

Nanotechnology in Cosmetics

6.1	Definition.....	2
6.2	Short Description.....	2
6.3	State of R&D	3
6.3.1	Vesicular Delivery Systems	3
6.3.2	Nanoemulsions	4
6.3.3	Solid Lipid Nanoparticles	4
6.3.4	Nanostructured Lipid Carriers	5
6.3.5	Dendrimers and hyperbranched polymers	6
6.3.6	Nanocrystals	6
6.3.7	Nanoencapsulation and controlled release	7
6.3.8	Cubosomes	7
6.3.9	Nanotechnology for UV protection	8
6.3.10	Nanomechanical and Nanotribological study of hair.....	8
6.4	Additional Demand for Research	9
6.5	Applications and Perspectives	9
6.6	References	11

Keywords: nano-emulsions, liposomes, niosomes, solid lipid nanoparticles, metal oxide nanoparticles, fullerenes, dendrimers, nanocapsules, cosmetics

6.1 Definition

For the purpose of this report, cosmetics covers different products applied to skin or hair.

6.2 Short Description

The applications of nanotechnology and nanomaterials can be found in many cosmetic products including moisturisers, hair care products, make up and sunscreen.

Almost all the major cosmetic manufacturers use nanomaterials in their products. L'Oréal has a number of nanotechnology-related products in the market and ranks 6th in US in the number of nanotech related patents in US¹. The European Commission estimated in 2006, that 5 % of cosmetic products contained nanoparticles.

The application of nanomaterials in cosmetic products has been the subject of continuous discussion in the media, scientific circles and among policy makers for the past few years. Toxicity issues have been raised due to conflicting research papers about the safety of nanomaterials and lack of agreement between researchers on whether the nanomaterials are safe for dermal use. There are a number of classes of nanoparticles used, or proposed for use, in cosmetic applications.

In cosmetics there are currently two main uses for nanotechnology. The first of these is the use of nanoparticles as UV filters. Titanium dioxide (TiO₂) and zinc oxide (ZnO) are the main compounds used in these applications. Organic alternatives to these have also been developed.

The second use is nanotechnology for delivery. Liposomes and niosomes are used in the cosmetic industry as delivery vehicles. Newer structures such as solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) have been found to be better performers than liposomes. In particular, NLCs have been identified as a potential next generation cosmetic delivery agent that can provide enhanced skin hydration, bioavailability, stability of the agent and controlled occlusion. Encapsulation techniques have been proposed for carrying cosmetic actives. Nanocrystals and nanoemulsions are also being investigated for cosmetic applications. Patents have been filed for the application of dendrimers in the cosmetics industry.

Other novel materials, such as fullerene, have also appeared in a small number of beauty products.

This report looks into some of the nanotechnologies used in the cosmetic industry and provides an overview of current activity in this area.

6.3 State of R&D

6.3.1 Vesicular Delivery Systems

Liposomes are vesicular structures with an aqueous core surrounded by a hydrophobic lipid bilayer, created by the extrusion of phospholipids. Phospholipids are GRAS (generally recognised as safe) ingredients, therefore minimising the potential for adverse effects. Solutes, such as drugs, in the core cannot pass through the hydrophobic bilayer however hydrophobic molecules can be absorbed into the bilayer, enabling the liposome to carry both hydrophilic and hydrophobic molecules. The lipid bilayer of liposomes can fuse with other bilayers such as the cell membrane, which promotes release of its contents, making them useful for drug delivery and cosmetic delivery applications. Liposomes can vary in size, from 15 nm up to several μm and can have either a single layer (unilamellar) or multilayer (multilamellar) structure. Liposomes that have vesicles in the range of nanometres are also called nanoliposomes. A new type of liposomes called transferosomes, which are more elastic than liposomes and have improved efficiency, have been developed². Transferosomes with sizes in the range of 200-300 nm can penetrate the skin with improved efficiency than liposomes³. These self assembled lipid droplets with elastic bilayers are capable of spontaneous penetration of the stratum corneum through intracellular or transcellular routes and have potential applications in cosmetics and drug delivery⁴.

The first liposomal cosmetic product to appear on the market was the anti-ageing cream 'Capture' launched by Dior in 1986. Since then several hundreds of products which utilise liposomal delivery capabilities have been introduced into the market, however only some contain liposomes in the nanoscale. Liposomes are unstable due to their susceptibility to oxidation and the breakdown of liposomal structure. However, formulations have been developed that are more stable by optimising the storage conditions and adding chelators and anti-oxidants⁵. It is also possible to add cryoprotectants (substances to protect biological tissue from freezing damage)¹ to liposomes to store them in frozen or lyophilized form.

One of the reasons for the widespread use of liposomes in the cosmetic industry is their ease of preparation and the ability to improve the absorption of active ingredients by skin. The ease of scale up made the widespread use of liposomes in cosmetic applications a reality.

Liposomes have been formed that facilitate the continuous supply of agents into the cells over a sustained period of time, making them an ideal candidate for the delivery of vitamins and other molecules to regenerate the epidermis⁶. Several active ingredients, biomolecules (e.g. vitamins A and E) and antioxidants (e.g. CoQ10, lycopene and carotenoids) have been incorporated into liposomal membranes to increase their delivery⁷. Efforts to improve the encapsulation capability of liposomes by adding emulsifiers have been proposed. However, this compromises the barrier integrity and the lipids are easily removed by washing.

