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Fragrance Allergens in detergents



Fragrance allergens in household detergents

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Abstract

Consumers are confronted with a large number of fragrance allergens from various sources. Until now, the discussion of exposure sources has mainly addressed cosmetic products and neglected other scented products in households. For the first time, fragrance allergens were evaluated in a complete set of detergents in households. In 131 households, we investigated the prevalence of detergents and searched their lists of ingredients for 26 fragrance allergens liable to be indicated on products according to the European Detergents Regulations. On the ingredient lists of 1 447 products, these 26 fragrance substances were named almost 2 000 times, most often limonene, linalool and hexyl cinnamal. Benzyl salicylate was used frequently in all-purpose cleaners. Linalool and limonene, hexyl cinnamal and butylphenyl methylpropional and citronellol and linalool co-occurred most often together in products. Fragrance allergens co-occurring together most frequently within households were eugenol, coumarin and cinnamyl alcohol. The study shows that detergents could play a relevant role for the exposure of consumers towards fragrance allergens and that they should not be underestimated as an exposure source during the exposure assessment.

Keywords

Aggregated exposure; co-exposure, contact allergy; detergents; fragrance allergens; product inventory; washing and cleaning agents

Highlights

- Product inventories were established for 131 households in 3 neighbourhoods.
- Inventories include all detergents (washing and cleaning agents).
- Lists of ingredients were searched for 26 fragrance allergens.
- Citronellol and linalool show the highest similarity of occurrence within products.
- Eugenol, coumarin, cinnamyl alc. show highest occurrence similarity in households.

1. Introduction

1.1 Allergy to fragrance substances in washing and cleaning agents

For contact allergy, fragrance substances belong to the major culprits (Schnuch and Mahler, 2015). A recent study in various geographic European regions came to the conclusion that 5 % of the general population reacted to any of the fragrance allergens (Diepgen et al., 2016). In the United States, prevalence of contact allergy to the fragrance mix I is even slightly higher than in Europe (Groot and Maibach, 2010).

Detergents are already under discussion as an exposure source for some substance groups associated with contact allergy, such as isothiazolinones used as preservatives (Ezendam et al., 2018; Gallo et al., 2016; Garcia-Hidalgo et al., 2017). They should not contain more than 2.5 % (w/w) of a fragrance, this international maximum level can be lowered based on the results obtained by quantitative risk assessment (IFRA, 2015). However, up to now, most exposure models used for risk assessments for consumers only consider cosmetic products as a possible exposure source and neglect the other sources, underestimating the real exposure to fragrance allergens (IDEA, 2016; Safford et al., 2017). Existing studies on fragrance allergens in detergents are describing the allergy risk from the exposure, e.g. through laundered fabric, as very low (Basketter et al., 2010; Corea et al., 2006; German Cosmetic, Toiletry, Perfumery and Detergent Association, 2016). Contact dermatitis through laundry detergents seems to be rare (Belsito et al., 2002). However, for certain users the exposure to fragrance allergens can indeed be mainly driven by the use of detergents (Nijkamp et al., 2015).

Even if household detergents might in general play a minor role for the induction of fragrance allergy, they can be relevant in the elicitation in already sensitized persons (Basketter et al., 2015) besides contributing to the aggregated exposure (Nijkamp et al., 2015). For this reason, the improvement of the assessment of aggregated exposure is an important approach to reduce the frequency of contact allergy further (Basketter and Safford, 2016; Peiser et al., 2012). Cross-reactions and co-exposures can aggravate the allergic reactions to fragrance allergens (Effendy and Maibach, 1995; Geier et al., 2012; Heydorn et al., 2003; Jacob and Amini, 2008; Schnuch et al., 2007). This enhanced sensitization due to the simultaneous exposure to mixtures of fragrances, which has been reported for cosmetics (Uter et al., 2013b), is relevant for detergents as well.

Consumers' daily exposure to fragrance allergens results from the multitude of scented products in their households (Dodson et al., 2012; Park et al., 2006; Rastogi et al., 2001) and from other applications (e.g. limonene is used as solvent in many products). In addition, exposure to fragrance allergens may be increased considerably by occupational exposure (Buckley et al., 2002; Uter et al., 2001). Further factors such as chemical transformation (e.g. by oxidation) into stronger allergens or new molecules of often unknown properties and individual use practices can increase the risk of allergy further (Bråred Christensson et al., 2016; Niu et al., 2017; Rossignol et al., 2013).

