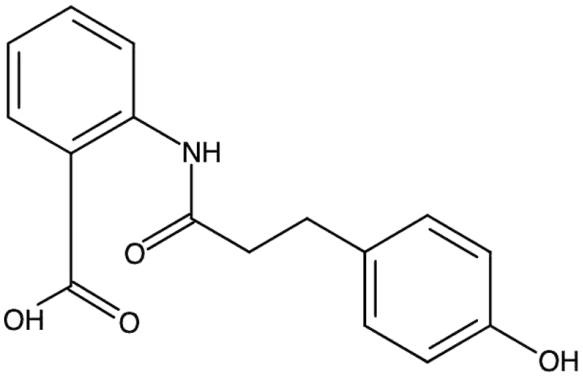
LITERATURE

1 Raison-Peyron N, Dereure O. Allergic contact dermatitis caused by 10-hydroxydecenoic acid contained in an emollient cream. Contact Dermatitis. 2019;81(5):386-387. doi: 10.1111/cod.13338.

2.16 HYDROXYPHENYL PROPAMIDOBENZOIC ACID

IDENTIFICATION

Description/definition : Hydroxyphenyl propamidobenzoic acid is the ortho-aminobenzoate that conforms to the structural formula shown below
Classification : Aminobenzoates
IUPAC name : 2-[3-(4-Hydroxyphenyl)propanoylamino]benzoic acid
Other names : Dihydroavenanthramide D
CAS registry number : 697235-49-7
EC number : 690-968-6
Functions in cosmetics : EU: skin conditioning. USA: skin-conditioning agents - miscellaneous
Patch testing : Symcalmin (a 5% solution of hydroxyphenyl propamidobenzoic acid in a vehicle of (1:1) butylene glycol and pentylene glycol (1)
Molecular formula : $C_{16}H_{15}NO_4$



GENERAL

Hydroxyphenyl propamidobenzoic acid (HPPBA) is a synthetic analogue of naturally occurring avenanthramide which can be found in oats. HPPBA is used as skin-conditioning agent in cosmetics, often in the form of Symcalmin. This is a 5% solution of HPPBA in a vehicle of (1:1) butylene glycol and pentylene glycol, which is commonly used by the pharmaceutical and cosmetic industry for its anti-inflammatory and anti-oxidant (i.e., anti-irritant and anti-itch) properties (1).

CONTACT ALLERGY (cosmetics)

Case report

A 29-year-old woman presented with a generalized eczema evolving for 1 week. The rash had initially appeared on her left forearm and had secondarily spread to the trunk and limbs. Three weeks earlier, the patient had been diagnosed with a left-handed tenosynovitis, for which she had applied an etofenamate-containing gel and a skin-calming cream. Patch tests with the European baseline, cosmetic, preservative and excipient series and with the patient's own products showed a positive reaction to the gel (D2 ++, D4 +++) and the cream (D2 -, D4 ++). Further patch testing confirmed contact allergy to etofenamate (D2 ++, D4 +++). Patch testing with the individual ingredients of the cream, provided by the manufacturer in the same concentrations as in the commercial product, showed a positive reaction to Symcalmin, a 5% solution of hydroxyphenyl propamidobenzoic acid (HPPBA) in a vehicle of (1:1) butylene glycol and pentylene glycol (D2 -, D4 ++). Additional patch tests with butylene glycol and pentylene glycol (both 5% in 50% water/50% alcohol) were negative. HPPBA itself could not be patch tested separately. Six unexposed controls were negative to the Symcalmin preparation. The patient was diagnosed with generalized allergic contact dermatitis caused by etofenamate and in addition due to Symcalmin, most likely to its component hydroxyphenyl propamidobenzoic acid in the skin-calming cream (which was actually also a topical pharmaceutical) (1).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 1/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 119/123,000.

LITERATURE

1 Blanchard G, Walker A, Dendooven E, Aerts O, Goossens A, Gilliet M, Seremet T. Allergic contact dermatitis from a skin-calming cream containing hydroxyphenyl propamidobenzoic acid. Contact Dermatitis. 2023;88(1):68-70. doi: 10.1111/cod.14221.

2.17 INDIGO DYE (NATURAL)

INDIGOFERA TINCTORIA LEAF POWDER

IDENTIFICATION

Description/definition : Indigofera tinctoria leaf powder is the powder obtained from the dried, ground leaves of *Indigofera tinctoria*
Classification : Botanical products and botanical derivatives
CAS number : Not available
EC number : : Not available
Wikipedia : https://en.wikipedia.org/wiki/Indigofera_tinctoria (Indigofera tinctoria)
SCCS opinions : SCCNFP/0790/04; SCCS/1439/11; SCCS/1615/20 Final Opinion
Functions in cosmetics : EU: skin conditioning; skin conditioning, miscellaneous. USA: skin conditioning agents - miscellaneous
Patch testing : 30% and 50% in water and in pet. (3); a D5 reading is recommended when negative or ?+ at D3 (3)

ISATIS TINCTORIA LEAF POWDER

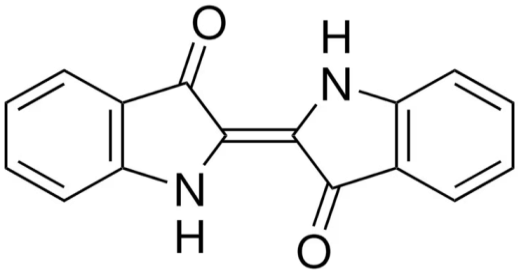
IDENTIFICATION

Description/definition : Isatis tinctoria leaf powder is the powder obtained from dehydrated, crushed leaves of the wild indigo, *Isatis tinctoria* L., Brassicaceae
Classification : Botanical products and botanical derivatives
CAS number : Not available
EC number : : Not available
Wikipedia : https://en.wikipedia.org/wiki/Isatis_tinctoria (Isatis tinctoria)
Functions in cosmetics : EU: hair conditioning – skin conditioning. USA: hair colorants
Patch testing : Unknown; suggested: 30% and 50% in water and pet.

INDIGO (CI 73000)

IDENTIFICATION

Description/definition : CI 73000 is the indigoid colour that conforms to the structural formula shown below
Classification : Hydroxyindoles
INCI name EU : CI 73000
INCI name USA : The INCI name CI 73000 may not be used for ingredient labeling in the USA
IUPAC name : 2-(3-Hydroxy-1*H*-indol-2-yl)indol-3-one
Other names : Indigo blue; indigotin; Vat blue 1
CAS registry number : 482-89-3
EC number : 207-586-9
Wikipedia : https://en.wikipedia.org/wiki/Indigo
Functions in cosmetics : EU: colorant. USA: colorants
Patch testing : Unknown; suggested: 1% pet.
Molecular formula : $C_{16}H_{10}N_2O_2$



GENERAL

Natural indigo dye may be obtained from the powdered dried leaves of *Indigofera tinctoria* and from *Isatis tinctoria*. These powders contain a high concentration of the active ingredient indigo (INCI name EU CI 73000). Indigo dyes and powders are most commonly used for coloring fabrics and yarn, but may also function as hair dye, often in combination with natural henna (1).

Extensive information on 'indigo' can be found in Wikipedia.

CONTACT ALLERGY (cosmetics)

Case report and case series

The patient presented here (1) was not the first who had allergic contact dermatitis from indigo powder. An earlier case was reported from Australia in 2016 (2). Both patients were also allergic to *p*-phenylenediamine, and its (undisclosed) presence in the powder was excluded in the case presented below (1) but not in the Australian report (2). In both cases, the actual allergenic ingredient in indigo powder remained unknown (1,2). In 2025, a case series of 3 patients with allergic contact dermatitis from natural indigo (Indigofera tinctoria leaf powder) was reported from France (3).

A 50-year-old woman was investigated for a 10-month history of intermittent eczema of the neck and ears. The symptoms had started after colouring her hair using commercial '100% natural' indigo powder mixed with natural henna. Physical examination at the time of presentation revealed hyperpigmented macules and patches on the lateral/posterior neck and earlobes. Patch testing with the North American Contact Dermatitis Group standard series, hairstyling series, textile dye series and the henna and indigo powders 'as is' on day 8 revealed strong or extreme (++ or +++) positive reactions to *p*-phenylenediamine (PPD), toluene-2,5-diamine sulfate, disperse orange 3, 3-aminophenol, 4-aminophenol, 4-aminoazobenzene, and indigo powder. There was no reaction to the natural henna powder. Because the patient desired to continue dyeing her hair, she was advised to use 100% natural henna or mineral-based dye. Three months later, she had persistent hyperpigmentation of the posterior neck but denied any recurrent dermatitis. Any undisclosed presence of *p*-phenylenediamine in the indigo powder was excluded by thin-layer chromatography (TLC) and high-resolution liquid chromatography-mass spectrometry (LC–MS)-analyses on 114 and 224 g packages of the indigo powder (1).

Three patients with allergic contact dermatitis from hair dyes containing natural indigo were reported early 2025 from France (3). The first was a 48-year-old woman who had developed scalp dermatitis after the third use of a natural hair dye. Patch tests with the European baseline series, hairstyling panel, plant series, cosmetic series, and various hair dyes (brown, dark brown and hazelnut) used by the patient were positive (+) at D3 for 'brown' powder, 'dark brown' powder, and 'hazelnut' powder, tested 30% and 50% petroleum (pet.). As these three hair dyes shared two components, Lawsonia inermis leaf extract (LILE) and Indigofera tinctoria leaf powder (ITLP), these two allergens were requested and received from the manufacturer. Patch tests at 50% pet. and open tests at 50% pet. and water were positive (+) for ITLP. The patch test with ITLP in water was negative, as were all tests for LILE (3).
A second patient was investigated for several episodes of scalp pruritus and facial dermatitis after application of natural hair dye. When patch tested, she had positive reactions at D5 (doubtful at D3) to 2 of her hair dyes. As in the case of patient one, both products contained LILE and ITLP. Patch testing with

these ingredients resulted in a positive (+) reaction to ITLP in pet. at D3 and a ++ reaction at D5. ITLP in water and LILE were negative (3).
The third patient, a 46-year-old woman, complained of scalp pruritus immediately after natural hair dyeing. The following day, she developed scalp dermatitis, which lasted a week. Patch tests for ITLP in water were positive (+) at D2 and doubtful at D3, whereas patch tests for ITLP in pet. and LILE were negative. Unfortunately, no delayed reading was possible. Prick tests for both extracts at D2 and D3 were negative (3). For unknown reasons, the result at 10-30 minutes was not mentioned.

INDIGOFERA TINCTORIA LEAF POWDER

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 0/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 16 /123,000.

ISATIS TINCTORIA LEAF POWDER

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 0/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 0/123,000.

LITERATURE

1 Voller LM, Elliott JF, Suzuki K, Reiz B, Neeley AB. Allergic contact dermatitis to natural indigo hair dye. Contact Dermatitis. 2020;83(3):222-224. doi: 10.1111/cod.13553.
2 Swan BC, Tam MM, Higgins CL, Nixon RL. Allergic contact dermatitis to substitute hair dyes in a patient allergic to para-phenylenediamine: Pure henna, black tea and indigo powder. Australas J Dermatol. 2016;57(3):219-21. doi: 10.1111/ajd.12454.
3 Charansol A, Bourdenet V, Hanniet A, Pelletier F, Aubin F, Castelain F. Contact dermatitis from natural indigo (Indigofera tinctoria Leaf Extract) contained in hair dye preparations: A case series. Contact Dermatitis. 2025 Feb 20. doi: 10.1111/cod.14769. Epub ahead of print.

2.18 IRIS GERMANICA ROOT EXTRACT

IDENTIFICATION

Description/definition : Iris germanica root extract is an extract of the roots of the German flag, *Iris germanica* L., Iridaceae
Classification : Botanical products and botanical derivatives
Other names : Orris root extract
CAS registry number : 85085-39-8 (generic)
EC number : 285-368-2
Wikipedia : https://en.wikipedia.org/wiki/Iris_%C3%97_germanica (*Iris* x *germanica*)
Functions in cosmetics : EU: skin conditioning. USA: skin-conditioning agents - miscellaneous
Patch testing : Iris germanica (florentina) root powder 1% and 5% in water and in pet. (1)

GENERAL

Iris is a genus encompassing 260–300 species of flowering plants (family Iridaceae). Nearly all species are encountered in temperate Northern hemisphere zones. Leaves, seeds, bulbs, or rhizomes contain irritant or allergenic substances (1). The bearded iris (*Iris germanica*) is one of the most popular irises growing from rhizomes. Root extracts of *Iris germanica* are used in cosmetics as skin-conditioning agents. The major components of Iris germanica root extract are myristic acid (>50%) and irones (20%–30%). The latter are methylionones, which are unsaturated ketones with several isomers (mainly α-irone and β-irone). α-Irone, or 6-methyl-β-ionone, is used as a fragrance ingredient in cosmetics as well as in household cleaners and detergents (1).

CONTACT ALLERGY (cosmetics)

Case report

A 45-year-old atopic woman with a history of allergic contact dermatitis from nickel had developed an acute itchy, erythematous and oedematous eruption on the face, that had appeared a few days after the application of a day cream containing, among others, Iris germanica root extract. Patch tests with the European baseline, additional and cosmetics series, and the patient's cosmetics showed positive reactions to cobalt chloride, nickel sulfate, linalool hydroperoxide 1% pet., limonene hydroperoxide 0.2% pet. (both D2 ?+, D3 +) and to the cosmetic cream (D2 +, D3 ++). Specific patch tests with individual ingredients of the cream could not be performed. By having the patient using various cosmetics with different but overlapping compositions, Iris germanica root extract and Hamamelis virginiana distillate were considered possible culprit allergens. Iris germanica root powder and Hamamelis virginiana distillate were purchased and diluted to both 1% and 5% in petrolatum and in water. When patch tested, positive reactions (D2 +, D3 ++) to Iris germanica florentina root extract (a white flowered variant of Iris germanica; CAS no. 90045-89-9) were observed with both concentrations and both vehicles. Five control patients were tested with the iris powder (1% pet. and 1% water) with negative results in all cases. The patient was diagnosed with allergic contact dermatitis from Iris germanica root extract. The allergen remained unknown. The linalool and limonene hydroperoxides patch tests results had apparently no clinical relevance because the patient tolerated a cream from the same brand containing both of these molecules without problems (1).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 5/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 11/123,000.

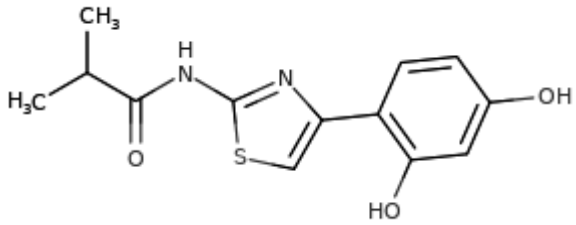
LITERATURE

1 Baudy A, Samaran Q, Dereure O, Raison-Peyron N. Allergic contact dermatitis to Iris germanica root in a "natural" cosmetic. Contact Dermatitis. 2021;85(1):111-112. doi: 10.1111/cod.13802.

2.19 ISOBUTYLAMIDO THIAZOLYL RESORCINOL

IDENTIFICATION

Description/definition : Isobutylamido thiazolyl resorcinol is the resorcinol-derivative that conforms to the structural formula shown below
Classification : Phenols
IUPAC name : *N*-[4-(2,4-Dihydroxyphenyl)-1,3-thiazol-2-yl]-2-methylpropanamide
Other names : Thiamidol
CAS registry number : 1428450-95-6
EC number : Not available
Functions in cosmetics : EU: antioxidant; bleaching; skin conditioning - miscellaneous. USA: antioxidants; skin bleaching agents; skin-conditioning agents - miscellaneous
Patch testing : 0.8% pet. (1)
Molecular formula : $C_{13}H_{14}N_2O_3S$



GENERAL

Isobutylamido thiazolyl resorcinol (thiamidol) is currently the most important inhibitor of human tyrosinase, an enzyme responsible for melanin production. As such, it is positioned as a revolutionary depigmenting agent, superior to hydroquinone, with temporary inhibition of melanogenesis. For this reason, it is currently highly valued in cosmetics and dermatological depigmenting formulations (1).

CONTACT ALLERGY (cosmetics)

Case reports

A 67-year-old woman suffered severe facial dermatitis for 4 months. She had been applying a depigmenting moisturiser daily for several months. A second patient, a 38-year-old woman, presented with a 3-month history of facial eczema following the use of a serum. Patch tests were performed in both patients with the European baseline series along with the suspected culprit products ('as is'). In the first patient, photopatch tests with the European photopatch baseline and extended series (5 J/cm^2 UVA) were also performed. There were strong positive reactions to the culprit products in both patients, in the first patient with equal intensity on the photo-irradiated side. Additional testing with the ingredients of the cream used by the first patient revealed positive reactions to thiamidol diluted 0.1%, 0.3%, 0.5% and 0.8% pet. on D4 in the first patient, with an intensity gradient that depended on the concentration (+ to ++). In the second patient, thiamidol 2% pet. showed a positive reaction (++) on D4. Four controls were negative to thiamidol 1% and 2% pet. Patch tests with resorcinol 1% pet. were negative (no-cross-reactions) (1). Quite curiously, although implied, the authors did not mention that / whether the cosmetic product used by the second patient contained thiamidol (I checked online, it does).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 1/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): unknown/123,000.

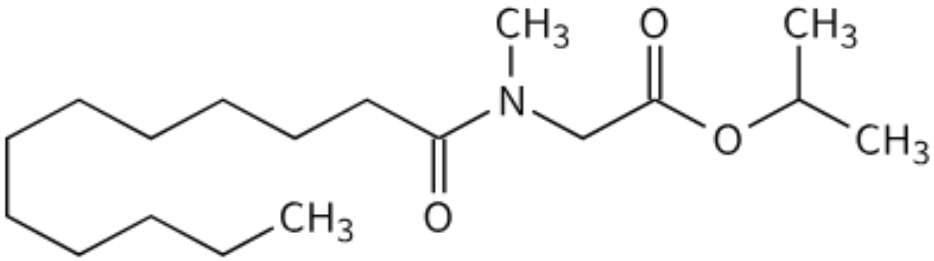
LITERATURE

1 Vernhet L, Dendooven E, Pasteur J, Belahssen L, Aerts O, Clement A. First two cases of allergic contact dermatitis from isobutylamido thiazolyl resorcinol ('thiamidol') in depigmenting skin care routine. Contact Dermatitis. 2025 Mar 26. doi: 10.1111/cod.14793. Epub ahead of print.

2.20 ISOPROPYL LAUROYL SARCOSINATE

IDENTIFICATION

Description/definition : Isopropyl lauroyl sarcosinate is the organic compound that conforms to the structural formula shown below
Classification : Sarcosinates
IUPAC name : Propan-2-yl 2-[dodecanoyl(methyl)amino]acetate
Other names : Glycine, *N*-methyl-*N*-(1-oxododecyl)-, 1-methylethyl ester
CAS registry number : 230309-38-3
EC number : 440-990-5
Functions in cosmetics : EU: skin conditioning. USA: binders; skin-conditioning agents - emollient
Patch testing : 5% alcohol (1,2)
Molecular formula : $C_{18}H_{35}NO_3$



GENERAL

Isopropyl lauroyl sarcosinate is an amino acid-based ester that is used in cosmetics as skin-conditioning agent. It is also employed to dissolve poorly soluble substances and in oily vehicles to improve the solubility, efficacy and photostability of ultraviolet filters (1).

CONTACT ALLERGY (cosmetics)

Case reports

A 43-year-old woman presented with a 3-year history of oedematous erythema and vesicles accompanied by a burning sensation and pruritus of the face. Allergic contact dermatitis caused by a cosmetic was suspected. Patch tests on the patient's upper arm (unspecified) were positive to an unspecified cosmetic used by the patient (D2 ?+, D3 +, D7 ++) and to gold sodium thiosulfate (a delayed reaction 2 months after application). Patch tests with 23 individual ingredients contained in the cosmetic, at concentrations as used in the product, yielded a positive reaction to isopropyl lauroyl sarcosinate 5% in alcohol (D2 ?+, D3 +, D7 +). Four controls were negative. A repeated open application test with isopropyl lauroyl sarcosinate 5% alcohol resulted in erythema on D3 (1).

A 35-year-old woman suffered an erythematous, oedematous, burning and itching eruption of the face, that had developed one day following the application of a product used to treat acne. The lesions disappeared without treatment 5 days after stopping the cream. Some months earlier, the patient had experienced a similar eruption following the application of a make-up base. Patch tests with the European baseline and cosmetic series and with the ant-acne cream showed a strong positive reaction to the cream on D4 (++), tested 'as is'. The ingredients of this cream, provided by the manufacturer, were subsequently patch tested and showed a doubtful reaction (?+) to isopropyl lauroyl sarcosinate 5% in alcohol on D4. A repeated open application test (ROAT) with this ingredient was strongly positive after 2 days; 3 controls were negative on D7. The previously used make-up base could not be patch tested, but similar products from the same brand were shown to contain isopropyl lauroyl sarcosinate (2).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 6/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 103/123,000.

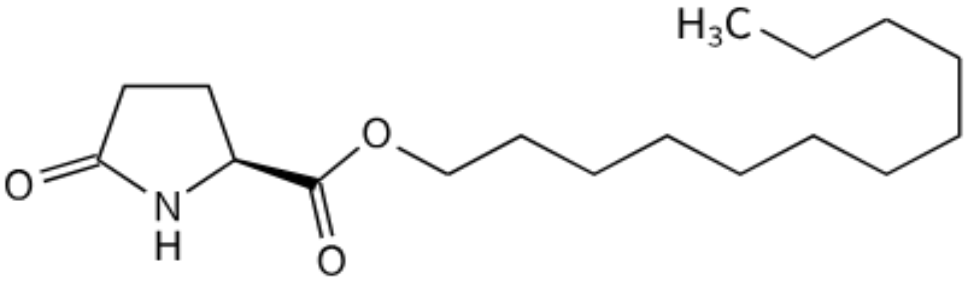
LITERATURE

1 Numata T, Okubo Y, Tsuboi R. Allergic contact dermatitis caused by isopropyl lauroyl sarcosinate. Contact Dermatitis. 2019;80(1):58-59. doi: 10.1111/cod.13117.
2 Badaoui A, Soria A. Allergic contact dermatitis to isopropyl lauroyl sarcosinate. Contact Dermatitis. 2021;85(1):119-120. doi: 10.1111/cod.13812.

2.21 LAURYL PCA

IDENTIFICATION

Description/definition : Lauryl PCA is the ester formed from L-pyrrolidone carboxylic acid and lauric alcohol that conforms to the structural formula shown below
Classification : Laurates; esters
IUPAC name : Dodecyl (2*S*)-5-oxopyrrolidine-2-carboxylate
Other names : Lauryl pyrrolidonecarboxylate; dodecyl 5-oxo-L-prolinate
CAS registry number : 22794-26-9
EC number : 245-224-1
Functions in cosmetics : EU: humectant; skin conditioning. USA: skin-conditioning agents – miscellaneous
Patch testing : 20% pet. (1)
Molecular formula : $C_{17}H_{31}NO_3$



GENERAL

Lauryl PCA is the ester formed from L-pyrrolidone carboxylic acid and lauric alcohol. It has humectant and skin-conditioning properties. According to the safety data sheet provided by the manufacturer of the lip balm that caused allergic reactions in 3 patients (presented below), its 10% dilution may be slightly irritant to eyes and skin (*ex vivo*), but not *in vivo* (1).

CONTACT ALLERGY (cosmetics)

Case reports

A 20-year-old woman had cheilitis of several months' duration. She had been treated with topical corticosteroids, but the lesions had always recurred. Patch tests with the extended Belgian baseline series, a cosmetic series, and her own cosmetics (lip balms, lipsticks, and toothpastes) resulted in a positive (D2 +, D4 ++) reaction to a lip balm, tested 'as is'. The patient was subsequently tested with the 14 ingredients of this lip balm, provided by the manufacturer. This resulted in ++ reactions on D2 and D4 to Laurydone (INCI name: lauryl PCA) 20% pet. The results with a dilution series (10% and 5% in pet.) also remained positive: a ++ reaction to 10% pet. and a + reaction to 5% pet. Five control subjects had negative results with the lip balm and with lauryl PCA 20% pet (1).

The authors presented two more (identical) patients who had also cheilitis from the same lip balm and who had positive patch tests to the lip balm 'as is' and lauryl PCA 20% pet. (1).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 33/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 57/123,000.

LITERATURE

1 Kerre S, Goossens A. Allergic contact cheilitis caused by lauryl PCA. Contact Dermatitis. 2018;79(5):318-319. doi: 10.1111/cod.13060.

2.22 LUFFA CYLINDRICA SEED OIL

IDENTIFICATION

Description/definition	: Luffa cylindrica seed oil is the fixed oil expressed from the seeds of the sponge loofah, *Luffa cylindrica*, Cucurbitaceae
Classification	: Fats and oils
Other names	: Pumpkin seed oil
CAS registry number	: 1242417-48-6
EC number	: Not available
CIR reviews	: Int J Toxicol 2017;36(Suppl.3):51-129
Wikipedia	: https://en.wikipedia.org/wiki/Luffa_aegyptiaca (Luffa aegyptiaca)
Functions in cosmetics	: EU: skin conditioning. USA: skin-conditioning agents - occlusive
Patch testing	: Insufficient data provided in the article reviewed

GENERAL

Luffa cylindrica seed oil is the fixed oil expressed from the seeds of *Luffa cylindrica*. This species belongs to the family Cucurbitaceae and is commonly known as the 'sponge gourd' or 'vegetable sponge'. It is widely cultivated for its fruit, which can be used as a natural sponge once mature, as well as for its edible young fruits. The seed oil is (uncommonly) used in cosmetics for its skin-conditioning properties.

CONTACT ALLERGY

Case report

One patient was reported to have both allergic contact dermatitis and immediate contact reactions (contact urticaria) from Luffa cylindrica seed oil (1). Her case is presented below under Immediate contact reactions (contact urticaria).

IMMEDIATE CONTACT REACTIONS

Case report

A 24-year-old woman developed, a few minutes after the first use of a face and body protective milk SPF 50 applied to the trunk, back and face, an urticarial rash on the application areas and hands, followed 5 days later by contact eczema with severe facial edema. Allergy skin tests revealed a positive open test at 20 minutes with the suspected product. On D2 and D3, the open test-site showed an acute eczema that spread to the arm, neckline, and face. Patch tests with the European baseline, preservatives, fragrances and cosmetics series were positive at D4 for cobalt (++), fragrance mix (+), nickel sulfate (+) and lanolin (++). None of these ingredients were present in the suspected product. Open tests and semi-open tests using the combination of oleic acid, Luffa cylindrica seed oil and oleoyl tyrosine provided by the manufacturer of the cosmetic were positive at 20 minutes (erythema) and at D3 (++). The patient was able to eat cucurbits without any problem before this episode, and did not wish further testing (1).

Comments: This author finds it curious that this report has been accepted for publication. A mixture of oleic acid, Luffa cylindrica seed oil and oleoyl tyrosine in an open and semi-open test induced erythema at 20 minutes and allergic contact dermatitis at D3. The 3 ingredients were not tested separately, and therefore, it remained unknown what the culprit was.

Yet, the authors stated: 'To our knowledge, allergy to oleic acid, oleoyl tyrosine which are two fatty acids, has never been described in the literature. We thus made the diagnosis of contact dermatitis to Luffa cylindrica seed oil, which may contain pumpkin proteins through contamination'. This is a highly unjustified and unscientific conclusion, apart from the fact that 'allergy', at least contact allergy, to oleic acid and oleoyl tyrosine in fact has been published. Also, the title suggests that proteins caused 'contact dermatitis', for which no evidence was provided.

Conclusion: this report is unreliable.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 34/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 28/123,000.

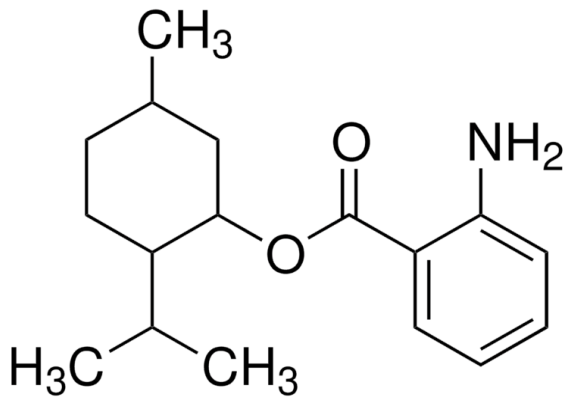
LITERATURE

1 Castelain F, Sueur P, Aubin F, Pelletier F. Protein contact dermatitis to a tan-extender lotion: Imputability of pumpkin seed oil (Luffa cylindrica seed oil). Contact Dermatitis. 2024;90(4):435-437. doi: 10.1111/cod.14492.

2.23 MENTHYL ANTHRANILATE

IDENTIFICATION

Description/definition : Menthyl anthranilate is the ester of menthol and *o*-anthranilic acid, that conforms to the structural formula shown below
Classification : Aminobenzoates
INCI name USA : Meradimate (name used in OTC drug products in the USA)
IUPAC name : (5-Methyl-2-propan-2-ylcyclohexyl) 2-aminobenzoate; menthyl o-amino-benzoate
Other names : Meradimate
CAS registry number : 134-09-8
EC number : 205-129-8
Wikipedia : https://en.wikipedia.org/wiki/Menthyl_anthranilate
Functions in cosmetics : EU: UV-absorber. USA: light stabilizers; sunscreen agents
Patch testing : 5% pet. for both patch testing and photopatch testing
Molecular formula : $C_{17}H_{25}NO_2$



GENERAL

Menthyl anthranilate is the ester of menthol and *o*-anthranilic acid. It is used as a broad-spectrum UVB- and UVA-absorber in cosmetics and in the USA in OTC products. It is currently required to be named as meradimate in all FDA approved OTC products. Meradimate is approved by the FDA and Health Canada to be used as an ingredient in sunblocking products in a maximum concentration of 5% (Drugbank online).

PHOTOCONTACT ALLERGY (cosmetics)

Case report

A 70-year-old man was referred with a 10-month history of recurrent pruritic, scaly, erythematous plaques in a photo-distributed pattern. Involved areas included the scalp, face, neck, and arms, with sparing of skin proximal to his shirt sleeves. The patient reported frequent outdoor activity and sun protection with a facial moisturizing lotion, which he applied to all sun-exposed areas. The active ingredients in this sunscreen include homosalate, meradimate, octinoxate (INCI name EU ethylhexyl methoxycinnamate), octocrylene, and zinc oxide. Patch tests were performed with the NACDG standard series, the personal care, preservative, emulsifier, and the NACDG photopatch test allergen series (applied twice, one for conventional patch testing and one for photopatch testing), as well as his personal products. At the D4 reading positive reactions were seen to menthyl anthranilate (meradimate) and the moisturizing lotion on the irradiated side only, confirming photo-allergic contact dermatitis. Strict avoidance of menthyl anthranilate-containing sunscreens was recommended, and at a 2-month follow-up the patient had significant improvement of symptoms (1).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 5/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 7/123,000.

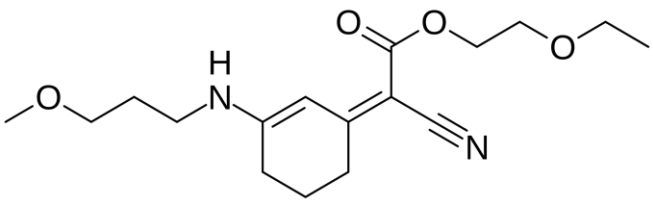
LITERATURE

1 Battis N, Ekstein SF, Neeley AB. Photoallergic contact dermatitis to menthyl anthranilate (Meradimate). Dermatitis. 2023;34(2):153. doi: 10.1089/derm.2022.0048.

2.24 METHOXYPROPYLAMINO CYCLOHEXENYLIDENE ETHOXYETHYLCYANOACETATE

IDENTIFICATION

Description/definition : Methoxypropylamino cyclohexenylidene ethoxyethylcyanoacetate is the organic compound that conforms to the structural formula shown below
Classification : Amines; esters; ethers
IUPAC name : 2-Ethoxyethyl-(2*Z*)-2-cyano-2-[3-(3-methoxypropylamino)cyclohex-2-en-1-ylidene] acetate
Other names : Acetic acid, 2-cyano-2-[3-[(3-methoxypropyl)amino]-2-cyclohexen-1-ylidene]-, 2-ethoxyethyl ester, (2*Z*)-
CAS registry number : 1419401-88-9
EC number : 700-860-3
Wikipedia : https://en.wikipedia.org/wiki/Methoxypropylamino_cyclohexenylidene_ethoxyethylcyanoacetate
SCCS opinions : SCCS/1605/19 Final opinion; SCCS/1587/17
Functions in cosmetics : EU: light stabilizer; UV-filter. USA: light stabilizers; sunscreen agents
Patch testing : 1% in 50% water/50% alcohol; UV-filters are usually tested 5-10% pet.
Molecular formula : $C_{17}H_{26}N_2O_4$



GENERAL

Methoxypropylamino cyclohexenylidene ethoxyethylcyanoacetate (MCE) is an organic compound used in sunscreens to absorb UVA radiation. It is marketed as Mexoryl 400 by L'Oréal. MCE has an absorption maximum of 385 nm, which is in the long-wave UVA range (UVA1, 360−400 nm) (Wikipedia).

CONTACT ALLERGY (cosmetics)

Case reports and case series

A 59-year-old woman with a history of atopic dermatitis presented with chronic and severe facial dermatitis persisting for 1 year. Physical examination revealed well-demarcated infiltrated erythematous plaques on the face. Patch tests with the European baseline series, preservatives, emulsifiers, corticosteroids and personal products were positive at D2 and D4 (++) for her sunscreen. Photopatch tests were also performed with the European baseline series and the sunscreen. The results were positive for the sunscreen product (++) both before and after exposure to 5 J/cm^2 of UVA, with a final reading at D4, confirming the diagnosis of allergic contact dermatitis to the sunscreen. Testing with the ingredients supplied by the manufacturer was positive for methoxypropylamino cyclohexenylidene ethoxyethylcyanoacetate 1% in 50% water/50% alcohol (++) at D2 and D4. Twelve controls were negative. Discontinuing the sunscreen resulted in the resolution of the lesions within 1 week (1).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): unknown/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 0/123,000.

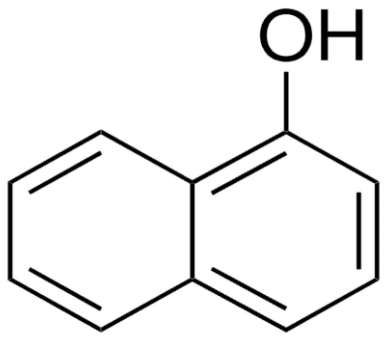
LITERATURE

1 Loretan A, Bertone F, Menzinger S, Piletta P, Tehrany YA. Severe allergic contact dermatitis caused by methoxypropylamino cyclohexenylidene ethoxyethylcyanoacetate. Contact Dermatitis 2025;92(1):80-81. doi: 10.1111/cod.14700.

2.25 1-NAPHTHOL

IDENTIFICATION

Description/definition : 1-Naphthol is the bicyclic phenol that conforms to the structural formula shown below
Classification : Naphthols
IUPAC name : Naphthalen-1-ol
Other names : 1-Naphthalenol; α-naphthol
CAS registry number : 90-15-3
EC number : 201-969-4
CIR reviews : Int J Toxicol 2011;30(Suppl.2):73-127; J Am Coll Toxicol 1989;8(4):749-768
Functions in cosmetics : EU: hair dyeing. USA: hair colorants
EU cosmetic restrictions : Annex III, 16. (max. 2%; in combination with hydrogen peroxide max. 0.1%; must label products containing it 'can cause an allergic reaction')
Patch testing : 1% pet. (1)
Molecular formula : $C_{10}H_8O$



GENERAL

In oxidative (permanent) hair dyes, a chemical reaction occurs between a precursor and a coupler, with an oxidizing agent. 1-Naphthol is a red coupler. Of 229 identified hair dye substances, it was 1 of 172 chemicals predicted to be strong/moderate sensitizers (2).

CONTACT ALLERGY (cosmetics)

Case report

A 43-year-old woman was hospitalized because of severe oedematous eczematous dermatitis on her scalp and face, and weeping eczema on the back of her neck, which appeared to have triggered secondary generalized eczema. She had applied a purple permanent oxidative hair dye 2 days before. Patch tests were performed with an extended British baseline series, hairdressing, clothing and dye, and corticosteroid series. Additionally, ingredients of the hair dye product, provided by the manufacturer, not present in these series, were tested, including 1-naphthol 1% pet. A positive reaction was observed to 1-naphthol 1% pet. (D2 +++, D4 +++), with additional positive reactions to nickel sulfate and cetearyl alcohol D2 -, D4 +). All other hair dyes, including *p*-phenylenediamine, were negative. Thus, allergic contact dermatitis from 1-naphthol was diagnosed. Cetearyl alcohol was also present in the hair dye, and may have been a contributory allergen. A further 8 patients presenting with a history suggestive of allergic contact dermatitis caused by hair dye were also tested with naphthol 1% pet., of who 7 had negative results and 1 had an irritant reaction to 1-naphthol (1).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 142/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 181/123,000.

LITERATURE

1 King T, Sabroe R, Holden C. Allergic contact dermatitis caused by 1-naphthol, a red coupler, in a purple permanent oxidative hair dye. Contact Dermatitis. 2018;79(2):99-100. doi: 10.1111/cod.12997.

2 Søsted H, Basketter D, Estrada E, Johansen JD, Patlewicz GY. Ranking of hair dye substances according to predicted sensitization potency: quantitative structure-activity relationships. Contact Dermatitis. 2004;51:241-254. doi: 10.1111/j.0105-1873.2004.00440.x.

2.26 NIGELLA SATIVA SEED OIL

IDENTIFICATION

Description/definition : Nigella sativa seed oil is the fixed oil expressed from the seeds of black caraway, *Nigella sativa* L., Ranunculaceae
Classification : Fats and oils
INCI name Europe : Nigella sativa seed oil
INCI name USA : Nigella sativa (black cumin) seed oil
Other names : Caraway seed oil
CAS registry number : 90064-32-7
EC number : 290-094-1
Wikipedia : https://en.wikipedia.org/wiki/Nigella_sativa (Nigella sativa)
Functions in cosmetics : EU: skin conditioning – emollient; skin conditioning; perfuming. USA: skin-conditioning agents - occlusive
Patch testing : 5% pet. (3); when tested undiluted, open test!

GENERAL

Contact allergy to Nigella sativa oil has been reported several times, but never before from its presence in cosmetics. In these products, it may be used as an emollient and for perfuming.

CONTACT ALLERGY (cosmetics)

Case report

A 31-year-old woman was referred for a 4-day history of acute erythema, pustules and scabs on the neck and lower face. Initially, no contact allergen was identified, but finally she reported living with a new partner for 2 months who used cosmetics for beard care: nigella oil, fenugreek oil, petrolatum jelly with Nigella 'Codex' (unknown manufacturer), a rub ointment (containing several essential oils), and an anti-ageing cream. The patient denied ever using essential oils on her own skin. Patch tests were performed with the European baseline, a cosmetic and an essential oils series, and the personal beard products of her partner and read at D2 and D4. Positive reactions were observed to Nigella sativa oil (5% in paraffin oil) (++/++), the cosmetic petrolatum jelly with Nigella Codex® 'as is' (-/++), limonene and linalool hydroperoxides (both -/++), *tert*-butylhydroquinone 1% pet. (++/++) and wood tar-mix 12% pet. (++/++). The patient was diagnosed with connubial allergic contact dermatitis from Nigella sativa seed oil present in beard cosmetics of her partner (1).

The main allergen in Nigella sativa oil is thymoquinone, which is also the main constituent of the oil. Thymoquinone itself was not tested, but the patient had a positive patch test reaction to *t*-butylhydroquinone, a structurally related compound. Cross-reactions between the two have been observed and *t*-butylhydroquinone is even considered to be a marker for sensitivity to Nigella sativa oil (2,3).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 53/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 215/123,000.

LITERATURE

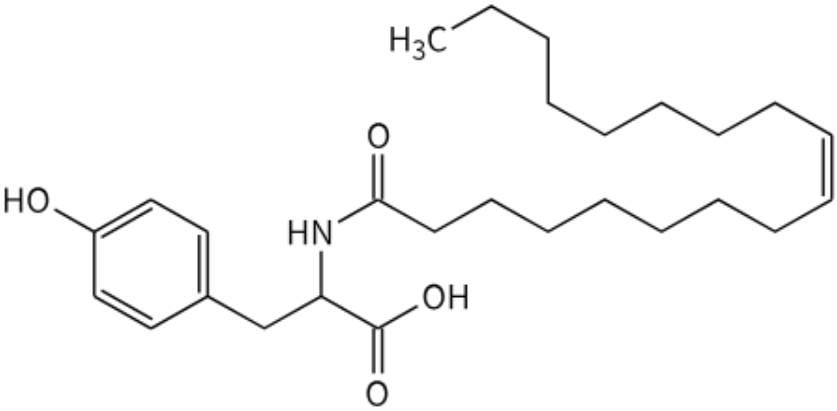
1 Assier H, Kouby F, Ingen-Housz-Oro S, Roux C. Severe allergic contact connubial dermatitis to Nigella Sativa Seed Oil due to repeated contacts to beard cosmetics. Contact Dermatitis. 2023;88(3):245-246. doi: 10.1111/cod.14266.

2 Kurihara F, Soria A, Lepoittevin JP, Chasset F, Barbaud A, Pecquet C. Thymoquinone as a causative allergen in Nigella sativa oil contact dermatitis with cross-reactivity to tert-butylhydroquinone. Contact Dermatitis. 2020;83(2):132-134. doi: 10.1111/cod.13542.
3 Seiller H, Kurihara F, Chasset F, Soria A, Barbaud A. Tert-butylhydroquinone is a marker for sensitivity to Nigella sativa oil allergy: Five new cases. Contact Dermatitis. 2021;84(6):447-449. doi: 10.1111/cod.13750.

2.27 OLEOYL TYROSINE

IDENTIFICATION

Description/definition : Oleoyl tyrosine is the amide formed from the reaction of oleoyl chloride and tyrosine that conforms to the structural formula shown below
Classification : Amino acids alkyl amides
IUPAC name : (2*S*)-3-(4-Hydroxyphenyl)-2-[[(*Z*)-octadec-9-enoyl]amino]propanoic acid
Other names : L-Tyrosine, *N*-(1-oxo-9-(*Z*)-octadecenyl)
CAS registry number : 147732-57-8
EC number : Not available
CIR reviews : Int J Toxicol 2017;36(Suppl.1):17-56
Functions in cosmetics : EU: skin conditioning; skin protecting. USA: skin-conditioning agents – miscellaneous
Patch testing : 1% pet. (1,2)
Molecular formula : $C_{27}H_{43}NO_4$



GENERAL

Oleoyl tyrosine is an amide formed from the reaction of oleoyl chloride and tyrosine and is used as a skin conditioning and a self-tanning agent. The authors of ref. 1 write: 'Few studies have evaluated the safe maximum concentration of oleoyl tyrosine as used in cosmetics, but, according to the Cosmetic Ingredient Review (CIR) panel, tyrosines did not produce any adverse cutaneous effects (irritation or sensitization) in rats, guinea pigs, or mouse skin models at concentrations up to 1%.' However, this sentence was related to tyrosine, not to tyrosine**S**. (CIR report).

CONTACT ALLERGY (cosmetics)

Case reports

A 13-year-old girl had developed an itchy erythematous and squamous eruption of the thighs, legs, and forearms 6 hours following the application of a sunscreen with SPF50+. The lesions spread secondarily to the face even though the sunscreen had not been applied there. Patch tests with the European baseline series, the cosmetic series and the sunscreen 'as is' showed a strong positive reaction (++) to the sunscreen on D4. The ingredients of this sunscreen, provided by the manufacturer, were subsequently patch tested and showed a ++ D4 reaction to oleoyl tyrosine 1% pet. Three controls were negative (1).

A 43-year-old woman was investigated for suspected (photo-)allergic contact dermatitis from her sunscreen or an after-sun product. The patient had used both sun care products in the past without problems. However, during a recent vacation, she had re-applied the same sunscreen and, following sunburn of the face, she applied the same after-sun product. A few days later, a pruritic, erythematous and strongly oedematous dermatitis occurred. Patch tests with the Belgian baseline, cosmetic and photo-patch test series (the latter *in duplo*, one irradiated with 5 J/cm^2 UVA) and both products, tested 'as is'

showed equally strong (++) positive patch and photopatch test reactions only to the after-sun product. As this cosmetic contained oleoyl tyrosine as a highly ranked ingredient, an additional patch test was performed to it in a concentration of 1% pet., yielding a ++ reaction on D3 (2).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 8/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 2/123,000.

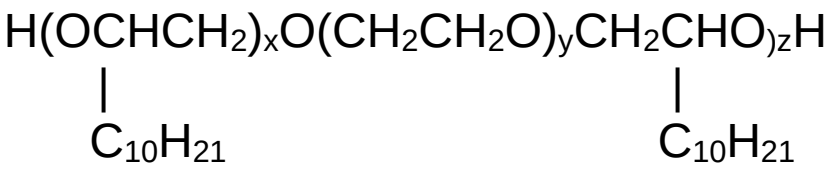
LITERATURE

1 Badaoui A, Vergez M, Soria A. Allergic contact dermatitis from oleoyl tyrosine in a sunscreen. Contact Dermatitis. 2021;85:255-256. doi: 10.1111/cod.13835.
2 De Fré C, Dendooven E, Aerts O. Oleoyl tyrosine: An emerging allergen in tan-enhancing sunscreens and cosmetics. Contact Dermatitis. 2022;87(1):110-112. doi: 10.1111/cod.14113.

2.28 PEG-45/DODECYL GLYCOL CO-POLYMER

IDENTIFICATION

Description/definition : PEG-45/dodecyl glycol copolymer is the polyoxyethylene, polydodecyl glycol block polymer that conforms generally to the formula shown below, in which the average value of x, y, and z are 11, 45 and 11, respectively
Classification : Alkoxylated alcohols; synthetic polymers
Other names : Poly(oxy-1,2-ethanediyl), α-(12-hydroxydodecyl)-ω-[(12-hydroxydodecyl)oxy]-
CAS registry number : 78336-31-9
EC number : Not available
Functions in cosmetics : EU: emulsion stabilising. USA: emulsion stabilizers; skin-conditioning agents – emollient
Patch testing : 10% pet. (1)
Molecular formula : $(C_2H_4O)_nC_{24}H_{50}O_3$



GENERAL

PEG-45/dodecyl glycol co-polymer is a polyoxyethylene polydodecyl glycol block polymer used in cosmetics as an emulsion stabilizer and emollient (1). The sensitising capacities of copolymers may have been underestimated because of their high molecular weight; the exact nature of the haptens in copolymers is still unknown (2).

CONTACT ALLERGY (cosmetics)

Case reports

A 16-year-old atopic boy had persistent dryness, episodes of swelling, and burning sensations affecting both lips for 3 months. A flare-up of the lesions, with scaling of the lips and eczema of the eyelids, was noted a couple of days after using a new lip balm. Patch tests with the European baseline series and supplements, the suspected product 'as is' and all its ingredients yielded a positive reaction to the lip balm (D2 ?+, D4 +) and doubtful reactions (D4 ?+) to some of its ingredients: PEG-45/dodecyl glycol co-polymer 10% pet., polyisobutene hydrogen 5% pet., and bis-diglyceryl polyacyladipate-2 16% pet. ROATs were subsequently performed twice a day on the patient's forearms with these three ingredients, and these were positive after 4 days to PEG-45/dodecyl glycol co-polymer and bis-diglyceryl polyacyladipate-2, with erythema and papules with a follicular pattern, graded ++, and a reaction evolving into plaques and lasting for almost a week after the end of the applications. Two controls were negative.
To explore these reactions further, new patch tests were performed with the three ingredients with an additional reading at D7. A positive test reaction was now observed to PEG-45/dodecyl glycol co-polymer 10% pet. (D4 ++, D7 +), and doubtful reactions to bis-diglyceryl polyacyladipate-2 16% pet. (D4 and D7 ?+), and polyisobutene hydrogen 5% pet. (?+ on D4 and negative on D7). The latter reaction was scored as negative (1).

A 27-year-old woman reported a vesicular rash around a scar on the back of the foot following the application of a 'protective repair cream' for the first time. Six days later, she developed an erythematous and pruritic oedema of the face. A few weeks after that, the patient reported a second pruritic vesiculobullous skin eruption on her hands after the first application of a hand cream of the same brand. Due to the severity of the initial reaction, semi-open skin tests were performed with the two creams, resulting in positive reactions on D2 to both products. Patch tests with the components of the two

creams, supplied by the manufacturer, were positive (++) on D2 and D4 to PEG-22/dodecyl glycol copolymer contained in the repair cream, and doubtfully positive (?+) on D2 and D4 to PEG-45/dodecyl glycol copolymer contained in the hand cream (concentrations not mentioned). A repeated open application test (ROAT) with the latter ingredient was, however, clearly positive (follicular aspect) after 5 days. The diagnosis of ACD caused by PEG-45/dodecyl glycol copolymer and PEG-22/dodecyl glycol copolymer on the initial application site associated with oedematous eczema of the face (via a transfer) was established. The authors suggested the possibility of cross-reactivity between PEG-22 and PEG-45 dodecyl glycol copolymers (2). Conversely, the genuine sensitizer might be an additive, an impurity, a product appearing during polymerization, a residual monomer, or a degradation product (3).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 7/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 80/123,000.

LITERATURE

1 Clark E, Samaran Q, Dereure O, Raison-Peyron N. PEG-45/dodecyl glycol co-polymer and bis-diglyceryl polyacyladipate-2: Two culprits responsible of an allergic contact dermatitis to a lip balm. Contact Dermatitis. 2021;85(1):117-119. doi: 10.1111/cod.13811.

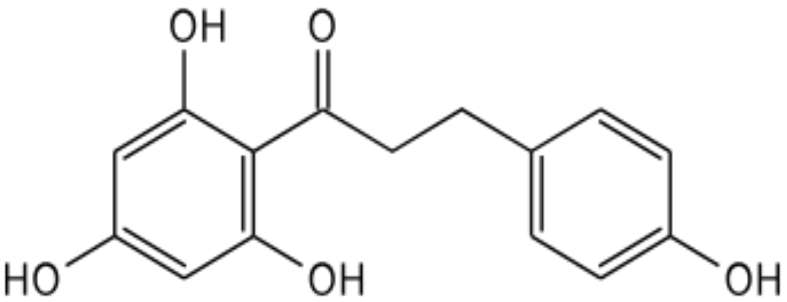
2 Brehon A, Soria A, Barbaud A, Amsler E. Allergic contact dermatitis caused by PEG-22 and PEG-45 dodecyl glycol copolymers in two skin-repairing creams. Contact Dermatitis. 2023;89(3):213-215. doi: 10.1111/cod.14369.

3 Quartier S, Garmyn M, Becart S, Goossens A. Allergic contact dermatitis to copolymers in cosmetics–case report and review of the literature. Contact Dermatitis. 2006;55(5):257-267. doi: 10.1111/j.1600-0536.2006.00960.x.

2.29 PHLORETIN

IDENTIFICATION

Description/definition : Phloretin is the polyphenolic flavonoid that conforms to the structural formula shown below
Classification : Dihydrochalcones; hydroxypropiophenones
IUPAC name : 3-(4-Hydroxyphenyl)-1-(2,4,6-trihydroxyphenyl)propan-1-one
Other names : 2',4',6'-Trihydroxy-3-(4-hydroxyphenyl)propiophenone; dihydronaringenin
CAS registry number : 60-82-2
EC number : 200-488-7
Wikipedia : https://en.wikipedia.org/wiki/Phloretin
Functions in cosmetics : EU: antioxidant; anti-sebum. USA: antiacne agents; antioxidants
Patch testing : 1% in 50% water/50% alcohol (1)
Molecular formula : $C_{15}H_{14}O_5$



GENERAL

Phloretin is a polyphenolic flavonoid naturally found in apple trees and other plants. It is used in cosmetic products for its antioxidant and anti-sebum properties, often together with ascorbic acid (vitamin C). Potential applications of phloretin have been investigated *in vitro* and in pre-clinical studies for several dermatological conditions including photo-aging, skin hyperpigmentation, acne, and melanoma (1).

CONTACT ALLERGY (cosmetics)

Case report

A 35-year-old woman with a personal history of atopic dermatitis and asthma was investigated for outbreaks of eczema of the face and neck since 5 months. Lesions predominantly involved the eyelid and lip areas where edema was also present. Patch tests with the Spanish baseline series (and apparently at least one cosmetic product) showed positive reactions to a luxury antioxidant serum product and thiomersal (relevance unknown). After discontinuing the use of the cosmetic product, it took several weeks for the eczematous lesions to heal. In a second test session, the patient was patch tested with a cosmetic series and the individual ingredients of the cosmetic product, obtained from the manufacturer; this showed a positive reaction to phloretin 2% 50 water/50 alcohol (D2 ?+, D4 ++, D7 ++). Twenty controls tested with the phloretin preparation were negative (1).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 2/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 6/123,000.

LITERATURE

1 Gatica-Ortega ME, Pastor-Nieto MA. Allergic contact dermatitis to phloretin, a luxury cosmetic ingredient, involving a woman with atopic dermatitis. Contact Dermatitis. 2024;91(2):172-174. doi: 10.1111/cod.14574.

2.30 POLYACRYLAMIDE/C13-14 ISOPARAFFIN/LAURETH-7 MIX

IDENTIFICATION

In the publication shown below, the name polyacrylamide/C13-14 isoparaffin/laureth-7 mix is used. Various other names are given by manufacturers as INCI names, but none of them can be found in the EU or USA INCI databases:

- Polyacrylamide (and) C13-14 Isoalkane (and) Laureth-7
- Polyacrylamide (and) C13-14 Isoalkane (formerly C13-14 Isoparaffin) (and) Laureth-7
- Polyacrylamide, C13-14 Isoparaffin, Laureth-7

Classification	: Polymers
INCI name Europe	: Not found
INCI name USA	: Not found
Other names	: Sepigel 305 ™
CAS registry number	: Not found
EC number	: Not found
Functions in cosmetics	: Described by the manufacturer as: emulsifier; emulsion stabilizer; stabilizer; viscosity modifier
Patch testing	: polyacrylamide/C13-4 isoparaffin/laureth-7 mix ‘as is’ (as supplied)

GENERAL

Polyacrylamide/C13-4 isoparaffin/laureth-7 mix (INCI name) or SEPIGEL 305 (trade name) is a non-ionic, pre-neutralized polymer included in an inverse emulsion. Used in cosmetics, it acts as a thickening, stabilizing and texture agent. According to regulation No. 1272/2008 (EC), this mixture is classified as an irritant for the eyes and skin, but is not known to elicit allergic skin reactions (1).

CONTACT ALLERGY (cosmetics)

Case report

A 33-year-old woman with a history of atopic dermatitis and seasonal rhinoconjunctivitis was referred for the investigation of eczema. The patient reported a recent flare-up of inflammatory skin lesions on her chest, arms and face after applying a moisturizing cream. Patch tests with the European baseline series, a cosmetic series and the suspected cream ‘as is’ were positive to the cream only (D2 +, D4 ++). In a second session, the ingredients of this cream, obtained from the manufacturer, were tested which resulted in a positive patch test to the mixture polyacrylamide/C13-4 isoparaffin/laureth-7 mix ‘as is’ ‘(D2 +, D4 ++). Five controls were negative. The corresponding individual ingredients could not be obtained from the manufacturer. Laureth-7 from another supplier (citrated, 1%, 5% and 10% water and pet.) was patch test-negative. Because the different ingredients of the mixture could not be tested separately, it is unknown whether the allergic skin reaction was caused by a compound allergy, by an impurity present in the mixture or one of its components, or by sensitization to C13-14 isoparaffin, laureth-7 or polyacrylamide (1).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): unknown/35,000.
EWG’s Skin Deep Cosmetics Database (February 2025): unknown/123,000.

LITERATURE

1 Jaulent C, Dereure O, Raison-Peyron N. Contact dermatitis caused by polyacrylamide/C13-4 isoparaffin/laureth-7 mix in an emollient cream for atopic skin. Contact Dermatitis. 2019;81(1):70-71. doi: 10.1111/cod.13234.

2.31 SALVADORA PERSICA BARK/ROOT EXTRACT

IDENTIFICATION

Description/definition : Salvadora Persica bark/root extract is the extract of the roots and bark of the mustard tree, *Salvadora persica* L., Moraceae
Classification : Botanical products and botanical derivatives
CAS registry number : Not available
EC number : Not available
Wikipedia : https://en.wikipedia.org/wiki/Salvadora_persica (Salvadora persica)
Functions in cosmetics : EU: skin conditioning. USA: skin-conditioning agents - miscellaneous
Patch testing : Extract 10%, 1% and 0.1% water (1)

GENERAL

Salvadora persica is a shrub belonging to the Salvadoraceae plant family, and is commonly known as the 'toothbrush tree', miswak, or meswak. Historically, the fibrous roots or twigs of the meswak tree were used as toothbrushes, especially in countries with large Muslim populations. Currently, the cosmetic industry is said to use extracts of *S. persica* roots or twigs as ingredients in toothpastes (1), although its functions are described in INCI databases as 'skin-conditioning'.

CONTACT ALLERGY (cosmetics)

Case report

A 28-year-old woman developed gingival pruritus and erythema 2 days after she brushed her teeth with an Indian toothpaste containing *Salvadora persica*. Her previous history showed an oral reaction to a *S. persica* chewing stick 6 months previously. Patch testing with the S. persica extract diluted 1:10, 1:100 and 1:1000 with water and all other ingredients tested 1% water resulted in +++ reactions to all dilutions of S. persica extract on D2 and D3 and a + reaction on D7. After switching to another toothpaste not containing this extract, follow-up 15 months later showed normal gingival and alveolar mucosa (1).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 2/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 9/123,000.

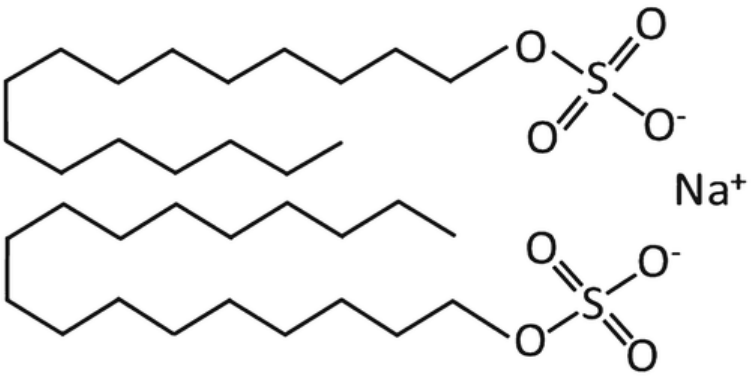
LITERATURE

1 Chaubal TV, Bapat RA, Bapat PR. Allergic contact stomatitis caused Salvadora persica in toothpaste. Contact Dermatitis. 2017;77(5):325-326. doi: 10.1111/cod.12819.

2.32 SODIUM CETEARYL SULFATE

IDENTIFICATION

Description/definition : Sodium cetearyl sulfate is the sodium salt of a mixture of cetyl and stearyl sulfate; it conforms generally to the formula shown below
Classification : Alkyl sulfates
IUPAC name : Sodium;hexadecyl sulfate;octadecyl sulfate
Other names : Sodium cetostearyl sulfate
CAS registry number : 59186-41-3
EC number : Not available
CIR reviews : Int J Toxicol 2010;29(Suppl.2):115-132; J Am Coll Toxicol 1992;11(1):145-155
Functions in cosmetics : EU: cleansing; foaming; surfactant - cleansing. USA: surfactants – cleansing agents; surfactants - emulsifying agents
Patch testing : 10% pet. (1)
Molecular formula : $C_{34}H_{70}NaO_8S_2$-



$CH_3(CH_2)_nCH_2OSO_3Na$ (n has a value of 16 and 18)

GENERAL

Sodium cetearyl sulfate (SCS) is a sulfated salt of cetearyl alcohol, a fatty alcohol composed of the mix of cetyl alcohol and stearyl alcohol. SCS is used in cosmetics mainly as an anionic emulsifier, because of its surfactant, emollient and opacifier properties. The Cosmetic Ingredient Review Expert Panel classified it as a safe product for the skin: not irritant or sensitizing (1) (see CIR reviews in the section Identification).

CONTACT ALLERGY (cosmetics)

Case report

A 51-year-old atopic woman with a past history of allergic contact dermatitis caused by MCI/MI presented with a 2-month history of eczematous lesions affecting predominantly the dorsal and lateral aspects of both hands and wrists. She admitted the use of multiple cosmetics. Patch testing with a cosmetics and fragrance series and with her own products resulted in positive reactions on D4 (one +, one ++) to a hand cream and a moisturising foot cream of the same brand. A repeated open application test (ROAT) performed with the hand cream elicited a positive reaction within 3 days. In a second session, patch testing with the 19 ingredients of the products, obtained from the manufacturer, were patch tested, resulting in a positive reaction (D1 ?+, D4 ++) to sodium cetearyl sulfate 10% pet. Ten controls were negative. Finally, the patient was tested with cetyl alcohol 5% pet., stearyl alcohol 30% pet. and cetearyl alcohol 20% pet. and there were no reactions to any of them (1).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 172/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 251/123,000.

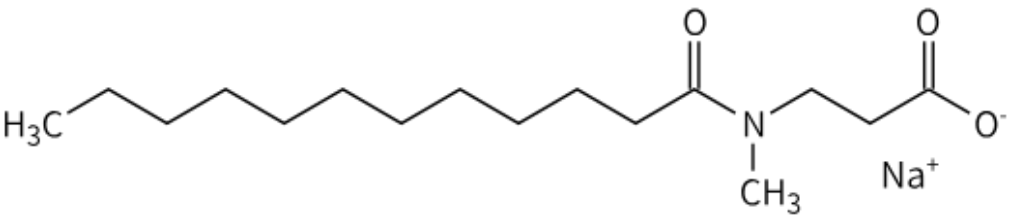
LITERATURE

1 Oscoz-Jaime S, Hervella-Garcés M, M de Espronceda-Ezquerro I, Yanguas-Bayona JI. Allergic contact dermatitis caused by sodium cetearyl sulfate. Contact Dermatitis. 2018;78(6):426-427. doi: 10.1111/cod.12968.

2.33 SODIUM LAUROYL METHYLAMINOPROPIONATE

IDENTIFICATION

Description/definition : Sodium lauroyl methylaminopropionate
Classification : Amino acid alkyl amides
IUPAC name : Sodium;3-[dodecanoyl(methyl)amino]propanoate
Other names : Sodium *N*-lauroyl *N*-methyl β-alanine; sodium *N*-methyl-*N*-(1-oxododecyl)-β-alaninate
CAS registry number : 21539-58-2
EC number : 244-429-3
Functions in cosmetics : EU: cleansing; surfactant – emulsifying; surfactant - cleansing. USA: surfactants - cleansing agents
Patch testing : 0.4% water (1)
Molecular formula : $C_{16}H_{31}NO_3 \bullet Na$



GENERAL

Sodium lauroyl methylaminopropionate is an anionic surfactant contained in shampoos, body soaps and shaving foams (1). Four, and possibly 5, cases of allergic contact dermatitis from this chemical have been reported, all from Japan (1-3).

CONTACT ALLERGY (cosmetics)

Case reports

A 53-year-old woman had a 3-year history of a generalized eruption, that had started as a pruritic eruption on the neck which gradually spread to the scalp, arms and trunk. She had been using a miconazole nitrate-containing shampoo after having tried several shampoos that did not resolve the eruption. Physical examination showed diffuse scaly erythema on the scalp and disseminated scaly erythematous papules and plaques on the neck, ears, arms and trunk. Patch tests with the patient's cosmetics, including her shampoo, conditioner, body soap and moisturizer, with the rinse-off products diluted to 1% in water, revealed a strong positive reaction to the miconazole nitrate-containing shampoo (D2 ++, D3 ++, D7 ++). Testing with the ingredients and a more diluted shampoo sample (0.1% water) showed strong positive reactions to the shampoo (D2 ++, D3 ++, D7 +) with a few micro-pustules and to sodium lauroyl methyl-aminopropionate (SLMA) 0.4% water (D2 ++, D3 ++, D7 +). Three controls were negative and the dermatitis resolved after discontinuation of the SLMA-containing shampoos (1).

The authors referred to 3 previously reported similar cases, of which 2 were published in Japanese journals and one in the JEADV (2). In another case report from Japan (3) a patient with allergic contact dermatitis from a hair colour shampoo (for details see Chapter 2.14 C12-14 Hydoxyalkyl hydroxyethyl sarcosine) had positive reactions to the ingredients C12–14 hydroxyalkyl hydroxyethyl sarcosine, basic blue 99, lauramide DEA and '*N*-methyl-*N*-(1-oxododecyl)-*β*-alaninate'. It is likely that the authors forgot the 'sodium', which would make this the 5th case of contact allergy to sodium lauroyl methylamino-propionate.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 8/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 12/123,000.

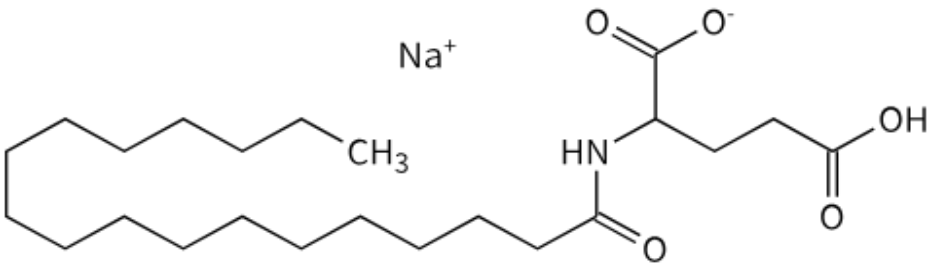
LITERATURE

1 Hirose A, Kawakami Y, Miyake T, Hirai Y, Morizane S. A case of generalized allergic contact dermatitis due to sodium lauroyl methylaminopropionate in a shampoo. Contact Dermatitis. 2022;87(6):546-548. doi: 10.1111/cod.14210.
2 Kato K, Igawa K, Nishizawa A, Takayama K, Yokozeki H. Allergic contact dermatitis induced by the anionic surfactant, sodium N-methyl-N-(1-oxododecyl)-beta-alaninate, contained in a daily-use shampoo. J Eur Acad Dermatol. 2016;30(11):e123-e124. doi: 10.1111/jdv.13393.
3 Kosumi H, Yanagi T, Izumi K, Ito T, Shimizu H. Hair colour shampoo dermatitis. Contact Dermatitis. 2017;77(6):419-421. doi: 10.1111/cod.12851.

2.34 SODIUM STEAROYL GLUTAMATE

IDENTIFICATION

Description/definition : Sodium stearoyl glutamate is the amino acid derivative that conforms to the structural formula shown below
Classification : Amino acid alkyl amides
IUPAC name : Sodium;(4*S*)-4-amino-5-octadecanoyloxy-5-oxopentanoate
Other names : L-Glutamic acid, *N*-(1-oxooctadecyl)-, monosodium salt
CAS registry number : 38517-23-6
EC number : 253-980-9
CIR reviews : Int J Toxicol 2017;36(Suppl.1):17-56
Functions in cosmetics : EU: cleansing; surfactant – emulsifying; hair conditioning; skin conditioning. USA: hair conditioning agents; skin-conditioning agents – miscellaneous; surfactants - cleansing agents
Patch testing : 1% water (1)
Molecular formula : $C_{23}H_{43}NO_5 \bullet Na$



GENERAL

Sodium stearoyl glutamate is an amino acid alkyl amide derived from glutamic acid, which is used in cosmetics for its conditioning, cleansing and emulsifying properties (1).