Phosphatidylcholine, one of the main ingredients of liposomes, has been widely used in skin care products and shampoos due to its softening and conditioning properties. Liposomes have proved to be a convenient way to deliver phosphatidylcholine.

Liposomes have also been used in the treatment of hair loss. Minoxidil, a vasodilator, is in the active ingredient in products like Regaine (www.regaine.co.uk) that claim to prevent or slow hair loss. It is formulated in liposomes to improve the flux of contents through the skin⁸. Minoxidil sulphate in propylene glycol (PG)-coated liposomes is also marketed as Nanominox-MS (http://www.sinere.com/nanominox-ms_en.html).

¹ <http://en.wikipedia.org/wiki/Cryoprotectant>

Niosomes are non-ionic surfactant based vesicles that have a similar structure to that of phospholipid vesicles like liposomes. They can be used to encapsulate aqueous solutes and act as drug and cosmetic carriers. They are formed by the self-assembly of non-ionic surfactants in aqueous media. The application of heat or physical agitation helps niosomes to attain a closed bilayer structure⁹. The hydrophobic parts are shielded from the aqueous solvent while the hydrophilic head groups are in contact with it. They have been used for the delivery of anti-inflammatory agents¹⁰ and anti-infective agents¹¹. They have also been used to enhance transdermal drug delivery.

Niosomes were developed and patented by L'Oréal (www.loreal.com) in the 1970s and 80s^{12,13}. The first product 'Niosome' was introduced in 1987 by Lancôme (www.lancome.com; a L'Oréal company). The advantages of using niosomes in cosmetic and skin care applications include their ability to increase the stability of entrapped drugs, improved bioavailability of poorly absorbed ingredients and enhanced skin penetration. However, niosomes do not contain GRAS components and are known to be more irritating than liposomes.

Van Hal *et al.*¹⁴ reported that niosome encapsulated estradiol can be delivered through the stratum corneum, which is known to be a highly impermeable protective barrier. Niosomes made from a novel surfactant (Bola surfactant), have been found highly effective for percutaneous drug delivery applications¹⁵. Studies have shown that they improve percutaneous passage of drugs through human stratum corneum and epidermis and are non-toxic.

There are hundreds of products on the market using these technologies, particularly liposomal based ones, so interest in new cosmetic applications has deteriorated. However, they are still of great interest for pharmaceutical applications (see Therapeutics subsector report).

6.3.2 Nanoemulsions

Nanoemulsions are dispersions of nanoscale droplets of one liquid within another¹⁶. These emulsions are metastable systems whose structure can be manipulated based on the method of preparation to give different types of product e.g. water-like fluids or gels¹⁷.

Nanoemulsions have a number of advantages over larger scale emulsions. They can be stabilised to increase the time before creaming occurs, therefore increasing the shelf life of products containing them¹⁸. They are transparent or translucent, and have a larger surface area due to the small particle size. It has been found that the smaller the size of the emulsion, the higher the stability and better suitability to carry active ingredients¹⁹. The components of nanoemulsions are usually GRAS compounds, therefore they are considered relatively safe systems which can break down to their safe components.

Several cosmetic products are available that use nanoemulsions, including Korres' Red Vine Hair sunscreen (www.korres.com).

Several companies supply ready to use emulsifiers for creating stable nanoemulsions for cosmetic applications, including Nanocream® from Sinerga (www.sinerga.it) and NanoGel from Kemira (www.kemira.com)²⁰. They produce a product called Nanogel- UV for sun care applications. L'Oréal own several patents on nanoemulsion based technologies²¹.

6.3.3 Solid Lipid Nanoparticles

Solid lipid nanoparticles (SLNs) are nanometre sized particles with a solid lipid matrix. They are oily droplets of lipids which are solid at body temperature and stabilised by surfactants. Their production is a relatively simple process where the liquid lipid (oil) in a nanoemulsion is exchanged by solid lipids²². This process does not require organic solvents.

SLNs offer a number of advantages for cosmetic products. They can protect the encapsulated ingredients from degradation. Compounds, including coenzyme Q10²³ and retinol²⁴ can remain stable in SLNs over a long time period. They can be used for the controlled delivery of cosmetic agents over a prolonged period of time and have been found to improve the penetration of active compounds into the stratum corneum.

SLNs have occlusive properties making them ideal for potential use in day creams. *In-vivo* studies have shown that an SLN-containing formulation is more efficient in skin hydration than a placebo²⁵. They have also been found to show UV resistant properties which were enhanced when a molecular sunscreen was incorporated and tested²⁶. Enhanced UV blocking by 3,4,5-trimethoxybenzoylchitin (a good UV absorber) was seen when incorporated into SLNs²⁷.

SLNs have also been tested in perfume formulations. Chanel's Allure perfume was incorporated into SLNs and nanoemulsions²⁸. SLN formulations delayed the release of perfume over a longer period of time. This slow release profile is also desirable for insect repellents.

