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Review Article

NANOTECHNOLOGY-BASED COSMECEUTICALS: A REVIEW

SANJUKTA DUARAH, KUNAL PUJARI, RAMYA DEVI DURAI, VEDHA HARI B NARAYANAN*

Department of Pharmaceutical Technology, School of Chemical and Biotechnology, Sastra University, Thanjavur 613401, India
Email: vedhahari@scbt.sastra.edu

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ABSTRACT

Nanotechnology signifies the evolving area of research and development, concerned in delivering innovative solutions to increase the efficacy of a product. In recent times, application of nanotechnology is rising in the arena of cosmeceuticals and seems to be promising in overcoming certain drawbacks associated with the traditional products. The nanotechnology-based delivery techniques have proved to offer advantages of greater stability, higher efficacy and have also been reported to show prolonged effects. Nanoparticles are also proficient in modifying the flux, targeting the drug to the location, tailoring the size of drug and in making the stratum corneum permeable in a selective manner. The rapid evolution of nanotechnology has given rise to great aspirations; however there are certain concerns still, regarding the possible hazards of nanoparticles to the human health, which could be neglected because of their less significant toxicity. This review gives a brief overview of the various novel nano-carriers for cosmeceuticals like nanoemulsions, liposomes, solid lipid nanoparticles(SLNs), dendrimers, inorganic nanoparticles, nanocrystals, etc. Safety of nanoparticles use and also the different routes of exposure to the nanoparticles have been discussed here.

Keywords: Cosmeceutical, Nanotechnology, Stratum corneum, Nano-carrier, Hazard.

INTRODUCTION

Nanotechnology is considered to be the most prospective technology of the 21st century, and can be defined as the nano-scale formulation, characterization, and application of compositions, devices, and structures by domineering shape and size [1]. This approach is being used to amend the penetration of the incorporated active components and is achieved by the variation of several aspects, for manipulating the release profile. The development of nanotechnology-based innovative formulations shows a good deal of potential for skin administration. In the present day, this escalating technology plays a significant role in rising above the traditional drawbacks related to cosmetics and allied products.

The Food and Drug Administration (FDA) defines cosmetics as "articles intended to be applied to the human body or any part thereof for cleansing, beautifying, promoting attractiveness, or altering the appearance" [2]. Cosmeceuticals refer to the combination of cosmetics and pharmaceuticals. They contain biologically active ingredients that are known to be beneficial to humans. The term 'cosmeceutical' is used in the professional skin care arena to portray a product that has measurable biological accomplishment in the skin, like a drug, but is regulated as a cosmetic since it claims to have an effect on appearance and is used for the treatment of conditions ranging from photo aging, wrinkles, hyperpigmentation to hair damage [3-5]. Their widespread use as products for skin, lips and nail care is also worth mentioning. Applying nanotechnology in the development of cosmeceuticals offers numerous advantages like targeting of the active therapeutic component to the desired site; greater skin retention; improvement in the stability of cosmetic ingredients; greater aesthetic appearance and sustained release of active drug for long-lasting effect [6, 7]. Some of the nanotechnology-based novel carriers of cosmetics include nanoemulsion, nanocapsule, liposome, niosome, nanocrystal, solid lipid nanoparticle, carbon nanotube, fullerene and dendrimers.

Industrial use of nanoparticles has created new dimensions, but there are also uncertainties regarding the safety and environmental impacts of this emerging technology. The type of toxicity and its extent varies based on the route of exposure to the nanoparticles [8]. The safety of the nanoparticles has to be explored by means of particular tests related to toxicity, including pre-clinical and clinical trials, before the wide-range application of the new technology [9-11].

