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The presence of fragrance allergens in scented consumer products

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RIVM letter report 340301002/2009

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Contents

1 Background

There are several products on the market that contain fragrance chemicals, for example personal health care products (perfumes, creams, shampoos, toothpaste) and household products (room fresheners, cleaning products, detergents). Many different fragrance chemicals are used in these consumer products and for some fragrances it is known that they can cause contact dermatitis after skin contact. Approximately 1-3% of the general population suffer from this type of allergy (Nielsen & Menne, 1992; Mortz et al., 2001; Nielsen et al., 2002; Dotterud, 2007; Dotterud & Smith-Sivertsen, 2007). In 1999 the EU Scientific Committee on Consumer and Non Food Products (SCCNFP, now known as the SCCS) has identified 24 fragrance chemicals that potentially could cause contact dermatitis. Of these fragrances, 13 are well-recognized contact allergens, whereas 11 are less well documented as contact allergens (SCCNFP, 1999) (summarized in Annex 1).Two botanical extracts, oak moss and tree moss, have been added to this list of 24 allergenic fragrances. According to EU legislation, labelling of these 26 fragrance allergens is mandatory when they are present in cosmetics (EU Directive 2003/15/EC, 2003).

Fragrances are not only present in cosmetics, such as creams and perfumes, but they are also used as ingredients in scented products intended to spread a pleasant smell in homes, cars and public buildings, i.e. room perfumes and air fresheners (Park et al., 2006). The exposure to fragrances in these products will be predominantly via inhalation, although dermal exposure to these products is possible as well. It is unknown if inhalation of fragrance allergens can lead to sensitization and subsequent induction of allergic symptoms in the respiratory tract. There are indications from an occupational setting that this is possible. A case report of a hairdresser describes the occurrence of occupational asthma caused by inhalation exposure to eugenol (Quirce et al., 2008). However, it is unknown if inhalation exposure to fragrance allergens present in consumer products can lead to respiratory allergies as well.

Within its responsibility to protect the safety of consumer products, the Dutch Food and Consumer Product Safety Authority (VWA) has initiated an project to gain more insight in the risks associated with the use of scented products. This project ultimately aims at developing a risk assessment strategy for these types of products. One important pillar for risk assessment is exposure assessment. This letter report will focus on this aspect. To gain insight in inhalation exposure to the 26 fragrance allergens a product inventory has been made of scented consumer products on the European market containing one or more of these fragrances.

2 Approach

For determination of the presence and concentrations of 26 allergenic fragrances in various products on the European market, different approaches were followed.

- Information on the fragrance products in scented products currently available on the Dutch market was obtained from the NVIC (Dutch National Poison Control Centre) database. The NVIC database contains information that was voluntarily provided by the manufacturer of the products. The list contains the names and CAS numbers of scented products for which inhalation exposure is likely to occur, together with ingredients and fractions of these ingredients. The database was searched for the 26 fragrance allergens by using their CAS numbers.
- The other source of information of this section is the website of Sara Lee (http://www.saralee-int.info/NL-NL/Our+Brands/AmbiPur). To our knowledge, Sara Lee is the only manufacturer of scented products with ingredient lists on their website.
- The information from the RIVM report “Allergens in consumer products” of Wijnhoven et al, (2008) was used to identify additional information from European market surveys, conducted in the last 10 years. Information of scented products from these BEUC (The European Consumers Organisation) and Danish EPA market surveys are reported in the current product inventory.
- Also Google and Scopus searches were performed with the following terms: scented products, fragrances, air fresheners etc. Unfortunately, this was without any useful result. Some Material Safety Data Sheets (MSDS) were found of scented products on the internet, however, no information on concentrations of the 26 allergenic fragrances was found in these sheets. In addition, websites of manufacturers of fragrances were found (for instance Givaudan), but these websites did not contain information on the type of products these fragrances were intended for.