Although SLNs are promising for cosmetic purposes they suffer some drawbacks. The production process needs improvement to increase loading capability and stop expulsion of the contents during storage. These problems are caused by the tendency for the particle matrix to form a perfect crystal lattice when solid lipids are used. The high water content of SLN dispersions can also be problematic.

6.3.4 Nanostructured Lipid Carriers

In order to overcome issues associated with SLNs, a second generation of lipid particles have been developed by mixing solid lipids with liquid lipids. These are known as nanostructured lipid carriers (NLCs). Compared to SLNs, NLCs have a distorted structure which makes the matrix structure imperfect and creates spaces to accommodate active compounds. The high loading capacity and long term stability offered by the NLCs make them superior to SLNs in many cosmetic applications. However, Müller *et al.*²⁹ suggest that SLNs are better for applications such as UV protection where a high level of crystallinity is required for the carrier.

Similar to SLNs, NLCs are also capable of preventing the active compounds from chemical degradation³⁰. They also possess a high occlusion factor and high level of skin adherence properties. When the particles adhere to the skin a thin film layer is created which prevents dehydration. As the size of the particles decreases the occlusion factor increases³¹. Due to this, NLCs offer the possibility of controlling occlusion without altering the properties e.g. increasing the occlusion of day creams without the glossiness of night creams. It has also been found that the release profile of the active compounds can be manipulated by changing the matrix structure of nanoparticle. Lipid nanoparticles have been found to increase the penetration capabilities of active compounds compared to microparticles³². The lubricating effect and mechanical barrier of lipid nanoparticles are also desired in skin care applications for reducing irritation and allergic reactions.

Lipid nanoparticles can make products appear white, rather than yellowish, which is more desirable for consumers³³.

The first products containing lipid nanoparticles appeared on the market in 2005 (Nanorepair cream and lotion, Dr. Rimpler GmbH, Germany), offering increased skin penetration. More than 30 cosmetic products containing NLCs are currently available worldwide (e.g. in South Korea, Superval products in the 'IOPE' line from AmorePacific). Recent reviews of these products and their ingredients have been written by Müller *et al.*^{34,35}.

6.3.5 Dendrimers and hyperbranched polymers

Dendrimers and hyperbranched polymers have also been considered for use in the cosmetic industry. Dendrimers are unimolecular, monodisperse, micellar nanostructures, around 20 nm in size, with a well-defined, regularly branched symmetrical structure and a high density of functional end groups at their periphery. They are known to be robust, covalently fixed, three-dimensional structures possessing both a solvent-filled interior core (nanoscale container) as well as a homogenous, mathematically defined, exterior surface functionality (nano-scaffold)³⁶. They are prepared in a step-wise fashion, with an architecture like a tree branching out from a central point. Hyperbranched polymers are effectively disorganised, unsymmetrical dendrimers that are prepared in a single synthetic polymerisation step, making them much more cost-effective than dendrimers. The large number of external groups suitable for multifunctionalisation which is a requirement for its use as a cosmetic agent carrier.

L'Oréal have a patent for a formulation containing hyperbranched polymers or dendrimers which form a thin film when deposited on a substrate³⁷. This formulation could be used for a wide variety of cosmetics e.g. mascara or nail polish. A problem of current polymers is that films are formed too soon after deposition. The new formulations will form highly adherent, water washable films only upon oxidation, usually by exposure to air. It is also possible to incorporate cosmetic agents into the medium to help form films for different applications. They have also developed a formulation comprising of a tanning agent and dendrimers for artificial skin tanning³⁸. Unilever have a patent for hydroxyl-functionalised dendrimers from polyester units to create formulations for use in sprays, gels or lotions³⁹. Several patents have been filed for the application of dendrimers in hair care, skin care and nail care products^{40,41}.

6.3.6 Nanocrystals

Nanocrystals have been used in the pharmaceutical industry for the delivery of poorly soluble actives (Elan; see Therapeutics subsector report). They are aggregates comprising several hundred to tens of thousands of atoms that combine into a "cluster". Typical sizes of these aggregates are between 10-400 nm and they exhibit physical and chemical properties somewhere between that of bulk solids and molecules. By controlling the size and surface area, other properties such as bandgap, charge conductivity, crystalline structure and melting temperature can be altered. The crystals must be stabilised to prevent larger aggregates from forming.

The first cosmetic products appeared on the market recently; Juvena in 2007 (rutin) and La Prairie in 2008 (hesperidin). Rutin and hesperidin are two, poorly soluble, plant glycoside antioxidants that could not previously be used dermally. Once formulated as nanocrystals, they became dermally available as measured by antioxidant effect. This dermal use of nanocrystals is protected by patents⁴². Other examples are resveratrol and ascorbylpalmitate nanocrystals. Incorporation of nanocrystals into cosmetic products is a straight forward process. Nanocrystals dispersed in water (i.e. a nanosuspension) is admixed with a cosmetic product (typical dilution factor: 50). Nanocrystals for cosmetic applications are commercially available via the contract manufacturer PharmaSol/Berlin.