1.2 Legal situation

In Europe, manufacturers are responsible for the safety of their products according to the Regulation (EC) 648/2004 on detergents (European Union, 2004). Twenty-six individual fragrance allergens must be listed with their INCI names (International Nomenclature of Cosmetic Ingredients) on the detergents containers if their concentrations exceed 0.01 % in the products (European Union, 2004). This labelling requirement is based on the Regulation (EC) 648/2004 on detergents, referring to the Regulation (EC) No 1223/2009 on cosmetic products (European Union, 2009). It is only applicable if the 26 fragrance allergens are added as single substances and does not apply if they are part of natural extracts or the like. All other fragrances are summarized under the term 'perfume' or similar wording, including concentrations below 0.01% of those fragrances that must be declared by INCI name above this concentration limit. Many other important fragrance allergens are known, and since several years it has been under debate whether the list of the 26 fragrance allergens to be declared should be extended (SCCS, 2012; Uter et al., 2013a). The regulation defines maximum concentrations only for certain fragrance allergens, there are no general concentration limits.

In other countries, such as Australia, there is no legal obligation to disclose fragrances on detergents, only voluntary initiatives from industry exist (Lunny et al., 2017). In the United States, labelling requirements for detergents are only starting to be implemented on State level. The Californian Cleaning Product Right to Know Act of

2017 directly refers to the labelling requirements for fragrance allergens laid down in the European regulations on cosmetics and detergents (State of California, 2017).

1.3 Objectives

The study evaluates fragrance allergens in a set of detergents present in households, covering a large number of single products. The aim is to analyze detergents as a further exposure source of fragrance allergens. This could help in identifying sources of fragrance allergens and minimizing consumers' exposure to them. Special emphasis is laid on the exposure to combinations of different fragrance allergens due the occurrence of two or more fragrance allergens in products and households (co-occurrence).

2. Methods

In this study, product inventories, which were collected as described in Wieck et al. (Wieck et al., 2016), were used to evaluate the presence of fragrance allergens in a large range of detergents. The product inventories included all types of detergents present in the households, for example including all-purpose cleaners, cleaning preparations for special purposes (e.g. bathroom, kitchen, dish-washing) and laundry detergents.

2.1 Study site

Members of 131 private households in Northern Germany were interviewed and product inventories were collected. The households were situated in three different neighborhoods, representing the three different urban–rural typologies in Europe:

predominantly urban, intermediate and predominantly rural regions (BBSR, 2009). In the rural neighborhood, 145 households were approached by letter supported by the mayor of the village. This letter contained information regarding the project and the planned study. The interviews were conducted from March until May 2015. Households were contacted several times during this period and only one member of each households was asked to answer the questions. In this neighborhood, members of 94 households (65 %) took part in this survey. In the intermediate neighbourhood, 80 households were approached by a letter of the Leuphana University of Lüneburg, containing information regarding the project and the planned study. The interviews were conducted from July until August 2015. Nineteen households took part in this study. In the urban neighborhood, a notice of the Leuphana University of Lüneburg containing information regarding the project and the planned study was displayed in multi-family homes. Twenty households took part in this neighborhood. In these latter two neighborhoods, a convenience sampling strategy was used. This type of sampling strategy is based on the willingness of potential participants to take part in the study (Robinson, 2014). An overview over the demographic characteristics is presented in Table 1. More details on the neighborhoods and the demographic characteristics of the households can be found in Wieck et al. (2016).

Table 1: Demographic characteristics of those 131 households in Northern Germany, where the product inventories were taken in 2015 (Wieck et al., 2016, modified).

	n	%
Household members ^a		
1 adult	27	20,3

2 adults	51	38,3
3 adults	13	9,8
2 adults, 1 child	19	14,3
2 adults, 2 children	4	3,0
2 adults, 3 children	3	2,3
Other	14	10,5
Time in school until graduation ^b		
Without graduation	3	2.3
Graduation after 9 years of education	35	26.7
Graduation after 10 years of education	34	26.0
Graduation after ≥ 12 years of education	52	39.7
Other	5	3.8
Not specified	2	1.5
Professional education ^{b,c}		
No job training (yet)	11	8.4
Apprenticeship	91	69.5
Foreman or similar	12	9.2
University degree	43	32.8
Other	1	0.8
Not specified	3	2.3
Total net household income per month		
< 850 €	9	6.9
851 – 1 500 €	17	13.0
1 501 – 2 000 €	15	11.5
2 001 – 3 000 €	26	19.8
3 001 – 4 000 €	30	22.9
4 001 – 5 000 €	10	7.6
5 001 – 6 000 €	7	5.3
> 6 000 €	7	5.3
Not specified	10	7.6