CONTACT ALLERGY (cosmetics)

Case report

A 40-year-old atopic female nurse had suffered two episodes of acute allergic contact dermatitis from two different cosmetic products. The first episode occurred 1 day following the application of a body lotion, and the dermatitis was localized on the face, trunk, legs and arms, at the application sites of the body lotion. Three months later, 1 day following the application of an after-sun, a similarly severe ACD occurred over the décolleté and arms. Patch tests with the European baseline series, a cosmetic series, and both creams tested 'as is' (also semi-open) showed ++ reactions on D3 and D4 to the two cosmetic products (both semi-open and patch tests). The ingredients common to both products were glycerin, sodium stearoyl glutamate, linalool and geraniol. Three months later, the ingredients of the after-sun, obtained from the manufacturer, were tested which revealed positive reactions to sodium stearoyl glutamate 1% water (D3/4 ++), and to capryloyl glycine 1% water (D3/4 +). The authors suggested possible cross-reactivity between sodium stearoyl glutamate and capryloyl glycine (1).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 206/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 1009/123,000.

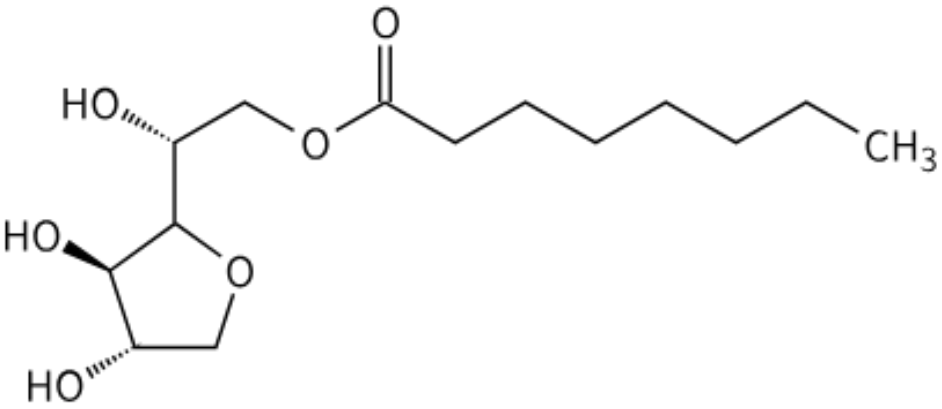
LITERATURE

1 Pralong P, Dendooven E, Aerts O. Sodium stearoyl glutamate: Another amino acid alkyl amide sensitizer in cosmetics. Contact Dermatitis 2022;87(5):453-454. doi: 10.1111/cod.14184.

2.35 SORBITAN CAPRYLATE

IDENTIFICATION

Description/definition : Sorbitan caprylate is the monoester of caprylic acid and hexitol anhydrides derived from sorbitol; it conforms to the structural formula shown below
Classification : Sorbitan fatty acid esters
IUPAC name : [(2*R*)-2-[(2*R*,3*R*,*4S*)-3,4-Dihydroxyoxolan-2-yl]-2-hydroxyethyl] octanoate
Other names : Sorbitan monocaprylate; sorbitan, monooctanoate
CAS registry number : 60177-36-8
EC number : 262-098-3
CIR reviews : Int J Toxicol 2019;38(Suppl.2):60-80; Int J Toxicol 2002;21(Suppl.1):93-112
Functions in cosmetics : EU: surfactant - emulsifying. USA: surfactants - emulsifying agents
Patch testing : 1% pet. (1)
Molecular formula : $C_{14}H_{26}O_6$



GENERAL

Sorbitan caprylate is a sorbitan derivative which is used in cosmetics as emulsifier.

CONTACT ALLERGY (cosmetics)

Case reports

Between December 2015 and February 2017, 4 female patients were investigated in a Belgian university hospital who had a history of eczema in the axillae after applying a deodorant. Patch tests with the European baseline series with Belgian extension, a cosmetic and pharmaceutical series, and the patients' own products (tested 'as is') showed positive reactions to the deodorant in the 3 patients in who the product had been tested; one of them also reacted to a shampoo of the same brand. Ingredient patch testing showed positive reactions to sorbitan caprylate 1% pet., which was present in both the deodorant and the shampoo. Two of 4 patients reacted to sorbitan monooleate, which were considered to be cross-reactions. One patient had a positive patch test to chitosan, which was also present in the deodorant (1).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 60/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 155/123,000.

LITERATURE

1 Vandeweghe J, Decoster E, Lapeere H. First report of allergic contact dermatitis caused by sorbitan caprylate. Contact Dermatitis. 2018;78(2):162-164. doi: 10.1111/cod.12876.

2.36 STANNOUS CHLORIDE

IDENTIFICATION

Description/definition : Stannous chloride is the inorganic salt that conforms to the formula $SnCl_2$
Classification : Inorganic salts
IUPAC name : Dichlorotin
Other names : Tin(II) chloride; tin dichloride
CAS registry number : 7772-99-8
EC number : 231-868-0
Wikipedia page : https://en.wikipedia.org/wiki/Tin(II)_chloride (Tin(II) chloride)
Function(s) in cosmetics : EU: reducing. USA: not mentioned
Patch testing : Tin 50% pet.; stannous chloride 1.0% pet.; tin(II)oxalate 1.0% pet. (Chemotechnique); tin(II) chloride 0.5% pet. (SmartPractice); stannous chloride may cause weak-positive and irritant reactions; tin 50% pet. is likely less sensitive; tin oxalate 1% pet. is possibly a good alternative (3)
Molecular formula : $SnCl_2$

GENERAL

Stannous chloride is mainly added to toothpastes for its antibacterial activity, resulting in reduction in the numbers of bacteria that cause dental plaque and gingivitis. The antibacterial action of tin salts also helps to improve breath odour by reducing the bacteria that cause bad breath (ChatGPT).

CONTACT ALLERGY (cosmetics)

General

In the patients presented here, the sensitizer is not stannous chloride *per se*, but tin, of which stannous chloride is a salt. See also Chapter 3.67.Stannous fluoride.

Case reports

A 23-year-old atopic woman suffered from recurrent episodes of oral stomatitis since >6 months. Each episode would start with itchy lips, without visible lesions, followed by the appearance of small itchy vesicles at the mucosal side of the lips and buccal mucosa, which subsequently broke down into small painful ulcers, and sometimes localized haemorrhages, together with a sensation of swelling of the tongue and oral mucosa. The patient had received multiple treatments for herpes simplex, aphthous ulcers, angioedema, Behçet disease and burning mouth syndrome without success. Because of the rather atypical complaint of associated pruritus, which also characterized the start of each new flare-up, the patient was patch tested with an extended baseline and cosmetic series; personal products were not brought in at the initial test session. At that time, the investigators had started to patch test various stannous (tin) salts as a supplement to their baseline series (tin 50% pet., tin chloride 1% pet. and tin oxalate 1% pet.). On D4 only positive reactions were observed to all three tin salts. Stannous chloride was found to be present in one brand of toothpaste the patient used. This product also contained stannous fluoride as did another toothpaste, hence stannous fluoride was also considered relevant for the recurrent oral stomatitis and aphthosis. Following the use of a sodium fluoride-containing toothpaste, the problem was completely resolved, with no recurrence after a follow-up time of 1 year (1).

Chinese investigators in 2022 reported three patients who had developed allergic contact stomatitis due to stannous chloride-containing desensitizing toothpastes. They all reacted to patch tests with their toothpastes and stannous chloride 1% pet. (2).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): Unknown/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 73/123,000.

LITERATURE

1 George H, Dendooven E, Leysen J, Aerts O. Recurrent allergic contact stomatitis and aphtosis, without cheilitis, due to stannous (tin)-containing toothpastes. Contact Dermatitis. 2023;89(6):509-511. doi: 10.1111/cod.14418.

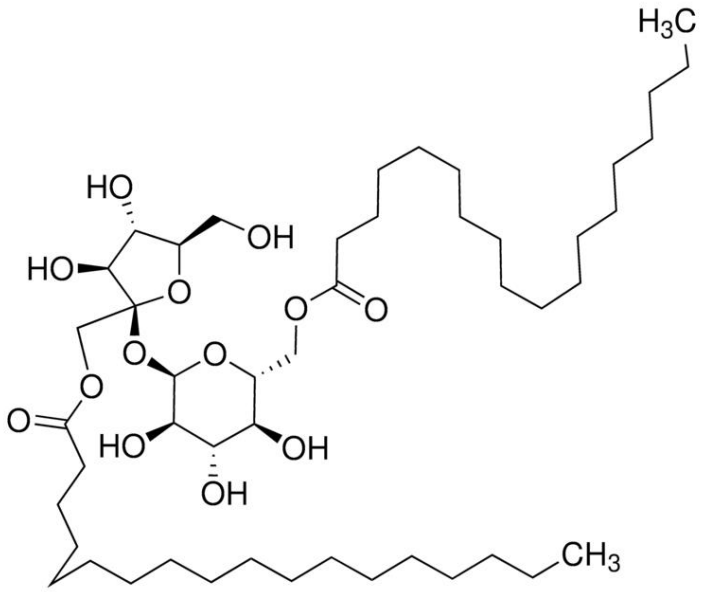
2 He W, Hu X, Hua H, Li K, Zhang C, Wei P. Allergic contact stomatitis due to desensitizing toothpastes. J Dermatol. 2022;49(6):648-651. doi: 10.1111/1346-8138.16338.

3 van Amerongen CCA, de Groot A, Volkering RJ, Schuttelaar MLA. Cheilitis caused by contact allergy to toothpaste containing stannous (tin) - two cases. Contact Dermatitis. 2020;83(2):126-129. doi: 10.1111/cod.13532.

2.37 SUCROSE DISTEARATE

IDENTIFICATION

Description/definition : Sucrose distearate is a mixture of sucrose esters of stearic acid consisting primarily of the diester (structural formula shown below)
Classification : Carbohydrates; disaccharides
IUPAC name : [(2*R*,3*S*,4*S*,5*R*,6*R*)-6-[(2*S*,3*S*,4*S*,5*R*)-3,4-Dihydroxy-5-(hydroxymethyl)-2-(octadecanoyloxymethyl)oxolan-2-yl]oxy-3,4,5-trihydroxyoxan-2-yl]methyl octadecanoate
Other names : Sucrose-1,5-distearate; α-D-glucopyranoside, β-D-fructofuranosyl, dioctadecanoate
CAS registry number : 27195-16-0
EC number : 248-317-5
CIR reviews : Int J Toxicol 2021;40(Suppl.2):52-116
Functions in cosmetics : EU: skin conditioning – emollient; surfactant – emulsifying; skin conditioning; surfactant - cleansing. USA: skin-conditioning agents – emollient; surfactants – emulsifying agents
Patch testing : 10% pet. (1)
Molecular formula : $C_{48}H_{90}O_{13}$



GENERAL

Sucrose distearate is mainly used in cosmetics for its emollient and emulsifying properties.

CONTACT ALLERGY (cosmetics)

Case report

An 11-month-old boy had been prescribed an unscented emollient cream to treat dry skin accompanying his atopic dermatitis. Two weeks later, he developed a generalized papular itchy rash. In the years thereafter the parents experienced difficulties to find suitable hydrating creams and sunscreens the child could tolerate. Patch tests with an in-house baseline series for children, with a selection of allergens from the European baseline series, and with the previously used emollient cream (tested 'as is') showed positive reactions to the emollient cream (++), the fragrance mix I (+) and Myroxylon pereirae resin (+). As the culprit emollient cream was unscented, additional patch tests were performed with its ingredients, provided by the manufacturer. Strong positive reactions were again observed to the emollient cream (other batch) as well as to 2 ingredients: candelilla cera 41% pet. (++) and sucrose distearate 10% pet.

(++). A weak reaction (+) was observed to sucrose stearate 10% pet. (which was apparently not present in the cream and may have been a cross-reaction to glucose distearate). Cosmetics without fragrances, candelilla cera, and sucrose stearate and distearate were advised and were well tolerated by the child (1).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 25/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 75/123,000.

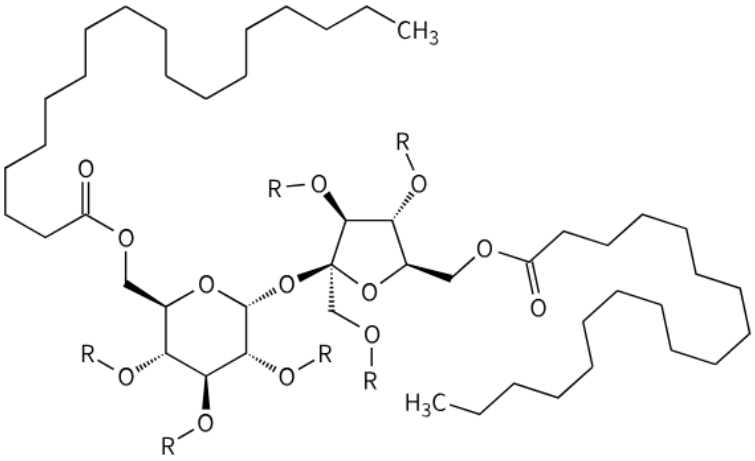
LITERATURE

1 Darrigade AS, Dendooven E, Mangodt E, Vermander E, Hagendorens M, Aerts O. A peculiar case of sensitization to Candelilla Cera and sucrose (di)stearate in a toddler. Contact Dermatitis. 2020;82(1):54-55. doi: 10.1111/cod.13381.

2.38 SUCROSE POLYSTEARATE

IDENTIFICATION

Description/definition : Sucrose polystearate is a mixture of esters of stearic acid and sucrose
Classification : Carbohydrates; esters
IUPAC name : α-d-Glucopyranoside, β-d-fructofuranosyl, esters with octadecanoic acid
CAS registry number : Not available
EC number : Not available
CIR reviews : Int J Toxicol 2021;40(Suppl.2):52-116
Functions in cosmetics : EU: skin conditioning – emollient; surfactant – emulsifying; skin conditioning; surfactant – cleansing. USA: skin-conditioning agents – emollient; surfactants – emulsifying agents
Patch testing : 1.5% pet. (1); this concentration is probably too low; testing in water may be preferable
Molecular formula : Undefined



R: stearoyl or H.

GENERAL

Sucrose polystearate is used in cosmetics as a surfactant, emulsifier, emollient, and skin-conditioning agent.

CONTACT ALLERGY (cosmetics)

Case report

A 13-year-old boy, with a history of atopic dermatitis during infancy, was referred for the evaluation of facial itchy, erythematous, and papular skin lesions. At the same time, the boy had started using a facial moisturizing cream two times a day because of dry skin. Following discontinuation of the cream, the dermatitis had spontaneously resolved within 2 weeks. Patch tests with the European baseline series, a cosmetic series, and the suspected facial cream 'as is' showed a doubtful reaction (?+) to the moisturizing cream on D3 only. However, a repeated open application test (ROAT) resulted in a clearly positive follicular skin reaction after 2 days. Testing with the ingredients, obtained from the manufacturer, gave a positive reaction to sucrose stearate 3.5% water (D2/3 ++). Five controls were negative. Another ingredient, related to glucose stearate, sucrose polystearate (tested 1.5% pet.), was negative, but an additional ROAT was positive after 2 days (1). It was suggested that the patch test concentration of sucrose polystearate (1.5% pet.) was probably too low, but it was also hypothesized that some residual sucrose monostearate is still present in the polymer, albeit at a low concentration (1).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 46/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 75/123,000.

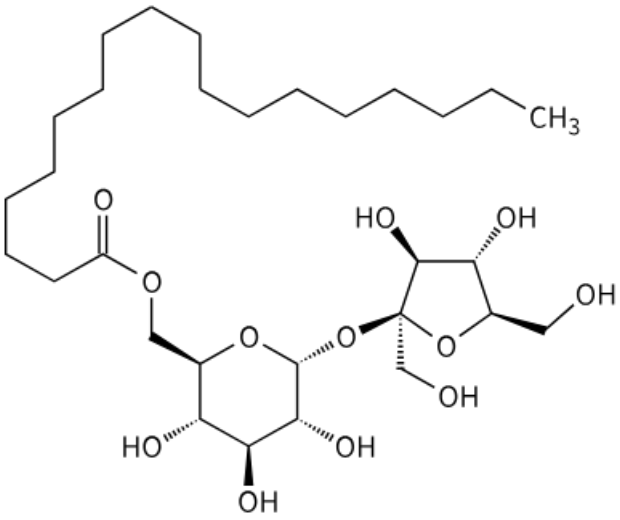
LITERATURE

1 Raison-Peyron N, Aerts O, Dereure O. Allergic contact dermatitis to sucrose stearate in a facial moisturizing cream. Contact Dermatitis. 2020;82(4):245-246. doi: 10.1111/cod.13449.

2.39 SUCROSE STEARATE

IDENTIFICATION

Description/definition : Sucrose stearate is the monoester of stearic acid and sucrose (q.v.), that generally conforms to the structural formula shown below
Classification : Carbohydrates; monosaccharides
IUPAC name : [(2*S*,3*S*,4*S*,5*R*)-3,4-Dihydroxy-5-(hydroxymethyl)-2-[(*2R,*3*R*,4*S*,5*S*,6*R*)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxyoxolan-2-yl]methyl octadecanoate
Other names : Sucrose monostearate; α-D-glucopyranoside, β-D-fructofuranosyl, monooctadecanoate
CAS registry number : 37318-31-3
EC number : 246-705-9
CIR reviews : Int J Toxicol 2021;40(Suppl.2):52-116
Functions in cosmetics : EU: skin conditioning – emollient; surfactant – emulsifying; skin conditioning; surfactant - cleansing. USA: skin-conditioning agents – emollient; surfactants – emulsifying agents
Patch testing : 3.5% water (1)
Molecular formula : $C_{30}H_{56}O_{12}$



GENERAL

Sucrose (mono)stearate is widely used in cosmetics as a surfactant, emulsifier, emollient, and skin-conditioning agent.

CONTACT ALLERGY (cosmetics)

Case report

A 13-year-old boy, with a history of atopic dermatitis during infancy, was referred for the evaluation of facial itchy, erythematous, and papular skin lesions. At the same time, the boy had started using a facial moisturizing cream two times a day because of dry skin. Following discontinuation of the cream, the dermatitis had spontaneously resolved within 2 weeks. Patch tests with the European baseline series, a cosmetic series, and the suspected facial cream 'as is' showed a doubtful reaction (?+) to the moisturizing cream on D3 only. However, a repeated open application test (ROAT) resulted in a clearly positive follicular skin reaction after 2 days. Testing with the ingredients, obtained from the manufacturer, gave a positive reaction to sucrose stearate 3.5% water (D2/3 ++). Five controls were negative. Another ingredient, related to glucose stearate, sucrose polystearate (tested 1.5% pet.), was negative, but an additional ROAT was positive after 2 days (1). It was suggested that the patch test concentration of

sucrose polystearate (1.5% pet.) was probably too low, but it was also hypothesized that some residual sucrose monostearate is still present in the polymer, albeit at a low concentration (1).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 108/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 291/123,000.

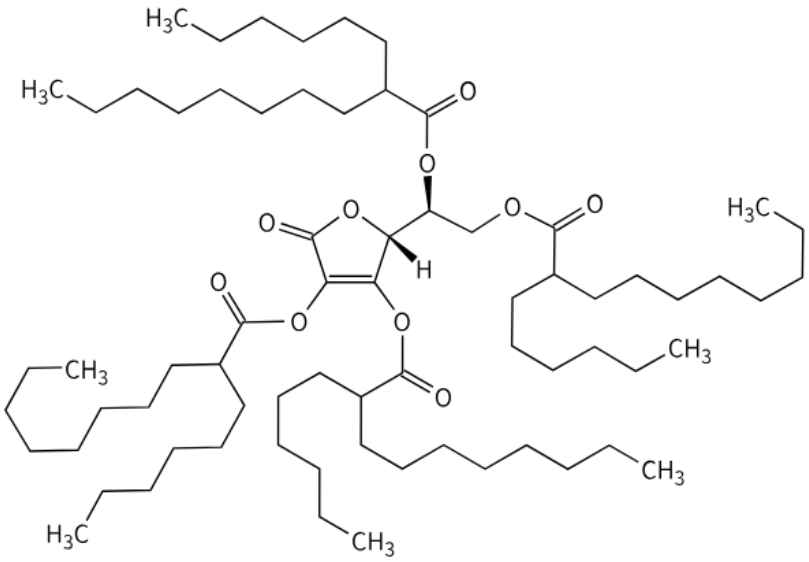
LITERATURE

1 Raison-Peyron N, Aerts O, Dereure O. Allergic contact dermatitis to sucrose stearate in a facial moisturizing cream. Contact Dermatitis. 2020;82(4):245-246. doi: 10.1111/cod.13449.

2.40 TETRAHEXYLDECYL ASCORBATE

IDENTIFICATION

Description/definition : Tetrahexyldecyl ascorbate is the ester resulting from the reaction of ascorbic acid (vitamin C) and the fatty acid tetrahexyldecanol; its structural formula is shown below
Classification : Esters; heterocyclic compounds
IUPAC name : [(2*S*)-2-[(2*R*)-3,4-bis(2-Hexyldecanoyloxy)-5-oxo-2*H*-furan-2-yl]-2-(2-hexyldecanoyloxy)ethyl] 2-hexyldecanoate
Other names : L-Ascorbic acid, tetrakis(2-hexyldecanoate); ascorbyl tetra-2-hexyldecanoate; ascorbyl tetraisopalmitate
CAS registry number : 183476-82-6
EC number : 430-110-8
CIR reviews : Int J Toxicol 2022;41(Suppl.2):57-75
Functions in cosmetics : EU: antioxidant; skin conditioning. USA: antioxidants; skin-conditioning agents - miscellaneous
Patch testing : No data provided (1)
Molecular formula : $C_{70}H_{128}O_{10}$



GENERAL

Tetrahexyldecyl ascorbate (THDA) is an ascorbic acid (vitamin C) derivative used in cosmetics as antioxidant and skin-conditioning agent. THDA is often used in skin care products because it is a more stable form of vitamin C than ascorbic acid itself. It is fat soluble and penetrates the skin better, making it more effective in caring for the skin.

CONTACT ALLERGY (cosmetics)

Case report

A 62-year-old woman experienced episodes of periocular inflammation, occurring 2-3 days after using two new eye creams. Patch testing with the American Contact Dermatitis Society core, cosmetic, and nail polish series plus additional potential allergens found in her current topical products and a sample of one of the eye creams resulted in a 3+ reaction to the cream at D4 only. In a second session, the ingredients of the cream, obtained from the manufacturer, and a face cream similar to the eye cream were tested, which showed a 3+ reaction to tetrahexyldecyl ascorbate (THDA) and a 2+ reaction to the face cream.

THDA was found in both eye creams and the face cream. 24 controls were negative. Discontinuation of both eye creams led to rapid healing and no further problems.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 255/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 1925/123,000.

LITERATURE

1 Scheman A, Fournier E, Kerchinsky L. Allergic contact dermatitis to two eye creams containing tetrahexyldecyl ascorbate. Contact Dermatitis. 2022;86(6):556-557. doi: 10.1111/cod.14082.

CHAPTER 3 UPDATES OF MONOGRAPHS PREVIOUSLY PRESENTED IN 'MONOGRAPHS IN CONTACT ALLERGY, VOLUME 1'

3.1 INTRODUCTION

By screening all issues of the journals *Contact Dermatitis*, *Dermatitis*, and *Cosmetics* between September/October 2017 and March 2025 and with a PubMed search as described in Chapter 1.2, the author found 74 single ingredients or substances that had caused allergic contact dermatitis from their presence in cosmetic products (i.e., causing allergic cosmetic dermatitis) and that had previously been reported as allergens/haptens in cosmetics. These allergens have been presented in monographs in the 2018 Monographs in Contact Allergy, Volume 1, covering the literature up to September 2017. The monographs presented here are an update to the corresponding chapters in that book.

Most monographs are limited to cosmetic allergy. However, whenever articles on the allergens were found during the screening of the journals mentioned above that were not (directly) related to cosmetics, their information was also included in the monographs in the section 'Other Publications', albeit only with brief descriptions. Examples of such data include (occupational) allergic contact dermatitis or contact urticaria from the allergen in non-cosmetic products, cross-reactivity, results of patch testing with different concentrations or materials, review articles, routine testing with the allergen (only when the article was entirely about the allergen, *not* results of testing multiple allergens in routine series such as the NACDG screening series or the European baseline series), market surveys of allergens in products, risk assessment studies and chemical analyses for identification of allergens in products. Non-cosmetic information for these allergens was *not* looked for in a PubMed search, so such data from journals other than *Contact Dermatitis* and *Dermatitis* is not covered.

The 74 allergens in cosmetics for which updates are provided here are shown in table 3.1.

Table 3.1 Chemicals and substances causing allergic cosmetic dermatitis for which updates are presented in this chapter

Alumina	bis-Ethylhexyloxyphenol methoxyphenyl triazine
m-Aminophenol	Ethylhexyl salicylate [b]
Ammonium persulfate [a]	Formaldehyde
Arachidyl glucoside	Glutaraldehyde
Basic blue 99 [a]	Glycyrrhetinic acid
Benzisothiazolinone	Glycyrrhiza inflata root extract
Benzoic acid	Hexylresorcinol
Bisabolol	Homosalate
Butylene glycol	Hydroxyethyl acrylate
Butyrospermum parkii (shea) butter	Iodopropynyl butylcarbamate
Candelilla cera	Lauramide DEA
Caprylic/capric triglyceride	Magnolia officinalis bark extract
Cera alba	Menthoxypropanediol
Cetearyl isononanoate	Methylchloroisothiazolinone (and) methylisothiazolinone [b]
CI 75470 (Carmine) [a]	
Cocamide DEA	Methyldibromo glutaronitrile
Coco-betaine	Methylisothiazolinone [b]
Colophonium	Methyl methacrylate
Decyl glucoside [b]	Nickel
Diethylamino hydroxybenzoyl hexyl benzoate	Panthenol [a]
bis-Diglyceryl polyacyladipate-2	PEG-22/dodecyl glycol copolymer
Drometrizole trisiloxane	Pentylene glycol
3-*o*-Ethyl ascorbic acid	Phenethyl resorcinol
Ethyl cyanoacrylate	Phenoxyethanol [a]
Ethylene glycol dimethacrylate	Phenylbenzimidazole sulfonic acid
Ethylhexylglycerin	*p*-Phenylenediamine [a]

Table 3.1 (*Continued*)

Phytonadione epoxide	Sodium cocoamphopropionate
Polyaminopropyl biguanide (polyhexamethylene biguanide)	Sodium metabisulfite
Polysilicone-15	Sorbitan sesquioleate
Propolis	Stannous fluoride
Propylene glycol	Thioctic acid [a]
Resveratrol	Tocopherol [a]
Retinyl palmitate	Tocopheryl nicotinate
Ricinus communis (castor) seed oil	Toluene-2,5-diamine [a]
Scutellaria baicalensis extract	Triclosan
Shellac	Triethanolamine
Sodium bisulfite	VP/eicosene copolymer
	Zinc ricinoleate

[a] Caused both allergic contact dermatitis and immediate-type reaction(s)
[b] (Also) caused photosensitivity (photoallergic contact dermatitis or photoaggravation of allergic contact dermatitis)

3.2 ALUMINA

IDENTIFICATION

Description/definition	: Alumina is an inorganic compound that conforms to the formula Al_2O_3
Classification	: Inorganics
IUPAC name	: Aluminium oxide
Other names	: Aluminii oxidum
CAS registry number	: 1344-28-1; 1333-84-2 (hydrate)
EC number	: 215-691-6
CIR reports	: Int J Toxicol 2016;35(Suppl.3):16-33
SCCS opinions	: SCCS 1525/14 (aluminium)
Wikipedia	: https://en.wikipedia.org/wiki/Aluminium_oxide (aluminium oxide)
Functions in cosmetics	: EU: abrasive; absorbent; anticaking; bulking; opacifying; viscosity controlling. USA: abrasives; absorbents; anticaking agents; bulking agents; opacifying agents
Patch testing	: Aluminum chloride hexahydrate 2% pet. (Chemotechnique); aluminum chloride hexahydrate 10% pet. (SmartPractice); aluminum hydroxide 10% pet. (Chemotechnique, SmartPractice)
Molecular formula	: Al_2O_3

Previous chapter to which this is an update

The literature on contact allergy to alumina from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.9, pp. 28-29.

CONTACT ALLERGY (cosmetics)

Case report

A 2-year-old boy with a history of atopic dermatitis developed an itchy eruption on the face, neck and forearms one day after the application of a sunscreen applied at the nursery. Patch tests with the European baseline series and the ingredients of the sunscreen showed a positive reaction to aluminium chloride hexahydrate 2% pet. (++) on D4. This was not present in the sunscreen, but it did contain alumina and aluminum hydroxide. The mother stated that her son had previously developed itchy lesions at the injection sites of aluminium-containing vaccines, which had very likely been the source of sensitization (2).

Previous cases of allergic cosmetic dermatitis

For previous case reports of allergic cosmetic dermatitis to alumina see ref. 1.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 669/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 5030/123,000.

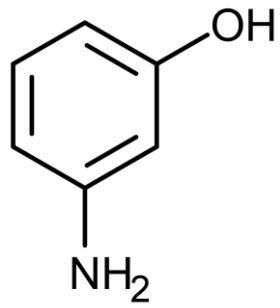
LITERATURE

1 Veien NK, Hattel T, Laurberg G. Systemically aggravated contact dermatitis caused by aluminium in toothpaste. Contact Dermatitis. 1993;28(3):199-200. doi: 10.1111/j.1600-0536.1993.tb03399.x.
2 Badaoui A. Allergic contact dermatitis to aluminium in a sunscreen. Contact Dermatitis. 2023;89(4): 305-307. doi:10.1111/cod.14387.

3.3 m-AMINOPHENOL

IDENTIFICATION

Description/definition : *m*-Aminophenol is the substituted phenol that conforms to the structural formula shown below
Classification : Amines; color additives - hair; phenols
IUPAC name : 3-Aminophenol
Other names : CI 76545
CAS registry number : 591-27-5
EC number : 209-711-2
CIR reports : J Am Coll Toxicol 1988;7(3):279-333
SCCS opinions : SCCP/0978/06
Wikipedia : https://en.wikipedia.org/wiki/3-Aminophenol (3-aminophenol)
Functions in cosmetics : EU: hair dyeing. USA: hair colorants
EU cosmetic restrictions : Regulated in Annex III/217 of the Regulation (EC) 2017/237
Patch testing : 1% pet. (Chemotechnique, SmartPractice)
Molecular formula : C_6H_7NO



Previous chapter to which this is an update

The literature on contact allergy to *m*-aminophenol from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.18, pp. 45-48.

CONTACT ALLERGY (cosmetics)

Case report

A 28-year-old woman had developed a severe eczematous reaction on the eyebrows one day after an eyebrow dyeing cream had been applied there by her beautician. The patient reported extreme burning and itching; erythema, swelling and exudation were clinically evident. She had never used hair dyes, but reported having a black henna tattoo applied on her forearm 14 years previously, which resulted in an intense vesicular reaction 15 days after application. Patch tests with the Italian Society of Allergological, Occupational and Environmental Dermatology (SIDAPA) baseline series, the dye at 10% pet. and 2 of its ingredients, *m*-aminophenol and toluene-2,5-diamine (TDA) resulted in positive reactions at D2 and D4 to *p*-phenylenediamine 1% pet. (+++), nickel (++), textile dye mix (++), the dye that had been applied (++), toluene-2,5-diamine (++), and *m*-aminophenol (++). In a second session, patch tests with the azo dye mix series showed positive reactions to disperse orange 3 (+++), disperse orange 1 (++), and disperse yellow 3 (++) (7).

Previous cases of allergic cosmetic dermatitis and immediate-type reactions

For previous cases of allergic cosmetic dermatitis to *m*-aminophenol see refs. 1-5 and for contact urticaria ref. 6.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 642/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 385/123,000.

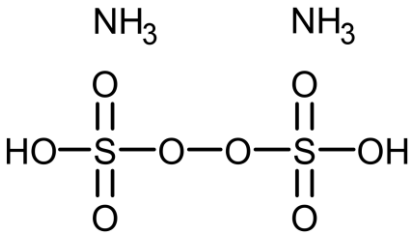
LITERATURE

1 Goossens A. Cosmetic contact allergens. Cosmetics 2016, 3, 5; doi:10.3390/cosmetics3010005
2 Laguna C, de la Cuadra J, Martín-González B, Zaragoza V, Martínez-Casimiro L, Alegre V. Allergic contact dermatitis to cosmetics. Actas Dermosifiliogr 2009;100(1):53-60. PMID: 19268112.
3 Zaragoza-Ninet V, Blasco Encinas R, Vilata-Corell JJ, Pérez-Ferriols A, Sierra-Talamantes C, Esteve-Martínez A, de la Cuadra-Oyanguren J. Allergic contact dermatitis due to cosmetics: A clinical and epidemiological study in a tertiary hospital. Actas Dermosifiliogr 2016;107(4):329-336. doi: 10.1016/j.ad.2015.12.007.
4 Søsted H, Rastogi SC, Andersen KE, Johansen JD, Menné T. Hair dye contact allergy: quantitative exposure assessment of selected products and clinical cases. Contact Dermatitis 2004;50(6):344-348. doi: 10.1111/j.0105-1873.2004.00362.x.
5 Gottlöber P, Gall H, Bezold G, Peter RU. Allergic contact dermatitis in beauty parlor clients. Hautarzt 2001;52(5):401-404. doi: 10.1007/s001050051332 (Article in German).
6 Tsunoda T, Horiuchi N, Sato M. Two cases of contact urticaria syndrome by hair dye. Hifu 1993;35 (suppl.16):178-183 (article in Japanese)
7 Romita P, Foti C, Mascia P, Guida S. Eyebrow allergic contact dermatitis caused by *m*-aminophenol and toluene-2,5-diamine secondary to a temporary black henna tattoo. Contact Dermatitis. 2018;79(1):51-52. doi: 10.1111/cod.12987.

3.4 AMMONIUM PERSULFATE

IDENTIFICATION

Description/definition : Ammonium persulfate is the inorganic salt that conforms to the structural formula shown below
Classification : Inorganic salts
IUPAC name : Diazanium sulfonatooxy sulfate
Other names : Ammonium peroxydisulfate; diammonium peroxodisulfate
CAS registry number : 7727-54-0
EC number : 231-786-5
CIR reports : Int J Toxicol 2001;20(Suppl.3):7-21; Int J Toxicol 2022;41(Suppl.3):5-21
Wikipedia : https://en.wikipedia.org/wiki/Ammonium_persulfate
Functions in cosmetics : EU: bleaching; oxidising. USA: oxidizing agents
Patch test allergens : 2.5% pet. (Chemotechnique, SmartPractice)
Molecular formula : $H_8N_2O_8S_2$



Previous chapter to which this is an update

The literature on contact allergy to ammonium persulfate from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.22, pp. 59-65.

CONTACT ALLERGY (cosmetics)

Case report

A 47-year-old non-atopic female hairdresser had a 2-year history of dermatitis with intense pruritus on her face and arms. Erythema, papules, and lichenification were noted on her face, arms, forearms, and the back of her hands. The patient had been treated previously with emollients and medium-potency topical corticosteroids with partial recovery. Patch testing using the standard and cosmetic series were negative. In a second session, the patient was patch tested with the hairdressing series, which resulted in a positive reaction to ammonium persulfate 2.5% pet. on D2 and D4. The patient was provided with written and verbal information about the allergen. Several preventive measures were advised: limit the number of bleaching and hair dye procedures per workday and have an assistant prepare the mixture, use protective equipment (gloves, facemask, face shield, long-sleeve coat), and work in well-ventilated areas. Frequent use of emollient was recommended. On this regime, the skin lesions gradually improved within a month, with no need of corticosteroid use. Four months after diagnosis, the patient was still working and had no longer any skin lesions (11).

Previous cases of allergic cosmetic dermatitis

For previous case reports of allergic cosmetic dermatitis to ammonium persulfate see refs. 1-9.

IMMEDIATE-TYPE REACTIONS

A 46-year-old woman with unknown allergies to drugs or foods had been dying her hair for more than 20 years every 2-3 months. She had used the same brand of dye in the last 3 years. Her hair was bleached before washing. The last time when the dye was applied, the patient after 5 minutes began to experience

intense itching on her palms, soles, ears, and external genitalia. The dyeing was stopped and her hair was washed immediately, but the itching did not stop. At the emergency centre, the patient manifested cutaneous erythema and acute generalized urticaria. After 2 months, the patient had a positive skin prick test (papule 13.7 mm) with the dye that contained a mix of ammonium and potassium persulfate diluted 20% in water and a positive rub test with 'the persulfate powder'. Skin prick tests with aeroallergens and foods were negative. Patch tests (TRUE Test) were negative at 48- and 96-hour readings, but persulfates themselves were not patch tested. Four controls were negative to the rub test and skin prick test. The patient was diagnosed with acute allergic contact urticaria to persulfates (10).
Comment: This is an unreliable or at least an unclear article. It is uncertain whether the prick and rub tests were done with a mix of ammonium and potassium persulfate, or that the tests were performed with the dye that contained the mix. In the latter case, the diagnosis of 'Acute contact urticaria to persulfate salts ….' could not reliably be made.

Previous cases of immediate-type reactions

There is extensive literature on immediate-type reactions to ammonium persulfate with contact urticaria, asthma and anaphylactic shock, especially in hairdressers. Please refer to the Monographs in Contact Allergy, Volume 1, Chapter 2.22, pp. 59-65, for this topic.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 24/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 18/123,000.

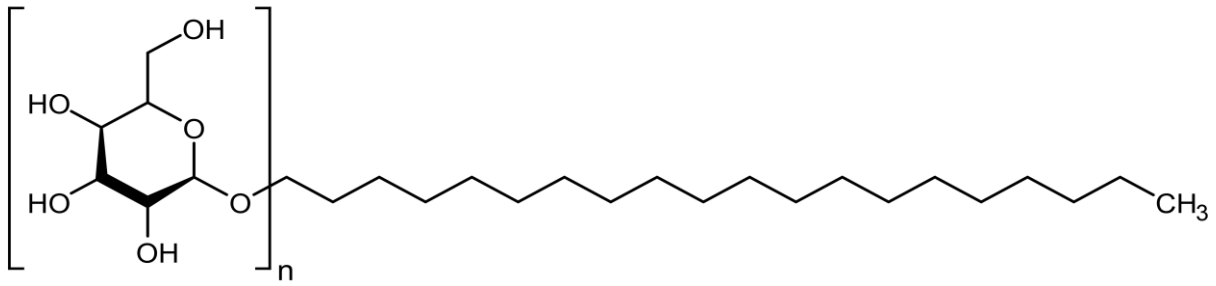
LITERATURE

1 Hougaard MG, Menné T, Søsted H. Occupational eczema and asthma in a hairdresser caused by hair-bleaching products. Dermatitis. 2012;23(6):284-287. doi: 10.1097/DER.0b013e318275968c.
2 Goossens A. Cosmetic contact allergens. Cosmetics 2016, 3, 5; doi:10.3390/cosmetics3010005.
3 Zaragoza-Ninet V, Blasco Encinas R, Vilata-Corell JJ, Pérez-Ferriols A, Sierra-Talamantes C, Esteve-Martínez A, de la Cuadra-Oyanguren J. Allergic contact dermatitis due to cosmetics: A clinical and epidemiological study in a tertiary hospital. Actas Dermosifiliogr. 2016;107(4):329-336. doi: 10.1016/j.ad.2015.12.007.
4 Fisher AA, Dooms-Goossens A. Persulfate hair bleach reactions. Cutaneous and respiratory manifestations. Arch Dermatol. 1976;112(10):1407-1409. PMID: 962335.
5 Widström L. Allergic reactions to ammonium persulphate in hair bleach. Contact Dermatitis. 1977;3(6):343. doi: 10.1111/j.1600-0536.1977.tb03703.x.
6 Yawalkar N, Helbling A, Pichler CE, Zala L, Pichler WJ. T cell involvement in persulfate triggered occupational contact dermatitis and asthma. Ann Allergy Asthma Immunol. 1999;82(4):401-404. doi: 10.1016/S1081-1206(10)63291-7.
7 Borelli S, Wüthrich B. Immediate and delayed hypersensitivity to ammonium persulfate. Allergy. 1999;54(8):893-894. doi: 10.1034/j.1398-9995.1999.00281.x.
8 Bregnhøj A, Søsted H. Type I ammonium persulfate allergy with no cross reactivity to potassium persulfate. Contact Dermatitis. 2009;61(6):356-357. doi: 10.1111/j.1600-0536.2009.01644.x.
9 Poltronieri A, Patrini L, Pigatto P, Riboldi L, Marsili C, Previdi M, Margonari M, Marraccini P. Occupational allergic "march". Rapid evolution of contact dermatitis to ammonium persulfate into airborne contact dermatitis with rhinitis and asthma in a hairdresser (article in Italian). Med Lav. 2010;101:403-408.
10 Gratacós Gómez AR, González Jimenez OM, Joyanes Romo JB, Palacios Cañas A, Garcia Rodriguez R, Gómez Torrijos E. Acute contact urticaria to persulfate salts diagnosed with positive skin prick tests. Contact Dermatitis. 2021;85(2):239-240. doi: 10.1111/cod.13817.
11 Valdés-Morales KL, Alonzo-Romero L. Occupational allergic contact dermatitis from ammonium persulfate in a hairdresser. Contact Dermatitis. 2021;85(3):362-364. doi: 10.1111/cod.13850.

3.5 ARACHIDYL GLUCOSIDE

IDENTIFICATION

Description/definition : Arachidyl glucoside is the product obtained by the condensation of arachidyl alcohol with glucose
Classification : Carbohydrates; ethers; glycosides
Other names : D-glucose, 1-eicosanol ether
CAS registry number : 144982-05-8
CIR reports : Int J Toxicol 2013;32(Suppl.3):22-48
Functions in cosmetics : EU: emulsifying; surfactant. USA: surfactants - emulsifying agents
Patch testing : 5% and 10% pet. (4)
Molecular formula : $C_{26}H_{52}O_6$



Previous chapter to which this is an update

The literature on contact allergy to arachidyl glucoside from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.26, pp. 74-75.

CONTACT ALLERGY (cosmetics)

Case report

A 47-year-old woman had developed acute facial dermatitis following a once-and-only application of a cosmetic cream, initially only on the left cheek, but later extending to the entire face and neck. Clinical examination showed sharply demarcated eczematous lesions at the application sites. The patient's history revealed intolerance to costume jewellery and a previous erythematous rash on her legs following the application of a body lotion. Patch tests with the extended Belgian baseline series and a cosmetic series (including decyl and lauryl glucoside), and all cosmetics used by the patient tested 'as is' were positive to nickel, the cosmetic cream, and to both alkyl glucosides. In a second session, patch testing was carried with coco glucoside, cetearyl glucoside and arachidyl glucoside 5% and 10% pet., provided by the cosmetic's manufacturer, and all were positive. The patient was given a list of cosmetic products not containing alkyl glucosides, after which her dermatitis did not recur (4). Somewhat surprising, it was not mentioned whether the cream actually contained arachidyl glucoside, but the fact that the test material was supplied by the manufacturer of the cosmetic suggests that it did.

Previous cases of allergic cosmetic dermatitis

For previous cases of allergic cosmetic dermatitis to arachidyl glucoside see refs. 1-3.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 130/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 407/123,000.

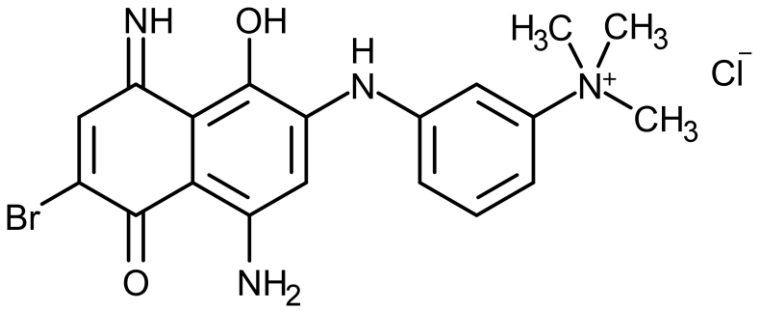
LITERATURE

1 Travassos AR, Claes L, Boey L, Drieghe J, Goossens A. Non-fragrance allergens in specific cosmetic products. Contact Dermatitis 2011;65(5):276-285. doi: 10.1111/j.1600-0536.2011.01968.x.
2 Goossens A. Cosmetic contact allergens. Cosmetics 2016, 3, 5; doi:10.3390/cosmetics3010005
3 Loranger C, Alfalah M, Ferrier Le Bouedec M-C, Sasseville Denis. Alkyl glucosides in contact dermatitis: a systematic review. Dermatitis 2017;28(1):5-13. doi: 10.1097/DER.0000000000000240.
4 Boucneau F, Goossens A, Huygens S, Gilissen L. Arachidyl glucoside: Another cosmetic allergen. Contact Dermatitis 2018;79(5):321-323. doi: 10.1111/cod.13077.

3.6 BASIC BLUE 99

IDENTIFICATION

Description/definition : Basic blue 99 is the naphthoquinoneimine color that conforms to the structural formula shown below
Classification : Color additives - hair
IUPAC name : [3-[(4,8-Diamino-6-bromo-1,5-dioxonaphthalen-2-yl)amino]phenyl]-trimethylazanium chloride
Other names : CI 56059; CI basic blue 99; 3-[(4-amino-6-bromo-5,8-dihydro-1-hydroxy-8-imino-5-oxo-2-naphtyl)amino]-*N*,*N*,*N*-trimethylanilinium chloride
CAS registry number : 68123-13-7
EC number : 268-544-3
CIR reports : Int J Toxicol 2007;26(Suppl.2):51-63
SCCS opinions : SCCS/1537/14; SCCS/1437/11; SCCS/1585/17
Functions in cosmetics : EU: hair dyeing. USA: hair colorants
Patch testing : 1% pet. or water (1); 0.1% saline for prick tests (6)
Molecular formula : $C_{19}H_{20}BrClN_4O_2$



Previous chapter to which this is an update

The literature on contact allergy to basic blue 99 from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.34, pp. 91-93.

CONTACT ALLERGY (cosmetics)

Case reports and case series

From Japan, five cases of allergic contact dermatitis caused by basic blue 99 contained in hair colour treatment products were reported (7). There were four female patients and one male, aged 51–81 years, all of who developed eczema on the head after using hair colour treatment products. In two cases, the condition was also observed on the face, and in one case on the trunk. Patch tests with 1% basic blue 99 showed positive reactions (+) on D2 and D3 in all 5 individuals. Open tests with the hair colour treatment products 'as is' were positive in four cases. Co-reactivities to *p*-phenylenediamine were observed in 3 individuals and to *p*-methylaminophenol sulfate in 2 (no cross-reactions, independent sensitizations from hair dyes). Quite remarkably, all 5 patients were atopic suffering from allergic rhinitis (n=4), asthma (n=1) and atopic dermatitis (n=1) (7).

Another patient from Japan, a 54-year-old man, was investigated for a 4-month history of itchy eruptions on the entire body. Physical examination showed pruritic erythema with thick scales on the scalp, face, and upper trunk. A skin biopsy specimen from a papule on the neck showed lymphocytic infiltration with marked spongiosis. A hair colour shampoo that the patient had used for one year was suspected to be the culprit. Patch testing with this shampoo (1% water) showed positive reactions on D2, D3, and D7 (all +).

Later, the ingredients of the product, provided by the manufacturer, were tested which yielded positive reactions to basic blue 99 0.5% pet. (++/++/++) and 3 other ingredients: C12–14 hydroxyalkyl hydroxyethyl sarcosine 0.3% water (+/+/+), , lauramide DEA 0.5% pet. (++/++/+) and *N*-methyl-*N*-(1-oxododecyl)-β-alaninate 0.3% water (+/+/+). Topical steroids were administered, and the patient was advised to stop using the shampoo. In just 10 days, the lesions had completely resolved, and no recurrence was observed for 6 months (8).

IMMEDIATE-TYPE REACTIONS

In Japan, a 54-year-old woman had a history of atopic dermatitis, cold urticaria, and contact dermatitis caused by *p*-phenylenediamine-containing hair dye. One month before presentation, the patient experienced a pruritic facial rash, throat irritation, sneezing, stomach pain, and vomiting 20 minutes after a non-PPD hair dye, a hair colour conditioning agent, and a hydrogen peroxide solution had been applied to her hair in a hair salon. Skin prick tests with the hair dye (1% saline), the colour conditioning agent and one to which she had previously had an immediate reaction (both 1% saline) and the hydrogen peroxide solution 'as is', were positive to both hair colour conditioning agents within 15 minutes after application. In a second session, skin prick tests with the ingredients were positive after 15 minutes to basic blue 99 (0.1% saline), which was present in both products (6).

Previous cases of allergic cosmetic dermatitis and immediate-type reactions

For previous cases of allergic cosmetic dermatitis to basic blue see ref. 1 and for immediate-type reactions refs. 2-5.

Presence in cosmetic products

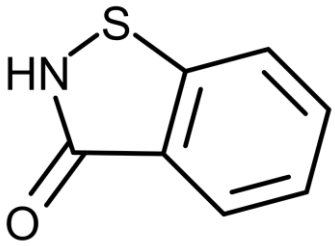
FDA's Voluntary Cosmetic Registration Program (March 2022): 38/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 103/123,000.

LITERATURE

1 De Groot AC, Weyland JW. Cosmetic allergy from the aminoketone colour Basic Blue 99 (CI 56059). Contact Dermatitis 1990;23(1):56-57. doi: 10.1111/j.1600-0536.1990.tb00092.x.
2 Jagtman BA. Urticaria and contact urticaria due to basic blue 99 in a hair dye. Contact Dermatitis 1996;35(1):52. doi: 10.1111/j.1600-0536.1996.tb02273.x.
3 Wigger-Alberti W, Eisner R, Wüthrich B. Immediate-type allergy to the hair dye basic blue 99 in a hairdresser. Allergy 1996;51(1):64-65. doi: 10.1111/j.1398-9995.1996.tb04555.x.
4 Peters KP, Drexler H, Heese A, Koch HU. Typ I-Allergie auf Friseursubstanzen. Fallbeispiel einer Soforttypallergie auf den Farbstoff Basic Blue 99 und auf Azofarben [Abstract]. Allergologie 1992;9:321.
5 Vanden Broecke K, Bruze M, Persson L, Deroo H, Goossens A. Contact urticaria syndrome caused by direct hair dyes in a hairdresser. Contact Dermatitis 2014;71:124-126. doi: 10.1111/cod.12211.
6 Numata T, Fujimori K, Kato K, Ito T, Harada K, Okubo Y. Type I hypersensitivity due to basic blue 99 in a hair colour conditioning agent. Contact Dermatitis 2025 Jan 13. doi: 10.1111/cod.14755. Epub ahead of print.
7 Nishioka K, Koizumi A, Takita Y. Five cases of allergic contact dermatitis caused by Basic Blue 99 contained in hair colour treatment products. Contact Dermatitis 2025;92(1):82-83. doi: 10.1111/cod.14704.
8 Kosumi H, Yanagi T, Izumi K, Ito T, Shimizu H. Hair colour shampoo dermatitis. Contact Dermatitis 2017;77(6):419-421. doi: 10.1111/cod.12851.

3.7 BENZISOTHIAZOLINONE

Description/definition	: Benzisothiazolinone is the heterocyclic compound that conforms to the structural formula shown below
Classification	: Amides; heterocyclic compounds; thio compounds
IUPAC name	: 1,2-Benzisothiazol-3(2*H*)-one; BIT
CAS registry number	: 2634-33-5
EC number	: 220-120-9
SCCS opinions	: SCCS/1482/12; SCCNFP/0811/04
Wikipedia	: https://en.wikipedia.org/wiki/Benzisothiazolinone
Functions in cosmetics	: EU: antimicrobial. USA: preservatives
Patch testing	: 0.1% pet. (Chemotechnique; SmartPractice); sodium salt, 0.1% pet. (SmartPractice)
Molecular formula	: C_7H_5NOS



Previous chapter to which this is an update

The literature on contact allergy to benzisothiazolinone from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.40, pp. 108-109.

CONTACT ALLERGY (cosmetics)

Case reports

A 35-year-old woman presented with a 3-month history of bilateral hand dermatitis coinciding with a household move. The rash began in the interdigital web spaces, spreading to both palms with erythema and desquamation. Patch testing with the North American Contact Dermatitis Group screening series as well as additional series (corticosteroid, emulsifiers, preservatives, rubber, medicament) and personal care products resulted in positive reactions to nickel and benzisothiazolinone (BIT) 0.1% pet. The patient did not react to methylchloroisothiazolinone/methylisothiazolinone (MCI/MI), MI, or octylisothiazolinone, indicating no cross-reactivity to BIT. BIT was found in the patient's hand soap, as well as her all-purpose surface cleaner and 2 laundry products. Further questioning revealed that the patient had purchased the hand soap shortly after moving. She was advised to switch to benzisothiazolinone-free hand soaps and handle cleaning chemicals with gloves (2).

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to benzisothiazolinone see ref. 1.

OTHER PUBLICATIONS [a]

- Allergic contact dermatitis from benzisothiazolinone in a soap for cleaning a continuous positive airway pressure mask (3).
- Allergic hand dermatitis in a 12-year-old non-atopic girl from benzisothiazolinone (and methylchloroisothiazolinone (and) methylisothiazolinone) in homemade 'slime' (4).
- Occupational allergic contact dermatitis of the forearms in a metal worker from undeclared benziso-thiazolinone in an emulsifying oil (5).

- Analyses of benzisothiazolinone in 10 children's toy slime products purchased in Japan (6).

[a] Literature on contact allergy to benzisothiazolinone that was found in *Contact Dermatitis* or/and *Dermatitis* from September 2017 through March 2025, in which there was no direct link with cosmetic products.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 1/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 8/123,000.

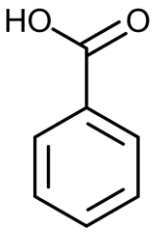
LITERATURE

1 Meysman T, Goossens A. Occupational allergic contact dermatitis caused by benzisothiazolinone in printing ink and soap. Contact Dermatitis 2017;76(1):51-53. doi: 10.1111/cod.12642.
2 Gupta R, Kullberg SA, Warshaw EM. Relevant contact allergy to benzisothiazolinone in a personal care product. Dermatitis. 2020 Mar/Apr;31(2):e13-e14. doi: 10.1097/DER.0000000000000558.
3 Felmingham C, Nixon R, Palmer A, Lee A. Allergic contact dermatitis caused by benzisothiazolinone in a continuous positive airway pressure mask liquid soap. Contact Dermatitis. 2019;81:152–153. doi: 10.1111/cod.13273
4 Alipour Tehrany Y, Quenan S, Bugey A, Piletta P. Contact dermatitis caused by homemade "slime": Report of two cases with chemical analysis. Contact Dermatitis. 2019;80(6):391-393. doi: 10.1111/cod.13230.
5 Corazza M, Forconi R, Bernardi T, et al. Occupational allergic contact dermatitis due to undeclared benzisothiazolinone in an emulsifying oil. Contact Dermatitis. 2020;83:408-409. doi: 10.1111/cod. 13559.
6 Kawakami T, Tahara M, Ikarashi Y. Analysis of isothiazolinone and paraben preservatives in children's toy slime in Japan. Contact Dermatitis. 2023;88(1):80-82. doi: 10.1111/cod.14229.

3.8 BENZOIC ACID

IDENTIFICATION

Description/definition	: Benzoic acid is an aromatic acid that conforms to the formula shown below
Classification	: Carboxylic acids
IUPAC name	: Benzoic acid
Other names	: Benzenecarboxylic acid
CAS registry number	: 65-85-0
EC number	: 200-618-2
CIR reports	: Int J Toxicol 2001;20(Suppl.3):23-50; Int J Toxicol 2017;36(Suppl.3):5-30
SCCS opinions	: SCCP/0891/05; SCCNFP/0532/01
EU cosmetic restrictions	: Regulated in Annex V/1 of the Regulation (EC) No. 2009/1223
Wikipedia	: https://en.wikipedia.org/wiki/Benzoic_acid
Functions in cosmetics	: EU: bulking; masking; preservative. USA: fragrance ingredients; preservatives; pH adjusters
Patch testing	: 5.0% pet. (Chemotechnique, SmartPractice); benzoic acid 5% causes irritant reactions (1)
Molecular formula	: $C_7H_6O_2$



Previous chapter to which this is an update

The literature on contact allergy to benzoic acid from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.41, pp. 110-113.

CONTACT ALLERGY (cosmetics)

Case report

A 4-year-old girl, with known severe pustular psoriasis, developed recurring flares of a pustular pruritic eruption, suspected to be caused by an allergic reaction to sunscreens. The rash resembled a severe flare of pustular psoriasis, with monomorphic pustular elements on an erythematous, slightly oedematous background, affecting the face, neck, and trunk. In addition, the patient had a history of a vaccination granuloma. Patch testing with the paediatric baseline series, a photopatch test series, additional allergens according to the ingredient label on sunscreens, and the sunscreens tested 'as is' resulted in multiple positive pustular reactions to triethanolamine, propolis, benzoic acid and aluminium (III) chloride hexahydrate. Triethanolamine and benzoic acid were present in several of the sunscreens used by the patient. The reaction to aluminium was of past relevance (vaccination granuloma) (9).

Previous cases of allergic cosmetic dermatitis and immediate-type reactions

For previous cases of allergic cosmetic dermatitis to benzoic acid see refs. 2-8. Benzoic acid is a contact urticariogen and is widely used in studies of immediate contact reactions, but there are no cases of such reactions to benzoic acid from its presence *in cosmetics*.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 890/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 3739/123,000.

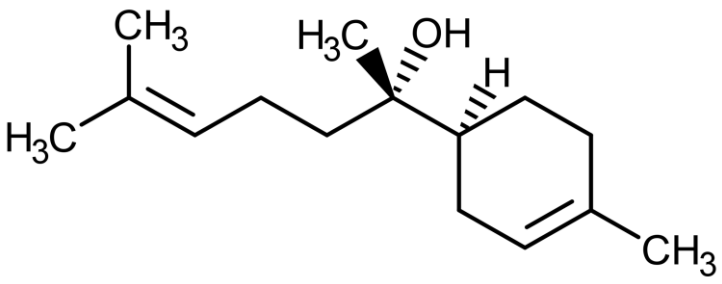
LITERATURE

1 De Groot AC, Weyland JW, Bos JD, Jagtman BA. Contact allergy to preservatives (I). Contact Dermatitis 1986;14(2):120-122. doi: 10.1111/j.1600-0536.1986.tb01179.x.
2 Travassos AR, Claes L, Boey L, Drieghe J, Goossens A. Non-fragrance allergens in specific cosmetic products. Contact Dermatitis 2011;65(5):276-285. doi: 10.1111/j.1600-0536.2011.01968.x.
3 Kohl L, Blondeel A, Song M. Allergic contact dermatitis from cosmetics: retrospective analysis of 819 patch-tested patients. Dermatology 2002;204(4):334-337. doi: 10.1159/000063379.
4 Goossens A. Cosmetic contact allergens. Cosmetics 2016, 3, 5; doi:10.3390/cosmetics3010005
5 Dooms-Goossens A, de Boulle K, Dooms M, Degreef H. Imidazolidinyl urea dermatitis. Contact Dermatitis 1986;14(5):322-324. doi: 10.1111/j.1600-0536.1986.tb05295.x.
6 García-Gavín J, Vansina S, Kerre S, Naert A, Goossens A. Methylisothiazolinone, an emerging allergen in cosmetics? Contact Dermatitis 2010;63(2):96-101. doi: 10.1111/j.1600-0536.2010.01754.x.
7 Wuyts L, van Hoof T, Lambert J, Aerts O. Allergic contact dermatitis caused by aftershave creams containing Glycyrrhiza inflata. Contact Dermatitis 2017(1);77:49-51. doi: 10.1111/cod.12725.
8 Martínez-González MI, González-Pérez R, García-Rio I, Heras-González S. Allergic contact dermatitis caused by benzoic acid and lauryl glucoside in a sunscreen. Contact Dermatitis 2017;77(3):186-187. doi: 10.1111/cod.12810.
9 Tracz ES, Sommerlund M, Bregnhøj A. Pustular allergic contact dermatitis caused by a sunscreen. Contact Dermatitis 2020;83(4):328-329. doi: 10.1111/cod.13621.

3.9 BISABOLOL

IDENTIFICATION

Description/definition : Bisabolol is the terpene that conforms to the structural formula shown below
Classification : Alcohols
IUPAC name : (2*S*)-6-Methyl-2-(4-methylcyclohex-3-en-1-yl)hept-5-en-2-ol
Other names : Levomenol
CAS registry number : 515-69-5
EC number : 208-205-9
Wikipedia : https://en.wikipedia.org/wiki/Bisabolol
CIR reports : Int J Toxicol 1999;18(Suppl.3):33-40
Functions in cosmetics : EU: masking; skin conditioning; soothing. USA: fragrance ingredients; skin-conditioning agents - miscellaneous
Patch testing : 5% pet. (2,8); 1% pet. may result in a false-negative reaction (4)
Molecular formula : $C_{15}H_{26}O$



Previous chapter to which this is an update

The literature on contact allergy to bisabolol from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.54, pp. 156-157.

CONTACT ALLERGY (cosmetics)

Case report

A 39-year-old non-atopic woman presented in the emergency department with pruritic oedematous eczema affecting the entire face, anterior and lateral neck and neckline. The symptoms had appeared within hours of applying a cosmetic cream on her face. The patient was treated with intramuscular methylprednisolone, followed by a course of oral prednisone. Despite discontinuing the use of the cream, lesions remained intense for 5 days and extended beyond the application area and then slowly improved. A single application of the cream on the inner side of the forearm provoked an eczematous reaction. Patch tests with the baseline Spanish Contact Dermatitis Research Group (GEIDAC) series and later with the 15 individual ingredients of the cream, provided by the manufacturer, resulted in positive reactions (++) on D3 to bisabolol 5% and to phytonadione epoxide 1% and 5% in petrolatum. Fifteen controls were negative to 5% bisabolol (8).

Previous cases of allergic cosmetic dermatitis

For previous cases of allergic cosmetic dermatitis to bisabolol see refs. 1-7.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 594/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 2462/123,000.

LITERATURE

1 Sarre, ME, Guérin-Moreau M, Lepoittevin JP, Martin L, Avenel-Audran M. Allergic contact cheilitis caused by polysilicone-15 (Parsol® SLX) in a lipcare balm. Contact Dermatitis 2014;70(2):119-121. doi: 10.1111/cod.12145.

2 Pastor N, Silvestre JF, Mataix J, Lucas A, Pérez M. Contact cheilitis from bisabolol and polyvinylpyrrolidone/hexadecene copolymer in lipstick. Contact Dermatitis 2008;58(3):178-179. doi: 10.1111/j.1600-0536.2007.01225.x.

3 Wilkinson SM, Hausen BM, Beck MH. Allergic contact dermatitis from plant extracts in a cosmetic. Contact Dermatitis 1995;33(1):58-59. doi: 10.1111/j.1600-0536.1995.tb00457.x.

4 Jacob SE, Matiz C, Herro EM. Compositae-associated allergic contact dermatitis from bisabolol. Dermatitis 2011;22(2):102-105. PMID: 21504695.

5 Goossens A, Beck MH, Haneke E, McFadden JP, Nolting S, Durupt G, Ries G. Adverse cutaneous reactions to cosmetic allergens. Contact Dermatitis 1999;40(2):112-113. doi: 10.1111/j.1600-0536.1999.tb06004.x.

6 Goossens A. Cosmetic contact allergens. Cosmetics 2016, 3, 5; doi:10.3390/cosmetics3010005.

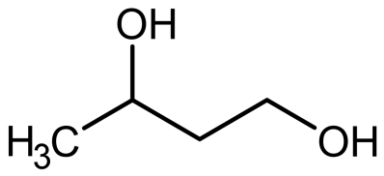
7 Jacob SE, Hsu JW. Reactions to Aquaphor: is bisabolol the culprit? Pediatr Dermatol 2010;27(1):103-104. doi: 10.1111/j.1525-1470.2009.01064.x.

8 de la Rosa-Fernández E, Gatica-Ortega ME, Feliciano-Divasson L, Loizate-Sarrionandia I, González-Carrillo E, Suárez-Hernández J, et al. Severe allergic contact dermatitis to bisabolol and phytonadione epoxide found in a moisturizing and strengthening facial cream. Contact Dermatitis 2024;91(2):174-176. doi: 10.1111/cod.14575.

3.10 BUTYLENE GLYCOL

IDENTIFICATION

Description/definition	: Butylene glycol is the aliphatic diol that conforms to the structural formula shown below
Classification	: Alcohols
IUPAC name	: Butane-1,3-diol
CAS registry number	: 107-88-0
EC number	: 203-529-7
CIR reports	: J Am Coll Toxicol 1985;4:223-248
Wikipedia	: https://en.wikipedia.org/wiki/Butanediol (Butanediol)
Functions in cosmetics	: EU: humectant; masking; skin conditioning; solvent; viscosity controlling. USA: fragrance ingredients; skin-conditioning agents – miscellaneous; solvents; viscosity decreasing agents
Patch testing	: 5-10% water; a test concentration of 20% in water causes irritant reactions (1)
Molecular formula	: $C_4H_{10}O_2$



Previous chapter to which this is an update

The literature on contact allergy to butylene glycol from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.62, pp. 181-183.

CONTACT ALLERGY (cosmetics)

Case report

A 62-year-old man had suffered two episodes of severe facial dermatitis. The first episode followed occasional use of a facial cream over a period of 2 years, with a progressively worsening skin reaction. The second followed a one-time application of an anti-age face gel. Use tests had been performed by the patient with both products with a positive outcome. Patch tests with the European baseline series, a series of the 26 fragrance allergens, a locally composed facial series and the ingredients that were common to both cosmetic products resulted in positive reactions to fragrance mix I with sorbitan sesquioleate (+ on D7) and butylene glycol 2% water (+ on D5 and D7). Only the facial cream contained perfume, while both the patient's products contained butylene glycol. The patient was advised to avoid future use of products containing perfume or butylene glycol and has not had any rash since (7).

Previous cases of allergic cosmetic dermatitis

Many cases of allergic cosmetic dermatitis to butylene glycol have previously been reported, e.g. in refs. 2-6. For a full literature review of this topic please refer to the Monographs in Contact Allergy, Volume 1, Chapter 2.62, pp. 181-183.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 6,909/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 16,082/123,000.

LITERATURE

1 Fan W, Kinnunen T, Niinimäki A, Hannuksela M. Skin reactions to glycols used in dermatological and cosmetic vehicles. Am J Cont Dermat 1991;2:181-183.

2 Sugiura M, Hayakawa R, Sugiura K. Contact dermatitis due to lipsticks and a cream containing isopalmityl diglyceryl sebacate. Contact Dermatitis 2006;54(4):213-214. doi: 10.1111/j.0105-1873.2006.0775a.x.

3 Magerl A, Pirker C, Frosch PJ. Allergic contact eczema from shellac and 1,3-butylene glycol in an eyeliner. J Dtsch Dermatol Ges 2003;1(4):300-302. German. PMID: 16285485.

4 Tamagawa-Mineoka R, Katoh N, Kishimoto S. Allergic contact dermatitis due to 1,3-butylene glycol and glycerol. Contact Dermatitis 2007;56(5):297-298. doi: 10.1111/j.1600-0536.2006.01027.x.

5 Diegenant C, Constandt L, Goossens A. Allergic contact dermatitis due to 1,3-butylene glycol. Contact Dermatitis 2000;43(4):234-235. PMID: 11011933.

6 Aizawa A, Ito A, Masui Y, Ito M. Case of allergic contact dermatitis due to 1,3-butylene glycol. J Dermatol 2014;41(9):815-816. doi: 10.1111/1346-8138.12603.

7 Blomberg M, Johansen JD. Allergic contact dermatitis due to butylene glycol in cosmetics. Contact Dermatitis. 2020;83(3):242-243. doi: 10.1111/cod.13581.