3 Results

3.1 Fragrance allergens in scented products available on the Dutch market

Two databases were used to obtain information on the presence of fragrance allergens in scented products that can be purchased in the Netherlands. The data from the NVIC database are summarized in Table 1 and the publicly available data from Sara Lee (http://www.saralee-int.info/NL-NL/Our+Brands/AmbiPur) are summarized in Table 2.

Table 1 NVIC database: fragrances used in scented products

Fragrances n =	% in all scented products 113
Geraniol	54%
Linalool	46%
Citronellol	42.5%
D-limonene	38.1%
Eugenol	37.2%
Lilial*	34.5%
Citral	32.7%
Hexyl cinnamal	20.4%
Benzyl salicylate	19.5%
Coumarin	19.5%
Lyral*	17.7%
Benzyl benzoate	13.3%
α-Isomethylionon	13.3%
Hydroxycitronellal	12.4%
Benzyl alcohol	11.5%
Cinnamyl alcohol	9.7%
Isoeugenol	8.0%
Amyl cinnamal	6.2%
Cinnamal	5.3%
Farnesol	3.5%
Benzyl cinnamate	2.6%
Oak moss	0.9%
Anisyl alcohol	0%
Amylcinnamyl alcohol	0%
Methyl heptine carbonate	0%
Tree moss	0%

* INCI names Lilial: butylphenyl methylpropional and Lyral: hydroxyisohexyl-3-cyclohexene carboxaldehyde

The NVIC database contained 113 scented products. Of these, 48 were air freshners and room perfurmes and the other products were intended for steam baths or saunas. The NVIC data show that the most frequently used fragrances in scented products (>40% of the products) were geraniol, linalool and citronellol. Almost all fragrance allergens from the SCCP list are used as ingredients in the

products, with the exception of anisyl alcohol, amyl cinnamyl alcohol, methyl heptine carbonate and tree moss. The fragrances cinnamyl alcohol, isoeugenol, amyl cinnamal, cinnamal, farnesol, benzyl cinnamate and oak moss were not frequently used (<10% of the products) in these scented products.

Table 2 Most frequently used fragrances in scented products[1]

Fragrances	% in all scented products	% in scented car products	% in sprays	% in electrical room perfumes	% in scented candles
n =	*49*	*12*	*15*	*18*	*4*
D-limonene	69.4%	83.3%	46.7%	77.8%	75%
Linalool	69.4%	83.3%	40%	83.3%	75%
Geraniol	53.1%	66.7%	13.3%	77.8%	50%
Citronellol	49%	41.7%	20%	77.8%	0%
α-Isomethylionon	42.9%	50%	13.3%	72.2%	0%
Citral	36.7%	50%	6.7%	61.1%	0%
Eugenol	32.7%	41.7%	0%	50%	50%
Benzyl alcohol	26.5%	0%	0%	66.7%	25%
Coumarin	26.5%	33.3%	6.7%	38.9%	25%
Benzyl benzoate	24.5%	16.7%	0%	44.4%	50%
Benzyl salicylate	22.4%	8.3%	13.3%	38.9%	25%
Hydroxycitronellal	20.4%	16.7%	6.7%	33.3%	25%
Lillial*	16.3%	8.3%	0%	38.9%	0%
Hexyl cinnamal	16.3%	0%	20%	27.8%	0%
Lyral*	16.3%	16.7%	0%	27.8%	25%
Cinnamyl alcohol	10.2%	8.3%	0%	22.2%	0%
Cinnamal	8.2%	8.3%	0%	11.1%	25%
Isoeugenol	6.1%	0%	0%	16.7%	0%
Amyl cinnamal	2.0%	0%	0%	11.1%	0%
Farnesol	2%	0%	0%	5.5%	0%
Anisyl alcohol	0%	0%	0%	0%	0%
Amyl cinnamyl alcohol	0%	0%	0%	0%	0%
Benzyl cinnamate	0%	0%	0%	0%	0%
Methyl heptine carbonate	0%	0%	0%	0%	0%
Oak moss	0%	0%	0%	0%	0%
Tree moss	0%	0%	0%	0%	0%

