

ORIGINAL ARTICLE

Fragrance contact allergens in 5588 cosmetic products identified through a novel smartphone application

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Abstract

Background More than 25% of the adult European population suffers from contact allergy, with fragrance substances recognized as one of the main causes. Since 2005, 26 fragrance contact allergens have been mandatory to label in cosmetic products within the EU if present at 10 ppm or above in leave-on and 100 ppm or above in wash-off cosmetics.

Objective To examine exposure, based on ingredient labelling, to the 26 fragrances in a sample of 5588 fragranced cosmetic products.

Methods The investigated products were identified through a novel, non-profit smartphone application (app), designed to provide information to consumers about chemical substances in cosmetic products. Products registered through the app between December 2015 and October 2016 were label checked according to International Nomenclature of Cosmetic Ingredients (INCI) for the presence of the 26 fragrance substances or the wording 'fragrance/parfum/aroma'.

Results The largest product categories investigated were 'cream, lotion and oil' ($n = 1192$), 'shampoo and conditioner' ($n = 968$) and 'deodorants' ($n = 632$). Among cosmetic products labelled to contain at least one of the 26 fragrances, 85.5% and 73.9% contained at least two and at least three of the 26 fragrances, respectively. Linalool (49.5%) and limonene (48.5%) were labelled most often among all investigated products. Hydroxyisohexyl 3-cyclohexene carboxaldehyde (HICC/Lyral[®]) was found in 13.5% of deodorants. Six of the 26 fragrance substances were labelled on less than one per cent of all products, including the natural extracts *Evernia furfuracea* (tree moss) and *Evernia prunastri* (oak moss). A total of 329 (5.9%) products had one or more of the 26 fragrance substances labelled but did not have 'parfum/fragrance/aroma' listed on the label.

Conclusions Consumers are widely exposed to, often multiple, well-established fragrance contact allergens through various cosmetic products intended for daily use. Several fragrance substances that are common causes of contact allergy were rarely labelled in this large sample of cosmetic products.

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Disclosures

NBO, SM, CSK, ABC and CJ are all employees at the Danish Consumer Council (DCC) THINK Chemicals, an initiative under the Danish Consumer Council (DCC), which is a non-governmental member organization (<https://taenk.dk/om-os/about-us>). The DCC is a member of International Consumer Research & Testing (ICRT), the only independent international organization for consumer research and testing. DCC THINK Chemicals is funded by a grant on the Danish Finance Act. NHB, CZ and JDJ have no competing or financial interests to declare.

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Introduction

More than 25% of the adult European population suffers from contact allergy, with fragrance chemicals recognized as one of the main causes both in the general population and among

dermatitis patients.^{1,2} In a case-control study among Danish eczema patients, fragrance contact allergy has previously been shown to be associated with decreased quality of life.³ Allergic contact dermatitis caused by fragrances is most often due to

exposure from cosmetics, defined in a broad term to include all personal care products used for hygiene and beautification purposes. More than 120 chemicals used for their scent in consumer products have been classified as possessing skin sensitizing properties.⁴ Among these, 26 well-established fragrance allergens have been mandatory to label since 2005 within the EU, if present at 10 ppm or above in leave-on cosmetics, and 100 ppm or above in wash-off cosmetics or household detergents, respectively.⁵ Cosmetic ingredient labelling within the EU is harmonized according to the International Nomenclature of Cosmetic Ingredients (INCI). Previous studies have established that a high proportion of eczema patients find it difficult to understand the INCI labelling of cosmetic products, especially among patients with lower educational background.^{6,7}

Danish Consumer Council (DCC) THINK Chemicals is an initiative under the Danish Consumer Council, a non-governmental organization with the overall aim of assisting consumers with information on problematic chemical substances when shopping for consumer products.⁸ In December 2015, DCC THINK Chemicals introduced the smartphone application (app) 'Kemiluppen', which roughly translates to 'the chemical magnifying glass', to download free of charge in Danish to iPhone™ and Android™ users. The app was developed with the overall aim of empowering consumers by creating transparency on the ingredients present in cosmetics and hence enables the individual to choose cosmetics without certain chemical substances such as fragrance contact allergens, without having to decipher the ingredients list on their own.