3.11 BUTYROSPERMUM PARKII (SHEA) BUTTER

IDENTIFICATION

Description/definition : Butyrospermum parkii butter is the fat obtained from the fruit of the shea tree, *Butyrospermum parkii,* Sapotaceae
Classification : Fats and oils
INCI name USA : Butyrospermum parkii (shea) butter
Other names : Shea butter; karite butter
CAS registry number : 194043-92-0
EC number : 293-515-7 (generic for extracts of *Butyrospernum parkii*)
CIR reports : Int J Toxicol 2017;36(Suppl.3):51-129; Int J Toxicol 2024;43(Suppl.1):82-95
Wikipedia : https://en.wikipedia.org/wiki/Shea_butter (Shea butter)
Functions in cosmetics : EU: skin conditioning; viscosity controlling. USA: skin-conditioning agents – miscellaneous; skin-conditioning agents – occlusive; viscosity increasing agents - nonaqueous
Patch testing : 30% pet. (4)

Previous chapter to which this is an update

The literature on contact allergy to Butyrospermum parkii butter from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.68, pp. 198.

CONTACT ALLERGY (cosmetics)

Case report

A 45-year-old woman developed cheilitis for which she successively applied two lip balms with no improvement. She then tried different topical antifungal and antiviral treatments, also with no benefit. Topical hydrocortisone aceponate finally resulted in improvement and clearance. Patch tests with the European baseline series and with suspected personal topical products, tested 'as is', including her lip balms and a toothpaste (which was also tested semi-open), were positive (++) to cobalt chloride 1% at D4 (no relevance found), to the toothpaste (+ for patch test, ++ for semi-open test), and to both lip balms (+). Ingredient patch testing yielded a positive (++) D4 reaction to Butyrospermum parkii butter, which was present in both products. The ingredients of the toothpaste, allergy to which may have been responsible for the initial episodes of cheilitis, could not be performed because of lack of cooperation by its manufacturer (3).

A 32-year-old atopic female patient suffered severe cheilitis lasting a few months, together with a longer standing mild dermatitis of the face and hand. Initially, she had developed dry cracked lips, diagnosed as atopic cheilitis, for which she had tried 6 different lip balms. Clinical examination showed a severe lip dermatitis complicated by bacterial superinfection. The patient was advised to use unscented toothpaste and petrolatum jelly as lip balm, and the cheilitis and infection were treated with oral antibiotics, topical compresses and a topical corticosteroid. After full healing, patch tests with a baseline, cosmetic, fragrance and bakery series together with four of six suspected lip balms showed + to ++ reactions to the four lip balms, and to several haptens (all +): fragrances (fragrance mix I, limonene and linalool hydroperoxides), fragrance indicators (Myroxylon pereirae resin, colophonium, propolis), octylisothiazolinone, HEMA and sorbitan sesquioleate (SSO). Although contact allergy to SSO potentially explained the positive patch tests to M. pereirae resin, the fragrance mix and HEMA, the patient also reacted to limonene hydroperoxides, which was considered relevant for the cheilitis and the facial and hand dermatitis, as limonene was present in several cosmetics, including her toothpaste. Only one of four tested lip balms was effectively scented, and therefore, ingredient patch testing was performed with preparations obtained from cosmetic manufacturers. Now, positive reactions were observed to Butyrospermum parkii (shea) butter

30% pet., cera alba (beeswax) 30% pet., candelilla cera 41% pet., and Helianthus annuus seed oil 10% pet., which were present in 4/6, 5/6, 1/6, and 1/6 of the previously used lip balms, respectively. Twenty controls were negative to all four test materials. Using cosmetics free from all demonstrated allergens led to complete resolution of the cheilitis, and significant improvement of the hand and face dermatitis (4).

Previous cases of allergic cosmetic dermatitis

For previous cases of allergic cosmetic dermatitis from Butyrospermum parkii butter see refs. 1 and 2.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 4/35,000 (unlikely to be correct).
EWG's Skin Deep Cosmetics Database (February 2025): 14,911/123,000.

LITERATURE

1 Travassos AR, Claes L, Boey L, Drieghe J, Goossens A. Non-fragrance allergens in specific cosmetic products. Contact Dermatitis 2011;65(5):276-285. doi: 10.1111/j.1600-0536.2011.01968.x.
2 Goossens A. Cosmetic contact allergens. Cosmetics 2016, 3, 5; doi:10.3390/cosmetics3010005
3 Castelain F, Aubin F, Pelletier F. Contact allergy to Butyrospermum parkii butter in a patient with cheilitis. Contact Dermatitis. 2024;90(3):323-324. doi: 10.1111/cod.14478.
4 Aerts O, Pyl J, Mangodt E, Dendooven E. Severe contact cheilitis from cera alba and other cosmetic oils, fats and waxes in lip balms. Contact Dermatitis 2023;88(4):322-323. doi: 10.1111/cod.14272.

3.12 CANDELILLA CERA

IDENTIFICATION

Description/definition	: Candelilla cera is the extract of the wax obtained from the candelilla, *Euphorbia cerifera*, Euphorbiaceae
Classification	: Waxes
Other names	: Candelilla wax; Euphorbia antisyphilitica wax; Euphorbia cerifera (candelilla) wax
CAS registry number	: 8006-44-8
EC number	: 232-347-0
CIR reports	: J Am Coll Toxicol 1984;3:1-41
Wikipedia	: https://en.wikipedia.org/wiki/Candelilla_wax (Candelilla wax)
Functions in cosmetics	: EU: emollient; film forming. USA: film formers; skin-conditioning agents – emollient
Patch testing	: 10% paraffin (1); 10% pet. (2); pure (3); 41% pet. (5); 50% pet. (5)

Previous chapter to which this is an update

The literature on contact allergy to candelilla cera from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.71, pp. 202.

CONTACT ALLERGY (cosmetics)

Case reports

A 25-year-old atopic female patient had a 3-year history of intermittent pruritic dermatitis of her lips and eyelids with occasional involvement on the trunk and limbs. Examination showed light pink thin scaly plaques of the lips, perioral area, and eyelids. Patch tests with a screening series, several supplemental series (corticosteroid, cosmetics, preservative, emulsifier, medicaments, antibiotics, hairstylist, fragrances, flavors, rubber, and acrylates), and 37 of her own personal products gave a positive reaction at D7 to 2 lipsticks and candelilla wax 50% petrolatum; a repeat test with the wax was again positive at D2. Both lipsticks contained candelilla wax (6).

An 11-month-old boy had been prescribed an unscented emollient cream to treat dry skin accompanying his atopic dermatitis. Two weeks later, he developed a generalized papular, itchy rash. In the years thereafter the parents experienced difficulties to find suitable, hydrating creams and sunscreens the child could tolerate. Patch tests with an in-house baseline series for children, with a selection of allergens from the European baseline series, and with the previously used emollient cream (tested 'as is') showed positive reactions to the emollient cream (++), the fragrance mix I (+) and Myroxylon pereirae resin (+). As the culprit emollient cream was unscented, additional patch tests were performed with its ingredients, provided by the manufacturer. Strong positive reactions were again observed to the emollient cream (other batch) as well as to 2 ingredients: candelilla cera 41% pet. (++) and sucrose distearate 10% pet. (++). Cosmetics without fragrances, candelilla cera, and sucrose stearate and distearate were advised and were well tolerated by the child (7).

A 32-year-old atopic female patient suffered severe cheilitis lasting a few months, together with a longer standing mild dermatitis of the face and hand. Initially, she had developed dry cracked lips, diagnosed as atopic cheilitis, for which she had tried 6 different lip balms. Clinical examination showed a severe lip dermatitis complicated by bacterial superinfection. The patient was advised to use unscented toothpaste and petrolatum jelly as lip balm, and the cheilitis and infection were treated with oral antibiotics, topical compresses and a topical corticosteroid. After full healing, patch tests with a baseline, cosmetic, fragrance and bakery series together with four of six suspected lip balms showed + to ++ reactions to the four lip balms, and to several haptens (all +): fragrances (fragrance mix I, limonene and linalool hydroperoxides),

fragrance indicators (Myroxylon pereirae resin, colophonium, propolis), octylisothiazolinone, HEMA and sorbitan sesquioleate (SSO). Although contact allergy to SSO potentially explained the positive patch tests to M. pereirae resin, the fragrance mix and HEMA, the patient also reacted to limonene hydroperoxides, which was considered relevant for the cheilitis and the facial and hand dermatitis, as limonene was present in several cosmetics, including her toothpaste. Only one of four tested lip balms was effectively scented, and therefore, ingredient patch testing was performed with preparations obtained from cosmetic manufacturers. Now, positive reactions were observed to candelilla cera 41% pet., Butyrospermum parkii (shea) butter 30% pet., cera alba (beeswax) 30% pet., and Helianthus annuus seed oil 10% pet., which were present in 1/6, 4/6, 5/6, and 1/6 of the previously used lip balms, respectively. Twenty controls were negative to all four test materials. Using cosmetics free from all demonstrated allergens led to complete resolution of the cheilitis, and significant improvement of the hand and face dermatitis (5).

Previous cases of allergic cosmetic dermatitis

For previous cases of allergic cosmetic dermatitis to candelilla cera see refs. 1-4.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): unknown/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 7.032/123,000.

LITERATURE

1 Barrientos N, Abajo P, Moreno de Vega M, Domínguez J. Contact cheilitis caused by candelilla wax contained in lipstick. Contact Dermatitis 2013;69(2):126-127. doi: 10.1111/cod.12080.
2 Tan BB, Noble AL, Roberts ME, Lear JT, English JSC. Allergic contact dermatitis from oleyl alcohol in lipstick cross-reacting with ricinoleic acid in castor oil and lanolin. Contact Dermatitis 1997;37(1):41-42. doi: 10.1111/j.1600-0536.1997.tb00380.x.
3 De Darko E, Osmundsen PE. Allergic contact dermatitis to Lipcare® lipstick. Contact Dermatitis 1984;11(1):46. doi: 10.1111/j.1600-0536.1984.tb00173.x.
4 Strauss RM, Orton DI. Allergic contact cheilitis in the United Kingdom: a retrospective study. Am J Contact Dermat 2003;14(2):75-77. PMID: 14749024.
5 Aerts O, Pyl J, Mangodt E, Dendooven E. Severe contact cheilitis from cera alba and other cosmetic oils, fats and waxes in lip balms. Contact Dermatitis 2023;88(4):322-323. doi: 10.1111/cod.14272.
6 Han J, Warshaw EM. Allergic contact cheilitis due to candelilla wax. Dermatitis 2023;34(6):548-550. doi: 10.1089/derm.2023.0062.
7 Darrigade AS, Dendooven E, Mangodt E, Vermander E, Hagendorens M, Aerts O. A peculiar case of sensitization to Candelilla Cera and sucrose (di)stearate in a toddler. Contact Dermatitis 2020;82(1):54-55. doi: 10.1111/cod.13381.

3.13 CAPRYLIC/CAPRIC TRIGLYCERIDE

IDENTIFICATION

Description/definition : Caprylic/capric triglyceride is the mixed triester of glycerin and caprylic and capric acids
Classification : Fats and oils
IUPAC name : 11-(2,3-Dihydroxypropoxycarbonyl)heptadecanoate
Other names : Decanoic acid, ester with 1,2,3-propanetriol octanoate; glycerides, mixed decanoyl and octanoyl; glyceryl caprylate-caprate
CAS registry number : 65381-09-1; 85409-09-2 (Glycerides, C8-10)
EC number : 265-724-3; 287-075-5 (Glycerides, C8-10)
CIR reports : J Environ Pathol Toxicol 1980;4:105-120; Int J Toxicol 2022;41(Suppl.3):22-68
Functions in cosmetics : EU: masking; perfuming; skin conditioning. USA: fragrance ingredients; skin-conditioning agents - occlusive; solvents
Patch testing : 1% pet. (1,3); 10% pet. (2; 10 controls were negative)

Previous chapter to which this is an update

The literature on contact allergy to caprylic/capric triglyceride from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.73, p. 204.

CONTACT ALLERGY (cosmetics)

Case reports

A 21-year-old atopic woman presented with a 6-month history of eyelid eczema, which had slowly progressed to involve the whole face. Treatment with mild topical corticosteroids had not helped, but on stopping all cosmetic products her dermatitis had settled completely. Patch tests with the British Society for Cutaneous Allergy standard, medicament, and facial series, as well as the patient's own products, gave one positive reaction only on D4 to an 'active revitalising eye cream', tested undiluted. The patient recalled having started daily application of this product a few months before the rash began. Patch testing with the eye cream ingredients, supplied by the manufacturer, revealed a positive reaction to caprylic/capric triglyceride (10% pet.), negative on D2 and positive on D4 (++). Ten controls were negative (2).

A 54-year-old non-atopic woman presented with eczema of the face that had developed over the preceding 3 months. The patient reported severe pruritus after application of a new cosmetic cream for 5 months. Examination revealed an erythematous and oedematous rash on the face. A repeated open application test (ROAT) with the cream showed a positive skin reaction after 5 days. Patch tests with the European comprehensive baseline series, a cosmetic series and ingredients of the cream supplied by the manufacturer showed a positive reaction to caprylic/capric triglyceride 1% pet. with an edge pattern. Ten controls were negative. After the cream was avoided the dermatitis cleared completely (3).

Previous cases of allergic cosmetic dermatitis

For previous cases of allergic cosmetic dermatitis to caprylic/capric triglyceride see ref. 1.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 4130/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 20,122/123,000.

LITERATURE

1 Laube S, Davies MG, Prais L, Foulds IS. Allergic contact dermatitis from medium-chain triglycerides in a moisturizing lotion. Contact Dermatitis 2002;47(3):171. doi: 10.1034/j.1600-0536.2002.470308_7.x.
2 Khan W, Stone N. Facial allergic contact dermatitis caused by caprylic/capric triglyceride in a cosmetic cream. Contact Dermatitis 2022;86(4):310-311. doi: 10.1111/cod.14019.
3 Navarro-Triviño FJ, Ruiz-Villaverde R. Allergic contact dermatitis caused by caprylic/capric triglyceride from an anti-aging cosmetic cream. Contact Dermatitis. 2020;83(6):508-510. doi: 10.1111/cod.13641.

3.14 CERA ALBA (BEESWAX)

IDENTIFICATION

Description/definition	: Cera alba is the wax obtained from the honeycomb of the bee, *Apis mellifera* L.; it consists primarily of myricyl palmitate, cerotic acid and esters and some high-carbon paraffins
Classification	: Waxes
INCI name USA	: Beeswax
Other names	: Beeswax; cera alba/cera flava; yellow/white beeswax
CAS registry number	: 8012-89-3
EC number	: 232-383-7
CIR reports	: J Am Coll Toxicol 1984;3:1-41
Wikipedia	: https://en.wikipedia.org/wiki/Beeswax (Beeswax)
Functions in cosmetics	: EU: emollient; emulsifying; film forming; perfuming. USA: binders; emulsion stabilizers; epilating agents; fragrance ingredients; skin-conditioning agents – miscellaneous; surfactants - emulsifying agents; viscosity increasing agents – nonaqueous
Patch testing	: 30% pet. (1,8,9); 20% pet. (2); pure (10); 20 controls were negative to yellow beeswax pure, but being a natural product, the composition of such substance can differ considerably depending on the source (3,10)

In the USA INCI system, Beeswax is described as 'The purified wax from the honeycomb of the bee, *Apis mellifera,* free from all other waxes. It is commonly named white wax when bleached and yellow wax when not bleached.'

The EU INCI system also has an entry termed '**Beeswax**', which largely seems to overlap with cera alba (even with the same CAS number), but appears to relate to the (more) purified forms.

IDENTIFICATION (Beeswax, CosIng)

Description/definition	: Beeswax is the purified wax from the honeycomb of the bee, *Apis mellifera*, free from all other waxes
Other names	: Beeswax absolute; beeswax concrete; beeswax, white (*Apis mellifera* L.); bleached beeswax; cera alba (EU); white beeswax; white wax; yellow wax
CAS registry number	: 8012-89-3
EC number	: 232-383-7
Functions in cosmetics	: Binding; emulsion stabilising; masking; skin conditioning; viscosity controlling

Previous chapter to which this is an update

The literature on contact allergy to cera alba from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.77, pp. 213-215.

CONTACT ALLERGY (cosmetics)

Case series

In a study from Sweden, 49 patients with contact cheilitis, facial eczema or a suspicion of contact allergy to beeswax were patch tested with cera alba (white beeswax, tested 'as is'), cera flava (yellow beeswax, tested 'as is') and propolis 10% pet. Nine patients (18%) reacted to cera alba, of who 9 (89%) co-reacted to both cera flava and propolis. In 8/9 cases, the reactions to 'beeswax' (i.e. either white, yellow or both) were considered to be relevant. The main product used was a brand of Swedish lip balm and emollient declared to contain beeswax. Nine of 17 patients with positive reactions (to white, yellow, or both) had used this type of product. Seven of the patients also had reactions to their own products containing

beeswax, tested 'as is'. Twenty controls were negative to yellow beeswax. No controls were apparently tested with cera flava (10), but, being the more refined product, irritant reactions may be considered unlikely.

Case reports

A 29-year-old atopic female patient suffered from a chronic, relapsing cheilitis and perioral dermatitis. The patient had used various lip balms, but without improvement. Patch tests with the extended British baseline series, fragrances, flavourings, a cosmetic and toiletry series, and her own lip cosmetics revealed multiple positive reactions, mostly to fragrances but also to one of her – non-fragranced – lip balms. Patch testing with the ingredients provided by the manufacturer at recommended concentrations confirmed an allergic reaction to the lip balm and to cera alba 30% pet. at D4. Twenty controls were negative to cera alba 30% pet. The patient's symptoms improved on allergen avoidance (9).

A 32-year-old atopic female patient suffered severe cheilitis lasting a few months, together with a longer standing mild dermatitis of the face and hand. Initially, she had developed dry cracked lips, diagnosed as atopic cheilitis, for which she had tried 6 different lip balms. Clinical examination showed a severe lip dermatitis complicated by bacterial superinfection. The patient was advised to use unscented toothpaste and petrolatum jelly as lip balm, and the cheilitis and infection were treated with oral antibiotics, topical compresses and a topical corticosteroid. After full healing, patch tests with a baseline, cosmetic, fragrance and bakery series together with four of six suspected lip balms showed + to ++ reactions to the four lip balms, and to several haptens (all +): fragrances (fragrance mix I, limonene and linalool hydroperoxides), fragrance indicators (Myroxylon pereirae resin, colophonium, propolis), octylisothiazolinone, HEMA and sorbitan sesquioleate (SSO). Although contact allergy to SSO potentially explained the positive patch tests to M. pereirae resin, the fragrance mix and HEMA, the patient also reacted to limonene hydroperoxides, which was considered relevant for the cheilitis and the facial and hand dermatitis, as limonene was present in several cosmetics, including her toothpaste. Only one of four tested lip balms was effectively scented, and therefore, ingredient patch testing was performed with preparations obtained from cosmetic manufacturers. Now, positive reactions were observed to cera alba (beeswax) 30% pet., Butyrospermum parkii (shea) butter 30% pet., candelilla cera 41% pet., and Helianthus annuus seed oil 10% pet., which were present in 5/6, 4/6, 1/6, and 1/6 of the previously used lip balms, respectively. Twenty controls were negative to all four test materials. Using cosmetics free from all demonstrated allergens led to complete resolution of the cheilitis, and significant improvement of the hand and face dermatitis (8).

A 25-year-old atopic woman had perioral eczema from contact allergy to cera alba (30% pet.; ++ at D4) and Ricinus communis (castor) seed oil in 2 lip balms (11).

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to cera alba/beeswax see refs. 1,2,4,5,6, and 7.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 0/35,000 (cera alba); 11/35,000 (beeswax).
EWG's Skin Deep Cosmetics Database (February 2025): 7/123,000 (cera alba); 9,099/123,000 (beeswax).

LITERATURE

1 Lucente P, Cavalli M, Vezzani C, Orlandi C, Vincenzi C. Contact cheilitis due to beeswax. Contact Dermatitis 1996;35(4):258. doi: 10.1111/j.1600-0536.1996.tb02378.x.
2 Jensen CD, Andersen KE. Allergic contact dermatitis from cera alba (purified propolis) in a lip balm and candy. Contact Dermatitis 2006;55(5):312-313. doi: 10.1111/j.1600-0536.2006.00801.x.
3 Nyman G, Hagvall L. A case of allergic contact cheilitis caused by propolis and honey. Contact Dermatitis 2016;74(3):186-187. doi: 10.1111/cod.12500.

4 Adams RM, Maibach HI, Clendenning WE, Fisher AA, Jordan WJ, Kanof N, et al. A five-year study of cosmetic reactions. J Am Acad Dermatol 1985;13 (6):1062-1069. doi: 10.1016/s0190-9622(85)70258-7.

5 Kohl L, Blondeel A, Song M. Allergic contact dermatitis from cosmetics: retrospective analysis of 819 patch-tested patients. Dermatology 2002;204(4):334-337. doi: 10.1159/000063379.

6 Baker L, Litzner B, Le EN, Cruz PD Jr. Ectopic periorbital dermatitis and mycosis fungoides-like dermatitis due to propolis. Dermatitis 2013;24(6):328-329. doi: 10.1097/DER.0b013e31829e0ff3.

7 Verheyden M, Rombouts S, Lambert J, Aerts O. Contact allergy to castor oil, but not to castor wax. Cosmetics 2017, 4, 5; doi:10.3390/cosmetics4010005.

8 Aerts O, Pyl J, Mangodt E, Dendooven E. Severe contact cheilitis from cera alba and other cosmetic oils, fats and waxes in lip balms. Contact Dermatitis 2023;88(4):322-323. doi: 10.1111/cod.14272.

9 Kapadia S, Kanji A, Wakelin SH. Contact dermatitis from cera alba in a lip balm - An overlooked allergen? Contact Dermatitis. 2023;88(4):324-325. doi: 10.1111/cod.14273.

10 Nyman GSA, Tang M, Inerot A, Osmancevic A, Malmberg P, Hagvall L. Contact allergy to beeswax and propolis among patients with cheilitis or facial dermatitis. Contact Dermatitis. 201981(2):110- 116. doi: 10.1111/cod.13306.

11 Verheyen M, Rombouts S, Lambert J, Aerts O. Contact allergy to castor oil, but not to castor wax. Cosmetics 2017, 4(1), 5; doi: 10.3390/cosmetics4010005.

3.15 CETEARYL ISONONANOATE

IDENTIFICATION

Description/definition : Cetearyl isononanoate is the ester of cetearyl alcohol and a branched chain nonanoic acid
Classification : Esters
IUPAC name : Hexadecyl 7-methyloctanoate
Other names : Isononanoic acid, C16-18 alkyl esters; isononanoic acid, hexadecyl ester; hexadecyl isononanoate
CAS registry number : 111937-03-2
EC number : 284-424-3
CIR reports : Int J Toxicol 2011;30(Suppl.3):228-269; Int J Toxicol 2015;34(Suppl.2):5-69
Functions in cosmetics : EU: emollient; hair conditioning; skin conditioning. USA: hair conditioning agents; skin-conditioning agents - emollient
Patch testing : 1% pet. (1); 4% in liquid mineral oil (2); 4% pet. (4)

Previous chapter to which this is an update

The literature on contact allergy to cetearyl isononanoate from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.86, pp. 229-230.

CONTACT ALLERGY (cosmetics)

Case report

A 38-year-old woman presented with widespread eczematous lesions on sun-exposed areas that had developed a few hours after she had been sunbathing. She denied previous similar reactions after sun exposure. The skin lesions resolved completely after application of a hydrocortisone cream. The patient did not relate the episode to the use of any specific product. Patch tests with the Spanish Contact Dermatitis and Skin Allergy Research Group (GEIDAC) baseline series and the European baseline photo-patch series were negative. There were no similar skin eruptions following episodes of sun exposure during the following weeks. However, 1 year later the patient sought dermatological advice again after two new flare-ups, one after using an anti-ageing night cream and the other after applying a sunscreen. Repeated open application tests were positive to both products and patch tests were also positive. In a second session, the patient was tested with the ingredients of the sunscreen, provided by its manufacturer, resulting in a positive reaction to cetearyl isononanoate 4% pet. (D2 and D4 ++). Patch tests with related compounds, such as cetearyl alcohol 20% pet. and stearyl alcohol 30% pet. were negative. Thus, the final diagnosis was allergic contact dermatitis caused by cetearyl isononanoate, which was present in both the sunscreen and the anti-ageing night cream. After avoidance of products containing cetearyl isononanoate, no recurrences have appeared (4).

Previous cases of allergic cosmetic dermatitis

For previous cases of allergic cosmetic dermatitis to cetearyl isononanoate see refs. 1-3.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 137/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 373/123,000.

LITERATURE

1 Ito K, Fujimura N, Uchida T, Ikezawa Z, Aihara M. Contact dermatitis with systemic reactions caused by cetearyl isononanoate. Contact Dermatitis 2013;69(5):315-316. doi: 10.1111/cod.12091.

2 Le Coz C-J, Bressieux A. Allergic contact dermatitis from cetearyl isononanoate. Contact Dermatitis 2003;48(6):343. doi: 10.1034/j.1600-0536.2003.00141.x.

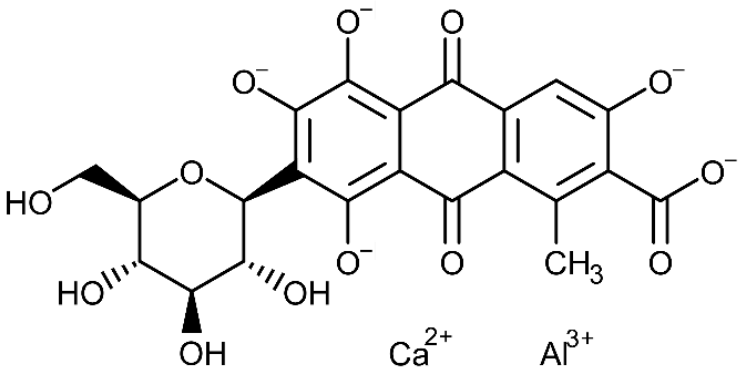
3 Sarre ME, Mancel E, Drouet M, Avenel-Audran MJ. Allergic contact dermatitis caused by cetearyl isononanoate in a sunscreen product. Contact Dermatitis 2017;76(6):357-358. doi: 10.1111/cod.12712.

4 Álvarez-Chinchilla P, Poveda-Montoyo I, González I, Silvestre JF. Cetearyl isononanoate, an underestimated contact allergen? Contact Dermatitis. 2018;79(4):243-244. doi: 10.1111/cod.13034.

3.16 CI 75470 (CARMINE)

IDENTIFICATION

Description/definition	: CI 75470 is the aluminum lake of the coloring agent cochineal; cochineal is a natural pigment derived from the dried female insect *Coccus cacti*
Classification	: Color additives
INCI name USA	: Carmine
IUPAC name	: 3,5,6,8-Tetrahydroxy-1-methyl-9,10-dioxo-7-[3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]anthracene-2-carboxylic acid
Other names	: Carmine; natural red 4; carminic acid aluminium lake; cochineal; E120 (food additive in EU); cochineal red
CAS registry number	: 1390-65-4
EC number	: 215-724-4
Wikipedia	: https://en.wikipedia.org/wiki/Carmine (Carmine)
Functions in cosmetics	: EU: cosmetic colorant. USA: colorants; fragrance ingredients
EU cosmetic restrictions	: Regulated in Annex IV/115 of the Regulation (EC) 2009/1223
Patch testing	: 2.5% pet. (Chemotechnique)
Molecular formula	: $C_{22}H_{20}O_{13}$



Previous chapter to which this is an update

The literature on contact allergy to CI 75470 (carmine) from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.109, pp. 294-296.

CONTACT ALLERGY (cosmetics)

An excellent review article on (systemic) contact dermatitis to carmine was published in 2018 (7).

Case series

In 2021, the members of the North American Contact Dermatitis Group (NACDG) published their 2011-2012 experience with patch testing carmine 2.5% pet. Of 4240 consecutive patients patch tested, 132 (3.1%) had reactions with a final interpretation of 'allergic' (positive). The face including the lips was the site mostly involved. At final reading, most carmine reactions (65%) were weakly positive (+). Approximately half of the positive patch tests were of current clinical relevance. The identified sources of contact with carmine were primarily personal care products (77%), especially makeup (31%) and lip products (8.6%). Food products were the source in 2.3%. It was concluded that weak patch test reactions to carmine should be interpreted with caution (apparently carmine was removed from the NACDG standard screening series in 2013, but it was added again in 2020 [9]). Allergic contact dermatitis to carmine should be suspected especially in women with facial and/or lip dermatitis (8).

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to CI 75470 see refs. 1-6.

IMMEDIATE-TYPE REACTIONS

A 24-year-old non-atopic woman sometimes experienced urticaria without anaphylaxis. Three years ago, she bought eyeshadow A but stopped using it because her eyelids turned red after application. A year ago, she noticed itchy erythema on her eyelids 3 hours after applying eyeshadow B and later also after applying eyeshadow C. Other than these eyeshadows, she used cosmetics without having any symptoms. She noticed that only eyeshadows A, B, and C contained carmine. Skin prick tests using carmine 1% in normal saline solution, carminic acid 1% water, cochineal dye 1% water, saline (negative control), and 10 mg/mL histamine dihydrochloride (positive control) were positive to carmine, carminic acid (the main component of cochineal dye), cochineal dye, and the positive control (mean wheal diameter: 4.5, 5.5, 4, and 5 mm, respectively) and negatively to saline. Specific immunoglobulin E antibodies binding to proteins against *Dactylopius coccus* Costa and carmine were identified in the patient's serum (11).

Previous cases of immediate-type reactions

Immediate-type reactions are frequently reported, especially to carmine in foods and drinks and in occupational settings, with urticaria, asthma, allergic rhinitis, diarrhea, and anaphylactic shock. Please refer to Monographs in Contact Allergy, Volume 1, Chapter 2.109, pp. 294-296

OTHER PUBLICATIONS [a]

A 4-year-old girl had recurrent intermittent bouts of systemic allergic dermatitis presenting as erythroderma with severe facial involvement and periorbital swelling, which was caused by delayed-type hypersensitivity to carmine in various foods including candies, juices, and, most notably, red velvet cupcakes (10).

[a] Literature on contact allergy to carmine that was found in *Contact Dermatitis* or/and *Dermatitis* from September 2017 through March 2025, in which there was no direct link with cosmetic products.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 1618/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 6077/123,000.

LITERATURE

1 Sarkany I, Meara RH, Everall J. Cheilitis due to carmine in lip salve. Trans Ann Rep St John's Hosp Dermatol Soc 1961;46:39.

2 Suzuki K, Hirokawa K, Yagami A, Matsunaga K. Allergic contact dermatitis from carmine in cosmetic blush. Dermatitis 2011;22(6):348-349. doi: 10.2310/6620.2011.11022.

3 Yamamoto A, Kono T, Kato A, et al. Contact dermatitis due to cochineal carmine. Environ Dermatol 1999;6:185-189 (in Japanese).

4 Endo Y, Onozawa N, Tamura A, Ishikawa O. Positive patch test reaction to carmine in lipstick. Environ Dermatol 2003;10:75-78 (in Japanese).

5 Shaw DW. Allergic contact dermatitis from carmine. Dermatitis 2009;20(5):292-295. PMID: 19808007.

6 Ferris GJ, Wat M, Nedorost S. Multifactorial dermatitis with probable systemic contact dermatitis to carmine. Dermatitis 2017;28(4):293-294. doi: 10.1097/DER.0000000000000295.

7 Rundle CW, Jacob SE, Machler BC. Contact dermatitis to carmine. Dermatitis. 2018;29(5):244-249. doi: 10.1097/DER.0000000000000386.

8 Warshaw EM, Voller LM, DeKoven JG, Taylor JS, Atwater AR, Reeder MJ, et al. Patch testing with carmine 2.5% in petrolatum by the North American Contact Dermatitis Group, 2011-2012. Dermatitis. 2021;32(2):94-100. doi: 10.1097/DER.0000000000000643.

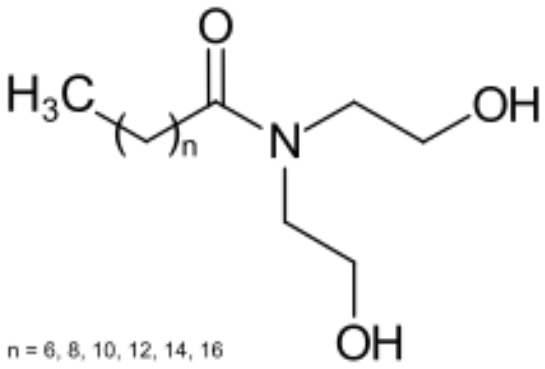
9 Schalock PC, Dunnick CA, Nedorost S, Brod B, Warshaw E, Mowad C, et al.; American Contact Dermatitis Society Core Allergen Series Committee. American Contact Dermatitis Society Core Allergen Series: 2020 update. Dermatitis. 2020;31(5):279-282. doi: 10.1097/DER.0000000000000621.

10 Machler BC, Jacob SE. Carmine red: A potentially overlooked allergen in children. Dermatitis. 2018; 29(2):92-93. doi: 10.1097/DER.0000000000000354.
11 Suzuki K, Futamura K, Sato N, Nakamura M, Matsunaga K, Yagami A. Contact urticaria caused by carmine-containing eyeshadows; the causative allergen is carminic acid rather than CC38K. Contact Dermatitis. 2021;84:468-469. doi: 10.1111/cod.13769.

3.17 COCAMIDE DEA

IDENTIFICATION

Description/definition : Cocamide DEA is a mixture of ethanolamides of coconut acid. It conforms generally to the structural formula shown below, where RCO- represents the fatty acids derived from *Cocos nucifera* (coconut) oil
Classification : Fatty acid dialkylamides and dialkanolamides
IUPAC name : Amides, coco, *N*,*N*-bis(hydroxyethyl)
Other names : Coconut diethanolamide; cocamine diethanolamine; coconut fatty acids diethanolamide
CAS registry number : 68603-42-9
EC number : 271-657-0
CIR reports : J Am Coll Toxicol 1986;5:415-454; J Am Coll Toxicol 1996;15:527-542; Int J Toxicol 2013;32(Suppl.3):36-58
Wikipedia : https://en.wikipedia.org/wiki/Cocamide_DEA
Functions in cosmetics : EU: emulsifying; emulsion stabilising; foam boosting; surfactant; viscosity controlling. USA: surfactants – foam boosters; viscosity increasing agents – aqueous
EU cosmetic restrictions : Regulated in Annex III/60 of the Regulation (EC) 2009/1223
Patch testing : 0.5% pet. (Chemotechnique, SmartPractice); the test material may sometimes cause irritant reactions (1)



Previous chapter to which this is an update

The literature on contact allergy to cocamide DEA from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.117, pp. 308-312.

CONTACT ALLERGY (cosmetics)

Case report

A 50-year-old nonatopic woman was investigated for a genital, pruritic eruption lasting for 2 months. She had started the daily use of a new intimate hygiene cosmetic 1 month before the onset of the dermatitis. The application of topical corticosteroids did not improve the dermatitis, but stopping the use of the gel made the dermatitis settle. A ROAT with the intimate gel (undiluted) on the forearm was positive after 3 days. Patch tests with the European comprehensive baseline series and cosmetic series, the intimate gel (tested 1% water), and its ingredients showed positive (+) reactions to the cosmetic gel and its ingredient cocamide DEA 0.5% pet. from both the cosmetic series and the ingredients received from the manufacturer. Ten controls were negative to the gel 1% water. Allergic contact dermatitis caused by cocamide DEA in the intimate gel was diagnosed (5).

Previous cases of allergic cosmetic dermatitis

Many cases of allergic cosmetic dermatitis to cocamide DEA have previously been reported, e.g. in refs. 1-4. For a full literature review of this topic please refer to the Monographs in Contact Allergy, Volume 1, Chapter 2.117, pp. 308-312.

Cross-reactions

It has been suggested that patients allergic to cocamide DEA may cross-react to lauramide DEA and to cocamide MEA (monoethanolamide), but that such reactions may not be common enough to be 'clinically relevant' (6).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 500/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 105/123,000.

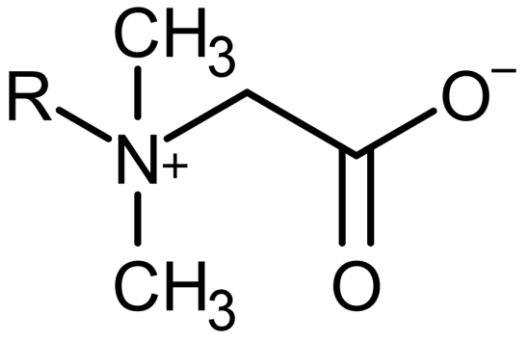
LITERATURE

1 Aalto-Korte K, Pesonen M, Kuuliala O, Suuronen K. Occupational allergic contact dermatitis caused by coconut fatty acids diethanolamide. Contact Dermatitis 2014;70(3):169-174. doi: 10.1111/cod.12151.
2 Kanerva L, Jolanki R, Estlander T. Dentist's occupational allergic contact dermatitis caused by coconut diethanolamide, N-ethyl-4-toluene sulfonamide and 4-tolyldiethanolamine. Acta Derm Venereol 1993;73(2):126-129. doi: 10.2340/0001555573126129.
3 Dejobert Y, Delaporte E, Piette F, Thomas P. Eyelid dermatitis with positive patch test to coconut diethanolamide. Contact Dermatitis 2005;52(3):173. doi: 10.1111/j.0105-1873.2005.0548n.x.
4 De Groot AC, de Wit FS, Bos JD, Weyland JW. Contact allergy to cocamide DEA and lauramide DEA in shampoos. Contact Dermatitis 1987;16:117-118. doi: 10.1111/j.1600-0536.1987.tb01401.x.
5 Navarro-Triviño FJ, Ruiz-Villaverde R. Genital allergic contact dermatitis caused by cocamide DEA. Contact Dermatitis 2021;85(6):701-703. doi: 10.1111/cod.13934.
6 Scheman A, Te R. Contact allergy to cocamide diethanolamine and cross-reactions. Dermatitis 2018; 29(2): 91-92. doi: 10.1097/DER.0000000000000350.

3.18 COCO-BETAINE

IDENTIFICATION

Description/definition : Coco-betaine is the zwitterion (inner salt) that conforms generally to the structural formula shown below, where R represents the alkyl groups derived from coconut oil
Classification : Betaines
IUPAC name : Betaines, coco alkyldimethyl
CAS registry number : 68424-94-2
EC number : 270-329-4
CIR reports : Int J Toxicol 2018;37(Suppl.1):28-46
Functions in cosmetics : EU: antistatic; cleansing; foam boosting; hair conditioning; skin conditioning; surfactant; viscosity controlling. USA: antistatic agents; hair conditioning agents; skin-conditioning agents - miscellaneous; surfactants – cleansing agents; surfactants- foam boosters; viscosity increasing agents – aqueous
Patch testing : 2% water (1); 6% water (2)



Previous chapter to which this is an update

The literature on contact allergy to coco-betaine from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.123, pp. 331-332.

CONTACT ALLERGY (cosmetics)

Case report

A 51-year-old man reported an itchy erythematous and desquamative eruption of the face and neck, that had developed some 12 hours following the application of a cosmetic beard cleansing product. The lesions disappeared without treatment 3 days after stopping the cream. He had used the same cleanser 1 month before without any reaction. Patch tests with the European baseline and cosmetic series, the cleanser 'as is' and the ingredients of this cream, provided by the manufacturer, showed a strong positive reaction to the cleanser (++) and to its ingredient coco-betaine 6% water (++) on D4. A repeated open application test with the cleanser on the forearm twice a day (washed off after rubbing in) was strongly positive after 24 hours. Three controls were negative to coco-betaine 6% water (2).

Previous cases of allergic cosmetic dermatitis

For previous cases of allergic cosmetic dermatitis to coco-betaine see ref. 1.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 209/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 620/123,000.

LITERATURE

1 Van Haute N, Dooms-Goossens A. Shampoo dermatitis due to cocobetaine and sodium lauryl ether sulphate. Contact Dermatitis 1983;9(2):169. doi: 10.1111/j.1600-0536.1983.tb04348.x.
2 Badaoui A. Allergic contact dermatitis to coco betaine in a beard cleanser. Contact Dermatitis 2024;90(6):632-633. doi: 10.1111/cod.14536.

3.19 COLOPHONIUM

IDENTIFICATION

Description/definition	: Colophonium is the residue left after distilling off the volatile oil from the oleoresin obtained from *Pinus palustris* and other species of Pinaceae
Classification	: Botanical products and derivatives
INCI name USA	: Rosin and Colophonium
Other names	: Gum rosin; colophony
CAS registry number	: 8050-09-7
EC number	: 232-475-7
Wikipedia	: https://en.wikipedia.org/wiki/Rosin (Rosin)
Functions in cosmetics	: EU: binding; depilatory; film forming; viscosity controlling. USA: binders; epilating agents; film formers; viscosity increasing agents - nonaqueous
Patch testing	: 20% pet. (Chemotechnique, SmartPractice); this test substance often does *not* detect contact allergy to modified (hydrogenated, esterified *et cetera*) colophony products and sometimes to colophony itself, when the allergen is in the neutral fraction

Previous chapter to which this is an update

The literature on contact allergy to colophonium from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.126, pp. 336-355.

CONTACT ALLERGY (cosmetics)

Case reports

A 40-year-old nonatopic woman presented with a pruritic pustular facial rash, which had appeared some 15 hours after wax epilation. The patient reported having applied a dispersible paracetamol and a cosmeceutical cream after the face waxing. She had a history of urticaria and angioedema to orally administered paracetamol. Dermatological examination revealed erythematous oedematous plaques with multiple pustules involving the eyebrows, the peri-orbicular region, and the upper lip. Patch tests with the European baseline series, paracetamol (30% pet. and water) and the cream (undiluted) and an open test with the depilatory wax were positive to colophonium (D2 ++, D3 +++) and the depilatory wax. The wax was found to contain colophonium. There were no positive reactions to paracetamol and the cosmetic cream and an oral provocation test with paracetamol was negative. Pustular allergic contact dermatitis caused by colophonium was diagnosed (3).

In 2020, a virtually identical case had been reported from Spain (4). The patient was a 44-year-old woman who presented with a 5-hour history of oedematous pruritic plaques involving the periorbital area and the upper lip. The skin lesions had developed 16 hours after wax epilation performed on her eyebrows and upper lip. A short course of systemic steroids was prescribed with resolution of the eruption in a few days. Patch tests were positive to nickel, ethylenediamine dihydrochloride, and colophonium (+) on D3 and D7. The wax epilation product used in the patient´s salon was found to contain colophonium. Hence, allergic contact dermatitis caused by colophonium contained in this product was diagnosed (4).

Previous cases of allergic cosmetic dermatitis

Colophonium is a well-known cause of allergic contact dermatitis (ACD) and is present in most international and national baseline series for patch testing. Most sources of ACD to colophonium are non-cosmetic (table below). Most previous case reports of allergic cosmetic dermatitis were to eye cosmetics such as eye shadow and mascara and were published over 25 years ago. There are at least 9 such cases, the most recent of which are from 1997 and 1998 (1,2).

Non-cosmetic colophony-containing product categories reported as causes of allergic contact dermatitis

Adhesives and adhesive materials	Paper and paper products
Colophony (products) used for string instruments	Pine trees, pine sawdust and pine wood
Colophony (products) used in sports	Soldering fluxes
Dental products	Topical pharmaceutical products
Inks	Waxes, polishes and depilatory products
Metalworking fluids	Miscellaneous products

Reproduced from Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.126, pp. 336-355.

OTHER PUBLICATIONS [a]

- A 28-year-old woman had (partially airborne) allergic contact dermatitis from the Christmas tree *Abies nordmanniana* from colophonium allergy (5).
- A 33-year-old professional football player had chronic eczema of the ankles and the dorsa of the feet, and also widespread eczematous dermatitis involving the trunk, limbs, and buttocks from contact allergy to colophonium in plasters used to tightly fixate his socks during daily professional training (6).
- Occupational ACD to colophonium at the Finnish Institute of Occupational Health 2002-2017 (7).
- Generalized ACD from colophonium(-derivatives) and fragrances in an insect repellent (8).
- ACD from colophonium(-derivatives) in: adhesive bandages (9); adhesives of a glucose sensor and sanitary pads (10); disposable paper napkin (11); bees wax wraps (12); resin creams (also occupational) (14).
- Occupational ACD from colophonium in wood dust (13,14).
- Allergic reactions to colophonium in dentistry are reviewed in ref. 15.

[a] Literature on contact allergy to colophonium that was found in *Contact Dermatitis* or/and *Dermatitis* from September 2017 through March 2025, in which there was no direct link with cosmetic products.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 102/35,000 (Rosin).
EWG's Skin Deep Cosmetics Database (February 2025): 251/123,000 (Rosin); 181/123,000 (Colophonium).

LITERATURE

1 Färm G. Contact allergy to colophony. Clinical and experimental studies with emphasis on clinical relevance. Acta Derm Venereol Suppl (Stockh) 1998;201:1-42. PMID: 9833065.
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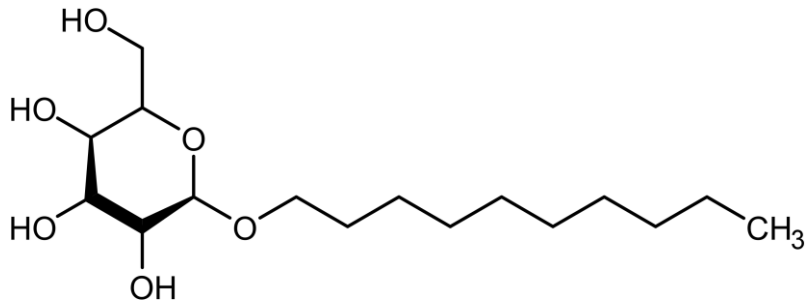
4 Tous-Romero F, Vico-Alonso C, Pinilla-Martín B, Ortiz de Frutos J. Allergic contact dermatitis from a depilatory wax. Contact Dermatitis 2020;83(1):65. doi: 10.1111/cod.13530.
5 Gether L, Gyldenløve M, Thyssen JP. Christmas tree dermatitis caused by colophonium allergy. Contact Dermatitis. 2017;77(6):412-414. doi: 10.1111/cod.12798.
6 Corazza M, Musmeci D, Scuderi V, Bernardi T, Cristofaro D, Borghi A. Occupational systemic allergic dermatitis in a football player sensitized to colophonium. Contact Dermatitis. 2018;79(5):325-326. doi: 10.1111/cod.13081.
7 Pesonen M, Suuronen K, Suomela S, Aalto-Korte K. Occupational allergic contact dermatitis caused by colophonium. Contact Dermatitis. 2019;80(1):9-17. doi: 10.1111/cod.13114.
8 Kullberg SA, Warshaw EM. Summertime dermatitis: When the repellent is the culprit, not the bugs! Dermatitis. 2020;31(4):e30-e32. doi: 10.1097/DER.0000000000000632.
9 Samaran Q, Clark E, Dereure O, Raison-Peyron N. Allergic contact dermatitis to Cupressus sempervirens resin and cross-reaction with colophonium. Contact Dermatitis. 2020;83(1):33-35. doi: 10.1111/cod.13496.

10 Salzano G, Galletta F, Caminiti L, Lonia P, Donia V, Pajno GB, Passanisi S, Lombardo F. Vulvar contact dermatitis caused by sensitization to colophonium in a patient with type 1 diabetes. Contact Dermatitis. 2021;85(3):364-366. doi: 10.1111/cod.13851.
11 Suzuki K, Futamura K, Kawakami T, Numata M, Sasaki K, Matsunaga K, Yagami A. Contact dermatitis caused by a disposable paper napkin containing colophonium. Contact Dermatitis. 2021 ;85(3):377-379. doi: 10.1111/cod.13864.
12 Hamid I, Stone N. Bees wax wraps-A novel source of colophonium allergic contact dermatitis. Contact Dermatitis. 2023;88(4):315-316. doi: 10.1111/cod.14267.
13 Hamwi S, Kunst A, Boust C, Bauvin O, Tetart F. Occupational allergic contact dermatitis caused by colophonium, an unsuspected sensitizer in a petrochemical worker. Contact Dermatitis. 2022; 87(6):548-550. doi: 10.1111/cod.14211.
14 Lievonen S, Pesonen M, Suomela S. Allergic contact dermatitis caused by colophonium in resin creams. Contact Dermatitis. 2024;91(1):70-72. doi: 10.1111/cod.14545.
15 Weber B, Karels S, Neeley A. Colophony in dentistry: Routes of exposure and reported reactions. Dermatitis. 2025 Jan 16. doi: 10.1089/derm.2024.0356. Epub ahead of print.

3.20 DECYL GLUCOSIDE

IDENTIFICATION

Description/definition : Decyl glucoside is the product obtained from the condensation of decyl alcohol with glucose, which generally conforms to the structural formula shown below
Classification : Carbohydrates; ethers
IUPAC name : (3*R*,4*S*,5*S*,6*R*)-2-Decoxy-6-(hydroxymethyl)oxane-3,4,5-triol
Other names : Decyl D-glucopyranoside
CAS registry number : 58846-77-8
EC number : 261-469-7
CIR reports : Int J Toxicol 2013;32(Suppl.3):22-48
Wikipedia : https://en.wikipedia.org/wiki/Decyl_glucoside
Functions in cosmetics : EU: cleansing; emulsion stabilising; surfactant. USA: surfactants – cleansing agents
Patch testing : 5.0% pet. (Chemotechnique, SmartPractice); 10% in water is not irritant (1)
Molecular formula : $C_{16}H_{32}O_6$



Previous chapter to which this is an update

The literature on contact allergy to decyl glucoside from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.134, pp. 366-369.

CONTACT ALLERGY (cosmetics)

General

Tinosorb M is a widely used UV filter complex consisting of methylene bis-benzotriazolyl tetramethylbutylphenol (active ingredient), propylene glycol, xanthan gum, water, and decyl glucoside. Sensitization to the latter has been responsible for several cases of allergic reactions to Tinosorb M. Contact allergy to the UV-filter itself, methylene bis-benzotriazolyl tetramethylbutylphenol (synonym: bisoctrizole) has thus far not been established. In the 2 new cases of allergic contact dermatitis from Tinosorb M reported from Portugal in 2020, decyl glucoside was again the culprit sensitizer (5).

Case reports

The first patient, a 48-year-old non-atopic woman, presented with a 6-month history of pruritic eczema on the face, predominantly affecting the eyelids, after the application of various cosmetic products. Patch testing revealed positive reactions to decyl glucoside (5% pet.), lauryl glucoside (3% pet.), Tinosorb M (containing decyl glucoside; 10% pet.), a face cream containing Tinosorb M, to lanolin alcohol and various fragrances. A ROAT with the cream was positive after 5 days. This facial cream was considered the culprit product as the remaining ones did not contain any fragrances nor the emulsifiers identified in the patch testing (5).

The second patient was a 44-year-old non-atopic female who presented with a 2-year history of pruritic erythema with papules on the face and neck with transient improvements. She mentioned that acute episodes tended to appear after outdoor work as an archaeologist. Patch tests were positive to MCI/MI, Myroxylon pereirae resin, benzoic acid, decyl glucoside, lauryl glucoside, Tinosorb M (containing decyl glucoside), and 2 sunscreens that contained this UV-filter. The patient was retrospectively able to relate flares to work periods during which sun protection with the sunscreens had been intensified (5).

Previous cases of allergic cosmetic dermatitis

Many cases of allergic cosmetic dermatitis to decyl glucoside have previously been reported, e.g. in refs. 1-4. For a full literature review of this topic please refer to the Monographs in Contact Allergy, Volume 1, Chapter 2.134, pp. 366-369.

PHOTOSENSITIVITY

A 21-year-old man presented with a 6-month history of recurrent pruritic facial rashes, worse after sun exposure whilst training in the army. He used green and black camouflage creams on the face and neck for training, 3-in-1 shower gels for shampoo/soap, and occasionally, colognes. Physical examination showed facial eczematous lesions, symmetrically photodistributed, and accentuated on his cheeks. The patient was patch and photopatch tested which yielded a weak positive (+) photopatch test reaction to decyl glucoside with UVA and a negative corresponding reaction without UVA, and weak positive (+) patch test reactions to Myroxylon pereirae resin and to his own black/green camouflage creams. The shower gels contained decyl glucoside. With careful avoidance of the allergens, complete resolution of symptoms was achieved (11) .

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 10/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 3255/123,000.

OTHER PUBLICATIONS [a]

- Allergic contact dermatitis from decyl glucoside, lauryl glucoside and polyhexamethylene biguanide in antimicrobial foam dressing (6).
- Patch testing with decyl glucoside and other alkyl glucosides in patients suspected of ACD from cosmetics (7,9).
- Routine testing with decyl glucoside and 3 other alkyl glucosides by the NACDG, 2019-2020 (8).
- Two patients had allergic contact dermatitis from surgical solutions and had positive patch test reactions to decyl glucoside and related alkyl glucosides. It was assumed that glucosides were present in the surgical solutions, but 'we were unable to confirm the specific surgical solutions used during surgery in both patients' (10).

[a] Literature on contact allergy to decyl glucoside that was found in *Contact Dermatitis* or/and *Dermatitis* from September 2017 through March 2025, in which there was no direct link with cosmetic products.

LITERATURE

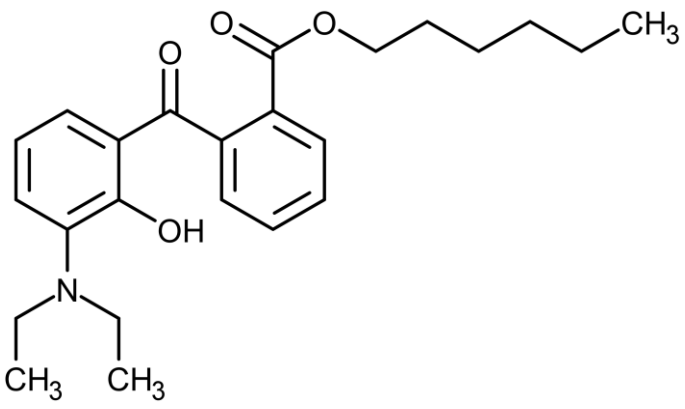
1 Le Coz CJ, Meyer MT. Contact allergy to decyl glucoside in antiseptic after body piercing. Contact Dermatitis 2003;48(5):279-280. doi: 10.1034/j.1600-0536.2003.00106.x.
2 Blondeel A. Contact allergy to the mild surfactant decylglucoside. Contact Dermatitis 2003;49(6):304-305. doi: 10.1111/j.0105-1873.2003.0251a.x.
3 Horn HM, Murray C, Aldridge RD. Contact allergy to decyl glucoside. Contact Dermatitis 2005;52(4):227. doi: 10.1111/j.0105-1873.2005.0566b.x.
4 Gijbels D, Timmermans A, Serrano P, Verreycken E, Goossens A. Allergic contact dermatitis caused by alkyl glucosides. Contact Dermatitis 2014;70(3):175-182. doi: 10.1111/cod.12154.
5 Monteiro AF, Paulino M, Máquina A, Amaro C, Viana I. Allergic contact dermatitis to decyl glucoside: Still an important allergen in Tinosorb M. Contact Dermatitis. 2020;82(2):126-128. doi: 10.1111/cod.13408.

6 Jaque A, DeKoven JG. Polyhexamethylene biguanide and alkyl glucosides: unexpected allergens in an antimicrobial foam dressing. Contact Dermatitis. 2017;77(6):421-422. doi: 10.1111/cod.12852.
7 Bhoyrul B, Solman L, Kirk S, Orton D, Wilkinson M. Patch testing with alkyl glucosides: Concomitant reactions are common but not ubiquitous. Contact Dermatitis. 2019;80(5):286-290. doi: 10.1111/cod.13186.
8 Warshaw EM, Xiong M, DeKoven JG, Taylor JS, Belsito DV, et al. Co-reactivity of glucosides: Retrospective analysis of North American Contact Dermatitis Group Data 2019-2020. Contact Dermatitis. 2023;88(2):153-156. doi: 10.1111/cod.14237.
9 Severin RK, Belsito DV. Patch testing with decyl and lauryl glucoside: How well does one screen for contact allergic reactions to the other? Dermatitis. 2017;28(6):342-345. doi: 10.1097/DER.0000000000000327.
10 Schlarbaum JP, Liou YL, Kimyon RS, Olson CL, Warshaw EM. Oh My glucosides! occult sources in medical products. Dermatitis. 2019;30(3):228-230. doi: 10.1097/DER.0000000000000476.
11 Tsang DA, Lim SPR. Photoallergic contact dermatitis to decyl glucoside. Dermatitis. 2025 Feb 20. doi: 10.1089/derm.2024.0554. Epub ahead of print.

3.21 DIETHYLAMINO HYDROXYBENZOYL HEXYL BENZOATE

IDENTIFICATION

Description/definition : Diethylamino hydroxybenzoyl hexyl benzoate is the organic compound that conforms to the structural formula shown below
Classification : Amines; esters; phenols
IUPAC name : Benzoic acid, 2-[4-(diethylamino)-2-hydroxybenzoyl]-, hexyl ester
Other names : 2-Hydroxy-4-diethylamino-2'-hexyloxycarbonylbenzophenone; hexyl 2-[4-(diethylamino)-2-hydroxybenzoyl]benzoate
CAS registry number : 302776-68-7
EC number : 443-860-6; 608-453-1
SCCS opinions : SCCP/1166/08
Wikipedia : https://en.wikipedia.org/wiki/Diethylamino_hydroxybenzoyl_hexyl_benzoate
Functions in cosmetics : EU: UV-filter. USA: light stabilizers
EU cosmetic restrictions : Regulated in Annex VI/28 of the Regulation (EC) 2013/344
Patch testing : 10% pet. (1)
Molecular formula : $C_{24}H_{31}NO_4$



Previous chapter to which this is an update

The literature on contact allergy to diethylamino hydroxybenzoyl hexyl benzoate from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.145, pp. 400-401.

CONTACT ALLERGY (cosmetics)

General

A very useful review article on sunscreen allergy was published in 2023 in *Dermatitis* (3).

Case report

A 49-year-old non-atopic female patient developed pruritic and progressive macular hyperpigmentation of the face and neck without clinically apparent eczematous lesions. She had related her symptoms to a particular sunscreen, which she had disposed of. As the pigmentation kept spreading, she increased the use of sunscreens, yet often switched brands because of intolerance to most of them. She also avoided perfumes because she recalled having 'reactions' from them. A skin biopsy showed abundant dermal melanophages without inflammation. Two years later, the patient started to notice hair loss of her eyebrows and, 2 years later, signs of frontal hairline regression compatible with frontal fibrosing alopecia. Patch tests with the GEIDAC baseline series and supplementary allergens, personal cosmetic products, as

well as an extended photopatch test series (5 J/cm^2 UVA) resulted in many positives, among which to diethylamino hydroxybenzoyl hexyl benzoate 10% pet. (D2 ++, D4/D7 +) without photo-aggravation, cinnamal 1% pet. (+++ on D2, D4 and D7) and cinnamyl alcohol 2% pet. (+++ on D2, D4 and D7). Diethylamino hydroxybenzoyl hexyl benzoate was found in one of her sunscreens, and cinnamal and cinnamyl alcohol in a facial moisturizer. After avoidance, the pruritus improved and further spreading of hyperpigmentation ceased. The patient was diagnosed with non-eczematous (lichenoid) pigmented contact dermatitis (2). This was the first reported case of contact allergy to diethylamino hydroxybenzoyl hexyl benzoate.

Previous cases of allergic cosmetic dermatitis

For previous cases of allergic cosmetic dermatitis to diethylamino hydroxybenzoyl hexyl benzoate see ref. 1 (in fact only one positive patch test, the relevance of which was not specified).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 135/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 140 /123,000.

LITERATURE

1 The European Multicentre Photopatch Test Study (EMCPPTS) Taskforce. A European multicentre photopatch test study. Br J Dermatol 2012;166(5):1002-1009. doi: 10.1111/j.1365-2133.2012.10857.x.
2 Gatica-Ortega ME, Vergara-de-la-Campa L, Alonso-Naranjo L, Pastor-Nieto MA. Relevant sensitization to diethylamino hydroxybenzoyl hexyl benzoate and fragrances in a patient with frontal fibrosing alopecia and acquired dermal macular hyperpigmentation. Contact Dermatitis 2022;87(3):287-289. doi: 10.1111/cod.14139.
3 Ekstein SF, Hylwa S. Sunscreens: A review of UV filters and their allergic potential. Dermatitis. 2023;34(3):176-190. doi: 10.1097/DER.0000000000000963.

3.22 BIS-DIGLYCERYL POLYACYLADIPATE-2

IDENTIFICATION

Description/definition	: Bis-diglyceryl polyacyladipate-2 is the adipic acid (q.v.) diester of a mixed diglyceryl ester of caprylic, capric, stearic, isostearic and hydroxystearic acids
Classification	: Glyceryl esters and derivatives
IUPAC name	: Not available
Other names	: Diglyceryl adipate mixed fatty acid ester; bis-diglyceryl caprylate/caprate/ isostearate/stearate/hydroxystearate adipate; Softisan 649 ®
CAS registry number	: 82249-33-0; 130905-60-1
EC number	: 406-144-4
CIR reports	: Int J Toxicol. 2013;32(Suppl.3):56-64
Functions in cosmetics	: EU: skin conditioning; skin conditioning - emollient. USA: skin-Conditioning agents - emollient
Patch testing	: Softisan 649 ® 100% (Chemotechnique)
Molecular formula	: Unspecified

Previous chapter to which this is an update

The literature on contact allergy to from bis-diglyceryl polyacyladipate-2 cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.149, pp. 406.

CONTACT ALLERGY (cosmetics)

Case report

A 16-year-old atopic boy had persistent dryness, episodes of swelling, and burning sensations affecting both lips for 3 months. Flare up of the lesions, with scaling of the lips and an eczema of the eyelids, was noted a couple of days after using a lip balm. Patch tests with the European baseline series and supplements, the suspected product ‘as is’ and all its ingredients, yielded a positive reaction to the lip balm (D2 ?+, D4 +) and doubtful reactions (D4 ?+) to some of its ingredients: bis-diglyceryl polyacyladipate-2 (16% pet.), polyisobutene hydrogen (5% pet.), and PEG-45/dodecyl glycol co-polymer (10% pet.). ROATs were subsequently performed twice a day on the patient's forearms with these three ingredients, and were positive after 4 days to bis-diglyceryl polyacyladipate-2 and PEG-45/dodecyl glycol co-polymer, with erythema and papules with a follicular pattern, graded ++, and a reaction evolving into plaques and lasting for almost a week after the end of the applications. Two controls were negative. To explore these reactions further, new patch tests were performed with the three ingredients with an additional reading at D7. A positive test reaction was observed to PEG-45/dodecyl glycol co-polymer 10% pet. (++ on D4 and + on D7), and doubtful reactions to bis-diglyceryl polyacyladipate-2 (16% pet.; D4 and D7 ?+), and polyisobutene hydrogen (5% pet.; ?+ on D4 and negative on D7) (1).

Previous cases of allergic cosmetic dermatitis

For previous cases of allergic cosmetic dermatitis to bis-diglyceryl polyacyladipate-2 see refs. 2-4.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 479/35,000.
EWG’s Skin Deep Cosmetics Database (February 2025): 4,392/123,000.

LITERATURE

1 Clark E, Samaran Q, Dereure O, Raison-Peyron N. PEG-45/dodecyl glycol co-polymer and bis-diglyceryl polyacyladipate-2: Two culprits responsible of an allergic contact dermatitis to a lip balm. Contact Dermatitis. 2021;85(1):117-119. doi: 10.1111/cod.13811.

2 Shaw DW. Allergic contact dermatitis caused by bis-diglycerylpolyacyladipate-2 (Softisan® 649) owing to its 12-hydroxystearic acid content. Contact Dermatitis 2011;65(6):369-370. doi: 10.1111/j.1600-0536.2011.01994.x.

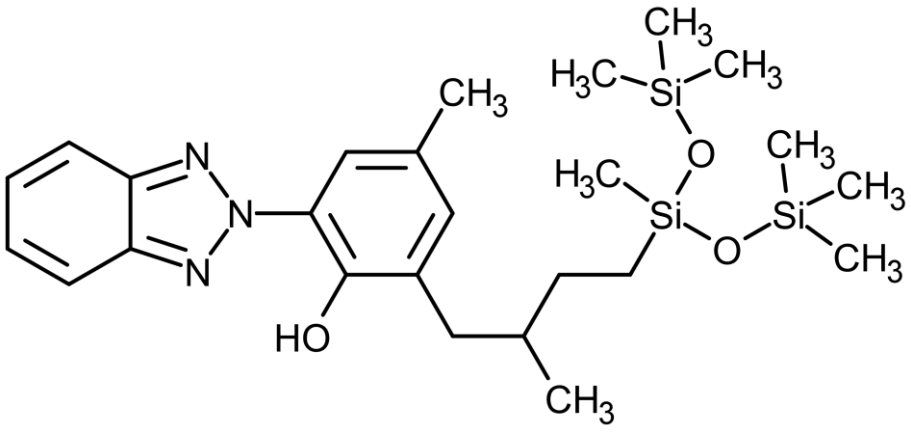
3 Shaw DW. Allergic contact dermatitis from 12-hydroxystearic acid, the principal fatty acid in hydrogenated castor oil. Dermatitis 2009;20:236 (Abstract)

4 Du-Thanh A, Raison-Peyron N, Guillot B. Bis-diglycerylpolyacyladipate-2: An emergent allergen in cosmetics? Contact Dermatitis 2011;64(6):358-359. doi: 10.1111/j.1600-0536.2011.01902.x.

3.23 DROMETRIZOLE TRISILOXANE

IDENTIFICATION

Description/definition : Drometrizole trisiloxane is the heterocyclic compound that conforms to the structural formula shown below
Classification : Heterocyclic compounds; phenols; siloxanes and silanes
IUPAC name : Phenol, 2-(2*H*-benzotriazol-2-yl)-4-methyl-6-(2-methyl-3-(1,3,3,3-tetramethyl-1-(trimethylsilyl)oxy)-disiloxanyl)propyl
CAS registry number : 155633-54-8
EC number : 687-624-2; 919-634-2
Wikipedia : https://en.wikipedia.org/wiki/Drometrizole_trisiloxane
Functions in cosmetics : EU: UV-absorber; UV-filter. USA: light stabilizers
EU cosmetic restrictions : Regulated in Annex VI/16 of the Regulation (EC) 2009/1223
Patch testing : 10.0% pet. (Chemotechnique) ; late readings at D7 and D14 may be warranted when negative at the second reading on D3/4 (6)
Molecular formula : $C_{24}H_{39}N_3O_3Si_3$



Previous chapter to which this is an update

The literature on contact allergy to drometrizole trisiloxane from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.172, pp. 449-450.

CONTACT ALLERGY (cosmetics)

General

A very useful review article on sunscreen allergy was published in 2023 in *Dermatitis* (7).

Case report

A 45-year-old non-atopic woman was referred for facial dermatitis, that she related to one particular sunscreen product (sunscreen A). The patient had been using sunscreens daily for years because of hyperpigmentation. She also recalled pruritic reactions involving several locations that she related to other sunscreens, cosmetics and other materials. Patch tests with the Spanish baseline (GEIDAC), sunscreen, fragrances and cosmetic series were positive for nickel sulfate and mercapto mix (past and unknown relevance, respectively). A ROAT with sunscreen A was positive on day 7. Yet, subsequent patch tests with its 24 individual ingredients, including drometrizole trisiloxane 10% pet. and ethylhexyl salicylate (EHS) 4% pet., obtained by the manufacturer, were negative on D2, D4 and D6.
One year later, the patient developed frontal, occipital, eyebrow, and axillary hair loss, diagnosed as frontal fibrosing alopecia. Since eczematous reactions persisted, further patch and photopatch tests with

the European photopatch extended series as well as the patient's cosmetics were performed and yielded positive reactions to drometrizole trisiloxane 10% pet. (D7 and D14, equal strength irradiated and unirradiated) and one compact sunscreen (sunscreen B) containing drometrizole trisiloxane (positive on D4, D7 and D14 irradiated and on D14 unirradiated). Drometrizole tested negative. One year thereafter, patch tests with 22 individual ingredients of sunscreen B including drometrizole trisiloxane 5% pet. and the patient's cosmetics were positive to EHS 5% pet. and two sunscreens containing EHS on D14. A significant improvement was noticed following avoidance of cosmetics containing drometrizole trisiloxane and ethylhexyl salicylate (6).
The authors state that diagnosis of sensitization to sunscreen compounds usually involves performing complex patch test investigations following a step-by-step approach. Patch/photopatch tests and ROAT with the patient's own sunscreen products, including the breakdown of the individual ingredients and high concentrations and multiple readings (including D7 and D14 late readings), should be performed in order to not miss the diagnosis (6).