^a Children: household members < 18 years

^b Of the household member with the highest income

^c Multiple selections possible

2.2 Data collection and analysis

The detergents present in the households were registered with barcode scanners as described in Wieck et al. (2016). All detergents present in the households were registered, including e.g. dish-washing liquids, all-purpose cleaners, textile detergents, toilet cleaners, glass cleaners, detergents for dish-washing machines, scouring agents and other detergents for special purposes. The barcodes were used to identify the products and their ingredients by using the public database www.codecheck.info. A similar approach has already been used for cosmetics in the Danish market (Bennike et al., 2018). The Swiss database "Codecheck" contains information on the ingredients of more than 40 000 products using data that is provided and kept up-to-date by users (Codecheck, 2018). The search system for products is based on barcodes. The 26 fragrance allergens legally required to be disclosed on the ingredient lists of detergents were compiled based on the results from this database (Figure 1). Several spellings and alternative names of the fragrance allergens were used to search the data because the entries are maintained by consumers and writing errors are likely to occur. For example, the exact declaration of limonene in the database was variable. As most listings did not specify the specific isomers of limonene. We summarized all entries under 'limonene'. In this publication, official INCI names of fragrance substances are used as recommended by the 'Scientific Committee on Cosmetic Products and Non-food products intended for Consumers' (SCCNFP, 2000). In addition, it was evaluated whether the product contained 'perfume', 'fragrances', 'aroma' or similar wording.

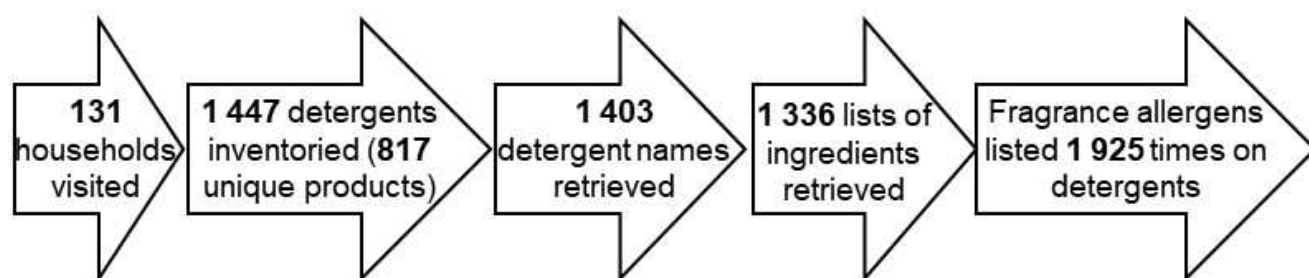


Figure 1: Flowchart presenting the data collection to identify the fragrance allergens in detergents in households in Northern Germany in 2015.

Data was analyzed using IBM SPSS Statistics 24.0.0.0 (IBM, Armonk, USA). To analyze the co-occurrence of fragrance allergens in products and households, we used hierarchical clustering. For the analysis of co-occurrence in products, we used complete linkage and Dice measure, for the analysis of the co-occurrence of fragrance allergens in households we used average linkage and Squared Euclidean Distance measure. This was only possible for the frequently occurring fragrances. Fragrances occurring in less than 20 products were not included in the cluster analysis.

3. Results

In the households, 1 447 detergents were scanned in total. Among them were 817 unique barcodes as the same products have been inventoried in several households. Duplicates were removed for the discussion of the presence of fragrance allergens in detergents ($n = 817$). The complete dataset was used for the discussion of fragrance allergens in households ($n = 1\,447$).

3.1 Fragrance allergens in detergents

Limonene (23.1 %), linalool (20.1 %), hexyl cinnamal (14.8 %) and butylphenyl methylpropional (14.7 %) were listed most often on the unique scanned detergents (Figure 2, n = 817). Looking at the different types of detergents, limonene and linalool are the most frequently listed fragrance allergens for all types, except for all-purpose cleaners. Benzyl salicylate was listed most often on these detergents. For dish-washing liquids (hand and machine) and toilet and glass cleaners, hexyl cinnamal was the fragrance allergen listed third. Butylphenyl methylpropional was listed third most often on textile detergents and citronellol on glass cleaners and scouring agents.