Novel nanocarriers for cosmeceuticals

Nanoemulsions

Nanoemulsions are considered to be the most advanced nanoparticulate system for cosmetics. These are also termed as sub-micron emulsions (SME) and are systems with uniform and extremely small droplet size (20-500 nm), optically transparent or translucent and having low viscosity that results in excellent spreadability. These are extensively used as medium for the controlled delivery of cosmeceuticals like lotions, shampoo, nail enamels, conditioners and hair serums [12, 13]. Their wide application is attributed to their intrinsic properties like stability, rapid penetration, texture and hydrating power. Korres' Red Vine Hair Sun protection is one of the many cosmetic products available as nanoemulsion. Recently, much research is being done for the fabrication of aqueous-based nail lacquers. A novel nitrocellulose based W/O emulsion nail enamel was developed by Yamazaki and team, which claims to protect and keep the nails in a fine state [14]. French company L'Oreal possess a number of patents on technologies based on nanoemulsions [15].

Liposomes

Liposome's are sphere-shaped, self-enclosed vesicles, composed of one or more phospholipids bilayers with dimensions from 20 nm to a few hundred micrometers [16]. They are used in an array of cosmeceuticals they are biocompatible, biodegradable, non-hazardous, flexible vesicles, can encapsulate active ingredients easily and are appropriate for delivery of both hydrophobic and hydrophilic compounds [17]. These intrinsic properties of the liposome's make them perfect aspirant for the deliverance of vitamins and many different vital components to revive the epidermis. These structures are useful in delivering incorporated components onto the skin surface and even transporting the drugs across it; in modifying the intercellular lipid lamellae by acting as penetration enhancers; or by controlling the release by creating a depot of active ingredients. Quite a few active components like vitamins A, E, K, including antioxidants such as Carotenoids, lycopene, and CoQ10 have been incorporated into liposomes, which amplified their physical and chemical stability when dispersed in water [18, 19]. In the year 1986, Dior introduced the first liposomal anti aging cream named "Capture"[20].

Niosomes

Niosomes are defined as vesicles made up of non-ionic surfactants, which are biodegradable and quite safe. Their stability is higher than liposome's [20]. Niosomesboost, the stability of the encapsulated components, augment skin penetration, improve the bioavailability of scantily absorbed elements and also helps in achieving site specific delivery by targeting the drug to the site where the therapeutic effect is desired [21]. In 1987, the first product

'Niosome' was launched by Lancôme [22]. Manconi *et al.* investigated that unilamellarniosomes are containing Brij®30 conferred best protection of tretinoin against photodegradation.

Nanocapsules

L'Oreal introduced the first nanocapsule-based cosmeceutical in 1995 with the intention of improving the market of their cosmetics, by introducing novel innovative solutions [23]. Nanocapsule is formed of a liquid/solid core in which the active ingredient is positioned into a cavity, which is enclosed by a polymer membrane fabricated of natural or synthetic polymers. Its dimension ranges from 10 nm to 1000nm [24].

Lipid nanoparticles

Solid lipid nanoparticles (SLNs) are defined as submicron colloidal vehicles composed of physiological lipid, dispersed in water or in an aqueous solution of surfactant and with dimensions ranging from 50 to 1000 nm [25]. These were developed at the beginning of the nineties as a substitute to other carriers such as liposomes, emulsions, and polymeric nanomaterials [26]. SLNs are widespread in the field of cosmeceuticals because of their inherent features such as controlled-release properties; reduced size which warrant close contact with the skin; low toxicity; enhanced skin penetration etc. [27]. Occlusive properties provided by SLNs bring about increased skin hydration [28]. Apart from performing as Ultra Violet (UV) rays blocker themselves, SLNs can even combine with organic sunscreens and improve the UV shield. This aids in reducing the concentration of the UVabsorber, which reduce the side effects [29]. In the arena of anti aging products, SLNs showed its impact with the launch of Nano Repair Q10 cream and Nano Repair Q10 Serum by Dr. Kurt Richter Laboratorien GmbH, Germany in 2005 [30]. In an *in vivo* study, it has been proved that the appliance of a conventional cream containing 4% SLNs for 4 w increases skin hydration by 31% [31]. SLNs are also used as topical vehicle for perfumes; e. g. Chanel's Allure perfume integrated into lipid nanoparticles to slow down the release for a prolonged effect [32]. Nanostructured lipid carriers (NLCs) are prepared by a combination of both solid and liquid lipids. The distorted structure of NLCs helps in creating more space and contributes to its higher loading capacity compared to SLNs. NLCs offer long term stability and this also makes them better than SLNs in various cosmeceuticals [33].