Previous cases of allergic cosmetic dermatitis

For previous cases of allergic cosmetic dermatitis to drometrizole trisiloxane see refs. 1-3. Photosensitivity has been reported in refs. 4 and 5.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 4/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 3/123,000.

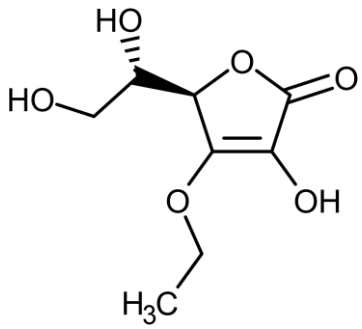
LITERATURE

1 Travassos AR, Claes L, Boey L, Drieghe J, Goossens A. Non-fragrance allergens in specific cosmetic products. Contact Dermatitis 2011;65(5):276-285. doi: 10.1111/j.1600-0536.2011.01968.x.
2 Kohl L, Blondeel A, Song M. Allergic contact dermatitis from cosmetics: retrospective analysis of 819 patch-tested patients. Dermatology 2002;204:334-337. doi: 10.1159/000063379.
3 Hughes TM, Martin JA, Lewis VJ, Stone NM. Allergic contact dermatitis to drometrizole trisiloxane in a sunscreen with concomitant sensitivities to other sun screens. Contact Dermatitis 2005;52(4):226-227. doi: 10.1111/j.0105-1873.2005.0566a.x.
4 Pigatto PD, Guzzi G, Schena D, Guarrera M, Foti C, Francalanci S, et al. Photopatch tests: an Italian multicentre study from 2004 to 2006. Contact Dermatitis 2008;59(2):103-108. doi: 10.1111/j.1600-0536.2008.01374.x.
5 The European Multicentre Photopatch Test Study (EMCPPTS) Taskforce. A European multicentre photopatch test study. Br J Dermatol 2012;166(5):1002-1009. doi: 10.1111/j.1365-2133.2012.10857.x.
6 Pastor-Nieto MA, Gatica-Ortega ME. Allergic contact dermatitis to drometrizole trisiloxane in a woman thereafter diagnosed with frontal fibrosing alopecia. Contact Dermatitis. 2023 Sep;89(3):215-217. doi: 10.1111/cod.14370.
7 Ekstein SF, Hylwa S. Sunscreens: A review of UV filters and their allergic potential. Dermatitis. 2023;34(3):176-190. doi: 10.1097/DER.0000000000000963.

3.24 3-O-ETHYL ASCORBIC ACID

IDENTIFICATION

Description/definition : 3-*o*-Ethyl ascorbic acid is the organic compound that conforms to the structural formula shown below
Classification : Alcohols; ethers; heterocyclic compounds
UPAC name : (2*R*)-2-[(1*S*)-1,2-Dihydroxyethyl]-3-ethoxy-4-hydroxy-2*H*-furan-5-one
Other names : Vitamin C ethyl
CAS registry number : 86404-04-8
EC number : 617-849-3
Functions in cosmetics : EU: skin conditioning. USA: skin-conditioning agents - miscellaneous
Patch testing : 0.05%-5% pet. (1); 1% water (2); 10% water (3,4,5); 5% pet. (6)
Molecular formula : $C_8H_{12}O_6$



Previous chapter to which this is an update

The literature on contact allergy to 3-*o*-ethyl ascorbic acid from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.177, p. 458.

CONTACT ALLERGY (cosmetics)

Case series

In Japan, 160 patients (153 women, 7 men) underwent patch tests from October 2018 to February 2021 with the Japanese baseline series, the cosmetic series (which includes 3-*O*-ethyl-L-ascorbic acid 10% water) and their personal cosmetics. Seven of the 160 patients (4.4%) showed a positive reaction to 3-*O*-ethyl-L-ascorbic acid 10% water. All seven patients had used one or more cosmetics containing this ascorbic acid-derivative, and in six of them, these products could also be patch tested. All six cosmetics clearly showed a positive reaction on D3, except for one lotion, which only showed a doubtful reaction. In all 7 patients facial dermatitis improved after the use of the causative product was discontinued. Among the 153 patients who had a final negative reaction to 3-*O*-ethyl-Lascorbic acid 10% water, 146 patients (95%) had shown negative reactions to this patch test preparation at all times of the analysis. Of these patients, 130 were also further observed until 1 month after patch testing and no late reactions were noted (4). The authors conclude that 3-*O*-ethyl-L-ascorbic acid is a frequent and relevant cosmetic sensitizer, and that the 10% water patch test preparation produces minimal skin irritation and no active sensitization (4).
Comment: It was not mentioned how the patient were selected. Undoubtedly, they were suspected of cosmetic dermatitis, possibly also on the presence of facial dermatitis.

Case reports

A 72-year-old nonatopic woman presented with a 4-year history of erythema on her face, which had worsened and spread over the last 3 weeks. Physical examination showed erythema and vesicles on her face, arms, and legs. She was advised to stop using her daily cosmetics and use only moisturizer and

foundation. With application of topical tacrolimus ointment her symptoms were eliminated completely. Patch tests with the Japanese baseline series, a cosmetic series and her own cosmetics, tested 'as is', were positive to a skin-whitening lotion (D3 ?+, D9 ?+), a skin-whitening cream (D3 +, D9 ?+), and 3-*O*-ethyl-L-ascorbic acid 10% water (D3 +, D9 +), which was an ingredient in both products. Discontinuation of the use of the skin-whitening cosmetics resulted in complete healing of the erythema without relapse (5).

A 42-year-old nonatopic woman presented with a 1-week history of itching eczematous lesions on her face, neck, and hands with intense swelling of the face. The lesions had appeared a few days after the third application of a few drops of an antioxidant concentrate applied once a month for aesthetic purposes. The cosmetic was stopped and lesions disappeared in 2 weeks with once daily application of mometasone furoate ointment. Patch tests with the Italian baseline series and her cosmetic 'as is' were positive (++) to the cosmetic drops. Subsequently, all ingredients of this product, provided by the manufacturer, were patch tested, which yielded an extreme positive (+++) reaction to 3-*O*-ethyl-L-ascorbic acid 5% pet. Twenty controls were negative. Taking oral vitamin C as a dietary supplement did not result in any skin changes (6).

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to 3-*o*-ethyl ascorbic acid see refs. 1-3.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 125/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 3/123,000.

LITERATURE

1 Yagami A, Suzuki K, Morita Y, Iwata Y, Sano A, Matsunaga K. Allergic contact dermatitis caused by 3-*o*-ethyl-l- ascorbic acid (vitamin C ethyl). Contact Dermatitis 2014;70(6):376-377. doi: 10.1111/ cod.12161.

2 Numata T, Kobayashi Y, Ito T, Harada K, Tsuboi R, Okubo Y. Two cases of allergic contact dermatitis due to skin-whitening cosmetics. Allergology International 2015;64(2):194-195. doi: 10.1016/ j.alit.2014.10.007.

3 Victoria-Martínez AM, Mercader-García P. Allergic contact dermatitis due to 3-*o*-ethyl-L-ascorbic acid contained in skin-lightening cosmetics. Dermatitis 2017;28(1):89. doi: 10.1097/DER. 0000000000000260.

4 Suzuki K, Futamura K, Nishimura A, Matsunaga K, Yagami A. Seven cases of allergic contact dermatitis caused by cosmetics containing 3-*O*-ethyl-L-ascorbic acid. Contact Dermatitis. 2022;86(5):421-423. doi: 10.1111/cod.14040.

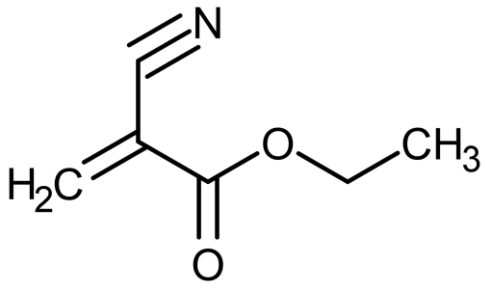
5 Hamanaka M, Kanto H, Mikai H, Tanaka H, Ito T, Washizaki K, et al. A rare case of allergic contact dermatitis caused by 3-*O*-ethyl-L-ascorbic acid in skin-whitening cosmetics identified under immunosuppressive therapy. Contact Dermatitis. 2020;83(6):520-521. doi: 10.1111/cod.13652.

6 Romita P, Foti C, Barlusconi C, Mercurio S, Hansel K, Stingeni L. Allergic contact dermatitis to 3-O-ethyl-L-ascorbic acid: An underrated allergen in cosmetics? Contact Dermatitis. 2020;83:63-64. doi: 10.1111/cod.13528.

3.25 ETHYL CYANOACRYLATE

IDENTIFICATION

Description/definition : Ethyl cyanoacrylate is the cyanoacrylate ester that conforms to the structural formula shown below
Classification : Esters
IUPAC name : Ethyl 2-cyanoprop-2-enoate
CAS registry number : 7085-85-0
EC number : 230-391-5
Wikipedia : https://en.wikipedia.org/wiki/Ethyl_cyanoacrylate
Functions in cosmetics : EU: film forming. USA: not reported
Patch testing : 10% pet. (Chemotechnique [March 2025 not available], SmartPractice)
Molecular formula : $C_6H_7NO_2$



Previous chapter to which this is an update

The literature on contact allergy to ethyl cyanoacrylate from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.178, pp. 459-462.

CONTACT ALLERGY (cosmetics)

Case report

A 13-year-old girl was referred on suspicion of acrodermatitis continua of Hallopeau. For the past 9 months, the patient had suffered from a painful rash on her fingers and disfiguring nail changes. When asked about exposure, she described nail art, regularly applying nail polish and pre-formed, press-on nails attached with nail glue. Physical examination revealed severe pulpitis with erythema, oedema, fissures, and scaling around the nails and dorsal aspects of her fingers and severe nail dystrophy. Patch tests were positive on D7 (+) to 2-hydroxyethyl methacrylate (HEMA) 2% pet., ethylene glycol dimethacrylate (EGDMA) 2% pet., ethyl acrylate 0.1% pet., methyl methacrylate (MMA) 2% pet. and ethyl cyanoacrylate (ECA) 10% pet. According to the ingredient list, the nail glue contained polymethyl methacrylate (poly MMA), polyethylene glycol dimethacrylate (poly EGDMA) and ECA. A diagnosis of allergic contact dermatitis caused by (meth)acrylates in nail glue was established (2).
Ethyl cyanoacrylate was undoubtedly the most important sensitizer, but assuming that polymethyl methacrylate and polyethylene glycol dimethacrylate released some amount of monomers, both MMA and EGDMA may have contributed to the allergic manifestations.

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to ethyl cyanoacrylate see ref. 1.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 25/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 451/123,000.

LITERATURE

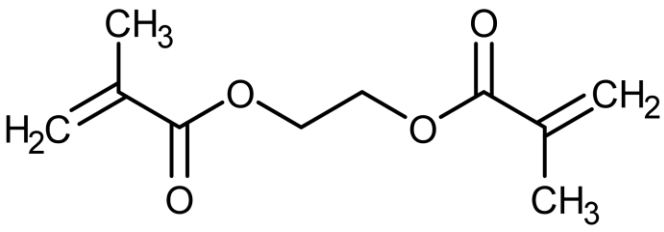
1 Goossens A. Cosmetic contact allergens. Cosmetics 2016, 3, 5; doi:10.3390/cosmetics3010005

2 Quaade AS, Simonsen AB. The bitter side of nail art: A teenage girl's encounter with (meth)acrylate-induced allergic contact dermatitis from nail glue. Contact Dermatitis. 2023;89(4):299-301. doi: 10.1111/cod.14382.

3.26 ETHYLENE GLYCOL DIMETHACRYLATE

IDENTIFICATION

Description/definition : Ethylene glycol dimethacrylate is the organic compound that conforms to the structural formula shown below
Classification : Esters
INCI name EU : Glycol dimethacrylate
IUPAC name : 2-(2-Methylprop-2-enoyloxy)ethyl 2-methylprop-2-enoate
Other names : Ethylene dimethacrylate; EGDMA
CAS registry number : 97-90-5
EC number : 202-617-2
CIR reviews : Int J Toxicol 2005;24(Suppl.5):53-100
Wikipedia : https://en.wikipedia.org/wiki/Ethylene_glycol_dimethacrylate
Functions in cosmetics : EU: nail conditioning
Patch testing : 2.0% pet. (Chemotechnique, SmartPractice)
Molecular formula : $C_{10}H_{14}O_4$



Previous chapter to which this is an update

The literature on contact allergy to glycol dimethacrylate from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.206, pp. 549-550 (incorrectly named Glycol HEMA-methacrylate).

CONTACT ALLERGY (cosmetics)

Case report

A 13-year-old girl was referred on suspicion of acrodermatitis continua of Hallopeau. For the past 9 months, the patient had suffered from a painful rash on her fingers and disfiguring nail changes. When asked about exposure, she described nail art, regularly applying nail polish and pre-formed, press-on nails attached with nail glue. Physical examination revealed severe pulpitis with erythema, oedema, fissures, and scaling around the nails and dorsal aspects of her fingers and severe nail dystrophy. Patch tests were positive on D7 (+) to ethylene glycol dimethacrylate (EGDMA) 2% pet., 2-hydroxyethyl methacrylate (HEMA) 2% pet., ethyl acrylate 0.1% pet., methyl methacrylate (MMA) 2% pet. and ethyl cyanoacrylate (ECA) 10% pet. According to the ingredient list, the nail glue contained polyethylene glycol dimethacrylate (poly EGDMA), polymethyl methacrylate (poly MMA), and ECA. A diagnosis of allergic contact dermatitis caused by (meth)acrylates in nail glue was established (1).
Ethyl cyanoacrylate was undoubtedly the most important sensitizer, but assuming that polyethylene glycol dimethacrylate and polymethyl methacrylate released some amount of monomers, both EGDMA and MMA may have contributed to the allergic manifestations.

Previous cases of allergic cosmetic dermatitis

For previous cases of allergic cosmetic dermatitis to glycol dimethacrylate see refs. 2-7.

Presence in cosmetic products

Ethylene glycol dimethacrylate is not a marketed as a cosmetic ingredient in the USA.

LITERATURE

1 Quaade AS, Simonsen AB. The bitter side of nail art: A teenage girl's encounter with (meth)acrylate-induced allergic contact dermatitis from nail glue. Contact Dermatitis. 2023;89(4):299-301. doi: 10.1111/cod.14382.

2 Travassos AR, Claes L, Boey L, Drieghe J, Goossens A. Non-fragrance allergens in specific cosmetic products. Contact Dermatitis 2011;65(5):276-285. doi: 10.1111/j.1600-0536.2011.01968.x.

3 Fisher AA. Cross reactions between methyl methacrylate monomer and acrylic monomers presently used in acrylic nail preparations. Contact Dermatitis 1980;6(5):345-347. doi: 10.1111/j.1600-0536.1980.tb04961.x.

4 Lazarov A. Sensitization to acrylates is a common adverse reaction to artificial fingernails. J Eur Acad Derm Venereol 2007;21(2):169-174. doi: 10.1111/j.1468-3083.2006.01883.x.

5 Erdmann SM, Sachs B, Merk HF. Adverse reactions to sculptured nails. Allergy 2001;56(6):581-582. doi: 10.1034/j.1398-9995.2001.056006581.x.

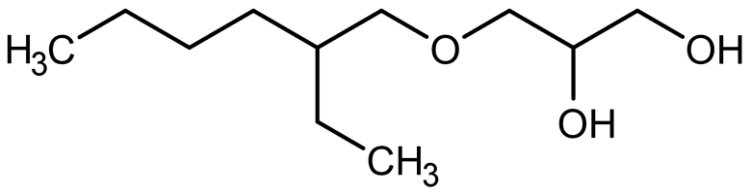
6 Goossens A. Cosmetic contact allergens. Cosmetics 2016, 3, 5; doi:10.3390/cosmetics3010005

7 Laguna C, de la Cuadra J, Martín-González B, Zaragoza V, Martínez-Casimiro L, Alegre V. Allergic contact dermatitis to cosmetics. Actas Dermosifiliogr 2009;100(1):53-60. Spanish. PMID: 19268112.

3.27 ETHYLHEXYLGLYCERIN

IDENTIFICATION

Description/definition : Ethylhexylglycerin is the organic compound that conforms to the structural formula shown below
Classification : Alcohols; ethers
IUPAC name : 3-(2-Ethylhexoxy)propane-1,2-diol
Other names : Octoxyglycerin;
CAS registry number : 70445-33-9
EC number : 408-080-2; 615-116-2
CIR reports : Int J Toxicol 2013;32(Suppl.3):5-21
Wikipedia : https://en.wikipedia.org/wiki/Ethylhexylglycerin
Functions in cosmetics : EU: skin conditioning. USA: deodorant agents; skin-conditioning agents – miscellaneous
Patch testing : 5.0% pet. (Chemotechnique, SmartPractice); sometimes, a higher concentration may be needed to identify contact allergy to ethylhexylglycerin (1)
Molecular formula : $C_{11}H_{24}O_3$



Previous chapter to which this is an update

The literature on contact allergy to ethylhexylglycerin from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.180, pp. 469-470.

CONTACT ALLERGY (cosmetics)

Case series

In the USA, the North American Contact Dermatitis Group (NACDG) published their results of patch testing with ethylhexylglycerin (EHG) 5% pet. in the period 2013-2018. Of 15,560 patients tested to EHG, 39 (0.25%) had positive (final interpretation of 'allergic') reactions, of who 72% were women. The most common anatomic sites of dermatitis were the face (28%) and scattered generalized distribution (26%). Current clinical relevance was high (80%). Personal care products (moisturizers/lotions/creams) were the most common source of exposure to EHG. There were no cases of occupational allergic contact dermatitis. It was concluded that ethylhexylglycerin is a rare contact allergen; the positive frequency of 0.25% is similar to other low allergenic preservatives including parabens, benzyl alcohol, and phenoxyethanol. The patch test concentration of 5.0% seems to be non-irritating (5).

Case report

A 63-year-old woman presented with hyperpigmentation of the face, neck, and chest. Four years prior, she had developed erythema and pruritus on the neck that healed with marked hyperpigmentation. Subsequently, the hyperpigmentation and itch worsened and had spread to the chest and face in the preceding 15 months. Hydrocortisone 2.5% cream provided some itch relief, and hydroquinone was not helpful. On physical examination, she had grey-brown patches on the forehead, upper eyelids, upper lip, and lateral cheeks and reticulated grey-brown patches on the chest and full circumference of the neck. A skin biopsy specimen of the left posterior neck revealed lichenoid dermatitis with prominent pigment incontinence and occasional eosinophils. Patch tests were positive to ethylhexylglycerin (2+) and a

skincare concealer used by the patient, which contained ethylhexylglycerin. She was diagnosed with pigmented contact dermatitis caused by ethylhexylglycerin. The patient was counselled on avoidance of ethylhexylglycerin in conjunction with strict sun protection and reported marked improvement in pruritus and pigmentation. For residual pigment, she was able to reinitiate hydroquinone 4% with further improvement and reported clearance at a 10-month follow-up visit (7).

Previous cases of allergic cosmetic dermatitis

Many cases of allergic cosmetic dermatitis to ethylhexylglycerin have previously been reported, e.g. in refs. 1-4. For a full literature review of this topic please refer to the Monographs in Contact Allergy, Volume 1, Chapter 2.180, pp. 469-470.

OTHER PUBLICATIONS [a]

A 63-year-old female patient had allergic contact dermatitis from ethylhexylglycerin in a lubricating gel for the treatment of vulval lichen sclerosus (a medical device) and 2 ultrasonic gels for Doppler ultrasound and cardiac echography (6).

[a] Literature on contact allergy to ethylhexylglycerin that was found in *Contact Dermatitis* or/and *Dermatitis* from September 2017 through March 2025, in which there was no direct link with cosmetic products.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 4724/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 22,656/123,000.

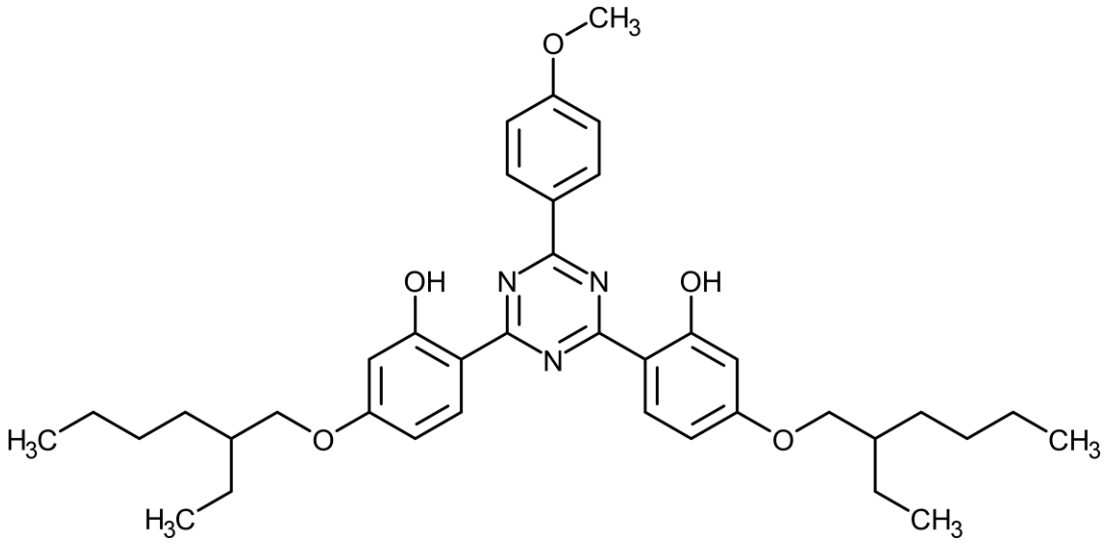
LITERATURE

1 Aerts O, Verhulst L, Goossens A. Ethylhexylglycerin: a low-risk, but highly relevant, sensitizer in 'hypo-allergenic' cosmetics. Contact Dermatitis 2016;74(5):281-288. doi: 10.1111/cod.12546.
2 Andersen KE. Ethylhexylglycerin – a contact allergen in cosmetic products. Dermatitis 2012;23(6):291. doi: 10.1097/DER.0b013e31827596b1.
3 Harries C, Mühlenbein S, Geier J, Pfützner W. Allergic contact dermatitis caused by ethylhexylglycerin in both an ointment and a skin aerosol. Contact Dermatitis 2016;74(3):181-182. doi: 10.1111/cod.12471.
4 Hagen SL, Warshaw E. The latest occult "hypoallergenic" allergen: Ethylhexylglycerin. Dermatitis 2017;28(3):220-222. doi: 10.1097/DER.0000000000000249.
5 Warshaw EM, Buonomo M, Maibach HI, Taylor JS, Zug KA, et al. Patch testing to ethylhexylglycerin: The North American Contact Dermatitis Group experience, 2013-2018. Dermatitis. 2022;33(1):36-41. doi: 10.1097/DER.0000000000000709.
6 Allichon S, Trebuchon F, Dereure O, Raison-Peyron N. A non-cosmetic allergic contact dermatitis to ethylhexylglycerin. Contact Dermatitis. 2024;90(3):310-312. doi:10.1111/cod.14467.
7 Hassan S, Chen JK. A case of pigmented contact dermatitis caused by ethylhexylglycerin. Dermatitis. 2022;33(3): e23-e24. doi: 10.1097/DER.0000000000000873.

3.28 BIS-ETHYLHEXYLOXYPHENOL METHOXYPHENYL TRIAZINE

IDENTIFICATION

Description/definition : bis-Ethylhexyloxyphenol methoxyphenyl triazine is the heterocyclic compound that conforms to the structural formula shown below
Classification : Heterocyclic compounds; phenols
Chemical/IUPAC name : 2,2'-[6-(4-Methoxyphenyl)-1,3,5-triazine-2,4-diyl]bis[5-[(2-ethylhexyl)oxy]-phenol]
Other names : Bemotrizinol; anisotriazine; Tinosorb® S
CAS registry number : 187393-00-6
EU number : 425-950-7
Wikipedia : https://en.wikipedia.org/wiki/Bemotrizinol (Bemotrizinol)
Functions in cosmetics : EU: skin conditioning; UV-absorber; UV-filter. USA: hair conditioning agents; sunscreen agents
EU cosmetic restrictions : Regulated in Annex VI/25 of the Regulation (EC) 2009/1223
Patch testing : 10.0% pet. (Chemotechnique, SmartPractice)
Molecular formula : $C_{38}H_{49}N_3O_5$



Previous chapter to which this is an update

The literature on contact allergy to bis-ethylhexyloxyphenol methoxyphenyl triazine from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.181, pp. 477-478.

CONTACT ALLERGY (cosmetics)

General

A very useful review article on sunscreen allergy was published in 2023 in *Dermatitis* (5).

Case reports

A 37-year-old woman reported an itchy erythematous and desquamative eruption of the face, neck, chest and forearms, that had emerged 6 hours following the application of 2 sunscreen products. A repeated open application test (ROAT) with both sunscreens on the forearm twice a day, without sun exposure, was strongly positive after one day. Patch tests with the European baseline series, the cosmetic series and the ingredients of these sunscreens, provided by their manufacturers, showed a strong positive reaction to

nickel (++) (past relevance) and to bis-ethylhexyloxyphenol methoxyphenyl triazine 10% pet. (++) provided by the manufacturer of one of the creams. The same ingredient, provided by the other manufacturer, tested at 2.5% pet, was negative (1).

A 51-year-old non-atopic woman presented with erythema and scales on her face for 3 months. Patch tests with the Japanese baseline series, her cosmetics, and several cosmetic allergens, were positive to a sunscreen cream tested 'as is', nickel sulfate, mercaptobenzothiazole and thiuram mix. When patch tested with the ingredients of this cosmetic, provided by its manufacturer, there were positive reactions to bis-ethylhexyloxyphenol methoxyphenyl triazine (Tinosorb S) 10% pet., polysilicone-15 10% pet. and an undisclosed fragrance 5% pet. Subsequent ROATs were positive to both UV-filters but negative to the fragrance (2).

A third patient with allergic contact dermatitis to bis-ethylhexyloxyphenol methoxyphenyl triazine was reported from Spain in 2020 (3). This was a 39-year-old nonatopic housewife who had a 2-year history of pruritic erythematous scaly plaques involving both eyelids and periorbital skin. Patch tests revealed positive reactions to a tinted sunscreen cream and 2 of its ingredients, ethylhexyloxyphenol methoxyphenyl triazine (tested 5% pet.) and Scutellaria baicalensis root extract (3).

Previous cases of allergic cosmetic dermatitis

For previous cases of allergic cosmetic dermatitis to bis-ethylhexyloxyphenol methoxyphenyl triazine see ref. 4 (in fact only one positive patch test, of which the clinical relevance was not mentioned).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 20/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 39/123,000.

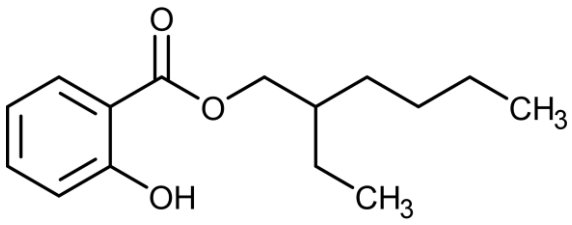
LITERATURE

1 Badaoui A. Allergic contact dermatitis to bis-ethylhexyloxyphenol methoxyphenyl triazine (Tinosorb S) in a sunscreen: An emerging allergen? Contact Dermatitis. 2024;91(5):443-445. doi: 10.1111/cod.14647.
2 Suzuki K, Futamura K, Sugiyama M, Matsunaga K, Yagami A. Allergic contact dermatitis caused by dimethicodiethylbenzalmalonate (polysilicone-15, Parsol SLX) and bis-ethylhexyloxyphenol methoxyphenyl triazine (Tinosorb S) in sunscreen cream. Contact Dermatitis. 2022 Jul;87(1):108-110. doi: 10.1111/cod.14112.
3 Luna-Bastante L, Gatica-Ortega M-E, Pastor-Nieto M-A, et al. Allergic contact dermatitis to Tinosorb S, Scutellaria baicalensis, and other emerging allergens in cosmetics. Contact Dermatitis. 2020;82(5):307-309. doi: 10.1111/cod.13460.
4 The European Multicentre Photopatch Test Study (EMCPPTS) Taskforce. A European multicentre photopatch test study. Br J Dermatol. 2012;166(5):1002-1009. doi: 10.1111/j.1365-2133.2012.10857.x
5 Ekstein SF, Hylwa S. Sunscreens: A review of UV filters and their allergic potential. Dermatitis. 2023;34(3):176-190. doi: 10.1097/DER.0000000000000963.

3.29 ETHYLHEXYL SALICYLATE

IDENTIFICATION

Description/definition : Ethylhexyl salicylate is the ester of 2-ethylhexyl alcohol and salicylic acid, that conforms to the structural formula shown below
Classification : Esters; phenols
IUPAC name : 2-Ethylhexyl 2-hydroxybenzoate
Other names : Octyl salicylate; octisalate
CAS registry number : 118-60-5
EC number : 204-263-4
CIR reports : Int J Toxicol 2003;22(Suppl.3):1-108
SCCS opinions : SCCNFP, 21 January 1998; Final report April 09, 2019
Wikipedia : https://en.wikipedia.org/wiki/2-Ethylhexyl_salicylate
Functions in cosmetics : EU: UV-absorber; UV-filter. USA: fragrance ingredients; light stabilizers; sunscreen agents
EU cosmetic restrictions : Regulated in Annex VI/20 of the Regulation (EC) 2009/1223
Patch testing : 5% pet. and 10% pet. (Chemotechnique); 10% pet. (Smartpractice [octisalate]); late readings at D7 and D14 may be warranted when negative at the second reading on D3/4 (5)
Molecular formula : $C_{15}H_{22}O_3$



Previous chapter to which this is an update

The literature on contact allergy to ethylhexyl salicylate from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.183, pp. 479-481.

CONTACT ALLERGY (cosmetics)

Case series

In Spain, from January 2021 to February 2022, 33 patients with frontal fibrosing alopecia (FFA) were patch tested and photopatch tested with the European Photopatch Series, including ethylhexyl salicylate (EHS) 10% pet. Positive patch tests to EHS were observed in 9 of 33 (27%) individuals. In seven cases, the patch test reactions to EHS were equally intense in both the UVA-irradiated and non-irradiated areas; in one patient, photosensitisation was suspected and in another photo-aggravation. Two patients had positive reactions to EHS 10% pet. provided by a sunscreen manufacturer, but were negative to the Chemotechnique commercial EHS 10% pet. test hapten.
Reactions to a variety of additional allergens were identified in all cases, with gallates (5/9) and propolis (3/9) being the most frequent. Regarding other salicylates, patch test reactions to benzyl salicylate were identified in 5 of 9 cases and to homosalate (homomenthyl salicylate) in 2 of 9. Four of nine patients also reacted to their personal sunscreens containing EHS. All were women with a mean age of 54 (30 - 65). Five patients had been diagnosed with FFA before the patch tests; four were diagnosed with FFA during the patch test investigations.
The authors are cautious in linking contact allergy with frontal fibrosing alopecia. Contact sensitisation from cosmetics including sunscreens in patients with FFA can be expected as a result of an increased

exposure. However, whether sensitisation to these allergens may impact the pathogenesis of FFA remains speculative, according to them (7).
This article provides an excellent literature review of contact allergy to ethylhexyl salicylate and allergic contact dermatitis to EHS and other allergens in patients with frontal fibrosing alopecia.

Case reports

A 39-year-old woman presented with facial dermatitis, suspected to have been caused by a cosmetic product, such as a moisturizer or sunscreen. Patch testing with the extended European baseline, fragrance, cosmetics and sunscreen chemical series and her facial sunscreen cream SPF 30 (tested 'as is') were positive (D4 +) to metals (nickel, cobalt; history of previous reactions to jewellery), fragrance substances (limonene, anise alcohol, benzyl salicylate), sunscreen chemicals (homosalate [homomenthyl salicylate], ethylhexyl salicylate) and to the sunscreen cream. This product contained homosalate, limonene, ethylhexyl salicylate, capryloyl salicylic acid and salicylic acid. Sensitisation to multiple salicylates was an unexpected finding. There was no relevant history of reactions to previous oral salicylate-containing medication such as Aspirin (acetylsalicylic acid). The patient was advised to discontinue all current products containing the identified allergens including all salicylate-containing products (6).

A 45-year-old non-atopic woman was referred for facial dermatitis, that she related to one particular sunscreen product (sunscreen A). The patient had been using sunscreens daily for years because of hyperpigmentation. She also recalled pruritic reactions involving several locations that she related to other sunscreens, cosmetics and other materials. Patch tests with the Spanish baseline (GEIDAC), sunscreen, fragrances and cosmetic series were positive for nickel sulfate and mercapto mix (past and unknown relevance, respectively). A ROAT with sunscreen A was positive on day 7. Yet, subsequent patch tests with its 24 individual ingredients, including ethylhexyl salicylate (EHS) 4% pet. and drometrizole trisiloxane 10% pet. obtained from the manufacturer, were negative on D2, D4 and D6.
One year later, the patient developed frontal, occipital, eyebrow, and axillary hair loss, diagnosed as frontal fibrosing alopecia. Since eczematous reactions persisted, further patch and photopatch tests with the European photopatch extended series as well as the patient's cosmetics were performed and yielded positive reactions to drometrizole trisiloxane 10% pet. (D7 and D14, equal strength irradiated and unirradiated) and one compact sunscreen (sunscreen B) containing drometrizole trisiloxane (positive on D4, D7 and D14 irradiated and on D14 unirradiated). Drometrizole tested negative. One year thereafter, patch tests with 22 individual ingredients of sunscreen B including drometrizole trisiloxane 5% pet. and the patient's cosmetics were positive to ethylhexyl salicylate (EHS) 5% pet. and two sunscreens containing EHS on D14. A significant improvement was noticed following avoidance of cosmetics containing ethylhexyl salicylate and drometrizole trisiloxane (5).
The authors state that diagnosis of sensitization to sunscreen compounds usually involves performing complex patch test investigations following a step-by-step approach. Patch/photopatch tests and ROAT with the patient's own sunscreen products, including the breakdown of the individual ingredients and high concentrations and multiple readings (including D7 and D14 late readings), should be performed in order to not miss the diagnosis (5).

A woman in her fifties with a history of polymorphous light eruption had suffered dermatitis on her face and both arms following the use of several sunscreen products and a day cream. Patch tests with the European baseline series, a cosmetic, a sunscreen and a fragrance series, and the products used along with their ingredients, were positive to ethylhexyl salicylate 10% pet. (D2 ?+; D4 +), and to four of her sunscreen products and a day cream, tested 'as is' (+ on D2 and D4), all of which contained this UV filter. Later, she was tested with benzyl salicylate 10% pet., which also elicited a positive reaction (D2 ?+; D4 +). No current relevance could be found, and it was suggested to be a cross-reaction (8).
These authors have tested 320 patients in their tertiary referral centre with ethylhexyl salicylate, and two more patients showed positive patch test reactions: a 44-year-old woman who had developed dermatitis caused by multiple sunscreens and a 62-year-old woman sensitized to EHS by the use of a day cream. Both patients were tested with benzyl salicylate and one had a positive reaction to this fragrance ingredient (8).

Cross-reactions

Ethylhexyl salicylate can very likely cross-react with benzyl salicylate (7,8).

Previous cases of allergic cosmetic dermatitis

For examples of previous case reports and case series of allergic cosmetic dermatitis to ethylhexyl salicylate see refs. 1-4. For a full literature review please refer to Chapter 2.183 of the Monographs in Contact Allergy, Volume 1.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 1966/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 2441/123,000.

LITERATURE

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6 Teo YX, White IR, McFadden JP. Allergic contact dermatitis to multiple salicylates: A case report. Contact Dermatitis. 2024;90(2):195-197. doi:10.1111/cod.14464.
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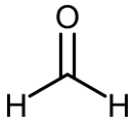
8 Dens A-C, Goossens A, Darcis J, Huygens S, Lambrecht C, Gilissen L. Allergic contact dermatitis caused by ethylhexyl salicylate with possible cross-reactivity with benzyl salicylate. Contact Dermatitis. 2019;81(4):317-318. doi: 10.1111/cod.13308.

3.30 FORMALDEHYDE

IDENTIFICATION

Description/definition : Formaldehyde is a volatile aldehyde that conforms to the structural formula shown below
Classification : Aldehydes
IUPAC name : Formaldehyde
Other names : Methanal; methyl aldehyde; methylene oxide; oxomethane; oxymethylene
CAS registry number : 50-00-0
EC number : 200-001-8
CIR reports : J Am Coll Toxicol 1984;3:157-184; Int J Toxicol 2013;32(Suppl.4):5-32
SCCS opinions : SCCS/1538/14; SCCNFP/587/02
Wikipedia : https://en.wikipedia.org/wiki/Formaldehyde
Functions in cosmetics : EU: preservative. USA: cosmetic biocides; denaturants; preservatives
EU cosmetic restrictions : Regulated in Annex II/1577 of the Regulation (EU) 2019/831 (prohibited)
Patch testing : 1.0% and 2% water (Chemotechnique, SmartPractice); 1.0% pet. (Chemotechnique)
Molecular formula : CH_2O



Previous chapter to which this is an update

The literature on contact allergy to formaldehyde from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.188, pp. 492-516.

CONTACT ALLERGY (cosmetics)

General

Currently, the use of formaldehyde is not allowed in cosmetic products in the European Union. Most cases of allergic cosmetic dermatitis to this preservative are caused by the use of formaldehyde-donors, e.g., imidazolidinyl urea, diazolidinyl urea, quaternium-15 and DMDM hydantoin.

Case reports

A 21-year-old non-atopic woman had worked as hairdresser for 3 years when bullous lesions appeared on both cheeks. She had suffered from facial dermatitis for 3 months before presentation. Patch tests with the Swedish baseline series, a hairdresser series, a cosmetic series and various work materials, such as shampoos, were negative on D3. On D6, 1 day before the intended second reading, the patient consulted the general dermatologist because of severe exacerbation of her facial lesions. The diagnosis at this point was nummular microbial eczema. Despite treatment, the patient's dermatitis always became worse when she worked. A new patch test session was started with the same series as before. The patient now had reactions to formaldehyde 1% water (D3+, D7?+) and ?+ reactions to 2 shampoos 5% water on D3. A chemical analysis with the chromotropic acid method showed relevant amounts of formaldehyde in both shampoos used at work and at home. The patient's dermatitis cleared after she avoided formaldehyde-containing skin care products. Two months later, facial papulopustules reappeared. When her current shampoo and new facial cream were checked, they both contained formaldehyde. DMDM hydantoin was labelled on the shampoo, but the patient had failed to identify this as a formaldehyde releaser. The cream was unlabelled. The patient remained clear at follow-up 3 months later (1).

A 15-year-old non-atopic girl suddenly developed pruritic papular dermatitis involving the face, body, and hands. The dermatologist suspected nummular dermatitis. Despite treatment, an exacerbation of the dermatitis was seen in the groins and axillae with crusts, and impetigo was suspected. Internal antibiotics were prescribed, and the patient was referred for patch testing. While waiting, she had a recurrence, and systemic corticosteroids were given. At presentation, she had suffered from skin lesions for 7 months. Patch tests with the Swedish baseline series showed a positive patch test to formaldehyde. The shampoo that she used was analysed for the presence of formaldehyde, and a concentration of >40 μg/ml was found. Because she also had perioral dermatitis, she was given tetracyclines, and the dermatitis eventually cleared. The skin lesions on the body and hands vanished when she stopped using skin care products containing formaldehyde or formaldehyde-releasing preservatives (1).

Previous cases of allergic cosmetic dermatitis

Formaldehyde is a well-known contact allergen, which is included in most international and national baseline series for patch testing. There is extensive literature on cosmetic allergy from formaldehyde. Please refer to the Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.188, pp. 492-516.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 6/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 33/123,000.

OTHER PUBLICATIONS [a]

Presence of formaldehyde in cosmetic products

- In the USA, high-performance liquid chromatography analysis found 5 of 29 nail polishes to contain formaldehyde, 4 of which were advertised as formaldehyde-free (2).
- In the USA, 54 baby and adult personal care products were tested with the chromotropic acid method. A blinded investigator graded the color change as mild, moderate, or strong. All 8 products declaring formaldehyde or/and formaldehyde-releasers resulted in a deep purple color change, indicating a strong reaction. Of the 46 products in which no formaldehyde(releasers) were declared, 4 (8.6%) were found to release formaldehyde. All 4 resulted in a light purple color change, indicating a mild reaction (4).
- In the USA, 51 popular and highly reviewed baby and toddler wet wipe products, none of which declared formaldehyde or formaldehyde-releasers, were tested for the presence of formaldehyde using the chromotropic acid method. Twelve wipes (24%) released formaldehyde (8 mild, 4 moderate/strong). Chromotropic acid method testing of 9 wipes (18%) was indeterminate and 30 (59%) were negative (6).

Allergic contact dermatitis from non-cosmetic products

- A 66-year-old woman had a 5-year-history of dermatitis of both hands. At work and when cleaning her house, she wore plastic, rubber or nitrile gloves. Patch tests were positive to formaldehyde, formaldehyde-releasers and several of the gloves. The strongest reaction was to a latex-free glove recommended as protective wear for patients with allergic hand dermatitis to natural rubber latex and rubber accelerators. The manufacturer was 99% sure that the glove did not contain formaldehyde. However, a chromotropic acid test showed a mild purple color change, indicating that a small amount of formaldehyde was released from the gloves (7).
- A 19-month-old child had airborne ACD from formaldehyde in cigarette smoke produced by his parents (14).

Presence of formaldehyde in non-cosmetic products

- Of 16 e-liquids of electronic cigarettes purchased in the USA, 4 (25%) were positive for the presence of formaldehyde as shown by the chromotropic acid method (3).

- In the USA, 77 clothing scraps from local department store tailors and 22 upholstery fabric cuttings from a furniture reupholstery store were collected and analysed with the chromotropic acid method to detect formaldehyde. All 99 clothing and upholstery fabrics tested negative for formaldehyde release. The authors concluded that textile manufactures may be using non-formaldehyde resins for durable press finishing in clothing likely to be tailored as well as fabrics used for furniture reupholstery (5).
- Thirteen products (seven eye drops [three eye lubricants, two topical antibiotics, and two antibiotic and corticosteroid combinations], two emollients, two oral anti-ulcer gels, and two first-aid antiseptics) were investigated in Lithuania for the presence of formaldehyde. Four products were positive in the chromotropic acid method, but this could not be confirmed in the high-performance liquid chromatography (HPLC) method. By rather complex calculations the authors tried to answer the question whether low formaldehyde contents (<10 ppm) is clinically relevant, i.e. whether it can cause allergic contact dermatitis in patients (highly) sensitized to formaldehyde (13).
- Analyses of formaldehyde in predispersed tattoo inks (15), commercial essential oils (16), and in eyelash glues (17) have been reported.

Test concentration of formaldehyde

- In a study from the International Contact Dermatitis Research Group, 2778 patients were tested with formaldehyde 1.0% water and 2766 of them to 2.0% water. Sixty-five patients (2.3%) had positive patch test reactions interpreted as contact allergy to formaldehyde. Thirty-six reacted only to 2.0% water, 21 patients reacted to both concentrations, and 8 patients reacted only to 1.0% water. There were 0.8% irritant reactions to 2% versus 0.1% to formaldehyde 1%. It was concluded that the increased formaldehyde patch test concentration to 2.0% water revealed more cases of formaldehyde contact allergy than the 1% concentration (8).
- In Spain, in 2017, 1136 patients were patch tested with the Spanish baseline series with two patch test support materials: formaldehyde (FA) at 180 µg/cm^2 (146 µg) in the TRUE Test and formaldehyde 2% water. A total of 52 patients reacted positively to FA 2% water (4.6%); only 13 patients (1.1%) reacted to formaldehyde in the TRUE Test and all of them showed a positive reaction to formaldehyde 2% water. In the 39 patients who reacted positively to FA 2% water but not to TRUE Test, 3 cases were assessed as irritant reactions. The authors concluded that the TRUE Test is a highly specific patch testing preparation (100% specificity), but with very low sensitive power (33% sensitivity) to detect formaldehyde sensitization compared with FA 2% water (10).
- The European Surveillance system of contact allergies (ESSCA) has studied the relationship between contact allergy to formaldehyde and allergy to formaldehyde-releasers (FR). A maximum of 15,067 patients were tested to formaldehyde 2% water and at least one FR. The percentage of isolated reactions to FR, without co-reactivity to formaldehyde 2% water, for each FR were 47% for quarternium-15 1% pet., 67% for imidazolidinyl urea 2% pet., 64% for diazolidinyl urea 2% pet., 83% for DMDM hydantoin 2% pet. and 96% for 2-bromo-2-nitropropane-1,3-diol (bronopol) 0.5% pet. It was concluded that formaldehyde 2% water is an inadequate screen for contact allergy to the formaldehyde-releasers (11).

Other information

- Patients with positive patch test to formaldehyde can be safely vaccinated with formaldehyde-containing vaccines (9).
- In a multicenter study in Spain performed in 2017, 2971 patients were patch tested with the Spanish baseline series including formaldehyde 2% water. 113 patients (3.80%) reacted positively, and only four irritant reactions were recorded. Twelve occupational cases were observed, mostly in women (health care workers and hairdressers), and the hands were the most frequently involved areas. The frequency of sensitization to formaldehyde was higher than in previous studies in Spain (ranging from 2.58% to 1.38%), which was ascribed to the fact that formaldehyde 2% water detects more cases of sensitization than the previously used 1% in water. The 14 authors concluded ‘that formaldehyde 2% water is the optimal concentration patch test in the Spanish baseline series’ (12).
  Comment: The conclusion of the authors that 2% water is the optimal concentration is not

substantiated by proper data, as they did not test formaldehyde 1% alongside 2%. But even when 2% would have detected more cases of formaldehyde allergy than 1% (which has indeed been demonstrated [8]), then the conclusion that 2% is 'optimal' would still be invalid, as no other concentrations or vehicles, which might have performed even better, were tested.

[a] Literature on contact allergy to formaldehyde that was found in *Contact Dermatitis* or/and *Dermatitis* from September 2017 through March 2025, in which there was no direct link with cosmetic products.

LITERATURE

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7 Liou YL, Schlarbaum JP, Kimyon RS, Hylwa SA. Formaldehyde in hypoallergenic household gloves. Dermatitis. 2019;30(1):75-77. doi: 10.1097/DER.0000000000000426.

8 Isaksson M, Ale I, Andersen KE, Goh CL, Goossens A, Jerajani H, et al. Patch testing with formaldehyde 2.0% (0.60 mg/cm2) detects more contact allergy to formaldehyde than 1.0. Dermatitis. 2019;30(6): 342- 346. doi: 10.1097/DER.0000000000000510.

9 Bindslev-Jensen U, Mortz CG, Andersen KE, Bindslev-Jensen C. Patients with positive patch test to formaldehyde can be safely vaccinated with formaldehyde-containing vaccines. Contact Dermatitis. 2023;89(2):107-110. doi: 10.1111/cod.14350.

10 Sanz-Sánchez T, Heras Mendaza F, González Pérez R, Córdoba Guijarro S, Gatica-Ortega ME, Fernández Redondo V, et al. Comparative study of formaldehyde 2% in aqueous solution vs TRUE Test in detecting formaldehyde sensitization. Contact Dermatitis. 2021;85(3):358-359. doi: 10.1111/cod.13848.

11 Whitehouse H, Uter W, Geier J, Ballmer-Weber B, Bauer A, Cooper S, et al. Formaldehyde 2% is not a useful means of detecting allergy to formaldehyde releasers- results of the ESSCA network, 2015-2018. Contact Dermatitis. 2021;84(2):95-102. doi: 10.1111/cod.13691.

12 Sanz-Sánchez T, Mercader García P, Silvestre Salvador JF, Heras Mendaza F, Gatica Ortega ME, González Pérez R, et al. Patch testing with formaldehyde 2% aq. - A multicenter study in Spain. Contact Dermatitis. 2019;81(6):458-459. doi: 10.1111/cod.13361.

13 Linauskiene K, Zimerson E, Malinauskiene L, Isaksson M. Low amount of formaldehyde in topical medication and cosmetics: Is it clinically relevant? Contact Dermatitis. 2019;81(1):60-61. doi: 10.1111/cod.13220.

14 Freeman T, Shmuylovich L, Sheinbein DM. Allergic contact dermatitis to formaldehyde in cigarette smoke in a nonsmoker. Dermatitis. 2024;35(5):519-520. doi: 10.1089/derm.2023.0219.

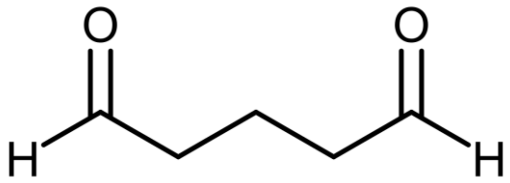
15 Liou YL, Voller LM, Liszewski W, Ericson ME, Siegel PD, Warshaw EM. Formaldehyde release from predispersed tattoo inks: Analysis using the chromotropic acid method. Dermatitis. 2021;32(5):327-332. doi: 10.1097/DER.0000000000000663.

16 Voller LM, Shaver R, Persson L, Bruze M, Hylwa SA. Investigation of commercial essential oils for formaldehyde content. dermatitis. 2023 Sep-Oct;34(5):460-461. doi: 10.1097/DER.0000000000000850.

17 Xiong M, Shaik JA, Hylwa S. Formaldehyde Release From Eyelash Glues: Analysis using the chromotropic acid method. Dermatitis. 2022;33(6):442-446. doi: 10.1097/DER.0000000000000910.

3.31 GLUTARALDEHYDE

Description/definition	: Glutaraldehyde is the dialdehyde that conforms to the formula shown below
Chemical class	: Aldehydes
INCI name USA	: Glutaral
UPAC name	: 1,5-Pentanedial
Other names	: Pentane-1,5-dial; glutardialdehyde
CAS registry number	: 111-30-8
EC number	: 203-856-5
CIR reports	: J Am Coll Toxicol 1996;15:98-139
Wikipedia	: https://en.wikipedia.org/wiki/Glutaraldehyde
Functions in cosmetics	: EU: preservative. USA: cosmetic biocides; fragrance ingredients; preservatives
EU cosmetic restrictions	: Regulated in Annex V/48 of the Regulation (EC) No. 1223/2009
Patch testing	: 0.2% pet. and 0.5% pet. (Chemotechnique); 0.3% pet. and 1% pet. (SmartPractice)
Molecular formula	: $C_5H_8O_2$



Previous chapter to which this is an update

The literature on contact allergy to glutaral from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.191, pp. 519-524.

CONTACT ALLERGY (cosmetics)

Case report

A 50-year-old woman had suffered lifelong atopic dermatitis. When she was around 50 years old, the dermatitis began to affect her face, resulting in bright erythema and edema of the entire face. Biopsy results revealed spongiotic dermatitis with eosinophils with mucin and spongiosis of several hair follicles. Patch testing with the NACDG standard series and an external agents and emulsifiers series revealed 2+ reactions to glutaraldehyde, MCI/MI, propolis, Myroxylon pereirae resin, and iodopropynyl butylcarbamate. Each of these allergens was relevant to her current personal care product usage (comment: this is not correct, as Myroxylon pereirae *as such* is not used in cosmetics). After 2 months of allergen avoidance, the patient exhibited dramatic improvement, with complete clearance of the dermatitis on the face and legs. Three years later, her face remains clear and she does not use any topical treatments on her face or body (1).

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to glutaraldehyde see ref. 2.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 3/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 3/123,000.

LITERATURE

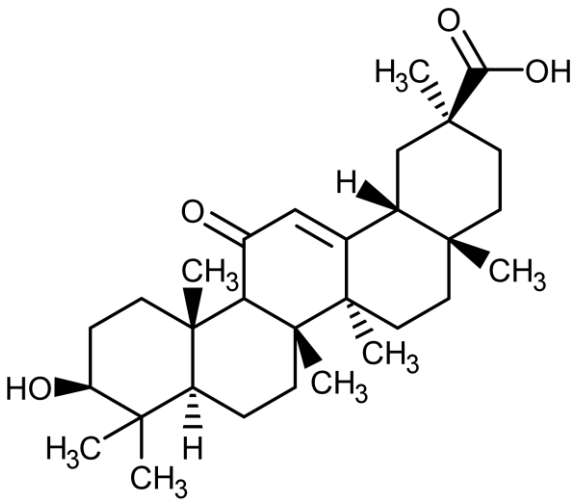
1 Semaan S, Raffi J, Murase JE. Allergic contact dermatitis masquerading as atopic dermatitis. Int J Womens Dermatol. 2020;6(4):329-330. doi: 10.1016/j.ijwd.2020.04.005.

2 Jaworsky C, Taylor JS, Evey P, Handel D. Allergic contact dermatitis to glutaraldehyde in a hair conditioner. Cleveland Clin J Med 1987;54(5):443-444. doi: 10.3949/ccjm.54.5.443.

3.32 GLYCYRRHETINIC ACID

IDENTIFICATION

Description/definition : Glycyrrhetinic acid is an organic compound derived from glycyrrhizic acid or shredded licorice roots, which conforms to the structural formula shown below
Classification : Sterols
IUPAC name : (2*S*,4a*S*,6a*R*,6a*S*,6b*R*,8a*R*,10*S*,12a*S*,14b*R*)-10-Hydroxy-2,4a,6a,6b,9,9,12a-heptamethyl-13-oxo-3,4,5,6,6a,7,8,8a,10,11,12,14b-dodecahydro-1*H*-picene-2-carboxylic acid
Other names : Enoxolone; glycyrrhetic acid; olean-12-en-29-oic acid, 3-hydroxy-11-oxo-, (3β,20β)-; uralenic acid; glycyrrhetin
CAS registry number : 471-53-4
EC number : 207-444-6
CIR reports : Int J Toxicol 2007;26(Suppl.2):79-112
Wikipedia : https://en.wikipedia.org/wiki/Enoxolone (Enoxolone)
Functions in cosmetics : EU: skin conditioning. USA: skin-conditioning agents - miscellaneous
Patch testing : 10% pet. (2)
Molecular formula : $C_{30}H_{46}O_4$



Previous chapter to which this is an update

The literature on contact allergy to glycyrrhetinic acid from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.207, pp. 551-552.

CONTACT ALLERGY (cosmetics)

Case report

A 9-year-old atopic girl had suffered an episode of acute eczema on both eyelids after applying an emollient cream for 12 days. The episode was treated in the emergency department with oral corticosteroids and discontinuation of the cream, with complete resolution of the symptoms. A ROAT became positive after 2 days. Patch tests were positive to potassium dichromate (++), cobalt chloride (++) and the cream 'as is' (++). Subsequently, patch testing with the 19 individual components of the eyelid emollient, supplied by the manufacturer in the concentrations present in the cream, showed a positive reaction only to glycyrrhetinic acid 10% pet. (D2 and D4 ++).

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to glycyrrhetinic acid see ref. 1.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 122/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 54/123,000.

LITERATURE

1 Sasseville D, Desjardins M, Almutawa F. Allergic contact dermatitis caused by glycyrrhetinic acid and castor oil. Contact Dermatitis 2011;64(3):168-169. doi: 10.1111/j.1600-0536.2010.01829.x.

2 Sánchez-García V, Taboada-Paz L, Hernández-Quiles R, Betlloch-Mas I, Silvestre JF. Allergic contact dermatitis from glycyrrhetinic acid contained in a cream for palpebral eczema. Contact Dermatitis. 2023;88(4):320-321. doi:10.1111/cod.14271.

3.33 GLYCYRRHIZA INFLATA ROOT EXTRACT

IDENTIFICATION

Description/definition : Glycyrrhiza inflata root extract is an extract of the roots of *Glycyrrhiza inflata*, Leguminosae
Classification : Botanical products and botanical derivatives
CIR reports : Final report, September 23, 2008
Wikipedia : https://en.wikipedia.org/wiki/Glycyrrhiza_inflata (Glycyrrhiza inflata)
Functions in cosmetics : EU: skin conditioning. USA: Skin-conditioning agents - miscellaneous
Patch testing : 1% pet.; 1% alc. (2);

Previous chapter to which this is an update

The literature on contact allergy to glycyrrhiza inflata root extract from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.209, pp. 555

CONTACT ALLERGY (cosmetics)

Case reports

A 31-year-old woman with acne had a 2-year history of pruritic erythematous-scaly plaques involving her eyelid, periorbital, and facial-cervical areas. Patch tests with the Spanish Contact Dermatitis Research Group (GEIDAC) baseline series, additional allergens, a fragrance and a cosmetic series, benzoyl peroxide 1% pet. and the patient's own products (tested 'as is') showed positive reactions to 2 cosmetic anti-acne products. Further patch tests with their individual ingredients, provided by the manufacturers, were positive to Glycyrrhiza inflata root extract 1% alc. (D4 and D7 ++) in one of the products. Twenty controls were negative. Of the ingredients of the other product, there was a reaction to benzoyl peroxide 2.6% pet., which was considered to be an irritant reaction (2).

Another patient had allergic contact dermatitis to 'licorice root extract' (tested 25% pet.) in a cosmetic 'eczema relief cream' and a post-shave balm, in the cream in the form of Glycyrrhiza inflata root extract and in the balm as dipotassium glycyrrhizate and ammonium glycyrrhizate (3). Rather annoying that the authors did not use INCI names in the title of their article and in the text.

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to glycyrrhiza inflata root extract see ref. 1.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 13/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 36/123,000.

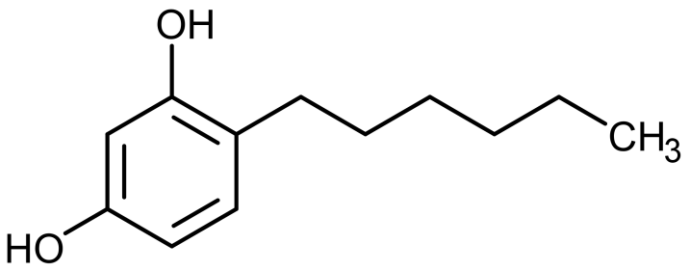
LITERATURE

1 Wuyts L, van Hoof T, Lambert J, Aerts O. Allergic contact dermatitis caused by aftershave creams containing Glycyrrhiza inflata. Contact Dermatitis 2017;77(1):49-51. doi: 10.1111/cod.12725.
2 Gatica-Ortega ME, Pastor-Nieto MA. Allergic contact dermatitis to Glycyrrhiza inflata root extract in an anti-acne cosmetic product. Contact Dermatitis. 2021;85(4):454–455. doi: 10.1111/cod.13872
3 Kimyon RS, Liou YL, Schlarbaum JP, Warshaw EM. Allergic Contact dermatitis to licorice root extract. Dermatitis. 2019;30(3):227-228. doi: 10.1097/DER.0000000000000475.

3.34 HEXYLRESORCINOL

IDENTIFICATION

Description/definition : Hexylresorcinol is the organic compound that conforms to the structural formula shown below
Chemical class : Phenols
IUPAC name : 4-Hexylbenzene-1,3-diol
CAS registry number : 136-77-6
EC number : 205-257-4
Wikipedia : https://nl.wikipedia.org/wiki/4-hexylresorcinol
Functions in cosmetics : EU: antimicrobial. USA: antimicrobial agents; antioxidants; cosmetic biocides; oral health care drugs
Patch testing : 1% pet. (2)
Molecular formula : $C_{12}H_{18}O_2$



Previous chapter to which this is an update

The literature on contact allergy to hexylresorcinol from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.229, pp. 604-605.

CONTACT ALLERGY

Case reports

A 62-year-old non-atopic woman presented with a 3-month history of pruritic, well-defined erythematous macules and desquamation on the face and neck. Patch tests with the Belgian baseline, cosmetic and photopatch series, along with the patient's own products, showed a positive (D3 ++) reaction to a cosmetic serum. Additional tests with its ingredients, obtained from the manufacturer, showed a positive reaction to hexylresorcinol 1% pet. (D4 +). Two other resorcinol-derivatives, resorcinol 2% pet. and methylresorcinol 1% pet., were negative (no cross-reactions) (2).

A 21-year-old non-atopic woman developed facial and neck eczema after using a tinted emulsion. Patch tests with the Belgian baseline, cosmetic and photopatch series, along with the patient's own products showed a strong positive reaction (+++) on D4 to this cosmetic, which had previously also been positive in a repeated open application test (ROAT). Ingredient patch testing showed a positive reaction to hexyl-resorcinol 1% pet. (D4 ++). Resorcinol 2% pet., methylresorcinol 1% pet., and phenylethyl resorcinol 0.3% alc./water 50/50 were, however, negative (no cross-reactions) (2).

In these skin care products, hexylresorcinol was used as a skin depigmenting agent (2).

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to hexylresorcinol see ref. 1.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 39/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 71/123,000.

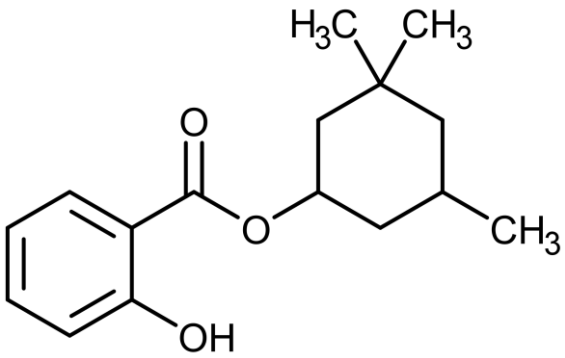
LITERATURE

1 Templeton HJ, Lunsford CJ. Cheilitis and stomatitis from ST 37 toothpaste. Arch Derm Syph 1932;25:439-443
2 Van Echelpoel C, Kanokrungsee S, Aerts O, Dendooven E. Two cases of facial allergic contact dermatitis from hexyl resorcinol, a 'new' resorcinol derivative in depigmenting products. Contact Dermatitis. 2025 Mar 9. doi: 10.1111/cod.14785. Epub ahead of print.

3.35 HOMOSALATE

IDENTIFICATION

Description/definition : Homosalate is the substituted phenolic compound that conforms to the structural formula shown below
Classification : Esters; phenols
IUPAC name : Benzoic acid, 2-hydroxy-, 3,3,5-trimethylcyclohexyl ester
Other names : Homomenthyl salicylate
CAS registry number : 118-56-9
EC number : 204-260-8
SCCS opinions : SCCP/1086/07; SCCS/1622/20 Final Opinion
Wikipedia : https://en.wikipedia.org/wiki/Homosalate
Functions in cosmetics : EU: skin conditioning; UV-absorber; UV-filter. USA: fragrance ingredients; light stabilizers; sunscreen ingredients
EU cosmetic restrictions : Regulated in Annex VI/3 of the Regulation (EC) 2009/1223
Patch testing : 5.0% and 10% pet. (Chemotechnique); 10% pet. (SmartPractice)
Molecular formula : $C_{16}H_{22}O_3$



Previous chapter to which this is an update

The literature on contact allergy to homosalate from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.231, pp. 607-609.

CONTACT ALLERGY (cosmetics)

General

A very useful review article on sunscreen allergy was published in 2023 in *Dermatitis* (4).

Case reports

A 39-year-old woman presented with facial dermatitis, suspected to have been caused by a cosmetic product, such as a moisturizer or sunscreen. Patch testing with the extended European baseline, fragrance, cosmetic and sunscreen chemical series and her facial sunscreen cream SPF 30 (tested 'as is') were positive (D4 +) to metals (nickel, cobalt; history of previous reactions to jewellery), fragrance substances (limonene, anise alcohol, benzyl salicylate), sunscreen chemicals (homosalate [homomenthyl salicylate], ethylhexyl salicylate) and to the sunscreen cream. This product contained homosalate, limonene, ethylhexyl salicylate, capryloyl salicylic acid and salicylic acid. Sensitisation to multiple salicylates was an unexpected finding. There was no relevant history of reactions to previous oral salicylate-containing medication such as Aspirin (acetylsalicylic acid). The patient was advised to discontinue all current products containing the identified allergens including all salicylate-containing products (2).

See also patients 6 and 8 in ref. 3.

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to homosalate see ref. 1. For photosensitivity to homosalate please refer to the Monographs in Contact Allergy, Volume 1, Chapter 2.231, pp. 607-609.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 50/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 1287/123,000.

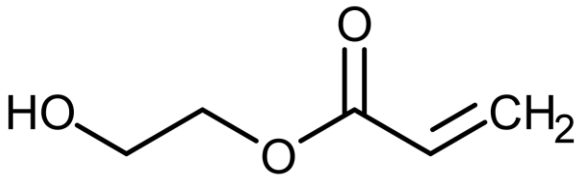
LITERATURE

1 Rietschel RL, Lewis CW Contact dermatitis to homomenthyl salicylate. Arch Dermatol 1978;114(3):442-443. PMID: 629582.
2 Teo YX, White IR, McFadden JP. Allergic contact dermatitis to multiple salicylates: A case report. Contact Dermatitis. 2024;90(2):195-197. doi:10.1111/cod.14464.
3 Pastor-Nieto MA, Gatica-Ortega ME, Borrego L. Sensitisation to ethylhexyl salicylate: Another piece of the frontal fibrosing alopecia puzzle. Contact Dermatitis. 2024;90(4):402-410. doi:10.1111/cod.14463
4 Ekstein SF, Hylwa S. Sunscreens: A review of UV filters and their allergic potential. Dermatitis. 2023;34(3):176-190. doi: 10.1097/DER.0000000000000963.

3.36 2-HYDROXYETHYL ACRYLATE

IDENTIFICATION

Description/definition : 2-Hydroxyethyl acrylate is the organic compound that conforms to the structural formula shown below
Classification : Acrylate esters
IUPAC name : 2-Hydroxyethyl prop-2-enoate
Other names : Ethylene glycol monoacrylate
CAS registry number : 818-61-1
EC number : 212-454-9
Wikipedia : https://en.wikipedia.org/wiki/Hydroxyethyl_acrylate
Functions in cosmetics : EU: film forming. USA: not mentioned
Patch testing : 0.1% pet. (Chemotechnique, SmartPractice)
Molecular formula : $C_5H_8O_3$



Previous chapter to which this is an update

The literature on contact allergy to 2-hydroxyethyl acrylate from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.240, pp. 636-637.

CONTACT ALLERGY (cosmetics)

Case reports

A 42-year-old woman was investigated for skin reactions after producing acrylic accessories and applying a facial moisturizing pack. She had started making acrylic accessories such as earrings and necklaces as a hobby 4 months previously. As the patient suspected that the reactions were attributable to contact with the acrylic accessories, she stopped making these, upon which the dermatitis disappeared. However, she subsequently developed facial dermatitis half a day after the first application of a cream-type moisturizing pack at a beauty salon. Patch tests with the Japanese baseline series, a (meth)acrylate series, the hardened acrylic accessory as a flat plate 7 mm in diameter, the moisturizing pack 'as is', and the components of the moisturizing pack at the concentrations used in the product were positive to the acrylic accessory (D2 +++, D3 +++, D7 +) and the moisturizing pack (D2 +, D3 ++, D7 +). The acrylic accessory components were 0.94% 2-hydroxyethyl acrylate (2-HEA) and 40% to 50% other (meth)acrylate monomers. Among the components of the moisturizing pack, only 2-HEA showed a positive reaction (D2 +, D3 ?+, D7 −). In the patch test with the (meth)acrylate series, positive reactions were observed to several (meth)acrylates, including 2-HEA, 2-hydroxyethyl methacrylate (2-HEMA), 2-hydroxypropyl methacrylate (2-HPMA), and ethyleneglycol dimethacrylate (EGDMA) (8).

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to 2-hydroxyethyl acrylate see refs. 1-7.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 2/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): unknown/123,000.

LITERATURE

1 Travassos AR, Claes L, Boey L, Drieghe J, Goossens A. Non-fragrance allergens in specific cosmetic products. Contact Dermatitis 2011;65(5):276-285. doi: 10.1111/j.1600-0536.2011.01968.x.