6.3.7 Nanoencapsulation and controlled release

Encapsulation technologies have been widely used for a long time in the pharmaceutical industry for drug delivery applications. The emergence of nanotechnology and the availability of novel tools have paved the way for new type of particles which can be used for targeted delivery and that can carry drug payloads for localised action. Such nanosized particles which have a shell and an interior space that can be used to load drugs are called nanocapsules. Different types of nanocapsules are required depending on the nature of the material (hydrophobic or hydrophilic) to be incorporated. It is also possible to functionalise these particles to target specific molecules. Polymers, proteins and different types of biomolecules have been proposed as suitable materials to coat nanocapsules. Polymers have been widely used to create nanocapsules which are then functionalised for various applications. The release of the payload could be organised by an external trigger (ultrasound or magnetic field etc.) or the materials can be designed to release the payload depending on the environment (pH, temperature, light exposure etc.). Such polymers that can respond to the changes and react accordingly are called adaptive polymers.

Hydrophobically modified polyvinylalcohol 10 000 (PVA) with fatty acids (FAs) have been used to create polymeric nanoparticles for cosmetic applications⁴³. PVA was substituted with saturated FAs to give the polymer sufficient lipophilicity and used to test the percutaneous absorption of benzophenone-3 (BZP), a widely used UV filter. As sunscreen filters are meant to work on the periphery of the skin, percutaneous absorption is highly discouraged. Studies showed that PVC nanoparticles can limit the adsorption of BZP, with nanoparticles with a high degree of substitution preventing absorption more efficiently.

The trend in the skincare applications of such polymers is moving from self repair (those that repair the skin damage according to changes in the environment using nanoencapsulation, controlled release etc.) to self predicting polymers that can predict future changes and change their property accordingly to prevent the damage. An example of this is a hydrogel developed by Hu and co-workers⁴⁴ which can respond to temperature and be used as a facial mask. The patented technology called Facial Switch™ shrinks the hydrogel if the temperature is increased and releases nutrients⁴⁵. They have also created smart fabrics with antibacterial properties that can respond to external stimuli and fabrics that turn from semi transparent to opaque in response to stimuli.

UK-based Vivamer (<http://www.vivamer.com/>) have developed a range of responsive polymers that can be attached to or encapsulate nanoparticles, films or gels that incorporate various ingredients. The polymer can be designed to release contents on response to external environment. The polymer capsules could be incorporated into perfumes to release the contents on exposure to sunlight or hot weather. The materials are stable in aqueous solution, non-toxic and biodegradable.

Hollow silica nanoshells, which have already found applications in drug delivery, have been proposed as suitable cosmetic agent carriers. Exilica Ltd (www.exilica.co.uk) have developed a method for making spherical polymer micro-beads and silica nano-shells to be used for molecular containment and slow release. Another company, MiCap (<http://www.micap.biz/>) is exploring the possibilities of using microbial cells and cell walls for the controlled delivery of perfumes.

6.3.8 Cubosomes

Cubosomes are discrete, sub-micron, nanostructured particles of bicontinuous cubic liquid crystalline phase⁴⁶. Bicontinuous cubic liquid crystalline phase is an optically clear, very viscous material that has a unique structure at the nanometer scale⁴⁷. It is formed by the self assembly of liquid crystalline particles of certain surfactants when mixed with water and a microstructure at a certain ratio.

Cubosomes offer a large surface area, low viscosity and can exist at almost any dilution level. They have high heat stability and are capable of carrying hydrophilic and hydrophobic molecules⁴⁸. Combined with the low cost of the raw materials and the potential for controlled release through functionalisation, they are an attractive choice for cosmetic applications as well as for drug delivery. However, at present cubosomes do not offer controlled release on their own⁴⁹. They have also been modified using proteins^{50,51}.

A number of companies including L'Oréal⁵², Nivia^{53,54,55,56} and Procter and Gamble are investigating cubosomes for cosmetic applications. Despite this interest, cubosomes have not yet led to products⁵⁷. The methods of formation must be efficient and cost-effective for scale up before this type of technology can be applied. The presence of large amounts of water during cubosome formation makes it difficult to load water soluble actives.

6.3.9 Nanotechnology for UV protection

Zinc oxide (ZnO) and titanium dioxide (TiO₂) particles have been widely used for many years as UV filters in sunscreens. Recently, nanoparticles of these oxides have become popular as they retain the UV filtration and absorption properties while eliminating the white chalky appearance of traditional sunscreens. Products using nanoparticles of ZnO or TiO₂ are transparent so have increased aesthetic appeal, are less smelly, less greasy and more absorbable by the skin. Many sunscreens and moisturisers available now use these nanoparticles, including products from Boots, Avon, The Body Shop, L'Oréal, Nivea and Unilever.

A number of modifications to the standard ZnO or TiO₂ UV protection system have been reported. Oxonica have developed Optisol, a UV absorption system which contains TiO₂ and 1 % manganese⁵⁸. Dispersing carnauba wax nanoparticles with TiO₂ nanoparticles was found to increase the sun protection factor (SPF)⁵⁹. Nanphase Technologies, who supply nanoparticles to companies including BASF, produce controllable polymeric nanocrystals of ZnO with a size less than 35 nm for personal care applications⁶⁰.

