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DEBATE ARTICLE

Changes in European Legislation Make it Timely to Introduce a Transparent Market Surveillance System for Cosmetics

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Marketing of cosmetics often makes strong claims linked to active ingredients. This is especially so for anti-ageing products, where the presentation and content of "active" ingredients may create new difficulties in their classification as cosmetics or medicinal products. A recent change in European legislation classifies a product as medicinal by virtue of its "function", in addition to the previous definition of "presentation" (i.e. marketing linked to diseases). Thus, formulations that also restore, correct or modify physiological functions by exerting a pharmacological, immunological or metabolic action should henceforth be covered by the Medicinal Products Directive. A cosmetic product must be suitable for its purpose and should not lead to adverse reactions that are disproportional in relation to its intended effect. However, the forthcoming ban on animal testing of cosmetic ingredients and the new European regulation, REACH (Registration, Evaluation and Authorisation of Chemicals), which aims to ensure a high level of chemical safety to protect human health and the environment, will probably have limited impact on the safety assessment of cosmetics. In order to enable consumers to make informed purchasing decisions, greater transparency in the process of assessing the performance of cosmetics is needed. Introduction of a more transparent system, enabling consumers and professionals to examine the scientific evidence for the claimed effect and the safety assessment of cosmetics, is therefore timely. Lack of transparency increases the risk of consumers wasting money on cosmetics that do not deliver the desired effects. This may jeopardize public trust in the cosmetic industry. ***Key words: claim substantiation; pharmaceuticals; efficacy; safety; misleading.***

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The cosmetics industry is global, characterized by companies marketing branded raw materials and finished products across international boundaries. The industry is competitive and highly innovative: on average, major cosmetic companies replace or reformulate approximately 25% of their products every year (1).

Cosmetics do not need marketing authorization, while medicinal products can only be marketed if and when marketing authorization is granted. The relevant authority grants this marketing authorization based upon detailed information about the quality, efficacy and safety of the medicinal product. Essential studies have to be undertaken, especially those concerning safety and efficacy.

The marketing and product presentation of cosmetics often makes strong claims linked to active ingredients and scientific evidence in order to persuade people of their efficacy. The presentation and content of relatively undefined ambivalent ingredients (e.g. some botanicals and vitamins) may create difficulties in their classification as cosmetics or medicinal products. The marketing of cosmetics in relation to their efficacy and safety is discussed in the present overview, using anti-wrinkle creams as an example. Furthermore, the aim of the present review is to promote transparency of the scientific evidence for product claims and safety, which may enhance public trust in the cosmetics industry. Taking ethics seriously is debated with regard to cosmetic dermatology (2).

REGULATORY FRAMEWORK FOR TOPICAL FORMULATIONS

Product claims and ingredients in topical formulations result in different regulatory procedures. The category "cosmetic product", as defined in the EU Cosmetics Directive (76/768/EEC) has borders with a range of product categories, including medicinal products, biocides and medical devices. The EU Cosmetics Directive defines a cosmetic product as:

> … any substance or preparation intended to be placed in contact with the various external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance and or/correcting body odours and/or protecting them or keeping them in good condition.

The new European medicinal legislation defines a medicinal product by virtue of either its "presentation" or its "function" (3). Thus, any substance or combination of substances presented for treating or preventing

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disease in humans is considered a medicinal product. Furthermore, products that are used in or administered to humans with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action are also covered by the Medicinal Products Directive, (i.e. definition by virtue of function) (3). These terms can be defined according to the following (4):

- *Pharmacological action:* interaction between the molecules of the substance in question and a cellular constituent usually referred to as a receptor, which either results in a direct response, or which blocks the response to another agent. Although not a completely reliable criterion, the presence of a dose-response correlation is indicative of a pharmacological effect.
- *Immunological action:* action in or on the body by stimulation and/or mobilization of cells and/or products involved in a specific immune reaction.
- *Metabolic action:* action which involves an alteration, including stopping, starting or changing the speed of the normal chemical processes participating in, and available for, normal body function. The fact that a product is metabolized *by* the human body does not necessarily mean that the substance contained in the product has a metabolic action *upon* the body.