2 Lazarov A. Sensitization to acrylates is a common adverse reaction to artificial fingernails. J Eur Acad Derm Venereol 2007;21(2):169-174. doi: 10.1111/j.1468-3083.2006.01883.x.

3 Lucidarme N, Aerts O, Roelandts R, Goossens, A. Hydroxyethyl acrylate: a potential allergen in cosmetic creams? Contact Dermatitis 2008;59(5):321-322. doi: 10.1111/j.1600-0536.2008.01436.x.

4 Kanerva L, Lauerma A, Estlander T, Alanko K, Henriks-Eckerman ML, Jolanki R. Occupational allergic contact dermatitis caused by photobonded sculptured nails and a review of (meth) acrylates in nail cosmetics. Am J Contact Dermatitis 1996;7(2):109-115. PMID: 8796752.

5 Dahlin J, Berne B, Dunér K, Hosseiny S, Matura M, Nyman G, et al. Several cases of undesirable effects caused by methacrylate ultraviolet-curing nail polish for non-professional use. Contact Dermatitis 2016;75(3):151-156. doi: 10.1111/cod.12608.

6 Goossens A. Cosmetic contact allergens. Cosmetics 2016, 3, 5; doi: 10.3390/cosmetics3010005.

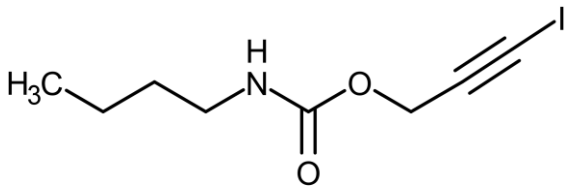
7 Zaragoza-Ninet V, Blasco Encinas R, Vilata-Corell JJ, Pérez-Ferriols A, Sierra-Talamantes C, Esteve-Martínez A, de la Cuadra-Oyanguren J. Allergic contact dermatitis due to cosmetics: A clinical and epidemiological study in a tertiary hospital. Actas Dermosifiliogr 2016;107(4):329-336. doi: 10.1016/j.ad.2015.12.007.

8 Mukaijo J, Inomata N, Higashihira M, Koh N, Togashi Y, Asai C, Watanabe Y, et al. Allergic contact dermatitis caused by 2-hydroxyethyl acrylate in a moisturizing face pack in a handmade acrylic accessory enthusiast. Contact Dermatitis. 2018;7996):383-385. doi: 10.1111/cod.13088.

3.37 IODOPROPYNYL BUTYLCARBAMATE

IDENTIFICATION

Description/definition : Iodopropynyl butylcarbamate is the organic compound that conforms to the structural formula shown below
Classification : Amides; esters; halogen compounds
IUPAC name : 3-Iodoprop-2-ynyl *N*-butylcarbamate
Other names : IPBC
CAS registry number : 55406-53-6
EC number : 259-627-5
CIR reports : Int J Toxicol 1998;17:1-37; Int J Toxicol 2017;36(Suppl2):14-58
SCCS opinions : SCCNFP/0826/04
Wikipedia : https://en.wikipedia.org/wiki/Iodopropynyl_butylcarbamate
Functions in cosmetics : EU: preservative. USA: pesticides; preservatives
EU cosmetic restrictions : Regulated in Annex V/56 of the Regulation (EC) 2009/1223
Patch testing : 0.2% pet. (Chemotechnique, SmartPractice); 0.5% pet. (SmartPractice); the concentration of 0.2% is already marginally irritant (1,2)
Molecular formula : $C_8H_{12}INO_2$



Previous chapter to which this is an update

The literature on contact allergy to iodopropynyl butylcarbamate from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.247, pp. 656-663.

CONTACT ALLERGY (cosmetics)

Case series

In a university hospital in Portugal, between 2011 and 2017, iodopropynyl butylcarbamate (IPBC) 0.2% pet. was added to the baseline series. Among 2276 patch tested patients, 12 positive reactions to IPBC (0.53% of the whole population and 1.9% of men) were found, with no increasing trend over the years. The positive patients included seven men and five women, ranging in age from 17 to 88 years (mean 58.3 ± 20.5 years). Five patients had disseminated dermatitis, four had leg dermatitis, and three had hand eczema. Reactions were considered to be possibly relevant in 9 of 12 patients (75%), of who 6 had used IPBC-containing cosmetic products. It was concluded that IPBC should be tested within the cosmetic series or in patients with leg ulcers/chronic venous insufficiency and in those who are occupationally exposed to household products, cooling fluids, paints, and chemicals used in the wood industry (4).

Case report

A 50-year-old woman had suffered lifelong atopic dermatitis. When she was around 50 years old, the dermatitis began to affect her face, resulting in bright erythema and edema of the entire face. Biopsy results revealed spongiotic dermatitis with eosinophils with mucin and spongiosis of several hair follicles. Patch testing with the NACDG standard series and an external agents and emulsifiers series revealed 2+ reactions to iodopropynyl butylcarbamate, propolis, Myroxylon pereirae resin, MCI/MI, and glutaraldehyde. Each of these allergens was relevant to her current personal care product usage. After 2

months of allergen avoidance, the patient exhibited dramatic improvement, with complete clearance of the dermatitis on the face and legs. Three years later, her face remains clear and she does not use any topical treatments on her face or body (5).

Previous cases of allergic cosmetic dermatitis

There is abundant literature on allergic contact dermatitis to iodopropynyl butylcarbamate, both in cosmetics and non-cosmetic products. Please refer to the Monographs in Contact Allergy, Volume 1, Chapter 2.247, pp. 656-663.

OTHER PUBLICATIONS [a]

In 7 patients sensitized to iodine or povidone-iodine who had suffered acute dermatitis during surgical interventions, co-reactivity was observed to iodopropynyl butylcarbamate (IPBC). The authors suspect that, despite the absence of firm evidence for IPBC being dehalogenated to produce free iodine in animals or in humans, the patch test reactions to IPBC in iodine-allergic subjects were possibly caused by free iodine released from this preservative agent (3).

[a] Literature on contact allergy to iodopropynyl butylcarbamate that was found in *Contact Dermatitis* or/and *Dermatitis* from September 2017 through March 2025, in which there was no direct link with cosmetic products.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 726/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 1936/123,000.

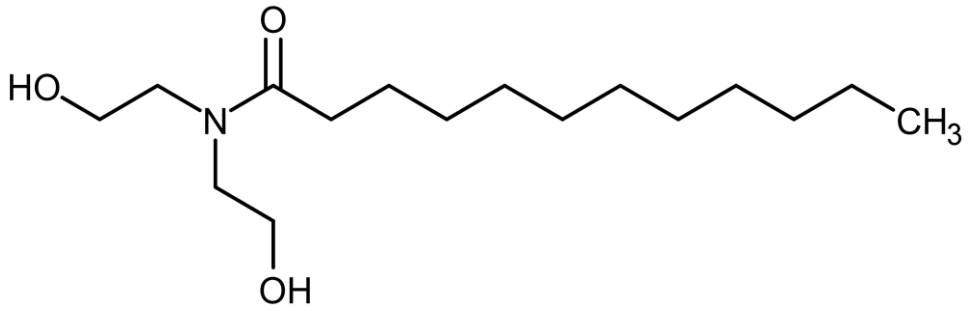
LITERATURE

1 Martin-Gorgojo A, Johansen JD. Contact dermatitis caused by iodopropynyl butylcarbamate in Denmark. Contact Dermatitis 2013;69(2):78-85. doi: 10.1111/cod.12062.
2 Bryld L E, Agner T, Rastogi S C, Menné T. Iodopropynyl butylcarbamate: a new contact allergen. Contact Dermatitis 1997;36(3):156-158. doi: 10.1111/j.1600-0536.1997.tb00400.x.
3 Vanhoutte C, Goossens A, Gilissen L, Huygens S, Vital-Durand D, Dendooven E, et al. Concomitant contact-allergic reactions to iodopropynyl butylcarbamate and iodine. Contact Dermatitis. 2019;81(1):17-23. doi: 10.1111/cod.13224.
4 Batista M, Morgado F, Gonçalo M. Patch test reactivity to iodopropynyl butylcarbamate in consecutive patients during a period of 7 years. Contact Dermatitis. 2019;81(1):54-55. doi: 10.1111/cod.13213.
5 Semaan S, Raffi J, Murase JE. Allergic contact dermatitis masquerading as atopic dermatitis. Int J Womens Dermatol. 2020;6(4):329-330. doi: 10.1016/j.ijwd.2020.04.005.

3.38 LAURAMIDE DEA

IDENTIFICATION

Description/definition : Lauramide DEA is a mixture of ethanolamides of lauric acid. It conforms generally to the structural formula shown below
Classification : Alkanolamides
IUPAC name : *N*,*N*-bis(2-Hydroxyethyl)dodecanamide
Other names : Lauric acid diethanolamide
CAS registry number : 120-40-1
EC number : 204-393-1
CIR reports : J Am Coll Toxicol 1986;5:415-454; Int J Toxicol 2013;32(Suppl.1):36-58
Functions in cosmetics : EU: antistatic; foam boosting; surfactant; viscosity controlling. USA: surfactants – foam boosting; viscosity increasing agents - aqueous
EU cosmetic restrictions : Regulated in Annex III/60 of the Regulation (EC) 2009/1223
Patch testing : 1% pet.
Molecular formula : $C_{16}H_{33}NO_3$



Previous chapter to which this is an update

The literature on contact allergy to lauramide DEA from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.265, p. 712.

CONTACT ALLERGY (cosmetics)

Case report

A 54-year-old man was investigated for a 4-month history of itchy eruptions on the entire body. Physical examination showed pruritic erythema with thick scales on the scalp, face, and upper trunk. A skin biopsy specimen from a papule on the neck showed lymphocytic infiltration with marked spongiosis. A hair colour shampoo that the patient had used for one year was suspected to be the culprit. Patch testing with this shampoo (1% water) showed positive reactions on D2, D3, and D7 (all +). Later, the ingredients of the product, provided by the manufacturer, were tested which yielded positive reactions to lauramide DEA 0.5% pet. (++/++/+), C12–14 hydroxyalkyl hydroxyethyl sarcosine 0.3% water (+/+/+), basic blue 99 0.5% pet. (++/++/++), and *N*-methyl-*N*-(1-oxododecyl)-β-alaninate 0.3% water (+/+/+). Two controls were negative at D2, D3 and D7. In addition, a lymphocyte transformation test (LTT) with the patient's lymphocytes using the four components showed positive reactions in the patient, but were negative in 5 healthy volunteers. Topical steroids were administered, and the patient was advised to stop using the shampoo. In just 10 days, the lesions had completely resolved, and no recurrence has been observed for 6 months (4).

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to lauramide DEA see refs. 1-3.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 55/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 38/123,000.

LITERATURE

1 Kohl L, Blondeel A, Song M. Allergic contact dermatitis from cosmetics: retrospective analysis of 819 patch-tested patients. Dermatology 2002;204(4):334-337. doi: 10.1159/000063379.
2 De Groot AC, de Wit FS, Bos JD, Weyland JW. Contact allergy to cocamide DEA and lauramide DEA in shampoos. Contact Dermatitis 1987;16(2):117-118. doi: 10.1111/j.1600-0536.1987.tb01401.x.
3 De Groot AC, Bruynzeel DP, Bos JD, van der Meeren HL, van Joost T, Jagtman BA, Weyland JW. The allergens in cosmetics. Arch Dermatol 1988;124(10):1525-1529. doi: 10.1001/archderm.124.10.1525.
4 Kosumi H, Yanagi T, Izumi K, Ito T, Shimizu H. Hair colour shampoo dermatitis. Contact Dermatitis. 2017;77(6):419-421. doi: 10.1111/cod.12851.

3.39 MAGNOLIA OFFICINALIS BARK EXTRACT

IDENTIFICATION

Description/definition : Magnolia officinalis bark extract is an extract of the bark of *Magnolia officinalis*, Magnoliaceae
Classification : Botanical products and botanical derivatives
Wikipedia : https://en.wikipedia.org/wiki/Magnolia_officinalis (*Magnolia officinalis*)
Functions in cosmetics : EU: antimicrobial; skin conditioning. USA: antimicrobial agents; skin-conditioning agents – miscellaneous
Patch testing : 0.5% pet. (1-5); 0.5% may sometimes be too low (4)

Previous chapter to which this is an update

The literature on contact allergy to Magnolia officinalis bark extract from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.282, p. 735.

CONTACT ALLERGY (cosmetics)

Case reports

A 58-year-old woman with frontal fibrosing presented with acute facial dermatitis. Patch tests showed positive reactions to nickel sulfate, cobalt chloride, propolis, gallates mix, dodecyl gallate, ethylhexyl salicylate, and two personal cosmetics tested 'as is'. Repeated open application tests (ROAT) performed at the inner side of the lower arm were intensely positive at day 7 with both cosmetics. Patch tests with their individual ingredients provided by the manufacturer only showed weak-positive reactions with Magnolia officinalis bark extract (MOBE) 0.5% pet. present in both creams. The individual ingredients were reapplied on D5 with 3 day occlusion, now yielding a more pronounced reaction to MOBE 0.5% pet. A ROAT with the extract 0.5% pet. was intensely positive after the fifth application (4).

A 65-year-old non-atopic woman was investigated for an itchy slate-grey hyperpigmentation affecting the cheeks and neck, which had developed over one year. Upon treatment with oral and topical corticosteroids, pruritus improved at first, but the grey hyperpigmentation persisted, together with several flares of pruritus. The patient acknowledged using a new anti-ageing cream and a vitamin C serum shortly before begin of symptoms. Patch tests with the European baseline series, the fragrance series and the patient's cosmetic products tested 'as is' were positive to an anti-age cream. Ingredient patch testing revealed sensitization to Magnolia officinalis bark extract 0.5% pet. at D2 and D4. Twenty controls were negative. The patient was advised to stop using the cream and has since not experienced further episodes of pruritus. The grey hyperpigmentation, which is an uncommon manifestation of allergic contact dermatitis, slowly resolved (5).

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to Magnolia officinalis bark extract see refs. 1-3.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 27/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 189/123,000.

OTHER PUBLICATIONS [a]

Vulvar allergic contact dermatitis caused by magnolol/honokiol, the major ingredients in Magnolia officinalis bark extract, in a vaginal gel (6).

[a] Literature on contact allergy to Magnolia officinalis bark extract that was found in *Contact Dermatitis* or/and *Dermatitis* from September 2017 through March 2025, in which there was no direct link with cosmetic products.

LITERATURE

1 Ghys K, De Palma A, Vandevenne A, Werbrouck J, Goossens A. *Magnolia officinalis* bark extract, a recently identified contact allergen in 'anti-ageing' cosmetics. Contact Dermatitis 2015;73(20):130-132. doi: 10.1111/cod.12415.

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3 Nilausen TD, Johansen JD, Thyssen JP. Allergic contact dermatitis of the face caused by *Magnolia officinalis* bark extract. Contact Dermatitis 2016;75(6):385-387. doi: 10.1111/cod.12655.

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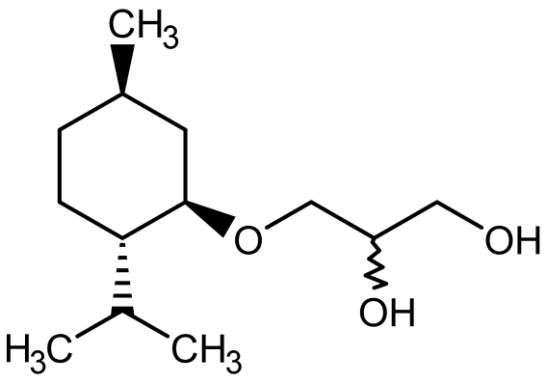
3.40 MENTHOXYPROPANEDIOL

IDENTIFICATION

Description/definition : Menthoxypropanediol is the organic compound that conforms to the structural formula shown below
Classification : Alcohols
IUPAC name : 3-(5-Methyl-2-propan-2-ylcyclohexyl)oxypropane-1,2-diol
Other names : 3-{[5-Methyl-2-(1-methylethyl)cyclohexyl]oxy}-; 3-l-menthoxypropane-1,2-diol; L-menthylglyceryl ether
CAS registry number : 87061-04-9
EC number : 289-296-2
Wikipedia : https://en.wikipedia.org/wiki/Menthoxypropanediol
Functions in cosmetics : EU: masking; refreshing. USA: flavoring agent; fragrance ingredient
Patch testing : 5% pet. (1)
Molecular formula : $C_{13}H_{26}O_3$



Previous chapter to which this is an update

The literature on contact allergy to menthoxypropanediol from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.285, pp. 738.

CONTACT ALLERGY (cosmetics)

Case report

A 45-year-old woman had developed itchy redness of the left wrist a few days after applying a skincare lotion there and covering it with a dressing tape. Patch tests with the Japanese baseline series, the lotion 'as is', and the dressing tape resulted in a + reaction to the lotion at day 3. The manufacturer provided the ingredients of the lotion unlabelled, prediluted in petrolatum for patch testing. The second patch test procedure showed a + reaction on D3 to the ingredient menthoxypropanediol (MPD). In a third session, MPD was patch tested in a dilution series of 5%, 2%, 1%, 0.5%, 0.1% and 0.05%; 2% and 5% appeared to be adequate test concentrations with positive results. The patient did not react to menthol 2% and 5% pet. Nine controls were negative to the dilution series of menthoxypropanediol (2).
The investigators suggested the test concentration of 2%; this author fails to see why they preferred 2% (D2 -, D3 +, D4 +, D7 ?+) over 5% (D2 ?+, D3 +, D4 +, D7 ?+). Nine controls had been negative to 5% and in the only previously reported case 5% had been appropriate (1).

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to menthoxypropanediol see ref. 1.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 92/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 164/123,000.

LITERATURE

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3.41 METHYLCHLOROISOTHIAZOLINONE (AND) METHYLISOTHISAZOLINONE

IDENTIFICATION

Description/definition : Methylchloroisothiazolinone (and) methylisothiazolinone is a mixture of methylchloroisothiazolinone and methylisothiazolinone with magnesium chloride and magnesium nitrate

Classification : Heterocyclic compounds

Other names : 5-Chloro-2-methyl-isothiazol-3(2*H*)-one and 2-methylisothiazol-3(2*H*)-one; 5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-4-isothiazolin-3-one; MCI/MI; best known trade name: Kathon® CG

CAS registry number : 55965-84-9 (mixture); 26172-55-4 (MCI); 2682-20-4 (MI)

EC number : 611-341-5 and 911-418-6 (mixture); 247-500-7 (MCI); 220-239-6 (MI)

CIR reports : J Am Coll Toxicol 1992;11:75-128; Int J Toxicol 2021;40(Suppl.1):20-33

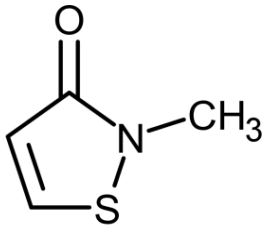
SCCS opinions : SCCS/1238/09; SCCP/0849/04; SCCNFP/0670/03

Wikipedia : https://en.wikipedia.org/wiki/Methylchloroisothiazolinone (Methylchloroisothiazolinone); https://en.wikipedia.org/wiki/Methylisothiazolinone (Methylisothiazolinone)

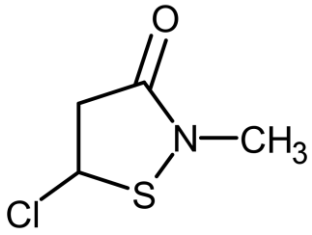
Functions in cosmetics : EU: preservative. USA: preservatives

Patch testing : 0.01% and 0.02% water (Chemotechnique, SmartPractice); 0.01% pet. (Chemotechnique); 0.215% water (Chemotechnique)

EU cosmetic restrictions : Regulated in Annex V/39 of the Regulation (EC) No. 2014/1003; EU legislation: maximum concentration 15 ppm in rinse-off products; not allowed in leave-on products from July 2016 on



Methylisothiazolinone



Methylchloroisothiazolinone

Previous chapter to which this is an update

The literature on contact allergy to methylchloroisothiazolinone (and) methylisothiazolinone from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.292, pp. 757-790.

CONTACT ALLERGY (cosmetics)

General

The use of MCI/MI in leave-on cosmetics has been prohibited in the European Union (EU) since 2016 and its permitted use in rinse-off products at a maximum level of 15 ppm seems to be largely safe. Therefore, current reports of cosmetic allergy from MCI/MI are mostly from countries outside the EU.

Case series

In 2016 and 2017, in 2 tertiary centers in Rio de Janeiro, 303 patients were patch tested with MI 0.2% water and 359 with MCI/MI 0.5% pet. (concentration 50 times higher than the at that time usual 0.01% and in another vehicle). MCI/MI was positive in 80 individuals (22.3%) with clinical relevance in 63 (79%).

MI was positive in 81 individuals (26.7%), with clinical relevance in 76 (94%). Eczema predominating in exposed areas was found in 30 patients who were allergic to isothiazolinones. Therefore, photopatch testing was performed in 18 patients. In 4, it was possible to observe a pattern of photoaggravation: 2 related to MCI/MI and 2 to MI. Although the number and percentage of clinically significant reactions were specified, nothing was, rather curiously, said about the culprit products. Probably the majority were cosmetics, as the high prevalence of MI sensitization was ascribed to the fact that, at that time, MI was allowed in a high concentration of 100 ppm in all cosmetics, also the leave-on products (nothing was mentioned of MCI/MI) (29).
Comments: This article is unreliable. It contains calculation errors, incorrect patch test material has been used and the lack of data on clinical relevance is an important omission.

Case reports

A 41-year-old locksmith presented with hand eczema that had lasted 2 years, primarily at the fingertips and dorsum of fingers. In his work he dismantled 20–30 locks per day and commonly came into contact with metals, oils from the locks and lubricants. He used gloves of various materials, washed his hands 10–15 times per day, and used wet wipes to clean his hands up to 5 times per day. Patch tests were positive to MCI/MI 0.02% in water (+), fragrance mix I 8% (++), cinnamal 1% pet. (+), and *tert*-butylhydroquinone (+++). MCI/MI was not declared in any safety data sheets of the products currently being used by the patient. However, a diagnostic spot test for isothiazolinones was used on the wet wipe, with positive results. The manufacturer of the wet wipes confirmed that MCI/MI had previously been used in the product and that the patient had used an old batch (10).

In a report from the USA, a 5-year-old boy was described who was brought to the clinic for persistent perianal pruritus and pain for 2 years. Affected areas also included the buttocks and posterior thighs. Physical examination was unremarkable except for excoriations on the buttocks, posterior thighs, and perianal area. The patient's mother was advised to discontinue the use of baby wipes and was prescribed topical corticosteroids as needed for pruritus. Patch testing with North American Standard Series-80 revealed positive reactions to MI (D2 2+, D6 2+) and to MCI/MI (D2 2+, D6 2+). MCI/MI was identified in several of the patient’s products, including wet wipes, liquid hand soap, body wash, shampoo, and detergent. With avoidance counselling, improvement in pain and pruritus was seen as early as 10 days after patch testing; after 1 month, the pain resolved, and pruritus has reduced dramatically (26).

A 64-year-old woman presented with dermatitis affecting both palms. The patient initially developed pruritic dermatitis on the left thenar eminence 3 years prior. On physical examination, a prominent eczematous plaque on the left thenar eminence and a thinner eczematous plaque covering the right palm diffusely was observed. Owing to the distinctive pattern of the plaques on her hands, contact allergy to shampoo was suspected. A skin biopsy to rule out psoriasis revealed acute spongiotic dermatitis consistent with contact dermatitis. Patch testing showed a 2+ reaction to MCI/MI, which was present in her shampoo. She was counselled on avoiding all products containing MCI/MI and the patient subsequently experienced resolution of her hand dermatitis after 3 months of allergen avoidance (27).

A 39-year-old nonatopic Turkish man presented with recurring hand eczema on the dorsum of both hands and fingers for 15 years, and additional face eczema mainly involving the periorbital area for the last 3 years. He had been working as a tramline worker for 16 years, and was mainly responsible for maintenance and repair. The patient had contact to surface cleaner and rust remover, machine oil, and metal-working fluids at work. Patch tests with the extended European baseline series, a cosmetic series including preservatives and emulsifiers, a rubber additive series, an oil and cooling fluid series, the ‘used machine oil’ from work and the patient's topical medications showed ++ positive reactions to MI 0.2% water, MCI/MI 3:1 0.02% water and a moisturizing cream ‘as is’. MCI/MI was identified on the product labels of both occupational (rust remover, surface cleaner) and nonoccupational (shampoo, moisturizing cream, floor detergent, and washing machine and dishwasher detergent) products. One year later, the patient presented with a severe attack of eyelid eczema, which was caused by MCI/MI in the paint he had used to paint a wall in his living room (28).

A 50-year-old woman had suffered lifelong atopic dermatitis. When she was around 50 years old, the dermatitis began to affect her face, resulting in bright erythema and edema of the entire face. Biopsy results revealed spongiotic dermatitis with eosinophils with mucin and spongiosis of several hair follicles. Patch testing with the NACDG standard series and an external agents and emulsifiers series revealed 2+ reactions to MCI/MI, propolis, Myroxylon pereirae resin, iodopropynyl butylcarbamate, and glutaraldehyde. Each of these allergens was relevant to her current personal care product usage. After 2 months of allergen avoidance, the patient exhibited dramatic improvement, with complete clearance of the dermatitis on the face and legs. Three years later, her face remains clear and she does not use any topical treatments on her face or body (30).

Previous cases of allergic cosmetic dermatitis

Methylchloroisothiazolinone (and) methylisothiazolinone is a preservative mixture that is a well-known contact allergen and is included in most international and national baseline series for patch testing. It has caused an epidemic of allergic cosmetic dermatitis from the mid-1980s on. Currently, in the European Union, it is allowed in rinse-off products up to a concentration of 15 ppm. For a full review (33 pages) please refer to the Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.292, pp. 757-790.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 2662/35,000 (methylchloroisothiazolino-ne); 2853 (methylisothiazolinone).
EWG's Skin Deep Cosmetics Database (February 2025): 4698/123,000 (methylchloroisothiazolinone); 5256/123,000 (methylisothiazolinone).

OTHER PUBLICATIONS [a]

Allergic contact dermatitis

Paints

- Photoallergic contact cheilitis from MCI/MI in hobby paint, transferred by the patient herself by the habit of touching the mouth while painting (5).
- Airborne allergic contact dermatitis from MCI/MI and MI in paint in a child (22), from MCI/MI in 2 paints in an adult with psoriasis (24), and in a Turkish man who also had occupational ACD from a rust remover and a surface cleaner (28).

Other products.

- Dermatitis, flushing and palpitations from contact allergy to MCI/MI (or/and MI) in a fabric softener (2).
- Pustular allergic contact dermatitis to MCI/MI from an electrocardiography gel (6).
- Contact allergy to MCI/MI caused ACD of the hands by its presence in homemade play material called 'slime' in 3 children (11), 2 children (12), and 1 child (13,14,15). A related product, 'noise putty' also caused hand dermatitis in a child allergic to MCI/MI. but the presence of the preservative in the toy was not ascertained (16).
- Ultrasound gel (33).

Occupational allergic contact dermatitis

- Significant increase in the number of cases of occupational allergic contact dermatitis to MCI/MI in cleaning professionals in Spain between 2005 and 2016 (3).
- Outbreak of allergic contact dermatitis in 8 (of who 4 were patch tested) workers at a water bottling plant secondary to high levels of MCI/MI in the cooling system (4).
- Pustular allergic contact dermatitis from MCI/MI in paints, lubricants, and adhesives in a patient working in a gas, plumbing and painting company (6).

- ACD with large blisters and ecchymotic purpura on the right hand of a service technician in the chemical industry from accidental exposition to a biocide containing MCI/MI during the maintenance of a cooling tower (8).
- A 64-year-old man processing traditional photographs had hand dermatitis from contact allergy to MCI/MI in a stabilizing agent used at his work (17).
- Five hospital employees had occupational allergic contact dermatitis from MCI/MI in a professional hospital hand soap (23).
- A Turkish man a combination of occupational allergic contact dermatitis from MCI/MI in a rust remover and a surface cleaner and non-occupational ACD from shampoo, moisturizing cream, floor detergent, washing machine and dishwasher detergent and later airborne ACD from MCI/MI in wall paint (28).
- A 46-year old woman, working in a box factory, operating in a cardboard box packaging process, developed occupational allergic hand dermatitis from MCI/MI and MI in glue (34). .

Patch testing

- The MCI/MI TRUE Test identified almost twice as many patients allergic to this preservative compared with MCI/MI 0.01% water (25).
- The MCI/MI TRUE Test has at least the same sensitivity and specificity as MCI/MI 0.02% water in detecting MCI/MI allergic patients (7).
- In a study of the Swedish Contact Dermatitis Group, a diagnostic mix of MCI 0.015% and MI 0.2% water detected significantly more patch test-positive individuals than both MCI/MI 0.02% water and MI 0.2% water, as well as either one of MCI/MI and MI. The authors stated that the results speak in favor of replacing the preparations MCI/MI 0.02% water and MI 0.2% water with MCI/MI 0.215% water as the screening substance in the Swedish baseline series, which has been implemented in 2020 (9).

Other information

- Risk assessment study of the skin sensitization induction potential of MCI/MI in rinse-off and leave-on personal care and cosmetic products (1).
- Usability of a spot test for isothiazolinones (10).
- Results of patch testing MI and MCI in Thailand, 2009 to 2018 (18).
- Market survey of the presence of MCI/MI and MI in cosmetic products in Thailand (19).
- Concomitant sensitivity to MCI/MI, imidazoles and nitroimidazoles is not rare. Whether this is merely a coincidence, or whether it represents cross-reactivity is currently unknown (20).
- Stronger sensitizing capacity of MCI and possible but not frequent cross-reactivity between MCI and MI (21).
- Analyses of MCI/MI in 10 children's toy slime products purchased in Japan (31).
- Analyses of MCI/MI and MI in dish soap and personal care products that do not declare isothiazolinones (32).

[a] Literature on contact allergy to methylchloroisothiazolinone (and) methylisothiazolinone that was found in *Contact Dermatitis* or/and *Dermatitis* from September 2017 through March 2025, in which there was no direct link with cosmetic products.

LITERATURE

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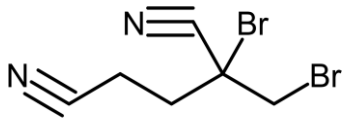
3.42 METHYLDIBROMO GLUTARONITRILE

IDENTIFICATION

Description/definition	: Methyldibromo glutaronitrile is the brominated methylene glutaronitrile that conforms to the structural formula shown below
Classification	: Halogen compounds
IUPAC name	: 2-Bromo-2-(bromomethyl)pentanedinitrile
Other names	: 1,2-Dibromo-2,4-dicyanobutane; bromothalonil; with phenoxyethanol in Euxyl® K 400
CAS registry number	: 35691-65-7
EC number	: 252-681-0
CIR reports	: J Am Coll Toxicol 1996;15:140-165
SCCS opinions	: SCCP/1013/06; SCCP/0863/05; SCCNFP/0806/04; SCCNFP/0585/02
Functions in cosmetics	: EU: formerly used as preservative. USA: preservatives
EU regulations	: Prohibited; delisted in 2008 (stay-on products) and 2010 (rinse-off products)
Patch testing	: 0.3% and 0.5% pet. (Chemotechnique, SmartPractice); 0.2% (SmartPractice)
Molecular formula	: $C_6H_6Br_2N_2$



Previous chapter to which this is an update

The literature on contact allergy to methyldibromo glutaronitrile from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.293, pp. 791-803.

CONTACT ALLERGY (cosmetics)

General

The use of methyldibromo glutaronitrile in cosmetics was prohibited in the EU in 2008 for stay-on products and in 2010 for rinse-off products. Yet, reports of cases of allergic cosmetic dermatitis from this preservative were still published in *Contact Dermatitis* in 2017 (1) and 2021 (2; see the section Other publications'), which were caused by cosmetics purchased outside the European Union (1,2).

Case report

A 41-year-old non-atopic woman developed a generalized eczematous rash during a 1-month vacation in Guatemala. After returning home, patch tests with the European baseline series and a fragrance series were positive to fragrance mix I (++), methyldibromo glutaronitrile (MDBGN) (+), nickel (++), and palladium(II) chloride (+). The minimal erythema dose (MED) was normal and photopatch testing yielded no evidence of photoallergy. On examination of the product labels of all cosmetic and household products used by the patient, MDBGN was found in a sunscreen agent, which she had bought and applied during the recent vacation. The rash was located on the skin areas where the product had been applied. Fragrances were found in a deodorant and body lotion, whereas the sunscreen agent did not contain 'perfume', according to labelling information. The patient was diagnosed with allergic contact dermatitis caused by MDBGN in the sunscreen (1).

Previous cases of allergic cosmetic dermatitis

Methyldibromo glutaronitrile, especially its presence in the preservative system Euxyl K400 with phenoxyethanol, has caused so many cases of allergic cosmetic dermatitis that it has been banned from cosmetics

in the European Union. For previous case reports and case series of allergic cosmetic dermatitis to methyldibromo glutaronitrile please refer to the Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.293, pp. 791-803

OTHER PUBLICATIONS [a]

- A 62-year-old woman had chronic hand eczema with periodic flare-ups for 3 years, which was caused by MDBGN in a detergent for leather, which she used for hand washing of her riding gloves (1).
- In a multicenter study in Spain, performed between June 2018 and June 2020, 5081 consecutive patients were tested with MDBGN and 114 (2.24%) were positive. Current relevance was found in only one case involving a 73-year-old woman who used cosmetics bought outside the EU. Four additional positive tests were considered of past relevance, involving a woman with a past history of contact allergy to cosmetics, two female patients who had previously worked as office cleaners in contact with several cleaning detergents and a man working as mechanic in contact with different oil products at work. The authors concluded that the clinical usefulness of this allergen seems weak and its continued inclusion in the European baseline series is questionable (2).
- This publication resulted in a fierce debate whether the (continued) inclusion of methyldibromo glutaronitrile is necessary and useful (4-6), also in the light of the commonly observed irritant reactions to MDBGN 0.5% pet., both in patients and in healthy controls (3). One year later the European Society of Contact Dermatitis decided to continue the inclusion of MDBGN in the 2023 European baseline series (7).

[a] Literature on contact allergy to methyldibromo glutaronitrile that was found in *Contact Dermatitis* or/and *Dermatitis* from September 2017 through March 2025, in which there was no direct link with cosmetic products.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 31/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 3/123,000.

LITERATURE

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3 García Castro R, Velasco Tirado V, González de Arriba M. Should methyldibromo glutaronitrile in the baseline series be tested? Results of the skin allergy unit of a fourth-level hospital in Spain. Contact Dermatitis. 2021;84(6):477-479. doi: 10.1111/cod.13774.
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5 Mercader-García P, Pastor-Nieto MA, Gonzalez-Perez R, Gimenez-Arnau AM, Ruiz-Gonzalez I, Mora-Fernández V, et al. Arguments in favour of excluding MDBGN from the European baseline series. In response to "Comment on MDBGN/DBDCB, the European baseline series, and EU legislation". Contact Dermatitis. 2021;85(5):611-613. doi: 10.1111/cod.13941.
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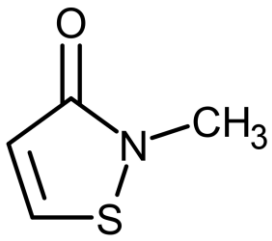
3.43 METHYLISOTHIAZOLINONE

IDENTIFICATION

Description/definition : Methylisothiazolinone is the heterocyclic organic compound that conforms to the structural formula shown below
Classification : Heterocyclic compounds
IUPAC name : 2-Methyl-1,2-thiazol-3-one
Other names : 2-Methyl-4-isothiazolin-3-one
CAS registry number : 2682-20-4
EC number : 220-239-6
CIR reports : J Am Coll Toxicol 1992;11:75-128; Int J Toxicol 2010;29(Suppl.3):187-213; Int J Toxicol 2019;38(Suppl.1):70-84; Int J Toxicol 2021;40(Suppl. 1):20-33; Int J Toxicol 2021;40(Suppl.1);5-19
SCCS opinions : SCCS/1557/15; SCCS/1521/13; SCCNFP/0805/04; SCCNFP/0625/02
Wikipedia : https://en.wikipedia.org/wiki/Methylisothiazolinone
Functions in cosmetics : EU: preservative. USA: preservatives
Patch testing : 0.2% water and pet. (Chemotechnique); 0.05% water and 0.2% water (SmartPractice)
EU cosmetic restrictions : Regulated in Annex V/57 of the Regulation (EC) No. 2017/1224; prohibited in stay-on cosmetics; allowed in rinse-off product in a maximum concentration of 0.0015% (15 ppm)
Molecular formula : C_4H_5NOS



Previous chapter to which this is an update

The literature on contact allergy to methylisothiazolinone from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.299, pp. 818-838.

CONTACT ALLERGY (cosmetics)

General

Methylisothiazolinone (MI) has caused an epidemic of allergic contact dermatitis from 2009 on in Europe (24), the USA and other countries such as Australia (28), which was mainly due to cosmetics containing the preservative (24,28). As complete avoidance of MI in cosmetics and other products was difficult, relapses of MI-induced allergic contact dermatitis were frequent (27). In 2017, MI was prohibited in the EU in stay-on cosmetics and only allowed in rinse-off product in a maximum concentration of 0.0015% (15 ppm). Since then, the prevalence of allergic contact dermatitis from MI started to decline considerably (24,25).

Case series

In 2016 and 2017, in 2 tertiary centers in Rio de Janeiro, 303 patients were patch tested with MI 0.2% water and 359 with MCI/MI 0.5% pet. (concentration 50 times higher than the at time usual 0.01% and in another vehicle). MI was positive in 81 individuals (26.7%), with clinical relevance in 76 (94%). MCI/MI was positive in 80 individuals (22.9%) with clinical relevance in 63 (79%). Eczema predominating in exposed

areas was found in 30 patients who were allergic to isothiazolinones. Therefore, photopatch testing was performed in 18 patients. In 4, it was possible to observe a pattern of photoaggravation: 2 related to MI and 2 to MCI/MI. Although the number and percentage of clinically significant reactions were specified, nothing was, rather curiously, said about the culprit products. Probably the majority were cosmetics, as the high prevalence of MI sensitization was ascribed to the fact that, at that time, MI was allowed in a high concentration of 100 ppm in all cosmetics, also the leave-on products (33).
Comments: This article is unreliable. It contains calculation errors, incorrect patch test material has been used and the lack of data on clinical relevance is an important omission.

Case report

A 56-year-old female patient with rosacea was investigated for acute, itching dermatitis of the face, with erythematous, slightly swollen eyelids, and erythematous papules and infiltrated patches on both cheeks and forehead. The dermatitis had occurred a few days following a facial treatment by a beautician who had applied a facemask, which had remained on her face for 15 minutes before being washed off, followed by the application of a moisturizing cream. Patch tests were performed with the extended Belgian baseline series, a cosmetic series, the patient's own cosmetics, and the products applied by the beautician. The culprit facial mask, together with two related facial masks from the same manufacturer, were tested semi-open. Readings on D3 showed +++ reactions to MCI/MI 0.02% water, MI 0.2% water and to all three masks. The ingredients on the label of the mask did not mention MCI/MI or MI, and both the distributor and the manufacturer denied their presence (1).
A first qualitative chemical analysis of the mask with an experimental isothiazolinone test kit showed the potential presence of isothiazolinones. Meanwhile, the manufacturer had provided samples of the individual ingredients of the mask, which were patch tested and showed a ++ reaction at D2 and D4 to sodium hyaluronate 0.1% water. Subsequently, chemical analyses (HPLC-UV) of the mask and the sodium hyaluronate showed the presence of 147 ppm MI in the facial mask and 326.5 ppm MI in the sodium hyaluronate solution. No other isothiazolinone derivatives could be detected. It was concluded that the preservation of the ingredient sodium hyaluronate with MI was responsible for this case of cosmetic allergy. The authors highlighted two particularities of this case: (i) a rinse-off cosmetic (i.e. a facial mask) caused severe allergic contact dermatitis attributable to MI that was shown to be present at a concentration of >100 ppm, although it was not labelled on the packaging; and (ii) MI was detected at a very high concentration (326.5 ppm) in one of the individual cosmetic raw materials, which probably explains the presence of the high final concentration of MI (147 ppm) in the finished product (1).

Previous cases of allergic cosmetic dermatitis

Methylisothiazolinone is a well-known allergen which has caused an epidemic of allergic contact dermatitis in cosmetics and a variety of other products including paints. For a full 20 page review up to September 2017 please refer to the Monographs in Contact Allergy, Volume 1, Chapter 2.229, pp. 818-838.

PHOTOSENSITIVITY

From the USA, 4 patients who had photoaggravated allergic contact dermatitis from MI were reported. Culprit products were sunscreens (n=4), shampoos (n=2), conditioner, and hand soap (both n=1) (20). Ten patients from Belgium and France had photoaggravated allergic contact dermatitis from MI. Sensitization to MI occurred possibly from cosmetics (including sunscreens and wet wipes) in 7 patients, and from work-related industrial biocides and paint in 2 patients and 1 patient, respectively. Besides cosmetics, subsequent elicitation took place through airborne contact with MI in 8 of 10 patients: from vapours in industrial biocides in 2 patients, and from water-based paints in 6. This resulted in airborne allergic contact dermatitis, which subsequently became photoaggravated. Four patients suffered from transient photosensitivity (29).

Presence of MI in cosmetic products

In Tunisia, where there are no restrictions on the use of MI in cosmetics, of 870 cosmetic products investigated in 2020, 118 (13.5%) contained MI, of which 44% were leave-on cosmetics. Percentages of

MI-positive cosmetics in the various cosmetics categories were 38 for shampoos, 36 for face cleansers, 24 for body cleansers, 23 for wet wipes, 12 for hair cosmetics, 12 for soap, 9 for sunscreens, 6.7 for deodorants, 6.6 for skin care leave-on cosmetics and 3.6 for hand creams (9).

Presence in cosmetic products in the USA

FDA's Voluntary Cosmetic Registration Program (March 2022): 2853/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 5256/123,000.

OTHER PUBLICATIONS [a]

Allergic contact dermatitis

- *Paints.* Cases of allergic contact dermatitis from MI in paint have been reported in refs. 2,5,7 (airborne, also from MCI/MI), 11 (mode to prevent relapses presented), 26 (also reactions from the hair dye of patient's partner [consort/connubial allergic contact dermatitis]), 34, and 35 (disfiguring angioedema-like ACD).
- *Medical mouthwashes.* Contact allergy caused by methylisothiazolinone in a mouthwash as the likely trigger of oral pemphigus vulgaris (6); angioedema-like contact dermatitis from MI in mouthwash (16).
- *Other products.* Glitter-glue used as make-up (8); home-made slime, 2 cases (9); dermatitis, flushing and palpitations from contact allergy to MI (or/and MCI/MI) in a fabric softener (15); MI (or another isothiazolinone) in a topical drug (38).
- *Occupational allergic contact dermatitis*: Ultrasound gel, 2 cases (3); cooling oil (13); liquid detergent solution containing 24% MI (31); nitrile gloves (36); glue (40); metalworking fluid (41).

Photoaggravated allergic contact dermatitis

- Eight patients previously sensitized to MI developed allergic contact dermatitis from airborne exposure to MI in vapors from industrial biocides (n=2) and water-based paints (n=6), which subsequently became photoaggravated (29).

Presence in non-cosmetic products

- Presence of MI and other isothiazolinones in water-based wall paints in 5 European countries (4).
- MI was present in 45/47 (96%) residential interior wall paints purchased in the USA, in concentrations of 1–358 ppm (17).
- MI was present in 17/44 (39%) consumer adhesives in the USA in amounts of 4-133 ppm (18).
- Very low concentrations of MI persisting in clothes (0.4 ppm) after machine washing; it is not necessary to recommend that patients sensitized to MI avoid isothiazolinones in machine detergents or fabric conditioners, or to double rinse (19).
- Isothiazolinones in children's toy slime: colorimetric spot test may have some utility as a screening assay, but is far from specific and likely not sensitive enough to reliably identify methylisothiazolinone (21).
- Presence of MI in cleaning products (12).
- Analyses of MI in 10 children's toy slime products purchased in Japan (37).
- Analysis of MI and MCI/MI in dish soap and personal care products that do not declare isothiazolinones (39).

Other information

- Usability of a spot test for isothiazolinones (13).
- Cross-reactivity between MI and octylisothiazolinone is likely, especially in patients with strong allergy to MI (14,30).
- Results of patch testing MI and MCI/MI in Thailand, 2009 to 2018 (22).
- Market survey of the presence of MCI/MI and MI in cosmetic products in Thailand (32).

[a] Literature on contact allergy to isothiazolinone that was found in *Contact Dermatitis* or/and *Dermatitis* from September 2017 through March 2025, in which there was no direct link with cosmetic products.

LITERATURE

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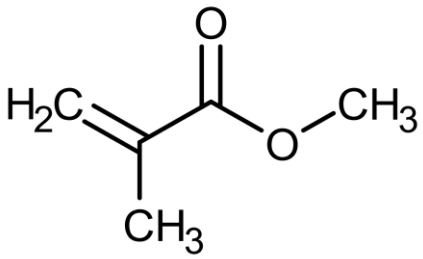
3.44 METHYL METHACRYLATE

IDENTIFICATION

Description/definition : Methyl methacrylate is the methyl ester of methacrylic acid, that conforms to the structural formula shown below
Classification : Esters
IUPAC name : Methyl 2-methylprop-2-enoate
CAS registry number : 80-62-6
EC number : 201-297-1
Wikipedia : https://en.wikipedia.org/wiki/Methyl_methacrylate
Functions in cosmetics : EU: Not reported
Patch testing : 2.0% pet. (Chemotechnique, SmartPractice)
Molecular formula : $C_5H_8O_2$



Previous chapter to which this is an update

The literature on contact allergy to methyl methacrylate from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.300, pp. 839-842.

CONTACT ALLERGY (cosmetics)

Case report

A 13-year-old girl was referred on suspicion of acrodermatitis continua of Hallopeau. For the past 9 months, the patient had suffered from a painful rash on her fingers and disfiguring nail changes. When asked about exposure, she described nail art, regularly applying nail polish and pre-formed press-on nails attached with nail glue. Physical examination revealed severe pulpitis with erythema, oedema, fissures, and scaling around the nails and dorsal aspects of her fingers and severe nail dystrophy. Patch tests were positive on D7 (+) to methyl methacrylate (MMA) 2% pet., 2-hydroxyethyl methacrylate (HEMA) 2% pet., ethylene glycol dimethacrylate (EGDMA) 2% pet., ethyl acrylate 0.1% pet., and ethyl cyanoacrylate (ECA) 10% pet. According to the ingredient list, the nail glue contained polymethyl methacrylate (poly MMA), polyethylene glycol dimethacrylate (poly EGDMA) and ECA. A diagnosis of allergic contact dermatitis caused by (meth)acrylates in nail glue was established (1).
Ethyl cyanoacrylate was undoubtedly the most important sensitizer, but assuming that polymethyl methacrylate and polyethylene glycol dimethacrylate released some amount of monomers, both MMA and EGDMA may have contributed to the allergic manifestations.

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to methyl methacrylate see refs. 2-5 (examples).

Presence in cosmetic products

Methyl methacrylate is in the USA not a marketed cosmetic ingredient.

LITERATURE

1 Quaade AS, Simonsen AB. The bitter side of nail art: A teenage girl's encounter with (meth)acrylate-induced allergic contact dermatitis from nail glue. Contact Dermatitis. 2023;89(4):299-301. doi: 10.1111/cod.14382.

2 Travassos AR, Claes L, Boey L, Drieghe J, Goossens A. Non-fragrance allergens in specific cosmetic products. Contact Dermatitis 2011;65(5):276-285. doi: 10.1111/j.1600-0536.2011.01968.x.

3 Fisher AA, Franks A, Glick H. Allergic sensitization of the skin and nails to acrylic plastic nails. J Allergy 1957;28(1):84-88. doi: 10.1016/0021-8707(57)90073-4.

4 Macedo NA, Carmona C, Piñeyro I. Contact dermatitis from acrylic nails. Contact Dermatitis 1995;32(6):362. doi: 10.1111/j.1600-0536.1995.tb00629.x.

5 Canizares O. Contact dermatitis due to the acrylic materials used in artificial nails. Arch Dermatol 1956;74(2):141-143. doi: 10.1001/archderm.1956.01550080027004.

3.45 NICKEL*

** Not an INCI name*

IDENTIFICATION

Description/definition	: Nickel is a metal, which may be present in pigmented make-up products as a contaminant
Classification	: Elements, transition metals
INCI name USA	: Neither in CosIng nor in the Personal Care Products Council Ingredient Database
CAS registry number	: 7440-02-0
EC number	: 231-111-4
Wikipedia	: https://en.wikipedia.org/wiki/Nickel
Functions in cosmetics	: No function, contaminant
EU cosmetic restrictions	: Regulated in Annex II/1093 of the Regulation (EC) 2009/1223 (prohibited)
Patch testing	: Nickel(II)sulfate hexahydrate 2.5% and 5.0% pet. (Chemotechnique, SmartPractice)

Previous chapter to which this is an update

The literature on contact allergy to nickel from cosmetic sources up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.310, pp. 866-868.

CONTACT ALLERGY (cosmetics)

Case reports

A 21-year-old woman presented with itchy erythematous and oedematous plaques on her eyebrows, eyelids and forehead of 4 days duration. Two months earlier, the patient had started to use a new eyebrow pencil. She also reported previous rashes caused by costume jewellery. Patch tests with the international baseline series, a cosmetic series and her own cosmetic products (tested 'as is') resulted in positive reactions to nickel (++ on D2 and D4), to the eyebrow pencil (+ on D2 and D4), to triclosan and to fragrances. The eyebrow pencil proved to contain the iron oxide pigments CI 77491, CI 77492 and CI 77499. Chemical analysis of 3 samples of the culprit eyebrow pencil with inductively coupled plasma mass spectrometry showed nickel levels of 8.13, 9.10, and 8.39 mg/kg, respectively. The patient's symptoms improved after avoidance of the eyebrow pencil. It was assumed that the nickel was a contamination in the manufacture of pigments and possibly other raw materials (3).
The authors presented a second very similar patient with ACD from nickel in the same eyebrow pencil (3).

Previous cases of allergic cosmetic dermatitis

There have been many case reports of allergic cosmetic dermatitis from nickel present in cosmetic products as a contaminant, examples of which are presented in refs. 1 and 2. For a full literature review of this topic please refer to the Monographs in Contact Allergy, Volume 1, Chapter 2.310, pp. 866-868.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): unknown/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): unknown/123,000.

LITERATURE

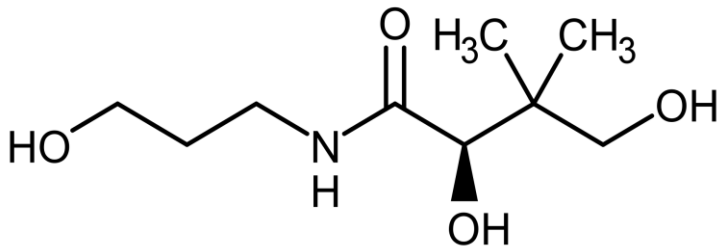
1 Travassos AR, Bruze M, Dahlin J, Goossens A. Allergic contact dermatitis caused by nickel in a green eye pencil. Contact Dermatitis 2011;65(5):307-308. doi: 10.1111/j.1600-0536.2011.01960.x.

2 Verhulst L, Persson L, Zimerson E, Bruze M, Vanden Broecke K, Goossens A. Palpebral eczematous dermatitis caused by nickel in an eye pencil. Contact Dermatitis 2014;70(4):247-249. doi: 10.1111/cod.12210.
3 Prasithirun P, Kasemsarn P, Boonchai W. Allergic contact dermatitis caused by nickel in an eyebrow pencil. Contact Dermatitis. 2019;80(2):125-126. doi: 10.1111/cod.13126.

3.46 PANTHENOL

IDENTIFICATION

Description/definition : Panthenol is the alcohol that conforms to the structural formula shown below
Classification : Alcohols; amides
IUPAC name : (2*R*)-2,4-Dihydroxy-*N*-(3-hydroxypropyl)-3,3-dimethylbutanamide
Other names : Dexpanthenol; pantothenol; provitamin B5
CAS registry number : 81-13-0
EC number : 201-327-3
CIR reports : J Am Coll Toxicol 1987;6:139-162; Int J Toxicol 2022;41(Suppl.3):77-128
Wikipedia : https://en.wikipedia.org/wiki/Panthenol
Functions in cosmetics : EU: antistatic; hair conditioning; skin conditioning. USA: hair conditioning agents
Patch testing : 5% pet. (Chemotechnique, SmartPractice)
Molecular formula : $C_9H_{19}NO_4$



Previous chapter to which this is an update

The literature on contact allergy to panthenol from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.331, pp. 910-913.

CONTACT ALLERGY (cosmetics)

Case series

In a retrospective study in Portugal, the files of patients patch tested between 2009 and 2017 were reviewed for allergic reactions to dexpanthenol 5% pet., which was tested initially in a cosmetic/vehicle series and in the last 3 years in consecutive patients. Among 2171 patients tested, 26 (1.2%) had positive reactions to panthenol. Relevance could be traced in 20 patients (77%), related to the use of one brand of pharmaceutical cream (n=15), moisturizers (n=3), topical medications (n=1), and a shampoo (n=1). Twenty-five of 26 patients (96%) reacted to several other allergens, mostly ingredients of cosmetic or pharmaceutical products. It was concluded that, although allergic contact dermatitis caused by panthenol is considered to be rare, it may be frequently overlooked. As a relatively high frequency of relevant cases was found, the authors encouraged inclusion of dexpanthenol in a patch test series, at least in a cosmetic and topical drug series (9).

Case reports

A 72-year-old nonatopic woman presented with a more than 10-year history of intermittent pruritic dermatitis on her eyelids, back, arms and legs. Patch testing with the 2020 to 2021 North American Contact Dermatitis Group screening series (80 allergens), as well as several supplemental series (corticosteroids, cosmetics, preservatives, emulsifiers, fragrances, sunscreens, and medicaments) and 29 of her own personal products on D6 showed + reactions to panthenol 5% pet. and a ‘healing ointment’

known to contain panthenol. Repeat patch tests with panthenol 5% pet. and the ointment were again positive. Examination of all patient's products found that panthenol was also listed as an ingredient in her sunscreen SPF 50, a blemish concealer, a black waterproof mascara and several hair and nail care products (7).

A 25-year-old atopic woman had perioral eczema from contact allergy to panthenol, cera alba and Ricinus communis (castor) seed oil in lip balms. Previously, she had suffered allergic contact dermatitis of the face from panthenol in a moisturizing cream (10).

A 26-year-old woman had eczema and delayed would healing from contact allergy to panthenol present in 3 cosmetic creams (12).

Previous cases of allergic cosmetic dermatitis

Panthenol is a well-known cause of allergic contact dermatitis in cosmetics and topical pharmaceutical products. The older literature on this topic has been reviewed in 1995 (1). Up to then, 40 cases had been reported. Most patients also reacted to several other allergens, mostly ingredients of cosmetic or pharmaceutical products (1). Recent reports of allergic cosmetic dermatitis to panthenol (especially from Bepanthen cream, which is actually a topical pharmaceutical) can be found in refs. 2-4. For a full literature review of this topic please refer to the Monographs in Contact Allergy, Volume 1, Chapter 2.331, pp. 910-913.

IMMEDIATE-TYPE REACTIONS

A female patient had eyelid dermatitis with a history of acute episodes of swelling resolving within a day in addition to more chronic redness and itching. Patch tests were performed with an extended series including known allergens in her hair products, eyeliner, and ointment applied to her lips, including panthenol, and with a contact urticaria series, all read at 1 hour with a final reading at D5. These showed a positive urticarial reaction at 1 hour to panthenol 5% pet. and a positive reaction to potassium dichromate at D5, which was relevant to her eyeliner containing chromic oxide green. The patient was advised to stop using her eyeliner, her hair products and the 'healing ointment' which contained panthenol. She reported complete resolution 8 weeks later (6).

Previous cases of immediate-type reactions

For a previous case of contact urticaria to panthenol in a hair conditioner and colouring product see ref. 5.

OTHER PUBLICATIONS [a]

- Most cases of ACD from panthenol are caused by the topical pharmaceutical product Bepanthen (8,11,13).
- A 49-year-old man presented had generalized eczema of the trunk, arms and legs caused by contact allergy to panthenol in a topical pharmaceutical (8). Two patients were allergic to Bepanthen cream. One also reacted to pantolactone, which was also present in 2 topical pharmaceuticals. Pantolactone is an impurity (~1%) of panthenol raw materials, and it is likely formed from panthenol in acidic aquatic media (i.e., sweat) (11).
- A 38-year-old man had extensive allergic contact dermatitis to dexpanthenol with distant facial and symmetrical intertriginous involvement after applying Bepanthen cream for 8 days to a newly engraved tattoo on his left lower forearm (13).
- A very useful review article on contact allergy to panthenol was published in 2014 in *Dermatitis* (14).

[a] Literature on contact allergy to panthenol that was found in *Contact Dermatitis* or/and *Dermatitis* from September 2017 through March 2025, in which there was no direct link with cosmetic products.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 273/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 14,135/123,000.

LITERATURE

1 Schmid-Grendelmeier P, Wyss M, Elsner P. Contact allergy to dexpanthenol – a report of seven cases and review of the literature. Dermatosen 1995;43:175-178.

2 Fernandes S, Macias V, Cravo M, Amaro C, Santos R, Cardoso J. Allergic contact dermatitis caused by dexpanthenol: report of two cases. Contact Dermatitis 2012;66(3):160-161. doi: 10.1111/j.1600-0536.2011.02005.x.

3 Chin MF, Hughes TM, Stone NM. Allergic contact dermatitis caused by panthenol in a child. Contact Dermatitis 2013;69(5):321-322. doi: 10.1111/cod.12116.

4 Clerens I, Goossens A. Allergic contact dermatitis caused by panthenol: a rare but relevant sensitizer. Contact Dermatitis 2017;76(2):122-123. doi: 10.1111/cod.12685.

5 Schalock PC, Storrs FJ, Morrison L. Contact urticaria from panthenol in hair conditioner. Contact Dermatitis 2000;43(4):223. doi: 10.1034/j.1600-0536.2000.043004223.x.

6 Ahuja KR, Nedorost S. Should we patch test to panthenol more often? Dermatitis. 2024;35(6):673-674. doi: 10.1089/derm.2023.0320.

7 Han J, Warshaw EM. Allergic contact dermatitis to panthenol in "hypoallergenic" products. Dermatitis. 2022 Nov 8. doi: 10.1097/DER.0000000000000883.

8 Miroux-Catarino A, Silva L, Amaro C, Viana I. Allergic contact dermatitis caused dexpanthenol—But is that all? Contact Dermatitis. 2019;81:391-392. doi: 10.1111/cod.13341.

9 Fernandes RA, Santiago L, Gouveia M, Gonçalo M. Allergic contact dermatitis caused by dexpanthenol-Probably a frequent allergen. Contact Dermatitis. 2018;79(5):276-280. doi: 10.1111/cod.13054.

10 Verheyen M, Rombouts S, Lambert J, Aerts O. Contact allergy to castor oil, but not to castor wax. Cosmetics 2017, 4(1), 5; doi: 10.3390/cosmetics4010005.

11 Blanchard G, Kerre S, Walker A, Dendooven E, Aerts O, Goossens A, et al. Allergic contact dermatitis from pantolactone and dexpanthenol in wound healing creams. Contact Dermatitis. 2022 ;87(5):468-471. doi: 10.1111/cod.14198.

12 Coco-Viloin M, Ramspacher J, Giordano F. Allergic contact dermatitis and delayed wound healing from panthenol. Contact Dermatitis. 2024 Dec;91(6):518-520. doi: 10.1111/cod.14666.

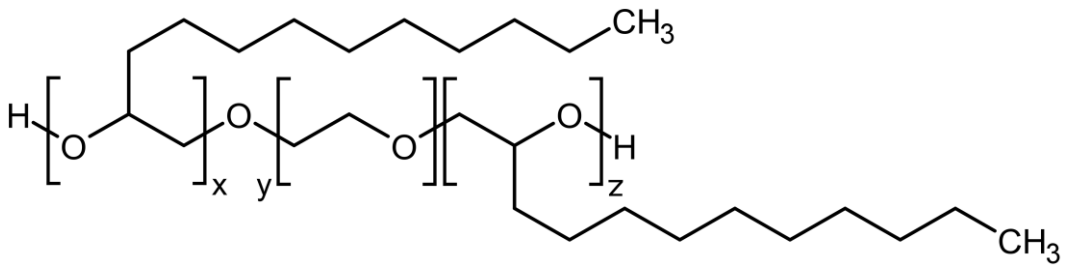
13 Goessinger EV, Merkel T, Chantraine S, Hartmann K. Extensive allergic contact dermatitis to dexpanthenol with distant facial and symmetrical intertriginous involvement: An unusual clinical presentation. Contact Dermatitis. 2025;92(1):75-77. doi: 10.1111/cod.14693.

14 Weber B, Hylwa S. Panthenol Allergic Contact Dermatitis: Sources of exposure, reported cases, and a call for more frequent testing. Dermatitis. 2024 Dec 23. doi: 10.1089/derm.2024.0489. Online ahead of print.

3.47 PEG-22/DODECYL GLYCOL COPOLYMER

IDENTIFICATION

Description/definition : PEG-22/dodecyl glycol copolymer is the polyoxyethylene, polydodecyl glycol block polymer that conforms generally to the formula shown below, in which the average value of x, y, and z are 4.5, 22 and 4.5 respectively
Classification : Alkoxylated alcohols; synthetic polymers
IUPAC name : Poly(oxy-1,2-ethanediyl), α-(12-hydroxydodecyl)- ω-[(12-hydroxydodecyl)oxy]-
Other names : Poly(oxy-1,2-ethanediyl), α-hydro-ω-hydroxy-, diethers with 1,2-dodecanediol homopolymer (22 mol EO, 9 mol dodecanediol average molar ratio)
CAS registry number : 78336-31-9
Functions in cosmetics : EU: emulsifying; stabilising. USA: emulsion stabilizers; skin-conditioning agents - emollient
Patch testing : 20% pet.



Previous chapter to which this is an update

The literature on contact allergy to PEG-22/dodecyl glycol copolymer from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.344, pp. 939.

CONTACT ALLERGY (cosmetics)

Case report

A 27-year-old woman reported a vesicular rash around a scar on the back of the foot following the application of a 'protective repair cream' for the first time. Six days later, she developed an erythematous and pruritic oedema of the face. A few weeks after that, the patient reported a second pruritic vesiculobullous skin eruption on her hands after the first application of a hand cream of the same brand. Due to the severity of the initial reaction, semi-open skin tests were performed with the two creams, resulting in positive reactions on D2 to both products. Patch tests with the components of the two creams, supplied by the manufacturer, were positive (++) on D2 and D4 to PEG-22/dodecyl glycol copolymer contained in the repair cream, and doubtfully positive (?+) on D2 and D4 to PEG-45/dodecyl glycol copolymer contained in the hand cream (concentrations not mentioned). A repeated open application test (ROAT) with the latter ingredient was, however, clearly positive (follicular aspect) after 5 days. The diagnosis of ACD caused by PEG-22/dodecyl glycol copolymer and PEG-45/dodecyl glycol copolymer on the initial application site associated with oedematous eczema of the face (via a transfer) was established. The authors suggested the possibility of cross-reactivity between PEG-22 and PEG-45 dodecyl glycol copolymers (2). Conversely, the genuine sensitizer might be an additive, an impurity, a product appearing during polymerization, a residual monomer, or a degradation product (3).

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to PEG-22/dodecyl glycol copolymer see ref. 1.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 3/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 1/123,000.

LITERATURE

1 Amsler E, Al-Raddadi R, Frances C. Allergic contact dermatitis caused by PEG-22/dodecyl glycol copolymer in a skin-repairing cream. Contact Dermatitis 2017;77(1):54-55. doi: 10.1111/cod.12743.

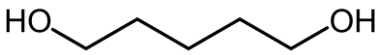
2 Brehon A, Soria A, Barbaud A, Amsler E. Allergic contact dermatitis caused by PEG-22 and PEG-45 dodecyl glycol copolymers in two skin-repairing creams. Contact Dermatitis. 2023;89(3):213-215. doi: 10.1111/cod.14369.

3 Quartier S, Garmyn M, Becart S, Goossens A. Allergic contact dermatitis to copolymers in cosmetics–case report and review of the literature. Contact Dermatitis. 2006;55(5):257-267. doi: 10.1111/j.1600-0536.2006.00960.x.

3.48 PENTYLENE GLYCOL

IDENTIFICATION

Description/definition : Pentylene glycol is the organic compound that conforms to the structural formula shown below
Classification : Alcohols
IUPAC name : Pentane-1,5-diol; 1,5-pentanediol
Other names : 1,2-Dihydroxypentane
CAS registry number : 5343-92-0
EC number : 226-285-3
CIR reports : Int J Toxicol 2012;31(Suppl.2):147-168
Wikipedia : https://en.wikipedia.org/wiki/1,5-Pentanediol (1,5-Pentanediol)
Functions in cosmetics : EU: skin conditioning; solvent. USA: preservatives; skin-conditioning agents – miscellaneous; solvents
Patch testing : 5% and 10% water (8); 10% water seems preferable over 5% water (6); 5% 50 water/50 alcohol (7,9)
Molecular formula : $C_5H_{12}O_2$



Previous chapter to which this is an update

The literature on contact allergy to pentylene glycol from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.351, p. 948.

CONTACT ALLERGY (cosmetics)

Case series

In Italy, from March 2021 to July 2022, members of the Società Italiana di Dermatologia Allergologica Professionale e Ambientale (SIDAPA) patch tested 1235 consecutive patients (880 women and 355 men, mean age 51 ± 19 years) with pentylene glycol (PTG) 5% and 10% water and propylene glycol (PG) 5% pet. and 30% water (6). Allergic reactions to both 5% and 10% PTG were seen in five patients and to 10% PTG alone in two (total n=7, 0.6%). The clinical relevance was judged certain/likely in two patients, possible/doubtful in three, and absent in two individuals. The sources of exposure to PTG in the two patients with certain/likely clinical relevance were face/body creams, and cosmetics were also (suspected) sources of exposure in the 3 patients with possible/doubtful relevance. Irritant reactions to both 5% and 10% PTG were seen in three patients and to 10% PTG alone in one. Overall, PTG gave 0.57% allergic reactions versus 0.32% irritant reactions. Only one patient showed simultaneous sensitization to PTG (5% and 10%) and PG (30%) with certain/probable relevance for allergic contact dermatitis. The authors conclude that pentylene glycol deserves to be considered as an audit allergen for the cosmetic series and that cross-reactivity with propylene glycol is infrequent (6).
For the results of propylene glycol see Chapter 3.57 Propylene glycol.

Case reports

A 37-year-old female patient, previously diagnosed with chronic (allergic) eyelid dermatitis due to (components in) cosmetics, scented candles, and essential oil diffusers, developed a relapse of her skin condition, despite using only ‘hypoallergenic’ products. Patch tests with the European baseline, cosmetic, preservative and excipient series and with the patient's own products (tested ‘as is’), showed positive reactions to an eye cream (D2 +++, D4 +++) and to a make-up remover (D2 +, D4 ++). Multiple positive reactions were observed to haptens from the commercial series (fragrances, propolis, neomycin, metals,

HEMA), yet these could not explain the positive patch test reactions to the two culprit cosmetics. The individual ingredients of the eye cream, provided by the manufacturer, were subsequently patch tested and showed a positive reaction only to pentylene glycol 5% 50 water/50 alcohol (D2 +++, D4 +++), which allergen was present in both the eye cream and the makeup remover. Two controls were negative. There were no (cross-)reactions to butylene glycol 5% 50 water/50 alcohol or propylene glycol 5% pet. and 5% water (7).

