

Fragrance chemicals in domestic and occupational products

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Epidemiological studies have described an increasing prevalence of fragrance allergy and indicated an association with hand eczema. 59 domestic and occupational products intended for hand exposure were subjected to gas chromatography-mass spectrometric (GC-MS) analyses to test the hypothesis that fragrance chemicals known to have the potential to cause contact allergy but not included in fragrance mix (FM) may be common ingredients in these products. A quantitative analysis of 19 selected fragrances was performed by GC-MS. Further analysis of GC-MS data revealed the presence of 43 other fragrance chemicals/groups of fragrance chemicals in the products investigated. Among the 19 target substances the most commonly detected were limonene in 78%, linalool in 61% and citronellol in 47% of the products investigated. The FM ingredients were present in these products with the following frequencies: oak moss (evernic acid methylester) 2%, cinnamic alcohol 2%, cinnamic aldehyde (cinnamal) 3%, isoeugenol 5%, α -amylcinnamic aldehyde (amyl cinnamal) 8%, hydroxycitronellal 12%, eugenol 27%, and geraniol 41%. Thus, the chemical analyses of domestic and occupational products indicates that investigation of potential contact allergy related to these products types should consider fragrance allergens additional to those in the FM, since these may occur with high frequency.

Key words: fragrance chemicals; domestic and occupational products; chemical analysis; fragrance mix (FM). © Munksgaard, 2001.

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Fragrances are one of the most common causes of allergic contact dermatitis. The generally applied diagnostic tool when suspecting fragrance allergy is a patch test with fragrance mix (FM). The FM, a combination of 8 different fragrance materials, gives a positive reaction in 4%–11% of dermatological patients tested (1–3). However, approximately 2500 substances are used in fragrances, which may contain from 10 to more than 300 different chemical compounds.

Previous studies have subjected cosmetic products to gas chromatography-mass spectrometric (GC-MS) analyses for the quantitative determination of selected fragrance allergens (4, 5). Deodorants, fine fragrances, skin care products, and children's products were analysed (5–7). FM chemicals were among the most common fragrance allergens in these products. However, the composition of fragrance chemicals in domestic and occupational products may differ from that in cosmetic products. This study subjected 59 dom-

estic and occupational products to GC-MS analysis to test the hypothesis that well-known sensitizing fragrance chemicals not included in the FM are common ingredients in these products.

Materials and Methods

Samples

59 domestic and occupational products for which hand exposure would occur were analysed. The products were purchased in retail outlets in Denmark, England, Germany and Italy. The product categories represented were liquid soap and soap bars (13 products), soft/hard surface cleaners (23 products), fabric conditioners/laundry detergents for hand wash (8 products), dish wash (10 products), furniture polish (1 product), car shampoo (1 product), stain remover (1 product) and 2 products used in occupational environments. Both well-known international companies and local small/medium-sized companies

in the above-mentioned geographical areas were represented.

Target fragrance chemicals

19 fragrance substances (including 3 FM ingredients) were selected for quantitative analysis according to the following 2 criteria (Table 1): known sensitizers; presumed to be common ingredients.

Sources of information required to fulfil the selection criteria included literature, advice from industry, published opinion of the EU Scientific Committee on Cosmetic and Non-Food Products (8), structure-activity relationship principles (4) and results obtained in a preliminary GC-MS analyses of 24 household products (unpublished data). The GC-MS data was also analysed for the presence of 43 other fragrance chemicals or groups of chemicals including the remaining 5 FM ingredients.

Analysis

As described in a previous publication, fragrance-rich extracts of the product samples were prepared from their solutions or homogeneous suspensions in methanol by silica gel column chromatography (9). Laundry detergents were dissolved in water

and diluted in methanol before extraction by column chromatography. Fragrances from aqueous solutions of soap bars were extracted in ethyl acetate (9). The fragrance-rich extracts were analysed by GC-MS and quantified using the intensity of a selected mass fragment of each substance in the total ion chromatograms of the extracts. Comparing both retention time and mass spectrum of the chromatographic peaks with the retention times and the mass spectra of the standard compounds identified fragrance chemicals. All of the target fragrance substances were analysed at a detection limit of approximately 1 ppm (0.0001%). The suitability of the method was evaluated by investigating linearity of the calibration curves as well as recoveries of the target fragrance substances from 3 products (a dish wash, a hard surface cleaner and a laundry detergent) spiked with these chemicals. Calibration curves for all of the substances were linear in the concentration range investigated (0.0002–0.0100%). Recoveries of the target fragrance substances from 3 products were found to be 72–110%. The repeatability of the determination of all target fragrance chemicals was within 10%.

Isomer-specific analyses were carried out for linalool and geraniol. They were determined as l-linalool and E (+) – geraniol.

