cosmetics

MDPI

Article

Cosmetic Contact Allergens

An Goossens

Department of Dermatology, University Hospitals K.U. Leuven, Kapucijnenvoer 33, B-3000 Leuven, Belgium; Tel.: +32-16-33-78-70; Fax: +32-16-33-78-72; an.goossens@uzleuven.be

Academic Editors: Emanuela Corsini and David Basketter
Received: 28 December 2015; Accepted: 15 February 2016; Published: 18 February 2016

Abstract: This article presents trends in the frequency of cosmetics as causal factors of allergic contact dermatitis during a 26-year period in 14,911 patients patch-tested between 1990 and 2014, and discusses the cosmetic allergens identified during the last six years (2010–2015) in 603 patients out of 3105 tested. The data were retrieved from, and evaluated with, a patient database developed in-house. The results show the increasing importance of cosmetic allergies, up to 25% of the patients tested during the last five-year period. As expected, fragrance materials, preservatives, and hair dyes were the most frequent culprits, but a great variety of other allergenic ingredients were involved as well. This underlines the need of additional and extensive patch testing with the patient's products used and their ingredients.

Keywords: allergens; allergic contact dermatitis; cosmetics; fragrances; preservatives; ingredients

1. Introduction

Allergic contact dermatitis is a common adverse reaction caused by cosmetics. We report here on trends in the occurrence of contact allergy to cosmetics during a 25-year period, and the cosmetic allergens detected in patients tested during the last six years (2010–2015).

2. Material and Methods

The data were retrieved from, and evaluated with, a patient database developed in-house in our Contact Allergy Unit of the University Hospitals of Leuven. This database contains patient information and results of all contact allergy investigations for patients with suspicion of allergic contact dermatitis, or with other diseases, such as irritant dermatitis or other forms of eczema for which an allergenic cause needed to be excluded.

During the 25-year period from January 1990 until December 2014, 14,911 patients presenting with an eczematous dermatitis were patch-tested with a modified European baseline series and those with a presumed cosmetic cause were also tested with a cosmetic series, or in case of a presumed photo-induced reaction, with a photo-patch test series. Most, if not all, subjects were also tested (or photo-patch tested) with the products to which they had been exposed and, whenever possible, also their ingredients. Formerly, the patch-test chambers applied on the upper back of the patients were Vander Bend® (Brielle, The Netherlands) fixed on Micropore® (3M Health Care, Borken, Germany), later on IQ Ultra® patch test chambers (Chemotechnique Diagnostics, Vellinge, Sweden), covered with Mefix® (Mölnlycke, Göteborg, Sweden). Following occlusion for two days, readings were performed at Day (D) 2 and D4, sometimes also at D7, according to the recently published guidelines from the European Society of Contact Dermatitis (ESCD) [1]. A +, ++, or +++ reaction at either reading was recorded as a positive patch test reaction; an irritant, doubtful, or negative response was recorded as a negative result. Some patients also received prick tests with the cosmetic products and the ingredients, in order to diagnose immediate contact urticarial reactions.

Concerning the cosmetic allergens identified, we will consider here the latest period, *i.e.*, between January 2010 and November 2015. For each test substance, the proportion of positive patch-test results over the total number of patch tests and the percentages (%) were calculated.

3. Results and Discussion

Among the most important sensitization sources in the total patient population tested (n = 14,911) at our department since 1990, "textile" and accessories (jewelry, shoes, gloves) were the main culprits of allergic contact dermatitis (25.9%), followed by cosmetics (19.4%) and pharmaceutical products (17.4%) (data not shown here).

3.1. Trends in Frequency

Table 1 shows trends in frequency over five-year periods of cosmetic dermatitis in patients tested between 1990 and 2014 (n = 14,911).

Table 1. Trends in frequency over five-year periods of cosmetic dermatitis in patients tested between 1990 and 2014 (n = 14,911).

Causal Factor	Total	1990–1994	1995–1999	2000–2004	2005–2009	2010–2014
	(n = 14,911)	(n = 3,228)	(n = 3,368)	(n = 3,177)	(n = 2,638)	(n = 2,559)
Cosmetics	2,886 (19.4%)	499 (15.5%)	562 (16.7%)	608 (19.5%)	576 (21.8%)	641 (25.1%)

Interestingly, contact allergy to cosmetic dermatitis has recently become increasingly important over the years, *i.e.*, from 19.4% between 1990 and 1994 to 25.1% between 2010 and 2014 (Table 1) compared to topical pharmaceutical products that are applied on diseased skin (results not shown here). Several factors may account for this: mandatory cosmetic labeling and consequently better identification of the allergenic culprits, growing cosmetic industry, the influence of fashion trends, and, since 2010 [2], the impact of the preservatives methylchloroisothiazolinone/methylisothiazolinone and, particularly, methylisothiazolinone as cosmetic allergens [2]; moreover, our specific interest in cosmetic dermatitis may also play a role.

