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ORIGINAL ARTICLE

Skin safety and health prevention: an overview of chemicals in cosmetic products

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Keywords

Health Prevention • Cosmetics • Cocktail Effect • Additive Effect

Summary

Introduction. *Cosmetic products contain a wide range of chemicals to which we are exposed every day. The aim of the study was to determine the presence of potential dangerous substances which can cause adverse health effects by examining product labels.*

Materials and methods. *A total of 283 products were collected from various shops in Lecce (Italy) and divided into 3 categories: rinse-off, leave-on and make-up. The label of every product was examined and a list including fragrances, preservatives and other chemicals of concern was created.*

Results. *Fragrances were present in 52.3% of the examined products, mostly limonene (76.9%) and linalool (64.6%) but also citronellol (34.1%), geraniol (31.5%), coumarin (30%) and hexyl cinnamal (29.2%). Preservatives showed a rate of 60% and the most frequently identified were phenoxyethanol (48.7%), sodium benzoate (35.6%), potassium sorbate (22%), methylparaben (15.2%) and MI/MCI (9.9%). The other chemicals of concern were detected in 58% of products; included PEGs (62.3%), acrylate copolymer (34%), petrolatum (17.2%), polysorbates (14,8%), BHT (14.7%), ethylhextyl methoxycinnamate (13.6%), benzophenone-1 (3.7%), benzophenone-3 (4.9%), BHA (1.6%), cocamide DEA and toluene (1.2%).*

Conclusions. *The use of many of these substances is allowed within certain limits, due to their toxicity at higher concentrations. Other important aspects should be considered as, for instance, the possibility of long-term effects. On the other hand, other substances may induce several acute adverse side-effects, i.e. contact dermatitis and allergic reactions. For these reasons, an enhancement of the criteria used for cosmetics formulation is required since many chemicals used singularly or combined are potentially unsafe.*

Introduction

In their everyday life people are exposed to a great range of chemicals most of which occur naturally in the environment, but others are derived from human activities, being present in foods, water and various daily use products. Because our skin is the largest surface of the body interacting with external environment, it is both involuntarily exposed to abiotic [1, 2] and biotic factors [3, 4], and voluntarily, due to personal care and cosmetic products use. Many of these are used or applied on a daily basis and in different ways, consequently, these products are assumed for enhancing our personal hygiene and appearance and they are reputed to be harmless for body's health.

In the light of the frequent and intimate nature of the contact on skin and mucosa with these products, it is important that they do not contain potentially dangerous substances.

As a matter of fact, all the ingredients used in cosmetic products meet certain regulatory requirements [5]. However, the use of many substances is allowed within certain limits, due to their toxicity at higher concentrations. Other important aspects should be considered as, for instance, the possibility of long-term effects [6, 7]. On the other hand, other substances may induce several acute adverse side-effects, i.e. contact dermatitis and allergic reactions [8]. Moreover, the everyday use and continuous exposition of humans to a wide range of personal care products and to different kinds of chemicals, derived from several sources, may cause the so-called "cocktail effect" due to the synergistic interaction of different substances and, also, the "additive effect" because of the presence of the same ingredient in many products [9, 10].

The purpose of the current study was to determine, among the ingredients listed on the label, the presence of substances with known adverse health effects in commonly used personal care and cosmetic products. We considered fragrances, preservatives and other substances known as skin sensitizers or potentially harmful on general health.

Materials and methods

Different kinds of beauty and hygiene products were selected between October and November 2017 from various shops in Lecce (Italy), mainly supermarkets with nationwide coverage, beauty shops, and pharmacies as well as online shops. Ingredient information from labels was collected by taking photos in the shops or downloading data sheets from webshops. Because of the lack

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of available data on sales rates of specific products to the public, as in other studies [11], a crude selection of products estimated to be sold in large volume was made, on the basis of information from shop assistants and the authors' own perceptions.

All products were divided into 3 categories: rinse-off products (shower gel, shampoo, toothpaste, liquid soap, intimate soap, shaving foam) leave-on products (body cream, face cream, hand cream, deodorant, sunscreen, aftershave) and make-up ones (lipstick, lipbalm, foundation, nail polish). Such a classification was based on the time of skin application: rinse-off products stay a very short time on it, as they are usually rapidly washed away (even if it would also be appropriate to consider the frequency of application); leave-on and make-up products stay longer on the skin, but the former are more usually used for skin care, in order to protect it, perfume it and keep it in good conditions (moisturising, nourishing, tonifying, etc.), the latter have an aesthetic purpose and are intended to improve someone's look.