Other nanoparticles have been developed for UV protection. Rohm and Haas (www.rohmhaas.com) produce hollow styrene acrylate copolymer nanoparticles, ~300 nm in size, that are reported to increase SPF by about 70 %⁶¹. Silica nanoshells have been used by Sol-Gel Technologies (<http://www.sol-gel.com>) to encapsulate cosmetic ingredients. Their first product 'UV Pearls™' contains UV filters encapsulated in silica shells kept on the top layers of the skin to block UV rays. The product provides improved photostability and reduces the filter uptake by the skin. Another product, 'Cool Pearls™ BPO', encapsulates benzoyl peroxide crystals in the silica shells for acne treatment.

Ciba Specialty Chemicals have developed TINOSORB®UV, a 50 % dispersion of a novel broad spectrum organic UV filter⁶². The particles are less than 200 nm in size, soluble in oils and can be used in sunscreens as an alternative to TiO₂ and ZnO.

6.3.10 Nanomechanical and Nanotribological study of hair

Nanotechnology has been used to study the mechanical characteristics of hair. Understanding the differences between hair types allows cosmetic companies to create products to suit individual hair types (e.g. ethnic differences between Caucasian, Asian and African hair) as these can respond differently to activities like shampooing, styling or colouring. The hair care industry is also interested in the effect of water on the nanomechanical properties of hair.

Bhusan *et al.* have conducted nanoscratch tests, using Nano Indenter II (MTS Nanosystems), to understand properties of different types of hairs at the nanoscale⁶³. The studies demonstrated the difference in scratch resistance of single hair fibres of different ethnic regions as well as the coefficient of friction of hairs. They found that the first 200nm of the hair surface, irrespective of origin, is softer than the underlying layer. A further study into the hair fatigue due to stress and tension using AFM has shown that the ethnic hairs vary in mechanical properties⁶⁴.

A good review of the nanotribological and nanomechanical properties of different types of skin and hair based on ethnicity, damage, conditioning treatment and various environments was written in 2008⁶⁵.

6.4 Additional Demand for Research

Although there are many products available in the market using nanomaterials, there are still opportunities to exploit the benefits of nanotechnology in the cosmetic industry.

- TiO₂ and ZnO are widely used in cosmetic formulations. There is a need for an in-depth study into the toxicity effects of these materials as the studies so far have brought mixed results.
- Encapsulation techniques and trigger-release mechanisms have been developed for the active delivery of cosmetic molecules. However, there is a need for reliable, cost effective triggers for controlled release.
- Improvements in the drug loading efficiency of lipid based nanoparticles (SLNs and NLCs) and nanocapsules are required.
- Better understanding of how lipid nanoparticles modify drug penetration into the skin, how they affect the drug penetration and how they interact with lipids of the stratum corneum is required⁶⁶.
- Fundamental conditions for the formation of SLNs and NLCs and the effect of surfactants used for modifications need to be studied further.
- Further *in vivo* studies on the effect of cosmetics that contain nanomaterials.

6.5 Applications and Perspectives

Although nanotechnology has featured in cosmetic formulations for many years, there are only a handful of technologies used, mainly liposomes, nanoemulsions and metal oxide nanoparticles. These offer advantages and improved characteristics compared with traditional formulations. Many of the newer technologies being investigated for drug delivery may also have applications in cosmetics. Along with the formulations discussed in this report, nanoparticles of silver, copper, silicone and silica have been reported as ingredients for cosmetics. A number of companies also claim to use fullerenes in their products due to the radical scavenging properties⁶⁷. However, there are concerns over their toxicity.

It should be assumed that research in this area is being affected by calls for bans and a moratorium on nanotechnology based cosmetic products by many organisations. This has led to reluctance to talk about nanotechnology in cosmetics by a number of organisations.

A list of products claiming to use nanomaterials has been compiled in the report 'Nanomaterials, sunscreens and cosmetics: Small ingredients, big risks'⁶⁸. (A response to this report was published in *Cosmetics & Toiletries Magazine* in January 2009⁶⁹). The Nanotechnology Consumer Products Inventory, run by the Project on Emerging Nanotechnologies at the Woodrow Wilson International Center for Scholars, aims to list all nanotechnology-based consumer products available. However, current regulation of cosmetics means that these products may or may not actually be using nanomaterials, and there may be many more that do.

Which?, the UK-based consumer group, published a report titled "Small Wonder? Nanotechnology and Cosmetics" in November 2008⁷⁰. In this they contacted a number of cosmetics companies about their use of nanotechnology. Only eight companies agreed to give details of their products. This could indicate a worrying silence and concealment of the use of nanomaterials in cosmetic products. The report highlighted a lack of information available on nanoscale ingredients in cosmetics and the safety concerns about this. They proposed the development of new regulation for reporting and assessing the use of nanomaterials in cosmetics.

Updated regulation and increased information sharing has also been called for by the SCCP (EU Scientific Committee on Consumer Products) and the European Commission. Recently, MEPs approved updates on cosmetic legislation⁷¹. The changes apply across all 27 member states and will come into effect from 2012. The new regulations introduce a safety assessment procedure for all products containing nanomaterials, which could lead to a ban on a substance if there is a risk to human health. Also, any nanomaterials present in cosmetics must be mentioned in the list of ingredients on the packaging. The establishment of an official EU-wide register for cosmetics was also proposed.