3.2. The Cosmetic Allergens

From 2010 till November 2015, 603 patients (115 men or 19%; 488 women or 81%) among 3105 tested (996 men or 32%; 2109 women or 68%), the youngest being 2 and the oldest 90 years old, suffered from cosmetic dermatitis (including other causal factors, such as textiles and accessories, *i.e.*, clothing, shoes, jewelry, *etc.*, but excluding topical pharmaceutical products because of potential common ingredients, such as vehicle components (e.g., lanolin, propylene glycol), preservatives (e.g., benzoic or sorbic acid), *etc.* As expected, fragrance materials, preservatives, and hair dyes were the most frequent culprits, but a great variety of other cosmetic ingredients were involved, as well. Table 2 lists the patch test results for the cosmetic products the patients brought with, and the individual allergens identified with the number of positive reactions/number of subjects tested and the percentages. Only the allergens encountered in this patient population will be discussed in detail.

Table 2. Cosmetic allergens identified during the period 2010–2015 among 603 patients suffering from cosmetic dermatitis (iatrogenic dermatitis excluded).

# Positive Tests	# Tested	%	Allergens
158	600	26.33	Fragrance-mix I
134	465	28.82	Linalool Hydroperoxides
128	598	21.4	*p*-Phenylene diamine
117	305	38.36	Cosmetic product

Table 2. *Cont.*

# Positive Tests	# Tested	%	Allergens
103	566	18.2	Methylisothiazolinone 500 ppm
92	465	19.78	Limonene Hydroperoxides
82	599	13.69	Fragrance-mix II
76	308	24.68	Methylisothiazolinone 2000 ppm
71	598	11.87	*Myroxylon Pereirae* resin
69	597	11.56	Methylchloro- and methylisothiazolinone 100 ppm
55	134	41.04	Toluene-2,5-diamine
49	252	19.44	Methylchloro- and methylisothiazolinone 200 ppm
48	172	27.91	*Evernia prunastri* (Oak moss)
44	598	7.36	Hydroxyisohexyl-3-cyclohexene carboxaldehyde
30	172	17.44	Iso-eugenol
29	596	4.87	Methyldibromo glutaronitrile (in Euxyl K 400®)
26	544	4.78	Formaldehyde 2%
25	172	14.53	Cinnamyl alcohol
23	597	3.85	Colophonium
23	597	3.85	Formaldehyde
23	171	13.45	Cinnamal
23	128	17.97	*p*-Aminophenol
19	93	20.43	Ammonium persulfate
18	596	3.02	Quaternium 15
17	340	5	Sodium pyrosulfite
16	381	4.2	Imidazolidinyl urea
16	117	13.68	*m*-Aminophenol
15	31	48.39	Deodorant
14	597	2.35	Wool alcohols
14	596	2.35	Amerchol L 101®
14	82	17.07	Coco-glucoside
13	365	3.56	Diazolidinyl urea
13	173	7.51	Hydroxycitronellal
13	66	19.7	Hydroxyethyl methylacrylate
12	172	6.98	Eugenol
11	362	3.04	2-Bromo-2-nitropropane-1,3-diol
11	68	16.18	Perfume
11	129	8.53	Farnesol
11	44	25	Ethyleneglycol dimethacrylate
11	245	4.49	Decyl gluco side
10	171	5.85	Geraniol
10	105	9.52	*o*-Nitro-*p*-phenylene diamine
9	87	10.34	Citral
8	345	2.32	Lauryl glucoside
7	28	25	Nail varnish
7	94	7.45	Hexyl cinnamal
6	279	2.15	Benzoic acid
6	183	3.28	Hydantoine
6	551	1.09	Compositae mix
5	171	2.92	Amyl cinnamal
5	50	10	Benzophenone-3
5	87	5.75	Citronellol
4	386	1.04	Cocamidopropyl betaine
4	117	3.42	Hydrochinon
4	145	2.76	Ethylhexylglycerin
3	147	2.04	Triclosan
3	192	1.56	Propyl gallate
3	596	0.5	Tosylamide/formaldehyde resin
3	84	3.57	Pyrogallol
3	290	1.03	Chlorhexidine
3	124	2.42	Benzyl salicylate
3	47	6.38	Methyl methacrylate
3	10	30	Propolis cera

