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A REVIEW ARTICLE ON NANOTECHNOLOGY BASED ON COSMECEUTICALS

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ABSTRACT

Nanotechnology has the potential to generate advancements and innovations in formulations and delivery systems. This fast- developing technology has been widely exploited for diagnostic and therapeutic purposes. Today, cosmetic formulations incorporating nanotechnology are a relatively new yet very promising and highly researched area. The application of nanotechnology in cosmetics has been shown to overcome the drawbacks associated withtraditional cosmetics and also to add more useful features to a formulation. Nanocosmetics and nanocosmeceuticals have been extensively explored for skin, hair, nails, lips, and teeth, and the inclusion of nanomaterials has been found to improve product efficacy and consumer satisfaction. This is leading to the replacement of many traditional cosmeceuticals with nanocosmeceuticals. However, nanotoxicological studies on nanocosmeceuticals have raised concerns in terms of health hazards due to their potential skin penetration, resulting in toxic effects. This review summarizes various nanotechnology-based approaches being utilized in the delivery of cosmetics as well as cosmeceutical products, along with relevant patents. It outlines theirbenefits, as well as potential health and environmental risks. Further,it highlights the regulatory status of cosmeceuticals and analyzes thedifferent regulatory guidelines in India, Europe, and the USA and discusses the different guidelines and recommendations issued by various regulatory authorities.

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

I. INTRODUCTION

"Articles intended to be applied to the human body or any part thereof for cleansing, beautifying, promoting attractiveness, or altering the appearance" is how the FDA defines cosmetics . The FDAis not legally able to approve cosmetics prior to their release on the market. Cosmetics must, however, be consumer-safe and appropriately labeled. Legal liability for the safety and labeling of cosmetics rests with persons and companies that promote them. Asubstance that fills the gap between medication and cosmetics is referred to as a "cosmeceutical."Among the Asian nations that are expected to draw significant players in the future are China, India, Japan, and other countries with enormous potential in the global cosmeceutical market. Japan has already established a notable presence in the global cosmetics market, and it is steadily strengthening its position in the cosmeceutical sector. According toa report titled "Cosmeceuticals market to 2018," the global market for cosmeceuticals is expected to reach $42.4 billion by that year.A "cosmeceutical" product is one that combines a medication and a cosmetic. In the professional skin-care industry, this term is used tocharacterize a substance that has measurable biological activity inthe skin and is classified as a cosmetic product because of its abilityto improve skin. Cosmetics are not classified as cosmeceuticals bythe FDA, but skin scientists, doctors, and other skin care experts use the term to persuade consumers to keep buying cosmetics. These products are specifically antiaging and sunscreen, and many manufacturers market them with natural recommendations and scientific declarations that emphasize the advantages of using these natural products. Some examples of nanotechnology-based innovations are nanoemulsions, which are colloidal particulate withunique perceptible texture properties; nanocapsules, which are used in skin care products; nanopigments, which are transparent and increase the effectiveness of sunscreen products; and liposome formulations, which are small vesicular systems made ofconventional cosmetic matter and also act as a shield in oxygen orlight-sensitive products. The production of cosmeceuticals benefits greatly from the use of these carbon nanotubes, niosomes, fullerenes, nanocrystals, solid lipid nanoparticles, and dendrimers. Because of their increased stability of cosmetic ingredients (such as vitamins, antioxidants, and unsaturated fatty acids), which are typically encapsulated within them, their ability to effectively protectskin from UV rays, and their visually appealing white form, nanoparticles are widely used in the cosmeceutical industries. Hence, in the case of cosmetic products, a major concernin the advancement of nanoformulations is that they may enhance the concentration of active ingredients reaching the blood and impact the toxicity . Figure 1 depicts the overall action ofnanoparticles in cosmetics and cosmeceuticals.

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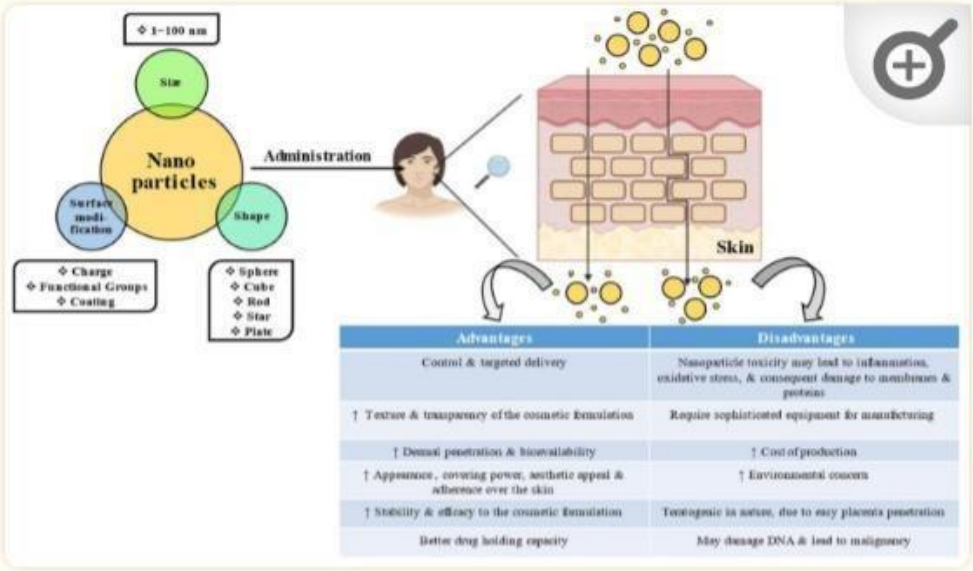
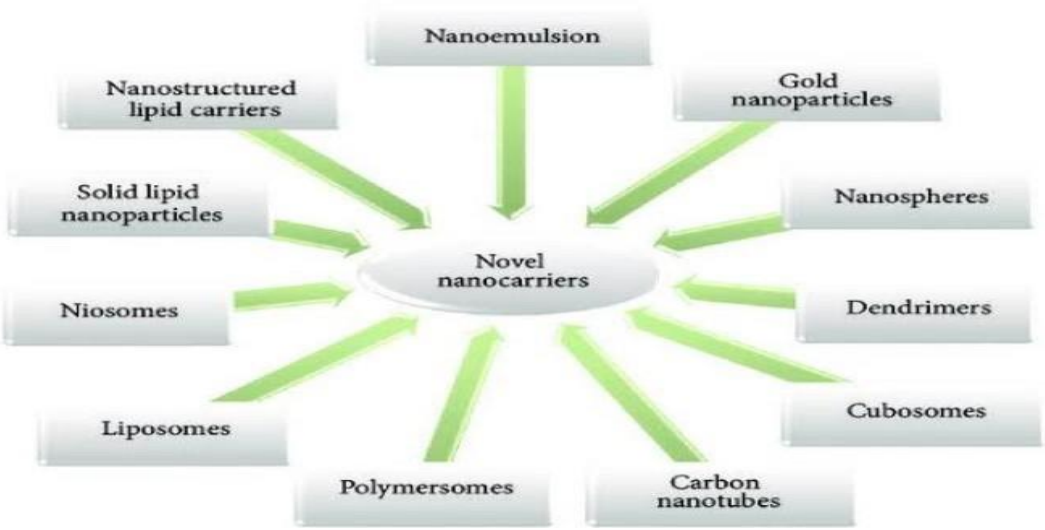