In this study, we wanted to examine exposure, based on ingredient labelling, to the 26 fragrance contact allergens with mandatory labelling in cosmetic products registered through the smartphone application.

Materials and methods

The app 'Kemiluppen' was developed by DCC THINK Chemicals in cooperation with Benjamin Client Media (Frederiksberg, Denmark). The app was launched on 10 December 2015 and publicized in a national newspaper as well as online and on social media. After downloading and installing the app, the consumer can scan the European Article Numbering (EAN) barcode of a cosmetic product of interest using the smartphone's camera function. If the product has already been assessed and label checked by DCC THINK Chemicals, the consumer instantly receives information on full ingredient labelling according to INCI. In assisting the consumer with deciphering the ingredient list, an information system is built into the app, assessing the presence of several classes of chemical substances in the product.⁹ If one or more of the 26 fragrance ingredients, or the word 'parfum', 'fragrance' or 'aroma', are listed on the product's ingredient label, the consumer is given the information: 'Contains fragrances'. If the scanned product has not been assessed by DCC THINK Chemicals, the consumer is asked via the app

to send in pictures of the product and the list of ingredients. The product's name, product category and full INCI labelling are reviewed and entered manually into an anonymized database, containing no information on the individual consumer contributing the product. Before being activated in the database, and hence instantly available in the app to the next consumer scanning the barcode of the same specific product, the ingredient list is sent to a check by the responsible company to ensure verification of the entered ingredients. Additionally, the ingredient list registered in the database for the single product is sent to the responsible company once a year to ensure it is up to date.

For the current study, full INCI labelling of activated cosmetic products available in the app between December 2015 and October 2016 was reviewed for the presence of fragrances, that is having labelled one or more of the 26 fragrance ingredients, or having 'parfum', 'aroma' or 'fragrance' listed. In addition, data on individual product name, date the product was added to the database, and total number of scans for the individual product was available. As products registered through the app are identified by their EAN barcode, these were reviewed for duplicates based on product name, product category and INCI labelling of ingredients, that is identical products available in different volumes or packages. For presentation of data, products were grouped into 14 major product categories (listed in Table 1), as well as the category miscellaneous which included the following products labelled to contain fragrances: Theatre make-up ($n = 20$), gift boxes containing several cosmetic products ($n = 17$), hand disinfectants ($n = 12$), adult wet wipes ($n = 4$), insect repellents ($n = 2$), nasal cleanser ($n = 1$) and talc powder ($n = 1$).

Data management and graphing were performed using SAS® Enterprise Guide® software, version 7.1 (SAS Institute Inc., Cary, NC, USA) and GraphPad Prism version 7 (GraphPad software, La Jolla, California, USA). Comparisons of total number of labelled fragrances in different product categories were performed using the Mann–Whitney *U*-test.

Results

During the study period, a total of 157 154 users downloaded the app 'Kemiluppen' for use on their smartphone, and contributed a total of 2 275 279 scans via the app of the ingredient labelling for 8727 cosmetic products. Of these, 5754 cosmetic products had at least one of the 26 fragrances listed, and/or had 'parfum', 'aroma' or 'fragrance' listed on the label. After exclusion of duplicates, 5588 unique fragranced products were identified and investigated further. The ten individual fragranced products scanned most often by the users of the app (all scanned more than 5000 times) were in descending order of total number of scans (including number of listed fragrances in parenthesis): (i) tooth paste (only 'aroma'), (ii) Hair wax (five fragrances and 'parfum'), (iii) body lotion (three fragrances and 'parfum'), (iv) body oil (13 fragrances and 'parfum'), (v) cream (seven

Table 1 Frequency of labelling of the 26 fragrance allergens in the investigated fragranced cosmetic products, stratified by product category