Thus, making the wrong claims or including ingredients in topical products that significantly modify the physiological functions of the skin can result in a medical classification of cosmetics and hence the need to comply with the comparatively onerous medicinal products regime. However, it does not make sense to classify insignificant modifications of physiological functions, for example via immunological actions induced by contact allergens, as medicinal actions. It is for the national competent authorities and national courts to assess on a case-by-case basis which regulatory framework applies for each formulation, based on the composition and physiological properties of the product and the risk that its use may entail (5).

In the USA there is a more pragmatic adherence to the definition of a medicinal product. For example, it is a serious violation of the *Federal Food, Drug, and Cosmetic Act* to influence the structure or any function of the body by application of cosmetics (6). Hence, claiming that products stimulate collagen synthesis, strengthen elastin fibres, reduce wrinkles or cellulite establishes the products' intended use to affect the structure or function of the body and causes them to be classified as drugs. Warning letters are then issued by the Food and Drug Administration (FDA) requesting the companies to take prompt action to correct such violations (7). Also, physical effects induced by sunscreens (reflection and ultraviolet (UV) quenching) and antiperspirants (mechanical obstruction of eccrine canal) classify these products as drugs in the USA, which forces the companies to adhere to the rules governing monographed over-the-counter (OTC) drugs.

COSMETICS AND THEIR INGREDIENTS

The great interest in maintaining a youthful appearance with minimal signs of ageing skin has led to a substantial market for prestigious and expensive skincare products that claim anti-ageing effects. Anti-ageing cosmetics are expected to generate pleasant emotions during their use and to improve facial appearance. The latter can be achieved by different means. Simply camouflaging the surface using coloured pigments (e.g. foundations) or adding reflecting pigments to ordinary creams to reduce shadows in the skin microstructure are physical methods of improving appearance. Cosmetics with anti-ageing claims usually also contain UV filters to reduce photo-ageing. UV filters quench the UV radiation from the sun by reflection or absorption. Furthermore, ordinary moisturizing creams remove signs of dryness, such as roughness and dullness, by physical occlusion and humectancy. Physical methods to reduce the signs of ageing skin may therefore be compatible with the EU Cosmetics Directive in contrast to the US directives, as described above.

However, the use of botanicals in cosmetic products creates a more multifaceted situation. We know that most of our foodstuff is derived from nature, substantiating its importance for human vitality in conjunction with harmlessness. We also know that several drugs are derived from nature (e.g. digitalis), making consumer perception of botanicals in topical formulations as having the potential to be as effective as drugs on the living tissue. Raw material suppliers and the cosmetic industry are therefore driven to discover new sources of ingredients to meet increasing consumer demand for natural products with positive effects on the skin (Table I) (8). For example, although oestrogen is not allowed in European cosmetics (9), phyto-oestrogens, such as genistein (isoflavone in soy), are targeted at women experiencing a reduction in hormonal activity and with skin displaying the effect of ageing (10). Growth factors and botanical extracts are frequently claimed to increase collagen content and skin density (8, 10, 11). Thus, if growth factors and botanicals (e.g. those listed in Table I) exert a significant pharmacological, immunological or metabolic action in the skin, then the formulations should be classified as medicinal products.

The use of complex mixtures, such as botanicals, is also challenging from a formulation viewpoint. To determine the optimum concentration of the "active" ingredients, and retain their concentration during processing and storage is resource demanding. Dose-response and shelf-life of active ingredients are essential parameters that need to be addressed in the claim-substantiation procedure. Therefore, information on raw material submitted by the suppliers must be validated carefully for the final performance in the product; otherwise public trust in the cosmetic industry may be jeopardized.