Every group included also organic and children's products. The first were identified on the basis of organic and natural certifications disclosed on the brand's website and indicated on the label (Cosmos, Ecolabel UE, Ecocert, Icea, Natrue, etc.); the latter showed on the label the word "baby" or "kids".

Subsequently, the label of every product was examined and chemicals which could possibly affect human health were detected. The selection of substances was based on scientific evidence: for fragrances the list of 26 allergens which have been identified as skin sensitizer by the Scientific Committee on Consumer Safety (SCCS) and whose names should be listed on the label [12] was considered; for the other substances a literature's review was conducted [13-15] and only those reporting possible harmful effects on human heath were selected.

A list with fragrances, preservatives and other chemicals of concern, including some UV filters, antioxidants, emulsifiers, surfactants and other synthetic compounds, was created. Data were recorded in Microsoft® Excel and analysed by calculating rate, median and maximum of substances for every category. No chemical analyses were performed in the present study.

Results

A total of 283 products were examined: 112 rinse-off, 103 leave-on and 68 make-up (Tab. I). Fragrances individuated on the labels were 19, preservatives were 16 and other chemicals of concern were 11.

Fragrances

The 19 fragrances individuated (Tab. II) are all included in the list of 26 allergens redacted by SCCS, whereas the missing seven ones were: amylcinnamyl alcohol, anise alcohol, benzyl cinnamate, cinnamal, evernia furfuracea, evernia prunastri, methyl 2-octynoate. More than fifty-two per cent of the products contained at least one of the fragrances investigated, especially rinse-off products (61.6%). Generally, the most frequently identified fragrances were limonene (76.9%), linalool (64.6%), citronellol (34.1%), geraniol (31.5%), coumarin (30%) and hexyl cinnamal (29.2%). Moreover, limonene was more present in rinse-off (70.7%) and make-up products (73.3%), whereas linalool was more found in leave-on ones (87.7%).

In addition, the presence of fragrances was found in organic and children's products (Tab. III), respectively 56.3% and 18.6%. Limonene was the fragrance most listed on the labels for both kinds of products (respectively 84.4 and 83.3%), followed by linalool (65.6 and 33.3%) (Not in the table).

Preservatives

Sixty per cent of the selected products contained at least one of the preservatives investigated, above all among rinse-off products (75%). The most frequently identified preservatives (Tab. IV) were phenoxyethanol (48.7%), sodium benzoate (35.6%), potassium sorbate (22%), methylparaben (15.2%) and methylisothiazolinone/methylchloroisothiazolinone (MI/MCI) (9.9%). Sodium benzoate was the most common preservative in rinse-off products (57.6%) and phenoxyethanol in leave-on (70.1%) and make-up ones (58.6%).

Four different parabens were identified (methylparaben, ethylparaben, propylparaben, butylparaben) and almost 15% of the products contained one or more parabens, mostly leave-on products (face and hand cream, sunscreen, aftershave). The most detected was methylparaben, found in all of those products containing at least one paraben, followed by ethylparaben (55.2%) and propylparaben (51.7%). All four parabens were contained in six products (foundation, face cream, lipstick, aftershave, two sunscreens) and three parabens in three products (aftershave, two face creams).

Tab. I. Products divided into rinse-off, leave-on and make-up categories with frequency of occurrence and proportion of products containing fragrances, preservatives and other chemicals of concern and their distribution in term of median and maximum.

	Examined products	Products containing fragrances			Products containing preservatives			Products containing other chemicals of concern		
		N (%)	Median	Max	N (%)	Median	Max	N (%)	Median	Max
Rinse-off	112	69 (61.6)	2	10	84 (75)	2	6	65 (58)	2	5
Leave-on	103	61 (59.2)	6	15	64 (62.1)	2	7	55 (53.4)	2	7
Make-up	68	18 (26.5)	2.5	6	22 (32.4)	2	7	44 (64.7)	2	5
Total	283	148 (52.3)	3	15	170 (60)	2	7	164 (58)	2	7

Tab. II. Frequency of occurrence and percentage of fragrances identified on the label of selected products and referring to rinse-off, leave-on and make-up categories.