	Baby product	Bodywash & soap	Cream, lotion & oil	Dental care	Deodorant	Facial cleanser	Hair colour	Hair styling	Make-up	Manicure & pedicure	Perfume	Shampoo & conditioner	Shaving & hair removal	Tanning & sun lotion
Fragranced/total products, <i>n</i>	49/230	565/751	1192/1864	205/215	632/732	463/776	73/95	416/516	262/741	287/472	51/52	968/1159	107/194	261/513
Only "parfum" listed*, %	42.9	44.8	35.5	34.6	19.5	43.2	28.8	31.7	28.6	45.0	11.8	28.2	40.2	45.2
No. of 26 fragrances labelled, mean (range)	1.8(0–6)	2.2(0–12)	3.5(0–14)	0.9(0–4)	5.4(0–17)	2.2(0–13)	3.1(0–10)	3.8(0–13)	2.7(0–15)	2.8(0–13)	6.8(0–15)	2.9(0–12)	1.9(0–9)	3.5(0–15)
Alpha-isomethyl ionone, %	0.0	9.7	16.2	0.0	38.0	11.2	2.7	20.7	8.8	12.9	31.4	10.1	6.5	24.5
Amyl cinnamal, %	6.1	1.4	3.6	0.0	2.5	1.5	8.2	10.1	3.8	1.1	5.9	4.8	2.8	1.9
Anise alcohol, %	0.0	0.2	0.4	0.5	0.0	0.9	0.0	0.5	1.2	0.0	2.0	0.0	0.0	0.8
Benzyl alcohol, %	16.3	15.0	24.7	9.8	22.5	20.1	42.5	26.0	27.5	18.1	21.6	30.5	2.8	31.0
Benzyl benzoate, %	14.3	5.1	11.5	0.0	11.9	5.6	0.0	10.6	18.7	8.0	23.5	6.0	2.8	8.1
Benzyl cinnamate, %	0.0	0.4	0.5	0.0	2.2	0.0	4.1	0.0	1.2	1.1	0.0	0.0	0.0	0.0
Benzyl salicylate, %	4.1	10.6	17.7	0.0	23.6	14.5	32.9	24.0	13.7	15.0	35.3	22.3	16.8	14.9
Butylphenyl methylpropional, %	0.0	19.1	19.4	0.0	35.3	12.7	21.9	28.9	5.3	12.2	51.0	22.5	16.8	26.1
Cinnamal, %	0.0	0.0	1.1	1.5	3.3	0.0	0.0	1.2	1.9	0.4	3.9	0.1	0.0	1.2
Cinnamyl alcohol, %	6.1	0.5	2.0	0.0	4.4	1.7	0.0	1.4	3.1	1.4	5.9	0.3	0.0	2.3
Citral, %	14.3	8.3	19.9	1.0	37.5	9.3	0.0	11.5	13.7	18.1	54.9	3.1	0.9	17.6
Citronellol, %	12.2	18.9	33.2	0.0	52.4	18.8	24.7	35.1	20.6	27.9	64.7	21.8	9.4	39.1
Coumarin, %	8.2	8.3	12.7	0.0	36.2	1.5	4.1	15.6	5.3	8.7	29.4	5.2	7.5	27.6
<i>E. furfuracea</i> extract, %	0.0	0.0	0.3	0.0	1.0	0.7	0.0	0.0	0.4	0.0	0.0	0.0	0.9	0.0
<i>E. prunastri</i> extract, %	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.2	0.4	0.0	0.0	0.0	0.0	0.0
Eugenol, %	0.0	4.4	9.3	7.8	15.0	4.3	5.5	5.1	11.5	8.7	23.5	2.3	3.7	20.7
Farnesol, %	4.1	0.7	3.3	0.5	9.3	0.9	0.0	1.0	5.0	4.5	5.9	0.5	0.9	1.9
Geraniol, %	20.4	13.8	30.5	0.5	46.8	17.9	6.9	27.4	17.2	26.5	66.7	15.9	4.7	20.3
Hexyl cinnamal, %	0.0	20.0	18.3	0.0	23.4	10.6	43.8	34.6	11.1	15.3	31.4	40.3	19.6	12.3
HICC, %	0.0	4.4	8.0	0.0	13.5	5.6	0.0	7.9	5.0	7.3	19.6	3.6	3.7	6.5
Hydroxycitronellal, %	2.0	2.1	7.6	0.0	16.8	4.5	1.4	10.8	8.8	4.5	41.2	5.3	0.0	2.7
Isoeugenol, %	0.0	0.5	2.8	0.0	3.8	0.2	1.4	1.4	1.5	1.7	7.8	0.5	2.8	0.8
Limonene, %	34.7	40.0	49.4	60.0	69.3	39.3	50.7	54.8	41.6	42.5	78.4	44.2	42.1	40.2
Linalool, %	38.8	41.2	54.3	3.9	69.0	35.9	56.2	54.6	43.5	44.6	76.5	53.5	40.2	48.7
Methyl 2-octynoate, %	0.0	0.0	0.1	0.0	0.3	0.0	0.0	0.0	1.2	0.0	3.9	0.0	0.0	0.0