Table 2. *Cont.*

# Positive Tests	# Tested	%	Allergens
3	311	0.96	Panthenol
3	4	75	Hydroxypropyl methacrylate
3	34	8.82	Benzophenone-10 (Mexenone)
3	87	3.45	Coumarin
3	3	100	C30–C38 Olefin/isopropyl maleate/MA copolymer
2	598	0.33	Propylene glycol
2	146	1.37	Potassium sorbate
2	151	1.32	Cocamide diethanolamine
2	64	3.13	Ethylhexyl methoxycinnamate
2	15	13.33	Lipstick
2	40	5	C12–15 alkylbenzoate
2	89	2.25	Hydroxy-ethylacrylate
2	52	3.85	Bisabolol
2	133	1.5	Butylene glycol
2	32	6.25	Isoamyl *p*-methoxycinnamate
2	247	0.81	Iodopropynylbutyl carbamate
2	60	3.33	Octocrylene
2	47	4.26	Pentylene glycol
2	17	11.76	*Melaleuca alternifolia* (Tea tree oil)
2	36	5.56	Cetearyl glucoside
2	11	18.18	Tetrahydroxypropyl ethylenediamine
2	6	33.33	*Magnolia grandiflora* bark extract
1	275	0.36	Cetrimide
1	147	0.68	Benzylalcohol
1	597	0.17	Parabens
1	97	1.03	Chloracetamide
1	278	0.36	Sorbic acid
1	159	0.63	Tocopherol acetate
1	272	0.37	Ethylenediaminetetraacetic acid (EDTA)
1	410	0.24	Cetyl alcohol
1	32	3.13	*Lavandula Angustifolia* (Lavender) oil
1	88	1.14	Glyceryl monothioglycolate
1	1	100	*Avena sativa* (Oat meal) extract *
1	32	3.13	Methylbenzylidene camphor
1	38	2.63	Benzalkonium chloride
1	27	3.7	*Ricinus communis* seed (Castor) oil
1	7	14.29	Triethyleneglycol dimetacrylate
1	121	0.83	Limonene
1	67	1.49	Benzyl benzoate
1	1	100	Bromonitrodioxane
1	79	1.27	Chlorphenesin
1	22	4.55	*Eucalyptus Globulus* Leaf (Eucalyptus) oil
1	2	50	Methyl nicotinate
1	5	20	*Mentha Viridis* Leaf (Spearmint) oil
1	56	1.79	Benzophenone-4 (Sulisobenzone)
1	40	2.5	Urethane dimethacrylate
1	1	100	Cyanoacrylate
1	3	33.33	Sodium omadine
1	48	2.08	Octyl salicylate
1	2	50	Hexandiol diacrylate
1	2	50	Tripropyleneglycol diacrylate
1	70	1.43	*Butyrospermum Parkii* (Shea) butter
1	2	50	Pentaerythritol triacrylate
1	14	7.14	*Evernia furfuracea* (Tree moss)
1	9	11.11	Glyceryl rosinate
1	7	14.29	Arachidyl glucoside
1	109	0.92	Butylfenyl methylpropional
1	15	6.67	Methyl 2-octynoate
1	37	2.7	Mascara (semi-open)
1	20	5	Diaminophenoxyethanol guanidine-hydrochloride (G-HCl)

Table 2. *Cont.*

# Positive Tests	# Tested	%	Allergens
1	6	16.67	Aminocresol
1	6	16.67	Bis(hydroxyethyl)-*p*-phenylenediamine
1	17	5.88	Cetearyl ethylhexanoate
1	12	8.33	Majantol
1	1	100	Phytonadione epoxide
1	6	16.67	Ascorbyl tetraisopalmitate
1	80	1.25	Dimethylcyclohexene carboxaldehyde
1	1	100	Basic blue 99 *
1	1	100	Basic brown 17 *
1	44	2.27	Polyhexamethylene biguanide *

* Prick testing.

3.2.1. Fragrance Components

Fragrance components are frequent causes of cosmetic dermatitis, most often due to toilet waters, after-shave lotions, and deodorants, although fragrance-containing skin-care products may also be involved. The results of patch testing with the individual fragrance ingredients of the Fragrance mix I (amyl cinnamal, cinnamal, cinnamyl alcohol, hydroxycitronellal, eugenol, isoeugenol, geraniol, and *Evernia prunastri* or oakmoss extract), and II (hydroxyisohexyl 3-cyclohexene carboxaldehyde, farnesol, citral, citronellol, coumarin, and alfa-hexyl cinnamal), as well as hydroxyisohexyl 3-cyclohexene carboxaldehyde separately in a higher (5%) concentration than in the mix (2.5%), together with trends over the years, have been extensively reported previously [3]. Additionally, their relation with other fragrance-allergy screening agents, *i.e.*, *Myroxylon pereirae* (balsam of Peru) and colophonium has been described. Recently, we also routinely tested with hydroperoxides of limonene and linalool, terpene compounds that act as prehaptens, which upon air exposure give rise to sensitizing air-autoxidation products. They are widely-used fragrance materials in consumer (cosmetic, household, and industrial) products and recognized as important sensitizers [4,5].

3.2.2. Preservatives

Shifts in frequency of positive patch-test reactions have occurred over the years [6], but more recently methylisothiazolinone (MI), in particular, both in leave-on and also rinse-off products [2,7], has created a worldwide epidemic of contact-allergic reactions. It is a weaker sensitizer than the chlorinated derivative methylchloroisothiazolinone (MCI), but also less efficient as a preservative, hence larger use concentrations (up to 100 ppm) than the mixture MCI/MI (max. 15 ppm) are admitted. Initially, most cases were due to the use of wet wipes (moist toilet paper) for intimate hygiene (also for babies—causing hand dermatitis in their parents) but, later on, facial skin-care products, body lotions, deodorants, and even rinse-off products, such as shampoos and liquid soaps turned out to be important sensitization sources (e.g., [7]). MI is sometimes responsible for severe skin lesions and atypical clinical symptoms, leading to a delay in the correct diagnosis (e.g., [8]), and respiratory problems may occur as well. Moreover, regarding the frequency of positive reactions observed, the studies carried out have even underestimated the true MI-epidemic given that patch tests have not always been conducted with the most optimal test concentrations [9,10]. Although the cosmetic industry advised its members to phase out the use of MI in leave-on products, there are still such products on the market and regulations are urgently needed by the European authorities.