Fragrances	CAS no.	Rinse-off		Leave-on		Make-up		Total	
		(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)
Alpha-isomethyl ionone	127-51-5	6	10.3	22	38.6	4	26.7	32	24.2
Amyl cinnamal	122-40-7	3	3.2	3	5.3	1	6.7	7	5.4
Benzyl alcohol	100-51-6	25	29.4	25	32.5	5	17.2	55	28.8
Benzyl benzoate	120-51-4	3	3.2	9	15.8	4	26.7	16	12.1
Benzyl salicylate	118-58-1	12	20.7	20	35.1	1	6.7	33	25.4
Butylphenyl methylpropional	80-54-6	12	20.7	16	28.1	-	-	28	21.5
Cinnamyl alcohol	104-54-1	1	1.7	3	5.3	-	-	4	3.1
Citral	5392-40-5	2	3.4	26	45.6	4	26.7	32	24.2
Citronellol	106-22-9	11	19	33	56.9	1	6.7	45	34.1
Coumarin	91-64-5	11	19	26	45.6	2	13.3	39	30
Eugenol	97-53-0	10	17.2	11	19.3	1	6.7	22	16.9
Farnesol	4602-84-0	-	-	3	5.3	-	-	3	2.3
Geraniol	106-24-1	7	12.1	32	56.1	2	13.3	41	31.5
Hexyl cinnamal	101-86-0	18	31	18	31.6	2	13.3	38	29.2
Hydroxycitronellal	107-75-5	2	3.4	8	14	1	6.7	11	8.5
Hydroxyisohexyl 3-cyclohexene carboxaldehyde	31906-04-4	-	-	12	21.1	-	-	12	9.2
Isoeugenol	97-54-1	-	-	6	10, 5	-	-	6	4.4
Limonene	138-86-3	41	70.7	48	84.2	11	73.3	100	76.9
Linalool	78-70-6	26	44.8	50	87.7	8	53.3	84	64.6

Tab. III. Frequency of occurrence and percentage of substances identified on the label of children's products.

Substances	Products	n	%
Limonene	Shower gel, toothpaste, sunscreen, lipstick, lipbalm	16	83.3
Linalool	Toothpaste, sunscreen, lipstick, lipbalm	7	33.3
Citral	Lipbalm	1	5
Benzyl alcohol	Shower gel, sunscreen, nail polish	5	25
Eugenol	Toothpaste	1	5
Alpha-isomethyl ionone	Sunscreen	1	5
Citronellol	Sunscreen	1	5
Coumarin	Sunscreen	1	5
Potassium sorbate	Shower gel, intimate soap, toothpaste, liquid soap	4	12.5
Sodium benzoate	Shower gel, shampoo, intimate soap, toothpaste, liquid soap, body cream	12	37.5
Phenoxyethanol	Shower gel, shampoo, toothpaste, body cream, sunscreen, lipstick, nail polish	14	43.8
Chlorphenesin	Shampoo, body cream	2	6.3
Imidazolidinyl urea	Shampoo	1	3.1
Diazolidinyl Urea	Nail polish	1	3.1
Methylparaben	Lipstick	1	3.1
Propylparaben	Lipstick	1	3.1
Benzoic acid	Sunscreen	1	3.1
Cocamide DEA	Shampoo	1	4
BHA	Shampoo	1	4
BHT	Shower gel, shampoo, lipbalm	4	16
PEG's	Shower gel, shampoo, intimate soap, toothpaste, liquid soap, body cream, sunscreen	17	68
MI/MCI	Shampoo, liquid soap	2	8
Ethylhextyl methoxycinnamate	Lipbalm	3	12
Petrolatum	Body cream, lipstick, lipbalm	6	24
Acrylate copolymer	Shampoo, sunscreen, lipstick, nail polish	6	24
Polysorbate-80/-60/-20	Shampoo, body cream	3	12

Tab. IV. Frequency of occurrence and percentage of preservatives identified on the label of selected products and referring to rinse-off, leave-on and make-up categories.