Figure 1

Advantages of nanocosmeceuticals.

II. NOVEL-NANOCARRIER USED IN COSMECEUTICALS



2.1 NANOLIPOSOMES:

The first work on liposomes was published by Bangham in 1963, and in the early 1980s, Mezei and Gulasekharam showed that liposomes Different types of nanoparticles. (a): liposome showing a phospholipid bilayer surrounding an aqucous interior, (b): nanocrystal, (C): solid lipid nanoparticle , and (d), nanocapstile with different drug-loading modalities may be effectively used to administer drugs topically. Phospholipid bilayers sequester part of the solvent that they freely float In, creating liposomes, which are colloidal spherical vesicles. Liposomes are available in a range of forms and sizes. The size of liposomes varies from 20 to several

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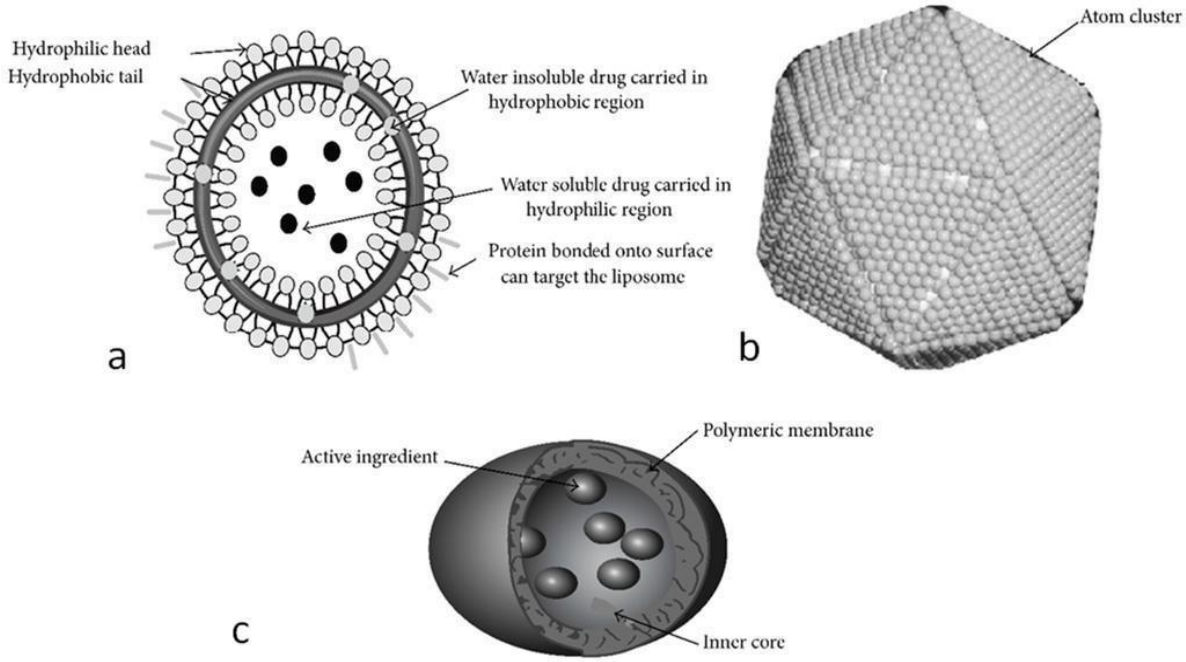
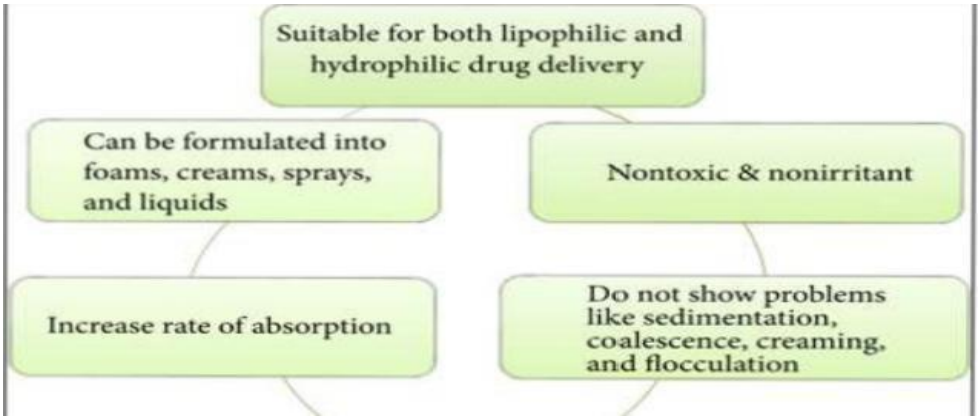
hundred nanometers. Liposomes are used in a variety of cosmeceuticals because they are nontoxic, biocompatible, biodegradable, and flexible vesicles that can easily encapsulate active compounds. Liposomes are helpful for delivering hydrophobic and hydrophilic medications because they may protect the treatment within from the external environment within a vesicular structure. Medications that dissolve in an aqueous media are added to the solvent portion, while medications that do not dissolve in an aqueous medium are stored in the lipid portion. Because of these qualities, they are a great option for supplying vitamins and other essential elements to promote epidermis renewal.