Table I. *Examples of botanicals marketed for use in anti-wrinkle creams (8)*

International Nomenclature Cosmetic Ingredient (INCI) name	Raw material supplier	Claimed properties
Aemella oleracea extract	Gattefossé Corp, Paramus, NJ, USA	From tropical plants. Ideal in wrinkle care dedicated to expression line smoothing. The ingredient limits microcontraction that aggravates facial wrinkles.
Argania spinosa kernel extract	Laboratoires Sérobiologiques, Pulnoy, France	Proteic fraction of Argan seeds, recommended for the use in anti-ageing care for its anti-wrinkle and tightening properties.
Curcuma longa (tumeric) root extract	Premier Specialties Middlesex, NJ, USA	Skin lightening via inhibition of tyrosinase for anti-aging products.
Dihydromyricetin	Provital Group, Barcelona, Spain	Acts on lipid metabolism and differentiation processes of adipocytes. Promotes lipolysis by selective inhibition of tyrosine kinase activity of the β-receptor subunit.
Euglena gracilis extract	Sederma SAS, Le Perray en Yvelines Cedex, France	Cell energizer which helps skin to recover its firmness and tone by triggering cell metabolism and stimulating calcium release.
Garcinia cambogia fruit extract	Premier Specialties, Middlesex, NJ, USA	Garcinol inhibits skin glycation that leads to reduced suppleness, inflammation and injury to the extracellular matrix.
Hydrolysed *Cucurbita pepo* (pumpkin) seed cake	Silab, Brive Cedex, France	The ingredient smoothes the skin and evens skin tone by controlling the protease activity and stimulating the extracellular matrix constitutive fibres.
Hydrolysed *Opuntia ficus indica* flower extract	Silab, Brive Cedex, France	Stimulates the activity of skin enzymes involved in the exfoliation process. It favours cell renewal and reduces lines and wrinkles.
Magnolia officinalis bark extract	Premier Specialties, Middlesex, NJ, USA	Potent anti-inflammatory used to reduce dark areas around eyes.
Melia azadirachta leaf extract	U.S. Cosmetics Corporation, Dayville, CT, USA	Whitens/brightens skin by decreasing the rate of melanin production.
Palmitoyl hydrolysed wheat protein	Seppic, Fairfield, USA	Quick mechanical action to smooth out expression lines and a long-term biological effect to re-densify skin and fill deep wrinkles.

CLAIM SUBSTANTIATION OF COSMETICS

According to the sixth amendment of the Cosmetics Directive 76/768/EEC, it is a regulatory demand to have: "proof of the effect claimed for the cosmetic product, where justified by the nature of the effect or product". This regulation has incited a search for improved methods to evaluate treatment effects, and non-invasive bioengineering test methodology has proven especially useful (12).

However, there are many pitfalls in the performance and interpretation of studies in humans. Therefore, the Danish competent authority has officially proposed guidelines for human efficacy studies (13) and a voluntary European group on efficacy measurements of cosmetics and other topical products (EEMCO) has addressed methods and study details in a number of reviews (14–24).

Commonly encountered problems in the interpretation of study results are the influence of possible product residues on the skin upon generation of test data in humans. For example, filling the microstructure of the skin with cream ingredients will not allow a true representation of the skin surface when the structure is evaluated. This may lead to high improvement percentages when the anti-wrinkle effects are calculated. Furthermore, non-blinded studies may influence judgement of the effects (25) as well as changing the consumption of creams (26). Double-blind, randomized controlled studies on the target group may therefore be necessary in order to support the effect of new active ingredients (13).

The development of *in vitro* methods, as alternatives to animal toxicity studies, has also increased the number of proposed methods that can be used to substantiate the efficacy of cosmetics. Whether the effects are detectable *in vivo* or are merely expectations is often not known. Due to their complexity, *in vitro* tests require even more careful validation than do studies in humans in order to become relevant for the outcome in the skin (13). *In vitro* studies in combination with open and uncontrolled *in vivo* studies were recently considered not to provide enough support to the claims for an anti-wrinkle cream in the UK and the advertisement for the cream was therefore considered misleading by the Advertising Standards Authority (27).

