"FOR" AND "AGAINST" THE USE OF NANOSTRUCTURES IN COSMETIC PRODUCTS

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ABSTRACT

Nanotechnology is a modern branch of science which is engaged with the design, characterization, formulation and implementation of devices, systems and structures with dimensions up to 100 nm. It finds a wide application in many areas – from electronics to medicine and pharmacy.

In recent years, a direction called nanocosmetics is formed. Many leading companies, producing cosmetic products use nanotechnology in their work to achieve better penetration, sustained effect, increase of the UV- protection of the skin, protection from the harmful effects of environmental factors. Commonly used nanostructures are: liposomes, nanosomes, nanoemulsions, nanocapsules, nanocrystals, niosomes, solid lipid nanoparticles, nanospheres, dendrimers, nanogols and nanosilver, micronized forms of ZnO and TiO_2, hydrogels and other. The expansion of nanosystems in cosmetics leads to the necessity to assess their impact on the human body and the environment.

This review focuses on the different nanostructures, their characteristics, their function, and the risks they pose to the human body, when they are included in various cosmetic products for hair, skin and nails. The stability, uniformity of size and shape, the control on the release of the substances included and the behavior in the human body are some of the major problems which need to be solved, before their wide entering in the cosmetics industry, and after strict compliance with the regulatory requirements placed upon them.

***Keywords**: nanostructures, cosmetic products, hazardous materials*

INTRODUCTION

Nanotechnology is the most rapidly developing field of modern science. According to some researchers it will be acknowledged as the technology of the 21st century (1). A research of one of the leading companies (Woodrow Wilson, Project on Emerging Nanotechnologies) indicates an approximately 1900% increase of the number of registered nanotechnology products in the period 2005-2009, respectively from 54 to 1015 (2). 137 from them are classified as nanotechnology products, which are used in cosmetics and 33 - as sunscreens (2). In the period 1994-2005 the company L'Oréal was ranked fifth in the world according to the total number of filed patents related to nanotechnology (3). The huge interest in this branch of science is due to the unique physical and chemical properties of the nanomaterials. Their widespread use in many aspects of life poses logical questions concerning their safety for humans and for the environment as well. As a result, the requirements relating to registration, labeling, terminology, safety, environmental impact and patent rights need to be regularly reconsidered and adapted in the context of the nanotechnology products.

EXPOSITION

On the recommendation of the European Commission (4), nanomaterials, in order to be determined as such, should meet at least one of the following criteria: 1) contain particles with one or more external dimensions in the size range 1 nm - 100 nm, which should be more than 1% in the number size distribution; 2) have internal or superficial structures with one or more dimensions in the range 1-100 nm; 3) have a specific surface area greater than 60 m^2 / cm^3, with the exception of materials, which consist of particles with dimensions less than 1 nm.

Another regulation of the European Union (EU, Cosmetic Products Regulation № 1223/2009) defines nanomaterials as insoluble or biopersistant materials with one or more external dimensions,

or an internal structure, on the scale from 1 to 100 nm (5). The aforementioned regulation applies only to those nanomaterials that are insoluble or biopersistant, but without any clear criteria for solubility and biopersistence. The regulation provides for compulsory labels on the product packaging, which contain information about all the ingredients, which are used in the form of nanomaterials. The names of such ingredients shall be followed by the word 'nano' in brackets. This should not be interpreted as a warning of hazard, but rather as an observation of the rights of the consumers to make an informed decision.

The same European regulation defines a cosmetic product as any substance or preparation, which is intended for "external" application on different parts of the human body (skin, hair and/or hair follicles, nails, lips and genitals) or on the teeth and the mucous membranes of the oral cavity with a view to cleaning them, perfuming them, changing their appearance, protecting them or keeping them in a good condition (5).

According to Adnan Nasir nanostructures are divided into nanomaterials, nanocomputers and nanodevices (6). We will refer only to some of the nanomaterials. They are most commonly classified in the literature according to their structural and morphological characteristics (6,7).