2.2 NANOCAPSULES:

In an effort to increase the popularity of their cosmetics, the French corporation L'Oréal introduced the first nano capsule-based cosmetic product in 1995, sparking investigation into the potential dermatological uses of these tiny capsules. "Nano capsules" are vesicular structures that range in size from 10 nm to 1000 nm, consisting of an inner liquid core surrounded by a polymeric membrane.The level of skin penetration can be regulated by the use of polymers and surfactants in the formulation.one study demonstrated the successful incorporation of perfluorodecalin (oxygen carrier) into a silica nanocapsule core as a new tactic for topical therapy of aging skin due to the inherent instability of perfluorocarbon emulsions. Furthermore, this combination displayed better delivery and stability compared to emultions.Nanocapsules are submicroscopic particles that are made of a polymeric capsule surrounding an aqueous or oily core. It has been found that the use of nanocapsules decreases the penetration of UV filter octyl methoxy cinnamate in pig skin when compared with conventional emulsions.

2.3 NANOEMULSION:



Merits of Nanoemulsion

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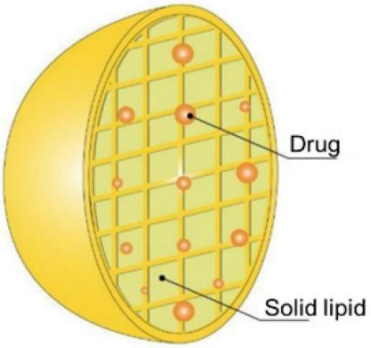
They are dispersions of Nanoscale droplets of one liquid within another. They are metastable systems whose structure can be manipulated based on the method of preparation. The components used for their preparation are GRAS products and are safe to use. Their smaller particle size provides higher stability and better suitability to carry active ingredients; they also increase the shelf life of the product.

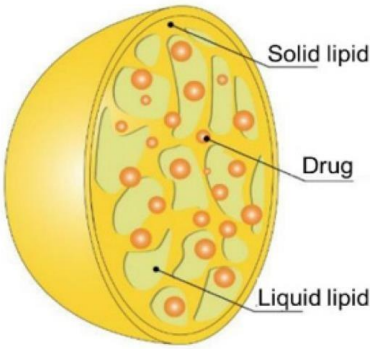
Nanoemulsions are normally water-in-oil (w/o) or oil-in-water (o/w) colloidal solutions that range from a couple of nanometers to 200 nm. The small size of the droplets is responsible for their alluring optical, rheological, and improved drug delivery properties, as compared to traditional formulations. Further, low viscosity, high solubilization ability, and increased kinetic stability due to sedimentation and flocculation make it more popular. Generally, these are transparent and stable and are employed for cleansing purposes, specifically in the cosmetic industry. These materials are used as powerful vehicles in the cosmetic industry for formulating body lotions, skin creams, sunscreens, etc.

2.4 Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs):

Solid lipid nanoparticles (SLNs) are submicron colloidal carriers made of physiological lipid that have been disseminated in water or an aqueous solution of surfactant. Their sizes range from 50 to 1000 nm. 51.Ns are widely used in cosmeceuticals due to a number of benefits. These include their low toxicity, physiologic and biodegradable lipid composition, close contact with the stratum corneum, increased penetration of active ingredients through the skin, and occlusive properties that lead to increased skin hydration. The success of lipid nanoparticles in the anti-aging sector was demonstrated by Dr. Kurt Richter Laboratorien GmbH, Berlin, Germany's Nano Repair Q10 cream and Nano Repair Q10 serum, which were released to the cosmetic market in October 2005.These are two novel delivery systems made up of a single layer of shells having a lipoidal center and are used for formulating pharmaceutical as well as cosmeceutical products . These formulations are characterized by a solid-state lipid matrix having a size in the nano range.



SOLID LIPID NANOPARTICLE



NANOSTRUCTURED LIPID CARRIER

2.5 DENDRIMERS:

The formation of dendrimers, which are highly branched, three- dimensional nanostructured macromolecules, explains their remarkable versatility. Usually composed of polymers, their durability makes them useful for distributing active substances through the skin. These compounds can be more effectively utilized in the formulation of shampoos and deodorants. The hydrophobic characteristics of dendrimers' peripheral parts and the hydrophilic characteristics of their center regions work together to cause surface movement and branching. Additionally, their reliability, polyvalence, and monodispersion make them the perfect transporters for the administration of drugs and cosmetics.Their dimensions are extremely small, having diameters in the range of 2 to 10 nm . Dendrimers are an exciting new class of macromolecular architecture and an important component in the area of nanotechnology- based cosmeceuticals to treat varieties of skin conditions. L'Oreal, Unilever, and The Dow Chemical Company have several patents for the application of dendrimers in hair care, skin care, and nail care products.

