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Study of the impurities present in the substances of cosmetic products

Abstract

Cosmetics have always been an integral part of our daily lives. There are different types of cosmetics for application to different sites on the body, which implies a different exposure depending on the product and the site of application. It is therefore essential to evaluate the safety of cosmetics by ensuring the safety of the substances and the finished product for the safety of the consumer. Nevertheless, impurities may persist, which may be due to a reaction of the substance or by contamination of the substance. The EXPERTOX laboratory, which regularly doses the impurities that may be present in cosmetics, has taken a closer look at the impurities that may be found in them through a bibliographical study. This study revealed that almost a third of the impurities were metals and that there was also a significant proportion of residual solvents. Moreover, on average 7 impurities can be found in substances used in cosmetic products. This study obviously requires further research, but it nevertheless makes it possible to realize that it is essential to measure metals when looking for impurities in a substance. This will allow the EXPERTOX laboratory to better target their research, as well as a better evaluation of safety and the development of new dosage methods.

Keywords: impurities, toxicology, cosmetics, dosage, epidermis,

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Introduction

Cosmetics have always been an integral part of our daily lives. According to one study, women use an average of 16 cosmetics.[1] The ANSM defines a cosmetic product as, "a substance or a mixture intended to be put in contact with the various superficial parts of the human body (epidermis, hair and capillary systems, nails, lips and external genitals) or with the teeth and oral mucous membranes, with a view, exclusively or mainly, to cleaning them, perfuming them, modifying their appearance, protecting them, maintaining them in good condition or correcting body odours". This definition includes a multitude of products used by men and women: creams, skin care products, lotions, powders, perfume, make-up, deodorants, baby products, toothpaste, etc. There are several exposure scenarios. Some cosmetics are not intended to remain on the skin and are rinsed off, while others will remain in contact with the skin for several hours. Also, a cosmetic spray may induce a possibility of inhalation and a cosmetic used around the eyes may come into contact with the eye.[2]

There is no prior marketing authorization for cosmetic products and it is the responsibility of manufacturers to ensure that their products meet legislative, regulatory and health safety requirements.[3] According to Article 1 of Regulation 1223/2009 cosmetics and their ingredients must be safe under normal conditions of use. In particular, a risk/benefit reasoning should not be used to justify a risk to human health. Furthermore, Article 10 stipulates that before placing a cosmetic product on the market, the responsible person shall ensure, in order to demonstrate that the product is in conformity, that its safety is assessed on the basis of appropriate information and that a report on the safety of the cosmetic product is drawn up in accordance with Annex I (Cosmetic Product Safety Report). The safety report must include at least (in part A): the quantitative and qualitative formula of the cosmetic product, its physical/chemical characteristics, its microbiological quality, impurities, traces and information concerning the packaging material, its normal and reasonably foreseeable use, data on exposure to the product and the substances contained in the cosmetic product, the toxicological profile of the substances, undesirable effects.[3,4]

Within the framework of the quality control of substances intended for use in cosmetics, possible impurities must be sought both in the substances, the raw materials and in the finished product. They must be characterized and quantified by an appropriate analytical method. In addition, there is no specific recommendation for assessing the limit of non-CMR impurities for cosmetic products.[4]

The data to be provided make it possible to assess whether the cosmetic product contains substances which have not been intentionally added and which could have an impact on its safety. They concern: the purity of the substances and mixtures; in the event of the presence of prohibited substances in trace amounts, the elements proving that it is technically unavoidable; and the relevant characteristics of the packaging material, in particular its purity and stability, insofar as substances may migrate from the packaging to the formulation. Thus, the presence of impurities, including for the packaging material, and traces must be assessed and this assessment must be included in the DIP. According to Article 17 of the Regulation, the unintentional presence of a small quantity of a prohibited substance, originating from impurities from natural or synthetic ingredients, the manufacturing process, storage, migration from the packaging, which is technically unavoidable in good manufacturing practices, is permitted.[3]

It is important to differentiate between ingredients and impurity/trace. An ingredient is defined as any substance or mixture intentionally used in the cosmetic product during the manufacturing process where an impurity is unintentionally present.[3] The presence of these traces can be assessed against the specifications and synthesis process of each substance and/or physico-chemical analyses of potential impurities in the substances and the finished product if necessary. The product safety assessor must justify that the presence of these traces is unavoidable and that the product remains safe for human health in accordance with Article 3 of the Regulation.[3] Particular attention must be paid to any possible impact on the toxicological profile resulting from particle size including nanomaterials, impurities of the substances and substances used, interaction of substances.

