Potentially Irritant Preservatives in Newborn Baby Cosmetics – Analysis of Labels of Products Sold in Portugal

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Abstract. *The use of cosmetics containing preservatives might pose a risk to the skin health of newborns, despite improving their adaptation to the external environment. The present work aimed at depicting the potentially hazardous preservatives in cosmetics sold in the district of Porto, Portugal. A total of 281 labels from newborn cosmetics were analyzed. From 729 different ingredients found in the analyzed labels, 15 were preservatives with previously recorded irritant activity, being sodium benzoate the most mentioned (n = 118). There was a significant difference between the means of number of preservatives with an irritant potential present in the products sold in pharmacies and in the products sold in supermarkets. Most analyzed products contained at least one preservative. Still, the choice of cosmetics for newborns should consider those with a minimum number of preservatives, being more probable to choose a less sensitizing product in pharmacies than in supermarkets.*

Keywords. Preservatives, cosmetics, allergic contact dermatitis, irritant contact dermatitis, labels

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1 Introduction

Despite the similarities between the thickness and lipid composition of neonatal epidermis of full-term infants and the epidermis of adults, there are several differences regarding morphological and functional features, which are accentuated in the case of preterm infants. Indeed, even in full-term babies, the pH is more alkaline [1-3], stratum corneum moisturization is deficient in the first days [1, 4], the capillary system is not fully formed [5, 6], and the production of sebum is inferior to that of adults (except for the first week in which it reaches its peak) [7, 8]. Several factors can influence the process of gradual adaptation to the external environment, especially the weather conditions, the use of diapers and the application of cosmetics [9].

The use of cosmetics may be important in the transition from the humid uterine environment to a dry atmosphere where it is necessary to ensure not only the correct development but also to protect the skin from possible irritations and inflammation and to create a feeling of comfort. In full term babies, the use of cleansers, mild surfactants and cosmetic products with a high percentage of water is considered appropriate and both newborns and young children have a good tolerance towards them [10, 11]. Additionally, the use of creams and emollients are considered beneficial in the recovery of the skin barrier function, for example in the case of irritant dermatitis in the diaper area, contributing significantly to a lower transepidermal water loss [11, 12].

Despite the benefits of the application of cosmetics in newborns, it is generally recognized that the formulations of the products used in this population group may present potentially irritant and harmful substances [13]. Thus, the evaluation of cosmetic formulations should be done carefully both by parents and by health professionals, being the information on the label the most accessible resource for this purpose. On the label, the presentation of the ingredients is obligatory and the presence of one or more preservatives (defined as substances whose main or exclusive purpose is the inhibition of microbial growth in the cosmetic product) is frequent [14].

Due to the potential adverse effects of the application of cosmetics in newborn babies, the present study aims to evaluate the prevalence of potentially hazardous preservatives in cosmetics and body hygiene products sold in pharmacies and supermarkets in the district of Porto, Portugal.

2 Methodology

The present cross-sectional study was based on the analysis of the labels of cosmetic and body hygiene products intended for newborns. The non-probability sampling allowed the inclusion of products sold in pharmacies and supermarkets located in the district of Porto (Portugal), in the period between November 2017 and January 2018, ultimately leading to the analysis of 281 product labels.

All included labels were characterized regarding their ingredients, intended function (cologne and perfumes, leave-on cleansers, rinse-off cleansers, diaper area creams, moisturizing products, sunscreens and other), origin (national or international) and place of sale (pharmacy or supermarket).

In parallel, a search was performed through Pubmed, regarding all the preservatives present in the labels, according to their "International Nomenclature of Cosmetic Ingredients" (INCI) designation. The case studies reporting allergic or hypersensitivity reactions resulting from the application to the skin or scalp of a particular preservative present in a cosmetic or body care product published until 2018 were considered for the identification of the preservatives with the greatest potential to cause an irritant effect. Studies reporting adverse effects from a non-transdermal route of administration (i.e. oral, intravenous, etc.) were excluded, as well as those reporting reactions resulting from the application of non-cosmetic products (such as paints, medical devices, etc.).

The statistical tool Statistical Package for the Social Sciences (SPSS) (version 25) was used for the purposes of registration and systematization of data. Student's t-test was applied and a p-value <0.05 was considered statistically significant.