TRANSPARENCY FACILITATES INFORMED PURCHASING DECISION

It is relatively easy for consumers to judge the benefits of the immediate superficial physical effects (e.g. filling and colouring) of anti-ageing creams. However, the marketing claims of several anti-wrinkle products also give the impression of deeper and more sustainable effects, which may become evident after weeks or months of treatment (Table II). Consumers are therefore, faced with difficult decisions in the selection of anti-wrinkle creams due to the absence of pre-marketing authorization and the limited transparency of the scientific evidence for the claim. For example, some consumers may prefer to use an ordinary sunscreen rather than an expensive face cream, the anti-ageing claims for which are substantiated solely by its content of UV filters.

Spurious and often confusing claims, considered to be of little benefit to the average consumer, have also prompted an initiative by the European Commission to improve the labelling of sunscreens (28). One competent authority has made comparative studies on sunscreens

Table II. *Examples of products on the market that claim anti-ageing effects*

Product	Active principles	Claimed effect on the skin	Source
Novadiol Anti-ageing skincare	”Phyto-flavone® an association of stimulating soya extract and two phytoactive ingredients in order to rebuild skin’s inner substance (epidermal cells + supporting collagen)”. ”Phyto-complex™ and Biophenonene™ to redensify and visibly smooth out the skin”.	”After 6 weeks the skin is redensified, plumped out and as if resculpted from within.” Accompanied with a photograph showing a weight attached to chin.	http://www.vichy.com
Myokine Vichy	New revolutionary complex with adenosine and magnesium. Limit the calcium-induced cellular contractions.	”Peri-ocular wrinkles appear visibly reduced. Smoothes the eye contour area and prevents the appearance of new wrinkles. Beneficial effects on ”dynamic” wrinkles. The groove of the wrinkle appears as if unfolded. The skin is smoothed.”	http://www.vichy.se http://www.vichy.fr/FR-FR/htmlref/produits/SCADA001.html
Alpha Lipoic Acid (ALA), Vitamin C Ester & DMAE Cream	”ALA helps promote the healthy production of nitric oxide, a substance that helps control blood flow to the skin (which is also the basis for the effect of the drug Viagra, increasing blood flow to the penis). This increased blood flow decreases swelling and edema, thus reducing under-eye puffiness. It also gives the skin the healthy glow of increased circulation. When mixed with nutrients and other antioxidants and applied topically, DMAE (dimethylaminoethanol) can improve the appearance of sagging skin, which results not just from free radical damage to collagen, but also to the nerves and muscles underneath the skin. Muscle tone and contraction are caused by the release of neurochemicals, specifically acetylcholine, at the neuromuscular junction – the microscopic space where the nerve acts on the underlying muscle. Topically applied DMAE works within minutes of application, its firming effect lasting for nearly 24 h. Those who use DMAE topically report a leaner look as their facial musculature improves. Some even notice that it lifts the tip of the nose.”	”Reviva Labs now offers a new answer to firming, tightening, ”lifting” skin with DMAE… as ALPHA LIPOIC ACID and Vitamin C Ester fight free radicals and future skin aging. As a special Reviva boost, this dramatic trio is encased in a soy liposome for deeper, time release action during the night. Allantoin and aloe vera are added to soothe and calm stressed skin, contributing to a healthy, vibrant glow. For supple, more youthful looking skin, it’s another major advance in the battle against skin aging.”	http://www.myskincare.biz/catalog/product_info.php?products_id = 163&osCsid = e08976647f08b48ef764fb719d5a47d2
Age Defying Anti-Wrinkle Replenishing Night Cream	”Niacinamide Also called vitamin B3, niacin, and nicotinic acid, this water-soluble ingredient has been shown to prevent skin from losing water content, as well as stimulate circulation in the skin. Recent studies have shown that it also improves the appearance of wrinkles, skin discolorations, reduces redness and improves skin elasticity.”	”Renews skin’s appearance at night when it needs it most while visibly reducing the appearance of fine lines and wrinkles – awake to skin that looks younger, smoother and overall firmer. Olay Anti-Wrinkle Replenishing Night Cream, with pro-retinol and beta-hydroxy, is a wrinkle-fighting formula that works deep within the skin’s surface to significantly reduce the appearance of fine lines and wrinkles. Olay intense”	http://www.olay.com/products/ge1007?tab = ingrelist
L’Oreal Dermo Expertise Wrinkle De-Crease with Boswelox Advanced Wrinkle Corrector & Dermo Smoother	”Boswelox is a phyto-complex that combines a power dose of boswellia serrata extract and manganese, which help reduce the appearance of lines caused by facial micro-contractions.”	”From age 30, targeted expression lines. Crow’s feet appear visibly reduced. 76% reported visible reduction in the appearance of expression lines. Tested in 50 women.”	http://www.lorealparis.co.uk