*Only 'parfum', 'fragrance' and/or 'aroma' listed and none of the 26 fragrances.

fragrances and 'parfum'), (vi) deodorant (only 'parfum' listed), (vii) deodorant (10 fragrances and 'parfum'), (viii) lip balm (two fragrances and 'parfum'), (ix) hair wax (four fragrances and 'parfum'), and (x) deodorant (seven fragrances and 'parfum'). Figure 1 displays the overall ranking of the individual fragrance substances among the total 5588 fragranced products. The terpenes linalool (49.5%) and limonene (48.5%) were the single fragrance substances most often labelled on the investigated products, followed by citronellol (28.5%), geraniol (23.8%) and benzyl alcohol (23.3%). The five fragrance substances benzyl cinnamate, anise alcohol, *Evernia furfuracea* (tree moss) extract, methyl 2-octynoate and *Evernia prunastri* (oak moss) extract were all labelled on less than one per cent of the investigated products. Amyl cinnamyl alcohol was the only one of the 26 fragrance substances that was not labelled on any of the investigated products.

In total, the 26 fragrance substances were labelled 17 870 times on the 5,588 cosmetic products (mean 3.2 fragrance substances per product, range 0–17). Of the investigated fragranced products, 1915 (34.3%) only had 'parfum/fragrance/aroma'

listed and none of the 26 fragrance substances. Detailed information on the presence of the 26 fragrances in the investigated fragranced cosmetic products, stratified by product category, is presented in Table 1 (excluding the category miscellaneous). Among the 3673 products labelled to contain at least one of the 26 fragrances, 85.5% contained at least two and 73.9% contained at least three of the 26 fragrances, respectively. Perfumes (fine fragrances and eaux de toilette) were labelled to contain the highest number of the 26 fragrances with a mean of 6.8 (range 0–15), followed by deodorants (mean 5.4, range 0–17). The difference between the two product categories was statistically significant ($P = 0.007$). For both of these product categories, the majority of all products scanned through the app (98.1% for perfumes and 86.3% for deodorants) were labelled to contain fragrances. Dental care products (mouth wash and tooth paste) were on average labelled to contain the lowest number of the 26 fragrances (mean 0.9, range 0–4). However of the 215 dental care products registered through the app, 205 (95.3%) were fragranced, with limonene being labelled on 60% of these. Of the total 230 baby-specific products registered through the app, 49