The unintentional presence of a small quantity of a prohibited substance, originating from impurities from natural or synthetic

ingredients, the manufacturing process, storage, migration from packaging, which is technically unavoidable under good manufacturing practice, is permitted provided that it is following Article 3 of the new Regulation (EC) No 1223/2009. This states that a cosmetic product made available on the market must be safe for human health when used under normal or reasonably foreseeable conditions.[3]

Among all the impurities frequently sought, metals are often found. As metals can be toxic at a certain concentration, it is very important to measure them in order to limit their presence. Poor quality products are more likely to contain traces and impurities in important quantities. This is the case for example with counterfeited products.[5]

There are, at present, few studies on impurities potentially found in substances used in cosmetic products. The EXPERTOX toxicological laboratory regularly looks for impurities in substances intended for use in cosmetics and therefore wondered if it was possible to carry out a study to allow a better targeting of the search for impurities, a better understanding of the purity certificates, an aid to the interpretation of trace tables and impurities as well as an aid to the toxicological evaluation of substances. Finally, this study would allow the development of new methods of assays by the EXPERTOX laboratory to complement those already existing. EXPERTOX studied the question through a bibliographical study which was punctuated by the writing of a scientific article.

Materials & methods

Setting up the study

We decided to study the impurities that can be found in substances used in cosmetic products through a bibliographic study over a fixed period of 3 months between July and September 2019. It should be noted that this is a work that must be updated regularly because regulations often change. In order to facilitate the collection of data and its interpretation, all the data have been noted on an excel file (Appendix 1). The definition of relevant information is described below.

Definition of relevant data

Selected substances: In order to study the impurities present in the substances, it is necessary to create tools that are appropriate for this study. First of all, it is therefore necessary to determine the substances being studied. To begin, we have identified all the substances present in Annexes III, IV, V, VI of Regulation 1223/2009. These data were collected between July and September 2019, and in view of the regular changes in the regulations we are aware that the data at this time may be slightly different without a significant impact on the data. It is therefore a work that needs to be updated regularly. We have decided to exclude the substances in Annex II because they are prohibited for use in cosmetic products.

The annexes are defined as such:

a. Annex III: list of substances that cosmetic products must not contain except under written restrictions.

b. Annex IV: list of colorants authorized in cosmetic products.

c. Annex V: list of preservatives authorized in cosmetic products.

d. Annex VI: list of UV filters authorized in cosmetic products.

Source of impurity data: As this study is a literature review, it is necessary to specify which sources were essential in the data collection as well as their description. The following are the data sources that were used to search for impurity data:

a. CIR: Cosmetic Ingredient review. It is a group of independent experts from the cosmetic industry that studies the safety of cosmetic ingredients.

b. Directive 95 corresponds to Commission Directive 95/45/EC laying down specific purity criteria for colorants for use in foodstuffs.

c. EFSA: European Food Safety Authority. This is the European Food Safety Authority. It provides independent scientific advice on risks related to food.

d. Regulation 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products.[3]

e. Scientific committee on cosmetic products and non-food products intended for consumers (SCCNFP): Scientific and technical questions concerning consumer health relating to cosmetic products and non-food products intended for consumers, in particular the substances used in the preparation of these products, their composition, their use and their types of packaging. Committee which operated from 1997 to 2004.

f. Scientific committee on consumer products (SCCP): the Committee issues opinions on the health and safety risks (chemical, biological, mechanical and other physical hazards) of non-food consumer products (e.g. cosmetic products and their ingredients, toys, textiles, clothing, personal care and household products) and services (e.g. tattooing, artificial tanning). Committee that served from 2004 to 2009.

g. Scientific Committee on Consumer Safety (SCCS): the Committee issues opinions on health and safety risks (chemical, biological, mechanical and other physical hazards) of non-food consumer products (e.g. cosmetics and their ingredients, toys, textiles, clothing, personal care and household products) and services (e.g. tattooing, artificial tanning). Committee that has been in operation since 2009.