Preservatives	CAS no.	Rinse-off		Leave-on		Make-up		Total	
		(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)
Methylparaben	99-76-3	8	9.4	16	20.8	5	17.2	29	15.2
Ethylparaben	120-47-8	2	2.4	11	14.3	3	10.3	16	8.4
Propylparaben	94-13-3	3	3.5	8	10.4	4	13.8	15	7.9
Butylparaben	94-26-8	-	-	4	5.2	2	6.9	6	3.1
Triclosan	3380-34-5	4	4.7	2	2.6	-	-	6	3.1
Imidazolidinyl Urea	39236-46-9	2	2.4	8	10.4	1	3.4	11	5.8
Diazolidinyl Urea	7849-02-8	-	-	-	-	1	3.4	1	0.5
5-bromo-5-nitro-1, 3 dioxane	30007-47-7	1	1.2	-	-	-	-	1	0.5
2-bromo-2-nitropropane-1, 3-diol	52-51-7	1	1.2	-	-	-	-	1	0.5
DMDM Hydantoin	6440-58-0	12	14.1	4	5.2	-	-	16	8.4
Phenoxyethanol	122-99-6	22	25.9	54	70.1	17	58.6	93	48.7
Methylisothiazolinone/ Methylchloroisothiazolinone	2682-20-4, 26172-55-4, 55965-84-9	19	22.4	-	-	-	-	19	9.9
Chlorphenesin	104-29-0	1	1.2	2	2.6	2	6.9	5	2.6
Benzoic acid	65-85-0	5	5.9	9	11.7	1	3.4	15	7.9
Sodium benzoate	1-23-235	49	57.6	17	22.1	2	6.9	68	35.6
Potassium sorbate	24634-61-5	23	27.1	15	19.5	4	13.8	42	22

Formaldehyde-releasers (imidazolidinyl urea, diazolidinyl urea, 5-bromo-5-nitro-1, 3 dioxane, 2-bromo-2-nitropropane-1, 3-diol, DMDM hydantoin) showed almost the same rate of parabens (15%) but they were more present in rinse-off products. Among the five formaldehyde-releasers, the most common were DMDM hydantoin (53.6%) and imidazolidinyl urea (39.3%), which were both found also in two body lotions.

MI/MCI was found in 9.9% of the examined products, especially in rinse-off ones. Six products contained triclosan (3.1%) (two deodorants, two intimate soaps, a liquid soap, a shaving foam).

As far as children's products are concerned, more than seventy-two per cent contained at least one of the preservatives among those considered, in particular the most present was phenoxyethanol (43.8%), followed by sodium benzoate (37.5%). Formaldehyde-releasers were found into two products (shampoo, nail polish), parabens in a lipstick, chlorphenesin in a body cream and a shampoo, MI/MCI in two rinse-off products (shampoo, liquid soap) (Tab. III).

Almost fifty-four per cent of organic products showed on the label at least one of the preservatives investigated, in particular the most common was sodium benzoate (50%) followed by potassium sorbate (47.2%). It is notable the presence of triclosan in an organic deodorant.

Other chemicals of concern

Fifty-eight per cent of the examined products contained at least one of the other chemicals of concern, especially make-up ones (64.7%). The substances most frequently identified in this group (Tab. V) were PEGs (polyethylene glycols) (62.3%) and acrylate copolymer (34%). The first were more common in rinse-off (81.5%) and leave-on products (69.1%), while make-up ones showed a high presence of acrylates (45.2%) and petrolatum (33.3%).

UV filters (ethylhextyl methoxycinnamate, benzophenone-1, benzophenone-3) were present in 19.1% of the products, especially in make-up ones (45.2%). BHT showed a rate of 14.7% and was found with BHA (butylated hydroxyanisole) in three products (a shampoo, two lipbalms). Noteworthy, two nail polishes which contained toluene.

Referring to children's products, almost fifty-eight per cent contained one or more of the aforementioned substances. Most of these (68%) showed PEGs on their label and the presence of ethylhextyl methoxycinnamate in three lipbalms is remarkable (Tab. III). Organic products contained this type of compounds for a rate of 10.9% and a nail polish contained benzophenone-3.

Discussion

In this study the presence of chemicals that can affect human health in consumer-available personal care and cosmetic products used by a large part of the population and frequently into contact with the body was examined. More attention should be given to leave-on and make-up products which stay longer on the skin. For this reason, dangerous substances could determine greater negative effects on human's health. Make-up products, in particular, are often applied close to mucosa and frequently used by more sensitive categories, such as teenagers.

Fragranced ingredients are widespread diffused in cosmetic products but many of these may cause sensitizations, allergies and skin irritations [11]. For this reason, the EU established limits to their utilization and the obligation to indicate their presence on products labels, when the concentration is higher than 0.01% in rinse-off products, and 0.001% in leave on products [5].