[1] Data are derived from the website of Sara Lee (http://www.saralee-int.info/NL-NL/Our+Brands/AmbiPur) * INCI names Lilial: butylphenyl methylpropional and Lyral: hydroxyisohexyl-3-cyclohexene carboxaldehyde

The Sara Lee database contained 49 scented products. When all scented products were analyzed, it was shown that the most frequently used fragrances (present in >40% of the products) were limonene, linalool, geraniol, citronellol and α-isomethylionon. The fragrances anisyl alcohol, amyl cinnamyl alcohol, benzyl cinnamate, methyl heptine carbonate, oak moss and tree moss were never used as ingredients in these products.

When the different product types were analyzed, it was shown that the distribution of the most frequently fragrances differed slightly between the products. For instance in scented products that were intended for cars, the most frequently used fragrances were similar to those in all products, but in addition citral en eugenol were found in 50% of the car products. Furthermore, 9 of the 24 fragrances

were not used in car products and two car products were free from fragrance allergens. Remarkably, the distribution in sprays is very different from the other scented products. In sprays, limonene and linalool were used frequently, whereas other fragrances were only found in a limited number of products ≤ 20%). Furthermore, 16 of the 26 fragrance allergens were never reported to be used in sprays. One difference is that in sprays only a few fragrances were used per product and two sprays were free of allergens. In contrast, in electrical room perfumes the individual products contained many different fragrances per product. There was one product that even contained 15 of the 26 fragrance allergens. In electrical room perfumes the most frequently used fragrances were linalool, limonene, geraniol, citronellol, α-isomethylionon, benzyl alcohol and eugenol. The fragrances anisyl alcohol, amyl cinnamyl alcohol, benzyl cinnamate, methyl heptine carbonate, oak moss and tree moss were not used as ingredients in electrical room perfumes. Finally, in scented candles the most often used fragrances were limonene, linalool, geraniol and eugenol. Of the 26 fragrance allergens, only 11 were used in candles (n=4).

3.2 Fragrance allergens in scented products: results from market surveys

Table 3 summarizes the data from a study from the European Consumers Organisation (BEUC). They have measured emission levels of different chemicals, including 11 fragrances, from 74 air fresheners in indoor air (BEUC, 2005). The most often detected fragrance was D-limonene and emissions ranged from 1 – 2003 μg/m^3. In almost 28% of the tested air fresheners, emission of linalool was detected, and concentrations ranged from 5-750 μg/m^3. The other fragrances that were detected but in a limited number of products were: lilial, cinnamal, coumarin, citral, benzyl benzoate, eugenol, benzyl alchohol, hydroxycitronellal and geraniol.

Table 3 Fragrance emission by air fresheners

Fragrances n =	% in all products 74	Emissions (μg/m^3)
D-limonene	88.1%	1 – 2003
Linalool	27.6%	5 – 750
Lilial*	13.2%	2 – 310
Cinnamal	6.5%	3 – 146
Coumarin	5.3%	4 – 22
Citral	2.6%	2 – 48
Benzyl benzoate	1.3%	9
Eugenol	1.3%	16
Benzyl alcohol	1.3%	22
Hydroxycitronellal	1.3%	51
Geraniol	1.3%	40

Data are derived from an European study from the BEUC (2005)* INCI names Lilial: butylphenyl methylpropional and Lyral: hydroxyisohexyl-3-cyclohexene carboxaldehyde.

The Danish Environmental Protection Agency (EPA) has performed a market survey in different stores and supermarkets that sell air fresheners for the home and the car (Pors & Fuhlendorff, 2003). A total of 19 products were selected and 6 of these were car products and 13 were products for use at home. In these products the presence and concentrations of 24 fragrance allergens were measured. The presence of oak moss and tree moss was not assessed in this study.