The incidence of positive reactions to formaldehyde—also a cause of contact-allergic reactions in cosmetics such as nail hardeners and hair-straightening products [11,12]—and its releasers has been slightly increasing as well [6], the latter also sensitizers by their own, most probably via degradation products [13,14]. A more recently introduced preservative is iodopropynyl butylcarbamate, the presence in cosmetics of which has been discussed, not because of its potentially allergenic properties,

but because of its iodine content; hence, it is not to be used in leave-on cosmetics in children under the age of 3.

Methyldibromoglutaronitrile—that was used in a mixture with phenoxyethanol (an exceptional cosmetic allergen), better known as Euxyl K400®—became such an important cosmetic allergen that the EU no longer permitted its further use in cosmetic products (March 2007). The few positive reactions observed have no present relevance. As seen in Table 2, triclosan does not seem to be much used anymore, and benzoic acid, sorbic acid and sorbates, and parabens are rare causes of cosmetic dermatitis; when allergy does occur, the sensitization source is most often via topical pharmaceutical products. Moreover, the withdrawal of parabens from cosmetics is merely a consumer, publicity, and political issue. Chlorphenesin cross-reacts with mefenesin, a rubefacient in topical pharmaceutical products, being the primary sensitizer in most cases. Recently, polyhexamethylene biguanide (Synonyms: polyaminopropyl biguanide, polyhexanide), a widely used hospital disinfectant and antiseptic, has shown to be another potential cosmetic allergen in wet wipes (and facial make-up cleansers), inducing both delayed-type eczematous [15], but also severe immediate-type reactions, expressed as the contact urticaria syndrome [16], as we described [17].

3.2.3. Hair-Dyes and Bleaching Agents

Regarding contact dermatitis from hair dyes, allergens other than para-phenylene diamine (PPD) are also concerned (e.g., [18]), both in hairdressers and clients, and diamino-2,5-toluene, more in use today, most often cross-reacts with it. PPD is even used for dying eyelashes and causes severe contact dermatitis and blepharoconjunctivitis [19,20]; this practice should be forbidden by EU legislation. In addition to severe cases of contact dermatitis, severe immediate-type reactions (the contact-urticaria syndrome) may also occur, not only to PPD [21], but also to direct hair dyes, such as basic blue 99 and basic brown 17 [22]. This is also the case with hair-bleaching agents based on persulfates [23] that, besides delayed-type allergens, have been recognized for several decades as causes of immediate-type reactions, such as asthma in hairdressers, in particular.

3.2.4. Nail Cosmetics

Allergic contact dermatitis from acrylates and (meth)acrylates have, during the last decade, become important causes of reactions to nail gel formulations, in particular, rarely in clients but most often in manicurists [24]. Hydroxyethyl methacrylate and ethyleneglycol dimethacrylate are the main culprits, but other derivatives may be responsible as well. These formulations not only cause fingertip eczema, but also often lesions on the face (eyelids) via airborne contact with the volatile acrylic monomers.

3.2.5. Sun Protectors

Sunscreen agents are increasingly used, not only in sun-protecting products but also in other cosmetics including moisturizers. They are also used to prevent degradation by sunlight exposure, hence a potential allergen in all product types including fragrances and hair-care products, such as benzophenone-4 (sulisobenzone) [25]. They may be responsible for allergic and photo-allergic reactions, and also immediate-type reactions, e.g., benzophenone-3 (see [26] for a review). Contact- and photo-contact allergy to octocrylene that also stabilizes other sunscreens, such as butyl methoxydibenzoylmethane, has been recently extensively discussed in the literature [27]. Its relation to simultaneous photosensitivity with ketoprofen, a non-steroidal anti-inflammatory drug used to treat muscle pain, needs to be further elucidated, since the chemical relationship, as in the case for benzophenones that clearly cross-react with ketoprofen [28], is not obvious.

3.2.6. Antioxidants and Chelating Agents

Although the number of contact-allergic reactions to propyl gallate (and other gallates, also used as food additives) was reported to have increased over the years [29], which was attributed to an

increased use in cosmetics concomitant to a reduced use in food (with oral tolerance reactions less likely to develop), we only observed few reactions to it. Sulfites and bisulfites often cause contact allergy and have shown to be relevant allergens in topical pharmaceutical products, but also in cosmetic creams and hair dyes [30]. Some antioxidants are used more specifically in sunscreen and anti-aging products; examples are vitamin C derivatives, such as ascorbyl tetraisopalmitate [31,32]. Furthermore, we observed six cases of contact allergy to tetrahydroxypropyl ethylenediamine, a chelating agent, due to its presence in skin care products; no cross-reactions to ethylenediamine or edetate (EDTA) were observed [33].