Classification of impurities

Chemical families: From our various sources, such as ingredient safety assessment reports, all impurities that can be found in the various substances have been noted. For some substances it is possible to find about ten impurities and for others none. As a comment we have noted the authorized thresholds if they were informed.

In addition, we decided to use the periodic table or Mendeleïev's table to classify all the metals and an internal list of the EXPERTOX laboratory (Appendix 2) to classify the rest. When impurities were found we were able to classify them according to a list of the following families:

a. Bisphenols (internal EXPERTOX laboratory list)

b. Phthalates (EXPERTOX laboratory internal list)

c. HAPs (internal EXPERTOX laboratory list)

d. Organochlorinated pesticides and pyrethroids (internal list of EXPERTOX laboratory)

e. Allergens" (internal list of EXPERTOX laboratory)

f. Polychrlorobiphenyls (PCBs) (EXPERTOX laboratory internal list)

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g. Residual solvents (EXPERTOX laboratory internal list completed by the European Pharmacopoeia list)

h. Dioxins (EXPERTOX laboratory internal list)

i. VOCs (EXPERTOX laboratory internal list)

j. Alkaline metals: Li, Na+, K+, rubidium, cesium, francium.

k. Halogens: fluorine, chlorine, bromine, iodine, astatine.

l. Non-metals: nitrogen, phosphorus, sulfur, carbon, hydrogen, oxygen, selenium.

m. Alkaline-earth metals: Beryllium, Mg, Ca, strontium, barium, radium.

n. Transition Metals: Silver, bohrium, chromium, cobalt, copper, darmstadtium, dubnium, iridium, iron, manganese, molybdenum, nickel, gold, osmium, platinum, palladium, rhenium, rhodium, tungsten, zirconium, titanium, vanadium.

o. Poor Metals: Zinc, gallium, cadmium, mercury, thallium, lead, bismuth, polonium, tin, aluminum

p. Metalloids: boron, silicon, germanium, arsenic, antimony, tellurium

q. Heavy Metals

It should be noted that some impurities were only defined as "heavy metals" in the various data sources without further detail. In the classification of families, we have therefore left "heavy metals". Finally, given the lack of known toxicological impact, we decided to exclude:

a. Water

b. Loss on drying

c. Loss through dehydration

d. Loss on ignition

e. Moisture content.

There were 30 of these. All other impurities identified that were not included in the family list were classified as "undefined". Most often they were synthetic metabolites.

By toxicological property: We noted the molecules that were classified as carcinogenic in the list of CMR classified chemicals provided by INRS.[6] It considers the 13th adaptation to technical and scientific progress of CLP and considers substances classified as CMR category 1A, 1B, 2 in Annex VI of the amended CLP Regulation. We simply noted O if the substance was classified as carcinogenic, without making any distinction on its classification and N if it was not.

Finally, it was considered to classify according to endocrine disrupting potential, but we had to discard this possibility as there is currently no exhaustive list.

Use of data

After having noted all the information of interest to us for the study, dynamic cross-tabulations were carried out on the excel file in order to analyze all the collected data. Each characteristic was studied. Then, from the data extracted from the pivot tables and statistical analyses were performed. We decided, when interpreting the results, to stop at the 1% threshold.We were first interested in the general analysis of the substances and impurities and then in more detail in the distribution of these according to the annex of the substance. Finally, we ended by studying the families of impurities and their carcinogenicity.