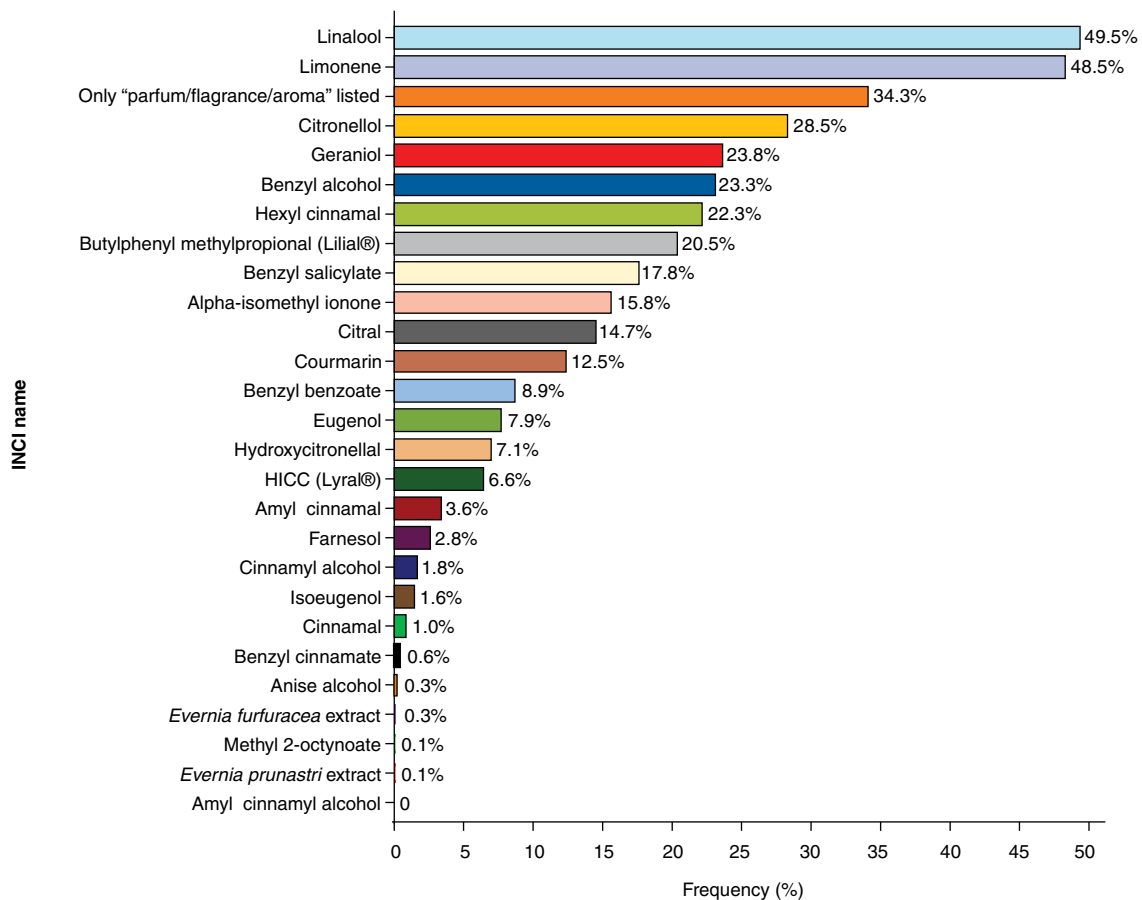


Figure 1 Labelling of the 26 fragrance allergens with mandatory labelling within the EU in 5588 fragranced cosmetic products.

(21.3%) were labelled to contain fragrances. The majority of these ($n = 41$) were leave-on cosmetic products (creams, lotions, oils and baby wet wipes).

Except for fragranced dental care products (with only 3.9% containing linalool), both limonene and linalool were the single fragrances labelled most often within all individual product categories. A few other fragrances were mainly present in specific product categories, such as hexyl cinnamal in different hair product categories. The natural extract *E. furfuracea* (tree moss) was only labelled on 14 products, and six of these were in a series of different products from the same brand. Of only eight products labelled to contain methyl 2-octynoate, one was a lip balm (make-up) marketed for children. A total of 329 (5.9%) products were labelled to contain one or more of the 26 fragrance substances but did not have 'parfum/fragrance/aroma' listed on the label. The fragrances most often labelled on these products were as follows: Limonene (78.4%), linalool (63.5%), geraniol (35.0%) and citral (31.3%). Of the 329 fragranced products without 'parfum/fragrance/aroma' labelled, 45 (13.7%) had a name containing one or more of the following terms: Organic/eco, sensitive, pure or natural. Among these were three baby lotions, labelled to contain one (benzyl alcohol in two products) and three (linalool, limonene and geraniol) of the 26 fragrance substances, respectively.