A 44-year-old female patient had suffered two episodes of severe facial eczema after the use of an antiaging cream. Patch testing with the SIDAPA (Società Italiana di Dermatologia Allergologica Professionale e Ambientale) baseline series and the integrative eyelids series showed positive reactions only to nickel sulfate (+++/+++) and cobalt chloride (+/++). A repeated open application test (ROAT) with the cream in the antecubital fossa was positive within 3 days. Due to the strong reaction in the ROAT, the patient refused further patch tests with the cream. The label on the cream reported pentylene glycol (PTG) among the top ingredients. Patch tests with PTG 5% and 10% water gave positive reactions (+) at D3 to both concentrations. Fifteen controls were negative. Propylene glycol was also tested (5% pet. and 30% water) with no reaction (8).
(**Comment**: why was the cream, which was strongly suspected, not tested in the first session?).

In another case report from Italy, a 90-year old female patient had allergic contact dermatitis from pentylene glycol (tested 5% in water/alcohol (equal parts) solution; + at D2, D3, and D4) in an eye contour cream (9).

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to pentylene glycol see refs. 1-5.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 1918/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 4901/123,000.

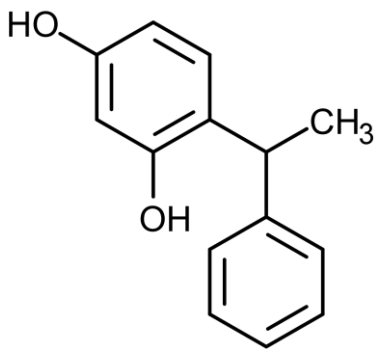
LITERATURE

1 Mortz CG, Otkjær A, Andersen KE. Allergic contact dermatitis to ethylhexylglycerin and pentylene glycol. Contact Dermatitis 2009;61(3):180. doi: 10.1111/j.1600-0536.2009.01586.x.
2 Gallo R, Viglizzo G, Vecchio F, Parodi A. Allergic contact dermatitis from pentylene glycol in an emollient cream, with possible co-sensitization to resveratrol. Contact Dermatitis 2003;48(3):176-177. doi: 10.1034/j.1600-0536.2003.00073.x.
3 Amado A, Taylor JS, Murray DA, Reynolds JS. Contact dermatitis to pentylene glycol in a prescription cream for atopic dermatitis: case report. Arch Dermatol 2008;144(6):810-812. doi: 10.1001/archderm.144.6.810.
4 Hausen BM. Contact allergy to pentylene glycol. Dermatitis 2007;18(2):99-100. doi:10.2310/6620.2006.06016.
5 Kerre S. Allergic contact dermatitis to pentylene glycol in a cosmetic cream. Contact Dermatitis 2008;58(2):122-123. doi: 10.1111/j.1600-0536.2007.01201.x.
6 Gallo R, Guarneri F, Ferrucci SM, Stingeni L, Hansel K, Corazza M, et al. Frequency of contact allergy to pentylene glycol. Retrospective cross-sectional study with data from the Società Italiana di Dermatologia Allergologica Professionale e Ambientale (SIDAPA). Contact Dermatitis. 2024;90(3):314-317. doi: 10.1111/cod.14469.
7 Seremet T, Aerts O, Walker A, Wüthrich H, Dendooven E, Goossens A, et al. Allergic contact dermatitis from pentylene glycol in 'hypoallergenic' eye cosmetics. Contact Dermatitis. 2023;88(1):73-75. doi:10.1111/cod.14224.
8 Corazza M, Schenetti C, Schettini N, Zedde P, Borghi A. Pentylene glycol: An emerging cosmetic allergen? Contact Dermatitis. 2022;86(1):44-46. doi: 10.1111/cod.13963.
9 Gallo R, Russo R, Trave I, Murgioni F, Parodi A. Allergic contact dermatitis to pentylene glycol in an eye contour cream. Contact Dermatitis. 2020;82(4):254-255. doi: 10.1111/cod.13454.

3.49 PHENYLETHYL RESORCINOL

IDENTIFICATION

Description/definition : Phenylethyl resorcinol is the organic compound that conforms to the structural formula shown below
Classification : Phenols
UPAC name : 4-(1-Phenylethyl)benzene-1,3-diol
Other names : Phenethyl resorcinol; 1,3-benzenediol, 4-(1-phenylethyl)-
CAS registry number : 85-27-8
Functions in cosmetics : EU: antioxidant. USA: antioxidants; skin-conditioning agents - miscellaneous
Patch testing : 0.1% and 1% pet. (1); 2% pet. (2,3); 5% pet. has also been used, no data on control testing available (3)
Molecular formula : $C_{14}H_{14}O_2$



Previous chapter to which this is an update

The literature on contact allergy to phenylethyl resorcinol from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.355, pp. 956.

CONTACT ALLERGY (cosmetics)

Case series

Apparently, in 2021, 3 Belgian cases of facial allergic cosmetic contact dermatitis from phenylethyl resorcinol have been published in *Contact Dermatitis* (4). However, according to PubMed, the article has been published online only, and it has not been included in the printed version. I am unable to locate the publication and present its results here.

In Spain, a systematic search in the Spanish Registry of Contact Dermatitis and Cutaneous Allergy (REIDAC) database was performed to identify patients with positive patch tests to phenethyl resorcinol or cosmetics that contain it between June 2018 and January 2023. Of 11,541 patients of who data were available, 13 individuals with positive patch tests to phenethyl resorcinol were identified. All 13 were women, with a mean age of 42 years (range 32–59 years). Eight of them had melasma and the Fitzpatrick skin phototype III was predominant. All 13 patients had lesions on their faces, which were mainly around the eyelids (n=9), around the lips (n=7) and on the forehead (n=4). Another common location was the neck (n=5). The main cosmetic implicated (in 11 out of 13 patients) was a sunscreen which is used frequently in Spain for patients with different types of facial pigmentations. Four individuals had shown positive patch test reactions to phenethyl resorcinol 2%, 2 to 5%, one to 0.5% in 50% water/50% alcohol and the remaining six to the chemical supplied by the manufacturer in an unknown concentration (3).

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to phenylethyl resorcinol see refs. 1 and 2.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 15/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 42/123,000.

LITERATURE

1 Gohara M, Yagami A, Suzuki K, Morita Y, Sano A, Iwata Y, et al. Allergic contact dermatitis caused by phenylethyl resorcinol [4-(1-phenylethyl)-1,3-benzenediol], a skin-lightening agent in cosmetics. Contact Dermatitis 2013;69(5):319-320. doi: 10.1111/cod.12114.

2 Pastor-Nieto M-A, Sánchez-Pedreño P, Martínez-Menchón T, Melgar-Molero V, Alcántara-Nicolás F, de la Cruz-Murie P. Allergic contact dermatitis caused by phenylethyl resorcinol, a skin-lightening agent contained in a sunscreen. Contact Dermatitis 2016;75(4):250-253. doi: 10.1111/cod.12617.

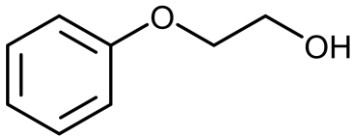
3 Mercader-García P, Gatica-Ortega ME, González-Pérez R, Pastor-Nieto MA, Carrillo A, Borrego L; REIDAC. Cosmetovigilance for infrequent allergens in Spain using a national online registry: The example of allergic contact dermatitis caused by phenylethyl resorcinol. Contact Dermatitis. 2024;90(3):245-252. doi:10.1111/cod.14460

4 Mairlot M, Aerts O, Dendooven E, Herman A. Three additional cases of facial allergic contact dermatitis from the powerful pigment-lightening agent phenylethyl resorcinol. Contact Dermatitis. 2021 Mar 21. doi: 10.1111/cod.13840. Epub ahead of print.

3.50 PHENOXYETHANOL

IDENTIFICATION

Description/definition : Phenoxyethanol is the aromatic ether alcohol that conforms to the structural formula shown below
Classification : Alcohols; ethers
IUPAC name : 2-Phenoxyethanol
Other names : Ethylene glycol monophenyl ether; in Euxyl® K 400 with methyldibromo glutaronitrile
CAS registry number : 122-99-6
EC number : 204-589-7
CIR reports : J Am Coll Toxicol 1990;9:259-277
SCCS opinions : SCCS/1575/16
Wikipedia : https://en.wikipedia.org/wiki/Phenoxyethanol
Functions in cosmetics : EU: preservative. USA: fragrance ingredients; preservatives
EU cosmetic restrictions : Regulated in Annex V/29 of the Regulation (EC) 2009/1223
Patch testing : 1% pet. (Chemotechnique, SmartPractice)
Molecular formula : $C_8H_{10}O_2$



Previous chapter to which this is an update

The literature on contact allergy to phenoxyethanol from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.356, pp. 957-961.

CONTACT ALLERGY (cosmetics)

Case report

A 59-year-old male toolmaker presented with therapy-resistant, 1-year lasting dermatitis of the hands and forearms suspected to be of occupational origin. Extensive patch tests were positive to phenoxyethanol only. Phenoxyethanol was not found in any of the available safety datasheets of the patient's workplace products, including the metalworking fluid. However, according to the product labels, it was an ingredient of 2 hand creams that he had regularly applied on his hands and lower arms after the onset of dermatitis. A repeated open application test (ROAT) with one of the creams twice daily for 6 days on the inner side of the patient's upper arm resulted in a positive reaction. The dermatitis of hands and lower arms improved significantly after avoidance of these skin care products, indicating clinical relevance of the sensitization to phenoxyethanol as causing secondary allergic contact dermatitis superimposed on the initially occupational irritant contact dermatitis (11).

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to phenoxyethanol (examples) see refs. 1-3.

IMMEDIATE-TYPE REACTIONS

A 26-year-old non-atopic man had suffered an erythematous-oedematous itching and burning eruption of his face following the application of a hydrating fluid. A 32-year-old woman, with a history of allergic

rhinitis and atopic dermatitis in childhood, reported itching erythema on her face after the use of a moisturising and soothing serum. In both cases, the manifestations appeared between 10 and 20 minutes after the application and disappeared after about 45 minutes. Contact urticaria was diagnosed. Patch tests with the baseline Italian SIDAPA series and three suspected ingredients that the cosmetics had in common (phenoxyethanol, citric acid, sodium benzoate) were negative after 15 and 30 minutes and at D2 and D3. Open tests with the cosmetics and these ingredients on the inner lower arm were also negative. However, open tests on the forehead showed a positive reaction with itching edema and erythema after 15 minutes with the personal product and with phenoxyethanol 1% and 5% pet. in both patients. Ten controls were negative (8).

A 29-year-old atopic woman had a 2-year history of recurrent episodes of urticarial reactions affecting her face, suspected to be caused by various cosmetics including a recently used facemask. Reactions developed within 30 minutes of exposure, initially lasting minutes, but progressed in terms of duration and severity over time. A photograph of a recent episode after applying the face mask showed marked oedema and erythema of the face and neck. Thirty minute patch testing to a modified European baseline series of 40 allergens was markedly positive to phenoxyethanol (>15 mm wheal). This preservative was found to be an ingredient in several of the products she had reacted to, including the facial mask. Contact urticaria to phenoxyethanol in various cosmetics was diagnosed (9).

A 20-year-old atopic woman had developed immediate pruritic erythematous reactions with hives at the areas where she had applied several cosmetics over the last year. The incriminated cosmetics had 4 common ingredients: water, glycerin, sodium hydroxide, and phenoxyethanol. Open tests performed with four moisturizers and one scrub ‘as is’, as well as phenoxyethanol 1% pet. all triggered erythematous pruritic reactions after 20 minutes, lasting 45 minutes. A prick-by-prick test with phenoxyethanol 1% pet. was negative. Open tests with phenoxyethanol in 10 controls were negative. The patient has remained asymptomatic for 2 years with the avoidance of cosmetics with phenoxyethanol except for rare accidental exposures to the preservative (10).

Previous cases of immediate-type reactions

For previously reported cases of immediate-type reactions to phenoxyethanol see refs. 4-7.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 11,089/35,000.
EWG’s Skin Deep Cosmetics Database (February 2025): 46,128/123,000.

OTHER PUBLICATIONS [a]

An 80-year-old woman had contact urticaria from phenoxyethanol in an ultrasound gel. Previously, she had developed swelling and pruritus a few minutes after the application of cosmetics such as moisturizers and wet wipes (12).

[a] Literature on contact allergy to phenoxyethanol that was found in *Contact Dermatitis* or/and *Dermatitis* from September 2017 through March 2025, in which there was no direct link with cosmetic products.

LITERATURE

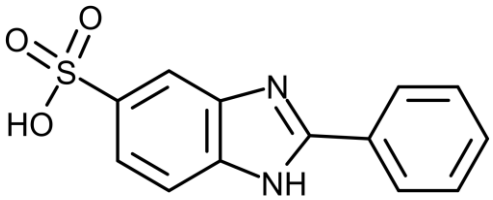
1 Lovell CR, White IR, Boyle J. Contact dermatitis from phenoxyethanol in aqueous cream BP. Contact Dermatitis 1984;11(3):187. doi: 10.1111/j.1600-0536.1984.tb00970.x.
2 Tosti A, Guerra L, Bardazzi F, Gasparri F. Euxyl K 400: a new sensitizer in cosmetics. Contact Dermatitis 1991;2592):89-93. doi: 10.1111/j.1600-0536.1991.tb01794.x.
3 Goossens A, Beck MH, Haneke E, McFadden JP, Nolting S, Durupt G, Ries G. Adverse cutaneous reactions to cosmetic allergens. Contact Dermatitis 1999;40(2):112-113. doi: 10.1111/j.1600-0536.1999.tb06004.x.
4 Birnie AJ, English JS. 2-phenoxyethanol-induced contact urticaria. Contact Dermatitis 2006;54(6)349. doi: 10.1111/j.0105-1873.2006.0645g.x.

5 Hernandez B, Ortiz-Frutos FJ, Garcia M, Palencia S, Garcia MC, Iglesias L. Contact urticaria from 2-phenoxyethanol. Contact Dermatitis 2002;47(1):54. doi: 10.1034/j.1600-0536.2002.470116.x.
6 Bohn S, Bircher AJ. Phenoxyethanol-induced urticaria. Allergy 2001;56(9):922-923. doi: 10.1034/j.1398-9995.2001.00218.x.
7 Núñez Orjales R, Carballas Vázquez C, Carballada González F, Boquete París M. 2-Phenoxyethanol-induced contact urticaria and anaphylaxis. J Investig Allergol Clin Immunol 2010;20(4):354-355. PMID: 20815317.
8 Marzola E, Melloni L, Caligiure A, Gianessi F, Bianchi A, Borghi A, et al. Site-related contact urticaria from phenoxyethanol. Contact Dermatitis. 2024;91(5):434-436. doi: 10.1111/cod.14637.
9 McCarthy S, White IR, McFadden JP, Cunningham L. Recurrent contact urticaria to cosmetics: An unexpected allergen. Contact Dermatitis. 2023;88(1):63-64. doi: 10.1111/cod.14217.
10 Pastor-Nieto MA, Peña-Arellano MI, Gatica-Ortega ME. Immunologic contact urticaria from phenoxyethanol in cosmetics. Contact Dermatitis. 2021;85(5):586-587. doi: 10.1111/cod.13911.
11 Kolodziej M, Kiewert A, Skudlik C, Brans R. Allergic contact dermatitis to phenoxyethanol: A rare, but possible cause of hand dermatitis. Contact Dermatitis. 2022;86(4):319-320. doi: 10.1111/cod.14029.
12 Aranzabal MA, Arruti N, Joral A, Lasa EM, Martínez S, Echenagusia MA. Contact urticaria caused by phenoxyethanol in ultrasound gel. Contact Dermatitis. 2019;81(2):132-133. doi: 10.1111/cod.13255.

3.51 PHENYLBENZIMIDAZOLE SULFONIC ACID

IDENTIFICATION

Description/definition : Phenylbenzimidazole sulfonic acid is the aromatic organic compound that conforms to the structural formula shown below
Classification : Heterocyclic compounds; sulfonic acids
IUPAC name : 2-Phenyl-3*H*-benzimidazole-5-sulfonic acid
Other names : Ensulizole; Eusolex® 232
CAS registry number : 27503-81-7
EC number : 248-502-0
SCCS opinions : SCCP/1056/06
Functions in cosmetics : EU: UV-absorber; UV-filter. USA: light stabilizers; sunscreen agents
EU cosmetic restrictions : Regulated in Annex VI/6 of the Regulation (EC) 2009/1223
Patch testing : 10% pet. (Chemotechnique, SmartPractice)
Molecular formula : $C_{13}H_{10}N_2O_3S$



Previous chapter to which this is an update

The literature on contact allergy to phenylbenzimidazole sulfonic acid from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.357, pp. 962-964.

CONTACT ALLERGY (cosmetics)

General

A very useful review article on sunscreen allergy was published in 2023 in *Dermatitis* (8).

Case report

A 79-year-old man presented with a generalized, extremely pruritic eruption that developed during his holidays. He had been exposed to the sun and had used two different sunscreens. Photopatch testing showed a positive reaction (++) to phenylbenzimidazole sulfonic acid 10% pet. 4 days after the allergens had been applied (2 days after irradiation) on both the irradiated and non-irradiated sites. No reaction was seen to the patient's own products, although phenylbenzimidazole sulfonic acid was present in one of the sunscreens (6).

A 75-year-old Japanese man developed discomfort after he had applied a phenylbenzimidazole sulfonic acid-containing skin lotion to his face for the first time. Two weeks later, the lotion was again applied mainly around the beard area of the face and neck, resulting in erythema and swelling the following day. The skin symptoms subsided in 1 week, but the patient noticed lighter skin spots at the previous sites of dermatitis. Five months after onset, depigmented lesions involving the face and the neck were observed. There was no depigmentation in other skin sites nor was there a family history of vitiligo. Histological findings showed vacuolar degeneration of the basal layer and an inflammatory cell infiltration around blood vessels in the upper dermis.
Patch tests with the Japanese baseline series and the lotion (tested 'as is') were positive (+) to the lotion, cobalt chloride and isothiazolinone mix. Patch and photopatch tests of the components of this lotion resulted in equally strong positive reactions to phenylbenzimidazole sulfonic acid 3% water at the

irradiated and non-irradiated sites. Three controls were negative. Depigmented allergic contact dermatitis was diagnosed. The depigmented lesions had partially improved one and a half year later, but they persist at most sites. The histological findings of the patch test reaction area suggested, according to the authors, the possibility of depigmentation due to inflammation at the epidermal-dermal interface (7).

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to phenylbenzimidazole sulfonic acid see refs. 1-4. For cases of photoallergic contact dermatitis see refs. 2 and 5 (examples).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 30/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 49/123,000.

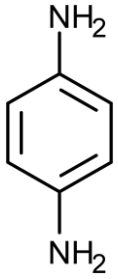
LITERATURE

1 Schauder S, Ippen H. Photoallergic and allergic contact eczema caused by dibenzoylmethane compounds and other sunscreening agents. Hautarzt 1988;39(7):435-440. PMID: 2975642.
2 Schauder S, Ippen H. Photoallergic and allergic contact dermatitis from dibenzoylmethanes. Photodermatology 1986;3(3):140-1473. PMID: 3748854.
3 Nedorost S. Ensulizole (phenylbenzimidazole-5-sulfonic acid) as a cause of facial dermatitis: two cases. Dermatitis 2005;16(3):148. doi: 10.1097/01206501-200509000-00014.
4 Gonçalo M, Ruas E, Figueiredo A, Gonçalo S. Contact and photocontact sensitivity to sunscreens. Contact Dermatitis 1995;33(4):278-280. doi: 10.1111/j.1600-0536.1995.tb00492.x.
5 Schauder S. Adverse reactions to sunscreening agents in 58 patients (part 3). Z Hautkr 1991;66:294-318 (article in German).
6 Barrientos N, Abajo P, de Celada RA, de Vega MM, Domínguez J. Allergic contact dermatitis caused by phenylbenzimidazole sulfonic acid included in a sunscreen. Contact Dermatitis. 2019;81(2):151-152. doi: 10.1111/cod.13271.
7 Tamagawa-Mineoka R, Taniguchi M, Ioka N, Hattori J, Mizutani H, Masuda K, et al. Depigmented contact dermatitis due to phenylbenzimidazole sulfonic acid contained in skin lotion. Contact Dermatitis. 2024;91(3):259-260. doi: 10.1111/cod.14588.
8 Ekstein SF, Hylwa S. Sunscreens: A review of UV filters and their allergic potential. Dermatitis. 2023;34(3):176-190. doi: 10.1097/DER.0000000000000963.

3.52 P-PHENYLENEDIAMINE

IDENTIFICATION

Description/definition : *p*-Phenylenediamine is the aromatic amine that conforms to the structural formula shown below
Classification : Amines; color additives - hair
IUPAC name : Benzene-1,4-diamine
Other names : CI 76060; 1,4-phenylenediamine; *p*-diaminobenzene; 1,4-benzenediamine
CAS registry number : 106-50-3
EC number : 203-404-7
CIR reports : J Am Coll Toxicol 1985;4:203-266; Final report, December 11, 2007; Tentative report, December 3, 2024
SCCS opinions : SCCS/1443/11; SCCP/0989/06; SCCNFP/0129/99
Wikipedia : https://en.wikipedia.org/wiki/P-Phenylenediamine
Functions in cosmetics : EU: hair dyeing. USA: hair colorants
EU cosmetic restrictions : Regulated in Annexes III/8a and III/8b of the Regulation (EC) 2013/344
Patch testing : 1% pet. (Chemotechnique, SmartPractice); 0.3% pet. (SmartPractice)
Molecular formula : $C_6H_8N_2$



Previous chapter to which this is an update

The literature on contact allergy to *p*-phenylenediamine from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.359, pp. 966-997.

CONTACT ALLERGY (cosmetics)

Case reports

A 24-year-old male patient with no personal/family history of autoimmune disease, but with a history of henna tattoo reaction at the age of 12, presented with acute exudative dermatitis on his scalp, ears and neck following the first self-application of a black-coloured hair dye. Two weeks later, he suddenly developed patchy non-scarring scalp and beard hair-loss compatible with alopecia areata (AA). Hair re-growth was slowly achieved upon treatment with oral and topical corticosteroids, and topical minoxidil within 5 months. Patch tests were strongly positive to *p*-phenylenediamine (PPD), PPD-related substances, hydroquinone and pyrogallol. The authors believe that allergic contact dermatitis should be considered a trigger for AA in predisposed individuals. It was hypothesized that interactions among overlapping inflammatory pathways underlying allergic contact dermatitis and AA have played a role in the AA elicitation in this patient (6).

A 30-year-old woman had been applying hair dyes of different brands every 2-3 months for 2 years. The last application, 6 months ago, had resulted in itchy, oozing plaques over the scalp, forehead, and ears. Clinical examination at presentation showed a residual violaceous pigmentation over the scalp, adjacent forehead, and superolateral portions of the ears, along with scarring and patchy hair loss (cicatricial

alopecia) of the scalp and forehead. A skin biopsy from a hyperpigmented alopecic lesion showed focal basal cell damage with moderate pigment incontinence and vertically oriented bands of scars, with loss of hair follicles and sebaceous glands, suggestive of follicular scarring. She was thus suspected to have cicatricial (lichenoid) alopecia with pigmentation due to allergic contact dermatitis from hair dye. Patch tests on D2 and D4 showed +++ reactions to four brands of PPD-containing hair dyes, three mixtures of hair dye with colour developer and to *p*-phenylenediamine 1% pet. Topical corticosteroids were unhelpful 6 weeks later, after which the patient was lost to follow-up (7).

A 29-year-old woman had a combination of allergic contact dermatitis to hair dye and 'anaphylactoid symptoms', which consisted of cough appearing a few hours after application of the dye, gradually worsening and accompanied by dyspnoea after 4 days. Open tests and scratch tests with 2 dyes and PPD 1% pet. were negative, but positive at D2 and D3. Meanwhile, five hours after the tests, pruritus had appeared at the sites of the open and closed patch test, and after 16 hours, the patient had developed hoarseness, pharyngeal symptoms, and dyspnoea. Although the open tests and scratch tests had been negative after 15 minutes, the authors suggested that 'the current case might likely be due to combined immediate and delayed hypersensitivity to hair dye, though the immediate hypersensitivity observed in this patient was atypical' (8).

A 22-year-old man had allergic contact dermatitis of the face from beard coloration. It was ascribed to PPD, but the patient also had positive patch tests to *p*- and *m*-aminophenol, toluene-2,5-diamine and the textile dye mix and there was no information provided on the contents of the beard coloration material. As the patch test reactions had been very strong to bullous, the authors suggested that a shorter contact time for PPD and textile dye mix would probably have been sufficient for diagnosis while avoiding the bullous patch test reactions observed. They feel that this encourages to minimize the contact time to one hour or 'until first symptoms' for all the patch tests with dyes when a dye-related ACD is strongly suspected (11).

A 49-year-old man presented with a 2-year history of recurrent pruritic eczema involving the left arm, left chest, and back. Patch testing with the European/Portuguese baseline series and a hairdressing series showed strong positive reactions on D2 and D3 to PPD, methylisothiazolinone 0.2% water, and various PPD-related para-chemicals. The patient denied dyeing his hair, having tattoos, or having contact with ink or textiles at work. However, his wife dyed her hair regularly with various products. The patient reported direct contact with his wife's hair, especially while sleeping at night, because she slept on his left side. Recommendations included the use of PPD-free hair dye for his wife, additional avoidance of the other allergens, and the use of topical corticosteroids as needed. In a reassessment 2 months later, the patient reported resolution of the lesions since his wife had been avoiding the culprit products and had cut her hair. This was a case of connubial/consort allergic contact dermatitis (16).

Another case of connubial ACD to PPD used by the partner is described in ref. 22.

A 42-year-old woman had suffered various episodes of allergic reactions to hair dyes. She also had a nasal bridge eruption after wearing certain eyeglasses. Patch tests were positive to PPD, many other para-compounds including diaminodiphenylmethane (DDM) and to scrapings of her eyeglass frame. These reactions were considered to be cross-reactions and the allergic contact dermatitis to the plastic eyeglass frame was ascribed to DDM, although no enquiries to the manufacturer were made for confirmation of its presence in the product or performing chemical analyses (19).

A 73-year-old woman presented with a 3-month history of a pruritic rash and erosions on her lips. The rash appeared on her scalp 2 weeks after using a brown hair dye, followed by facial and peri-areolar lesions and mucosal erosions 1 month later. Physical examination revealed annular erythematous plaques with a violaceous border and a slightly atrophic center on the scalp, forehead, neck, and right breast, along with erosive crusted cheilitis and white lacy streaks on the jugal mucosa. Biopsies from the forehead and peri-areolar area revealed civatte bodies, a band-like lymphocytic infiltrate, and pigment

incontinence. Biopsy of the oral mucosa confirmed mucosal lichen planus. Patch tests using the European comprehensive baseline series and the hairdressing series were positive to PPD and toluene-2,5-diamine on D2 and D3 (+/++). Further investigation confirmed that her hair dye contained PPD and that she had previously used black henna. Five months after PPD eviction, the patient developed depigmented macules around the lichenoid lesions that later resolved, leaving patches of leukoderma at the sites of prior involvement (22).

Previous cases of allergic cosmetic dermatitis

p-Phenylenediamine is a well-known allergen, which has caused a large number of cases of allergic contact dermatitis from hair dyes, henna tattoos and a large spectrum of other products. For a full literature review of this topic (32 pages) please refer to the Monographs in Contact Allergy, Volume 1, Chapter 966-997.

IMMEDIATE-TYPE REACTIONS

A 54-year-old atopic man felt generally unwell within minutes of dyeing his scalp hair, and developed severe itching of the scalp and an urticarial rash. Patch tests with the baseline, cosmetic and hairdressing series were negative. *p*-Phenylenediamine (PPD) 1% pet. was also negative after 20 minutes. A prick test with the colour blend formula gave a positive result (7-mm wheal) with appropriate positive (10 mm) and negative (2 mm) control reactions (five controls were negative to the dye formula). Prick tests with PPD 1% pet., *m*-aminophenol 1% pet., resorcinol 1% pet., propylene glycol 20% water, EDTA 1% pet., limonene 10% pet., linalool 10% pet., citronellal 1% pet., cocamidopropyl betaine 1% water, and sodium metabisulfite 1% pet. (as a proxy for sodium sulfite), which were listed as ingredients, were also negative. The manufacturers of the hair dye supplied 50-mg weighed aliquots of PPD, *m*-aminophenol, resorcinol, and sodium sulfite, which were thought to be the most likely sensitizers. Immediately prior to use, these samples were diluted with water to produce fresh 1% aqueous solutions for prick testing. There was a positive reaction to PPD 1% water (5 controls negative), the others were negative (12).
The authors mention that this case highlights the fact that water may better present the allergen to the immune system. The reason for the increased sensitivity to PPD dissolved in water may be increased bioavailability or that the allergen is an oxidation product formed rapidly on dilution in water. They concluded that, when a patient is investigated for suspected allergic contact urticaria caused by hair dye, an essential first step is to test/challenge with the product in question, and not to rely on commercially available patch test allergens, which, in their experience, have consistently given false-negative results. Graded challenge (touch, prick, and scratch) with the dye and dye/developer mixture and subsequently with the individual constituents diluted in water, if the product gives positive results, would appear to be the best way of increasing the sensitivity of the test with the least risk of a significant adverse reaction (12).

A 29-year-old woman had a combination of allergic contact dermatitis to hair dye and ‘anaphylactoid symptoms’, which consisted of cough appearing a few hours after application of the dye, gradually worsening and accompanied by dyspnoea after 4 days. Open tests and scratch tests with 2 dyes and PPD 1% pet. were negative, but positive at D2 and D3. Meanwhile, five hours after the tests, pruritus had appeared at the sites of the open and closed patch test, and after 16 hours, the patient had developed hoarseness, pharyngeal symptoms, and dyspnoea. Although the open tests and scratch tests had been negative after 15 minutes, the authors suggested that ‘the current case might likely be due to combined immediate and delayed hypersensitivity to hair dye, though the immediate hypersensitivity observed in this patient was atypical’ (8).

Previous cases of immediate-type reactions

There are at least 13 previous case reports of immediate-type reactions with contact urticaria, respiratory symptoms or anaphylactic shock to *p*-phenylenediamine; the most recent were presented in 2000 (ref. 1), 2003 (ref. 2), and 2007 (ref. 3).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 803/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 302/123,000.

OTHER PUBLICATIONS [a]

Allergic contact dermatitis from non-cosmetic products

A 49-year-old woman had extensive bullous allergic contact dermatitis from PPD in black henna applied to the hair. It healed within a week on methylprednisolone and antihistamines except for the thighs and legs, later leaving a 'livedoid pattern'. This was tentatively ascribed to the presence of PPD or textile dyes cross-reacting with PPD in her black nylon lowers (9).

Other information

- Twenty-six patients previously diagnosed with PPD allergy were tested with dilution series of PPD and PPD dihydrochloride (PPD-DHC) and followed-up for 28 days. 23 of 26 (88%) reacted to PPD 1.0%, and 69% to PPD 0.32%; 42% and 27% reacted to PPD-DHC 1% resp. 0.32%. No late-appearing reactions after D7 were observed. It was shown that lowering the test concentration of PPD from 1% to 0.32% results in a number of false-negative reactions (10).
- Cross-reactions between PPD and 2-methoxymethyl-*p*-phenylenediamine (13).
- A study of the IVDK has confirmed that hair dyeing (odds ratio 6.0), henna tattoos (OR 2.4) and being a hairdresser (OR 2.1) increases the risk of PPD sensitization. Neither dyeing of own hair nor application of a temporary henna tattoo seems to affect PPD sensitization in hairdressers (14).
- PPD may be a marker of sulfasalazine allergy (15).
- Patch testing with different concentrations and volumes of *p*-phenylenediamine in pet. (17).
- Self-testing for PPD-allergy is recommended by almost all manufacturers of permanent hair dyes. However, the procedures vary greatly regarding the method of application, the amount of hair dye applied, the location and size of the application area, the number of applications, whether or not rinsing must be performed after application, the reading times, and how a positive reaction is defined. Not a single test has been validated. There are not only concerns about validity, but also regarding safety, notably the risk of active sensitization by these self-tests (20). A self-test protocol for an allergy alert test that can elicit a self-noticeable alert signal in *p*-phenylenediamine (PPD)–allergic consumers was developed by dermatologists and major German and French companies producing and marketing hair-colouring products. Unfortunately, the study was conducted in a group of individuals with known contact allergy to PPD, and not in the target group for such self-tests, consumers of hair dyeing products (18).
- Routine testing with PPD in USA and Canada. North American Contact Dermatitis Group, 1994-2018 (4).
- Review article. Cross-reactions among hair dye-related allergens; Management in clinical practice; Prevalence of hair dye-related allergens in patch-tested populations (5).
- Review article. Ingredients and chemistry of oxidative hair dyeing; sensitization to hair dye ingredients; cross-reactivity; metabolism; new hair dye ingredient: 2-methoxymethyl-*p*-phenylenediamine (21).

[a] Literature on contact allergy to *p*-phenylenediamine that was found in *Contact Dermatitis* or/and *Dermatitis* from September 2017 through March 2025, in which there was no direct link with allergic cosmetic dermatitis.

LITERATURE

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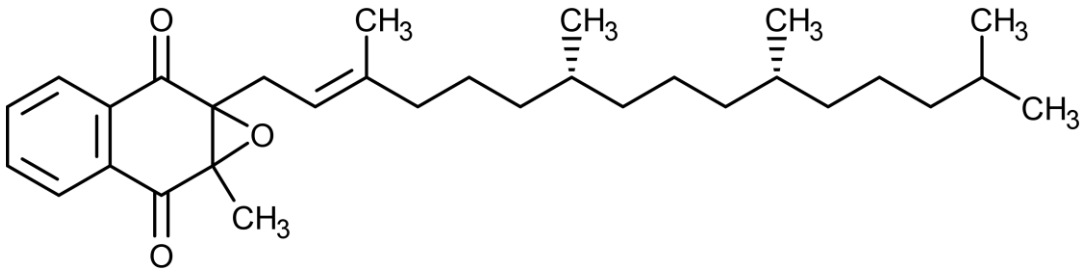
21 Schuttelaar M-L, Vogel TA. Contact allergy to hair dyes. Cosmetics 2016, 3, 21; doi:10.3390/cosmetics3030021

22 Sboui K, Lahouel I, Belhadjali H, Soua Y, Youssef M, Zili J. Para-phenylenediamine-induced lichenoid eruption with involvement of the oral mucosa and subsequent contact leukoderma. Dermatitis. 2025 Jan 27. doi: 10.1089/derm.2024.0249. Epub ahead of print.

3.53 PHYTONADIONE EPOXIDE

IDENTIFICATION

Description/definition : Phytonadione epoxide is the organic compound that conforms to the structural formula shown below
Classification : Ethers; ketones
IUPAC name : 1a,7a-Dihydro-1a-methyl-7a-(3,7,11,15-tetramethyl-2-hexadecen-1-yl)-naphth[2,3-b]oxirene-2,7-dione
Other names : Vitamin K1 oxide; phylloquinone oxide; 2,3-epoxyphytyl)menaquinone
CAS registry number : 25486-55-9
EC number : 247-022-9
Functions in cosmetics : EU: adstringent. USA: drug astringents - skin protectant drugs
Patch testing : 1% pet. (1); 1% and 5% pet. (3,5); 5% pet.; test with 10% pet. when contact allergy is strongly suspected but there is a negative reaction to 5% pet. (4)
Molecular formula : $C_{31}H_{46}O_3$



Previous chapter to which this is an update

The literature on contact allergy to phytonadione epoxide from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.366, pp. 1012-1013.

CONTACT ALLERGY (cosmetics)

Case series

From January 2019 to June 2023, 20 patients were evaluated in 15 Dermatology Departments across Spain who had positive patch test and/or ROAT reactions to cosmetic products containing phytonadione epoxide (PE), of who 3 were excluded from the study. All 17 patients were female with a mean age of 48 years at diagnosis (range: 32–67 years). All individuals presented with eyelid involvement; in some patients, the lesions spread to involve other areas such as the cheeks, the neck, the chest or the antecubital folds. Nine of the 17 (53%) required medical attention at the emergency care unit, and 8 of the 17 (47%) oral corticosteroids. Cosmetics containing PE causing the reactions were identified to be eye contour products in 14 of the 17 cases (82%), of who twelve had used one particular brand of eye cream. Patch tests with cosmetic products containing PE were performed in 14 of the 17 patients. Positive results were seen in 13 of the 14 patients, and 12 of the 14 women developed strong-to-extreme reactions (++ in 5/12 and +++ in 7/12); however, only 6 of the 13 became positive as early as D2. ROATs with cosmetic products containing PE were performed on 10 of the 17 patients and positive results were observed in all, of who 9 developed strong-to-extreme positive reactions (+++ in 5/10, ++ in 4/10). The mean reading day for the ROAT to become positive was D4 (range: D2–D7). The patients were patch tested with PE 1% pet. (6/8 positive), 5% pet. (14/17 positive), 10% pet. (11/11 positive), 20% pet. (8/8 positive) or a combination. The authors suggested 5% pet. as test concentration for PE, but 10% should be considered whenever a 5% concentration is negative and the clinical suspicion is high (4).

Case reports

A 39-year-old non-atopic woman presented in the emergency department with pruritic oedematous eczema affecting the entire face, anterior and lateral neck and neckline. The symptoms had appeared within hours of applying a cosmetic cream on her face. The patient was treated with intramuscular methylprednisolone, followed by a course of oral prednisone. Despite discontinuing the use of the cream, lesions remained intense for 5 days and extended beyond the application area and then slowly improved. A single application of the cream on the inner side of the forearm provoked an eczematous reaction. Patch tests with the baseline Spanish Contact Dermatitis Research Group (GEIDAC) series and later with the 15 individual ingredients of the cream, provided by the manufacturer, resulted in positive reactions (++) on D3 to phytonadione epoxide 1% and 5% pet. and bisabolol 5% in petrolatum (3).

A 57-year-old woman developed acute eczema on her cheeks and eyelids after assisting in a cosmetics show, where an eye contour cream that contained vitamin K1 oxide (phytonadione epoxide) had been applied. Thirteen years earlier, this patient had been examined for a similar episode, after applying an eyelid cream containing vitamin K1 (phytomenadione). She had shown a positive patch test to the cream then, but had missed her appointment for ingredient patch testing. At the current consultation, patch tests with the Spanish baseline series and a cosmetic series, Konakion (= phytomenadione, vitamin K1) aqueous solution 10 mg/mL, the eye contour cream 'as is', and the individual components of the cream, provided by the manufacturer, were positive to the eye cream (++ on D3), phytonadione epoxide 1% pet. and 5% pet. (++ on D4), and Konakion (++ on D5). Patch tests with the cream and Konakion in 15 control subjects gave negative results (why was phytonadione epoxide not tested in controls?). The authors suggested that the current reaction to phytonadione epoxide (oxidised vitamin K1) was a cross-reaction to (unoxidised) vitamin K1, to which the patient had previously become sensitized (5).

Two patients with erythema multiforme-like allergic contact dermatitis from arnica gel were reported from Spain, a 6-year-old boy and a 35-year old woman. Both had developed a pruritic eruption with erythema and targetoid papules at the application sites. Patch tests were positive in both individuals to the gel tested 'as is' and to its ingredient vitamin K1 oxide 5% pet. (one D2 +, D4 +; the other +++ at D7). A biopsy of the positive patch test reaction of the female patient showed changes consistent with eczema, such as spongiosis and intraepidermal vesicles (6).

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to phytonadione epoxide see refs. 1 and 2.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 2/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 2/123,000.

LITERATURE

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2 Goossens A. Cosmetic contact allergens. Cosmetics 2016, 3, 5; doi:10.3390/cosmetics3010005.
3 de la Rosa-Fernández E, Gatica-Ortega ME, Feliciano-Divasson L, Loizate-Sarrionandia I, González-Carrillo E, Suárez-Hernández J, et al. Severe allergic contact dermatitis to bisabolol and phytonadione epoxide found in a moisturizing and strengthening facial cream. Contact Dermatitis 2024;91(2):174-176. doi: 10.1111/cod.14575.
4 Gatica-Ortega ME, Pastor-Nieto MA, Giménez-Arnau AM, Mercader-García P, Serra-Baldrich E, Zaragoza-Ninet V, et al. An emerging epidemic of allergic contact dermatitis due to phytonadione epoxide (oxidised vitamin K1). Contact Dermatitis. 2024;91(5):379-386. doi: 10.1111/cod.14675.

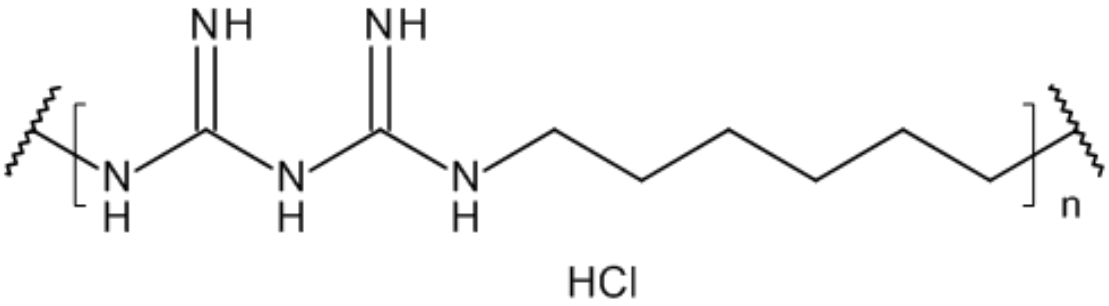
5 Schneller-Pavelescu L, Ochando-Ibernón G, Vergara-de Caso E, Silvestre-Salvador JF. "Crossed" allergic contact dermatitis caused by oxidized vitamin K1 in a patient previously sensitized to non-oxidized vitamin K1. Contact Dermatitis. 2019 Jan;80(1):64-65. doi: 10.1111/cod.13128.
6 Pastor-Nieto MA, Gatica-Ortega ME, Melgar-Molero V, González-Muñoz P, Mollejo M, Schoendorff C, et al. Erythema multiforme-like reaction resulting from vitamin K1 oxide (phytomenadione epoxide). Contact Dermatitis. 2017;77(5):343-345. doi: 10.1111/cod.12837.

3.54 POLYAMINOPROPYL BIGUANIDE

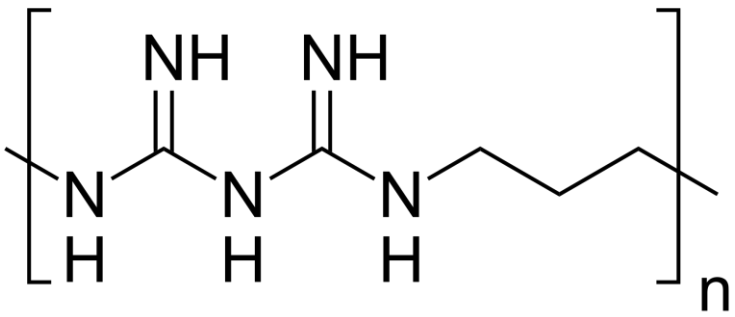
In both the EU and the USA INCI nomenclature system the INCI name polyaminopropyl biguanide (CAS 133029-32-0) is (incorrectly) used for poly(hexamethylenebiguanide) hydrochloride (CAS 32289-58-0). The latter is used as a preservative, but polyaminopropyl biguanide itself is currently (March 2025) not allowed in cosmetics in the EU.

IDENTIFICATION

Description/definition	: Poly(hexamethylenebiguanide) hydrochloride is the synthetic polymer that generally conforms to the structural formula shown below
Classification	: Synthetic polymers
Chemical name	: Polyhexamethylene biguanide hydrochloride
Other names	: Polyhexanide; PHMB
CAS registry number	: 32289-58-0
EU number	: 608-723-9
Wikipedia	: https://en.wikipedia.org/wiki/Polyhexanide (Polyhexanide)
CIR reports	: Int J Toxicol 2020;39(Suppl. 3):26-73
SCCS opinions	: SCCS/1535/14; Final opinion 5 May 2017; SCCS/1581/16
Functions in cosmetics	: EU: preservative. USA: preservatives
EU cosmetic restrictions	: Regulated in Annex V/28 of the Regulation (EU) 2019/831
Patch testing	: 5% water (may rarely be irritant); higher concentrations (10-20%) may be necessary in some cases
Molecular formula	: $(C_8H_{17}N_5)_n.{}_n$HCl (poly[hexamethylenebiguanide] hydrochloride); $(C_5H_{11}N_5)_n$ (polyaminopropyl biguanide)



Poly(hexamethylenebiguanide) hydrochloride (CAS nr. 32289-58-0)



Polyaminopropyl biguanide (CAS nr. 133029-32-0)

Previous chapter to which this is an update

The literature on contact allergy to polyaminopropyl biguanide from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.371, pp. 1018-1021.

CONTACT ALLERGY (cosmetics)

Case report

A 52-year-old male kitchen aid had a 3-year history of work-related hand eczema. Patch tests with the German Contact Dermatitis Research Group (DKG) baseline series, topical preparations, preservatives, rubber, and disinfectants as well as a selection of the patient's own products, including skin care products (tested 'as is'), were positive to polyhexamethylene biguanide (PHMB) 2.5% water at D3 (+), D4 (++), and D7 (++). A skin care product containing polyaminopropyl biguanide (PAPB) according to product labelling caused a doubtful reaction at D3 with slight increase (+) until D7. The patient had applied this product on his hands several times a day for >1 year. A repeated open application test (ROAT) with the cream on the inner sides of both forearms caused an erythema at D4 and a papulovesicular reaction at D7 in both test areas. Work-related hand eczema consisting of both irritant contact dermatitis and allergic contact dermatitis caused by sensitization to PHMB was diagnosed (3).

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to polyaminopropyl biguanide see refs. 1 and 2.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 13/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 202/123,000.

OTHER PUBLICATIONS [a]

- Routine testing with polyhexamethylene biguanide hydrochloride 2.0% water in Sweden 2016-18 (4).
- Allergic contact dermatitis from polyhexamethylene biguanide, decyl glucoside and lauryl glucoside in antimicrobial foam dressing (5).
- A 55-year-old female hospital cleaner developed hand dermatitis, spreading to the arms, eventually also involving the neck and the trunk from contact allergy to poly(hexamethylenebiguanide), didecyldimethylammonium chloride and benzalkonium chloride in surface cleaning wipes (6).

[a] Literature on contact allergy to polyaminopropyl biguanide / polyhexamethylene biguanide that was found in *Contact Dermatitis* or/and *Dermatitis* from September 2017 through March 2025, in which there was no direct link with cosmetic products.

LITERATURE

1 Leysen J, Goossens A, Lambert J, Aerts O. Polyhexamethylene biguanide is a relevant sensitizer in wet wipes. Contact Dermatitis 2014: 7095): 323-325. doi: 10.1111/cod.12208.

2 Aerts O, Smeets J, Adriaenssens K, Lambert J, Goossens A. Contact allergy to biguanides might explain cases of unresolved eyelid dermatitis. J Eur Acad Dermatol Venereol 2015;29(10):2064-2065. doi: 10.1111/jdv.12598.

3 Kolodziej M, Kiewert A, Skudlik C, Brans R. Allergic contact dermatitis caused by polyhexamethylene biguanide may contribute to work-related hand eczema. Contact Dermatitis. 2021;85(1):97-98. doi: 10.1111/cod.13792

4 Sukakul T, Dahlin J, Pontén A, Antelmi A, Bruze M, Hamnerius N, et al. Contact allergy to polyhexamethylene biguanide (polyaminopropyl biguanide). Contact Dermatitis. 2021;84(5):326-331. doi: 10.1111/cod.13728.

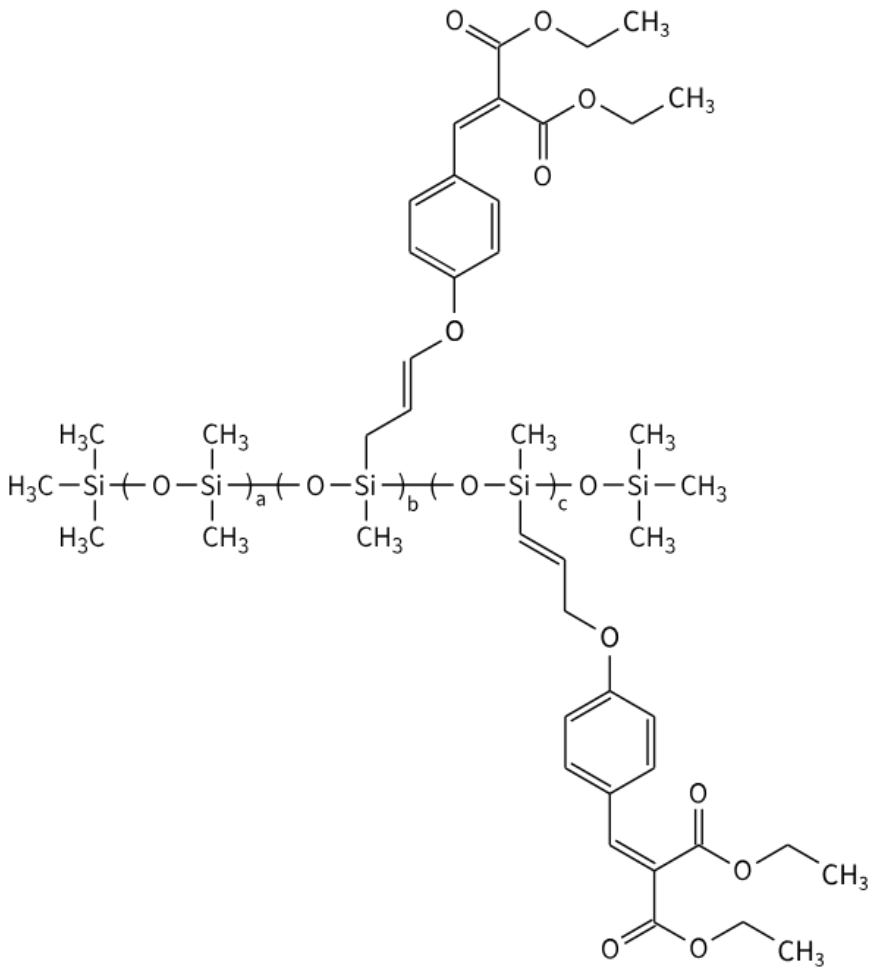
5 Jaque A, DeKoven JG. Polyhexamethylene biguanide and alkyl glucosides: unexpected allergens in an antimicrobial foam dressing. Contact Dermatitis. 2017;77(6):421-422. doi: 10.1111/cod.12852.

6 Ulicki M, Dendooven E, Aerts O. Triple relevant sensitization to didecyldimethylammonium chloride, benzalkonium chloride, and polyhexamethylene biguanide in a hospital cleaner. Contact Dermatitis. 2022; 86(6):546-547. doi: 10.1111/cod.14062.

3.55 POLYSILICONE-15

IDENTIFICATION

Description/definition : Polysilicone-15 is the siloxane polymer that conforms generally to the structural formula shown below
Classification : Siloxanes and silanes; synthetic polymers
IUPAC name : Siloxanes and silicones, dimethyl, 3-(4-(2,2-di(ethoxycarbonyl)ethenyl) phenoxy)propen-2-yl methyl, 3-(4-(2,2-di(ethoxycarbonyl)ethenyl) phenoxy)propen-1-yl methyl, trimethylsilyl terminated
Other names : Diethylbenzylidene malonate dimethicone; dimethicodiethylbenzalmalonate; benzylidenemalonatepolysiloxane; Parsol® SLX
CAS registry number : 207574-74-1
EC number : 606-621-9
Wikipedia : https://en.wikipedia.org/wiki/Polysilicone-15
SCCS opinions : SCCS/1346/10
Functions in cosmetics : EU: UV-filter. USA: light stabilizers
EU cosmetic restrictions : Regulated in Annex VI/26 of the Regulation (EC) 2009/1223
Patch testing : 10% pet. (Chemotechnique)



Previous chapter to which this is an update

The literature on contact allergy to polysilicone-15 from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.376, pp. 1026-1027.

CONTACT ALLERGY (cosmetics)

General

A very useful review article on sunscreen allergy was published in 2023 in *Dermatitis* (4).

Case report

A 51-year-old non-atopic woman presented with erythema and scales that had been present on her face for 3 months. Patch tests with the Japanese baseline series, her cosmetics, and several cosmetic allergens were positive to a sunscreen cream tested 'as is', nickel sulfate, mercaptobenzothiazole and thiuram mix. When patch tested with the ingredients of this cosmetic, provided by its manufacturer, there were positive reactions to polysilicone-15 10% pet., bis-ethylhexyloxyphenol methoxyphenyl triazine (Tinosorb S) 10% pet., and an undisclosed fragrance 5% pet. Subsequent ROATs were positive to both UV-filters but negative to the fragrance (2).

Another case of allergic contact dermatitis from polysilicone-15, for which no details are available, was published in a Japanese dermatological journal (3).

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to polysilicone-15 see ref. 1.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 12/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 194/123,000.

LITERATURE

1 Sarre, ME, Guérin-Moreau M, Lepoittevin JP, Martin L. Avenel-Audran M. Allergic contact cheilitis caused by polysilicone-15 (Parsol® SLX) in a lipcare balm. Contact Dermatitis 2014;70(2):119-121. doi: 10.1111/cod.12145.

2 Suzuki K, Futamura K, Sugiyama M, Matsunaga K, Yagami A. Allergic contact dermatitis caused by dimethicodiethylbenzalmalonate (polysilicone-15, Parsol SLX) and bis-ethylhexyloxyphenol methoxyphenyl triazine (Tinosorb S) in sunscreen cream. Contact Dermatitis. 2022;87(1):108-110. doi:10.1111/cod.14112

3 Hiratsuka R, Hisaoka H, Sekine M. A case of allergic contact dermatitis caused by polysilicone-15 in a sunscreen cream. Practical Dermatology. 2017;39(7):723-726 (In Japanese).

4 Ekstein SF, Hylwa S. Sunscreens: A review of UV filters and their allergic potential. Dermatitis. 2023;34(3):176-190. doi: 10.1097/DER.0000000000000963.

3.56 PROPOLIS

PROPOLIS CERA

IDENTIFICATION

Description/definition : Propolis cera is the waxy component of the resinous material found in beehives
Classification : Waxes (natural and synthetic)
Other names : Propolis wax (US)
CAS registry number : 85665-41-4
EC number : 288-130-6
Wikipedia : https://en.wikipedia.org/wiki/Propolis
Functions in cosmetics : EU: antiseborrhoeic; moisturising; smoothing; USA: not mentioned
Patch testing : Propolis 10% pet. (Chemotechnique); propolis and propolis B 10% pet. (SmartPractice)

PROPOLIS WAX

IDENTIFICATION

Description/definition : Propolis wax is the material obtained from the extraction of propolis, a resinous substance found in beehives
Classification : Waxes (natural and synthetic)
Other names : Propolis (European Pharmacopoeia); propolis cera (EU); propolis resin
CAS registry number : 9009-62-5
EC number : 288-130-6
Wikipedia : https://en.wikipedia.org/wiki/Propolis
Functions in cosmetics : EU: emollient; skin conditioning. USA: skin-conditioning agents - emollient; skin-conditioning agents - miscellaneous
Patch testing : Propolis 10% pet. (Chemotechnique); propolis and propolis B 10% pet. (SmartPractice)

PROPOLIS EXTRACT

IDENTIFICATION

Description/definition : Propolis extract is an extract of propolis wax
Classification : Biological products
CAS registry number : 85665-41-4
EC number : 288-130-6
Wikipedia : https://en.wikipedia.org/wiki/Propolis
Functions in cosmetics : EU: skin conditioning. USA: skin-conditioning agents - miscellaneous
Patch testing : Propolis 10% pet. (Chemotechnique); propolis and propolis B 10% pet. (SmartPractice)

Propolis is not an INCI name, because the raw propolis has to be chemically and/or physically modified to be suitable for use in cosmetic products. The exact nature of the materials with INCI names propolis cera and propolis wax as described above is not clear.

Previous chapter to which this is an update

The literature on contact allergy to propolis from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.385, pp. 1042-1055.

CONTACT ALLERGY (cosmetics)

General

Propolis 10% pet. was added to the European baseline series in 2019 (1) and its continued inclusion was confirmed in 2023 (2). The literature on allergy to propolis has been reviewed by the author in an article published in 2013 in *Dermatitis* (3) and in the in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.385, pp. 1042-1055. An update 2013-2025 to the review article is planned for 2025 and, therefore, the content of this chapter is strictly limited to well-described cases of dermatitis from contact allergy to propolis verified to be present in cosmetic products.

Case reports

A 58-year-old woman had a 1-year history of dermatitis of both ears, followed by blepharoconjunctivitis 8 months later. After learning about the allergenicity of methylisothiazolinone, she stopped all cosmetics containing isothiazolinones and switched to 'natural' products. However, her dermatitis progressively worsened. Patch tests with the NACDG standard series, supplemented with a comprehensive cosmetics series and the 17 personal products that the patient had previously stopped using, showed only one positive (+) reaction to propolis at D2 and D4. Propolis was found to be present in many of her products, including the newly bought natural products she had been using as a substitute for her previous cosmetics (and which she had not brought in for patch testing). Propolis-containing products included mascara, eyeshadow, eyebrow pencil, eyeliner, shampoos and a 'therapeutic' cream for eczema. She also admitted applying a homemade cream containing beeswax and ingesting propolis. After avoidance of all propolis- (and probably beeswax-) containing products, the dermatitis cleared within 3 weeks (4).

A 42-year-old woman had eczema of the head and neck for 6 months, which was initially diagnosed and treated as atopic dermatitis, but without improvement. During re-interview, the focus was put on cosmetic products, and the patient then reported the use of a new shampoo containing propolis in the last 8 months and intense pruritus after the use of the shampoo. Nevertheless, she continued using it, as she considered it as a natural and harmless product. Physical examination showed subacute eczema located on the head and neck, with more marked desquamation on the eyelids and erythematous and oedematous confluent papules and plaques on the neckline. Patch tests with the European comprehensive baseline series, a cosmetic series, and caffeic acid phenyl ester 1% pet. were positive to propolis 10% pet. and to caffeic acid phenyl ester 1% pet. Allergic contact dermatitis caused by propolis present in the shampoo was diagnosed. After proper avoidance counselling, complete clearance of the lesions was achieved within 6 weeks, and no recurrence was observed at 3 month follow-up (5).

A 32-year-old woman presented with a 15-day history of severe cheilitis and perioral dermatitis, associated with patchy eczematous lesions affecting her trunk, arms and legs. The patient was taking topical and oral preparations containing propolis to treat what she thought was a herpetic infection of her lips. She had used lip balms containing propolis several times previously. The patient was advised to avoid propolis, and was treated with systemic steroids, with complete resolution of the skin lesions. Patch tests performed 2 months later showed positive reactions to propolis 10% pet. and Myroxylon pereirae resin on D2 and D4. The patient was diagnosed with allergic contact dermatitis and systemic allergic dermatitis from propolis (6).

A 50-year-old woman had suffered lifelong atopic dermatitis. When she was around 50 years old, the dermatitis began to affect her face, resulting in bright erythema and edema of the entire face. Biopsy results revealed spongiotic dermatitis with eosinophils with mucin and spongiosis of several hair follicles. Patch testing with the NACDG standard series and an external agents and emulsifiers series revealed 2+ reactions to propolis, Myroxylon pereirae resin, MCI/MI, iodopropynyl butylcarbamate, and glutaraldehyde. Each of these allergens was relevant to her current personal care product usage. After 2 months of allergen avoidance, the patient exhibited dramatic improvement, with complete clearance of the dermatitis on the face and legs. Three years later, her face remains clear and she does not use any topical treatments on her face or body (7).

Previous cases of allergic cosmetic dermatitis

There are at least 40 previous case reports and 6 case series of allergic cosmetic dermatitis to propolis. Please refer to the Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.385, pp. 1042-1055 and to the 2013 review article written by the author (3).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 9/35,000 (propolis wax); 178/35,000 (propolis extract).
EWG's Skin Deep Cosmetics Database (February 2025): 3/123,000 (propolis cera); 18/123,000 (propolis wax); 178/123,000 (propolis extract).

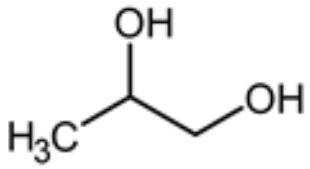
LITERATURE

1 Wilkinson M, Gonçalo M, Aerts O, Badulici S, Bennike NH, Bruynzeel D, et al. The European baseline series and recommended additions: 2019. Contact Dermatitis. 2019;80(1):1-4. doi: 10.1111/cod.13155.
2 Wilkinson SM, Gonçalo M, Aerts O, Badulici S, Dickel H, Gallo R, et al. The European baseline series and recommended additions: 2023. Contact Dermatitis. 2023;88(2):87-92. doi: 10.1111/cod.14255.
3 De Groot AC. Propolis: a review of properties, applications, chemical composition, contact allergy, and other adverse effects. Dermatitis. 2013;24(6):263-82. doi: 10.1097/DER.0000000000000011.
4 Besner Morin C, Alipour Tehrany Y, Sasseville D. Severe allergic contact blepharitis from propolis. Contact Dermatitis. 2020;82(6):399-400. doi: 10.1111/cod.13484.
5 Navarro-Triviño FJ, Ruiz-Villaverde R. Allergic contact dermatitis of head and neck by propolis contained in a shampoo. Contact Dermatitis. 2020;82(6):409-410. doi: 10.1111/cod.13491.
6 Freedman J, Griggs J, De Padova MP, Tosti A. What's the "buzz" about propolis? Propolis-induced systemic contact dermatitis. Contact Dermatitis. 2019;80(1):65-67. doi: 10.1111/cod.13131.
7 Semaan S, Raffi J, Murase JE. Allergic contact dermatitis masquerading as atopic dermatitis. Int J Womens Dermatol. 2020;6(4):329-330. doi: 10.1016/j.ijwd.2020.04.005.

3.57 PROPYLENE GLYCOL

IDENTIFICATION

Description/definition : Propylene glycol is the aliphatic alcohol that conforms generally to the formula shown below
Chemical class : Alcohols
IUPAC name : Propane-1,2-diol
Other names : 1,2-Dihydroxypropane
CAS registry number : 57-55-6
EC number : 200-338-0
CIR reports : J Am Coll Toxicol 1994;13:437-491; Int J Toxicol 2012;31(Suppl.2):245-260
Wikipedia : https://en.wikipedia.org/wiki/Propylene_glycol
Functions in cosmetics : EU: humectant; fragrance; solvent; viscosity controlling; skin conditioning – humectant; skin conditioning – miscellaneous. USA: fragrance ingredients; skin-conditioning agents – humectants; skin-conditioning agents – miscellaneous; solvents; viscosity decreasing agents – humectants
Patch testing : 5% pet. (Chemotechnique); 20% water (SmartPractice); 30% water (Chemotechnique, SmartPractice); pure (SmartPractice); the test concentrations of 20% and higher may cause irritant reactions, the lower test concentrations false-negative results
Molecular formula : $C_3H_8O_2$



Previous chapter to which this is an update

The literature on contact allergy to propylene glycol from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.386, pp. 1056-1066.

CONTACT ALLERGY (cosmetics)

Case report

A 39-year-old non-atopic housewife was investigated for a 2-year history of pruritic erythematous scaly plaques involving both eyelids and periorbital skin. Lesions resolved after application of topical corticosteroids and pimecrolimus ointment; however, a quick relapse after treatment discontinuation was observed. Patch tests with the baseline series of the Spanish Contact Dermatitis Research Group (GEIDAC), a fragrance series and the patient's own products were positive to a sunscreen and a foundation. Ingredient patch testing identified bis-ethylhexyloxyphenol methoxyphenyl triazine (Tinosorb S) and Scutellaria baicalensis root extract as the sensitizers in the sunscreen. Patch testing with the components of the foundation yielded positive reactions to propylene glycol and a mixture of talc, CI 77491, and dimethicone/methicone copolymer. The patient refused further patch testing with the separate chemicals of the mixture. Following specific avoidance recommendations, no new recurrences of the dermatitis have occurred (7).

Previous cases of allergic cosmetic dermatitis

There is extensive literature on case series and case reports of allergic cosmetic dermatitis to propylene glycol and of allergic contact dermatitis to other product types, notably topical pharmaceutical products,

conductive gels, lubricant jellies and wound dressings. Please refer to the Monographs in Contact Allergy, Volume 1, Chapter 2.386, pp. 1056-1066 for these topics.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 7918/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 13,092/123,000.

OTHER PUBLICATIONS [a]

- Allergic contact dermatitis from propylene glycol in diclofenac gel (2).
- Cross-reactions to and from butylene glycol (3).
- Propylene glycol: ACDS Contact allergen of the year 2018 (4).
- Systematic review of propylene glycol in contact dermatitis (5).
- Patients allergic to propylene glycol (PG) are unlikely to cross-react to its derivatives dipropylene glycol, PG monostearate, and PG diacetate, and to hexylene glycol, pentylene glycol, and butylene glycol (9).
- Results of patch testing consecutive patients with propylene glycol: refs. 1, 6 and 8.
- Acute generalized exanthematous pustulosis (AGEP)-like contact dermatitis from propylene glycol and other allergens in topical pharmaceuticals (10).

[a] Literature on contact allergy to propylene glycol that was found in *Contact Dermatitis* or/and *Dermatitis* from September 2017 through March 2025, in which there was no direct link with cosmetic products.

LITERATURE

1 Gallo R, Guarneri F, Ferrucci SM, Stingeni L, Hansel K, Corazza M, et al. Frequency of contact allergy to pentylene glycol. Retrospective cross-sectional study with data from the Società Italiana di Dermatologia Allergologica Professionale e Ambientale (SIDAPA). Contact Dermatitis. 2024;90(3):314-317. doi: 10.1111/cod.14469.

2 Barakat L, Dereure O, Raison-Peyron N. A police case: Finding propylene glycol guilty as culprit allergen. Contact Dermatitis. 2021;85(4):475-476. doi: 10.1111/cod.13900.

3 Ekstein SF, Battis N, Dabrowski D, Neeley AB. Cross-reactivity between propylene glycol and butylene glycol. Dermatitis. 2024;35(2):149-151. doi: 10.1089/derm.2023.0143.

4 Jacob SE, Scheman A, McGowan MA. Propylene glycol. Dermatitis. 2018;29(1):3-5. doi: 10.1097/DER.0000000000000315.

5 McGowan MA, Scheman A, Jacob SE. Propylene glycol in contact dermatitis: A systematic review. Dermatitis. 2018 Jan-Feb;29(1):6-12. doi: 10.1097/DER.0000000000000307.

6 Lalla SC, Nguyen H, Chaudhry H, Killian JM, Drage LA, Davis MDP, et al. Patch testing to propylene glycol: The Mayo Clinic experience. Dermatitis. 2018;29(4):200-205. doi: 10.1097/DER.0000000000000393.

7 Luna-Bastante L, Gatica-Ortega ME, Pastor-Nieto MA, Vergara-de-la-Campa L, Gómez-Dorado BA, Alonso-Naranjo L, et al. Allergic contact dermatitis to Tinosorb S, Scutellaria baicalensis, and other emerging allergens in cosmetics. Contact Dermatitis. 2020;82(5):307-309. doi: 10.1111/cod.13460.

8 Lalla SC, Nguyen H, Chaudhry H, Killian JM, Drage LA, Davis MDP, et al. Patch testing to propylene glycol: The Mayo Clinic experience. Dermatitis. 2018;29(4):200-205. doi: 10.1097/DER.0000000000000393.

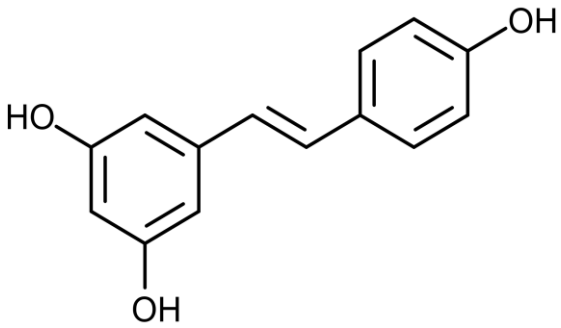
9 Scheman A, Roszko K. Contact allergy to propylene glycol and cross-reactions. Dermatitis. 2018;29(6):350-351. doi: 10.1097/DER.0000000000000416.