Table 1. Frequency and concentration of 19 fragrances in 59 domestic and occupational products

Target fragrance chemicals	Frequency of fragrance chemicals in 59 domestic and occupation products	Mean concentrations (ppm)±SD	Concentration range (ppm)
limonene	78% (n=46)	826.7±195.1	6–9443
linalool	61% (n=36)	147.9±107.5	3–439
citronellol	47% (n=28)	275.3±326.1	18–1579
eucalyptol	41% (n=24)	77.5±101.6	15–446
geraniol*	41% (n=24)	234.4±360.0	53–1758
α-pinene	39% (n=23)	41.3±51.5	5–157
Galaxolide®	36% (n=21)	111.8±117.2	6–346
isoamyl salicylate	34% (n=20)	193.9±254.7	29–1157
α-hexylcinnamic aldehyde (hexyl cinnamal)	32% (n=19)	327.6±209.1	53–674
eugenol*	27% (n=16)	121.9±96.4	32–349
Lilial®	27% (n=16)	99.3±53.1	36–214
coumarin	25% (n=15)	149.0±87.1	45–309
citral	25% (n=15)	217.9±257.8	48–1088
piperonal	22% (n=13)	75.8±44.2	18–150
hexyl salicylate	19% (n=11)	634.1±1200.2	61–4060
hydroxycitronellal*	12% (n=7)	68.8±47.0	15–140
Lyrall®	10% (n=6)	74.8±23.9	36–103
benzyl benzoate	10% (n=6)	97.2±63.0	51–223
benzyl salicylate	8% (n=5)	801.1±515.7	293–1614

n=number of products containing the fragrance chemical concerned.

ppm=parts per million (1 ppm=0.0001%).

SD=standard deviation.

* Constituent of fragrance mix (FM) in the European standard series.

Galaxolide®: 4,6,6,7,8-hexamethyl-1,3,4,6,7,8-hexahydrocyclopenta[g]benzopyran.

Lilial®: 2-methyl-3-(4-tert-butyl-phenyl)propanal.

Lyrall®: 4-(4-hydroxy-4-methylpentyl)-3-cyclohexene carbaldehyde.

Table 2. Other fragrance materials identified in 59 domestic and occupational products

Fragrance chemical	Present in no. of products
cinnamic aldehyde (cinnamal)	2
cinnamic alcohol	1
α -amylcinnamic aldehyde (amyl cinnamal)	5
isoeugenol	3
p-anisaldehyde: 4-methoxy benzaldehyde	4
nerol	17
α - β -ionone	5
Hedione®: methyl dihydrojasmonate	14
α -isomethyl ionone	5
methyl anthranilate	7
vanillin and related aromatic aldehydes	3
C ₉ -C ₁₁ aliphatic aldehydes and ketones	3
cyclohexanol and cyclohexanone derivatives	23
cyclamen aldehyde	4
Rosephenone®: trichloromethylphenyl-carbinyl acetate	5
polycyclic musks, other than Galaxolide®	8
geranyl acetate	1
anisketone: 1-(4-methoxyphenyl)-2-propanone	1
geranyl/neryl acetate	14
linalyl acetate	16
tetrahydro-/dihydro- linalool	12
<i>tert</i> -butyl cyclohexyl acetate	18
dihydromyrcenol	12
isobornyl acetate	19
borneol/isoborneol	15
camphor	7
terpenes, other than limonene and α -pinene	22
sesquiterpenes	14
musk ketone	1
oakmoss (evernic acid methyl ester)	1
nopyl acetate	1
butanolides	4
benzyl acetate	8
terpineols	30
linalool oxide	2
amyl salicylate	6
Ambrox®: 1,6,10,10-tetramethyl-2-oxatricyclo[3,0,4,2]tridecane	1
Helional®: 2-methyl-3-(3,4-methylenedioxyphenyl)propanal	1
Triplal®: 2,4-dimethyl-3-cyclohexene carboxaldehyde	5
patchouli alcohol	3
3-hexenyl salicylate	1
dimethyl cyclopentadione	1
fenchol/fenchylacetate	4

Results

We determined the contents of 19 selected fragrance substances (Table 1) in 59 domestic and occupational products by GC-MS. The 5 most frequently used fragrances in domestic and occupational products were limonene (78%), linalool (61%), citronellol (47%), eucalyptol (41%), geraniol (41%), and α -pinene (39%) (Table 1). Limonene had the highest concentration range value (9443 ppm) and the highest mean concentration value (826.7 ppm) as well as the highest frequency in these 59 products. The least frequent fragrance in the 59 products was benzyl salicylate (8%). The fragrances with the 5 highest mean concentration values in the 59 products were limonene (826.7 ppm), benzyl salicylate (801.1 ppm), hexyl salicyl-

ate (634.1 ppm), α -hexylcinnamic aldehyde (hexyl cinnamal) (327.6 ppm), and citronellol (275.3 ppm). The lowest mean concentration value was found for α -pinene (41.3 ppm) (Table 1).