Liposomes are microscopic vesicles composed of an aqueous core surrounded by a hydrophobic bilayer, which is usually prepared by extrusion of phospholipids (7). The lipid bilayer of the liposomes is similar to that of the cell membranes and that makes them very suitable to be used in cosmetic products as systems with controlled release of the active substances, which they contain. The first cosmetic product on the market with liposomes is the cream Capture, presented by the company Dior in 1986 (7). Despite their instability and the necessity to add anti-oxidants, cryoprotectants etc., the application of liposomes continues to grow due to their ease of preparation and the ability to enhance the penetration of active substances through the skin. *Niosomes* are bi-layered vesicular structures similar to the liposomes, but they consist of nonionic surfactants, which can have both hydrophilic and lipophilic compounds. They were tested, developed and patented by L'Oréal in the 70s and 80s (7,8). In 1987 Lancome release on the market the first Niosome product. Some of the reasons to use niosomes in cosmetics are their abilities to increase the stability of the included active substance and to enhance its absorption through the skin (7).

Nanoemulsions are microdispersions, characterized by a high thermodynamic stability and small size (100 nm) of the dispersed phase - nanosized droplets of one insoluble liquid into another (9). Nanoemulsions have a pleasant, light and non-greasy texture and enhance the penetration of the active ingredients into the skin and the hair. They are effective drug-delivery system of some essential hydrophobic substances (antioxidants, fat-soluble vitamins, lipids, etc.) at therapeutic concentrations (10). Nanoemulsions are used to reduce transdermal loss of water by increasing the barrier capability of the skin (9,10).

Solid lipid nanoparticles are nanometer sized particles with a solid lipid matrix (11), which preserves its structure at body temperature. The advantages of their application in cosmetic products are their ability to prevent degradation of the substances, which are encapsulated in the lipid matrix, their controlled release and the enhanced penetration through stratum corneum (coenzyme Q10 and retinol) (11,12). They also increase the hydration of the skin, due to their occlusive properties. The delayed release of substances from the solid lipid nanoparticles is also used in the perfume industry (Allure, Chanel) and for insect repellents (13). The second group of lipid particles are the so-called *nanostructured lipid carriers*, which are developed by mixing liquid and solid lipids. They have the same properties as the solid lipid nanoparticles. They are also used for reducing the redness in allergic reactions due to their lubricating effect and the mechanical barrier, which they create on the skin. Nanorepair cream and lotion, Dr. Rimpler GmbH, Germany is the first product containing lipid nanoparticles. It has been on the market since 2005 (7).

Dendrimers are systems of branched liquid or semi-solid polymers containing amine, carboxyl and hydroxyl groups on their surface and may include hydrophilic and lipophilic substances (14). The selection of the external functional groups (amine, carboxyl and hydroxyl), the

size and the molecular weight of the dendrimers are the most important parameters for their design and application in various cosmetic products. L'Oréal have patented a formula of hyper-branched polymers and dendrimers, which form a thin film on the substrate (15). They are used in mascara and nail polish products. The rapid formation of the film after application turns out to be a serious problem. That is why the new formulations include film-forming agents for different applications. They are used in cosmetics for artificial tanning, hair, skin care and nails (7).

According Sahoo et al. (16), the *nanoparticles* are defined as particles with a diameter smaller than 1 μm, which consist of different biodegradable and non-biodegradable polymers, lipids, phospholipids or metals. They are classified as *nanospheres* or *nanocapsules* according to whether the active substance is uniformly distributed into the polymer matrix or it is coated by the polymer. Polymers, proteins and other biomolecules can be used for the coating of the active substance in the nanocapsules. The release of the substances can be controlled by external factors (e.g. ultrasound) or different environmental conditions (pH, temperature, sun exposure, etc.). A thermosensitive gel, which is applied on the facial skin, releases the included in it active substances when the temperature reaches that of the human body (Facial SwitchTM) (17).