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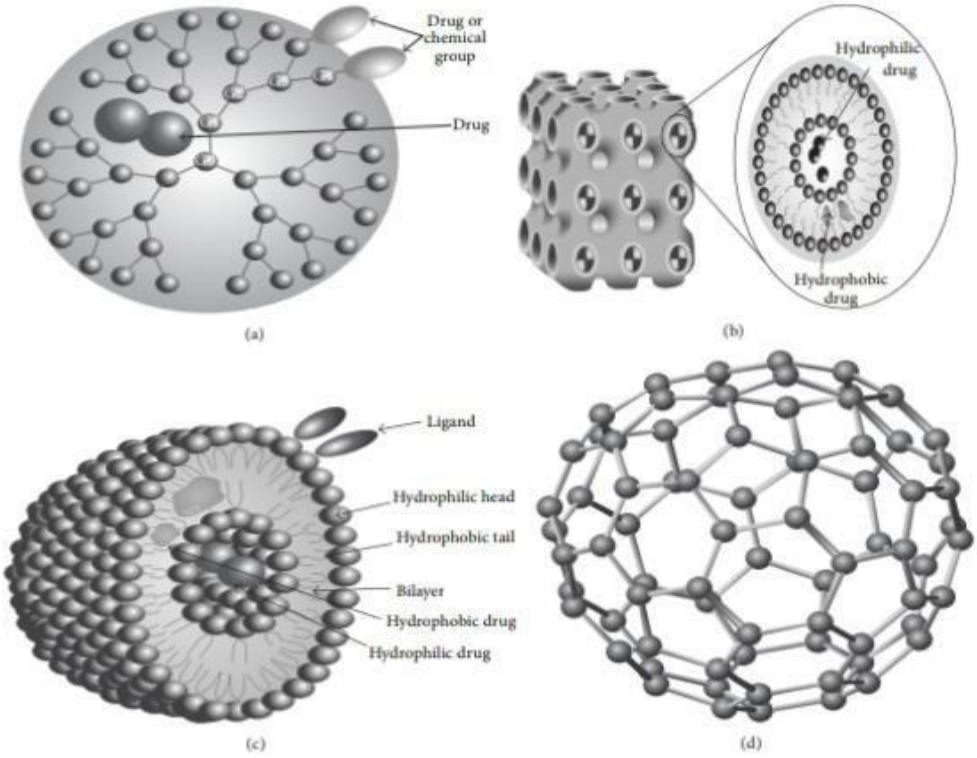
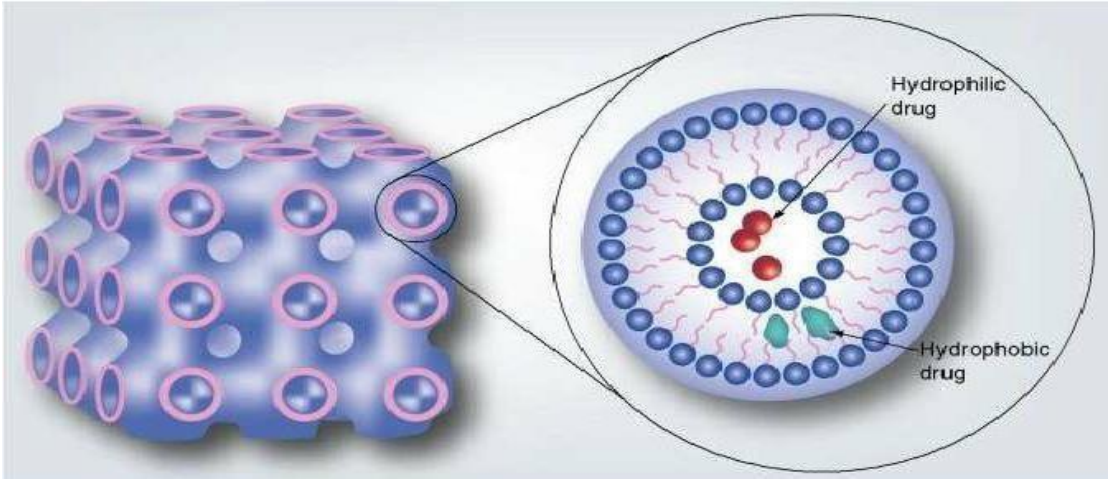


FIGURE 2: Different types of nanoparticles. (a): dendrimer with its different drug-loading modalities, (b): cubosome and its membrane composition with different drug-loading modalities. (c): niosome and its internal synthetic surfactant surrounding drug, and (d): fullerene [13].

2.6 CUBOSOMES:

Cubosomes are discrete particles of bicontinuous cubic liquid crystalline phase that are submicron in size and nanostructured. Recent studies on the application of cubosomes in skin care, hair care, and antiperspirant products were conducted. Numerous studies conducted in collaboration with L'Oreal and Nivea, among other cosmetic businesses, are attempting to use cubosome particles as pollution absorbents and stabilizers for oil-in-water emulsions in cosmeceuticals .Cubosomes are being used as a stabilizer for oil-in-water emulsions and as a means of absorbing contaminants from cosmeceutical formulations in a number of studies conducted in association with cosmetic organizations. Khan et al. described a prolonged-release cubosome formulation that contained erythromycin. They determined that this non-invasive formulation had greater activity and effectiveness in treating and preventing acne.



Structure of cubosomes

2.7 NANOCRYSTAL:

Nanocrystals are aggregates composed of several hundreds to thousands of atoms that combine into a cluster and are in the size range of 10-400 nm used for the delivery of poorly soluble actives . Nanocrystals appeared

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first in the cosmeceutical market in 2000 by Juvena with the product Juvedical having rutin (27) In a study it was observed that, compared to the water-soluble rutin glucoside (rutin with attached glucose), the nanocrystal formulation of original rutin molecule possesses 500 times higher bioactivity .In one of the latest studies carried out by Köpke et al. on the anti-pollution agent SymUrban, the solubility and the penetration profiles were observed to remarkably increase in its nanocrystal form. These nanocrystals increased the dermal bioavailability of the poorly soluble active ingredient in SymUrban and appeared to be a favorable delivery system for this material .It was observed that, despite the 500 times lower concentration of dissolved rutin in the water phase of the nanocrystal suspension, the nanosuspension was about 25% more effective in photoprotection and the concentration of actives formulated as nanocrystals in the skin were much higher compared to water-soluble derivative or using the active in normal powder form.