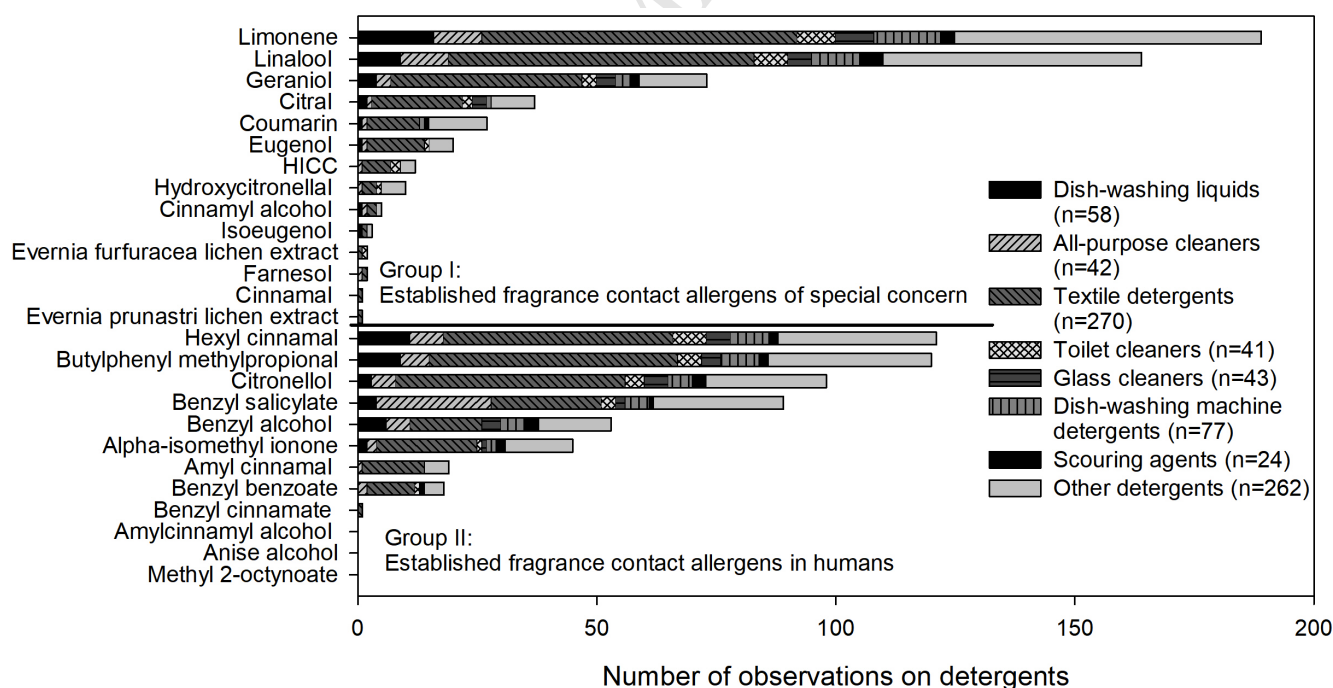


Figure 2: The 26 fragrance allergens to be named on detergents in the EU and their appearance on lists of ingredients on detergents (n=817). The substances are grouped by the categorization of established contact allergens in humans. Group I includes the established fragrance contact allergens of special concern due to the high number of reported cases, group II includes other established contact

allergens in humans (Uter et al., 2013a). HICC: Hydroxyisohexyl 3-cyclohexene carboxaldehyde.

Detailed data can be found in the supplementary material.

The average number of the 26 fragrance allergens per product was 1.4, the maximum number of fragrance allergens on a single product label being 8 substances (Table 2).

The detergent group containing the highest share of products listing fragrance allergens were textile detergents and toilet cleaners. The average number of fragrance allergens per product is highest for textile detergents and all-purpose cleaners. Detergents listing the least fragrance allergens on average were detergents used in dishwashing machines.