3.2.7. Emulsifiers, Emollients, Excipients, Surfactants, and Humectants

In examples of the most recent sensitizing emollients (and skin conditioning agents) we also identified fatty alcohol esters that are not known to be reactive chemicals and, hence, are not notable contact allergens (but are sometimes used in rather high concentrations), *i.e.*, cetearyl isononanoate [34], a compound closely related to other isononanoates [35], neopentanoates and hexanoates, within which cross-reactions may occur. Additionally C12–15 alkyl benzoate may be an occasional sensitizer [36]. Contact allergy to ethylhexylglycerin (Synonym: octoxyglycerin), another widely-used ingredient that also has antimicrobial properties (hence its use in preservative-free cosmetics), has been reported a few times in the literature, the most recent case concerning its presence in sunscreens [37]. Cocamidopropyl betaine, an amphotheric surfactant, has caused sensitization due to impurities in it; however, it was also a cause of irritant patch-test reactions [38]. We recently identified Cocamide Diethanolamine (DEA), a non-ionic surfactant as an occupational allergen in hairdressers [39]. Alkyl glucosides, *i.e.*, condensation products of fatty alcohols with glucose, such as coco- and lauryl-glucosides that are often used as mild surfactants and cleansing agents, but also as emulsifiers, particularly cetearyl- and decyl-glucoside, are known allergens, the latter being a hidden source in sunscreens (see [40] for a review). Humectants such as butylene-, pentylene-, and hexylene-glycol, *i.e.*, aliphatic alcohols with similar uses (solvent, humectant, and antibacterial) to propylene glycol that are considered to be more irritant and allergenic, have become very popular in recent years. They sometimes cross-react with each other and may also cause immediate-type reactions [41]. Finally, copolymers are also potential cosmetic allergens (see [42] for a review), although the allergenic culprits (degradation products?) in them have not been identified. The latest reports concerned C30–38 olefin/isopropyl maleate/MA copolymer as an allergen in a sunscreen product [43] and also a moisturizer [44].

3.2.8. Natural Ingredients

Plant extracts or other natural substances have become very popular in recent years, many of which have induced contact dermatitis problems [45,46]. A few examples are glycyrrhetinic acid and castor oil [47], *Magnolia grandiflora* bark extract [48], *Melaleuca altenifolia* or tea tree oil, also containing (oxidized) terpenes [49], propolis, which often cross-reacts with *Myroxylon pereirae* [50], and bisabolol, a component of *Compositae* plants [51]. Moreover, vitamins and their derivatives are potential allergens as well, e.g., panthenol, a vitamin B derivative [52] and also Vitamine K oxide (phytonadione epoxide) [53].

There are, however, several problems involved regarding the allergenic behavior of natural products [54]: these are complex mixtures of many chemical ingredients, the exact nature of which is, in most cases, not known; their chemical nature and, hence, their allergenic potency, may vary from batch to batch according to their origin, which also influences patch testing since standardization is not possible. Moreover, there is the role of autoxidation (prehaptens), skin penetration, and/or skin metabolism (prohaptens). Multiple positive reactions to different natural products may be observed in such patients; for example, those reacting to plant species from the *Compositae* or *Asteraceae* family (tested as *Compositae*-mix) are frequently positive to fragrance ingredients and also to colophonium [55], which is caused by the common presence of air-oxidized terpene compounds. This broadens, of course, the spectrum of sensitization sources to which the allergic subject is being exposed. Moreover, cosmetic

labelling of plant products leads to confusion, not only because their INCI names are in Latin and, hence, not easily understandable by most consumers, but sometimes they are used because of other properties than being fragrances, and as such even in "non-scented" products [56].

Nowadays, skin-care products, especially in those intended to treat dry skin in atopic subjects (often children) often contain potentially sensitizing protein-containing plant extracts, and hydrolyzed proteins in particular, which may, besides delayed-type reactions, also cause IgE-mediated contact urticaria. Examples are *Avena sativa* (oat meal) extract [57] and hydrolyzed wheat proteins. Recently, a three-year old atopic boy was described who had probably been sensitized to hydrolyzed wheat protein contained in a moisturizer via maternal skin contact (by proxy) [58]. With regard to percutaneous sensitization, high molecular weight wheat hydrolysates seem to be more allergenic than the lower ones [59]. The use of protein-containing cosmetic ingredients has, however, given rise to controversies since subjects may get sensitized through topical preparations and, subsequently, develop food allergies [57,60].

4. Conclusions

Cosmetics as causes of allergic reactions are increasingly being observed, recently up to 25% of the patients investigated in our contact allergy unit. Many different allergens are involved; hence the need of additional patch testing with the patient's products used and the ingredients.

Conflicts of Interest: The author declares no conflict of interest.