Table II. continued

Olay Regenerist Targeted Tone Enhancer	”Amino-peptides have demonstrated a remarkable anti-inflammatory effect deep within the skin’s surface that promotes anti-aging properties, including tissue regeneration.”	”uses an exclusive amino-peptide complex combined with pro-retinol to renew the outer layer of your skin for a more youthful brightness. It allows you to target damaged cells by diminishing the appearance of age spots and discoloration without drastic measures. **The results? Beautifully regenerated skin – the appearance of age spots and discoloration diminished.” **Results not equal to medical procedures.	http://www.olay.com
Nivea Visage. DNAge Cell Renewal Day Cream	Contains an SPF 15 and ”combines two powerful, active ingredients: folic acid shown to support healthy skin cell development and creatine known to act as powerful energy source for cells”.	”it protects the cell division process from the damage that is caused by external influences (UV light, pollution...)” and ”.. reduces DNA damage in your skin whilst promoting healthy skin cell production. This will give improved skin vitality, tangibly firmer skin and visibly reduction of wrinkles and fine lines”.	http://www.nivea.co.uk
Nivea visage beauty boost night	Creatine	”designed to stimulate the skin’s natural anti-ageing process” contains multi-active Creatine to enhance the production of collagen helping to improve your skin’s strength and suppleness.	http://www.nivea.co.uk

and found important differences in their efficacy (29). To our knowledge no studies have been made on anti-wrinkle products. Independent studies of anti-ageing creams are hampered by the required length of the study and by complicated techniques for evaluation of the effects. Vehicle-controlled studies are also complicated, since the effect of cosmetics is often claimed to be due to a “balanced and precise mixture of cosmetic ingredients”(30), usually covered by trade names.

In a recent study, no differences in facial appearance were demonstrated between treatment with a conventional moisturizer and an expensive anti-wrinkle cream, as judged by a trained assessor, the subjects themselves and by objective replica technique (26). It was claimed in the marketing of the cream that as many as 94% of the test subjects were satisfied regarding wrinkles/fine lines after only 4 weeks of treatment (31). The cream contained 51 substances, including 2 UV filters and cost almost €100 for 50 ml. Anti-wrinkle creams may vary in price from €5 to €500 for 50 ml. Extract of liquorice root, “Adhesioderm” and “Life Cycle Regenerator” are mentioned as active principles in the formulation (31). “Adhesioderm” and “Life Cycle Regenerator” are claimed to “stimulate the production of the anchor molecules, which form the junction between the dermis and the epidermis” and to “boost the skin’s metabolism”, respectively (31). Furthermore, the cream contains extract of liquorice root, which was claimed to “help regulation of the production of melanin” and counter dark spots (31).

Absence of differences in efficacy between expensive products and own-brands was also found recently by an independent nonprofit consumer organisation (Consumers Union) when they compared 9 face creams (32). The best performers reduced the average depth of wrinkles by less than 10%, a magnitude of change that was barely visible to the naked eye. Furthermore, no relationship between the active ingredients in the products and their overall performance were detected. The price of the tested products ranged from €38 to €335.

The price of face creams is comparable with, for example, medicinal products, where a new innovative dermatological drug costs approximately €100 for 50 ml (Protopic, Astellas Pharma GmbH, München, Germany). The approval procedure and marketing of new medicinal products is accompanied by extensive clinical trials, whereas the scientific evidence for the performance of anti-wrinkle cosmetics are neither approved by an outside party, nor easily accessible to the users of the products. To enable consumers to make informed purchasing decisions there is a need for greater transparency in the process of identifying the performance of cosmetics.