Results and discussion

Analysis of sources of impurities

Impurities were identified from different sources: the scientific committees of the European Commission (SCCNFP, SCCP, SCCS and SSCNFP) represent 74% of the data, the CIR represents 12%, the Directive 95, 11%, and the Regulation 1223/2009, 3% (Figure 1).

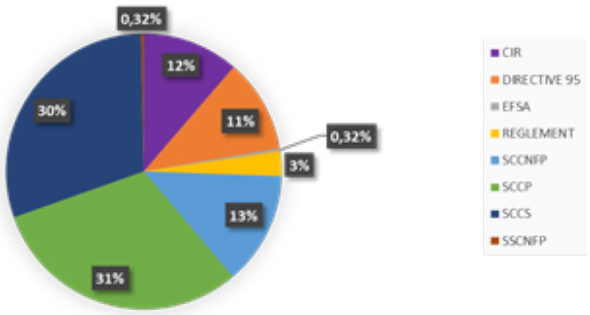

Figure 1 Proportion of impurity data sources.

Analysis of substances

540 substances are listed in Annexes III, IV, V and VI of Regulation 1223/2009 and from our various sources, 169 substances have impurities declared and identified. Furthermore, there is a homogeneous distribution of the substances listed in the different annexes. It is interesting to note that the substances in Annexes III and IV (which contain 305 and 154 substances respectively) have the same ratio of 1/3 while for Annex VI, the ratio is about 1/6th and 1/4th for Annex V (Tables 1).

Table 1 Ratio of substances with data

Origin of the SUBSTANCES studied according to the appendix	Number of substances with data	Total number of substances
Annex III (1223:2009)	103	305
Annex IV (1223:2009)	48	154
Annex V (1223:2009)	13	52
Annex VI (1223:2009)	5	29
Total	169	540

Impurity analysis

General: 1318 impurities were identified among the 169 substances with data. It appears that the metals are the most found with lead, mercury and arsenic with an average frequency of 6%. Cadmium is found at 4.6%, heavy metals at 3.0%, antimony at 3.0% and iron and antimony at 2% respectively. Finally, methanol and nickel are found at a frequency of about 1% (Figure 2).

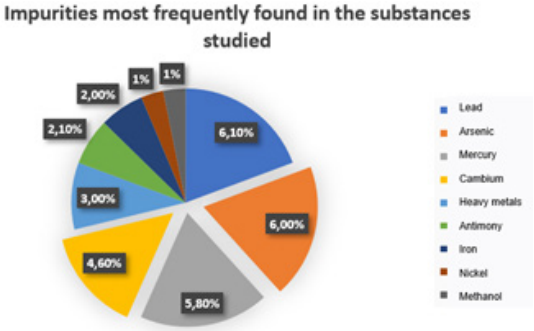

Figure 2 Impurities most frequently found for the substances studied.

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Distribution of impurities: What is the breakdown of the number of impurities per Annex? The vast majority of impurities (90%) are found in Annexs III and IV with 689 and 529 impurities respectively. These are also the Annexs in which the average number of impurities found per substance is the highest: 11 for Annex IV and 6.7 for Annex III. For Annexs V and VI the average number is lower, with an average of between 5.3 and 5.8 respectively. Finally, the overall average number of impurities that can be found per substance is 7(Table 2).

Table 2 Distribution and average number of impurities by substance by Annex

Origin of the substances studied	Number of substances with data	Number of impurities found	Average impurities found per substance
Annex III (1223:2009)	103	689	6,7
Annex IV (1223:2009)	48	529	11,0
Annex V (1223:2009)	13	69	5,3
Annex VI (1223:2009)	5	31	5,8
Total	169	1318	7,2