The most common fragrance identified in the present study was limonene (76.9%) which, together with citral

Tab. V. Frequency of occurrence and percentage of other chemicals of concern identified on the label of selected products and referring to rinse-off, leave-on and make-up categories.

Other chemicals	CAS no.	Rinse-off		Leave-on		Make-up		Total	
		(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)
PEGs*	25322-68-3	53	81.5	38	69.1	10	23.8	101	62.3
Acrylate copolymer	25133-97-5	16	24.6	20	36.4	19	45.2	55	34
Petrolatum	8009-03-8	2	3.1	12	21.8	14	33.3	28	17.2
Polysorbate-80/-60/-20	9005-65-6, 9005-67-8, 9005-64-5	16	24.6	7	12.7	1	2.4	24	14.8
Ethylhextyl methoxycinnamate	5466-77-3	-	-	9	16.4	13	31	22	13.6
BHA	25013-16-5	1	1.2	-	-	2	6.9	3	1.6
BHT	128-37-0	3	3.5	14	18.2	11	37.9	28	4.7
Benzophenone-1	131-56-6	-	-	-	-	6	14.3	6	3.7
Benzophenone-3	131-57-7	-	-	3	5.5	5	11.9	8	4.9
Cocamide DEA	68603-42-9	2	3.1	-	-	-	-	2	1.2
Toluene	108-88-3	-	-	-	-	2	4.8	2	1.2

*we considered all ingredients indicated on labels as "PEG" or "-eth", followed by a number.

(24.2%), is classified as skin sensitizers (H317), according to the regulation on the classification, labelling and packaging of substances and mixtures (CLP) [16]. In addition, many fragrance ingredients were categorized as weak allergens [17]; since a large number of products contains a mixture of fragrances, the consumers are more likely to be exposed to mixtures of allergens. Bonefeld et al. [18] found that mixtures of fragrance allergens have an increased potency in sensitization and elicitation of contact allergy as compared with an isolated fragrance allergen.

Among preservatives, parabens are considered as a class of endocrine disruptors, especially propylparaben and butylparaben. Many studies observed that parabens were able to chemically imitate the oestrogenic activity leading to adverse health outcomes [19, 20]. Moreover, parabens could play a role in the development of human breast, ovary and testicles cancer [21, 22]. For these reasons, many countries have banned the use of some parabens in personal care products intended for newborns and children [23].

Formaldehyde-releasers are important sources of formaldehyde exposure and allergic Contact Dermatitis They are able to release formaldehyde that has the capability to cause hypersensitivity reactions [24]. For some time now, formaldehyde is considered carcinogenic to humans [25] and, even if concentrations of these kinds of preservatives added to cosmetics are very low, they are still present in a large number of products whose use occurs frequently and daily.

MCI and MI are preservatives whose use has recently increased in cosmetics, but there is a limit of concentration both for the single ingredient and for the MI/MCI mixture [5]. Many studies focused on contact allergies associated with the use of MI/MCI, even if the dose allowed is respected [26, 27]. The use of chlorphenesin is allowed in concentration lower than 0.3% [28]. At a higher concentration it may cause irritations and contact dermatitis, especially on sensitive skin [29]. Due to the possibility of collateral side-effects on children, in particular on the respiratory tract and the central nervous system, the Food and Drug Administration (FDA) advised against the use of products containing chlorphenesin for children and women while breastfeeding [30]. In this work we underlined the presence of clorphenesin in two children's products.

We found triclosan in few products, however, because of its relevance, it is important to focus attention on it. It is an antimicrobial additive considered potentially harmful for health as an endocrine disruptor, as a result of a prolonged use [31-33]. It may be found together with dioxin, formed during its synthesis process, which could also be formed by photodegradation of triclosan in the urban wastewater [34]. Moreover, the massive diffusion of this antimicrobial compound may determine an increase in the bacterial resistance to the most common antibiotics used in the medical field [35]. The widespread use of this substance is demonstrated by the detection of triclosan traces in fish's fatty tissues and, even worse, in maternal milk. That evidence confirms the continuous exposition to very low or minimal concentrations of triclosan may lead to living organisms to absorb that compound [36, 37]. For all these reasons, triclosan was banned in 2013 by the FDA [38]. Nevertheless, in Europe the use of triclosan is still allowed in cosmetic products.