SAFETY ASSESSMENT PRIOR TO THE MARKETING OF COSMETICS

A cosmetic product must be suitable for its purpose and must not cause adverse reactions under normal use that are disproportionate to the intended effect of the product.

The European Inventory of ingredients employed in cosmetic products includes some 8000 chemical substances belonging to 36 different cosmetic functions.

Chemical substances within the EU must undergo a risk assessment to examine the risks posed to humans prior to their use. Every cosmetic product marketed in the EU must also be evaluated by a qualified professional. The safety assessment is based on the toxicological profile of the ingredients, their chemical structure and the exposure level (9). However, the identification and assessment of chemical risks are slow and there is a lack of toxicological data on compounds already in industrial use. Therefore, the forthcoming European regulation REACH (Registration, Evaluation and Authorisation of Chemicals) aims to ensure a high level of chemical safety to protect human health and the environment. However, REACH is considered to have limited impact on the availability of toxicological data for substances used in cosmetics, since animal testing will be phased out and, perhaps more importantly, less toxicological data are needed on low-volume chemicals in Europe. The testing ban on finished products has applied since September 2004, while the testing ban on ingredients or combination of ingredients will apply step by step as soon as alternative methods are validated and adopted, but with a maximum cut-off date of 6 years after entry into force of the Directive, i.e. March 2009, irrespective of the availability of alternative non-animal tests (33).

The limited data requirements on low-volume chemicals may influence the toxicological data on "active ingredients" in cosmetics, since no tests at all are required for production volumes below 1 tonne (1000 kg), which is a change for the worse as the previous limit was 100 kg (34). This change in limit aims to facilitate the innovation and competitiveness of the EU chemical industry. Toxicological test programmes may be too resource demanding for small- and medium-sized enterprises. Furthermore, for production volumes of 1–10 tonnes, the only test required that may give some indication of a potential of carcinogenic, mutagenic or reproductive effect (CMR) is a mutagenicity test in bacteria. A mutagenicity test is insufficient for proper toxicological evaluation of the potential for substances to be classified as CMR compounds. The use of CMR compounds in cosmetics is prohibited, but this does not trigger any additional toxicological studies (33). Not even for substances to be included in the annexes to the Council Directive 76/768/EEC is it compulsory to perform carcinogenicity and reproductive toxicity tests, as this is judged on a case-by-case basis (34). Hence, it remains the responsibility of the safety assessor at the cosmetic company to justify whether enough information on the ingredients, the finished product and exposure is available for safety evaluation (34). This is a difficult situation, as in most cases it can be argued that more information is needed to be able to make a reliable evaluation. In particular, the evaluation of complex mixtures such as botanicals is very difficult, as they often contain numerous loosely defined substances, the content of which may vary with the production method, the part of the plant used, the growing conditions, the time of harvest, etc. (35).

Hence, the introduction of REACH and alternatives to animal testing of cosmetics (9) will not immediately solve the problem of lack of toxicity data and increase confidence in the safety evaluation of cosmetics. Therefore, selection of chemicals for further studies has to be performed by other strategies, e.g. studying structural alerts, using methods for quantitative structure-activity relationship (QSAR), etc. Furthermore, epidemiological studies on compounds already in use can be employed to substantiate their innocuousness. The statistical resolution in epidemiological studies is usually not high enough to determine risk levels of particular substances that are of interest to society (36). Such studies can never replace conventional safety studies.

COSMETO-VIGILANCE MORE THAN CONTACT ALLERGY

Undesirable effects caused by cosmetics may lead to acute and chronic suffering, for example lifelong intolerance to specific substances, with negative consequences for the individual as well as for the healthcare and social insurance systems. Some of the undesirable effects that may be caused by the use of cosmetic products are listed below:

- contact dermatitis caused by allergy or irritation;
- contact dermatitis caused by photo-allergy or photo-toxicity;
- conjunctivitis;
- urticaria;
- acne cosmetica/acne-folliculitis;
- hypo- or hyper-pigmentation;
- granuloma;
- onycholysis, subungal haemorrhage, anocychia;
- alopecia;
- cancer;
- desquamation and irritation of the membrane of the oral cavity;
- sensitization of teeth;
- different systemic effects.

