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LETTER TO THE EDITOR

Contact haptens in emollients marketed in two European countries (Poland and Spain)

Abstract

Introduction and objectives: Atopic dermatitis (AD) is the most common skin disease among pediatric patients, which affects up to 20% of children worldwide. Characterized by pruritus and eczema, it is also associated with improper skin barrier function and allergen sensitization. Here, we aimed to assess the presence of haptens in emollients marketed in two European countries: in Poland and Spain, as, firstly, these products are considered to be AD's basic therapy, and, secondly, frequent application of potent sensitizers on atopic skin may result in contact dermatitis.

Materials and methods: We systematically searched for moisturizers explicitly described as ''*Atopic skin care*'' products in the most frequently visited online pharmacies in Poland and Spain.

Subsequently, we created a database of all products and compared their composition with 139 contact haptens listed in the European Baseline Series (EBS), Fragrance and Cosmetic Series.

Results: As of December 2018, our list comprised 159 and 111 emollients available on the Polish and Spanish markets, respectively. There were no ingredients listed in 28 (17.5%) products in Poland and 24 (21.6%) in Spain. Only 23 (17.5%) and 13 (14.8%) products were hapten free. The pattern of most common haptens was similar in both countries, including phenoxyethanol, tocopherol and tocopheryl acetate, undefined parfum in Poland and tocopherol, phenoxyethanol, tocopheryl acetate and undefined parfum in Spain.

Conclusions: This study shows that a vast majority of products taken into consideration contain at least one potential contact hapten. These findings indicate a need for patient education about potentially allergenic ingredients and stronger cooperation between academia and cosmetic manufacturers.

Introduction

Atopic dermatitis (AD), the pathophysiology of which is yet to be entirely understood, is a common chronic inflammatory skin disease, which often begins in infancy and affects up to 20% of children worldwide. It is associated with improper skin barrier function and increased skin absorption facilitating allergen permeation and sensitization.[1]

The available data on the connection between contact sensitization and atopic dermatitis is still inconclusive. However, several reviews indicate that children with AD may be at higher risk of developing contact sensitization, especially to fragrances, preservatives, and other components of skin care products.[2–5]

Methods

The five most frequently visited online pharmacies were identified by using Website traffic tools: Gemius report about the most searched on-line drugstores in Poland in 2017: https://www.gemius.pl/wszystkie-artykuly-aktualnosci/leki-sprawdzamy-w-sieci-kupujemy-tradycyjnie.html, and the most popular pharmacies as stated on the website:

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https://www.esdemarketing.com/mejores-farmacias-online in Spain (listed in Appendix 1, on-line repository materials). Subsequently, we systematically screened the most frequently visited online pharmacies for emollients and moisturizers indicated for atopic eczema section or using ''atopic'' as a keyword in a pharmacy-page search. Then we cross-checked whether all the products found were marketed by their producers for atopic skincare on their official websites. To evaluate the frequency of allergenic haptens, we compared their composition based on the International Nomenclature of Cosmetic Ingredients (INCI) with 139 contact allergens listed in the European Baseline Series, the Fragrance Series and the Cosmetic Series (listed in Appendix 2). Because of commonly used fragrance ingredients in emollient, the ''undefined parfum'' category was added to our study.

Results

As of December 2018, our list comprised 159 and 111 emollients available on the Polish and Spanish markets, respectively. Ingredients could not be determined in 28 (17.6%) products in Poland and in 24 (21.6%) in Spain (INCI composition neither available on the internet nor upon mailing to manufacturers). Only 17.5% ($n = 23$) products in Poland and 14% ($n = 13$) in Spain were devoid of the haptens listed in the European Baseline Series, the Fragrance Series and the Cosmetic Series, while the remaining emollients contained at least one contact allergen, with the maximum number of 12 and 14 haptens. The average was 3.5 and 3.6 different haptens per product in Poland and Spain respectively (Fig. 1). The pattern of the most common haptens was similar in both countries, with: phenoxyethanol (32.8%), tocopherol (32.1%) and tocopheryl acetate (29.0%), undefined parfum (21.4%), cethyl alcohol (18.3%), propylene glycol (17.5%) in Poland; and tocopherol (44.8%), phenoxyethanol and tocopheryl acetate (both in 37.9% of emollients), undefined parfum (35.6%), cethyl alcohol (32.2%), propylene glycol and ethylhexylglycerin (both in 18.4% of products) in Spain (Fig. 2 and Table 1).