Table 2: The total number of unique products, the products containing fragrance allergens and the average number of fragrance allergens per product for the different detergent types (n = 817)

	Total number of unique products	Products containing fragrance allergens		Average number of fragrance allergens per product
	[n]	[n]	[%]	[n]
Dish-washing liquids	58	28	47.5	1.2
All-purpose cleaners	42	20	47.6	1.6
Textile detergents	270	135	50.0	1.7
Toilet cleaners	41	20	48.8	1.2
Glass cleaners	43	14	32.6	1.0
Dishwashing machine detergents	77	26	33.8	0.9
Scouring agents	24	8	33.3	1.0
Other detergents	262	114	43.7	1.2

Looking at the co-occurrence of fragrance allergens, hexyl cinnamal and butylphenyl methylpropional next to citronellol and linalool showed the most similar use patterns of all detergents (n = 817, Figure 3). Hexyl cinnamal and butylphenyl methylpropional also often appear together with benzyl salicylate and benzyl alcohol. Citronellol and

linalool often appear in combination with limonene and citral (see also supplementary material for a cross table).

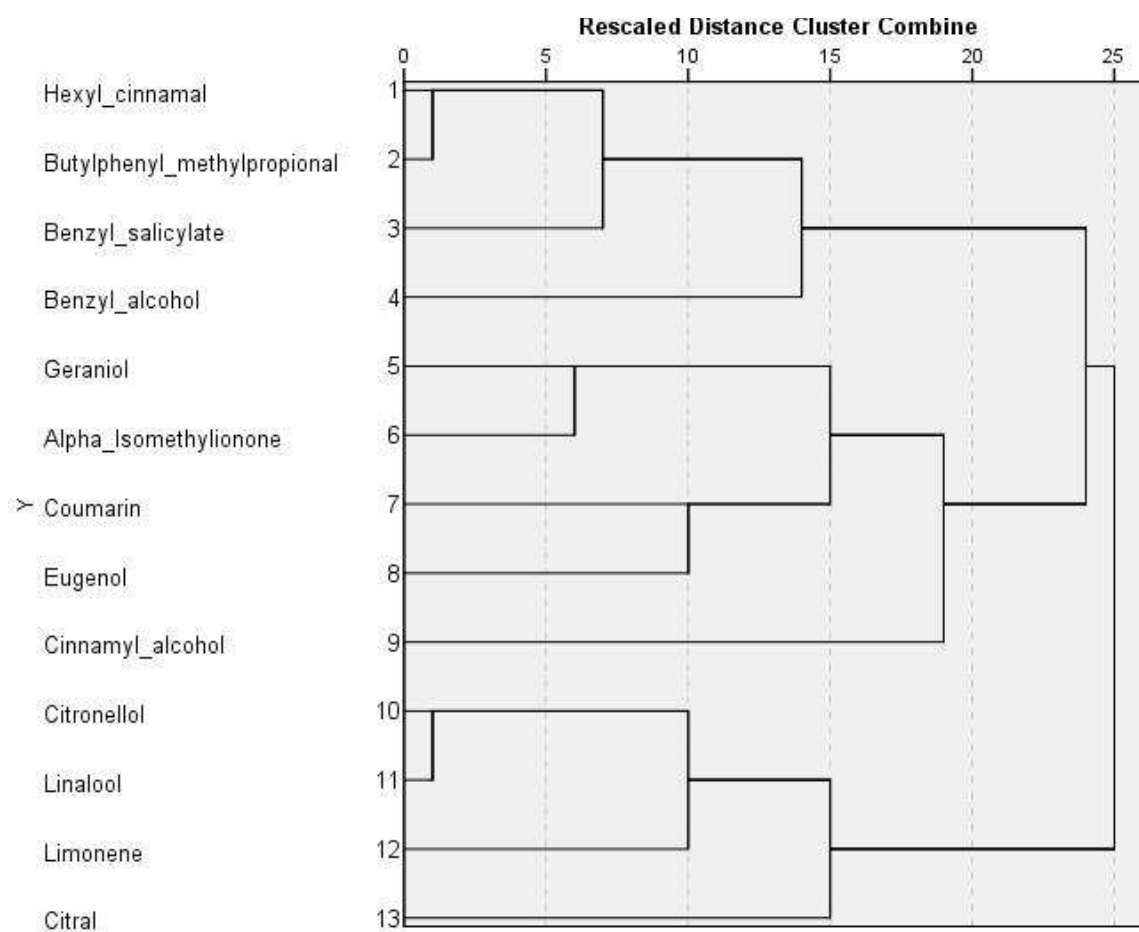


Figure 3: Dendrogram (complete linkage, Dice measure) showing the co-occurrence of those fragrance allergens that were listed on more than 20 products (n = 817).