Lastly other chemicals, considered in our investigation, were substances different from fragrances and preservatives. Benzophenone-1 and benzophenone-3 are chemical filters used for the protection from UV radiations, reputed endocrine disruptors. Exposure to these ingredients, although definitive studies are lacking, could cause negative effects on humans, as well as a neuronal delay and alterations in behavioural development, congenital malformations, fertility deficiency for men, etc. [39, 40]. In addition, the International Agency for Research on Cancer (IARC) classified benzophenone as a possibly carcinogenic to humans (2B group) [41]. These ingredients have good lipophilic properties and after only a few hours from their application on the skin, it is possible to detect them in biological fluids like maternal milk [42]. Also ethylhexyl methoxycinnamate is a UV filter added to cosmetics, and some studies show how it can affect and modify the regulation of the endocrine system [43].

Considering BHA and BHT, the Cosmetic Ingredient Review (CIR) Expert Panel established concentration limits for these substances (0.5% max) because of their uncertain toxicological profile and the potential irritating power on skin and mucosa [44, 45].
Cocamide DEA is a skin irritant [46], classified in 2B group by the IARC [47]. Moreover, in 2012 the California Office of Environmental Health Hazard Assessment added cocamide DEA to the list of chemical compounds that cause cancer [48].
PEGs are characterised by low cutaneous toxicity and generally they are weakly irritants. They come from the polymerization of ethylene oxide, a well-known carcinogenic agent [49]. These substances can contain residual impurities derived from the ethoxylation process: ethylene oxide, dioxane, polycyclic aromatic compounds, heavy metals like lead, iron, cobalt, nickel, cadmium, arsenic [50].
Petrolatum (indicated on labels as paraffinum liquidum/petrolatum/paraffin/vaseline/mineral oil) is widely used in cosmetics but there are some potential health risks linked to its utilization, especially for the possible presence of impurities. In 2011 a scientific study showed that hydrocarbons derived from petrolatum are the most present contaminants in human body and the contamination occurs, above all, through the inhalation of polluted air, the ingestion of contaminated food and cutaneous absorption. This study also underlined that cosmetics can represent one of the most significant source of these compounds [51].
Toluene exposure from nail polish application was assumed to occur through both dermal and inhalation routes: a high concentration can cause irritation on the mucosa and skin irritation. It was listed in 1991 under State of California Proposition 65, as a chemical known for causing reproductive toxicity and having adverse effects on the central nervous system [52].
Finally, acrylates and polysorbates are considered weakly irritants: the concern related to the first compounds is the possible presence of toxic residuals like acrylic and methacrylic acid which are characterized by allergenic activity [53]; while the second ones are less irritants, even if cases of contact dermatitis due to these substances have been proved [54].

Conclusions

As a result of what explained, it is evident how, through the use of cosmetics, most people are exposed worldwide to a variety of potentially harmful substances.
Although the amounts may be small, and their effects sometimes poorly understood, continuous exposure to a mix of these chemicals over long periods could have consequences for the health and well-being of people and society. Actually, the current legislation takes these risks into account and many substances are subject to a threshold concentration, but there is a potential "cocktail effect" due to the utilization of combined products during the daytime. In addition, the same substance can be found in more than one product and can derive from different sources ("additive effect"), in this way, the safety threshold established could be overcome. For example, we can think about formaldehyde which is found in a variety of consumer products: clothing, plastics, dry cleaning agents, paper, glue, drywall board, resins, wood panelling, etc.
It is necessary to improve the legislative approach, since there are chemicals whose use is not completely safe, but still allowed, so that it would be suitable to resort to the precautionary principle. Moreover, it would be appropriate to enhance cytotoxicity studies in order to assess the actual harmlessness of the formulations in vitro [55] and to prefer alternative substances [56] compared to those potentially dangerous used for the stability and the attractiveness of the products.

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Conflict of interest statement

None declared.

Authors' contributions

All authors made substantial contributions to the conception and design of the study and were involved in drafting and critically revising the manuscript in terms of intellectual content. In addition, AP conceived the study, performed the analysis and interpreted the results. FS contributed in the interpretation of results. FB contributed in the analysis and interpretation of data. TG was involved in the study design and methodology. AI and MDG were involved in collection and management of data. MG and MC were involved in planning and supervising the work. ADD was involved in study design, interpretation of results and supervised the findings of this work.

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