2.8 NIOSOMES:

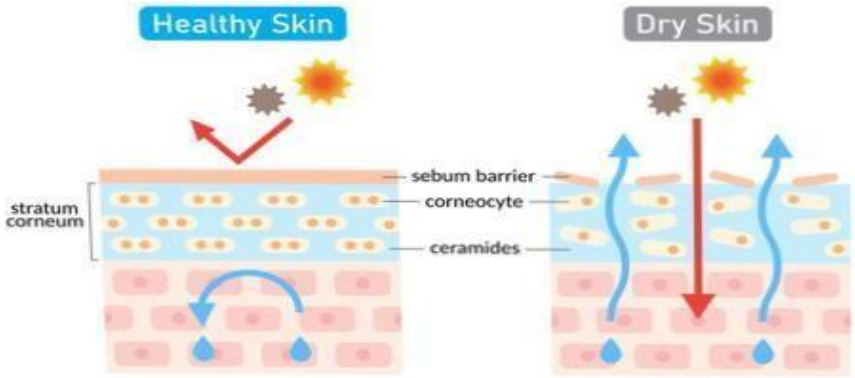
Niosomes are nonionic surfactant vesicles devised by using nonionic surfactants . These vesicles possess high entrapment efficiency, improved chemical stability, and enhanced penetration, as well as lower production cost as compared to liposomes. A niosome is a nanostructure that ranges in diameter from 100 nm to 2 m. Its center is an aqueous cavity that is surrounded by layers of lamellar phase nonionic surfactant. These have been tested as topical vesicular carriers for a range of medications and cosmetics. Since niosomes can lengthen the active ingredient's residence duration in both the stratum corneum and the epidermis and decrease system absorption, they are shown to be effective for topical distribution of active substances. Targeted delivery is also possible with niosomes because the active ingredient is delivered straight to the chosen therapeutic spot. 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 . Niosomes can be multilamellar or unilamellar vesicles in which an aqueous solution of solute and lipophilic components are entirely enclosed by a membrane which are formed when the surfactant macromolecules are organized as bilayer . Size ranges from 100 nm to 2 μm in diameter. Size of small unilamellar vesicles, multilamellar vesicles, and large unilamellar vesicles ranges from 0.025–0.05 μm, =>0.05 μm, and 0.10 μm, respectively . Major niosomes components include cholesterol and nonionic surfactants like spans, tweens, brijs, alkyl amides, sorbitan ester, crown ester, polyoxyethylene alkyl ether, and steroid-linked surfactants which are used for its preparation.

2.9 FULLERENES:

Other nanoscale materials like carbon fullerene are utilized in some cosmetic products thanks to their antioxidative properties. They display potent Scavenging capacities against radical oxygen species which they're considered for his or her use within the preparation of skin rejuvenation cosmeceutical formulations. These structures are comprised of carbon rings and contain odd-numbered (like Pentagon and heptagon) carbon rings. Conferring a 3dimensional spherical shape. These structures are known as Fullerenes ("Bucky Balls"). Fullerenes are highly hydrophobic and thus aren't soluble in aqueous solutions, which initially limited their applications, but the utilization of surfactants or surface modifications has increased the power of fullerenes to solubilize in water and get more attention to their potentialpharmaceuticaluses.

III. MAJOR CLASSES OF NANOCOSMETICALS

3.1 MOISTURIZER:



How does moisturizer protect the skin

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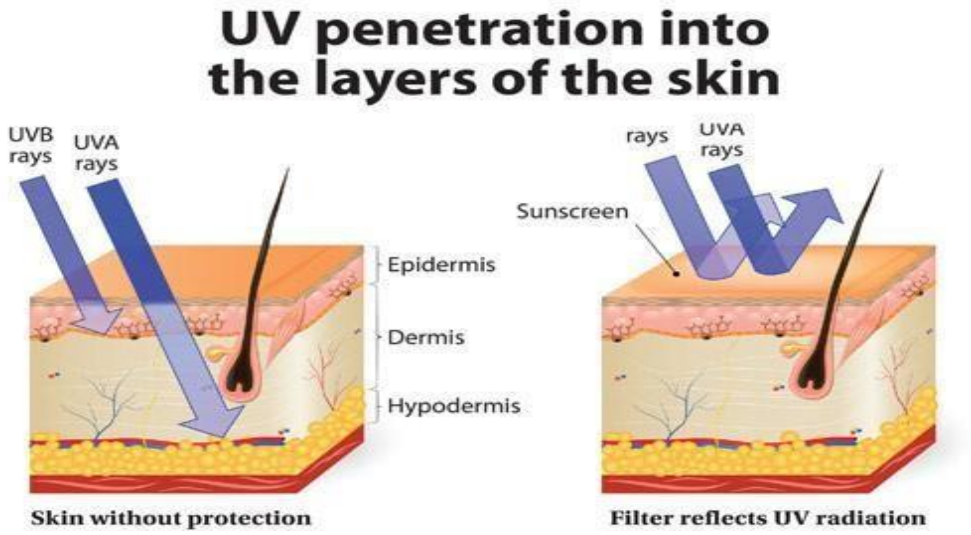
Stratum corneum is the primary barrier of the skin whose main purpose is to keep inside in and outside out. Water from the stratum corneum gets evaporated quickly leading to dehydration. This dehydration of skin can be averted by using moisturizers which provide flexibility to the skin. A thin layer of humectant is created onthe skin when moisturizers are applied, helping the skin look nicer and retain moisture. Because of their long-lasting benefits, liposomes, nanoemulsions, and SLNs are often used moisturizing formulations. These are thought to be the best products for treating different skin problems.