References

1. Johansen, J.D.; Aalto-Korte, K.; Agner, T.; Andersen, K.E.; Bircher, A.; Bruze, M.; Cannavó, A.; Giménez-Arnau, A.; Gonçalo, M.; Goossens, A.; *et al*. European Society of Contact Dermatitis guideline for diagnostic patch testing—Recommendations on best practice. *Contact Dermat.* **2015**, *73*, 195–221. [CrossRef] [PubMed]
2. Gonçalo, M.; Goossens, A. Whilst Rome Burns: The Epidemic of Contact Allergy to Methylisothiazolinone. *Contact Dermat.* **2013**, *68*, 257–258. [CrossRef] [PubMed]
3. Nardelli, A.; Carbonez, A.; Drieghe, J.; Goossens, A. Results of patch testing with fragrance mix 1, fragrance mix 2 and their ingredients and Myroxylon pereirae and colophonium, over a 21-year period. *Contact Dermat.* **2013**, *68*, 307–313. [CrossRef] [PubMed]
4. Bråred Christensson, J.; Andersen, K.E.; Bruze, M.; Johansen, J.D.; Garcia-Bravo, B.; Gimenez Arnau, A.; Goh, C.-L.; Nixon, R.; White, I.R. Positive patch test reactions to oxidized limonene: Exposure and relevance. *Contact Dermat.* **2014**, *71*, 264–272.
5. Bråred Christensson, J.; Andersen, K.E.; Bruze, M.; Johansen, J.D.; Garcia-Bravo, B.; Gimenez Arnau, A.; Goh, C.-L.; Nixon, R.; White, I.R. Air-oxidized linalool—A frequent cause of fragrance contact allergy. *Contact Dermat.* **2012**, *67*, 247–259.
6. Svedman, C.; Andersen, K.; Brandão, F.M.; Bruynzeel, D.P.; Diepgen, N.; Frosch, P.J.; Rustemeyer, T. Follow-up of the monitored levels of preservative sensitivity in Europe: Overview of the years 2001–2008. *Contact Dermat.* **2012**, *67*, 312–314. [CrossRef] [PubMed]
7. Aerts, O.; Baeck, M.; Constandt, L.; Dezfoulian, B.; Jacobs, M.C.; Kerre, S.; Lapeere, H.; Pierret, L.; Wouters, K.; Goossens, A. The dramatic increase in the rate of methylisothiazolinone contact allergy in Belgium: A multicentre study. *Contact Dermat.* **2014**, *71*, 41–48. [CrossRef] [PubMed]
8. Knackstedt, T.J.; Zug, K.A. T-cell lymphomatoid contact dermatitis: A challenging case and review of the literature. *Contact Dermat.* **2015**, *72*, 65–74. [CrossRef] [PubMed]
9. Bruze, M.; Engfeldt, M.; Gonçalo, M.; Goossens, A. Recommendation to include methylisothiazolinone in the European baseline patch test series—On behalf of the European Society of Contact Dermatitis and the European Environmental and Contact Dermatitis Research Group. *Contact Dermat.* **2013**, *69*, 263–270. [CrossRef] [PubMed]