We have been able to discuss the source data, the Annexs, the distribution of the number of impurities, now let's look at the different impurities that can be found according to the Annex of the substance. Certain impurities are in the majority in several Annexes: this is the case for arsenic and lead which are found in Annexs III and IV, respectively from 4.9 to 8.3% for arsenic and 4.9% to 8.5% for lead. Mercury and cadmium are also found in common in these two annexes at a frequency of 4.6% to 8.1% for mercury and 3.8% to 6.2% for cadmium. Metals are therefore the most common impurities found in Annexs III and IV, representing 37% of the total impurities in Annex III and 36% in Annex IV. For Appendices V and VI, heavy metals are found mostly at 8.7% and 6.5% respectively. However, residual solvents are present at a frequency of 4.4% acetic acid for Annex V and 6.5% methanol for Annex VI. Finally, for Annexes V and VI (which contain few impurities) we can find the unique presence of different impurities such as phenol, benzene and 1,6-diguanidinohexane dihydrochloride for Annex V and formaldehyde, cadmium or synthetic metabolites for Annex VI.

The following table summarizes the different impurities that can be found according to the annex of the substance above the threshold of 1.5% (Table 3).

Table 3 Frequency of occurrence of impurities according to the Annex of the substance

Annex III	Annex IV	Annex V	Annex VI
Arsenic 4,9%	Lead 8,5%	Heavy metals 8,7%	Heavy metals 6,5%
Lead 4,9%	Arsenic 8,3%	Acetic acid 4,4%	Methanol 6,5%
Mercury 4,6%	Mercury 8,1%		Formaldehyde
Cadmium 3,8	Cadmium 6,2%		Cadmium Camphor
Antimoine 3,5%	Heavy metals5,3%		Toluene
Iron 2,6%	Coloring materials 3,2 %		1-hexanol4-
Sulphated ash1,7%	Water-insolublematerials 2,8%		Dimethylaminobenzaldehyde-
			4-Dimethylaminobenzoic- acid
			4-tert-butyl-o-xylène9-decyn-1-
		1,6-	ol Arsenic
		diguanidinohexane	Sulphated ashIron
	Ether extractable materials	dihydrochloride Phénol	
Nickel 1,5%	2,0%		Mercure
		BenzenSulfate	Lead Nickel
		2,9 %*	3,2 %**

*For information, this frequency represents 1 out of 69

**For information, this frequency represents 1 in 29

Family analysis

General: Half (55%) of the 1318 impurities could not be defined because they do not fit into any of the above-mentioned families. Therefore, 715 impurities could not be classified and 603 were classified into 12 different families. Out of the 12 families found, 7 have a frequency of appearance higher than 1%. We find 18% of poor metals, 8% of metalloids and 8% of residual solvents. There are also 7% transition metals, 4% heavy metals and 1% alkaline-earth metals. The rest of the families not shown on the graph were less than 1% (Figure 3).

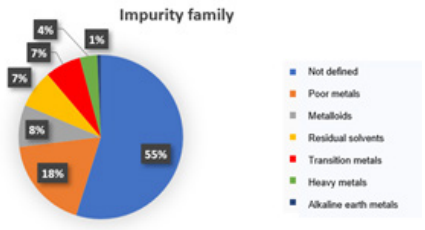

Figure 3 General analysis of the most frequently found families of impurities.

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By grouping together all the families of metals, we can see that they represent more than 1/3 of the impurities found with a proportion of 38%. These findings confirm many studies that had found different metals in cosmetic products.[2,7–9] During the manufacture of a substance, it sometimes seems thorny to avoid certain impurities. Some may result from a chemical reaction, others from the contamination of a solvent by metals, for example, or pesticides.

Moreover, good industrial practices do not prevent the residual presence of traces of metals in the environment and therefore in drinking water, food and cosmetics. Metals may thus be present in ingredients of natural mineral and vegetable origin used in cosmetics. A strict and regular quality control allows us to limit these traces as much as possible so that they do not represent any risk to the health of the consumer. Acceptable limits vary for metals depending on the population concerned (children, pregnant women ...), the quantity of product used and its site of application (lips, body...). In addition, the European cosmetic regulation allows the unintentional presence of a small quantity of these substances when its presence is unavoidable and without risk for the end user. Here are the 12 families that we have defined. We find one pesticide, one dioxin, and one HAP (Table 4).