Discussion

Allergic Contact Dermatitis (ACD) is not uncommon among children, and according to the European Academy of Allergy and Clinical Immunology Task Force on Allergic Contact Dermatitis in Children its prevalence appears to be on the rise.[6] In the pediatric population, the most frequent sensitizers are metals, fragrances, and preservatives.[3] It is still debated whether children with atopic dermatitis are at higher risk of developing contact allergy. However, recent studies indicate that they might be more susceptible to ACD development caused by their skincare products and allergens such as fragrance mix I, peruvian balsam, and lanolin alcohol.[2,7,8]

This study shows that a vast majority of emollients indicated for the treatment of atopic dermatitis contain at least one potential contact allergen listed in the European Baseline Series, the Cosmetics and the Fragrance Series (Appendix 2). Even though tocopherol (32.1% and 44.8%), phenoxyethanol (32.8% and 37.9%), and tocopheryl acetate (29.0% and 37.9%) were the most frequently found allergens in all products in both countries, they seem to be of little consequence in ACD in children.[9,10] However, another commonly identified sensitizer, propylene glycol, found in 17.5% and 18.4% of emollients in Poland and Spain, respectively, might be an easily irritating hapten responsible for toxic reactions in children under two years of age, according to European Guidelines for the treatment of atopic eczema.[11]

According to a recent report by Lubbes et al., fragrances are among the five most frequent sensitizers in the pediatric population and that children with AD react more often to fragrances (such as fragrance mix I and myroxylon pereirae).[4] Similarly, a study by Thyssen et al. reported a higher prevalence of contact allergy to fragrances among children with mild to moderate AD, with contradicting results for children with severe AD.[5]

In our study, there were 17 (18 with undefined parfum) different fragrances in 108 emollients in Poland and 75 in Spain (Fig. 2). Fragrance mix I was found in 4.64% and 12% of emollients in Poland and Spain, respectively, whereas myroxylon pereirae was not included in the tested series.

Benzyl alcohol and linalool were the fragrance haptens most frequently found in both countries (Table 1). In a recent retrospective study, Kreft and Geier have shown that benzyl alcohol rarely causes ACD.[12] However, linalool was recognized as a frequent sensitizer among the US population.[13] Similarly, in a study conducted in Spain, a primary oxidation product of linalool – linalool hydroperoxides – was found to be a frequent cause of contact allergy to fragrances.[14] Limonene was another common allergen mentioned in both studies. While in Poland it was not present in any of the products, in Spain it could be found in 4% of emollients. It is worth mentioning that neither linalool nor limonene are included in the European Baseline Series. Therefore, in suspected contact allergy, it should be of high importance to extend the search for culprit allergens using the Fragrance Series.

'Undefined parfum' was the most prevalent fragrance ingredient in both countries, and occurred in 25.9% and 41.33% of emollients in Poland and Spain, respectively. By definition, '*undefined parfum*' is a mix of fragrances that are not listed as potential haptens. However, this does not necessarily mean that its potential allergenicity can be dismissed. Hence, the risk of contact allergy should be further investigated.

To the best of our knowledge, the prevalence of contact allergy to allergens listed in the Fragrance Series has yet to be comparatively analyzed between an AD cohort and a non-AD control group. Therefore, one cannot dismiss a concept – that there are indeed more patients with AD – who also suffer from ACD at the same time.

Furthermore, two reviews, by Simonsen et al. and Lubbes et al. suggest that lanolin alcohol is found more frequently as a potential sensitizer in children with AD than in children without atopic dermatitis.[3,4] On the Spanish market, no emollients containing lanolin nor lanolin alcohol were detected, whereas, on the Polish market, lanolin alcohol (lanolin derivative) was present in three products, whereas lanolin was in 13 another emollients, indicating the need to check the composition of the purchased product in this respect.

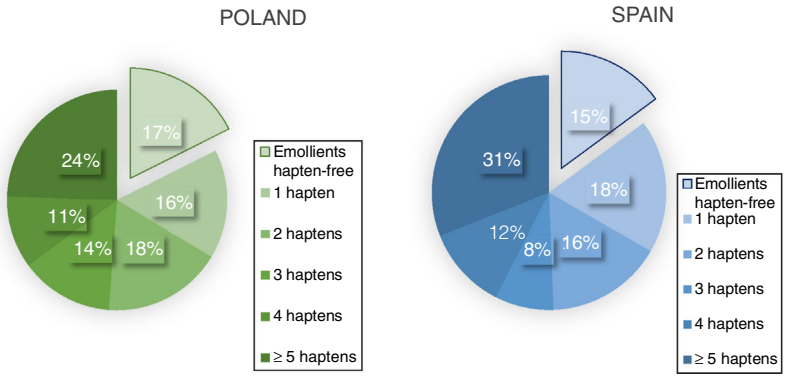

Figure 1 Percentages of products containing haptens in Poland and Spain.