Nanocrystals are aggregates, which consist of several hundred to tens of thousands of atoms that form "clusters" with average size of about 10-400 nm. They are used in the cosmetic industry mainly for incorporation of water-insoluble substances such as rutin, hesperidin (a flavanone glycoside with antioxidant properties), resveratrol, ascorbyl palmitate, etc., which are patented (18).

In recent years, a number of nanoparticles with ZnO and TiO_2 have been developed as sunscreen systems (6,7). As an alternative to ZnO and TiO_2, 50% dispersions of a new range of organic UV-filters have been developed- TINOSORB ® UV of Ciba Specialty Chemicals, in the form of nanoparticles with a size smaller than 200 nm, soluble in oil, with sun protective properties (19).

The application of nanoparticles raises some safety concerns for the human health and their impact on the environment. Some important questions about the safety of nanoparticles derive from their ability to pass through tissue barriers and their biocompatibility and biodegradation.

Cosmetic products are applied mainly to the skin, which is composed of epidermis, dermis and hypodermis. The epidermis consists of five layers. Its outermost layer- *stratum corneum* – executes a vital barrier function. The hair follicles are located in the dermis, but their outer parts protrude in the epidermis. There are three pathways of percutaneous penetration - intercellular, transcellular and transfollicular (through the hair follicles and the sweat and sebaceous glands which are connected to them). The passive transport of nanoparticles through the *stratum corneum*, which is rich in proteins, is less possible due to the dense matrix of corneocytes and the lipid bilayer with intercellular spaces (20). The multilayer epidermis is less permeable for active molecules than the single-layer capillary epithelium. The passage of the active substances through the transcellular pathway depends on their size, lipophilic properties and degree of ionization. For example, the raising of the weight of molecules with identical lipophilicity only two times (from 400 to 800 g/mol), reduces the permeability by a coefficient approximately 2,5 log units. Only particles, which size is less than ~ 36 nm, can pass through the intercellular spaces. On the other hand the follicular ducts (smaller than 200 nm) are permeable for nanoparticles (20). The human skin acts as a defence barrier and has low permeability for external particles, nevertheless special attention should be paid when substances that increase the permeability are included into nanoparticles.

Nanoparticles have a large specific surface area and high surface energy. Therefore the biological environment, in which they are located, can have a serious impact on their behavior (21). In the biological fluids nanoparticles are often surrounded by enzymes, glycoproteins or lipoproteins, which can provoke a specific biological response or to conceal specific defense mechanisms (21). The large surface area of the nanoparticles enhances the adsorption of various pathogens, allergens or proteins. Thus nanoparticles become carriers of these structures and can transport them through tissue barriers and reach different organs. For example, bactericidal

nanoparticles, which contain silver, can adsorb lipopolysaccharides (well known exogenous pyrogens) from dead bacterial cells, which can cause fever when they enter the systemic circulation.

It should be taken into consideration that the protein coating around the nanoparticles is not constant. It can vary depending on the environment (21, 22). The morphology of the nanoparticles is essential for their safe application.

Based on the above mentioned Gregory Morose from University of Massachusetts Lowell in his work "The 5 principles of "Design for Safer Nanotechnology"" determine size, surface and structure, alternative materials, functionalization, encapsulation and reduce the quantity are the most important items in designing of safe nanomaterials (23).

CONCLUSION

Using nanomaterials in cosmetics has many advantages: a possibility to include hydrophilic and hydrophobic substances, greater stability, controlled release, targeted transport to the target cells and the ability to provoke a biological response at lower than the therapeutic concentrations.

When using cosmetic products with nanomaterials there are also some risks for the human health, which derive from the possibility for the nanoparticles to have different properties, compared to these of the same material, but with larger particles. The ability of some of them to pass through biological membranes provides the possibility of their deposition in various organs. The process of their elimination is still a subject for debates and is not quite clear yet. In a conclusion, nanomaterials should be used in cosmetics only after a thorough study of their safety and observing the established regulations.

REFERENCES:

1. Bowman, D., Hodge, G., 2006. Nanotechnology: mapping the wild regulatory frontier. Futures 38(9):1060-1073

2. http://www.nanotechproject.org/inventories/consumer/analysis_draft/.