Toxicity of nanomaterials is currently the subject of an increasing amount of research. Further investigation by academia and industry is required before materials can be deemed as safe. This research, along with better regulation and reporting, will enable consumers to choose products with confidence. This in turn will allow companies to benefit from these novel technologies in the long term while retaining customer confidence.

6.6 References

- ¹ Nano, Nano, On The Wall... L'Oréal and others are betting big on products with microparticles. Business Week, 12 December 2005.
- ² G. Cevc, Transfersomes, liposomes and other lipid suspensions on the skin: permeation enhancement, vesicle penetration, and transdermal drug delivery. Crit. Rev. Ther. Drug Career Syst. 13, 257-388, 1996
- ³ H.-Y. Thong, H. Zhai, H.I. Maibach, Percutaneous penetration enhancers: An overview. Skin Pharmacol. Physiol. 20, 272-282, 2007
- ⁴ S. Jain, R. Sapee, N.K. Jain, Proultraflexible lipid vesicles for effective transdermal delivery of norgesterol. Proceedings of 25th conference of C.R.S. USA, 32-35, 1998
- ⁵ D.D. Lasic, Novel applications of liposomes. Trends in Biotechnology 16, 7, 307-321, 1998
- ⁶ H. Lautenschläger, Liposomes, Handbook of Cosmetic Science and Technology, 155-163, CRC Press Taylor & Francis Group, Boca Raton, 2006
- ⁷ http://www.encapsula.com/contract_manufacturing.html
- ⁸ Non-crystalline minoxidil composition, US Patent 5030442, <http://www.freepatentsonline.com/5030442.html>
- ⁹ I.F. Uchegbua, S.P. Vyas, Non-ionic surfactant based vesicles (niosomes) in drug delivery. International Journal of Pharmaceutics 172, 1-2, 33-70, 1998
- ¹⁰ D.N. Reddy, N. Udupa, Formulation and evaluation of oral and transdermal preparations of flurbiprofen and piroxicam incorporated with different carriers. Drug Dev. Ind. Pharm. 19, 843-852, 1993
- ¹¹ W. Walker, J.M. Brewer, J. Alexander, Lipid vesicle-entrapped influenza A antigen modulates the influenza A-specific human antibody response in immune reconstituted SCID-human mice. Eur. J. Immunol. 26, 1664-1667, 1996
- ¹² Procédé de fabrication de dispersions aqueuses de spérules lipidiques et nouvelles compositions correspondantes, L'Oréal, French Patent 2315991, 1975
- ¹³ Cosmetic and pharmaceutical compositions containing niosomes and a water-soluble polyamide, and a process for preparing these compositions, L'Oréal, US Patent 4830857, 1989
- ¹⁴ D. Van Hal, A. Vanrensen, T. Devringer, H. Junginger, J. Bouwstra, Diffusion of estradiol from non-ionic surfactant vesicles through human stratum-corneum in-vitro. STP Pharm. Sci. 6, 72-78, 1996
- ¹⁵ D. Paolino, R. Muzzalupo, A. Ricciardi, C. Celia, N. Picci, M. Fresta, In vitro and in vivo evaluation of Bola-surfactant containing niosomes for transdermal delivery. Biomed. Microdevices 9, 421-433, 2007
- ¹⁶ T.G. Mason, J.N. Wilking, K. Meleson, C.B. Chang, S. M. Graves, Nanoemulsions: formation, structure, and physical properties. J. Phys. Condens. Matter 18, R635-R666, 2006
- ¹⁷ O. Sonneville-Aubrun, J.-T. Simonnet, F. L'Alloret, Nanoemulsions: a new vehicle for skincare products. Advances in Colloid and Interface Science 108 -109, 145-149, 2004
- ¹⁸ T. Tadros, P. Izquierdo, J. Esquena, C. Solans, Formation and stability of nanoemulsions. Adv. Colloid Interface Sci. 109, 303-318, 2004
- ¹⁹ A. Dingler, S. Gohla, Production of solid lipid nanoparticles (SLN): scaling up feasibilities. Microencapsulation 19, 11-6, 2002
- ²⁰ <http://www.in-cosmetics.com/ExhibitorLibrary/162/NanoGel - Brochure - Nano Emulsion Chassis 2.pdf>, Accessed 24 April 2009
- ²¹ Nanoemulsion based on phosphoric acid fatty acid esters and its uses in the cosmetics, dermatological, pharmaceutical, and/or ophthalmological fields. L'Oréal, US Patent 6274150
- Nanoemulsion based on oxyethylenated or non-oxyethylenated sorbitan fatty esters, and its uses in the cosmetics, dermatological and/or ophthalmological fields. L'Oréal, US Patent 6335022
- Nanoemulsion based on ethylene oxide and propylene oxide block copolymers and its uses in the cosmetics, dermatological and/or ophthalmological fields. L'Oréal, US Patent 6464990
- Nanoemulsion based on glycerol fatty esters, and its uses in the cosmetics, dermatological and/or ophthalmological fields. L'Oréal, US Patent 6541018
- Nanoemulsion based on sugar fatty esters or on sugar fatty ethers and its uses in the cosmetics, dermatological and/or ophthalmological fields. L'Oréal, US Patent 6689371
- Transparent nanoemulsion less than 100 NM based on fluid non-ionic amphiphilic lipids and use in cosmetic or in dermopharmaceuticals. L'Oréal, US Patent 5753241