3.2 Fragrance allergens in households

In 131 households, 1 447 detergents were inventoried. The 26 selected fragrances were named 1 925 times on their lists of ingredients (n=1 447 products). 46 % of the 1 447 products listed at least one of the 26 fragrance allergens on their ingredient lists, 60 % listed 'perfume' or the like.

The co-occurrence of fragrance allergens in the households was analyzed. For this analysis, all fragrance allergens that were listed on the detergents scanned were summed up per household (see also supplementary material for a cross table). Figure 4 shows that products listing eugenol, coumarin and cinnamyl alcohol often are present together in one household. Also, the co-occurrence within a household of the fragrances geraniol and citronellol or alpha-isomethyl ionone and benzyl salicylate was often seen.

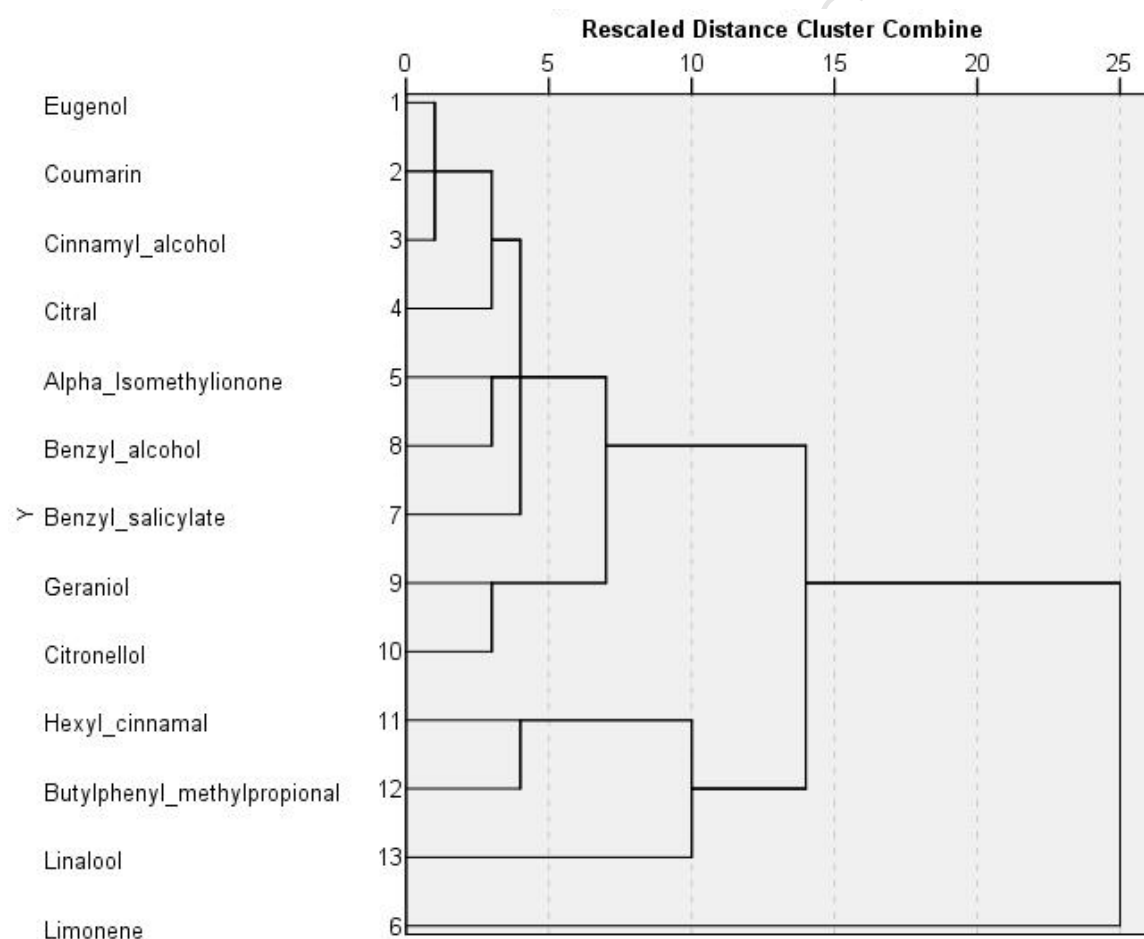


Figure 4: Dendrogram (average linkage, Squared Euclidean Distance measure) showing the co-occurrence within households of those fragrance allergens that were listed on more than 20 products (n = 1 447).