Nanocrystals

A nanocrystal is a particle having, at least, one dimension smaller than 100 nanometres (nm) and composed of atoms in either a single or poly-crystalline arrangement. Their dimension ranges from 10–400 nm and are applicable for the delivery of scantily soluble active ingredients [34]. Nanocrystal was first launched in the market in 2007 by Juvena with the skin renewing serum Juvedical, having rutin (flavonoid) as the active ingredient [35]. In a study, it was observed that, compared to the water-soluble rutin glucoside (rutin attached with glucose) the nanocrystal formulation of original rutin molecule possesses 500 times elevated bioactivity [36]. Another product containing nanocrystal carrier is La Prairie having hesperidin, a glycoside plant antioxidant. Ant wrinkle cream, Renergie Microlift by the French company, Lancôme also contains nanocrystals [37, 38].

Dendrimers

Dendrimers are well-defined, regularly branched symmetrical entities with a tree-like configuration and the terminals of the branches imparting a high density of surface functionality. Their dimensions are extremely small, having diameters in the range of 2 to 10 nm[39]. L'Oreal, Unilever and The Dow Chemical Company possess several patents for the use of dendrimers in cosmeceuticals for skin, hair and nail application [40, 41]. A patent on cosmetic formulation containing carbo siloxane dendrimer claimed that it can provide good water resistance, sebum resistance, glossiness, tactile sensation, and/or adhesive properties to the hair and/or skin [42]. In dendrimers, active ingredients are integrated both in the internal part as well as attached on the surface. They are accounted to provide controlled release from the central core.

Nanogold and nanosilver

Gold and silver nanoparticles are considered to be more valuable in cosmeceuticals because of their antibacterial and antifungal properties. Their use in cosmeceutical products like deodorant, face pack and anti aging cream is widespread. An ointment containing silver nanoparticle was claimed to have antibacterial activity and can be used for skin inflammation and skin wound disinfection [43]. French scientist Dr. Philippe Walter and teamper formed a study in which they tried to synthesize fluorescent gold nanoparticles inside human hair. They showed that the gold color remained even after repeated washings [44].

Cubosomes

Cubosomes are defined as discrete, nanoparticles of bicontinuous cubic liquid crystalline phase comprising much larger specific surface area compared to the parent cubic phase [45]. Research activities are trying to use cubosomes for skin care, hair care and antiperspirants [46-48].

Fullerenes

Carbon fullerenes have been used in a number of cosmetic products because of their antioxidant properties; thus recognized for their application in the formulation of skin rejuvenation cosmeceutical products [49, 50]. Fullerenes, like other carbon allotropes, are extremely hydrophobic and this insolubility in aqueous solutions limited their relevance in the beginning, but the utilization of surfactants or surface alterations has augmented their capability to solubilise in aqueous medium and brought more awareness to their possible cosmeceutical applications [51]. Radical Sponge–world's first fullerene-based cosmetic was launched in 2005. Inui *et al.* evaluated the clinical efficacy of fullerene in treating acne vulgaris. They formulated a Lipo Fullerene gel, which significantly reduced the number of inflammatory lesions by 23% and 38% after 4 and 8 w, respectively [52].

Chitin nanofibrils

A chitin nanofibril is a crystalline form of a natural polysaccharide obtained from the crustacean exoskeleton with needle-shaped configuration and its dimensions range from 24-75 nm. It is easily metabolized by the endogenous enzymes of our body and hence employed in personal care products. The efficacy of the chitin nanofibrils in reducing skin wrinkling and improving the signs of aging has been widely demonstrated [53-57]. Chitin nanofibrils have been shown to encourage wound healing activity by reducing hypertrophic scar formation [58, 59].