The GC-MS data were analysed for the presence of other fragrance chemicals in the investigated products. 43 other fragrance chemicals/groups of fragrance chemicals, including the 5 remaining FM ingredients (not comprising the group of target substances) were identified in the products analysed (Table 2). Quantitative analyses of these substances were not performed. Of these 43 chemicals/groups of chemicals, the 5 most frequently found were: terpineols in 51% of the 59 analysed products, derivatives of cyclohexanol and cyclohexanone in 39%, terpenes (other than limonene and α -pinene) in 37%, isobornyl acetate in 32% and

Table 3. Frequency of fragrance mix ingredients in 59 domestic and occupational products

Fragrance mix ingredients	Frequency of presence in the domestic and occupational products
oak moss (evernic acid methylester)	2% (<i>n</i> =1)
cinnamic alcohol	2% (<i>n</i> =1)
cinnamic aldehyde (cinnamal)	3% (<i>n</i> =2)
isoeugenol	5% (<i>n</i> =3)
α -amylcinnamic aldehyde (amyl cinnamal)	8% (<i>n</i> =5)
hydroxycitronellal	12% (<i>n</i> =7)
eugenol	27% (<i>n</i> =16)
geraniol	41% (<i>n</i> =24)

n=number of products containing the fragrance chemical concerned.

tert-butyl cyclohexyl acetate in 31% of the 59 analysed domestic and occupational products. Among the 5 remaining FM ingredients (cinnamic alcohol, cinnamic aldehyde (cinnamal), α -amylcinnamic aldehyde (amyl cinnamal), isoeugenol, and oak moss), the most frequently found was α -amylcinnamic aldehyde in 5 of 59 products (8%), Table 3. The other 4 FM ingredients were identified less frequently: cinnamic alcohol (1/59 products), oak moss (evernic acid methylester, 1/59 products), cinnamic aldehyde (2/59 products), and isoeugenol (3/59 products), Table 3.

No obvious difference was found with respect to the contents of fragrance ingredients in the 4 largest product categories: liquid soap and soap bar, soft/hard surface cleaner, fabric conditioner/laundry detergent for hand wash and dishwash products.

Discussion

Epidemiological studies have shown that fragrance allergy was associated with hand eczema (10–12). Employing GC-MS analyses, we determined the levels of presumably common and known sensitizing fragrance chemicals in 59 domestic and occupational products. These 59 products were especially relevant in terms of risk assessment for allergic hand eczema, as they were all intended for hand exposure.

Limonene was found to be the most common ingredient, and had the highest mean concentration value and the highest concentration range. Karlberg et al. (13) demonstrated in animal experiments that autoxidized limonene was an allergen. In the same publication, they referred to the concentration of d-limonene in perfumes and household products described in a publication from 1975 (14). At that time, the concentration of d-limonene was found to be low in this type of prod-

ucts (below 0.03% in detergents). Our analyses of 59 domestic and occupational products support the view of Karlberg et al. (13), that this has changed in recent decades. It seems that the industrial use of limonene has increased because of the pressure to replace chlorinated hydrocarbons, chlorofluorocarbons (CFC) and other organic solvents with less hazardous substances.

Geraniol ranked number 4 in frequency (41%) and had a mean concentration value of 234.4 ppm (Table 2). Comparison of this finding with previously published GC-MS analyses of 73 deodorants, 23 various cosmetic products and 10 best selling perfumes does not show a clear difference (5, 15, 6). However, it appears that the frequency of geraniol is higher in cosmetic products than household products. The frequency of geraniol in these studies was 53/73 (70%), 12/23 (52%) and 9/10 (90%) respectively. Mean concentrations were reported in the 2 last mentioned studies and they were 5 to 10 $\times$ higher than in domestic and occupational products. The result of this comparison does not reject the hypothesis that household products in most cases contain other fragrance chemicals than cosmetic products.

The above analyses of 73 deodorants, 23 cosmetics and 10 perfumes also described the levels of eugenol, hydroxycitronellal and isoeugenol (5, 15, 6), giving the following frequencies: eugenol was found in 40/73 (55%) deodorants, in 17/23 (74%) of cosmetics, and in 9/10 (90%) of perfumes; hydroxycitronellal was found in 35/73 (48%) deodorants, in 20/23 (87%) cosmetics and in 9/10 (90%) of perfumes; isoeugenol was found in 20/73 (27%) deodorants, in 6/23 (26%) cosmetics, and in 7/10 (70%) of perfumes. In the present study, we found eugenol in 27% of the household products, hydroxycitronellal in 12% of the household products and isoeugenol in 5% of the household products (Table 3). Thus, the frequency of eugenol, hydroxycitronellal, and isoeugenol was much higher in the cosmetic products than in household products.

The demonstration that known allergens are present in relatively high concentrations in a large number of household products with hand contact means that the consumers are exposed to these allergens. The prevalence of allergy to these fragrances in hand eczema patients need to be studied to clarify a possible lack of diagnostic tools. However, a number of other variables, such as the use concentration of the product, the frequency of the exposure and the individual(s) exposed, have to be taken into account when performing a risk assessment on the fragrance allergens identified.

Patch testing is an important diagnostic tool in the evaluation of allergic contact dermatitis. Most European dermatologists use the FM when diag-

nosing fragrance allergy. According to our chemical analyses of domestic and occupational products (Tables 1, 2) most of the FM ingredients were relatively infrequent ingredients when compared to other fragrance allergens. This finding suggests the possibility of diagnostic failures, as patch testing may not be undertaken with the most appropriate fragrance allergens for the type of products we have examined. This may be especially important to patients with hand eczema, who are exposed to these domestic and occupational products.

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