Discussion

In the current study, we investigated exposure to 26 well-established fragrance contact allergens in 5588 fragranced cosmetic products based on ingredient labelling. According to current legislation within the EU, the 26 fragrance substances are to be labelled when present at 10 ppm or above in leave-on cosmetic and 100 ppm or above in wash-off cosmetic products.⁵ The products examined in the current study were selected by consumers from the general Danish population who registered these using a free and non-profit smartphone application. No information is stored in the app's database on the individual consumer submitting a cosmetic product for investigation of ingredient labelling. Hence, it is not possible to state that the investigated products were selected at random. On the contrary, it is likely that users of the smartphone app are biased towards selecting personal care products free from problematic chemical substances, such as labelled fragrance contact allergens. This is evident as fragranced products, based on labelling of the 26 fragrance allergens as well as the wording 'parfum', 'fragrance' or 'aroma', only made up around two-thirds of all cosmetic products registered through the app. Despite this, the internal ranking of the frequency of labelling of the 26 fragrance substances in the current study is to a large extent comparable to a German random sample of approximately 5000 cosmetic products investigated between 2006 and 2009.¹⁰ A similar internal ranking was observed in a smaller sample of 300 various cosmetic products examined for

fragrance ingredient labelling in the UK in 2006.¹¹ As the specific concentration of single fragrance substances is not available from the ingredient label of a fragranced consumer product, estimates of exposure to the investigated fragrance allergens based on INCI labelling is qualitative. However, based on data from the aforementioned German survey, Schnuch *et al.*¹² have recently shown a very high correlation coefficient (Spearman's rank = 0.94, $P < 0.0001$) between actual use volumes (in tonnage) of the 26 fragrance substances in cosmetic products produced in Europe, and exposure estimates for these based on frequency of ingredient labelling.

Among the cosmetic products labelled to contain any of the 26 fragrances, 85% of these had two or more of the investigated fragrance contact allergens labelled. When tested one by one in animal studies, the majority of the 26 fragrance contact allergens have been categorized as only moderate skin sensitizers based on the murine local lymph node assay.⁴ It has previously been shown that exposure to a combination of two fragrance contact allergens has a synergistic effect on the elicitation response in eczema patients sensitized to both, compared to the expected response based on testing with either substance alone.¹³ Experimental studies in mice have additionally shown that a mixture of fragrance contact allergens has an increased potency with regard to sensitization risk compared to exposure to individual sensitizing fragrance substances.¹⁴ In a clinical patch test setting, this 'cocktail effect' of exposure to multiple fragrance contact allergens could explain the often observed negative break down test in patients sensitized to the screening markers fragrance mix I and fragrance mix II.¹⁵ In addition, the 26 fragrance contact allergens constitute less than one-third of fragrance substances already established as contact allergens in humans.^{4,16} As the use of any or several of these in a cosmetic product is only identified by labelling 'parfum', 'fragrance' or 'aroma' on the product, exposure estimates to multiple fragrance contact allergens based on ingredient labelling will be underestimated.

The fragrance terpenes limonene and linalool were labelled on almost half of all fragranced cosmetic products in the current study. With regard to causing contact allergy, both fragrance terpenes are prehaptenes, meaning that the pure fragrance chemicals, with low sensitizing potency, are modified outside the skin by air oxidation resulting in an increased allergenic potential.¹⁷ For both linalool and limonene, specific hydroperoxides formed during oxidation of these have been identified as the primary haptens causing sensitization.^{18,19} Among consecutive Danish eczema patients patch tested with the 26 fragrance contact allergens, oxidized linalool and oxidized limonene have been shown to be top sensitizers within recent years.²⁰ Among European patch test populations, sensitization to the standard patch test concentrations of the oxidized terpenes is frequent, with prevalences of positive reactions ranging from 3.3% to 14.3% for oxidized linalool 6% pet., and 2.3% to 7.7% for oxidized limonene 3% pet., respectively.^{21–24} The International Fragrance