10 González-Cantero Á, Gatica-Ortega ME, Pastor-Nieto MA, Martínez-Lorenzo ER, Gómez-Dorado BA, Mollejo-Villanueva M, Tapia-de-Pedro G, et al. Acute generalized exanthematous pustulosis (AGEP)-like contact dermatitis resulting from topical therapy in a polysensitized patient. Contact Dermatitis. 2019;80(5):329-333. doi: 10.1111/cod.13204.

3.58 RESVERATROL

IDENTIFICATION

Description/definition : Resveratrol is the organic compound that conforms to the formula shown below
Classification : Phenols
IUPAC name : 1,3-Benzenediol, 5-[(1*E*)-2-(4-hydroxyphenyl)ethenyl]-
Other names : 3,5,4'-*trans*-Trihydroxystilbene
CAS registry number : 501-36-0
Wikipedia : https://en.wikipedia.org/wiki/Resveratrol
Functions in cosmetics : EU: antioxidant; skin protecting. USA: antioxidants; skin protectants
Patch testing : 5% pet. (1); 10% paraffin (3); 1% water (4)
Molecular formula : $C_{14}H_{12}O_3$



Previous chapter to which this is an update

The literature on contact allergy to resveratrol from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.398, pp. 1107.

CONTACT ALLERGY (cosmetics)

Case reports

A 69-year-old female patient had a 7-month history of recurrent dermatitis of the face and neck, accentuated in the skin folds and sometimes accompanied by itchy erythema on the arms. Patch tests with the European baseline series, a cosmetic series with preservatives and fragrances and the patient's own products were positive only to one cosmetic cream. In a second session, patch testing with the ingredients of this product, provided by the manufacturer and already diluted for patch testing, showed a positive reaction to resveratrol 10% paraffin at D4 (−/++). Her dermatitis disappeared within a week after stopping the use of this cream. Three controls tested with the same sample of resveratrol showed no reaction (3).

A 37-year-old woman had suffered an itchy papular and vesicular eruption of the face and neck, which had started 2 days after the application of a new facial cream with resveratrol. Patch tests with the European baseline series, a cosmetic series, and the resveratrol cream 'as is' were positive to the cream (++) on D4 and to chromium (++) and *p-tert*.-butylphenolformaldehyde resin (++) with past relevance. The ingredients of this cream, provided by the manufacturer, were patch tested in a second session, which yielded positive reactions (++) to resveratrol 1% water and Scutellaria baicalensis root extract 0.5% water (++) at D4. Four controls were negative (4).

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to resveratrol see refs. 1 and 2.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 143/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 326/123,000.

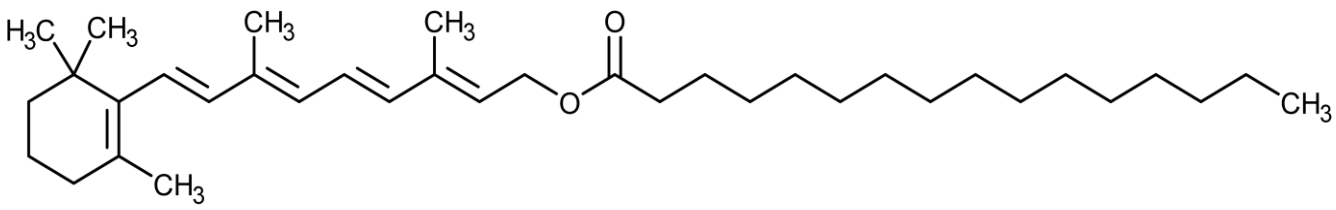
LITERATURE

1 Gallo R, Viglizzo G, Vecchio F, Parodi A. Allergic contact dermatitis from pentylene glycol in an emollient cream, with possible co-sensitization to resveratrol. Contact Dermatitis 2003;48(3):176-177. doi: 10.1034/j.1600-0536.2003.00073.x.
2 Gallo R, Pastorino C, Gasparini G, Ciccarese G, Parodi A. Scutellaria baicalensis extract: a novel botanical allergen in cosmetic products? Contact Dermatitis 2016;75(6):387-388. doi: 10.1111/cod.12659.
3 Degraeuwe A, Jacobs MC, Herman A. Allergic contact dermatitis caused by resveratrol in a cosmetic cream. Contact Dermatitis. 2020;82(6):412-413. doi: 10.1111/cod.13493.
4 Badaoui A. Allergic contact dermatitis to resveratrol and Scutellaria baicalensis root extract in a cosmetic product. Contact Dermatitis. 2022;87(3):282-283. doi:10.1111/cod.14134.

3.59 RETINYL PALMITATE

IDENTIFICATION

Description/definition : Retinyl palmitate is the ester of retinol (vitamin A) and palmitic acid, that conforms to the structural formula shown below
Classification : Esters
IUPAC name : [(2*E*,4*E*,6*E*,8*E*)-3,7-Dimethyl-9-(2,6,6-trimethylcyclohexen-1-yl)nona-2,4,6,8-tetraenyl]hexadecanoate
Other names : Retinol palmitate; vitamin A palmitate; retinol, hexadecanoate
CAS registry number : 79-81-2
EC number : 201-228-5
CIR reports : J Am Coll Toxicol 1987;6:279-320
SCCS opinions : SCCS/1576/16
Wikipedia : https://en.wikipedia.org/wiki/Retinyl_palmitate
Functions in cosmetics : EU: skin conditioning. USA: skin-conditioning agents - miscellaneous
Patch testing : 5% pet. (1); this concentration may cause occasional irritant reactions (1); 1% and 10% MEK (methyl ethyl ketone) (2)
Molecular formula : $C_{36}H_{60}O_2$



Previous chapter to which this is an update

The literature on contact allergy to retinyl palmitate from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.400, pp. 1109-1110.

CONTACT ALLERGY (cosmetics)

Case report

A 33-year-old atopic man was investigated for erythematous and squamous lesions located on the eyelids of the right eye associated with ipsilateral conjunctivitis. Bacterial conjunctivitis was initially suspected and he was treated with fusidic acid gel and oral pristinamycin for 1 week. As this gave no improvement, treatment with a corticosteroid ointment, an emollient palpebral cream, anti-allergic eye drops and artificial tears were prescribed for 3 months. After a brief improvement, lesions relapsed on the right eyelids and now allergic contact dermatitis was suspected. Patch tests with the European baseline series, additional haptens, a cosmetic series and the patient's personal products tested 'as is' were negative. Next, repeated open application tests (ROAT) were carried out with all products and the ROAT with the palpebral cream was positive at D7. However, ingredient patch testing was negative. Therefore, ROATs with each ingredient of the cream were carried out, beginning with the most suspected ones. The ROAT with vitamin A palmitate 5% pet. was positive on D7 with a few erythematous vesicles and papules on the application area. Despite discontinuation of the applications of this product, the lesions kept spreading to the ipsilateral axillary fold, the chest, the back, the contralateral arm and the legs. ROATs with vitamin A palmitate 5% pet. were subsequently conducted in 4 control patients with a negative result on D10 (3).

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to retinyl palmitate see refs. 1 and 2.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 816/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 1/123,000.

LITERATURE

1 Clemmensen A, Thormann J, Andersen, KE. Allergic contact dermatitis from retinyl palmitate in polycaprolactone. Contact Dermatitis 2007;56(5):288-289. doi: 10.1111/j.1600-0536.2006.00988.x.
2 Manzano D, Aguirre A, Gardeazabal J, Eizaguirre X, Pérez J LD. Allergic contact dermatitis form tocopheryl acetate (vitamin E) and retinol palmitate (vitamin A) in a moisturizing cream. Contact Dermatitis 1994;31(5):324. doi: 10.1111/j.1600-0536.1994.tb02030.x.
3 Saadi S, Dereure O, Raison-Peyron N. Case report: A severe repeated open application test reaction to an ingredient of cosmetic. Contact Dermatitis. 2024;91(3):255-257. doi:10.1111/cod.14586.

3.60 RICINUS COMMUNIS (CASTOR) SEED OIL

IDENTIFICATION

Description/definition	: Ricinus communis seed oil is the fixed oil obtained from the seeds of castor, *Ricinus communis,* Euphorbiaceae
Classification	: Fats and oils
INCI name USA	: Ricinus communis (castor) seed oil
Other names	: Castor oil; ricinus oil; oleum ricini; oil of Palma Christ
CAS registry number	: 8001-79-4
EC number	: 232-293-8
CIR reports	: Int J Toxicol 2007;26(Suppl.3):31-77
Wikipedia	: https://en.wikipedia.org/wiki/Ricinus (Ricinus)
Functions in cosmetics	: EU: emollient; masking; moisturising; skin conditioning; smoothing; solvent. USA: fragrance ingredients; skin-conditioning agents - occlusive
Patch testing	: Pure

Previous chapter to which this is an update

The literature on contact allergy to Ricinus communis seed oil from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.402, pp. 1113-1114.

CONTACT ALLERGY (cosmetics)

Case reports

A 13-year-old atopic boy had a 3-week history of cheilitis, which started as 'cracked and dry lips' and had worsened after he had used 2 different brands of lip balm. On physical examination, the patient had erythema and oedema of the lips accompanied by yellow crusting from secondary infection with *Staphylococcus aureus*. The patient was treated with topical betamethasone and gentamicin, and was told to stop using all of his lip care products, which resulted in resolution of the lesions within a week. No recurrences were observed in the following 3 months. Patch tests with a baseline series, a cosmetic series, and both lip care products 'as is' were positive on D4 to neomycin sulfate (++; past relevance), one of his lip balms (++), Myroxylon pereirae resin (+), fragrance mix I (+), and colophonium (+). Both lip balms were perfume-free, ergo these positives could not explain the allergic cheilitis. In a second session, the components of the lip balm that reacted positively, obtained from the manufacturer at the same concentrations as used in the product, were tested, resulting in a ++ positive reaction to castor oil 20% pet. Ten controls were negative. The other lip balm that the patient had used did not contain this ingredient (3).

A 25-year-old atopic woman suffered from perioral eczema which she related to the use of several lip balms. Her history revealed that a facial rash had occurred in the past, following the use of a day cream. Patch tests with the Belgian baseline series, a cosmetic series (in which castor oil is present at 100%), hydrogenated castor oil 30% pet. (obtained from a cosmetic manufacturer), the patient's own cosmetic products, and their available ingredients, were positive at D4 to castor oil ('as is') (+) and to cera alba 30% pet. (++), both of which were present in the lip balms she had been using. Furthermore, the patient reacted to panthenol 5% pet., also present in two lip balms, and in the moisturizing cream which had provoked a facial dermatitis in the past. There was no positive patch test reaction to hydrogenated castor oil 30% pet. The perioral dermatitis completely healed upon avoidance of all contact allergens (4).

The authors of the previous case report also described a second patient. A 50-year-old male patient presented with perioral eczema following the use of two different brands of lip balms. Initial patch tests (performed as in the previous patient) were positive to castor oil ('as is') (++). A patch test with the lip balms could not be performed, but a repeated open application test (ROAT) with one of two lip balms,

twice daily on a forearm, resulted in a positive reaction after three days. Upon request, the manufacturer of this particular lip balm provided the individual ingredients, among which were castor oil ('as is') and hydrogenated castor oil (30% pet.). Positive reactions were again seen to castor oil 'as is' (D2++, D4+++) but not to hydrogenated castor oil 30% pet. Castor oil was, according to the packaging, present in both lip balms he had been using. The patient also showed a positive patch test reaction to benzyl salicylate, explaining a previous axillary dermatitis from deodorant. Following avoidance of all contact allergens, the patient's perioral eczema healed and has not recurred since (4).
The authors state that their cases illustrate that, in order to achieve a correct diagnosis, one should patch test castor oil 'as is', and not rely on patch test materials containing only hydrogenated castor oil (4).

Previous cases of allergic cosmetic dermatitis

There are at least 12 previous case reports and case series of allergic cosmetic dermatitis to Ricinus communis (castor) seed oil; the most recent are refs. 1 and 2. For a full literature review of this topic please refer to the Monographs in Contact Allergy, Volume 1, Chapter 2.402, pp. 1113-1114.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 143/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 8907/123,000.

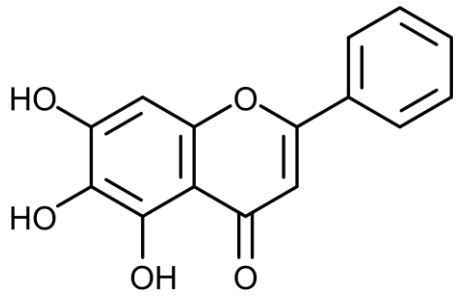
LITERATURE

1 Sasseville D, Desjardins M, Almutawa F. Allergic contact dermatitis caused by glycyrrhetinic acid and castor oil. Contact Dermatitis 2011;64(3):168-169. doi: 10.1111/j.1600-0536.2010.01829.x.
2 Verheyden M, Rombouts S, Lambert J, Aerts O. Contact allergy to castor oil, but not to castor wax. Cosmetics 2017, 4, 5; doi:10.3390/cosmetics4010005.
3 Sánchez-Herrero A, Mateos-Mayo A, Rodríguez-Lomba E, Molina-López I, Campos-Domínguez M, Suárez Fernández R. Allergic contact cheilitis in an adolescent to Ricinus communis seed oil (castor oil) in a lip balm. Contact Dermatitis. 2018;79(3):176-178. doi: 10.1111/cod.13016.
4 Verheyen M, Rombouts S, Lambert J, Aerts O. Contact allergy to castor oil, but not to castor wax. Cosmetics 2017, 4(1), 5; doi: 10.3390/cosmetics4010005.

3.61 SCUTELLARIA BAICALENSIS EXTRACT

IDENTIFICATION

Description/definition : Scutellaria baicalensis extract is the extract of the whole plant, *Scutellaria baicalensis*, Lamiaceae
Classification : Botanical products and botanical derivatives
CAS registry number : 94279-99-9
EC number : 304-845-9
Wikipedia : https://en.wikipedia.org/wiki/Scutellaria_baicalensis (*Scutellaria baicalensis*)
Functions in cosmetics : EU: antimicrobial. USA: antimicrobial agents
Patch testing : 0.5% water (1,2); 0.2% in 50/50 water/alcohol (4)



Structural formula of baicalein, one of the main flavonoids in *Scutellaria baicalensis.*

Previous chapter to which this is an update

The literature on contact allergy to Scutellaria baicalensis extract from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.405, pp. 1118.

CONTACT ALLERGY (cosmetics)

Case reports

A 37-year-old woman had suffered an itchy papular and vesicular eruption of the face and neck, which had started 2 days after the application of a new facial cream with resveratrol. Patch tests with the European baseline series, a cosmetic series, and the resveratrol cream 'as is' were positive to the cream (++) on D4 and to chromium (++) and *p-tert*.-butylphenolformaldehyde resin (++) with past relevance. The ingredients of this cream, provided by the manufacturer, were patch tested in a second session, which yielded positive reactions (++) to resveratrol 1% water and Scutellaria baicalensis root extract 0.5% water (++) at D4. Four controls were negative (2).

A 39-year-old nonatopic housewife had a 2-year history of pruritic erythematous scaly plaques involving both eyelids and periorbital skin. Patch tests revealed positive reactions to a tinted sunscreen cream and 2 of its ingredients, Scutellaria baicalensis root extract (0.2% 50/50 water/alcohol) and ethylhexyloxyphenol methoxyphenyl triazine (5% pet.) (3).

A 53-year-old man returned home from a 10-day vacation in the Caribbean with facial eczema. He had carefully applied a sunscreen several times a day there and after his return. The eczema occurred only when he returned home to France and he noted that the more he applied the sunscreen, the worse the eczema became. Patch tests and photopatch tests with the European baseline series, a series of photoallergens and with the sunscreen 'as is' were positive at the irradiated (+) and nonirradiated (+++) sites of the sunscreen at day 2. Subsequently, patch tests and photopatch tests were performed with the

ingredients of the sunscreen, provided by the manufacturer. This time, the only positive patch test was to Scutellaria baicalensis extract, tested 0.2% in 50/50 water/alcohol at the non-irradiated site at D2 (++) (4). The author mentioned that the fact that the patch test with S. baicalensis extract was negative at the irradiated site but positive when non-irradiated is consistent with the clinical history, i.e. that the dermatitis only started when the patient returned from his sunny holidays. Possible explanations given by the author were the potential immunosuppressive effect of ultraviolet A radiation, a molecular interaction between components of the sunscreen when irradiated, or a concentration problem in the S. baicalensis patch test applied to the irradiated site (4).

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to Scutellaria baicalensis extract see ref. 1.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 38/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 9/123,000.

LITERATURE

1 Gallo R, Pastorino C, Gasparini G, Ciccarese G, Parodi A. *Scutellaria baicalensis* extract: a novel botanical allergen in cosmetic products? Contact Dermatitis 2016;75(6):387-388. doi: 10.1111/cod.12659.

2 Badaoui A. Allergic contact dermatitis to resveratrol and Scutellaria baicalensis root extract in a cosmetic product. Contact Dermatitis. 2022;87(3):282-283. doi:10.1111/cod.14134.

3 Luna-Bastante L, Gatica-Ortega M-E, Pastor-Nieto M-A, et al. Allergic contact dermatitis to Tinosorb S, Scutellaria baicalensis, and other emerging allergens in cosmetics. Contact Dermatitis. 2020;82(5):307-309. doi: 10.1111/cod.13460.

4 Adam T, Bursztejn A-C, Schmutz J-L. Facial eczema from a sunscreen: Scutellaria baicalensis, a novel allergen beginning to attract attention. Contact Dermatitis. 2020;82:253-254. doi: 10.1111/cod.13453.

3.62 SHELLAC

IDENTIFICATION

Description/definition	: Shellac is the resinous secretion of the insect *Laccifer (Tachardia) lacca,* Coccidae
Classification	: Biological products
Other names	: Lacca; lac resin; gum lac
CAS registry number	: 9000-59-3
EC number	: 232-549-9
CIR reports	: J Am Coll Toxicol 1986;5:309-327
Wikipedia	: https://en.wikipedia.org/wiki/Shellac
Functions in cosmetics	: EU: binding; emollient; film forming; hair fixing; viscosity controlling. USA: binders; film formers; hair fixatives
Patch testing	: 20% alc. (Chemotechnique, SmartPractice); high risk or false-positive, irritant reactions (7)

Previous chapter to which this is an update

The literature on contact allergy to shellac from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.408, pp. 1124-1127.

CONTACT ALLERGY (cosmetics)

Case report

An otherwise healthy 66-year-old nonatopic woman was investigated for pruritus and progressive hair loss involving the frontotemporal follicular implantation line, present for 14 months, diagnosed as frontal fibrosing alopecia (FFA). This had become associated with outbreaks of localized eczematous lesions in the last 8 months. The patient used a shellac-containing ecological hairspray daily. A repeated open application test (ROAT) with the hairspray twice daily on the antecubital flexure resulted in an eczematous reaction after 3 days. Patch tests with the European Comprehensive Baseline Series, hairdresser series, and shellac 20% alcohol (alc.) showed a positive reaction only to shellac 20% alc. (D4 ++). Shellac was the second most important ingredient in the hairspray. Following discontinuation of the hairspray the pruritic dermatitis completely resolved and did not recur. Her FFA remained unchanged at 6 month follow-up (4).

Previous cases of allergic cosmetic dermatitis

There have been at least 12 previous case reports and case series of allergic cosmetic dermatitis to shellac, the most recent in references 1-3. For a full literature review of this topic please refer to the Monographs in Contact Allergy, Volume 1, Chapter 2.408, pp. 1124-1127.

OTHER PUBLICATIONS [a]

- A 21-year-old woman had a recurrent lower median lip fissure as a result of contact allergy to shellac present in a mouthguard (5).
- A 38-year-old woman had occupational allergic dermatitis of the hands from shellac present in an alcoholic dispersion of wax and shellac, used for the glazing of hard-coated sugar-free and sugar-containing sweets (6).
- A 25-year-old woman working in a fruit warehouse had occupational allergic contact dermatitis of the hands and forearms from contact allergy to shellac (E904) used as a coating agent for lemons (6).
- In 2021, in Germany, members of the Information Network of Departments of Dermatology (IVDK) patch tested 2167 consecutive patients with shellac 20% alc. and 76 (3.5%) had a positive reaction, for none of which certain relevance was found. 185 patients (8.5%) had non-allergic reactions (90 irritant, 95 doubtful). The authors concluded that the high incidence of weak positive, doubtful, and irritant reactions assigns shellac (20% alc.) as a problematic allergen preparation with a presumably high

share of false-positive reactions. There was a significant association with positive reactions to colophonium (7).

- In Leeds Teaching hospital, in the period 2013-2022, 5458 patients were tested with the cosmetic series which included shellac 20% alc. and there were 21 (0.4%) positive reactions. Eleven (53%) were deemed of current relevance, but no culprit products or possible sources of shellac were mentioned. There was an association between shellac positivity and markers of fragrance allergy, particularly colophonium and propolis (8).
- In the Mayo clinics in the USA, from 2014 to 2016, shellac 20% alcohol was patch tested in 612 (35%) of 1764 unique patients in an extended standard series. Five patients (0.8%) had an irritant reaction. In addition, 64 patients (10.5%) had a positive reaction to shellac with reactions graded as weak (n = 57 [9.3%]), strong (n = 7 [1.1%]), or extreme (n = 0 [0.0%]). A further 70 patients (11.4%) had reactions graded as macular erythema; these reactions were excluded from the calculation of positive reaction rates. No mention was made of the clinical relevance of the reactions. The author claim that, although it has been reported that shellac in alcohol tends to be a common irritant, they found shellac to have a relatively low irritant rate (0.8%) (9), which quite obviously is a rather embarrassingly wrong statement.

[a] Literature on contact allergy to shellac that was found in *Contact Dermatitis* or/and *Dermatitis* from September 2017 through March 2025, in which there was no link with cosmetic products.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 9/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 55/123,000.

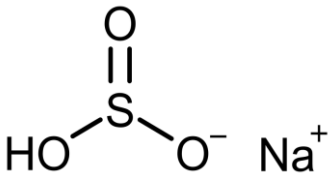
LITERATURE

1 Shaw T, Oostman H, Rainey D, Storrs F. A rare eyelid dermatitis allergen: shellac in a popular mascara. Dermatitis 2009;20(6):341-345. PMID: 19958740.
2 Strauss RM, Orton DI. Allergic contact cheilitis in the United Kingdom: a retrospective study. Am J Contact Dermat 2003;14(2):75-77. PMID: 14749024.
3 Gallo R, Marro I, Pavesi A. Allergic contact dermatitis from shellac in mascara. Contact Dermatitis 2005;53(4):238-239. doi: 10.1111/j.0105-1873.2005.0670f.x.
4 Navarro-Triviño FJ. Allergic contact dermatitis from shellac in an ecological hair spray occurring in a patient with frontal fibrosing alopecia. Contact Dermatitis. 2022;86(6):544-545. doi: 10.1111/cod.14061.
5 Melchers RC, Quint KD, van Zuuren EJ. Contact allergy to a shellac-containing mouthguard. Contact Dermatitis. 2022;86(6):554-556. doi: 10.1111/cod.14081.
6 Mercader-García P. Occupational allergic contact dermatitis caused by shellac. Contact Dermatitis. 2022;86(6):557-559. doi: 10.1111/cod.14083.
7 Schubert S, Worm M, Dickel H, Wagner N, Brans R, Schröder-Kraft C, Bauer A, Koch A, Geier J; IVDK. Patch testing shellac in consecutive patients-Data of the Information Network of Departments of Dermatology (IVDK) 2021. Contact Dermatitis. 2023;88(1):77-80. doi: 10.1111/cod.14227.
8 Ghadiri SJ, Sambi P, Wilkinson SM, Whitehouse H. Contact sensitisation to shellac: A possible marker of fragrance allergy. Contact Dermatitis. 2023;89(3):205-206. doi: 10.1111/cod.14364.
9 Veverka KK, Killian JM, Yiannias JA, Hall MR, Drage LA, Davis MDP. Shellac: A tertiary care center experience. Dermatitis. 2018;29(4):226-227. doi: 10.1097/DER.0000000000000394.

3.63 SODIUM BISULFITE

IDENTIFICATION

Description/definition : Sodium bisulfite is the inorganic salt that conforms to the structural formula shown below
Classification : Inorganic salts
IUPAC name : Sodium hydrogen sulfite
CAS registry number : 7631-90-5
EC number : 231-548-0
CIR reports : Int J Toxicol 2003;22(Suppl.2):63-88
SCCS opinions : SCCNFP/0648/03, final
Wikipedia : https://en.wikipedia.org/wiki/Sodium_bisulfite
Functions in cosmetics : EU: antioxidant; preservative; reducing. USA: antioxidants; hair waving/straightening agents; reducing agents
EU cosmetic restrictions : Regulated in Annexes III/99 and V/9 of the Regulation (EC) 2009/1223
Patch testing : 1% pet. (SmartPractice)
Molecular formula : HO_3NaS



Previous chapter to which this is an update

The literature on contact allergy to sodium bisulfite from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.412, pp. 1134-1136.

CONTACT ALLERGY (cosmetics)

Case series

In 2017 and 2018, 4885 consecutive patients suspected of contact dermatitis were patch tested by the members of the North American Contact Dermatitis Group (NACDG) with sodium bisulfite 1% pet. and 132 (2.7%) had a positive reaction. Reactions were most commonly + (50%) or ++ (34%); 65% were considered to be currently relevant. Specific sources of sodium bisulfite exposure were cosmetics/beauty preparations/skin and healthcare products (n=25, of which 15 hair care products), drugs/medications (n=12), food products (n=10) and other (n=4) (3).

Previous cases of allergic cosmetic dermatitis

For previous cases of allergic cosmetic dermatitis to sodium bisulfite see ref. 1.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 53/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 81/123,000.

OTHER PUBLICATIONS [a]

- A 62-year-old caregiver had occupational allergic contact dermatitis of the hands from sodium bisulfite in dish soap (2).
- Occupational ACD from sulfites (unspecified) used as preservatives on shrimps (4).

- Review article sulfites: Allergen of the year 2024 (5).

[a] Literature on contact allergy to sodium bisulfite that was found in *Contact Dermatitis* or/and *Dermatitis* from September 2017 through March 2025, in which there was no direct link with cosmetic products.

LITERATURE

1 Adams RM, Maibach HI, Clendenning WE, Fisher AA, Jordan WJ, Kanof N, et al. A five-year study of cosmetic reactions. J Am Acad Dermatol 1985;13(6):1062-1069. doi: 10.1016/s0190-9622(85)70258-7.

2 Kullberg SA, Hylwa S. Sodium disulfite/bisulfite allergy manifesting from dish soap: Not limited to hairdressing or food industries. Dermatitis. 2020;31(5):e51-e52. doi: 10.1097/DER.0000000000000576.

3 Warshaw EM, Buonomo M, DeKoven JG, Atwater AR, Reeder MJ, Belsito DV, et al. Patch testing with sodium disulfite: North American Contact Dermatitis Group experience, 2017 to 2018. Contact Dermatitis. 2021;85(3):285-296. doi: 10.1111/cod.13860.

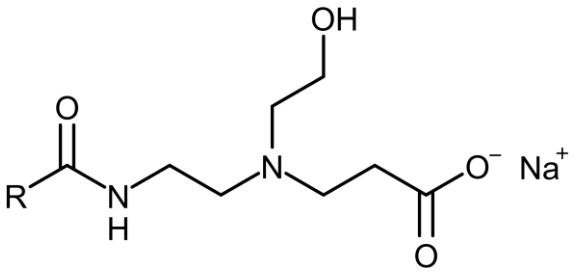
4 Raison-Peyron N, Roulet A, Dereure O. Occupational allergic contact dermatitis caused by sulfite in a seafood section worker of a supermarket. Contact Dermatitis. 2019;80(6):412-414. doi: 10.1111/cod.13244.

5 Ekstein SF, Warshaw EM. Sulfites: Allergen of the Year 2024. Dermatitis. 2024;35(1):6-12. doi: 10.1089/derm.2023.0154.

3.64 SODIUM COCOAMPHOPROPIONATE

IDENTIFICATION

Description/definition : Sodium cocoamphopropionate is the amphoteric organic compound that conforms generally to the structural formula shown below, where RCO- represents the fatty acids derived from coconut oil
Classification : Alkylamido alkylamines
Other names : Fatty acids, coco, reaction products with 2-((2-aminoethyl)amino)ethanol, mono(2-carboxyethyl) derivs., monosodium salts
CAS registry number : 132647-08-6; 93820-52-1
EC number : 298-632-7
Functions in cosmetics : EU: cleansing; foam boosting; foaming; hair conditioning; surfactant. USA: hair conditioning agents; surfactants - cleansing agents; surfactants – foam boosters; surfactants - hydrotropes
Patch testing : 1% water (1,4); 10% pet. (2); 20 controls were negative to 10% pet. (3)



Previous chapter to which this is an update

The literature on contact allergy to sodium cocoamphopropionate from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.415, pp. 1140-1141.

CONTACT ALLERGY (cosmetics)

Case series

Four patients, a male car mechanic, a system operator in metal processing, a tool mechanic and a male grinder, had hand eczema of 6 months – 7 years duration. They all had applied the same skin protection cream at the workplace several times a day for >1 year. Patch tests with the cream 'as is' and all of its single components, including sodium cocoamphopropionate 1% water, showed positive reactions to the cream and sodium cocoamphopropionate in all 4 individuals at D3/D4. No further positive reactions to the other ingredients were observed. In all patients, eczema improved after avoidance of exposure to sodium cocoamphopropionate (4).

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to sodium cocoamphopropionate see refs. 1-3.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 28/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 14/123,000.

LITERATURE

1 Hagvall L, Bråred-Christensson J, Inerot A. Occupational contact dermatitis caused by sodium cocoamphopropionate in a liquid soap used in fast-food restaurants. Contact Dermatitis 2014;71(2):122-124. doi: 10.1111/cod.12209.

2 Pesonen M, Kuuliala O, Suomela S, Aalto-Korte K. Epidemic of occupational contact dermatitis caused by sodium cocoamphopropionate in a hand cleanser among fast-food restaurant workers. Contact Dermatitis 2016;75(Suppl.1):37.

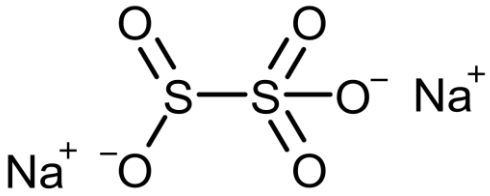
3 Pesonen M, Suomela S, Kuuliala O, Aalto-Korte K. Occupational contact allergy to sodium cocoamphopropionate in a hand cleanser. Contact Dermatitis 2016;74(4):246-248. doi: 10.1111/cod.12474.

4 Skudlik C, Markthaler M, John SM. Occupational contact allergy to sodium cocoamphopropionate in a skin protection cream. Contact Dermatitis. 2018;78(4):295-296. doi: 10.1111/cod.12932.

3.65 SODIUM METABISULFITE

IDENTIFICATION

Description/definition : Sodium metabisulfite is the inorganic salt that conforms to the structural formula shown below
Classification : Inorganic salts
IUPAC name : Disodium disulfite
Other names : Sodium pyrosulfite; sodium disulfite
CAS registry number : 7681-57-4
EC number : 231-673-0
CIR reports : Int J Toxicol 2003;22(Suppl.2):63-88
SCCS opinions : SCCNFP/0648/03, final
Wikipedia : https://en.wikipedia.org/wiki/Sodium_metabisulfite
Functions in cosmetics : EU: antioxidant; preservative; reducing. USA: antioxidants; reducing agents
EU cosmetic restrictions : Regulated in Annexes III/99 and V/9 of the Regulation (EC) 2009/1223
Patch testing : 1% pet. (Chemotechnique, SmartPractice)
Molecular formula : $H_2Na_2O_5S_2$



Previous chapter to which this is an update

The literature on contact allergy to sodium metabisulfite from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.422, pp. 1154-1159.

CONTACT ALLERGY (cosmetics)

Case report

A 41-year-old woman with a history of recurrent erythematous plaques on the cheeks was prescribed three cosmetic creams. After 2 days of application, the patient noted worsening of her facial lesions with more itching and burning. She was then prescribed desonide 0.1% cream and ketoconazole 2% cream. One day later, her dermatosis had worsened even more and she presented at the dermatology emergency room, where erythematous and very oedematous plaques on her cheeks and nose were noted. Acute contact dermatitis was suspected, which resolved in 1 week with desonide cream. Patch tests with the European baseline series, a cosmetics series and the suspected products tested 'as is' (three facial creams, ketoconazole cream, desonide cream) were positive to sodium metabisulphite 1% pet. (++/++), ketoconazole cream (++/++) and one of the cosmetic creams (-/++). The cosmetic cream contained sodium metabisulfite and ketoconazole cream sodium sulfite. The patient first had worsening of eczema from sodium metabisulfite in the cosmetic cream, which was further aggravated by contact allergy to sodium sulfite in the pharmaceutical cream. It is uncertain whether the patient had primarily become sensitized to both sulfites or that there was a cross-reaction between the two (5).

Previous cases of allergic cosmetic dermatitis

There are at least 10 previous case reports and case series of allergic cosmetic dermatitis to sodium metabisulfite, the most recent ones are refs. 1-4. For a full literature review of this topic please refer to the Monographs in Contact Allergy, Volume 1, Chapter 2.422, pp. 1154-1159.

IMMEDIATE-TYPE REACTIONS

Immediate reactions such as urticaria, angioedema, asthma, rhinoconjunctivitis and anaphylaxis from sodium metabisulfite in foods, drinks, medications and other products are well recognized, but no cases have resulted from the presence of sodium metabisulfite in cosmetic products.

OTHER PUBLICATIONS [a]

- A 42-year-old woman, allergic to sodium metabisulfite, had intermittent unilateral lip swelling from ingestion of this (or/and other?) sulfites in beer, wine and other food products: systemic allergic dermatitis (6).
- An operating room nurse had hand dermatitis from contact allergy to sodium metabisulfite which was present in lidocaine decanted during surgery (7).
- A 48-year-old woman developed localized allergic dermatitis and a generalized eczematous rash (systemic allergic dermatitis) from delayed-type hypersensitivity to sodium metabisulfite which was present in a lidocaine local anesthetic injected for surgical removal of a mole (8).
- Systemic allergic dermatitis from sodium metabisulfite in a rectal enema (9).
- A 46-year-old man had 3 episodes of dermatitis after orthopedic surgeries from delayed-type hypersensitivity to sodium metabisulfite in gentamicin injection solution (10).
- Occupational ACD from sulfites (unspecified) used as preservatives on shrimps (11).
- Systemic allergic dermatitis to sodium metabisulfite in local anesthetic solution (12).
- Occupational allergic contact dermatitis to sodium metabisulfite in shredded coconut (13).
- Allergic contact dermatitis to sodium metabisulphite in a rotigotine transdermal therapeutic system (14).
- Review article sulfites: Allergen of the year 2024 (15).
- ACD from sodium metabisulfite and lidocaine in a local anesthetic (16).

[a] Literature on contact allergy to sodium metabisulfite that was found in *Contact Dermatitis* or/and *Dermatitis* from September 2017 through March 2025, in which there was no direct link with cosmetic products.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 586/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 551/123,000.

LITERATURE

1 Garcia-Gavin J, Parente J, Goossens A. Allergic contact dermatitis caused by sodium metabisulfite: a challenging allergen. A case series and literature review. Contact Dermatitis 2012;67(5):260-269. doi: 10.1111/j.1600-0536.2012.02135.x.

2 Aalto-Korte K, Suuronen K, Alanko K. Sodium metabisulfite – a contact allergen? Contact Dermatitis 2009;60(2):115-117. doi: 10.1111/j.1600-0536.2008.01484.x.

3 Madan V, Walker SL, Beck MH. Sodium metabisulfite allergy is common but is it relevant? Contact Dermatitis 2007;57(3):173-176. doi: 10.1111/j.1600-0536.2007.01188.x.

4 Ralph N, Verma S, Merry S. What is the relevance of contact allergy to sodium metabisulfite and which concentration of the allergen should we use? Dermatitis 2015;26(4):162-165. doi: 10.1097/DER.0000000000000120.

5 Beaulieu V, Matei I, Hajjar N, Ingen-Housz-Oro S, Assier H. Acute allergic contact dermatitis caused by sulphites in a cosmetic and a pharmaceutical cream. Contact Dermatitis. 2024;90(3):312-314. doi:10.1111/cod.14468.

6 Johnson H, Yu J. Systemic contact dermatitis to sodium metabisulfite presenting as episodic, unilateral lip swelling. Dermatitis. 2023;34(5):451. doi: 10.1089/derm.2023.0039.

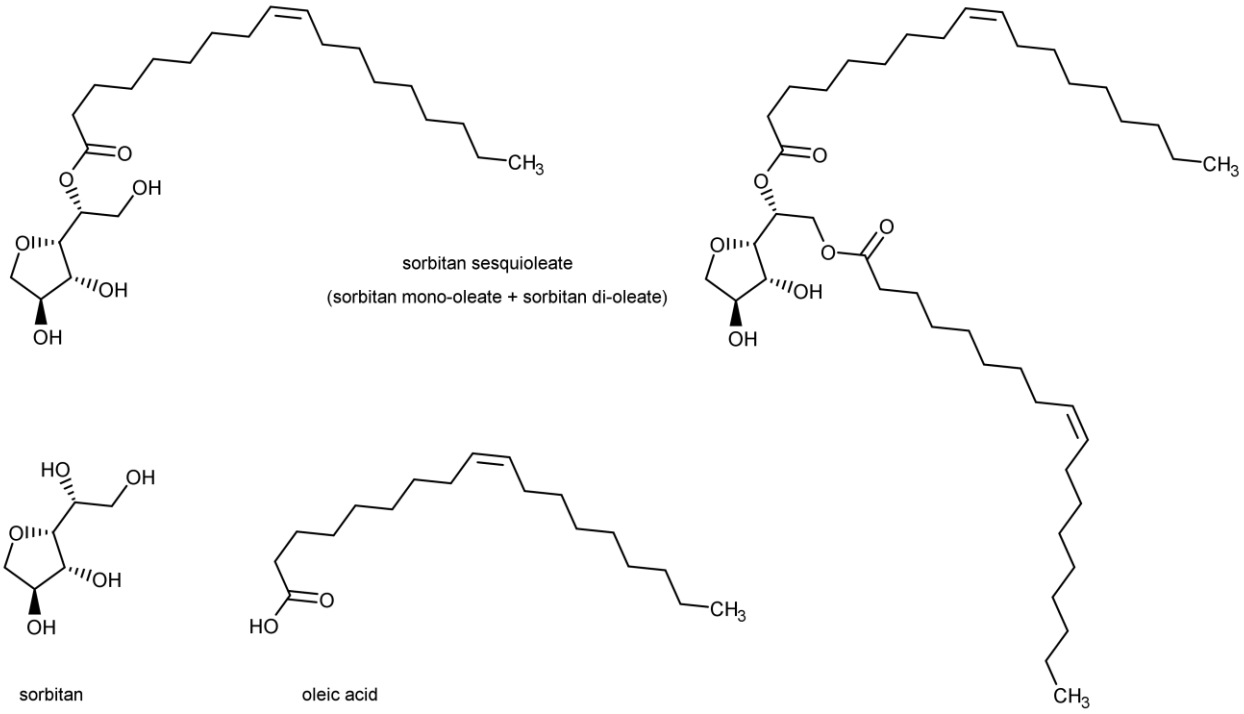
7 Ibanez MA, Levoska MA, Zheng DX, Nedorost ST. Sodium metabisulfite allergic contact dermatitis from lidocaine exposure in an operating room nurse. Dermatitis. 2021;32(6):e108-e109. doi: 10.1097/DER.0000000000000710.

8 Guha-Niyogi B, Sabroe R, Holden C. An unusual case of a systemic delayed hypersensitivity reaction to sodium metabisulfite. Contact Dermatitis. 2018;79(4):246-247. doi: 10.1111/cod.13037.
9 Borges AS, Valejo Coelho MM, Fernandes C, Brasileiro A, Gonçalo M. Systemic allergic dermatitis caused by sodium metabisulfite in rectal enemas. Contact Dermatitis. 2018;78(6):429-430. doi: 10.1111/cod.12971.
10 Boyd AH, Warshaw EM. Sulfites: No longer a zebra? Dermatitis. 2017;28(6):364-366. doi: 10.1097/DER.0000000000000312.
11 Raison-Peyron N, Roulet A, Dereure O. Occupational allergic contact dermatitis caused by sulfite in a seafood section worker of a supermarket. Contact Dermatitis. 2019;80(6):412-414. doi: 10.1111/cod.13244.
12 Tan MG, Li HO, Pratt MD. Systemic allergic dermatitis to sodium metabisulfite in local anesthetic solution. Contact Dermatitis. 2022;86(2):120-121. doi: 10.1111/cod.13978.
13 Hamann CR, Baker C, O'Hern K, Zug KA. Occupational allergic contact dermatitis to sodium metabisulfite in shredded coconut. Contact Dermatitis. 2022;87(4):385-386. doi: 10.1111/cod.14175.
14 Antunes-Duarte S, Sun L, Sousa D, Alpalhão M. Allergic contact dermatitis to sodium metabisulphite in a rotigotine transdermal therapeutic system. Contact Dermatitis. 2024;91(6):528-529. doi: 10.1111/cod.14676.
15 Ekstein SF, Warshaw EM. Sulfites: Allergen of the Year 2024. Dermatitis. 2024;35(1):6-12. doi: 10.1089/derm.2023.0154.
16 Hoyos CNF, Jessup CJ, Goldminz AM. Allergic contact dermatitis to lidocaine and sodium metabisulfite. Dermatitis. 2025;36(1):83-84. doi: 10.1089/derm.2024.0024.

3.66 SORBITAN SESQUIOLEATE

IDENTIFICATION

Description/definition : Sorbitan sesquioleate is a mixture of mono- and diesters of oleic acid and hexitol anhydrides derived from sorbitol
Classification : Sorbitan derivatives
IUPAC name : (2*R*,3*R*,4*R*,5*S*)-Hexane-1,2,3,4,5,6-hexol; (*Z*)-octadec-9-enoic acid
Other names : Arlacel® C
CAS registry number : 8007-43-0
EC number : 232-360-1
CIR reports : J Am Coll Toxicol 1985;4:65-121; Int J Toxicol 2019;38(Suppl.2):60-80
Functions in cosmetics : EU: emulsifying. USA: surfactants - emulsifying agents
Patch testing : 20% pet. (Chemotechnique, SmartPractice)
Molecular formula : $C_{66}H_{126}O_{16}$



Previous chapter to which this is an update

The literature on contact allergy to sorbitan sesquioleate from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.432, pp. 1177-1182.

CONTACT ALLERGY (cosmetics)

Case series

In 11 clinics homogeneously distributed across Italy, 5336 consecutive patients (1702 men and 3634 women; mean age 46.1 years) were patch tested between January and December 2018 with sorbitan sesquioleate 20% pet. in the SIDAPA baseline series. Of these, 27 (0.5%) showed positive reactions to SSO,

12 men (0.6%) and 15 women (0.4%). In 59% (16/27) of these patients the reactions were strong (++) or extreme (+++). In 19 of the 27 SSO-positive patients (70%) the patch tests were considered to be relevant. Culprit products were cosmetics (n=10, 53%), topical corticosteroids (n=4, 21%), and other topical medications (n=5, 26%) (10).

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to sorbitan sesquioleate see refs. 1-4. For cases of immediate-type reactions to sorbitan sesquioleate in a corticosteroid ointment see refs. 5 and 6 (article twice published in the same journal).

IMMEDIATE-TYPE REACTIONS

A 64-year-old female cashier had contact urticaria from a topical corticosteroid, which was caused by its ingredient sorbitan sesquioleate (11).

OTHER PUBLICATIONS [a]

- Commercial fragrance mix I, Myroxylon pereirae resin, and 2-hydroxymethyl methacrylate test allergens, which are present in most standard/baseline series, may contain sorbitan sesquioleate (SSO) as emulsifier. As it is well-known that SSO may occasionally cause contact allergy itself, positive patch tests to the abovementioned allergens in patients allergic to SSO may be misinterpreted. Therefore, some authors have advised to add SSO 20% pet. to the baseline series (7). Others, however, do not recommend SSO for screening in the baseline series due to the relatively low prevalence and difficulty in evaluating clinical relevance (8).
- Allergic contact dermatitis to sorbitan sesquioleate in a non-adhering surgical dressing (9).

[a] Literature on contact allergy to sorbitan sesquioleate that was found in *Contact Dermatitis* or/and *Dermatitis* from September 2017 through March 2025, in which there was no direct link with cosmetic products.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 343/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 1879/123,000.

LITERATURE

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10 Stingeni L, Tramontana M, Bianchi L, Foti C, Romita P, Patruno C, et al. Patch test with sorbitan sesquioleate in Italian consecutive patients: A 1-year multicenter SIDAPA study. Contact Dermatitis. 2019;81(6):454-456. doi: 10.1111/cod.13359.
11 Sandhu VK, Huang CM, DeKoven JG. A case of contact urticaria to sorbitan sesquioleate in topical corticosteroids. Contact Dermatitis. 2022;86(5):436-437. doi: 10.1111/cod.14054.

3.67 STANNOUS FLUORIDE

IDENTIFICATION

Description/definition : Stannous fluoride is the inorganic salt with the molecular formula SnF_2 (F_2Sn)
Classification : Inorganic salts
IUPAC name : Difluorotin
Other names : Tin difluoride
CAS registry number : 7783-47-3
EC number : 231-999-3
Wikipedia : https://en.wikipedia.org/wiki/Tin(II)_fluoride (Tin(II) fluoride)
Functions in cosmetics : EU: antiplaque; oral care. USA: anticaries agents; oral care agents; oral health care drugs
EU cosmetic restrictions : Regulated in Annex III/35 of the Regulation (EC) 2013/344
Patch testing : Tin 50% pet.; stannous chloride 1.0% pet.; tin(II)oxalate 1.0% pet. (Chemotechnique); tin(II) chloride 0.5% pet. (SmartPractice); stannous chloride 1% pet. may cause weak-positive, irritant, reactions; tin 50% pet. is likely less sensitive; tin oxalate 1% pet. is possibly a good alternative (5)
Molecular formula : SnF_2; F_2Sn

Previous chapter to which this is an update

The literature on contact allergy to stannous fluoride from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.435, p. 1185.

CONTACT ALLERGY (cosmetics)

General

In the patients presented here, the sensitizer is not stannous fluoride *per se*, but tin, of which stannous fluoride is a salt. See also Chapter 2.36 Stannous chloride.

Case reports

A 23-year-old atopic woman suffered from recurrent episodes of oral stomatitis since >6 months. Each episode would start with itchy lips, without visible lesions, followed by the appearance of small itchy vesicles at the mucosal side of the lips and buccal mucosa, which subsequently broke down into small painful ulcers, and sometimes localized haemorrhages, together with a sensation of swelling of the tongue and oral mucosa. The patient had received multiple treatments for herpes simplex, aphthous ulcers, angioedema, Behçet disease and burning mouth syndrome without success. Because of the rather atypical complaint of associated pruritus, which also characterized the start of each new flare-up, the patient was patch tested with an extended baseline and cosmetic series; personal products were not brought in at the initial test session. At that time, the investigators had started to patch test various stannous (tin) salts as a supplement to their baseline series (tin 50% pet., tin chloride 1% pet. and tin oxalate 1% pet.). On D4, positive reactions were observed to all three materials. Stannous fluoride was found to be present in two brands of toothpastes the patient used, the latter also containing stannous chloride, hence also considered relevant for the recurrent oral stomatitis and aphthosis. Following the use of a sodium fluoride-containing toothpaste, the problem was completely resolved, with no recurrence after a follow-up time of 1 year (2).

A 52-year-old woman had a 2-month history of repeated episodes of lip swelling accompanied by small blisters, itching and redness on her lip, without intra-oral symptoms. The patient had recently started using a new toothpaste. Patch tests were positive to stannous oxalate 1% pet. (D3 ++, D7 +++). Her new

toothpaste proved to contain stannous fluoride. A semi-open patch test with the toothpaste 1% water and patch tests with the product at 5%, 10%, 20% and 30% in water were negative at D2. However, erythema and vesiculation of the upper lip were noticed at that moment, likely due to the absorption of the allergen. During the day 3 and day 7 assessments, the 20% and 30% dilutions exhibited positive results, with stronger positive reactions at D7. The patient was diagnosed with allergic contact cheilitis from stannous fluoride in toothpaste. After the product was substituted with a toothpaste not containing stannous fluoride, no symptoms have been observed anymore (3).

A 50-year-old atopic female patient with pre-existing chronic spontaneous urticaria presented with episodes of lip swelling, (angular) cheilitis, and small aphthous ulcers, accompanied by perianal itching and mild flexural dermatitis involving the elbow folds, axillae, and groins. Patch tests with a baseline series, cosmetic, fragrance and dental (metal) series, along with personal hygiene products, were positive to one of two toothpastes (D2 +, D4 ++, D7 ++) and to tin 50% pet. (D4 ++, D7 ++). The toothpaste that reacted positively contained stannous fluoride. The perianal itching and mild flexural dermatitis were considered symptoms of systemic allergic dermatitis from absorption of tin through the oral mucosa. New patch tests with tin 50% pet., tin chloride 1% pet. and tin(II) oxalate 1% pet. were strongly positive on D4. The suspected toothpaste was also retested, and again gave a positive reaction (+) on D4; a dilution series with the toothpaste (30% down to 0.003%), in both water and pet., was positive down to 3% in both vehicles. Following replacement of the culprit toothpaste with a sodium fluoride-containing toothpaste, the dermatitis in the patient resolved and did not recur. The urticaria, however, persisted (4).

Two years later, 2 patients were reported from The Netherlands who had used the same stannous fluoride-containing toothpaste as the previous patient and who were also shown to be allergic to tin. The first was a 69-year-old atopic retired painter, who reported recurrent swelling with small blisters and red spots intra-orally and on his tongue and, in addition, crusts on his lips for 6 months. The second patient was a 62-year-old non-atopic housewife who suffered from an erythematous gingiva and who had episodes of red and flaking skin changes on and below her lip prior. Both reacted to patch tests with (dilutions of) their toothpaste, tin 50% pet., and tin salts (stannous oxalate, chloride, fluoride). Contact allergy to fluoride was excluded by negative reactions to sodium fluoride in dilution series in pet. and water from 0.015% up to 0.5%. After avoidance of tin and tin salts, all symptoms resolved in both patients. Control patch testing showed that the test material of stannous chloride 1% pet. caused many ?+ and IRR reactions, whereas there were no irritant reactions to stannous oxalate 1% pet. As tin 50% gave only + reactions, the authors suggested that testing with stannous oxalate 1% pet. may be preferable for patch testing in patients suspected of allergy to tin (5).

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to stannous fluoride see ref. 1 (dubious report).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 0/35,000 (toothpastes in the USA are OTC drugs, not cosmetics).
EWG's Skin Deep Cosmetics Database (February 2025): 8/123,000.

LITERATURE

1 Enamandram M, Das S, Chaney KS. Cheilitis and urticaria associated with stannous fluoride in toothpaste. J Am Acad Dermatol 2014;71(3):e75-76. doi: 10.1016/j.jaad.2014.01.912.
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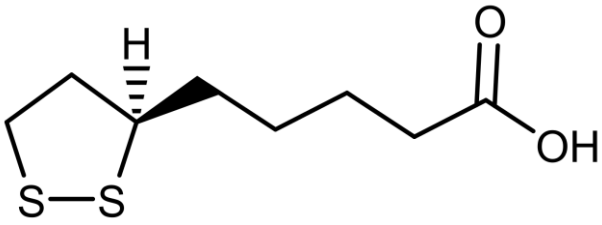
4 Toma N, Horst N, Dandelooy J, Romaen E, Leysen J, Aerts O. Contact allergy caused by stannous fluoride in toothpaste. Contact Dermatitis. 2018 Apr;78(4):304-306. doi: 10.1111/cod.12940.

5 van Amerongen CCA, de Groot A, Volkering RJ, Schuttelaar MLA. Cheilitis caused by contact allergy to toothpaste containing stannous (tin) - two cases. Contact Dermatitis. 2020;83(2):126-129. doi: 10.1111/cod.13532.

3.68 THIOCTIC ACID

IDENTIFICATION

Description/definition : Thioctic acid is the organic compound that conforms to the structural formula shown below
Classification : Carboxylic acids; thio compounds
IUPAC name : 1,2-Dithiolane-3-pentanoic acid, (+/-)-
Other names : α-Lipoic acid; 1,2-dithiolane-3-valeric acid; 5-(dithiolan-3-yl)valeric acid
CAS registry number : 1077-28-7
EC number : 214-071-2
Wikipedia : https://en.wikipedia.org/wiki/Lipoic_acid (Lipoic acid)
Functions in cosmetics : EU: antioxidant. USA: antioxidants
Patch test allergens : 1% and 5% pet. (may sometimes cause very strong reactions [4])
Molecular formula : $C_8H_{14}O_2S_2$



Previous chapter to which this is an update

The literature on contact allergy to thioctic acid from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.458, pp. 1247.

CONTACT ALLERGY (cosmetics)

Case report

An 86-year-old woman presented with an acute itching rash, at the site where she had used a cosmeceutical for chronic venous insufficiency. Examination showed a severe erythematous, oozing dermatitis of her lower legs and thighs. The patient was advised to stop the use of the cream and topical and systemic corticosteroids were prescribed. Six months later, patch tests with the Società Italiana Dermatologia Allergologica Professionale Ambientale baseline series and the topical product, tested 'as is', were positive to the cream (+++) on D2 and D3. Additional patch tests were performed with its main component, α-lipoic acid, at 0.5%, 1% and 5% in petrolatum. All three concentrations gave a strong positive reaction (+++) at D2 and D3. Seven controls were negative (4).

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to thioctic acid see refs. 1 and 2.

IMMEDIATE CONTACT REACTIONS

A 47-year-old woman with vulvar lichen sclerosus refractory to treatment was investigated for a pruritic vulvar rash that had been evolving for months. Recently, the patient had applied a 5% vulvar serum (retinol palmitate 0.09 g, water-soluble vitamin E 50%, vitamin C 1.5 g, sodium hyaluronic acid 0.15 g, lipoic acid [thioctic acid] 0.9 g), which she reported to have caused an urticarial pruritic rash within a few hours after application, and disappearing within a day. A ROAT was positive 4 hours after the first application, triggering an acute urticarial rash in the antecubital fossa, and, remotely, in the palpebral

area. Next, an open test was performed with all ingredients separately, which was negative at 20 minutes. However, after 4 hours, an erythematous reaction was visible at the site of α-lipoic acid (thioctic acid) with distant lesions on the forearm. Complete clearance of the eruption occurred after stopping to apply the serum. Contact urticaria syndrome, probably allergic in nature, to alpha-lipoic acid was diagnosed (3).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 46/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 2/123,000.

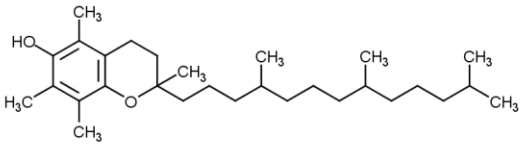
LITERATURE

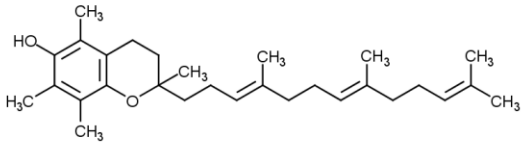
1 Bergqvist-Karlsson A. Thelin I, Bergendorff O. Contact dermatitis to α-lipoic acid in an anti-wrinkle cream. Contact Dermatitis 2006;55(1):56-57. doi: 10.1111/j.0105-1873.2006.0847c.x.
2 Leysen J, Aerts O. Further evidence of thioctic acid (α-lipoic acid) being a strong cosmetic sensitizer. Contact Dermatitis 2016;74(3):182-184. doi: 10.1111/cod.12472.
3 Velasco-Amador JP, Prados-Carmona A´ , Navarro-Triviño FJ. Contact urticaria syndrome caused by alpha-lipoic acid in a master formula for vulvar lichen sclerosus. Contact Dermatitis. 2023;89(2): 136-137. doi:10.1111/cod.14353
4 Corazza M, Arlotti E, Schettini N, Pacetti L, Bianchi A, Borghi A. Allergic contact dermatitis due to α-lipoic acid in a topical over-the-counter product: A case report. Contact Dermatitis. 2023;89(4): 297-299. doi: 10.1111/cod.14381.

3.69 TOCOPHEROL

IDENTIFICATION

Description/definition : Tocopherol is a racemic mixture of naturally occurring tocopherols, including α-tocopherol, β-tocopherol, γ-tocopherol and δ-tocopherol
Classification : Heterocyclic compounds
IUPAC name : 3,4-Dihydro-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)-2*H*-benzo-pyran-6-ol
Other names : Vitamin E; natural vitamin E; mixed tocopherols; DL-α-tocopherol
CAS registry number : 1406-66-2 (tocopherols); 59-02-9 (α-tocopherol); 10191-41-0 (DL-α-tocopherol); 148-03-8 (β-tocopherol); 54-28-4 (γ-tocopherol); 119-13-1 (δ-tocopherol)
EC number : 233-466-0; 218-197-9; 200-412-2; 205-708-5; 204-299-0; 200-201-5
CIR reports : Int J Toxicol 2002;21(Suppl.3):51-116; Int J Toxicol 2018;37(Suppl.2):61-94
Wikipedia : https://en.wikipedia.org/wiki/Tocopherol
Functions in cosmetics : EU: antioxidant; masking; skin conditioning. USA: antioxidants; fragrance ingredients; skin-conditioning agents – miscellaneous; skin-conditioning agents – occlusive
Patch testing : DL-α-Tocopherol 100% (Chemotechnique, SmartPractice)
Molecular formula : $C_{29}H_{50}O_2$ (α-tocopherol; DL-α-tocopherol); $C_{28}H_{48}O_2$ (β-tocopherol; γ-tocopherol); $C_{27}H_{46}O_2$ (δ-tocopherol)


α-tocopherol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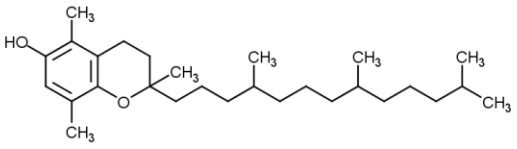
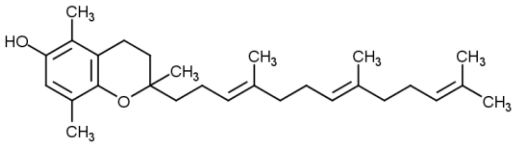

β-tocopherol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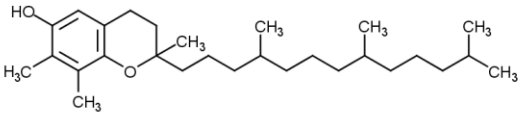
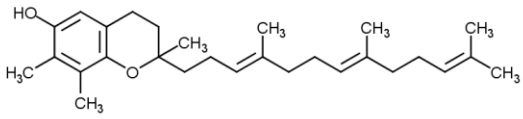
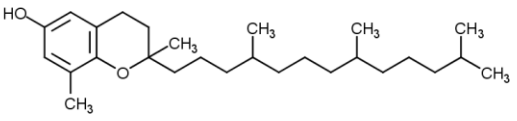
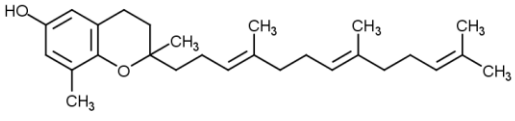

γ-tocopherol


γ-tocotrienol


δ-tocopherol


δ-tocotrienol

Previous chapter to which this is an update

The literature on contact allergy to tocopherol from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.463, pp. 1253-1257.

CONTACT ALLERGY (cosmetics)

Case series

In the period 2001 to 2016, the members of the North American Contact Dermatitis Group (NACDG) patch tested 38,699 consecutive patients suspected of contact dermatitis with DL-α-tocopherol 100% and DL-α-tocopheryl acetate 100% (only 2001-2002) and reviewed the literature on contact allergy to these chemicals (4). During the 2001–2002 cycle (when both tocopherol and tocopheryl acetate were tested), 56 patients (1.1%) were positive to tocopherol, 25 (0.5%) were positive to tocopheryl acetate, and 7 (0.1%) reacted to both. The frequency of positive reactions to tocopherol (2003–2016) was 0.8%. There was a significant decrease in frequency of positive reactions over time. 349 patients had positive allergic reactions to 'tocopherol' (which included tocopheryl acetate) and 39 patients had doubtful reactions coded as 'allergic'. Most (87.6%) allergic reactions were considered currently clinically relevant, but only 30 (9.1%) were 'definitely' relevant. One hundred twelve (33.8%) were considered 'probably' clinically relevant, and 148 (44.7%) were scored as 'possibly' relevant. Relevant reactions were mainly associated with personal care products (65.7%), especially moisturizers, lotions and creams (4).

Case report

A 13-year-old boy with a history of poorly controlled atopic dermatitis since early childhood presented with widespread dermatitis on the face, neck, scalp, and back. Treatment for many years included topical ammonium lactate, 'hypoallergenic' emollients recommended by dermatologists, and corticosteroids with minimal relief. Topical steroids had been applied to the patient's skin at least on a weekly basis since infancy. Patch tests with the North American Comprehensive 80 series, sunscreen, fragrance, and emulsifier series were positive to cobalt (1+), limonene hydroperoxides (1+) and tocopherol (2+). The patient was counselled to avoid tocopherol in his diet and tocopherol and limonene in personal care products. Within 3 months, this resulted in a dramatic improvement of his widespread eczema previously presumed 'atopic dermatitis'. When the patient attempted to reintroduce dietary products high in tocopherol, his dermatitis recurred, and removal of the allergen again led to resolution of his rash (5).
Comment: The authors, in their PRECÍS, stated that '……. was ultimately attributed solely to allergic contact dermatitis (ACD)'. However, they did not mention which of the topical products that the patient used actually contained tocopherol (if at all). Instead they wrote 'When he attempted to reintroduce dietary products high in tocopherol, his dermatitis recurred, and removal of the allergen again led to resolution of his rash', which suggests systemic allergic dermatitis rather than allergic contact dermatitis.

Previous cases of allergic cosmetic dermatitis

There have at least been 4 case series and 9 case reports of allergic cosmetic dermatitis to tocopherol; the most recent ones are refs. 1-3. For a full literature review of this topic please refer to the Monographs in Contact Allergy, Volume 1, Chapter 2.463, pp. 1253-1257.

IMMEDIATE CONTACT REACTIONS

A healthy 11-year-old girl was investigated for an episode of pruritus and facial oedema which developed minutes after applying a cleansing water. An open test on the forearm with the cleansing water 'as is' was positive after 30 minutes, with the appearance of a 28 × 15-mm wheal reaction that disappeared within 24 hours. Five controls were negative. Next, those components of this cosmetic product that were commercially available as test allergen (Chemotechnique) were tested in duplicate by open application on both forearms. With the application of tocopherol 10% pet., a wheal developed after 30 minutes on both arms, that disappeared within one day. Further tests with all of the other ingredients could not be

performed because of an uncooperative manufacturer. There have been no recurrences since the patient avoided products containing tocopherol (6).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 1/35,000 (probably incorrect data).
EWG's Skin Deep Cosmetics Database (February 2025): 21,330/123,000.

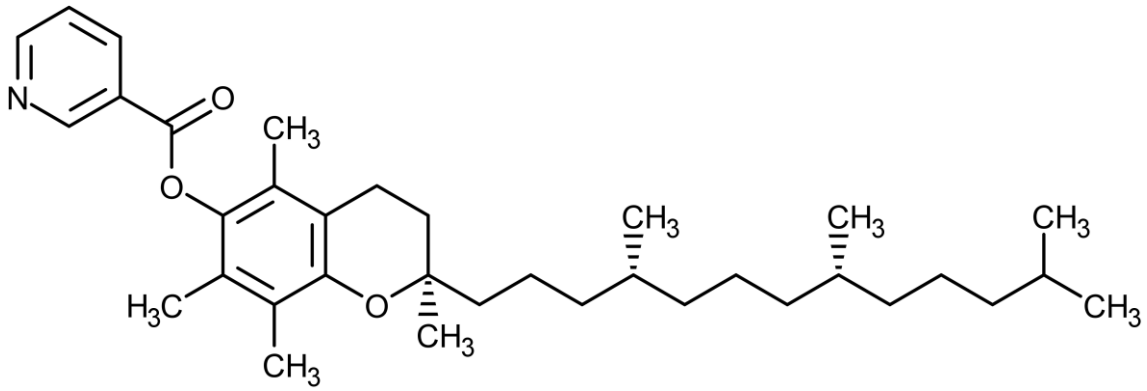
LITERATURE

1 De Groot AC, Rustemeyer T, Hissink D, Bakker M. Contact allergy to capryloyl salicylic acid. Contact Dermatitis 2014;71(3):185-187. doi: 10.1111/cod.12239.
2 Simonsen AB, Koppelhus U, Sommerlund M, Deleuran M. Photosensitivity in atopic dermatitis complicated by contact allergy to common sunscreen ingredients. Contact Dermatitis 2016;74:56-58. doi: 10.1111/cod.12477.
3 Ramírez Santos A, Fernández-Redondo V, Pérez Pérez L, Concheiro Cao J, Toribio J. Contact allergy from vitamins in cosmetic products. Dermatitis 2008;19(3):154-156.
4 Warshaw EM, Ruggiero JL, DeKoven JG, Silverberg JI, Maibach HI, et al. Patch testing with tocopherol and tocopherol acetate: The North American Contact Dermatitis Group experience, 2001 to 2016. Dermatitis. 2021;32(5):308-318. doi: 10.1097/DER.0000000000000706.
5 Chen R, Raffi J, Murase JE. Tocopherol allergic dermatitis masquerading as lifelong atopic dermatitis. Dermatitis. 2020;31(1):e3-e4. doi: 10.1097/DER.0000000000000543.
6 Sanz-Sánchez T, Núñez Acevedo B, Rubio Flores C, Díaz-Díaz RM. Contact urticaria caused by tocopherol. Contact Dermatitis. 2018;79(6):395. doi: 10.1111/cod.13099.

3.70 TOCOPHERYL NICOTINATE

IDENTIFICATION

Description/definition : Tocopheryl nicotinate is the ester of tocopherol and nicotinic acid that conforms to the structural formula shown below
Classification : Esters; heterocyclic compounds
IUPAC name : [2*R*-[2*R**(4*R**,8*R**)]]-3,4-Dihydro-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)-2*H*-1-benzopyran-6-yl nicotinate
Other names : Vitamin E nicotinate
CAS registry number : 43119-47-7
EC number : 256-101-7
CIR reports : Int J Toxicol 2002;21(Suppl.3):51-116; Int J Toxicol 2018;37(Suppl.2):61-94
Functions in cosmetics : EU: antioxidant; skin conditioning; skin protecting. USA: antioxidants; skin-conditioning agents - miscellaneous
Patch testing : 1% pet. or 10% pet. (1); 1% pet. (3)
Molecular formula : $C_{35}H_{53}NO_3$



Previous chapter to which this is an update

The literature on contact allergy to tocopheryl nicotinate from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.466, pp. 1263-1264.

CONTACT ALLERGY (cosmetics)

Case report

A 52-year-old woman had developed a pruritic eczematous rash on the scalp after using cosmetic anti-hair loss ampoules since 2 weeks. After discontinuing its use, the rash resolved completely within 7 days. A repeated open application test (ROAT) with the content of the ampoule was positive after 2 days. Patch tests with the European comprehensive baseline series and the 13 ingredients of the anti-hair loss preparation, obtained from the manufacturer, showed a positive reaction to tocopheryl nicotinate 1% pet. Tocopherol 100% pet. and tocopheryl acetate 10% pet. were negative. Ten controls were negative to tocopheryl nicotinate 1% pet. Based on these findings, allergic contact dermatitis caused by tocopheryl nicotinate was diagnosed. The patient was instructed to avoid the allergen. There was no recurrence of the rash after 3 months of follow-up (3).

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to tocopheryl nicotinate see refs. 1 and 2.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 23/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 61/123,000.