-
- ²² R.H. Müller, M. Radtke, S.A. Wissing, Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) in cosmetic and dermatological preparations, *Adv. Drug Deliv. Rev. Suppl.* 54, S131-S15, 2002
- ²³ R.H. Müller, A. Dingler Feste Lipid-Nanopartikel (Lipopearls) als neuartiger Carrier für kosmetische und dermatologische Wirkstoffe. *PZ Wiss* 49, 11-15, 1998
- ²⁴ V. Jenning, S. Gohla, Encapsulation of retinoids in solid lipid nanoparticles (SLN). *J. Microencapsul.* 18, 149-158, 2001
- ²⁵ S.A. Wissing, R.H. Müller, Cosmetic applications for solid lipid nanoparticles (SLN). *International Journal of Pharmaceutics* 254, 65-68, 2003
- ²⁶ S.A. Wissing, R.H. Müller, A novel sunscreen system based on tocopherol acetate incorporated into solid lipid nanoparticles (SLN). *Int. J. Cosm. Sci.* 23, 233-243, 2001
- ²⁷ C. Song, S. Liu, A new healthy sunscreen system for human: Solid lipid nanoparticles as carrier for 3,4,5-trimethoxybenzoylchitin and the improvement by adding vitamin E. *International Journal of Biological Macromolecules* 36, 116-119, 2005
- ²⁸ S.A. Wissing, K. Mäder, R.H. Müller, 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, 2000
- ²⁹ R.H. Müller, M. Radtke, S.A. Wissing, Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) in cosmetic and dermatological preparations. *Adv. Drug Deliv. Rev. Suppl.* 54, S131-S15, 2002
- ³⁰ V. Jenning Feste, Lipid-Nanopartikel (SLN) als Trägersystem für die dermale applikation von Retinol, Free University Berlin, 1999
- ³¹ R.H. Müller, A. Dingler, The next generation after the liposomes: solid lipid nanoparticles (SLN, Lipopearls) as dermal carrier in cosmetics. *Eurocosmetics* 7, 8, 18-26, 1998
- ³² R.H. Müller, A. Dingler, The next generation after the liposomes: solid lipid nanoparticles (SLN, Lipopearls) as dermal carrier in cosmetics. *Eurocosmetics* 7, 8, 18-26, 1998
- ³³ A. Dingler, R.P. Blum, H. Niehus, R.H. Müller, S. Gohla, Solid lipid nanoparticles (SLN/Lipopearls)-a pharmaceutical and cosmetic carrier for the application of vitamin E in dermal products. *J. Microencapsul.* 16, 751-767, 1999
- ³⁴ R.H. Müller, R.D. Petersen, A. Hommos, J. Pardeike, Nanostructured lipid carriers (NLC) in cosmetic dermal products. *Adv. Drug Deliv. Rev.* 59, 522-530, 2007
- ³⁵ J. Pardeike, A. Hommos, R.H. Müller, Lipid nanoparticles (SLN, NLC) in cosmetic and pharmaceutical dermal products. *International Journal of Pharmaceutics* 366, 170-184, 2009
- ³⁶ S. Svenson, D.A. Tomalia, Dendrimers in biomedical applications - reflections on the field. *Adv. Drug Deliv. Rev.* 57, 2106-2129, 2005
- ³⁷ 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 pharmaceuticals, L'Oréal, US Patent 6432423, 2002
- ³⁸ Self-tanning cosmetic compositions, L'Oréal, US Patent 6399048, 2002
- ³⁹ G. Adams, M.R. Ashton, E. Khoshdel, Hydroxyl-functionalized dendritic macromolecules in topical cosmetic and personal care compositions, Unilever Home & Personal Care, US Patent 6582685
- ⁴⁰ Cosmetic or dermatological topical compositions comprising dendritic polyesters, L'Oréal, US Patent 6287552, 2001
- ⁴¹ M. Franzke, K. Steinbrecht, T. Clausen, S. Baecker, J. Titze, Cosmetic compositions for hair treatment containing dendrimers or dendrimer conjugates, US Patent 6068835, Wella Aktiengesellschaft, 2000
- ⁴² R. Petersen, Nanocrystals for use in topical cosmetic formulations and method of production thereof. Abbott GmbH & Co., US Patent 60/866233, 2008
- ⁴³ B. Luppi, T. Cerchiara, F. Bigucci, R. Basile, V. Zecchi, Polymeric nanoparticles composed of fatty acids and polyvinylalcohol for topical application of sunscreens. *JPP* 56, 407-411, 2004
- ⁴⁴ J. Hu, Active Polymers and textile products for skincare applications, 3rd International Conference on Nanotechnology and Smart Textiles for Industry, Healthcare and Fashion, Institute of Nanotechnology, 2008
- ⁴⁵ US patent pending; China patent CN1883438, 2006
- ⁴⁶ P.T. Spicer, M.L. Lynch, M. Visscher, S. Hoath, Bicontinuous Cubic Liquid Crystalline Phase and Cubosome Personal Care Delivery Systems, in M. Rosen (Ed.), *Personal Care Delivery Systems and Formulations*. Noyes Publishing, 2003
- ⁴⁷ G. Gopal, S. Shailendra, S. Swarnlata, Cubosomes: An overview. *Biol. Pharm. Bull.* 30, 2, 350-353, 2007
- ⁴⁸ E. Kesselman, R. Efrat, N. Garti, D. Danino, Formation of cubosomes as vehicles of biologically active substances, http://materials.technion.ac.il/ism/Docs/2007/Life-Abstracts/Poster/E_Kesselman.pdf