4. Discussion

4.1 Listed fragrance allergens on detergents

The study shows the widespread use of fragrances and fragrance allergens in household detergents. Limonene and linalool were listed most often on the labels of detergents (Figure 2). They belong to the established fragrance contact allergens of special concern in their oxidized form (Uter et al., 2013a). Hexyl cinnamal and butylphenyl methylpropional were also listed frequently. Both belong to the group of established fragrance contact allergens in humans, although they are associated with a low frequency of incidence of contact allergy. A high occurrence combined with lower sensitization rates may indicate a lower potential of sensitization associated with these substances (Schnuch et al., 2015). During the evaluation of the different product categories in more detail, it became clear that the occurrence to the 26 fragrance allergens varies over the different product categories (Figure 2). Benzyl salicylate was listed on 28.2 % of the all-purpose cleaners, while it was only listed on 7.0 % of the dish-washing liquids within our study. Differences between the fragrance allergens listed on these two product categories have been reported previously (Magnano et al., 2009; Yazar et al., 2011), although for other substances.

Our ranking of frequency of the fragrance allergens in detergents is generally in good agreement with previous studies that had analyzed much smaller number of products (Buckley, 2007; Gerster et al., 2014; Magnano et al., 2009; Yazar et al., 2011). However, the average number of listed fragrances is lower in our study than in the study performed in the U.K. in 2006, where, on average, three fragrance allergens have been listed (Buckley, 2007). We also found considerably less dish-washing liquids and

all-purpose cleaners listing one of the 26 fragrance allergens than Magnano et al. (2009). It has already been discussed by Tanaka et al. (2004) that if substances do not need to be declared, they might be used more frequently. It is possible that today producers apply less fragrance allergens that need to be declared and on occasion substitute them with other fragrance compounds with unknown allergy potential, which are summarized on the label in the term 'perfume'. This term was listed on 60 % of the detergents. This corresponds to previously published results, where for example 73.5% of the liquid household cleaning products analyzed in Italy listed 'parfum' (Magnano et al., 2009).

4.2 Aggregate exposure to fragrance allergens

Our results demonstrate that detergents could contribute to the aggregated exposure to fragrance allergens. To enhance the risk assessment for the fragrance allergens, detergents (as a possible exposure source) need to be included in the existing exposure models as it has already been done recently by Nijkamp et al. (2015) and Ezendam et al. (2018).

4.3 Co-exposure to fragrance allergens

The exposure of consumers to combinations of two or more fragrance allergens (co-exposure) may enhance sensitization and has already been described for some fragrance allergens in cosmetics (Uter et al., 2013b). The results of our study highlight that detergents can also lead to co-exposure of consumers (Figure 3). Several fragrance substances were listed simultaneously on one detergent within our study, as has already been reported for German detergents in 2001 (Luger, 2001). A Danish

survey also found up to nine different fragrance allergens in detergents (Rastogi, 2002).

The two pairs of fragrance allergens showing the highest similarity in hierarchical cluster analysis were hexyl cinnamal and butylphenyl methylpropional next to citronellol and linalool (Figure 3). This means that they more often occurred together than with other fragrance allergens. The combination of these fragrances is also frequent in cosmetic products (Uter et al., 2013b). Preferably, these pairs of fragrance allergens should be further investigated regarding potential enhancing effects on sensitization.

The co-occurrence of citral and geraniol, both leading to the exposure of consumers to geranial, has been discussed previously for cosmetics (Uter et al., 2013b). These two fragrance allergens also co-occurred in twelve detergents (n=817).

However, the co-exposure of consumers to different fragrance allergens can not only happen due to their co-occurrence within one product but can also be due to the occurrence in different products that are used in the same household in parallel, e.g. during cleaning activities. The evaluation of the household data by hierarchical clustering shows that the composition of the fragrance allergen mixture across the entire range of products within a household is very different from the co-occurring fragrance allergens in one product. Over the entire range of detergents within one household, the highest similarity was calculated for the combination of eugenol, coumarin and cinnamyl alcohol (Figure 4). Also, alpha-isomethylionone and benzyl alcohol were often used together in the same household, as well as geraniol and

citronellol. These combinations of fragrance allergens should also be further investigated regarding potential enhancing effects on sensitization.