Insoluble, mineral-based nanoparticles

The mineral UV filters, used widely in sun-blocking formulations to elevate their Sun Protection Factor (SPF), form a noticeable pigmented layer on the surface of the skin. The currently available man-sized oxides such as Titanium dioxide (TiO_2) and Zinc oxide (ZnO) help to avoid this problem. TiO_2can disperse UV radiation most effectively in the range of 65-130 nm [60], while in case of ZnO; the most favourable size is within20–30 nm[61]. The inclusion of these components in sunscreens is beneficial on account of their capacity to raise the SPF; greater range of UV defence; and their inherent non-irritant character [62]. These properties of the nanoformulations eventually lead to their greater market acceptance. The first sunscreen containing nanoparticles of TiO_2 was introduced in 1989, whereas product containing nano forms of ZnO was launched in the year 1991 [63].

Available nano-cosmeceuticals in the market

Some of the nanotechnology-based cosmeceuticals existing in the market are tabulated in table 1.

Safety of nanoparticles

Increasing production and application of nanomaterial-based products marks an escalating number of the workforce and customers exposed to nanomaterials. A wide diversity of cosmeceutical products containing nanoparticles exists in the market. However, despite their huge potential benefits in the realm of environmental, biomedical and industrial applications, very little is known about the short and long-term health effects in organisms and the environment [64]. Concerns have been raised on the subject of the probable dangers which may arise on their skin penetration after the application to the skin [65, 66]. The toxicity of

nanomaterials is affected by their properties, which are attributable to their smaller size, chemical composition, exterior arrangement, solubility, nature and aggregation [67]. Widespread research is crucial to assess the behaviour of the nanoparticles and to resolve whether the nanoparticles stay on the surface of the skin and/or stratum corneum or absorbed into the blood stream to arrive at different organs [68]. According to the Royal Society, in order to ensure complete safety, elements in the form of nanoparticles should be evaluated by the appropriate scientific advisory committee, prior to their application in products intended for human use [69].

Table 1: Various nanotechnology-based cosmeceutical products in the market

S. No.	Trade name	Proposed use	Manufacturer	Type of nanotechnology used
1.	Hydra Flash Bronzer DailyFace moisturizer	Moisturizer	Lancome	Nanocapsule
2.	Hydra Zen Cream	Moisturizer	Lancome	Nanoparticles
3.	RenergieMicrolift	Antiwrinkle	Lancome	Nanocrystals
4.	Revitalift Double Lifting	Antiwrinkle	L'Oreal	Nanosomes
5.	Eye Tender	Antiwrinkle	Kara Vita	Nanospheres
6.	Eye Contour Nanolift	Antiwrinkle Antiaging	Euoko	Nanocapsules
7.	Zelens Fullerene C-60 Night Cream	Antiaging	Zelens	Fullerene C-60
8.	Royal Jelly Lift Concentrate	Antiwrinkle	Jafra Cosmetics	Liposomes
9.	NanoSun™	Sunscreen	Micronisers Pty Ltd	Nanoparticles
10.	Elixir Skin Up	Make-up Foundation	Shiseido	Nanoparticles
11.	Radical Sponge	Skin Treatment	Vitamin C60 BioResearch	C_{60} nanoparticles
12.	Nanorama—Nano Gold Mask Pack	Face mask	LEXON NanoTech	Nanoparticles
13.	CosilWhitening Mask	Face mask	Natural Korea	Nanocolloids
14.	Cosil Nano Beauty Soap	Cleanser	Natural Korea	Nanoparticles
15.	Fresh As A Daisy Body Lotion	Body lotion	Kara Vita	Nanospheres
16.	Lip Tender	Lip moisturizer	Kara Vita	Nanoparticles
17.	Primordiale Optimum Lip	Lip treatment	Lancome	Nanocapsule
18.	Dior Snow Pure UV Base SPF 50	Sunscreen	Dior	Nano-UV filters
19.	Clearly It! Complexion Mist	Antiacne	Kara Vita	Nanosphere
20.	Nanosphere Plus	Antiaging	DermaSwiss	Nanosphere
21.	Nano-In Hand and Nail Moisturizing Serum and Foot Moisturizing Serum	Moisturizer	Nano-Infinity Nanotech	Nanocrystals
22.	TEGO® Sun TS plus	Sunscreen	Degussa	Nanoparticles
23.	Nano Sal™Moisture Key	Moisturizer	Salvona	Nanospheres
24.	Capture	Antiaging	Dior	Liposomes

Routes of exposure to nanoparticles

Health hazards that nanoparticles cause to the humans depend on the route and degree of exposure to such materials. Nanoparticles gain access to the body primarily through three routes i.e. inhalation, ingestion, and dermal routes [70].