Table 4 Distribution of Impurities in the 12 families

Family of impurities	Number of appearances
Poor Metals	237
Métalloides	108
residual solvents	97
Transition Metals	92
Heavy Metals	45
Alkaline-earth metals	9
Non-metals	6
Alkali metals	4
VOC	2
Dioxin	1
HAP	1
Pesticide	1
Total	603

Out of the 18% of poor metals found, lead, mercury and cadmium are the metals mostly found with respectively 34%, 32% and 25% frequency of occurrence (Figure 4).

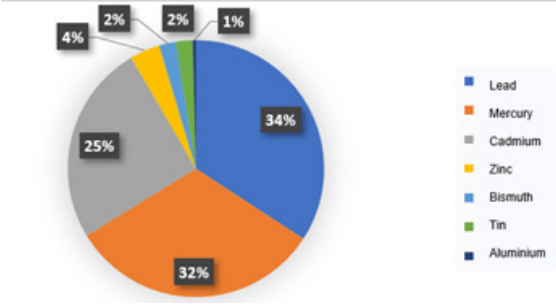

Figure 4 Frequency of occurrence of different metals in the poor metal family.

Distribution of families by Annex: According to the table below, summarizing the families of impurities found according to the Annex of the substance, the most common impurities are poor metals for Annexs III and IV and residual solvents for Annexs V and VI. Residual solvents can be found in all substances in the different Annexs ranging from 6.2% to 13.0%. There are also poor metals in each annex ranging from 9.7% to 24.4% except for Annex VI where they are not present. Finally, on average, 9% metalloids may be present in the substances in Annexs III and IV. Grouping the families of metals together, these represent 37% for Annex III (Table 5).

Table 5 Family of impurities according to the Annex of substances

Annex III		Annex IV		Annex V		Annex VI	
Family	**Frequency**	**Family**	**Frequency**	**Family**	**Frequency**	**Family**	**Frequency**
undefined	55,6%	undefined	46,3%	undefined	63,8%	undefined	58,1%
Poor metal	15,2%	Poor metal	24,4%	Residual solvents	13,0%	Residual solvents	12,9%
Transition metal	9,3%	Metalloid s	9,1%	Heavy metal	10,1%	Poor metal	9,7%
Metalloids	8,6%	Residual solvents	7,8%	Dioxin	1,4%*	Heavy metal	6,5%**
Residual solvents	6,2%	Heavy metal	5,3%	Alkaline metal	1,4%*	Transition metal	6,5%**
Heavy metal	1,2%	Transition metal	4,7%	Transition metal	1,4%*	Meta lloids	3,3%***
Total families	10	9		5		6	

*this frequency represents 1 in 69

**this frequency represents 2 out of 31

***this frequency represents 1 in 31

Analysis of carcinogenicity

After analyzing the families of impurities, their frequency, their distribution, we looked if among them there were carcinogens. Thanks to the list of CMR classified chemical substances provided by INRS, we were able to classify the impurities classified as carcinogenic without distinction for the category. Approximately 5% of the impurities found are listed as carcinogenic (see excerpt from the table).

Conclusion

It is a delicate and still insufficiently documented subject that the EXPERTOX laboratory has tried to decipher through its study. It was difficult to step back and compare all our data given the lack of scientific articles on this subject.

It was highlighted that metals are a major problem with a potential presence of 38% in the substances. This shows the importance of

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quality control and safety assessment of substances and FPs. Of course, this information comes from potential declarations but there may be other degradations, interactions of substances and raw materials due to e.g. pollution, packaging, transport, or other factors, which were not considered in this study. Further research is needed to confirm our interpretations. It could be interesting to compare these bibliographical data with real data of impurity dosages of substances and finished products in order to compare this information with ours. The results would allow a better targeting when searching for impurities and assessing the safety of cosmetic products. This study is a tool to better apprehend and evaluate potential contaminations. It also allows the EXPERTOX laboratory to consider new method developments for impurities it was not looking for before.

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None.

Conflicts of interest

The authors declare that there are no conflicts of interest.

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