10. Bruze, M.; Goossens, A.; Isaksson, M. Recommendation to increase the test concentration of methylchloroisothiazolinone/methylisothiazolinone in the European baseline patch test series—On behalf of the European Society of Contact Dermatitis and the European Environmental and Contact Dermatitis Research Group. *Contact Dermat.* **2014**, *71*, 35–40.
11. Mestach, L.; Goossens, A. Allergic contact dermatitis and nail damage mimicking psoriasis caused by nail hardeners. *Contact Dermat.* **2016**, *74*, 112–114. [CrossRef] [PubMed]
12. Van Lerberghe, L.; Baeck, M. A case of acute contact dermatitis induced by formaldehyde in hair-straightening products. *Contact Dermat.* **2014**, *70*, 384–386. [CrossRef] [PubMed]
13. Takeda, A.; Asada, A.; Kajimura, K. Characterization of the decomposition of compounds derived from imidazolidinyl urea in cosmetics and patch test materials. *Contact Dermat.* **2012**, *67*, 284–292.
14. Kajimura, K.; Taguchi, S. The different decomposition properties of diazolidinyl urea in cosmetics and patch test materials. *Contact Dermat.* **2011**, *65*, 81–91.
15. Leysen, J.; Goossens, A.; Lambert, J.; Aerts, O. Polyhexamethylene biguanide is a relevant sensitizer in wet wipes. *Contact Dermat.* **2014**, *70*, 323–325. [CrossRef] [PubMed]
16. Kautz, O.; Schumann, H.; Degerbeck, F.; Venemalm, L.; Jakob, T. Severe anaphylaxis to the antiseptic polyhexanide. *Allergy* **2012**, *65*, 1058–1072.
17. Creytens, K.; Faber, M.; Aerts, O.; Goosens, A. Severe contact urticaria syndrome from wipes for intimate hygiene. *Contact Dermat.* **2014**, *71*, 307–309. [CrossRef] [PubMed]
18. Sösted, H.; Rustemeyer, T.; Gonçalo, M.; Bruze, M.; Goossens, A.; Giménez-Arnau, A.M.; Le Coz, C.J.; White, I.R.; Diepgen, T.L.; Andersen, K.E. Contact allergy to common ingredients in hair dyes. *Contact Dermat.* **2013**, *69*, 32–39. [CrossRef] [PubMed]
19. Teixeira, M.; de Wachter, L.; Ronsyn, E.; Goossens, A. Contact allergy to para-phenylenediamine in a permanent eyelash dye. *Contact Dermat.* **2006**, *55*, 92–94. [CrossRef] [PubMed]
20. Vogel, T.A.; Coenraads, P.-J.; Schuttelaar, M.-L.A. Allergic contact dermatitis presenting as severe and persistent blepharoconjunctivitis and centrofacial oedema after dyeing of eyelashes. *Contact Dermat.* **2014**, *71*, 304–306. [CrossRef] [PubMed]
21. Sahoo, B.; Handa, S.; Penchallaiah, K.; Kumar, B. Contact anaphylaxis due to hair dye. *Contact Dermat.* **2000**, *43*, 244.
22. Vanden Broecke, K.; Bruze, M.; Persson, L.; Deroo, H.; Goossens, A. Contact urticaria syndrome caused by direct hair dyes in a hairdresser. *Contact Dermat.* **2014**, *71*, 124–126. [CrossRef] [PubMed]
23. Hoekstra, M.; van der Heide, S.; Coenraads, P.-J.; Schuttelaar, M.-L.A. Anaphylaxis and severe systemic reactions caused by skin contact with persulfates in hair-bleaching products. *Contact Dermat.* **2012**, *66*, 317–322. [CrossRef] [PubMed]
24. Ramos, L.; Cabral, R.; Gonçalo, M. Allergic contact dermatitis caused by acrylates and methacrylates—A 7-year study. *Contact Dermat.* **2014**, *71*, 102–107. [CrossRef] [PubMed]
25. Hughes, T.M.; Stone, N.M. Benzophenone 4: An emerging allergen in cosmetics and toiletries? *Contact Dermat.* **2007**, *56*, 153–156. [CrossRef] [PubMed]
26. Heurung, A.R.; Raju, S.I.; Warshaw, E.M. Benzophenones. *Dermatitis* **2014**, *25*, 3–10. [CrossRef] [PubMed]
27. De Groot, A.C.; Roberts, D.W. Contact and photocontact allergy to octocrylene: A review. *Contact Dermat.* **2014**, *70*, 193–204. [CrossRef] [PubMed]
28. Karlsson, I.; Vanden Broecke, K.; Mårtensson, J.; Goossens, A.; Börje, A. Clinical and experimental studies of octocrylene's allergenic potency. *Contact Dermat.* **2011**, *64*, 343–352. [CrossRef] [PubMed]
29. Perez, A.; Basketter, D.A.; White, I.R.; McFadden, J. Positive rates to propyl gallate on patch testing: A change in trend. *Contact Dermat.* **2008**, *58*, 47–48. [CrossRef] [PubMed]
30. García-Gavín, J.; Parente, J.; Goossens, A. Allergic contact dermatitis caused by sodium metabisulfite: A challenging allergen. A case series and literature review. *Contact Dermat.* **2012**, *67*, 260–269. [CrossRef] [PubMed]
31. Swinnen, I.; Goossens, A. Allergic contact dermatitis from ascorbyl tetraisopalmitate. *Contact Dermat.* **2011**, *64*, 241–242. [CrossRef] [PubMed]
32. Assier, H.; Wolkenstein, P.; Grille, C.; Chosidow, O. Contact dermatitis caused by ascorbyl tetraisopalmitate in a cream used for the management of atopic dermatitis. *Contact Dermat.* **2014**, *71*, 60–61. [CrossRef] [PubMed]
33. Goossens, A.; Baret, I.; Swevers, A. Allergic contact dermatitis from tetrahydroxypropyl ethylenediamine in cosmetic products. *Contact Dermat.* **2011**, *64*, 161–164. [CrossRef] [PubMed]