-
- ⁴⁹ B.J. Boyd, Characterisation of drug release from cubosomes using the pressure ultrafiltration method. *Int. J. Pharmaceutics*, 260, 239-47, 2003
- ⁵⁰ A. Angelova, B. Angelov, B. Papahadjopoulos-Sternberg, M. Ollivon, C. Bourgaux. Proteocubosomes: nanoporous vehicles with tertiary organized fluid interfaces. *Langmuir*, 21, 4138- 4143, 2005
- ⁵¹ P. Spicer, Progress in liquid crystalline dispersions: Cubosomes. *Curr. Opin. Colloid Int. Sci.* 10, 274-279, 2005
- ⁵² I. Afriat, B. Biatry, Use of cubic gel particles as agents against pollutants, especially in a cosmetic composition. *Eur. Pat. Appl.*, L'Oréal, 2001
- ⁵³ J. Schreiber, H. Albrecht, Hair care products with a content of disperse phase liquid crystals which form cubic phases. *Ger. Offen.*, Beiersdorf AG, Germany, 2002
- ⁵⁴ J. Schreiber, H. Albrecht, Cosmetic cleaning products with a content of disperse phase liquid crystals which form cubic phases. *Ger. Offen.*, Beiersdorf AG, Germany, 2002
- ⁵⁵ J. Schreiber, A. Eitrich, Deodorant and antiperspirant products with a content of disperse phase liquid crystals which form cubic phases. *Ger. Offen.*, Beiersdorf AG, Germany, 2002
- ⁵⁶ J. Schreiber, C. Schwarzwaelder, T. Cassier, Skin care products with a content of disperse phase liquid crystals which form cubic phases. *Ger. Offen.*, Beiersdorf AG, Germany, 2002
- ⁵⁷ P. Spicer, Cubosome processing: Industrial nanoparticle technology development. *Chemical Engineering Research and Design* 83, 1283-1286, 2005
- ⁵⁸ http://www.oxonica.com/materials/materials_optisol.php
- ⁵⁹ J.R. Villalobos-Hernández, C.C. Müller-Goymann, Sun protection enhancement of titanium dioxide crystals by the use of carnauba wax nanoparticles: The synergistic interaction between organic and inorganic sunscreens at nanoscale. *International Journal of Pharmaceutics* 322, 161-170, 2006
- ⁶⁰ V. McDonald, Nanotechnology finds some growing applications. *Chemical Week*, 11 May 2005
- ⁶¹ Polymeric nanoparticles in consumer products, Rohm & Haas (US), European Patent EP1447074
- ⁶² Time and Extent Application, Bisotrizole, Prepared to support the Inclusion of Bisotrizole into FDA's Monograph for Sunscreen Drug Products for Over-the-Counter Human Use; (64 FR 27666-27693, as amended by 66 FR 6748567487, Docket No. 78N- 0038), Ciba Specialty Chemicals Corporation, April 2005
- ⁶³ G. Wei, B. Bhushan, Nanotribological and nanomechanical characterization of human hair using a nanoscratch technique. *Ultramicroscopy* 106, 742-754, 2006
- ⁶⁴ I. P. Seshadri, B. Bhushan, Effect of ethnicity and treatments on in situ tensile response and morphological changes of human hair characterized by atomic force microscopy. *Acta Materialia* 56, 3585-3597, 2008
- ⁶⁵ B. Bhushan, Nanoscale characterization of human hair and hair conditioners. *Progress in Materials Science* 53, 585-710, 2008
- ⁶⁶ R.H. Müller, M. Radtke, S.A. Wissing, Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) in cosmetic and dermatological preparations. *Adv. Drug Deliv. Rev. Suppl.* 54, S131-S15, 2002
- ⁶⁷ B. Halford, Fullerene for the face. *C&EN* 84, 13, 47, 2006
- ⁶⁸ Nanomaterials, sunscreens and cosmetics: Small ingredients, big risks. *Friends of the Earth*, 2006
- ⁶⁹ J. Wiechers, Nanotechnology and skin delivery: Infinitely small or infinite possibilities? *Cosmetics & Toiletries Magazine*, January 2009
- ⁷⁰ Which? Report - Small wonder: Nanotechnology in cosmetics, November 2008
<http://www.which.co.uk/documents/pdf/nanotechnology-and-cosmetics-161175.pdf>
- ⁷¹ European Parliament Press Release - MEPs approve new rules on safer cosmetics, 24 March 2009
http://www.europarl.europa.eu/news/expert/infopress_page/066-52333-082-03-13-911-20090323IPR52331-23-03-2009-2009-true/default_en.htm