3. Mihranyan, A., Ferraz, N., Strømme, M., 2012. Current status and future prospects of nanotechnology in cosmetics. 57:875-910

4. http://ec.europa.eu/environment/consultations/pdf/recommendation_nano.pdf.

5. http://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:342:0059:0209:en:PDF

6. Nasir, A., 2010. Nanotechnology and dermatology: Part I-potential of nanotechnology, Clinics in Dermatology, 28, 458-466

7. Raj, S., Jose, S., Sumod, U., Sabitha, M., 2012. Nanotechnology in Cosmetics: Opportunities and challenges. J Pharm Bioallied Sci. 4:186-93

8. Paolino, D., Muzzalupo, R., Ricciardi, A., Celia, C., Picci, N., Fresta, M., 2007. In vitro and in vivo evaluation of Bola-surfactant containing niosomes for transdermal delivery, Biomed. Microdevices, 9, 421-433

9. Mason, T., Wilking, J., Meleson, K, Chang, C., Graves, S., 2006. Nanoemulsions: formation, structure, and physical properties. J. Phys. Condens. Matter 18, R635-R666

10. Aubrun-Sonneville, O., Simonnet, J.-T., L'Alloret, F., 2004. Nanoemulsion: a new vehicle for skincare products. Advances in Colloidal and Interface Science 108-109, 145-149

11. Jenning, V., Gysler, A., Schafer-Korting, M., Gohla, S.H., Vitamin A loaded solid lipid nanoparticles for topical use: properties and drug targeting to the upper skin, Eur J Pharm Biopharm, 49, 211-8

12. Müller, R.H, Wissing, S.A., 2003. Cosmetic applications for solid lipid nanoparticles (SLN), Int J Pharm, 254, 65-68

13. Wissing, S., Mäder, K., Müller, R., 2000. Solid lipid nanoparticles (SLN) as a novel carrier system offering prolonged release of the perfume Allure (Chanel), Int. Symp. Control Release Bioact. Mater., 27, 311-312

14. Svenson, S., Tomalia, D., 2005. Dendrimers in biomedical applications – reflections on the field, Adv. Drug Deliv, Rev. 57, 2106-29

15. Use of hyperbranched polymers and dendrimers comprising a particular group as film-forming agent, film-forming compositions comprising same and use particularly in cosmetics and pharmaceutics, 2002. L'Oréal, US Patent 6432423,

16. Sahoo, S., Dilnawaz, F., Krishnakumar, S., 2008. Nanotechnology in ocular drug delivery. Drug Discov Today. 13:144–151

17. US patent pending, 2006. China patent CN1883438

18. Petersen, R., 2008. Nanocrystals for use in topical cosmetic formulations and method of production thereof. Abbott GmbH & Co., US Patent 60/866233

19. Time and Extent Application, Bisoctrizole, Prepared to support the Inclusion of Bisoctrizole into FDA'S Monograph for Sunscreen Drug Products for Over-the-Counter Human Use, 2005. (64 FR 27666-27693, as amended by 66 FR 6748567487, Docket №78N-0038), Ciba Specialty Chemicals Corporation

20. Baroli B., 2010. Penetration of nanoparticles and nanomaterials in the skin: fiction or reality? J Pharmaceut Sci, 99:21-50.

21. Lövestam G, Rauscher H, Roebben G, Kluttgen BS, Gibson N, et al., 2010. Considerations on a Definition of Nanomaterial for Regulatory Purposes, Reference Reports EU JRC, 24403, p.8

22. Poland, C., Duffin, R., Donaldson, K., 2009. High Aspect Ratio Nanoparticles and the Fibre Pa-thogenicity Paradigm. In: Nanotoxicity. Chichester, UK: John Wi-ley& Sons, ltd

23. Morose, G., 2010. The 5 principles of “Design for Safer Nanotechnology”. Journal of Cleaner production, 18:285-289