34. Ito, K.; Fujimura, N.; Uchida, T.; Ikezawa, Z.; Aihara, M. Contact dermatitis with systemic reactions caused by cetearyl isononanoate. *Contact Dermat.* **2014**, *69*, 315–316. [CrossRef] [PubMed]
35. Goossens, A.; Verbruggen, K.; Cattaert, N.; Boey, L. New cosmetic allergens: Isononyl isononanoate and trioleyl phosphate. *Contact Dermat.* **2008**, *59*, 320–321. [CrossRef] [PubMed]
36. Werbrouck, J.; Lambrecht, C.; Goossens, A. C12–15 alkyl benzoate: A new cosmetic allergen? *Contact Dermat.* **2015**, *73*, 249–250. [CrossRef] [PubMed]
37. Sasseville, D.; Stanciu, M. Allergic contact dermatitis form ethylhexylglycerin in sunscreens. *Dermatitis* **2014**, *25*, 42–43. [CrossRef] [PubMed]
38. Schnuch, A.; Lessmann, H.; Geier, J.; Uter, W. Is cocamidopropyl betaine a contact allergen? Analysis of network data and short review of the literature. *Contact Dermat.* **2011**, *64*, 203–211. [CrossRef] [PubMed]
39. Aalto-Korte, K.; Pesonen, M.; Kuuliala, O.; Suuronene, K. Occupational allergic contact dermatitis caused by coconut fatty acids diethanolamide. *Contact Dermat.* **2014**, *70*, 169–174. [CrossRef] [PubMed]
40. Gijbels, D.; Timmermans, A.; Serrano, P.; Verreycken, E.; Goossens, A. Allergic contact dermatitis caused by alkyl glucosides. *Contact Dermat.* **2014**, *70*, 175–182. [CrossRef] [PubMed]
41. Spoerl, D.; Scherer, K.; Bircher, A.J. Contact urticaria with systemic symptoms due to hexylene glycol in a topical corticosteroid: Case report and review of hypersensitivity to glycols. *Dermatology* **2010**, *220*, 238–242. [CrossRef] [PubMed]
42. Quartier, S.; Garmyn, M.; Becart, S.; Goossens, A. Allergic contact dermatitis to copolymers in cosmetics—Case report and review of the literature. *Contact Dermat.* **2006**, *55*, 257–267. [CrossRef] [PubMed]
43. Kai, A.C.; White, M.L.; White, I.R.; Johnston, G.; McFadden, J.P. Contact dermatitis caused by C30–38 olefin/isopropyl-maleate/MA copolymer in a sunscreen. *Contact Dermatitis* **2011**, *64*, 353–354. [CrossRef] [PubMed]
44. Swinnen, I.; Goossens, A.; Rustemeyer, T. Allergic contact dermatitis caused by C30–38 olefin/isopropyl maleate/MA copolymer in cosmetics. *Contact Dermat.* **2012**, *67*, 318–320. [CrossRef] [PubMed]
45. Corazza, M.; Borghi, A.; Gallo, R.; Schena, D.; Pigatto, P.; Lauriola, M.M.; Guarneri, F.; Stingeni, L.; Vincenzi, C.; Foti, C.; *et al*. Topical botanically derived products: Use, skin reactions, and usefulness of patch tests. A multicenter Italian study. *Contact Dermatitis* **2014**, *70*, 90–97. [CrossRef] [PubMed]
46. Jack, A.R.; Norris, P.L.; Storrs, F.J. Allergic Contact Dermatitis to Plant Extracts in Cosmetics. *Semin. Cutan. Med. Surg.* **2013**, *32*, 140–146. [PubMed]
47. Sasseville, D.; Desjardins, M.; Almutawa, F. Allergic contact dermatitis caused by glycyrrhetinic acid and castor oil. *Contact Dermat.* **2011**, *64*, 168–169. [CrossRef] [PubMed]
48. Ghys, K.; Gilissen, G.; Vandevenne, A.; Werbrouck, J.; Goossens, A. *Magnolia officinalis* bark extract, a recently identified contact allergen in "anti-aging" cosmetics? *Contact Dermat.* **2015**, *73*, 130–132. [CrossRef] [PubMed]
49. Larson, D.; Jacob, S.E. Tea tree oil. *Dermatitis* **2012**, *23*, 48–49. [CrossRef] [PubMed]
50. De Groot, A. Propolis: A review of properties, applications, chemical composition, contact allergy, and other adverse effects. *Dermatitis* **2014**, *24*, 263–282. [CrossRef] [PubMed]
51. Jacob, S.E.; Matiz, C.; Herro, E.M. Compositae-associated allergic contact dermatitis from bisabolol. *Dermatitis* **2011**, *22*, 102–105. [PubMed]
52. Fong Chin, M.; Hughes, T.M.; Stone, N.M. Allergic contact dermatitis caused by panthenol in a child. *Contact Dermat.* **2013**, *69*, 321–322. [CrossRef] [PubMed]
53. Garcia-Gavin, J.; Tennstedt, D.; Goossens, A. Allergic contact dermatitis due to cosmetics containing vitamin K1 oxide. *Contact Dermat.* **2011**, *62*, 248–250. [CrossRef] [PubMed]
54. Goossens, A. Les allergies de contact aux produits naturels des cosmétiques. *Rev. Fr. Allerg.* **2015**, *55*, 171–173. (In French). [CrossRef]
55. Paulsen, E.; Andersen, K.E. Colophonium and compositae mix as markers of fragrance allergy: Cross-reactivity between fragrance terpenes, colophonium and compositae plant extracts. *Contact Dermat.* **2005**, *53*, 285–291. [CrossRef] [PubMed]
56. Nardelli, A.; Thijs, L.; Janssen, K.; Goossens, A. Rosa centifolia in a "non-scented" moisturizing body lotion as a cause of allergic contact dermatitis. *Contact Dermat.* **2009**, *61*, 306–309. [CrossRef] [PubMed]
57. Vansina, S.; Debilde, D.; Morren, M.-A.; Goossens, A. Sensitizing oat extracts in cosmetic creams: Is there an alternative? *Contact Dermat.* **2010**, *63*, 169–171. [CrossRef] [PubMed]

58. Leheron, C.; Bourrier, T.; Albertini, M.; Giovannini-Chami, L. Immediate contact urticaria caused by hydrolysed wheat proteins in a child via maternal skin contact sensitization. *Contact Dermat.* **2013**, *68*, 379–380. [CrossRef] [PubMed]
59. Chinuki, Y.; Takahashi, H.; Dekio, I.; Kaneko, S.; Tokuda, R.; Nagao, M. Higher allergenicity of high molecular weight hydrolysed wheat protein in cosmetics for percutaneous sensitization. *Contact Dermat.* **2013**, *68*, 86–93. [CrossRef] [PubMed]
60. Pecquet, C.; Lauriere, M.; Huet, S.; Leynadier, F. Is the application of cosmetics containing protein-derived products safe? *Contact Dermat.* **2002**, *46*, 123. [CrossRef]