The EU has an intergovernmental rapid alert system (Rapex) that operates when unsafe consumer products appear on the market. Recent cases have included illegal levels of a carcinogen in a British-made eyeliner, and skin-lighteners produced in Italy and India that contained glucocorticoids. Statistics compiled by the cosmetic industry imply that relatively few and minor undesirable effects can be assumed to be caused by cosmetics, given the number of units sold (www.colipa.com).

Epidemiological studies show the frequency of adverse reactions to cosmetics to be 10–15% (37, 38). Among patients referred for standard patch-testing due

to suspected contact dermatitis, 47% (54% women and 31% men) reported current or previous adverse skin reactions to cosmetics and skincare products in Sweden (39). Some of the adverse reactions to cosmetics can be attributed to contact allergens, identified by patch-testing. Case-reports on contact allergy have also influenced dermatological clinics to monitor and report more systematically the frequency of sensitization to identified allergens, such as preservatives and fragrances. The recent finding of an increased frequency of fragrance allergies (40) has caused the Cosmetics Directive to be amended to require labelling of products containing the 26 most common fragrance allergens. The increase in allergy-induced illnesses in the population also highlights the need to improve post-marketing surveillance system for cosmetics. Furthermore, prohibition of animal testing (9) also highlights the need for an efficient post-marketing surveillance system to confirm the appropriateness of alternative methods.

Introduction of an efficient post-marketing system may therefore be timely, in order to elicit consumers' and professionals' awareness of the potential disadvantages of cosmetic products. Most adverse reactions are not reported and recorded in a standardized way. Currently, the quality of collected data is poor, due to insufficient involvement of the industry, dermatologists and the affected consumer. Pharmaco-vigilance is long-established, whereas cosmeto-vigilance is in its infancy. As the cosmetic industry is global, multinational companies have the opportunity to collect data from a large number of exposed persons, giving the basis for extensive epidemiological studies and/or early indications of potential side-effects. The industry is obliged to record complaints and inform customers on request about undesirable effects reported to them by other customers (9). Consumer associations should encourage, by any appropriate means, those consumers who notice an undesired reaction to consult a health professional or to report to the competent authorities or at least to the person responsible for placing the product on the market. The establishment of national networks of health professionals that test and report to health authorities in a standardized procedure should also be encouraged (41). Harmonization in handling of undesirable effects and proper aggregation of data would significantly enhance the quality of the collected information.

Making such information publicly available along with the quantitative composition should enable more efficient assessment of the substances with insufficient toxicological data. For some biological end-points reflecting acute problems, this seems a simple strategy. A more challenging problem would be the time lag from exposure to appearance of adverse effect for some end-points, such as cancer, which would require more complicated follow-up analyses. For this, risk management might prioritize those cosmetics marketed for their stimulating and cell-renewal activities.

CONCLUSION

Regulatory authorities and consumer groups place great responsibility on the manufacturers to ensure the efficacy and safety of cosmetic products. If a cosmetic is found to qualify as a medicinal product, then the consequences for the manufacturer are expensive. On the other hand, harmful consequences for the consumers could arise if cosmetics interact with structures below the stratum corneum and induce adverse effects.

The authors therefore suggest the introduction of a transparent system that enables consumers and professionals to access scientific evidence regarding the claimed effect on the skin of cosmetic products, the safety assessment and potential adverse effects. Evidence regarding the claimed effects and safety assessment of cosmetics could be published on company websites, or be administered by some other independent organization or regulatory authority. The marketing of anti-wrinkle products that have no noticeable effects on the skin may be misleading. If the products induce significant physiological changes in the skin via pharmacological, immunological or metabolic mechanisms, then they should be classified as medicinal products.

In order to ensure adequate safety of newly introduced active ingredients in cosmetics, the professionals concerned must be encouraged to act properly in order to give transparency to findings that may be important for consumers. Efficient post-marketing surveillance, focusing on undesirable effects, their analyses, evaluation and dissemination of the conclusions and follow-up measures is essential for the cosmetic industry and its stakeholders.

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