3.2 SUNSCREENS:

Sunscreens are widely used to protect the skin from harmful effects of sun rays on exposure. Zinc oxide (ZnO) and titanium dioxide (TiO_2)are the most effective approved mineral-based ingredient which protects the skin from sun damage. This mineral forms a materialistic barrier on the skin, reflects UVA and UVB rays from penetrating down to the deeper layers of skin, and is less irritating .This mineral forms materialistic barrier on the skin. Reflects both UVA and UVB rays from penetrating right down to the deeper layers of skin, and may be a smaller amount irritating the most drawback of traditional or conventional sunscreen is that, when applied, it leaves a white chalky layer on the skin this is often where nanoparticles are available. Improved sunscreens are just one of the varied innovative uses of nanotechnology. Sunscreen products using nanoparticles of ZnO or TiO_2 are transparent, less greasy, and less smelly and have increased aesthetic appeal.



How does sunscreens protect the skin

3.3 ANTIAGING PRODUCTS:

Chemical products, pollution, stress, irradiation from infrared (IR) and ultraviolet (UV) sources, and abrasion are involved in skin aging. Collagen plays an important role in skin rejuvenation and wrinkle reversal effect. The quantity of collagen in the skin decreases alongwith age. The aging of the skin manifests itself in many ways: drying out, loss of elasticity and texture, thinning, damaged barrier function, appearance of spots, modification of surface line isotropy, and, finally, wrinkles. Most of the cosmeceuticals have been developed with claims of antiwrinkle and firming, moisturizing and lifting, and skin toning and whitening activity. Antiaging products are the main cosmeceuticals in the market currently being made using nanotechnology. L'Oreal has employed nanotechnology in products such as Revitalift antiwrinkle cream which contains nanosomes of ProRetinol A, and claims that it instantly retautens the skin and reduces the appearance of wrinkles . Application of retinol can increase epidermal water content, epidermal hyperplasia, and cell renewal while enhancing collagen synthesis .Application of retinol can increase epidermal hyperplasia. Epidermal water content, and cell renewal while enhancing the collagen synthesis. Retinol also interferes with melanogenesis and they also inhibit matrix metalloproteinases, which are involved in the breakdown of collagen.The clinical benefits include a discount within the looks of wrinkles, fine lines and lightening of lentigines. Hydra Zen Cream is introduced by Lancôme to renew the skin's healthy Look which contains nanoencapsulated Triceamide.

3.4 HAIR CARE:

Hair care is another promising field for nanotechnology. Companies are using nanotechnology in hair care products and research is ongoing to discover the ways of how nanoparticles can be used to prevent hair loss and

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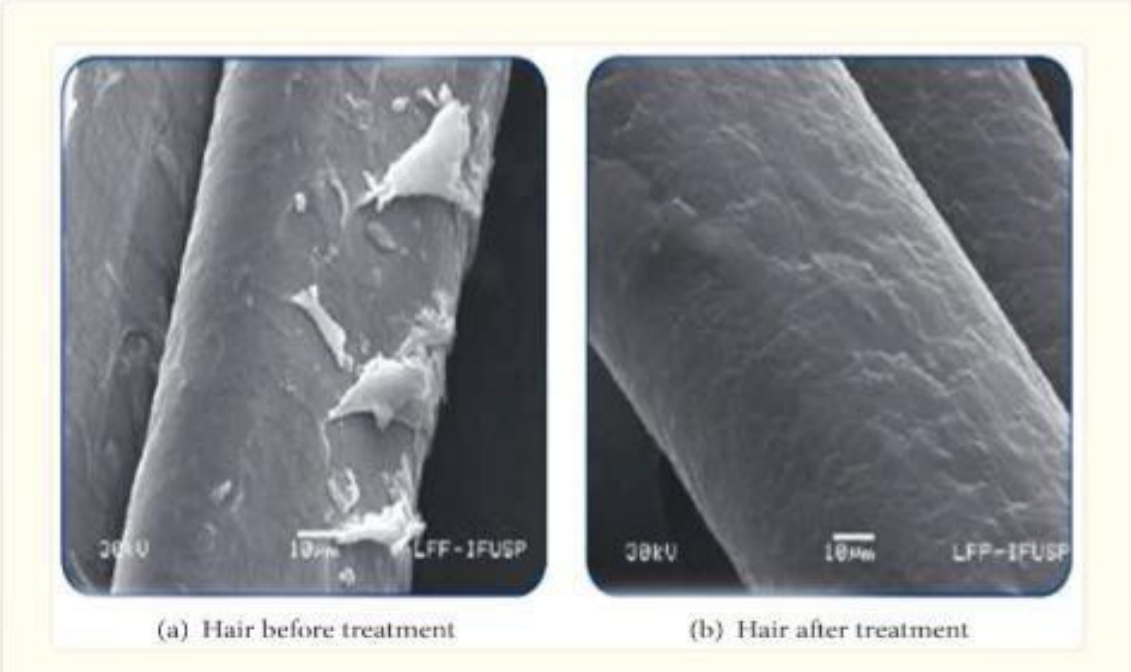
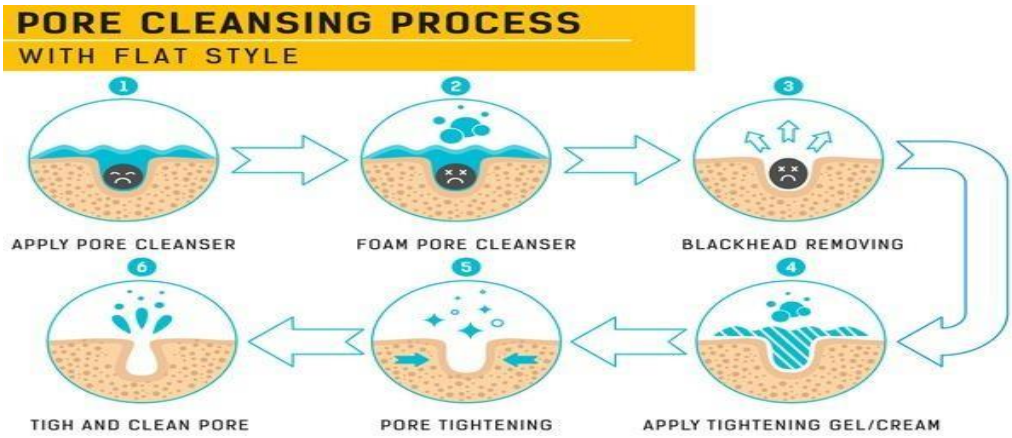
to maintain shine, silkiness, and health of hairs.Unlike ordinary hair straightening products nanoemulsion in hair cosmetics does not destroy the outer structure of the hair fibers, called cuticles, to penetrate into the hair strands . Unlike ordinary hairstraightening products nanoemulsion in hair cosmetics doesn't destroy the outer structure of the hair fibers, called cuticles, to penetrate into the hair strands. Sericin (composed of cationic sericin nanoparticles) is a lively area of hair cosmeceuticals. Studies have shown that sericin nanoparticles in hair cosmeceuticals easilyadheretothesurfaceofearlesssealandtreatthedamagedcuticles.