Inhalation

According to the National Institute of Occupational Health and Safety, inhalation is the most common route of exposure of airborne nanoparticles [71]. As the most toxic component of airborne particulate matter, nanoparticles have uncontrolled access to the cells of the airway and even intracellular components because of their size. Hence, deposition of NPs in the alveolar spaces of the lung plays a central role to pulmonary toxicity [72]. If the correct safety strategies are not employed, workers may breathe in nanomaterials while production, while customers can inhale nanoparticles by means of using the products such as perfumes, sprays, mist etc. Recent studies on intratracheal instillation of nanoparticles in rats showed that ferric oxide nanoparticles (20 nm) induced some clinical, pathological changes such as follicular hyperplasia, protein effusion, pulmonary capillary vessel hyperaemia and alveolar lipoproteins is in lungs [73]. National Institute of Health has said that though the greater part of inhaled elements enter the pulmonary tract, proof from animal studies implies that a small portion of the inhaled nano-components may pass through the nasal nerves to the brain and get straightforward entry to the blood, nervous system, and additional organs [74].

Ingestion

Ingestion of nanoparticles may perhaps take place from accidental hand to mouth transfer or from those cosmeceuticals that are applied in the vicinity of mouth or lips (e. g., lipstick, lip balm, etc). Large fractions of nanoparticles rapidly pass out of the body after intake, but a small fraction might get absorbed by the body, which subsequently migrate into the different organs [75]. When mice were orally administrated with 20 nm and 120 nm ZnO Nanoparticles at different doses, it was found that the liver, spleen, heart, pancreas and bone became the target organs, where different dose-response relationship were observed [76].

Dermal route

There are three pathways of infiltration across the skin and these have been recognized as intercellular, trans follicular and transcellular [77]. The transfer of nano components across the skin is associated to the physicochemical characteristics of the nanoparticles and carriers, the character of the drug, and also the skin conditions [78]. Even though cosmeceuticals are supposed to be used on normal skin, they are also applied on non-healthy or broken skin with a possibly weakened obstructive nature. Certain works have accounted that nanosized products used on the skin penetrate only through hair follicles and pores present in the skin, with negligible quantity being noticed beneath the stratum corneum [79]. Gulson *et al.*, in their work on dermal absorption of ZnO nanoparticles from a sunscreen product, have revealed that zinc from ZnO particles penetrate healthy skin and are detected in blood and urine, but whether theZn was present as particles or soluble Zn ion was unidentified at that period [80]. A US-based NGO named Environmental Working Group did a review on the utilization of nanoparticles in cosmetics. After peer review of more than 400 papers, it was concluded that zinc and titanium-based products are amongst the safest, highly efficient sun blocking creams available based inaccessible data. Out of the16 studies on skin absorption, none showed absorption of zinc and titanium nanoparticles through healthy and undamaged skin [81].

CONCLUSION

Cosmeceutical industry is expanding day-by-day; and nanotechnology, being the most potential technology of this era, has the competence to revolutionize the cosmeceutical market. We just need to invent ways for their effective application in improving our wellbeing. Novel cosmeceutical delivery systems considered in this review relish the possibility to build up as the 'new generation smarter carrier systems'. Nanotechnology can be effectively used to enhance the safety, efficacy, stability and aesthetic appeal of the

product which will ultimately lead to greater consumer compliance. Nanoproducts should be fabricated and dealt in a manner that improves its values and also accomplish the health of customers and the environment.

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CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest.

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