3 Results

The present study resulted in the analysis of 151 products commercialized in pharmacies and 130 products sold in supermarkets. From 729 different ingredients found in the analyzed labels, 28 are classified as preservatives, according to the Regulation (EC) Number 1223/2009 of the European Parliament and of the Council of 30 November 2009 [14]. There were 81 products (29%) that had no preservatives in their composition, while 200 products (71%) had at least one preservative.

Fifteen preservatives deserved special attention throughout the present work owing to the attribution of hypersensitive effects due to their presence in cosmetics applied directly to the skin or scalp in previously published case studies: phenoxyethanol, benzyl alcohol, parabens, polyaminopropyl biguanide, chlorhexidine digluconate, diazolidinyl urea, imidazolidinyl urea, 2-bromo-2-nitropropane-1,3-diol, chlorphenesin, iodopropynil butylcarbamate, methylchloroisothiazolinone, methylisothiazolinone, sodium benzoate, sodium metabisulfite and sorbic acid (Table 1). Of these 15 preservatives, the most commonly mentioned in the labels of the analyzed products are sodium benzoate (n = 118), phenoxyethanol (n = 62), sorbic acid (n = 23), parabens (n = 16) and benzyl alcohol.

Table 1. Case reports of hypersensitivity reactions to preservatives following cosmetics application on skin or hair

	Alcohols		Derivates of phydroxy-benzoic acid	Diquanides		Formaldehyde -releasing preservatives		Halogenated			Izothiazoline derivates		Others		
	Benzyl Alcohol	**Phenoxyethanol**	**Parabens**	**Chlorhexidine Digluconate**	**Polyaminopropyl Biguanide**	**Imidazolidinyl Urea**	**Diazolidinyl Urea**	**Iodopropynil Butylcarbamate**	**Chlorphenesin**	**2-Bromo-2-Nitropropane-1,3-diol**	**Methyl-isothiazolinone**	**Methylchloro-isothiazolinone**	**Sorbic Acid**	**Sodium Metabisulfite**	**Sodium Benzoate**
Case Reports in neonates and infants (0-2 years old)			[15]	[16]											
Case Reports in Young Child (2-6 years old)				[17]							[51]	[51, 52]			
Case Reports in Child (7-11 years old)	[18]				[19]		[20]				[51, 52]	[51-54]			
Case Reports in Adolescents (12-18 years old)					[20]		[20]			[55]	[62-67]	[62-71]			[72]
Case Reports in Adults	[21-25]	[26-30]	[28, 31-35]	[36-38]	[39-42]	[43-47]	[47-49]	[59-61]	[56-58]					[73-75]	[76-80]
Patients Age not mentioned							[50]								

Concerning the number and types of preservatives presented by the product labels, there is a highly variable distribution, especially regarding the preservatives used in leave-on and rinse-off cleansers, diaper area creams and moisturizing products, all of them presenting 5 or more types of compounds (Figure 1). Nevertheless, these are the products that present a larger number of units in the present sample, which may justify the variability found. Sun protection products, colognes and perfumes and other products have 4 or fewer types of preservatives but only represent 32 products of the final sample (Figure 1 and Table 2).