Effect of sericin nanoparticles on hair cuticle. Increased hair gkasa (b) obtained in damaged hair (a) after treating with sericin nanoparticles.

3.5 SKIN CLEANSER:

The skin is covered with a hydrolipid film that, depending on the area of the body, comprises secretions from sebaceous glands and fromapocrine and eccrine sweat glands. Decomposition products from corneocytes and cornification (cellular debris and stratum corneumlipids) in the process of being shed are also present. This film provides a natural defense against pathogenic organisms but also attracts dirt and pollutants from the environment. Sometimes the microorganisms present on the skin surface act on components ofthe surface film and create undesirable by-products, such as those resulting from the metabolism of compounds found in apocrine sweat that create body odor . Thus, periodic cleansing to urge obviatedirt, debris, and odor is significant to needcareofskinhealth.



Cleansing is additionally necessary to urge obviate soil (which mayinclude bacteria) from the skin surface that's acquired by incidental contact or by intentional application (medications or makeup and other cosmetic products). Nano Cyclic Inc. produces Nano Cyclic cleanser pink soap which is a scientifically balanced blend of

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nanosilver and natural ingredients and claims that it kills harmful bacteria and fungi, fights acne, and diminishes age spots and sundamagedskin.

3.6 LIPCARE:

Lip care is another promising class of cosmeceuticals. Different nanoparticles Can be incorporated into lipstick and lip gloss which will soften or soothe the lips. By preventing transepidermal water loss. Korea Research Institute of Bioscience and Biotechnology holdsa patent that described that it is possible to prepare Pigments exhibiting wide range of colors using gold or silver nanoparticles bymixing in various compositional ratios and whose color can be maintained for a long period of time. Silica nanoparticles used in lipsticks improve the homogenous distribution of pigments. Once applied, they prevent the pigments from migrating or bleeding into thefinelineoflips.

3.7 NAILCARE:

Nanotechnology-based nail cosmeceuticals have various advantages over conventional products. A study revealed that nailpaints having nanosized particles improve toughness, mar resistance, and impact resistance of the mammalian nails [56]. NanoLabs Corp. (a nanotechnology research and development company)was awarded a provisional patent for its original nanonail polish andlacquer having advantages that it dries to a very hard state, resistsshock, cracking, scratching, and chipping and its elasticity offers superior ease of application without cracking. One of the new strategies which may have great potential in the cosmeceuticals is the incorporation of nanoparticles having antifungal activity (like silver and metal oxide nanoparticles) in nail polish to treat fungal toenailinfections.

IV. EXPOSURE TO NANOPARTICLES

Although the industrial usage of nanoparticles has opened up newpossibilities, there are risks and uncertainties involved as well. Workers and consumers are exposed to nanoparticles in greater quantities as a result of the growing production and use ofnanomaterials. This indicates that knowledge about their exposureroutes is more important. There are three ways that humans might beexposed to nanoparticles: through their food, drink, or skin. The mosttypical way to be exposed to airborne nanoparticles is through inhalation. As production or consumers utilize aerosolizedcosmeceuticals (deodorant, fragrances, etc.), they run the risk of inhaling nanoparticles. The way that nanoparticles interact with therespiratory epithelial membrane determines how much of them endup in the respiratory system. Therefore, there should be pronounced demand for the details of exposure of nanoparticles route. Humans exposed to nanoparticles mainly through ingestion, inhalation and dermal routes. Airborne nanoparticles mostly exposed through inhalation. Customers inhale nanoparticles through use of aerosol cosmeceuticals whereas employees inhale during production of nanoparticles. The other route of exposure of nanoparticles into thesystemic circulation is dermal absorption. Majority of cosmeceuticalsareappliedtotheskin.