Association (IFRA) has stated that for both linalool²⁵ and limonene,²⁶ cosmetic products containing either of the fragrance terpenes should have a hydroperoxide fraction of no more than 20 mM according to industry standards. Experimental investigations of the essential oils sweet orange oil (main compound limonene) and petitgrain oil (main compounds include linalool) have shown that the concentration of allergen-specific hydroperoxides increases over time in these, irrespective of storage and handling conditions, to levels that can elicit an allergic reaction in sensitized individuals.^{27,28}

The product categories 'cream, lotion and oil' and 'shampoo and conditioner' were the largest groups of investigated products in the current study. It is of interest that the very same product categories are the cosmetic exposures most often causing allergic contact dermatitis due to fragrance allergy within a large Danish patch test population in recent years.^{29,30} In the current study, deodorants were the third largest product category, with 632 products investigated. We identified linalool, limonene, citronellol and geraniol as the fragrances labelled most often among these, which is comparable to a Danish market survey from 2007 reporting on ingredient labelling of 88 deodorants.³¹ However in the current study, hydroxyisohexyl 3-cyclohexene carboxaldehyde (HICC/Lyral®) was only labelled on 13.5% of deodorants compared to 33.0% in the 2007 survey, which is significantly lower (Chi-square test, $P < 0.0001$). In an extensive opinion on fragrance contact allergens from 2012, the Scientific Committee on Consumer Safety (SCCS), advisory to the European Commission, concluded that HICC should not be used in consumer products due to an exceptionally high number of documented cases of contact allergy to the synthetic compound.¹⁶ Within recent years, sensitization to HICC has shown a tendency to decrease in several European patch test populations,^{15,20} which could indicate a general decrease in exposure. Currently, the European Commission is drafting an amendment to Annex II (banned substances) of the Cosmetics Directive to ban HICC, along with the two potent sensitizers atranol and chloroatranol, from being used in cosmetic products.³² Atranol and chloroatranol have been identified as potent sensitizers present in extracts from *E. prunastri* (oak moss) and *E. furfuracea* (tree moss), and a large reduction in the total tonnage of both natural extracts used in cosmetic products within the EU has been reported from 1997 to 2007.^{33,34} In the current study, we only identified three and 14 products labelled to contain *E. prunastri* and *E. furfuracea*, respectively. The rare occurrence of labelling of the two natural extracts in the investigated cosmetic products is in contrast to data from patch test populations where these are still common causes of sensitization.^{15,20,35} A likely explanation for this discrepancy could be that the two natural extracts are used in leave-on and wash-off cosmetic products below the limits specified above and hence are not required to be labelled. It has previously been shown that among eczema patients sensitized to oak moss and chloroatranol, an allergic reaction can be elicited

when exposed daily to as low levels as 5 ppm of chloroatranol in a use test.³⁶

In the current study, 329 cosmetic products were labelled to contain one or more of the 26 fragrance allergens but did not have 'fragrance', 'parfum' or 'aroma' labelled concomitantly. The misleading marketing accompanying several of these 'natural' or 'pure' products is exemplified in the series of six men's products from the same brand labelled to contain *E. furfuracea* extract. These were marketed with the text 'Be loyal to your skin. Our products never contain artificial colors, synthetic fragrances [...]'. In line with this, a recent market survey from the US of 187 'hypoallergenic' products, identified that 89% of these contained at least one contact allergen with fragrance substances being the second most prevalent allergen group.³⁷

In summary, we assessed exposure to 26 fragrance contact allergens with mandatory labelling within the EU in more than 5000 fragranced cosmetic products, sampled by consumers from the general population through the use of a novel non-profit smartphone application. Exposure to multiple fragrance contact allergens in various cosmetic products, including products intended for daily use, continues to be frequently occurring and could pose an increased risk of sensitization to the individual consumer. Several fragrance contact allergens that are common causes of sensitization were rarely labelled on the investigated products which we speculate could be due to their use in concentrations below those required for labelling in cosmetic products. Full ingredient labelling of not just the 26 fragrance allergens but all fragrance substances with skin sensitizing potential, irrespective of use concentration, would be of value to both the clinician in diagnosing patients suspected of fragrance contact allergy, as well as the sensitized individual trying to avoid future exposure.

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