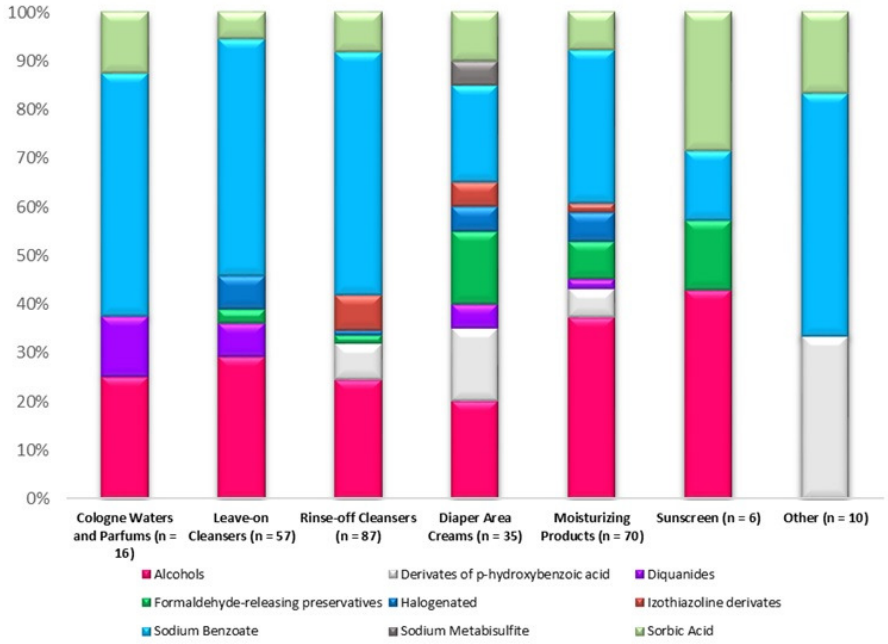

Figure 1. Relative frequencies of analyzed preservatives in skin care and cosmetic product for babies, in Portugal

Table 2. Absolut frequencies of products per category and number of preservatives in each group

Category	Cologne waters and parfums	Leave-on cleansers	Rinse-off cleansers	Diaper area creams	Moisturizing products	Sunscreen	Other
Total of products (n)	16	57	87	35	70	6	10
Mean of targeted conservatives ± standard deviation	0.6 ± 0.7	1.3 ± 0.7	1.3 ± 1.4	0.6 ± 0.9	0.7 ± 1.0	1.3 ± 1.5	0.6 ± 1.0

Sunscreen products, leave-on cleansers and rinse-off cleansers have the highest average number of preservatives with irritant potential, whereas moisturizing products, cologne and perfumes, diaper area creams and other products are those with a lower average of preservatives with sensitizing potential in their composition (Table 2).

The comparison of the preservatives identified as potentially irritant in the products sold in pharmacies with those present in the products sold in supermarkets showed a notable difference (Figure 2). Using the t-test, it was demonstrated that there is a statistically significant difference between the mean number of preservatives with an irritant potential present in the cosmetic and body hygiene products for newborns sold in pharmacies (1.01 ± 1.358) and the mean number of preservatives with an irritant potential present in the cosmetic and body hygiene products for newborns sold in supermarkets (1.55 ± 1.114).

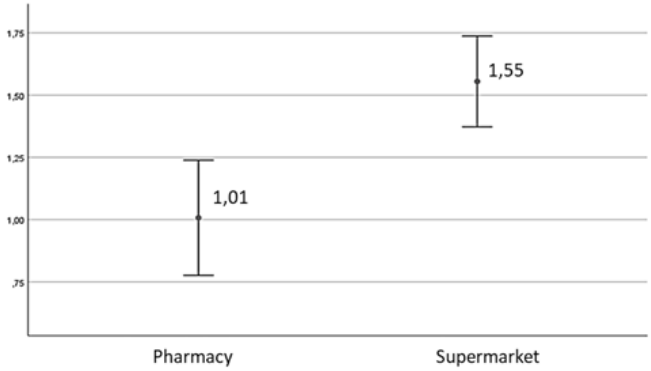

Figure 2. 95% Confidence intervals and average of the number of potentially irritant preservatives in cosmetics sold in Portugal

The observed difference between the average number of potentially irritant preservatives in cosmetics sold in pharmacies and in supermarkets does not seem to be influenced by the categories of the products. In fact, a slightly higher number of the products belonging to the categories in which a higher mean of potentially irritant preservatives is more likely (leave-one cleansers, rinse-off cleansers and sunscreens, according to table 2) were analyzed from pharmacies, than from supermarkets (Table 3).

Table 3. Absolut frequencies of products commercialized in pharmacies and supermarkets, per category

Categories of products	Pharmacy	Supermarket	Total
Cologne waters and parfums	7	9	16
Leave-on cleansers	30	27	57
Rinse-off cleansers	45	42	87
Diaper area creams	22	13	35
Moisturizing products	35	35	70
Sunscreen	4	2	6
Other	8	2	10
Total	**151**	**130**	**281**

As regards to the comparison of the mean number of potentially irritant preservatives in products produced in Portugal and products produced in other countries, there is no statistically significant difference ($p > 0.05$). Cosmetic and body hygiene products produced in Portugal have an approximate mean of one potentially irritant preservative in their composition (0.98 ± 1.30), as well as imported products (0.97 ± 1.03). Therefore, it can be assumed that the tendency for the inclusion of potentially irritant preservatives in Portugal is similar to the tendency of the other countries, being the leave-on and the rinse-off cleansers the categories of products with the highest number of potentially irritant preservatives.