V. SKIN PENITRATION OF NANOPARTICLES

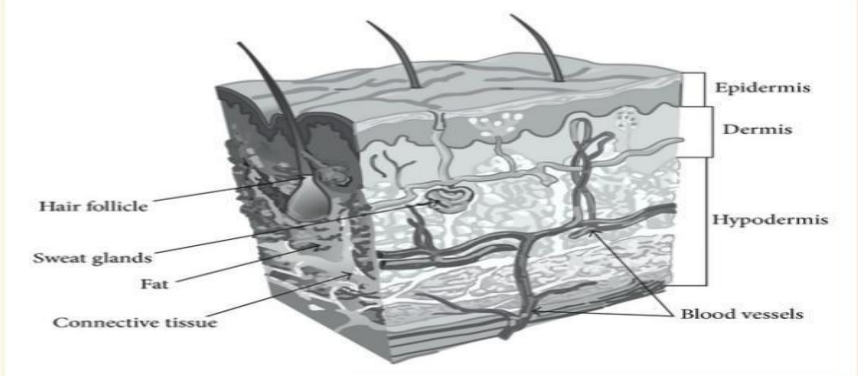

Figure 4

Human skin layers.

The skin is the largest organ of the body. Human skin is made up of three layers , the epidermis (the outermost layer of skin), the dermis (contains tough connective tissue, hair follicles, and sweat glands), and the hypodermis (made up of fat and connective tissue). The epidermis is divided into several layers and its

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outermost layer, the stratum corneum, is responsible for the barrier function of the skin due to its lipophilicity and high cohesion between cells. Passive routes by which a molecule can cross the stratum corneum are intercellular, transcellular, and appendageal routes.

A vast number of cosmeceutical products containing nanoparticles are present at the market place and are applied all over skin, which may raise possible dangers when exposed to skin penetration. Nanoparticles are mainly classified into two groups, that are soluble biodegradable nanoparticles and insoluble nonbiodegradable nanoparticles. Cosmetics products are meant to apply on the normalskin but it is also applied on skin which is not healthy. In case of that type of conditions the skin may got damaged. Mostly studies showed that nanoparticles contained products are mainly penetrate through the hair follicle and skin pore openings present below the stratumcorneum.

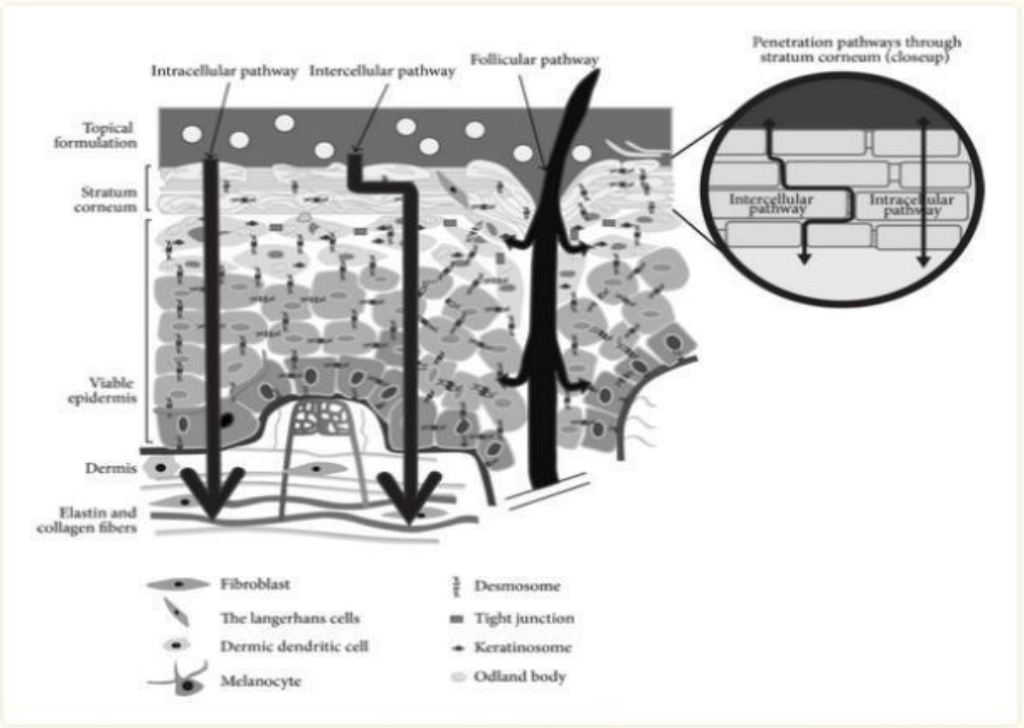

Figure 5

Skin penetration pathways (intracellular, intercellular, and follicular) by which a molecule can cross the stratum corneum [64].

VI. TOXICITY OF NANOPARTICLE

When used topically, nanoparticles from different cosmeceutical treatments have the potential to enter the bloodstream and have harmful effects. According to a study on the toxicity of TiO_2 nanoparticles, brain damage and decreased sperm production in male progeny were caused by subcutaneous administration of nano-sized TiO_2 to pregnant mice. Numerous studies have demonstrated that when exposed to UV light, TiO nanoparticles can generate free radicals and cause cell damage in test tube experiments. Research has demonstrated that human fibroblast cells can be killed by cobalt-chromium nanoparticles (29.5 nm in diameter) even when the cellular barrier is intact. Accidental inhalation and consumption of nanoparticles or its absorption through skin can cause severe skin and lung damage or organ damage. But silver nano particles are used as an antimicrobial agent. Silver concentration used are lethal for bacteria which is also lethal for keratinocytes and fibroblasts. Concentration of silver that is lethal for bacteria is also lethal for both keratinocytes and fibroblasts . The cosmeceutical industry debatesthat consumer risks are low, as there is no evidence that nanoparticles from the productpenetratehealthy,intactadultskin.

VII. CONCLUSION

Growth of cosmeceutical industry is increasing day by day as the cosmeceuticals market is highly diversified, with products coming from major and small manufacturers and local companies around the world. Nanotechnology represents the key technologies of the twenty-first century, offering excellent opportunities for both research and business. The rapid spread and commercialization of nanotechnology in cosmeceuticals have given rise to great technical and economic aspirations but also question about the emerging risks to health and safety of consumers. Thus, cosmeceutical products based on nanotechnology should be designed and sold in a way that fully respects the health of consumers and the environment.

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