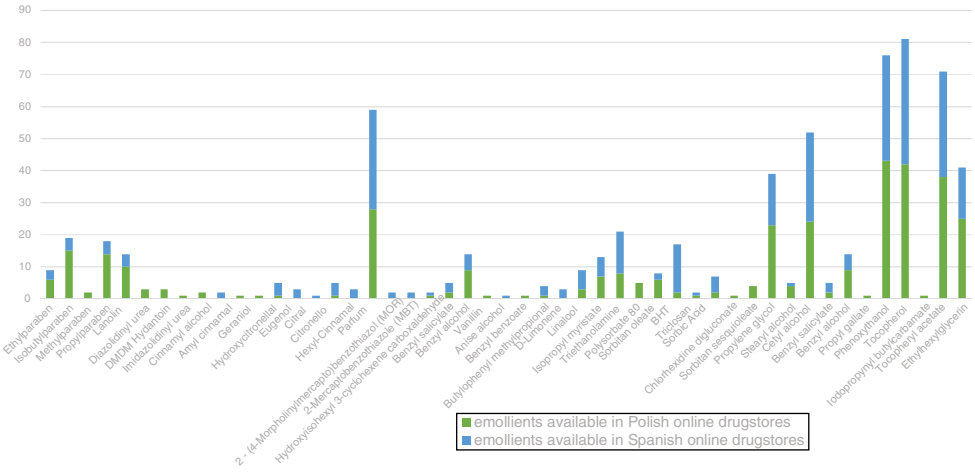

Figure 2 Frequency of haptens form the European Baseline Series, Cosmetic and Fragrance Series in emollients available in Polish and Spanish online drugstores.

Table 1 The prevalence of different fragrance haptens in emollients available in Polish and Spanish online drugstores.

Fragrance haptens present in emollients	Poland		Spain	
	n	% of emollients	*n*	% of emollients
Parfum	28	25.93%	31	41.33%
Benzyl alcohol	9	8.33%	5	6.67%
Linalool	3	2.78%	6	8.00%
Benzyl salicylate	2	1.85%	3	4.00%
Amyl cinnamal	1	0.93%	0	0.00%
Benzyl benzoate	1	0.93%	0	0.00%
Butylphenyl methylpropional	1	0.93%	3	4.00%
Vanillin	1	0.93%	0	0.00%
Citronellol	1	0.93%	3	4.00%
Eugenol	1	0.93%	3	4.00%
Geraniol	1	0.93%	4	5.33%
Hydroxycitronellal	1	0.93%	0	0.00%
Hydroxyisohexyl 3-cyclohexene carboxaldehyde	1	0.93%	1	1.33%
Anise alcohol	0	0.00%	1	1.33%
Cinnamyl alcohol	0	0.00%	2	2.67%
Citral	0	0.00%	1	1.33%
D-Limonene	0	0.00%	3	4.00%
Hexyl-cinnamal	0	0.00%	3	4.00%

The results of our research are in accordance with the data presented in a few previous studies. In our previous papers, we have shown that around 60% of products designed for AD contain incipients listed in the European Baseline Series, and 85% of ''hypoallergenic'' products destined for infants and neonates also contained haptens.[15,16] Similarly, in the US, Hamman et al. reported that 89% of the skin products labeled as ''hypoallergenic'' contained haptens.[17]

There are several limitations to this study. Firstly, we have analyzed cosmetic compounds without evaluating skin reactions to every single hapten. In order to evaluate the impact of the most common haptens found in emollients, a comprehensive clinical study is needed. Secondly, the European Baseline Series, the Fragrance, and the Cosmetics Series are lists of the most popular haptens. Hence, they do not comprise all sensitizing substances. Thirdly, the search was narrowed to the internet, which precludes emollients from smaller and less known producers from our list. Moreover, the list of ingredients presented according to the International Nomenclature of Cosmetic Ingredients (INCI) was not always available on both the pharmacy and the producer websites and only a few producers replied upon request and provided us with the full ingredients list. Consequently, some emollients, potentially containing more haptens, were not included in our list. Nevertheless, the emollients that are included are the most popular and readily available on the market.

Last but not least, the list was created for two European countries only, and although there are only minor differences between them, our results might not apply to other European markets.

This is the first study targeted to compare available emollients in different European countries. In future studies, a patient-oriented analysis could be performed to determine whether hapten-deprived emollients would be associated with a lower risk of sensitization in patients with atopic dermatitis.

Conclusion

These findings point out the need for patient education on potentially allergenic ingredients. The presence of multiple fragrance ingredients in emollients should raise concerns, considering that those components might not have any other function than to entice potential customers. Moreover, it is vital to effectively co-operate with the cosmetic industry on current trends and needs in manufacturing cosmetics designed for atopic skin. Strengthened cooperation between academia and cosmetic manufacturers would help to design further studies on potential sensitizers in skincare products as risk factors in ACD.

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Conflicts of interest

None declared.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.aller.2020.04.002.

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