4 Discussion and Conclusion

Most of the analyzed products in the present study have preservatives in their composition. This result might be justified by the fact that the presence of microorganisms in cosmetics and body hygiene products may change their composition, possibly resulting in irritations and infections, especially when these products are applied in injured skin, in the skin area surrounding the eyes or in baby skin [81-83]. Pathogenic strains of Staphylococcus aureus and Pseudomonas aeruginosa are amongst the microorganisms most frequently identified in cosmetic products, [83] and cases of hospitalization of individuals due to the use of contaminated cosmetics, namely by bacteria Burkholderia cepacia, have already been reported [84, 85]. However, contrary to what was described in a similar study performed in Bangkok, where all cosmetic products contained preservatives in their composition [86], the preservatives are absent in a substantial number of products. This result can be justified by the fact that, contrary to the mentioned study, all the analyzed products are intended to be applied in newborns and can frequently cause undesirable side effects. Indeed, it is estimated that approximately 6% of the population is allergic to preservatives and fragrances, the two main groups of compounds responsible for hypersensitivity reactions in cosmetics [87, 88]. Particularly as regards to the preservatives identified in the analyzed labels, parabens, formaldehyde-releasing preservatives (diazolidinyl urea, imidazolidinyl urea and 2-bromo-2-nitropropane-1,3-diol) and methylisothiazolinone were already linked to negative effects in clinical trials. Butylparaben and propylparaben revealed a significant increase in the likelihood of allergen sensitization [89] and in vitro studies about the activity of parabens demonstrated the induction of phenotypic transformations in breast epithelial cells [90], increased proliferation, migration and acquisition of invasive properties of cancer cells [91, 92] and the generation of reactive oxygen species and DNA damage in spermatozoa [93], hence confirming the estrogenic, anti-androgenic and genotoxic potential of the parabens. It is noteworthy that the presence of propylparaben in a product for application in the diaper area violates the Regulation (EU) No 1004/2014 (that amends the Annex V to Regulation (EC) No 1223/2009 of the European Parliament and of the Council on cosmetic products), that states that "butylparaben and propylparaben should be prohibited in leave-on cosmetic products designed for application on the nappy area of children below three years." [94]. Concerning formaldehyde-releasing compounds, they have already caused contact allergies in humans [95] and particularly methylisothiazolinone gave rise to in vitro neurotoxicity effects [96, 97].

According to the Commission Regulation (EU) 2017/1224 of 6 July 2017 amending Annex V to Regulation (EC) No 1223/2009 of the European Parliament and of the Council on cosmetic products, methylisothiazolinone "should (…) be further restricted in rinse-off products". Additionally, it is acknowledged that, in non-rinsed cosmetic products, it has not been yet demonstrated any safe concentrations of methylisothiazolinone, regarding the elicitation of contact allergies [98]. In the studied sample, one product intended to be used as a diaper area cream and one body moisturizer product presented methylisothiazolinone in their composition as well as four rinse-off cleansers.

The inclusion of a greater number of potentially irritating preservatives in cosmetics and body hygiene products intended for newborns marketed in hypermarkets than in pharmacies may result in hypersensitization more frequently [99]. Additionally, the use of various cosmetics or body care products containing the same preservative necessarily increases the risk of sensitization due to repeated exposure [100]. For example, studies regarding the use of cosmetic products in French children (0-3 years old) [101] and Portuguese children (0-5 years old) showed that, on average, six cosmetic products are applied daily. The cumulative potential for causing hypersensitivity reactions in infants exposed to a high number of cosmetics is thus evident, and particularly if they are leave-on products rather than rinse-off products, since those stay in contact with the cutaneous surface for longer periods.

In order to ensure a better adaptation of the skin and its annexes to the outside environment by newborns and infants, the use of cosmetics is undeniably pertinent. However, the inclusion of preservatives in a balanced manner in these products is imperative and the minimum number of preservatives required to ensure the preservation of products must be used in order to avoid excessive exposure to these compounds with a recognized sensitizing potential. Regulating authorities play a central role in market surveillance and should ensure that only legally permitted preservatives are present in marketed cosmetic products.

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