In Table 4, the results are summarized and the most frequently used fragrances (in >50% of the products) were D-limonene, linalool, benzyl benzoate, hexyl cinnamal, eugenol, lilial, benzyl alchohol and benzy salicylate. When the products intended for use at home or in the car were analyzed separately, the distribution shifted slightly. In products for at home 22 of the 24 fragrance allergens were used, with the exception of anisyl alcohol and farnesol. In car products, 5 of the 24 fragrance allergens were not used, these products contained no anisyl alcohol, farnesol, benzyl cinnamate, methyl heptine carbonate, and isoeugenol.

In this study, the concentrations of the fragrances were measured as well. There was a large variation when the individual products were analyzed. In addition, some fragrance chemicals were used in higher concentrations than others. In general, cinnamal, isoeugenol, amyl cinnamal alcohol and methyl heptine carbonate were used in the lowest concentrations. The fragrances that were used in the highest concentrations were (in weight % of a product) : lyral (6.2%), linalool (3.9%), citral (2.6%), hexyl cinnamal (2.2%), and D-limonene (2.1%).

Table 4 Most frequently used fragrances in air freshners from a Danish market survey

Fragrances	% in all products	Concentration range (ppm)	% in all products for at home	% in all car products
n =	19		13	6
D-limonene	78.9%	41 – 21,000	84.6%	80%
Linalool	78.9%	970 – 39,000	84.6%	80%
Benzyl benzoate	68.4%	7.7 – 10,000	61.5%	100%
Hexyl cinnamal	68.4%	39 – 22,000	69.2%	80%
Eugenol	63.2%	11 – 9,000	61.5%	80%
Lilial*	57.9%	450 – 12,000	61.5%	60%
Benzyl alcohol	52.6%	7.7 – 10,000	53.9%	60%
Benzyl salicylate	52.6%	4.1 – 13,000	46.2%	80%
Citronellol	52.6%	190 – 18,000	61.5%	40%
α-Isomethylionon	52.6%	220 – 11,000	61.5%	40%
Coumarin	47.4%	15 – 13,000	46.2%	60%
Lyral*	47.4%	310 – 62,000	53.9%	40%
Geraniol	42.1%	390 – 8,900	46.2%	40%
Citral	36.8%	200 – 26,000	38.5%	40%
Amyl cinnamal	26.3%	640 – 16,000	15.4%	60%
Hydroxycitronellal	26.3%	440 – 2,600	23.1%	40%
Cinnamal	15.8%	10 – 63	15.4%	20%
Isoeugenol	15.8%	23 – 120	23.1%	0%
Methyl heptine carbonate	15.8%	3.5 – 270	23.1%	0%
Benzyl cinnamate	10.5%	170 – 500	15.4%	0%
Cinnamyl alcohol	10.5%	19 – 230	7.7%	20%
Amylcinnamyl alcohol	5.3%	17 – 50	7.7%	0%
Anisyl alcohol	0%	--	0%	0%
Farnesol	0%	--	0%	0%
Oak moss	NA			
Tree moss	NA			

Data are derived from market survey conducted by the Danish EPA (Pors and Fuhlendorff, 2003)* INCI names Lilial: butylphenyl methylpropional and Lyral: hydroxyisohexyl-3-cyclohexene carboxaldehyde. NA: not assessed.

4 Summary

This letter report provides information on the use of 26 fragrance allergens that are known as contact allergens, in scented products.

- In scented products that are available on the Dutch market the majority of the 26 fragrances are used as ingredients. Anisyl alcohol, amyl cinnamyl alcohol, methyl heptine carbonate, and tree moss were not used as ingredients.

- In the Danish market survey it was shown that anisyl alcohol and farnesol could not be detected in any of the scented products. In this study, the presence of the botanical extracts oak moss and tree moss was not assessed.