LITERATURE

1 De Groot AC, Berretty PJM, Van Ginkel CJW, Den Hengst CW, Van Ulsen J, Weyland JW. Allergic contact dermatitis from tocopheryl acetate in cosmetic cream. Contact Dermatitis 1991;25(5):302-304. doi: 10.1111/j.1600-0536.1991.tb01878.x.

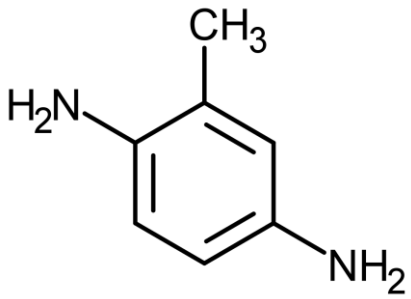
2 Oshima H, Tsuji K, Oh-I T, Koda M. Allergic contact dermatitis due to *dl*-α-tocopheryl nicotinate. Contact Dermatitis 2003;48(3):167-168. doi: 10.1034/j.1600-0536.2003.00052.x.

3 Navarro-Triviño FJ, Linares-González L, Ayén-Rodríguez A, Ruiz-Villaverde R. Allergic contact dermatitis caused by tocopheryl nicotinate. Contact Dermatitis. 2021;84:479-480. doi: 10.1111/cod.13775.

3.71 TOLUENE-2,5-DIAMINE

IDENTIFICATION

Description/definition : Toluene-2,5-diamine is the substituted aromatic amine that conforms to the structural formula shown below
Classification : Amines; color additives - hair
IUPAC name : 2-Methylbenzene-1,4-diamine
Other names : *p*-Toluenediamine; 2-methyl-*p*-phenylenediamine; CI 76042; 2,5-diaminotoluene; 2-methyl-1,4-benzenediamine
CAS registry number : 95-70-5
EC number : 202-442-1
CIR reports : J Am Coll Toxicol 1992;11:423-445; Int J Toxicol 2010;29(Suppl.2):61-83
SCCS opinions : SCCS/1553/15; SCCS/1479/12; SCCS/1390/10; SCCP/1084/07
Functions in cosmetics : EU: hair dyeing. USA: hair colorants
EU cosmetic restrictions : Regulated in Annex III/9a of the Regulation (EC) 2013/1197
Patch testing : 1% pet. (Chemotechnique, SmartPractice)
Molecular formula : $C_7H_{10}N_2$



Previous chapter to which this is an update

The literature on contact allergy to toluene-2,5-diamine from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.467, pp. 1265-1269.

CONTACT ALLERGY (cosmetics)

General

A review article on hair dyes focusing on cross-reactions among hair dye-related allergens, management in clinical practice and prevalence of hair dye-related allergens in patch-tested populations was published in 2024 in *Dermatitis* (10).

Case reports

A 28-year-old woman had developed a severe eczematous reaction on the eyebrows one day after an eyebrow dyeing cream had been applied there by her beautician. The patient reported extreme burning and itching. Erythema, swelling and exudation were clinically evident. She had never used hair dyes, but reported having a black henna tattoo applied on her forearm 14 years previously, which resulted in an intense vesicular reaction 15 days after application. Patch tests with the Italian Society of Allergological, Occupational and Environmental Dermatology (SIDAPA) baseline series, the dye at 10% pet. and 2 of its ingredients, toluene-2,5-diamine (TDA) 1% pet. and *m*-aminophenol 1% pet., resulted in positive

reactions at D2 and D4 to toluene-2,5-diamine (++), *p*-phenylenediamine 1% pet. (+++), nickel (++), textile dye mix (++), the dye that had been applied (++), and *m*-aminophenol (++). In a second session, patch tests with the azo dye mix series showed positive reactions to disperse orange 3 (+++), disperse orange 1 (++), and disperse yellow 3 (++) (8).

A 55-year-old non-atopic male office worker developed extensive urticarial lesions starting on the scalp and face followed by abdominal cramps, nausea and vomiting less than 30 minutes after hair dye application. His condition rapidly improved upon treatment with prednisolone and antihistamines. The patient had no previous history of immediate reactions to hair dyes and never had any temporary black henna tattoos done. However, for more than 1 year, he had noticed itching of the scalp associated with eczematous lesions of the ears and forehead some days after dyeing his hair. Semi-open patch tests with the patient's personal dyes diluted to 10% water were positive after 20 minutes to 2 dyes with a localised papular reaction. Patch tests with the baseline, cosmetic, and hairdressing series as well as his dyes showed +++ positive reactions to *p*-phenylenediamine and toluene-2,5-diamine 1% pet. on D2 and D4, and ++ positive reactions to the dyes. Prick tests with appropriate positive and negative controls were positive to the dyes and to toluene-2,5-diamine. The authors diagnosed a combination of allergic contact dermatitis (delayed-type hypersensitivity) and immediate-type reaction to toluene-2,5-diamine in hair dye products (9).

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to toluene-2,5-diamine see refs. 1-5.

IMMEDIATE-TYPE REACTIONS

A combined immediate-type and delayed-type reaction to toluene-2,5-diamine has been reported in ref. 9 and is presented in the section Case reports above.

Previous cases of immediate-type reactions

For previous cases of immediate-type reactions to toluene-2,5-diamine in hair colours see refs. 6 and 7.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 66/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 55/123,000.

LITERATURE

1 Goossens A. Cosmetic contact allergens. Cosmetics 2016;3. doi: 10.3390/cosmetics3010005.
2 Søsted H, Rastogi SC, Andersen KE, Johansen JD, Menné T. Hair dye contact allergy: quantitative exposure assessment of selected products and clinical cases. Contact Dermatitis 2004;50(6):344-348. doi: 10.1111/j.0105-1873.2004.00362.x.
3 Gottlöber P, Gall H, Bezold G, Peter RU. Allergic contact dermatitis in beauty parlor clients. Hautarzt 2001;52(5):401-404 (Article in German). doi: 10.1007/s001050051332.
4 Madsen JT, Andersen KE. 2-Amino-4-hydroxyethylaminoanisole sulfate – a coupler causing contact allergy from use in hair dyes. Contact Dermatitis 2016;74(2):102-104. doi: 10.1111/cod.12494.
5 Søsted H, Rastogi SC, Thomsen JS. Allergic contact dermatitis from toluene-2,5-diamine in a cream dye for eyelashes and eyebrows – quantitative exposure assessment. Contact Dermatitis 2007;57(3):195-196. doi: 10.1111/j.1600-0536.2007.01105.x.
6 Pasche-Koo F, French L, Piletta-Zanin PA, Hauser C. Contact urticaria and shock to hair dye. Allergy 1998;53(9):904-905. doi: 10.1111/j.1398-9995.1998.tb04001.x.
7 Taniguchi T, Higashi N, Kume A, Miyomoto T, Ogiwara S, Higami K. A case of anaphylaxis due to para-toluenediamine in a hair dye. Jpn J Dermatoallergol 2000;8:7-11 (in Japanese).
8 Romita P, Foti C, Mascia P, Guida S. Eyebrow allergic contact dermatitis caused by *m*-aminophenol and toluene-2,5-diamine secondary to a temporary black henna tattoo. Contact Dermatitis. 2018;79(1):51-52. doi: 10.1111/cod.12987.

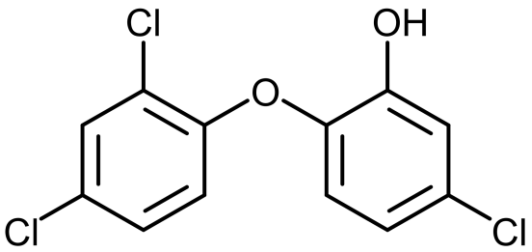
9 Piletta-Zanin A, Marchal O, Pastor D, Piletta-Zanin P, Harr T. An unusual case of a combined severe type I immediate hypersensitivity reaction and delayed type IV allergic contact dermatitis caused by hair dyes including toluene-2,5-diamine in the same patient. Contact Dermatitis. 2024;91(3):257-259. doi: 10.1111/cod.14587.

10 Tsimpidakis A, Katoulis A, Nicolaidou E, Rigopoulos D, Stratigos A, Gregoriou S. Hair dyes sensitization and cross-reactions: Challenges and solutions: A systematic review of hair dye allergens' prevalence. Dermatitis. 2024;35(1):13-23. doi: 10.1089/derm.2023.0019.

3.72 TRICLOSAN

IDENTIFICATION

Description/definition	: Triclosan is the substituted organic ether that conforms to the structural formula shown below
Classification	: Ethers; halogen compounds; phenols
IUPAC name	: 5-Chloro-2-(2,4-dichlorophenoxy)phenol
Other names	: Irgasan® DP 300
CAS registry number	: 3380-34-5
EC number	: 222-182-2
Wikipedia	: https://en.wikipedia.org/wiki/Triclosan
CIR reports	: Final report, December 14, 2010
SCCS opinions	: SCCS/1414/11; SCCP/1192/08; SCCP/1040/06; SCCNFP/0600/02; SCCP/1251/09
Functions in cosmetics	: EU: deodorant; preservative. USA: cosmetic biocides; deodorant agents; preservatives
EU cosmetic restrictions	: Regulated in Annex V/25 of the Regulation (EU) 2024/996
Patch testing	: 2% pet. (Chemotechnique, SmartPractice); according to some authors, this concentration may cause some irritant reactions (1)
Molecular formula	: $C_{12}H_7Cl_3O_2$



Previous chapter to which this is an update

The literature on contact allergy to triclosan from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.475, pp. 1294-1299.

CONTACT ALLERGY (cosmetics)

Case report

A 65-year-old woman had suffered swelling, redness, and itching of her lips (lower more than upper) since more than 6 months. At the time of consultation, her main complaint was dry mouth; she also had some persisting redness and swelling of her lips. The patient had been evaluated by her dentist and ophthalmologist and denied dry eyes or sun sensitivity. She also denied any particular oral habits or use of any devices. Using topical hydrocortisone ointment several times weekly helped with her lip symptoms. Laboratory testing ordered at the time of consultation showed an antinuclear antibody titre of 1:80 and negative Sjogren's syndrome A and B autoantibodies. Patch tests with a modified American Contact Dermatitis Society 80 allergen series plus an extended flavouring and fragrance series showed 1+ reactions to cobalt and triclosan at D4. The cobalt reaction was thought not likely to be relevant, but triclosan proved to be present in her toothpaste. Two weeks after stopping its use, a nearly complete resolution of oral and lip symptoms was reported by the patient (5).

Previous cases of allergic cosmetic dermatitis

There are at least 14 previous case reports and case series of allergic cosmetic dermatitis to triclosan, most of them in older literature; the most recent ones are refs. 3 and 4. For a full literature review of this topic please refer to the Monographs in Contact Allergy, Volume 1, Chapter 2.475, pp. 1294-1299.

Previous cases immediate-type reactions

For a case of immediate-type reactions to triclosan in a toothpaste and moisturizing lotion see ref. 2.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 102/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 54/123,000.

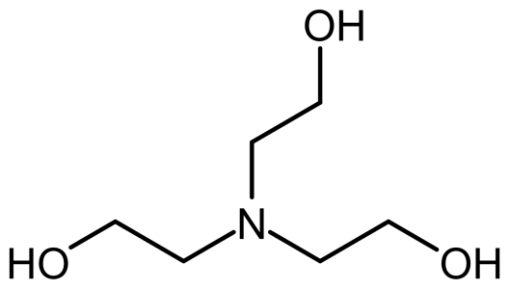
LITERATURE

1 Buhl T, Fuchs T, Geier J. Contact hypersensitivity to triclosan. Ann Allergy Asthma Immunol 2014; 113(1): 119-120. doi: 10.1016/j.anai.2014.04.027.
2 Özkaya E, Bozkurt PK. An unusual case of triclosan-induced immunological contact urticaria. Contact Dermatitis 2013;68(2):121-123. doi: 10.1111/j.1600-0536.2012.02166.x.
3 Robertshaw H, Leppard B. Contact dermatitis to triclosan in toothpaste. Contact Dermatitis 2007;57(6):383-384. doi: 10.1111/j.0105-1873.2005.00771.x.
4 Wong CSM, Beck MH. Allergic contact dermatitis from triclosan in antibacterial handwashes. Contact Dermatitis 2001;45(5):307. doi: 10.1034/j.1600-0536.2001.450517.x.
5 Watsky KL. Allergic contact cheilitis and stomatitis due to triclosan in toothpaste. Dermatitis. 2021;32(1):e15-e16. doi: 10.1097/DER.0000000000000636.

3.73 TRIETHANOLAMINE

IDENTIFICATION

Description/definition : Triethanolamine is an alkanolamine that conforms generally to the structural formula shown below
Classification : Alkanolamines
IUPAC name : 2-[bis(2-Hydroxyethyl)amino]ethanol
Other names : 2,2',2'-Nitrilotriethanol; trolamine
CAS registry number : 102-71-6
EC number : 203-049-8
CIR reports : J Am Coll Toxicol 1983;2:183-235; Int J Toxicol 2013;32(Suppl.1):59-83
Wikipedia : https://en.wikipedia.org/wiki/Triethanolamine
Functions in cosmetics : EU: buffering; emulsifying; masking; surfactant. USA: fragrance ingredients; surfactants – emulsifying agents; pH adjusters
EU cosmetic restrictions : Regulated in Annex III/62 of the Regulation (EC) 2009/1223
Patch testing : 2% pet. (Chemotechnique); 2.5% pet. (SmartPractice); the 2.5% pet. test substance is slightly irritant (1)
Molecular formula : $C_6H_{15}NO_3$



Previous chapter to which this is an update

The literature on contact allergy to triethanolamine from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.477, pp. 1301-1305.

CONTACT ALLERGY (cosmetics)

Case report

A 4-year-old girl, with known severe pustular psoriasis, developed recurring flares of a pustular pruritic eruption, suspected to be caused by an allergic reaction to sunscreens. The rash resembled a severe flare of pustular psoriasis, with monomorphic pustular elements on an erythematous, slightly oedematous background, affecting the face, neck, and trunk. In addition, the patient had a history of a vaccination granuloma. Patch testing with the paediatric baseline series, a photopatch test series, additional allergens according to the ingredient label in sunscreens, and the sunscreens tested 'as is' resulted in multiple positive pustular reactions to triethanolamine, propolis, benzoic acid and aluminium (III) chloride hexahydrate. Triethanolamine and benzoic acid were present in several of the sunscreens used by the patient. The reaction to aluminium was of past relevance (vaccination granuloma) (5).

Previous cases of allergic cosmetic dermatitis

There are at least 17 previous case reports and case series of allergic cosmetic dermatitis to triethanolamine; the most recent ones are refs. 2-4. For a full literature review of this topic please refer to the Monographs in Contact Allergy, Volume 1, Chapter 2.477, pp. 1301-1305.

OTHER PUBLICATIONS [a]

Allergic contact dermatitis from triethanolamine in an ultrasound gel (6).

[a] Literature on contact allergy to triethanolamine that was found in *Contact Dermatitis* or/and *Dermatitis* from September 2017 through March 2025, in which there was no link with cosmetic products.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 2987/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 3388/123,000.

LITERATURE

1 Lessmann H, Uter W, Schnuch A, Geier J. Skin sensitizing properties of the ethanolamines mono-, di-, and triethanolamine. Data analysis of a multicentre surveillance network (IVDK) and review of the literature. Contact Dermatitis. 2009;60(5):243-255. doi: 10.1111/j.1600-0536.2009.01506.x.

2 Chu C-Y, Sun C-C. Allergic contact dermatitis from triethanolamine in a sunscreen. Contact Dermatitis. 2001;44(1):59. doi: 10.1034/j.1600-0536.2001.440107-8.x.

3 Schmutz J-L, Barbaud A, Tréchot P. Allergie de contact à la triéthanolamine contenue dans des gouttes auriculaires et dans un shampooing. Ann Dermatol Venereol. 2007;134(1):105. doi: 10.1016/s0151-9638(07)89009-0.

4 Milanesi N, Berti S, Gola M. Allergic contact dermatitis to triethanolamine in a child. Pediatr Dermatol. 2015;32(3):e112-113. doi: 10.1111/pde.12537.

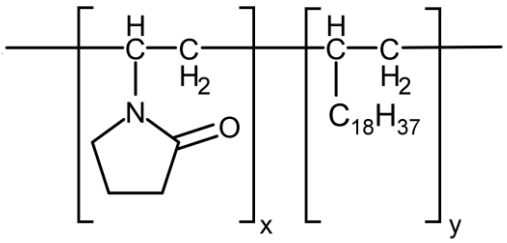
5 Tracz ES, Sommerlund M, Bregnhøj A. Pustular allergic contact dermatitis caused by a sunscreen. Contact Dermatitis. 2020;83(4):328-329. doi: 10.1111/cod.13621.

6 Almeida FT, Caldas R, Pereira T. Allergic contact dermatitis caused by triethanolamine in an ultrasound gel. Contact Dermatitis. 2020;82:64-65. doi: 10.1111/cod.13391.

3.74 VP/EICOSENE COPOLYMER

IDENTIFICATION

Description/definition : VP/eicosene copolymer is a polymer of vinylpyrrolidone and eicosene monomers, that conforms generally to the structural formula shown below
Classification : Synthetic polymers
Other names : PVP/eicosene copolymer; 2-pyrrolidinone, 1-ethenyl-, polymer with 1-eicosene
CAS registry number : 77035-98-4
CIR reports : Int J Toxicol 2024;43(Suppl.4):5-41
Function in cosmetics : EU: binding; film forming; viscosity controlling. USA: binders; dispersing agents – nonsurfactant; film formers; viscosity increasing agents – nonaqueous
Patch testing : 10% pet. (6); 5% pet. (5)



Previous chapter to which this is an update

The literature on contact allergy to VP/eicosene copolymer from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.492, pp. 1328-1329.

CONTACT ALLERGY (cosmetics)

Case reports

A 46-year-old man had recurrent eczematous rashes at body sites where he had applied a particular sunscreen. He also developed a similar rash on his hands and wrists after applying the same sunscreen to his children and when he picked up his children after they had been using the sunscreen. Patch tests with the baseline, medicaments, sunscreen and fragrance test series, as well as with his own sunscreen, tested 'as is', were positive (+) to triclosan on day D2 and D4 only, for which no relevance was found. When tested with the ingredients of the sunscreen, obtained from the manufacturer, a ?+ reaction to vinylpyrrolidone (VP)/eicosene copolymer 5% pet. on D2, which increased to a ++ reaction on D4, was observed (5).

A 25-year-old atopic woman had an 18-month history of dermatitis involving the face, eyelids, and scalp. Her symptoms began as pruritic papules along the hairline and scalp, which progressed to oedematous red scaly plaques involving the eyelids, forehead, and cheeks. The patient suspected that a 'hypoallergenic' moisturizer had exacerbated her symptoms. Patch tests with the NACDG screening series and several supplemental series including corticosteroids, personal care product series, preservatives, emulsifiers, and multiple personal items, were positive to the moisturizer, tested 'as is' (++), to a mascara, tested semi-open 'as is' (+), and to multiple other cosmetic allergens and cosmetic products. The cream and the mascara both contained polyvinylpyrrolidone (PVP)/eicosene copolymer. The manufacturer was uncooperative with providing purified ingredients, so PVP/eicosene copolymer was purchased and diluted in-house to 10% pet. Subsequent patch testing to the three ingredients of the cream (petrolatum, paraffin, PVP/eicosene copolymer) showed ++/+++ reactions to PVP/eicosene copolymer on D2 and D4. Five controls were negative to the cream and the copolymer (6).

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to VP/eicosene copolymer see refs. 1-4.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 201/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 1131/123,000.

LITERATURE

1 Gallo R, Dal Sacco D, Ghigliotti G. Allergic contact dermatitis from VP/eicosene copolymer (Ganex® V-220) in an emollient cream. Contact Dermatitis 2004;50(4):261. doi: 10.1111/j.0105-1873.2004.0301k.x.

2 Le Coz CJ, Lefebre C, Ludmann F, Grosshans E. Polyvinylpyrrolidone (PVP)/eicosene copolymer: an emerging cosmetic allergen. Contact Dermatitis 2000;43(1):61. PMID:10902604.

3 Smith HR, Armstrong K, Wakelin SH, White IR. Contact allergy to PVP/eicosene copolymer. Contact Dermatitis 1999;40(5):283. doi: 10.1111/j.1600-0536.1999.tb06067.x.

4 Le Coz CJ. Le copolymère de polyvinylpyrrolidone et d'eicosene (PVP/eicosene copolymer): un nouvel allergène cosmétique. La lettre du Gerda 2000;17:54.

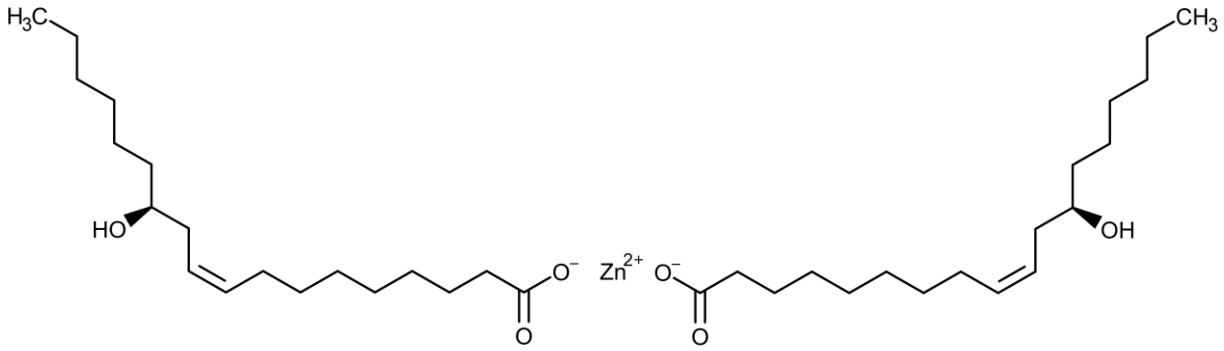
5 Waas RLV, Hill G. Allergic contact dermatitis caused by vinylpyrrolidone/eicosene copolymer in a sunscreen. Contact Dermatitis. 2019;80(1):63. doi: 10.1111/cod.13127.

6 Buonomo M, Warshaw EM. Allergic contact dermatitis due to polyvinylpyrrolidone (PVP)/eicosane copolymer. Contact Dermatitis. 2021;85(4):458-460. doi: 10.1111/cod.13878.

3.75 ZINC RICINOLEATE

IDENTIFICATION

Description/definition : Zinc ricinoleate is the zinc salt of ricinoleic acid, which conforms to the structural formula shown below
Classification : Soaps
IUPAC name : Zinc (*Z*,12*R*)-12-hydroxyoctadec-9-enoate
Other names : Zinc diricinoleate; 12-hydroxy-9-octadecenoic acid, zinc salt
CAS registry number : 13040-19-2
EC number : 235-911-4
CIR reports : Int J Toxicol 2007;26(Suppl.3):31-77; Int J Toxicol 2024;43(Suppl.2):5-69
Patch testing : 75% pet. (1,3); a penetration enhancer may be necessary (1)
Functions in cosmetics : EU: anticaking; deodorant; opacifying. USA: anticaking agents; deodorant agents; opacifying agents
Molecular formula : $C_{36}H_{66}O_6Zn$



Previous chapter to which this is an update

The literature on contact allergy to zinc ricinoleate from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.497, pp. 1338.

CONTACT ALLERGY (cosmetics)

Case report

A 15-year-old atopic boy had developed inflammatory skin lesions affecting the axillae after applying a 'natural' deodorant. The patient also reported the intermittent occurrence of cheilitis since childhood with an exacerbation during the last 3 years. Patch tests with the European baseline series along with additional haptens, a cosmetic series, a fragrance series, zinc ricinoleate 75% and 30% pet. (in-house prepared), castor oil (Ricinus communis seed oil) 'as is', zinc 2.5% pet., hydrogenated castor oil 30% pet. (provided by the cosmetic manufacturer) and the patient's personal products, were positive to the deodorant 'as is' (D2 +, D3 ++), to zinc ricinoleate 75% pet. and 30% pet. (D2 +, D3 +) and to castor oil 'as is' (D2 and D3 ++). Patch testing with zinc ricinoleate 75% pet. in 6 controls was negative. The patient was advised to avoid any further contact with zinc ricinoleate and castor oil and all its derivatives (3).

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to zinc ricinoleate see refs. 1 and 2.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 21/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 236/123,000.

LITERATURE

1 Magerl A, Heiss R, Frosch PJ. Allergic contact dermatitis from zinc ricinoleate in a deodorant and glyceryl ricinoleate in a lipstick. Contact Dermatitis 2001;44(2):119-121. doi: 10.1034/j.1600-0536.2001.44020919.x.
2 Dooms-Goossens A, Dupré K, Borghijs A, Swinnen C, Dooms M, Degreef H. Zinc ricinoleate: sensitizer in deodorants. Contact Dermatitis 1987;16(5):292-294. doi: 10.1111/j.1600-0536.1987.tb01468.x.
3 Samaran Q, Dereure O, Raison-Peyron N. Allergic contact dermatitis to zinc ricinoleate in a 'natural' deodorant. Contact Dermatitis. 2024;91(1):76-78. doi: 10.1111/cod.14550.

CHAPTER 4 MONOGRAPHS OF CHEMICALS AND SUBSTANCES IN COSMETICS THAT HAVE CAUSED IMMEDIATE-TYPE REACTIONS

4.1 INGREDIENTS OF COSMETICS THAT HAVE CAUSED IMMEDIATE-TYPE REACTIONS

In this chapter, non-fragrance chemicals are presented that have caused immediate-type reactions from their presence in cosmetics (September/October 2017 to March 2025). Possible symptoms (single or in combination) of immediate-type reactions (from any product) include localized erythema, itching or tingling, localized urticaria, angioedema, generalized urticaria, respiratory symptoms (wheezing, dyspnoea, asthma, rhinitis, nasal discharge), cardiac problems (hypotension, bradycardia, ventricular fibrillation or cardiac arrest), gastrointestinal symptoms (abdominal pain, diarrhoea, nausea, vomiting) or even anaphylactic shock, which may be life-threatening in some patients and has proven fatal in exceptional cases.

There are several possible pathomechanisms for immediate-type reactions. Some chemicals may induce non-immunological immediate-type reactions (mostly non-immunological contact urticaria), such as benzoic acid, benzyl nicotinate, Capsicum frutescens resin, methyl nicotinate, sodium benzoate, and sorbic acid. As these effects are well-known and dose-dependent, non-immunological contact urticaria from these chemicals in cosmetics is rare nowadays. For some other chemicals, the pathomechanism of producing immediate contact reactions is not clear, for example for ammonium persulfate, which is widely used in hair-bleaching products.

In most published case reports of immediate-type reactions, an immunological mechanism was suspected or claimed on the basis of the rarity of such cases for a particular substance, positive skin tests (open application, scratch, prick, intradermal) and negative controls. True allergic immediate-type reactions to cosmetics with positive skin tests or/and positive basophil activation tests or/and specific IgE antibodies have been caused by, for example, their ingredients casein, equae lac (mare milk), goat milk, hydrolysed wheat protein, and milk protein.

Chemicals that have produced immunological immediate-type reactions from their presence in non-cosmetic products include chlorhexidine (in lubricant gel for urinary catheterization, skin disinfectants, chlorhexidine-coated central venous lines, disinfectants for mucous membranes, mouthwashes, corticosteroid cream) and CI 75470 (carmine) in foods, drinks, and pharmaceuticals (Monographs in Contact Allergy, Volume 1, Chapter 3, pp. 1339-1360).

Table 4.1 (next page) lists the ingredients that have caused immediate-type reactions from their presence in cosmetic products (September/October 2017 – March 2025).

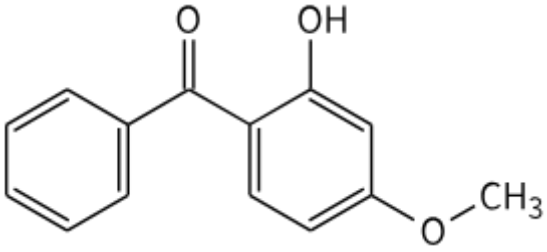
Table 4.1 Chemicals that have caused immediate-type reactions from their presence in cosmetic products

Chemicals that have caused allergic contact dermatitis AND immediate-type reactions. These are presented in Chapters 2 and 3.	
Ammonium persulfate	(Chapter 3.4)
Basic blue 99	(Chapter 3.6)
Caprylyl glycol	(Chapter 2.6)
CI 75470 (Carmine)	(Chapter 3.16)
Luffa cylindrica seed oil	(Chapter 2.22)
Panthenol	(Chapter 3.46)
Phenoxyethanol	(Chapter 3.50)
p-Phenylenediamine	(Chapter 3.52)
Thioctic acid	(Chapter 3.68)
Tocopherol	(Chapter 3.69)
Toluene-2,5-diamine	(Chapter 3.71)
Chemicals that have caused immediate-type reactions only and are presented in this chapter.	
Benzophenone-3	(Chapter 4.2)
Benzophenone-8	(Chapter 4.3)
Benzophenone-10	(Chapter 4.4)
Chamomilla recutita extract	(Chapter 4.5)
1,2-Hexanediol	(Chapter 4.6)
Hydrolysed wheat protein	(Chapter 4.7)
Octocrylene	(Chapter 4.8)
Potassium persulfate	(Chapter 4.9)
Silk powder	(Chapter 4.10)

4.2 BENZOPHENONE-3

IDENTIFICATION

Description/definition : Benzophenone-3 is a benzophenone derivative that conforms to the structural formula shown below
Classification : Benzophenones
IUPAC name : (2-Hydroxy-4-methoxyphenyl)-phenylmethanone
Other names : Oxybenzone; 2-hydroxy-4-methoxybenzophenone; Eusolex® 4360
CAS registry number : 131-57-7
EC number : 205-031-5
CIR reports : J Am Coll Toxicol 1983;2:35-77; Final report 2021
SCCS opinions : SCCP/1201/08; SCCP/1069/06; SCCS/1625/20
Wikipedia : https://en.wikipedia.org/wiki/Oxybenzone (Oxybenzone)
Functions in cosmetics : EU: UV-absorber; UV-filter. USA: light stabilizers; sunscreens
EU cosmetic restrictions : Regulated in Annex VI/4 of the Regulation (EU) 2022/1176
Patch testing : 10.0% pet. (Chemotechnique, SmartPractice)
Molecular formula : $C_{14}H_{12}O_3$



Previous chapter to which this is an update

The literature on contact allergy to benzophenone-3 from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.43, pp. 116-126.

CONTACT ALLERGY

The results of patch testing benzophenone-3 by the members of the North American Contact Dermatitis Group between 2013 and 2020 can be found in ref. 2.

IMMEDIATE-TYPE REACTIONS

A 49-year-old woman had suffered two episodes of a skin eruption and systemic symptoms. The first episode occurred one day after the application of a sunscreen. The patient described an oedematous, painful, pruritic eruption on her arms and neck. She also experienced an increased amount of phlegm, voice changes, and tachycardia, and required hospitalization. There was a similar episode 9 months later. Patch tests were performed with the North American Contact Dermatitis Group (NACDG) routine series, supplemental panels, NACDG 2018 photopatch series, and the personal care products used by the patient. Two hours after application she reported a raspy voice, dry mouth, difficulty in swallowing, and a 'racing heart'. The patient removed her patches and was evaluated in the emergency department, where she received oral prednisone and diphenhydramine. On the next day, the 24-hour patch test reading showed positive reactions to fragrance mix I (+), 2(2-hydroxy-5-methylphenyl) benzotriazole (++), triclosan (+), and urticarial reactions at the benzophenone-3, benzophenone-8 and benzophenone-10 test sites. Two days after patch application, the patient experienced recurrent symptoms of dry mouth, lip swelling, and lip numbness, and she started taking prednisone. At the day 4 final reading, while she was on prednisone, her symptoms had resolved, and the only positive reaction was to propyl gallate (+). The results were interpreted as immediate urticarial reactions to benzophenone-3, benzophenone-8, and benzophenone-

10, and a + delayed reaction to propyl gallate. The patient was instructed to avoid benzophenones and propyl gallate. At her 2-month follow-up appointment, her symptoms had resolved (1).

Comments: There appear to be some curious omissions in this report. Were one or more of the benzophenones present in the sunscreens or cosmetic products used by the patient, i.e. where they the actual cause of the episodes that the patient had experienced? Where there already urticarial lesions when she was seen after 2-3 hours at the emergency department (has nobody looked and taken a photograph? The patient must have informed the physician at the emergency department of her patch tests). Why did the authors use the name 2(2-hydroxy-5-methylphenyl) benzotriazole, a name that nobody recognizes, but which is a synonym for the UV-filter drometrizole? Was drometrizole present in the patient's products? And why were the patch tests (except the benzophenones) not repeated? They may not have been reliable as the patient took (an undefined dose of) prednisone. What was the relevance of the positive patch test to propyl gallate? And can these results indeed be interpreted, as the authors have done, as '*immediate* urticarial reactions to benzophenone-3, benzophenone-8, and benzophenone-10', when symptoms occurred after 2 hours only and urticarial reactions at the test sites were first seen one day after application? Why were these not repeated under medical supervision? The authors further stated that 'At her 2-month follow-up appointment, her symptoms had resolved'. But had they not already resolved at D4?

Previous cases of allergic cosmetic dermatitis and immediate-type reactions

There is extensive literature on case series and case reports of allergic contact dermatitis to benzophenone-3. The UV-absorber has also been tested in many groups of unselected and selected dermatitis patients. There are also many reports of photoallergic contact dermatitis, which is the most frequent side effect of benzophenone-3. In addition, a number of immediate-type reactions and some immediate-type photoreactions have been recorded. Please refer to the Monographs in Contact Allergy, Volume 1, Chapter 2.43, pp. 116-126, for these topics.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 311/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 600/123,000.

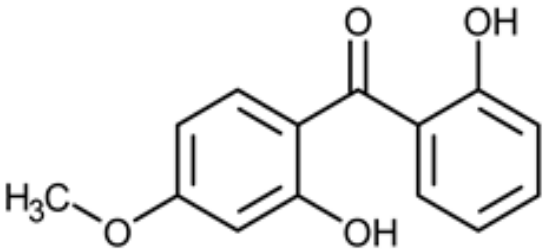
LITERATURE

1 Tawfik ME, Atwater AR. Anaphylactoid reaction to benzophenones, with recurrence during patch testing. Contact Dermatitis 2019;81(4):303-304. doi: 10.1111/cod.13293.
2 Warshaw EM, Xiong M, Belsito DV, Adler BL, Atwater AR, DeKoven JG, et al. Patch testing with benzophenone-3 and -4: The North American Contact Dermatitis Group experience, 2013-2020. Dermatitis. 2023;34(2):105-112. doi: 10.1089/derm.2022.29013.ewa.

4.3 BENZOPHENONE-8

IDENTIFICATION

Description/definition : Benzophenone-8 is a benzophenone derivative that conforms to the structural formula shown below
Classification : Benzophenones
IUPAC name : (2-Hydroxy-4-methoxyphenyl)-(2-hydroxyphenyl)methanone
Other names : 2,2'-Dihydroxy-4-methoxybenzophenone; dioxybenzone
CAS registry number : 131-53-3
EC number : 205-026-8
CIR reports : J Am Coll Toxicol 1983;2(5):79-84; Final report March 12, 2021
Wikipedia : https://en.wikipedia.org/wiki/Dioxybenzone (Dioxybenzone)
Functions in cosmetics : EU: UV-absorber. USA: light stabilizers; sunscreen agents
Patch testing : 2% pet. (1); most benzophenones are tested 10% pet.
Molecular formula : $C_{14}H_{12}O_4$



Previous chapter to which this is an update

The literature on contact allergy to benzophenone-8 from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.45, pp. 132-133.

IMMEDIATE-TYPE REACTIONS

A 49-year-old woman had suffered two episodes of a skin eruption and systemic symptoms. The first episode occurred one day after the application of a sunscreen. The patient described an oedematous, painful, pruritic eruption on her arms and neck. She also experienced an increased amount of phlegm, voice changes, and tachycardia, and required hospitalization. There was a similar episode 9 months later. Patch tests were performed with the North American Contact Dermatitis Group (NACDG) routine series, supplemental panels, NACDG 2018 photopatch series, and the personal care products used by the patient. Two hours after application she reported a raspy voice, dry mouth, difficulty in swallowing, and a 'racing heart'. The patient removed her patches and was evaluated in the emergency department, where she received oral prednisone and diphenhydramine. On the next day, the 24-hour patch test reading showed positive reactions to fragrance mix I (+), 2(2-hydroxy-5-methylphenyl) benzotriazole (++), triclosan (+), and urticarial reactions at the benzophenone-8, benzophenone-3, and benzophenone-10 test sites. Two days after patch application, the patient experienced recurrent symptoms of dry mouth, lip swelling, and lip numbness, and she started taking prednisone. At the day 4 final reading, while she was on prednisone, her symptoms had resolved, and the only positive reaction was to propyl gallate (+). The results were interpreted as immediate urticarial reactions to benzophenone-3, benzophenone-8, and benzophenone-10, and a + delayed reaction to propyl gallate. The patient was instructed to avoid benzophenones and propyl gallate. At her 2-month follow-up appointment, her symptoms had resolved (1).

Comments: There appear to be some curious omissions in this report. Please refer to Chapter 4.2 Benzophenone-3 for comments.

Previous cases of allergic cosmetic dermatitis

For previous cases of allergic cosmetic dermatitis to benzophenone-8 see refs. 2-4.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): unknown/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): not mentioned in the database.

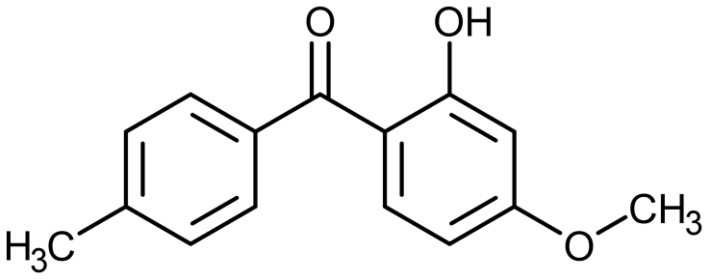
LITERATURE

1 Tawfik ME, Atwater AR. Anaphylactoid reaction to benzophenones, with recurrence during patch testing. Contact Dermatitis 2019;81(4):303-304. doi: 10.1111/cod.13293.
2 Pariser RJ. Contact dermatitis to dioxybenzone. Contact Dermatitis 1977;3(3):172. doi: 10.1111/j.1600-0536.1977.tb03638.x.
3 Thompson G, Maibach H, Epstein J. Allergic contact dermatitis from sunscreen preparations complicating photodermatitis. Arch Dermatol 1977;113(9):1252-1253. PMID: 143242.
4 Adams RM, Maibach HI, Clendenning WE, Fisher AA, Jordan WJ, Kanof N, et al. A five-year study of cosmetic reactions. J Am Acad Dermatol 1985;13(6):1062-1069. doi: 10.1016/s0190-9622(85)70258-7.

4.4 BENZOPHENONE-10

IDENTIFICATION

Description/definition : Benzophenone-10 is a benzophenone derivative that conforms to the structural formula shown below
Classification : Benzophenones
IUPAC name : (2-Hydroxy-4-methoxyphenyl)-(4-methylphenyl)methanone
Other names : 2-Hydroxy-4-methoxy-4'-methylbenzophenone; mexenone
CAS registry number : 1641-17-4
EC number : 216-688-2
CIR reports : Final report March 12, 2021
Wikipedia : https://en.wikipedia.org/wiki/Mexenone (Mexenone)
Functions in cosmetics : EU: UV-absorbers. USA: light stabilizers
Patch testing : 10.0% pet. (Chemotechnique, SmartPractice)
Molecular formula : $C_{15}H_{14}O_3$



Previous chapter to which this is an update

The literature on contact allergy to benzophenone-10 from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.46, pp. 134-137.

IMMEDIATE-TYPE REACTIONS

A 49-year-old woman had suffered two episodes of a skin eruption and systemic symptoms. The first episode occurred one day after the application of a sunscreen. The patient described an oedematous, painful, pruritic eruption on her arms and neck. She also experienced an increased amount of phlegm, voice changes, and tachycardia, and required hospitalization. There was a similar episode 9 months later. Patch tests were performed with the North American Contact Dermatitis Group (NACDG) routine series, supplemental panels, NACDG 2018 photopatch series, and the personal care products used by the patient. Two hours after application she reported a raspy voice, dry mouth, difficulty in swallowing, and a 'racing heart'. The patient removed her patches and was evaluated in the emergency department, where she received oral prednisone and diphenhydramine. On the next day, the 24-hour patch test reading showed positive reactions to fragrance mix I (+), 2(2-hydroxy-5-methylphenyl) benzotriazole (++), triclosan (+), and urticarial reactions at the benzophenone-10, benzophenone-3 and benzophenone-8 test sites. Two days after patch application, the patient experienced recurrent symptoms of dry mouth, lip swelling, and lip numbness, and she started taking prednisone. At the day 4 final reading, while she was on prednisone, her symptoms had resolved, and the only positive reaction was to propyl gallate (+). The results were interpreted as immediate urticarial reactions to benzophenone-3, benzophenone-8, and benzophenone-10, and a + delayed reaction to propyl gallate. The patient was instructed to avoid benzophenones and propyl gallate. At her 2-month follow-up appointment, her symptoms had resolved (1).

Comments: There appear to be some curious omissions in this report. Please refer to Chapter 4.2 Benzophenone-3 for comments.

Previous cases of allergic cosmetic dermatitis and immediate-type reactions

For previous cases of allergic cosmetic dermatitis to benzophenone-10 see refs. 2-5; for cases of photo-contact dermatitis see refs. 6-9; for an immediate-type photoreaction see ref. 10.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): unknown/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): not mentioned in the database/123,000.

LITERATURE

1 Tawfik ME, Atwater AR. Anaphylactoid reaction to benzophenones, with recurrence during patch testing. Contact Dermatitis 2019;81(4):303-304. doi: 10.1111/cod.13293.
2 Millard LG, Barrett PL. Contact allergy from Mexenone masquerading as an exacerbation of light sensitivity. Contact Dermatitis 1980;6(3):222-223. doi: 10.1111/j.1600-0536.1980.tb05610.x.
3 English JSC, White IR, Cronin K. Sensitivity to sunscreens. Contact Dermatitis 1987;17(3):159-162. doi: 10.1111/j.1600-0536.1987.tb02698.x.
4 Goossens A. Cosmetic contact allergens. Cosmetics 2016, 3, 5; doi:10.3390/cosmetics3010005.
5 Cronin E. Contact Dermatitis. Edinburgh: Churchill Livingstone, 1980: 453.
6 Burry JN. Photo allergies from benzophenones and beta carotene in sunscreens. Contact Dermatitis 1980;6(3):211-212. doi: 10.1111/j.1600-0536.1980.tb05600.x.
7 Ang P, Ng SK, Goh CL. Sunscreen allergy in Singapore. Am J Cont Derm 1998;9(1):42-44. PMID: 9471986.
8 Green C, Catterall M, Hawk JLM. Chronic actinic dermatitis and sunscreen allergy. Clin Exp Dermatol 1991;16(1):70-71. doi: 10.1111/j.1365-2230.1991.tb00305.x.
9 Gudmunsen KJ, Murphy M, O'Sullivan D, Powell FC, O'Loughlin S. Polymorphic light eruption with contact and photocontact allergy. Br J Dermatol 1991;124(4):379-382. doi: 10.1111/j.1365-2133.1991.tb00603.x.
10 Bourrain JL, Amblard P, Béani JC. Contact urticaria photoinduced by benzophenones. Contact Dermatitis 2003;48(1):45-46. doi: 10.1034/j.1600-0536.2003.480108_1.x.

4.5 CHAMOMILLA RECUTITA (MATRICARIA) EXTRACT

IDENTIFICATION

Description/definition : Chamomilla recutita extract is the extract of the whole plant of the matricaria, *Chamomilla recutita* (L.), Asteraceae (Asteraceae is the old name for Compositae)
Classification : Botanical products and botanical derivatives
INCI name USA : Chamomilla recutita (matricaria) extract
Other names : Camomille extract; chamomile extract, German; chamomile extract, Hungarian; matricaria extract
CAS registry number : 84082-60-0
EC number : 282-006-5
CIR reports : Final report, January 10, 2014; Int J Toxicol 2018;37(Suppl.3):51-79
Wikipedia : https://en.wikipedia.org/wiki/Chamomile (Chamomile)
Functions in cosmetics : EU: skin conditioning. USA: skin-conditioning agents – miscellaneous
Patch testing : 1.0% pet. (Chemotechnique); also present in the Compositae mix II 2.5% and 5% pet. (Chemotechnique); 1% physiologic saline for immediate open testing (1)

It should be realized that the colloquial plant name 'Chamomile' (sometimes termed camomile) has been used interchangeably for at least three different species: German chamomile (*Chamomilla recutita* (L.) Rauschert), Roman chamomile (*Chamaemelum nobile* (L.) All.; synonym *Anthemis nobilis* L.) and dog fennel (*Anthemis cotula* L.). German and Roman chamomile are both important medicinal plants, but despite their allegedly similar properties, they differ considerably in their chemical composition (2).

Previous chapter to which this is an update

The literature on contact allergy to Chamomilla recutita (matricaria) extract from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.89, pp. 238-243.

IMMEDIATE-TYPE REACTIONS

Case report

An 8-year-old atopic girl had developed an acute rash after applying a wet wipe to her face. Her personal history revealed abdominal pain after ingestion of chamomile tea in two previous episodes. The mother provided a photo showing the itchy erythematous facial rash that appeared within minutes of applying the wet wipe, which disappeared after 30 minutes. Chamomile was found among the ingredients of the wipe. The girl had used the same wipes on a previous occasion with the same skin reaction. Patch tests with the European comprehensive baseline series, plant series and chamomile extract 2% pet. (home preparation) and photopatch tests with the wet wipe 'as is' (2x2 cm), Compositae mix II 2.5% pet., sesquiterpene lactone mix 0.1% pet., and chamomile extract 2% pet. were negative. However, a semi-open test with the wet wipe and chamomile extract 2% pet. showed a positive test reaction to the wet wipe with erythema and mild oedema at 20 minutes (10 controls were negative). Specific IgE for chamomile was 20.8 UI/mL (normal <0.1 UI/mL). A skin prick test with the wipe was positive with an urticarial reaction after 15 minutes (7x5 mm), positive histamine control 8x8 mm, negative saline control 0x0 mm. Contact urticaria caused by the wet wipe was diagnosed, and the suspected culprit was chamomile. Avoidance of cosmetic products and foods/drinks containing chamomile was recommended. Follow-up at 3 months showed no rash or digestive problems (9).
It should be realized that the exact nature of the 'chamomile' was not specified, but looking at the discussion, it most likely was Chamomilla recutita extract.

Previous cases of allergic cosmetic dermatitis and immediate-type reactions

For previous case reports and case series of allergic cosmetic dermatitis to Chamomilla recutita extract see refs. 3-8. There have been several cases of immediate-type reactions to chamomile, especially to chamomile tea. It appears that these represent type-1 allergic reactions to chamomile pollens cross-reacting to other pollens, notably from *Artemisia* and *Ambrosia* species (Monographs in Contact Allergy, Volume 1, Chapter 2.89, pp. 238-243).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 43/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 582/123,000.

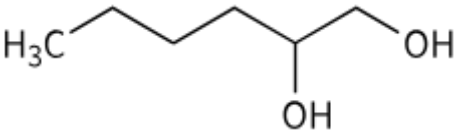
LITERATURE

1 West I, Maibach HI. Contact urticaria syndrome from multiple cosmetic components. Contact Dermatitis 1995;32(2):121. doi: 10.1111/j.1600-0536.1995.tb00770.x.
2 Paulsen E. Contact sensitization from Compositae-containing herbal remedies and cosmetics. Contact Dermatitis 2002;47(4):189-198. doi: 10.1034/j.1600-0536.2002.470401.x.
3 Travassos AR, Claes L, Boey L, Drieghe J, Goossens A. Non-fragrance allergens in specific cosmetic products. Contact Dermatitis 2011;65(5):276-285. doi: 10.1111/j.1600-0536.2011.01968.x.
4 Beetz B, Cramer HJ, Mehlhorn HCh. Zur Häuftigkeit der epidermalen Allergie gegenüber Kamille in kamillenhaltigen Arzneimitteln und Kosmetika. Dermatologische Monatschrift 1971;157(7):505-510. PMID: 5116600
5 Hausen BM. A 6-year experience with Compositae mix. Am J Contact Dermatitis 1996;7(2):94-99. PMID: 8796749.
6 Cusack C, Buckley C. Compositae dermatitis in a herbal medicine enthusiast. Contact Dermatitis 2005;53(2):120-121. doi: 10.1111/j.0105-1873.2005.0650g.x.
7 Rudzki E, Rapiejko P, Rebandel P. Occupational contact dermatitis, with asthma and rhinitis, from camomile in a cosmetician also with contact urticaria from both camomile and lime flowers. Contact Dermatitis 2003;49(3):162. doi: 10.1111/j.0105-1873.2003.0185e.x.
8 Wilkinson SM, Hausen BM, Beck MH. Allergic contact dermatitis from plant extracts in a cosmetic. Contact Dermatitis 1995;33(1):58-59. doi: 10.1111/j.1600-0536.1995.tb00457.x.
9 Navarro-Triviño FJ, Ayén-Rodríguez Á, Ruiz-Villaverde R. Contact urticaria caused by chamomile in a wet wipe. Contact Dermatitis. 2022;86(6):548-549. doi: 10.1111/cod.14067.

4.6 1,2-HEXANEDIOL

IDENTIFICATION

Description/definition : 1,2-Hexanediol is the fatty alcohol that conforms to the structural formula shown below
Classification : Fatty alcohols
IUPAC name : Hexane-1,2-diol
Other names : 1,2-Dihydroxyhexane
CAS registry number : 6920-22-5
EC number : 230-029-6
CIR reviews : Int J Toxicol 2012;31(Suppl.2):147-168
Functions in cosmetics : EU: skin conditioning; solvent. USA: preservatives; skin-conditioning agents – miscellaneous; solvents
Patch testing : Open test and closed test read after 15 minutes with 1,2-hexanediol 2% dissolved in cetyl ethylhexanoate (1); the report is unreliable
Molecular formula : $C_6H_{14}O_2$



GENERAL

1,2-Hexanediol is used frequently in cosmetics for its solvent, preservative, and skin-conditioning properties. It was not included in the 'Monographs in Contact Allergy, Volume 1' book.

IMMEDIATE CONTACT REACTIONS (CONTACT URTICARIA)

Case report

A 31-year-old woman developed an urticarial reaction on her face after using facial moisturizers for 2 months. After the first month, she switched to another moisturizer, and the same urticarial reaction occurred. During her examination, when she applied her moisturizer onto half of her face, wheals appeared within 5 minutes. Patch tests with the Korean standard series on the back, read after 30 and 60 minutes and 48 and 72 hours, were negative. Next, an open test was conducted on her forearm using common substances in moisturizers, distilled water, ceramide, caprylic triglyceride, polyglyceryl-3 methylglucose distearate, glyceryl stearate, stearic acid, squalene, and 1,2-hexanediol dissolved by cetyl ethylhexanoate to a 1% concentration. The results showed a slight erythematous reaction to 1,2-hexanediol in 15 minutes, and all other components tested negative up to 60 minutes. Next, closed chamber testing on the forearm with 1% and 2% 1,2-hexanediol was conducted and the 2% test material produced intense wheals. The patient was instructed to use cosmetic products without 1,2-hexanediol (1).

Comments: This author finds it curious that this report has been accepted for publication. There are several questions that need to be answered:
1 why was cetyl ethylhexanoate, a synthetic ester used as a texture enhancer and emollient in cosmetics, chosen as vehicle for diluting 'common substances in moisturizers'?
2 How were the test substances chosen? Were they even present in the moisturizer or moisturizers that the patient had used? The last sentence 'In summary, this case highlights how 1,2-hexanediol, a popular ingredient in cosmetics, can cause contact urticaria' suggests it was not.
3 Why have the authors not performed control tests with 2% 1,2-hexanediol in cetyl ethylhexanoate in unexposed subjects to exclude that this material has non-immunological contact urticaria-inducing properties?

4 Why was it not mentioned whether avoiding cosmetic products with 1,2-hexanediol solved the problem and no more recurrences were noted?

Also, the pictures shown were far from convincing.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 2681/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 7,202/123,000.

LITERATURE

1 Han HJ, Kang HY. Facial contact urticaria caused by a moisturizer containing 1,2-hexanediol. Dermatitis. 2023;34(6):565-566. doi: 10.1089/derm.2022.0091.

4.7 HYDROLYSED WHEAT PROTEIN

IDENTIFICATION

Description/definition	: Hydrolyzed wheat protein is the hydrolyzate of wheat protein derived by acid, enzyme or other method of hydrolysis. It is composed primarily of amino acids, peptides, and proteins. It may contain impurities consisting chiefly of carbohydrates and lipids along with smaller quantities of miscellaneous organic substances of biological origin
Classification	: Protein derivatives
Other names	: Protein hydrolyzates, wheat germ
CAS registry number	: 94350-06-8; 222400-28-4; 70084-87-6
EC number	: 305-225-0
CIR reports	: Int J Toxicol 2018;37(Suppl.1):55-66
SCCS opinions	: SCCS/1534/14
Wikipedia	: https://en.wikipedia.org/wiki/Wheat_allergy (Wheat allergy)
EU cosmetic restrictions	: Regulated in Annex III/307 of the Regulation (EU) 2017/2228
Functions in cosmetics	: EU: antistatic; hair conditioning; skin conditioning. USA: film formers; hair conditioning agents; skin-conditioning agents - miscellaneous

Previous chapter to which this is an update

The literature on contact allergy to hydrolyzed wheat protein from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.236, pp. 620-624.

CONTACT ALLERGY

Previous cases of allergic cosmetic dermatitis

For previous case reports and case series of allergic cosmetic dermatitis to hydrolyzed wheat protein see refs. 1-3.

IMMEDIATE-TYPE REACTIONS

A 35-year-old female patient with atopic dermatitis developed facial swelling and contact wheals after applying a face mask or a shampoo, both containing hydrolysed wheat protein (HWP). Four months later, swelling of her lips and face, generalized urticaria and diarrhoea arose after eating wheat noodles followed by fast walking. Symptoms recurred after eating noodles and exercise weeks later, but never by exercise alone. In allergy tests, skin prick tests were positive for wheat, the patient's HWP-containing own cosmetics (face mask, shampoo and their ingredient hydrolysed wheat protein provided by the manufacturer), but negative in three controls. Ten minutes after successive challenge with 1. 20 ml ethanol, 2. intake of 64 g gluten and 3. aerobic treadmill exercise, generalized urticaria confirmed wheat-dependent exercise-induced anaphylaxis (WDEIA). Her eczema was of moderate severity (SCORAD 12.5), transepidermal water loss was elevated (24.7), signifying skin barrier dysfunction which probably resulted in percutaneous sensitization of wheat protein from the patient's cosmetic products. The sequence of 1. applying HWP-containing cosmetics, 2. facial contact urticaria/angioedema and 3. WDEIA to wheat after a few weeks or months indicate percutaneous sensitization to HWP with cross-reactivity to normal wheat (4).

A 34-year-old technician working in industrial maintenance for a cosmetic manufacturer developed two immediate hypersensitivity reactions with a 1-year interval 5 minutes after cleaning a tank containing an anti-wrinkle cream, despite wearing a protective suit and gloves. The first reaction was characterized by rhinitis, conjunctivitis, and sneezing, whereas the second episode was more severe, with immediate contact urticaria, conjunctivitis, and dyspnoea. The offending cosmetic product contained 12% of a powder, mainly composed of hydrolysed wheat protein (HWP), which represented 10% of the final

cosmetic product. The results of open tests were negative with the cosmetic product and all of the ingredients provided by the manufacturer, including the HWP powder. However, prick tests gave positive results at 20 minutes (>50% of the positive control response induced by histamine chloride at 10 mg/ml) for the cosmetic product (10% water), the HWP powder (10% water), and wheat extract. Titration of IgE specific for wheat protein fractions showed low amounts of specific IgE for some native wheat proteins, whereas IgEs specific for the cosmetic product, the HWP in the powder and deamidated gluten were strongly detected, confirming the diagnosis of occupational immediate IgE-mediated hypersensitivity to HWP. The patient did not report a history of food reactions to wheat protein between or after the two hypersensitivity episodes. After avoidance of all cosmetics and foods containing HWP and wheat protein, and optimization of the personal protective equipment at work (gloves, mask, goggles, and full protective suit), no further reactions were observed (5).

Previous cases of immediate-type reactions

There is extensive literature on immediate-type reactions to hydrolysed wheat protein with symptoms including (occupational) contact urticaria, rhinitis, asthma, angioedema, generalized urticaria and exercise-induced anaphylaxis. Please refer to the Monographs in Contact Allergy, Volume 1, Chapter 2.236, pp. 620-624 for these topics.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 6/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 1449/123,000.

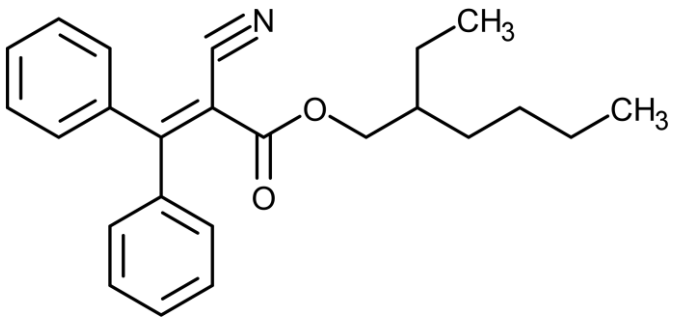
LITERATURE

1 Sanchez-Perez J, Sanz T, Garcia-Diez A. Allergic contact dermatitis from hydrolyzed wheat protein in cosmetic cream. Contact Dermatitis 2000;42(6):360. PMID: 10871108.
2 Hann S, Hughes M, Stone N. Allergic contact dermatitis to hydrolyzed wheat protein in a cosmetic cream. Contact Dermatitis 2007;56(2):119-120. doi: 10.1111/j.1600-0536.2007.00977.x.
3 Bordalo O. Allergic contact dermatitis from hydrolyzed wheat protein. Contact Dermatitis 2004;50: 183-184.
4 Brockow K, Reidenbach K, Kugler C, Biedermann T. Wheat-dependent exercise-induced anaphylaxis caused by percutaneous sensitisation to hydrolysed wheat protein in cosmetics. Contact Dermatitis. 2022;87(3):296-297. doi: 10.1111/cod.14144
5 Delaunay J, Hacard F, Denery-Papini S, Garnier L, Bérard F, Nicolas JF, et al. Occupational immediate contact allergy to hydrolysed wheat protein after cosmetic exposure. Contact Dermatitis. 2018;78(4):291-292. doi: 10.1111/cod.12929.

4.8 OCTOCRYLENE

IDENTIFICATION

Description/definition : Octocrylene is the substituted acrylate that conforms to the structural formula shown below
Classification : Esters
IUPAC name : 2-Ethylhexyl 2-cyano-3,3-diphenylprop-2-enoate
Other names : 2-Cyano-3,3-diphenylacrylic acid 2'-ethylhexyl ester; 2'-ethylhexyl 2-cyano-3-phenylcinnamate; 2-ethylhexyl-2-cyano-3,3-diphenylacrylate
CAS registry number : 6197-30-4
EC number : 228-250-8
Wikipedia : https://en.wikipedia.org/wiki/Octocrylene
SCCS opinions : SCCS/1627/21 Final Opinion
Functions in cosmetics : EU: UV-absorber; UV-filter. USA: light stabilizers; sunscreen agents
EU cosmetic restrictions : Regulated in Annex VI/10 of the Regulation (EC) 2022/1176
Patch testing : 10% pet. (Chemotechnique, SmartPractice). It appears that photopatch testing with the commercial octocrylene test substance may sometimes be false-negative (1)
Molecular formula : $C_{24}H_{27}NO_2$



Previous chapter to which this is an update

The literature on contact allergy to octocrylene from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.315, pp. 876-881.

CONTACT ALLERGY

Previous cases of allergic cosmetic dermatitis

There is abundant literature on allergic contact dermatitis and photodermatitis to octocrylene. For a full literature review of this topic please refer to the Monographs in Contact Allergy, Volume 1, Chapter 2.315, pp 876-881.

IMMEDIATE-TYPE REACTIONS

A 15-year-old healthy non-atopic female patient had for the past 5 years repeatedly developed a generalized urticarial skin reaction within five to 8 hours after localized application of sunscreen products that disappeared within 2 to 3 days. The reaction occurred with different brands of sunscreens. She did not notice any worsening of the complaints after sun exposure, and minimal erythema dose testing showed normal sensitivity to both UVA and UVB. Patch tests and photopatch tests were negative after 20 minutes. At D1, there were + urticarial reactions to octocrylene 10% pet. and 3 of the sunscreens used by the patient and ?+ reactions to 2 other sunscreens. At D3, three of the sunscreens still showed a ?+

reaction, the other two and octocrylene were negative. The reactions were not aggravated by UVA. All 5 sunscreens contained octocrylene. The authors considered this to be a case of delayed-onset contact urticaria (2).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 94/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 1526/123,000.

OTHER PUBLICATIONS [a]

Photopatch testing with octocrylene in Italy 2010-2017: ref. 3.

[a] Literature on contact allergy to octocrylene that was found in *Contact Dermatitis* or/and *Dermatitis* from September 2017 through March 2025, in which there was no direct link with cosmetic products.

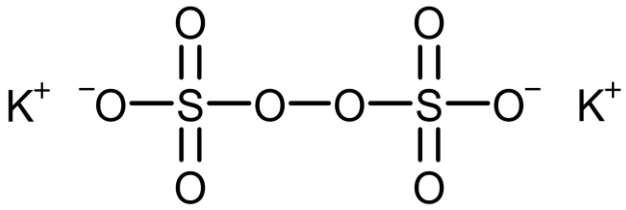
LITERATURE

1 Aerts O, Goossens A, Bervoets A, Lambert J. Almost missed it! Photo-contact allergy to octocrylene in a ketoprofen-sensitized subject. Dermatitis 2016;27(1):33-34. doi: 10.1097/DER.0000000000000156.
2 Haisma MS, Schuttelaar ML. Contact urticaria caused by the ultraviolet absorber octocrylene in sunscreens. Contact Dermatitis. 2017;77(4):254-256. doi: 10.1111/cod.12806.
3 Romita P, Foti C, Hansel K, Stingeni L. Photo-contact allergy to octocrylene: a decreasing trend? Contact Dermatitis. 2018;78(3):224-225. doi: 10.1111/cod.12904.

4.9 POTASSIUM PERSULFATE

IDENTIFICATION

Description/definition : Potassium persulfate is the inorganic salt that conforms to the structural formula shown below
Classification : Inorganic salts
IUPAC name : Dipotassium sulfonatooxy sulfate
Other names : Dipotassium peroxodisulfate
CAS registry number : 7727-21-1
EC number : 231-781-8
CIR reports : Int J Toxicol 2001;20(Suppl.3):7-21; Int J Toxicol 2022;41(Suppl.3):5-21
Wikipedia : https://en.wikipedia.org/wiki/Potassium_persulfate
Functions in cosmetics : EU: oxidising. USA: oxidizing agents
Patch testing : 2.5% pet.
Molecular formula : $K_2O_8S_2$



Previous chapter to which this is an update

The literature on contact allergy to potassium persulfate from cosmetic and non-cosmetic sources, photosensitivity, immediate-type reactions, other non-eczematous contact reactions, systemic side effects, and other relevant information up to September 2017, has been reviewed in Monographs in Contact Allergy, Volume 1. Non-fragrance Allergens in Cosmetics, Chapter 2.380, pp. 1035-1036.

IMMEDIATE-TYPE REACTIONS

A 46-year-old woman with unknown allergies to drugs or foods had been dying her hair for more than 20 years every 2-3 months. She had used the same brand of dye in the last 3 years. Her hair was bleached before washing. The last time when the dye was applied, the patient after 5 minutes began to experience intense itching on her palms, soles, ears, and external genitalia. The dyeing was stopped and her hair was washed immediately, but the itching did not stop. At the emergency centre, the patient manifested cutaneous erythema and acute generalized urticaria. After 2 months, the patient had a positive skin prick test (papule 13.7 mm) with the dye that contained a mix of ammonium and potassium persulfate diluted 20% in water and a positive rub test with 'the persulfate powder'. Skin prick tests with aeroallergens and foods were negative. Patch tests (TRUE Test) were negative at 48- and 96-hour readings, but persulfates themselves were not patch tested. Four controls were negative to the rub test and skin prick test. The patient was diagnosed with acute allergic contact urticaria to persulfates (3).

Comment: This is an unreliable or at least an unclear article. It is uncertain whether the prick and rub tests were done with a mixture of ammonium and potassium persulfate, or that the tests were performed with the dye that contained the mix. In the latter case, the diagnosis of 'Acute contact urticaria to persulfate salts ….' could not reliably be made.

Previous cases of allergic cosmetic dermatitis and immediate-type reactions

For previous case reports and case series of allergic cosmetic dermatitis to potassium persulfate see ref. 1. For immediate-type reactions see ref. 2.

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 43/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 34/123,000.

LITERATURE

1 Cronin E. Contact Dermatitis. Edinburgh: Churchill Livingstone, 1980:128.
2 Estrada Rodríguez JL, Gozalo Reques F, Cechini Fernandez C, Rodríguez Prieto MA. Contact urticaria due to potassium persulfate. Contact Dermatitis 2001;45(3):177. doi: 10.1034/j.1600-0536.2001.045003177.x.
3 Gratacós Gómez AR, González Jimenez OM, Joyanes Romo JB, Palacios Cañas A, Garcia Rodriguez R, Gómez Torrijos E. Acute contact urticaria to persulfate salts diagnosed with positive skin prick tests. Contact Dermatitis. 2021;85(2):239-240. doi: 10.1111/cod.13817.

4.10 SILK POWDER

IDENTIFICATION

Description/definition : Silk powder is finely pulverized silk
Classification : Proteins
CAS registry number : 9009-99-8
EC number : Not available
CIR reviews : Int J Toxicol 2020;38(Suppl.3):127-144
Functions in cosmetics : EU: bulking; skin conditioning. USA: bulking agents; skin-conditioning agents – miscellaneous; slip modifiers
Patch testing : Prick-to-prick tests with silk powder

GENERAL

Silk is used to improve texture, powder base, and surface treatment in make-up, skin care, cosmetic, body care, cleansing, and nail products (1).

IMMEDIATE CONTACT REACTIONS

Case report

A 26-year-old woman developed erythema and wheals on her face both after using a facial cleansing powder and a face powder, which improved within 3-4 hours. She suffered from pollinosis and experienced oral discomfort when eating peaches and kiwi fruits, but had no history of atopic dermatitis. Prick-to-prick tests with the 2 powders, tested 'as is', moistened with a drop of saline, were positive, each causing wheals of 6 × 3 mm (histamine 6×6 mm; negative control 0×0 mm). Next, prick-to-prick and scratch closed tests were performed on the single ingredients of both powders. In the cleansing powder, the prick test to silk powder was positive, causing a wheal of 6×7 mm (histamine 4×4 mm; negative control 1×1 mm). Of the ingredients of the other powder, the prick-to-prick test was positive for the mixture of silk-lauroyl lysine, causing a wheal of 4 mm (histamine 3 mm; negative control 0 mm). All other components in both powders tested negative. Thus, patient was diagnosed with facial contact urticaria caused by a facial cleansing powder (1). (apparently not the face powder, as silk had been tested in combination with lauroyl lysine).

Presence in cosmetic products

FDA's Voluntary Cosmetic Registration Program (March 2022): 96/35,000.
EWG's Skin Deep Cosmetics Database (February 2025): 260/123,000.

LITERATURE

1 Yasuda R, Nagai A, Saito K, Sugiura K. Facial contact urticaria caused by a facial cleanser and cosmetics. Contact Dermatitis. 2021;85(1):106-107. doi: 10.1111/cod.13798.

INDEX

Chemicals and side effects can be easily located in the **CONTENTS** and in chapters 2.1 and 3.1