4.4 Limitations

Despite our extensive effort to get a realistic picture of fragrance allergens in household detergents, there are still limitations leading to a possible underestimation of the exposure to fragrance allergens. There are already known allergenic fragrances which so far are not required to be declared by law (Uter et al., 2013a). Further on, many natural extracts or oils have been identified to be established contact allergens, such as various *Citrus* preparations or *Lavandula hybrida* (SCCS, 2012). The allergenic components of these natural substances contribute to the aggregated as well as the combined exposure in addition to the 26 individual fragrance allergens listed on the containers (Klaschka, 2016). Those natural oils and extracts have also been listed on the inventoried detergents (data not presented here), demonstrating that our study probably underestimates the occurrence.

In addition, there are also methodological reasons, why our exposure estimation by exclusively using the ingredient lists has to be considered as an underestimate of occurrence. The 26 fragrance allergens are only listed if they are present above the thresholds for declaration (0.01%) and if they are used as fragrance ingredients, otherwise they do not need to be disclosed. Furthermore, it has been shown in the previous analyses of the data that it had a significant effect, whether the interviewees were bringing the products to the interviewers or whether the interviewer was allowed to walk around in the houses for scanning (Wieck et al., 2016). With the latter

scenario, higher numbers of products were detected in a household. This leads to an additional possible underestimation of the number of detergents as not all household members allowed us to walk around.

The use of the public database was successful for identifying the products scanned in the households and their ingredients. For 95.7 % of the barcodes, the names of the products could be retrieved, and for 89.6 %, the ingredients were available (n = 817). These retrieval rates were slightly lower than in a previous study based on the same database, where not only detergents were analyzed but also some cosmetics and biocidal products (Wieck et al., 2016). As the database is maintained by public users, it is possible, that it contains wrong declarations. Regarding product names, a study on the database used showed that the correctness of product names was 98 % (n = 13 702, Karpischek et al., 2014). Problems were encountered with spelling errors, as already described in the Methods section. These were solved by manual review and correction of the retrieved lists of ingredients.

The derivation of quantitative usage and exposure estimates was not possible, as amounts used per household member over time were not collected and the listing of the fragrance allergens on the labels only gives qualitative information on occurrence. The survey could not discriminate between products never or rarely used and products regularly used. We also did not collect any information whether consumers applied measures to reduce their personal exposure such as using gloves and whether the measures were effective. The households participating in the study are not necessarily representative for the general population. The voluntary participation

of household members might lead to a bias towards participants who are more aware of fragrance allergens and suggests that the occurrence of fragrance allergens might be even higher for the general population than derived from the presented data. Regional differences in user behavior might reduce the transferability of our results to users in other regions.

5. Conclusions

The present study focuses on the analysis of the occurrence of fragrance allergens in a very large number of detergents found in households. This is the first study of this size and contributes to the discussion of consumers' exposure to the 26 fragrance allergens to be declared on the labels of detergents in the EU. The results indicate that detergents, next to cosmetics, should be included in exposure scenarios calculating the aggregate exposure. Furthermore, detergents can also contribute to the co-exposure of consumers, possibly leading to enhanced sensitization. The combinations of fragrance allergens that are relevant for co-exposure are not necessarily only the ones that co-occur in detergents or cosmetics but also those that are present in other types of products, such as do-it-yourself products, scented candles or air fresheners for houses and cars.

The results emphasize the ubiquitous exposure of consumers to fragrance allergens. It would be desirable to enable consumers to decide consciously whether they want to be exposed to these substances. The necessity to declare the names of potential allergens on the product, as requested by the Regulation (EC) 648/2004 on

detergents for the European Union, is a tool for consumers wanting to avoid specific substances. However, other countries, for example the United States or Australia, do not have such legislation. Implementation of regulations similar to the European regulation on detergents could enable equally informed buying decisions of consumers in these countries. On the other hand, lists of ingredients on products can only inform consumers with detailed knowledge on potential sensitizers. Further strategies that also protect consumers without this detailed knowledge should be implemented to avoid new sensitizations and elicitations of skin effects.

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Conflict of interest

Stefanie Wieck is also working at the German Environment Agency. This paper does not necessarily reflect the opinion or the policies of the German Environment Agency.

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