- There are some differences in the most frequently used fragrances per product type, but in general it can be concluded that the most frequently used fragrances in products for the Dutch market are D-limonene, linalool, geraniol, and citronellol. Fragrance allergens that are less frequently used in scented products are benzyl cinnamate, cinnamyl alcohol, cinnamal, isoeugenol, methyl heptine carbonate and oak moss

- The most frequently used fragrances in the Danish market survey were also D-limonene and linalool. In addition, benzyl benzoate, hexyl cinnamal and eugenol were detected in the majority of Danish products. Apparently, some differences exist between the products on the Dutch and the Danish market. However, it should be noted that the number of products in the Danish study was much lower than in the two Dutch databases, which might explain the differences.

- The Danish EPA study provides data on the levels of fragrances that are present in these products and shows that large differences exist, dependent on the product and the fragrance. The lowest levels were found for amyl cinnamyl alcohol, cinnamyl alcohol, cinnamal, isoeugenol, methyl heptine carbonate, benzyl cinnamate. The highest levels were found for lyral, linalool, citral, hexyl cinnamal and D-limonene.

- The BEUC study measured emissions and shows that D-limonene is emitted from the majority of scented products. Other fragrances that were emitted, but by much less products, were linalool, lilial, cinnamal, coumarin and citral. Only a few products emitted detectable levels of benzyl benzoate, eugenol, benzyl alcohol, hydroxitronellal and geraniol.

5 Conclusion

From this product inventory it can be concluded that exposure to fragrance allergens via inhalation is possible for the majority of the 26 fragrances listed by the SCCS. The most frequently used fragrances in scented products are also frequently used as ingredients in other consumer products, for example in cosmetics, i.e. D-limonene, linalool, lilial and geraniol. The potency of these fragrances to induce contact dermatitis is weak and although they are present in many consumer products, these fragrances do not often cause contact dermatitis. The product inventory also shows that strong and moderate skin sensitizers, such as isoeugenol, methyl heptine carbonate and cinnamal, are not frequently used as ingredients in scented products. These fragrances are also not often used in cosmetics, but for instance isoeugenol and cinnamal are important contact allergens. Hence, the skin sensitizing potency is an important determinant in the risk on developing contact dermatitis.

It is currently unknown whether skin sensitizing potency can be used to predict the hazard on respiratory sensitization. In this project, experiments have been performed to assess the hazard of inhalation of fragrances; these data will be published separately this year. Furthermore, in this project it will be investigated in experimental animal models, if inhalation of fragrance allergens can induce respiratory allergic manifestations in people with an existing fragrance allergy, due to skin contact. Ultimately, the information on hazard identification and human exposure will be used to develop a strategy to evaluate the risk of scented consumer products.

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Annex 1: Overview of fragrances identified by the SCCNFP[1]

Fragrances - most frequently reported as consumer allergens

Common name	CAS no
Amyl cinnamal	122-40-7
Amylcinnamyl alcohol	101-85-9
Benzyl alcohol	100-51-6
Benzyl salicylate	118-58-1
Cinnamyl alcohol	104-54-1
Cinnamal	104-55-2
Citral	5392-40-5
Coumarin	91-64-5
Eugenol	97-53-0
Geraniol	106-24-1
Hydroxycitronellal	107-75-5
Hydroxymethylpentyl-cyclohexenecarboxaldehyde (HMPCC)	31906-04-4
Isoeugenol	97-54-1

Fragrances - Less frequently reported as consumer allergens

Common name	CAS no
Anisyl alcohol	105-13-5
Benzyl benzoate	120-51-4
Benzyl cinnamate	103-41-3
Citronellol	106-22-9
Farnesol	4602-84-0
Hexyl cinnamaldehyde	101-86-0
Lilial	80-54-6
d-Limonene	5989-27-5
Linalool	78-70-6
Methyl heptine carbonate	111-12-6
3-Methyl-4-(2,6,6-trimethyl-2-cyclohexe-1-yl)-3-buten-2-one (= γ-methylionone)	127-51-5

[1] SCCNFP (1999) Opinion concerning fragrance allergy in consumers. SCCNFP/0017/98.

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