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# A REVIEW ON POTENTIAL ROLE OF NANOTECHNOLOGY IN SKIN DRUG DELIVERY SYSTEM:

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## ABSTRACT.

Skin as a drug delivery method has attracted great attention in recent years because it eliminates many of the limitations of oral and parenteral administration. However, the excellent barrier properties of skin are a major obstacle to effective drug delivery via this route. The top layer of the skin, the “stratum corneum”, is the tightest layer and is responsible for most resistance. This requires a reversal and change in the resistance of the stratum corneum to achieve significant cure in systemic or localized skin diseases. In the last few years, many methods have been developed to increase the permeability of drugs through the stratum corneum. A good way is to use nanoparticle materials, as they not only facilitate the delivery of drugs into the skin, but also prevent negative effects on the skin structure. This review focuses on nanoparticle carriers, including liposomes, deformable liposomes, ethosomes, liposomes, and lipid nanoparticles designed for topical and transdermal delivery. Special attention is paid to their composition, structure, access process and final applications. The data presented demonstrate the potential of the nanoparticle carrier for dermal and transdermal delivery.

**KEYWORDS**. Nanoparticle carrier, Skin penetrating, Liposomes, Deformable liposomes, Allosomes, Liposomes, Lipids Nanoparticles.

## INTRODUCTION.

Nanomaterials are a large “part” of materials and their applications are very popular due to their excellent physical and chemical properties. The cosmetic industry was one of the first industries to use nanotechnological materials and nanocomponents have been used in the cosmetic industry for more than 30 years. In the European Union, the definition of nanomaterial in cosmetics is “an insoluble or biopersistent and deliberately produced material with one or more external dimensions or structures with dimensions between 1 and 100. Cosmetics based on nanomaterials, compared with microcosmetics It shows some special advantages. The purpose of using nanomaterials (NM) in the cosmetics industry is to obtain long-term results and increase stability. The high surface area of nanomaterials allows better delivery of

ingredients through the skin. Some of the main purposes for using nanomaterials in cosmetics are to penetrate the skin to improve the distribution of ingredients, new colors (like lipstick and nail polish), transparency (like sunscreen), and long-lasting effects (for example, in cosmetics). The ultimate goal of using NMs in the cosmetic industry is to deliver the right ingredients to suit the body's needs and ensure long-term stability. Today, the most common use of NM in cosmetics is in UV filters in skin care products, especially sunscreens.In 1986, Christian Dior created the liposome-based anti-aging product Capture™. Over the years hundreds of cosmetic products have started to use NM and many more. World-famous cosmetic brands use NM in their products . L'Oréal invested most of its profits in nanotechnology. The number of patents it has received related to nanotechnology ranks sixth in the United States and uses approximately four nnanocomponents. Shiseido uses nano. -TiO2 and ZnO are available in wet formulations (e.g. emulsions), but not in aerosols due to inhalation risk. They are slowly incorporating nanomaterials (carbon black) into some formulations of their products. Shiseido is using nanoscale TiO2 and ZnO in wet-based formulations such as cosmetics, however, it does not include them due to the risk of inhalation used in aerosols. Generally speaking, The world's famous cosmetic industry is gradually incorporating nanomaterials into its products, and the World Health Organization (WHO), non-governmental organizations, political organizations and organizations have expressed concerns about the safety and use of nanomaterials. Currently, the European Commission (EC) has updated its guidelines on the safety assessment of nanomaterials in cosmetics and the US Food and Drug Administration (FDA) has also developed its own guidelines on the use of nanotechnology in cosmetics. In Europe, future toxicological data for hazard analysis will be available in FC Cosmetics Regulation No. It should not include animal testing according to. Decision 1223/2009 banning these tests and other methods (such as in vivo or in vitro) In 2020, the European Union Observatory for Nanomaterials (EUON). Announced that: All companies that produce, use or import nanomaterials According to the registration regulations.

## TYPES OF NANOMATERIAL IN COSMETICS.

### Inorganic Nanoparticles.

Compared to organic nanoparticles, inorganic nanoparticles are non-toxic, hydrophilic, biocompatible and very stable. The main difference between these and the above is that inorganic nanoparticles are synthesized from inorganic elements (Ag, Au, Ti, etc.) while organic nanoparticles are synthesized from polymers. TIO is one of the most commonly used inorganic nanoparticles in sunscreens. On the nanoscale, it has a higher sun protection factor (SPF), which makes it better and better compared to it because of its transparency. Cosmetic effect on TiO2 pigment. In the market, companies often use words like "transparent" or "invisible" when using nanoscale TiO2 or ZnO. Nanoscale TiO and ZnO have been reported to exhibit good properties at larger nanometer sizes. Micro-TiO2 and ZnO are used as ingredients in sunscreens due to their ability to absorb UVA and UVB. ZnO and TiO2 nanoparticles are also widely used in sunscreens as UV filters with sizes starting from 20 nm. They show good distribution and leave a nice effect. The combination of transmission electron microscopy (TEM) and X-ray powder diffraction (XRD) is considered a good method for the analysis of ZnO and TIO in cosmetics. Regarding their safety, it has been reported that high absorption of ZnO nanoparticles may harm health. However, a different route (e.g., dermal route) for ZnO content in sunscreen samples is considered safe because there is no evidence of skin penetration.

**Silica (SiO2)**

Silica nanoparticles have attracted the attention of the cosmetic industry because they have a hydrophilic surface that supports extended production time and low cost. Nano silica is used to improve the performance, texture and shelf life of cosmetics. It increases absorbency and acts as an anti-caking agent. Research shows that silica nanoparticles can help improve the appearance and distribution of pigments on the lips and prevent the movement of pigment towards the lips . Silica nanoparticles are stable nanodispersions with sizes ranging from 5 to 100 nm, providing lipophilicity. Hydrophilic drugs are delivered to their site of action by encapsulation. Silica nanoparticles can be found in rinse-off and rinse-off cosmetics for hair, skin, lips, face and nails, and the presence of silica nanoparticles in cosmetics should be increased. Regarding the safety of silica-based nanoparticles, results are conflicting, and properties such as size and surface modification should be taken into account when assessing toxicity. Therefore, speculation regarding the use and exposure of silica nanoparticles in cosmetics continues.

**Carbon Black (Nano)**

Carbon black, CI 77266, is a cosmetic product known to be used as a pigment in eye makeup, skin care products and mascara. Its nanoform is now approved in the EU and can be used as a colorant at a maximum level of 10%. Studies on carbon black nanoparticles have shown that, compared to micron-sized nanoparticles, they exhibit a greater tendency to induce cytotoxicity, inflammation, and alter phagocytosis of human monocytes [28]. Considered safe when there is no respiratory risk.

**Nanoorganic Materials**

Triphenyltriazine is an excellent and light-stable filtering agent, making it a particular ingredient of choice in sunscreen formulations. Triphenyltriazine (Nano) is a broad-spectrum UV filter suitable for use in sunscreen and anti-aging facial products. It has excellent photostability and is a European approved UV filter. BASF SE uses its own brand Methylenebisbenzotriazolyltetramethylbutylphenol (Nano) or MBBT is a UV filter authorized on the EU market for use cosmetics for skin applications at up to 10% w/w. In the opinion of the SCCS MBBT does not pose a risk to humans when applied to healthy skin. However, SCCS Is concerned about irritation and potential bioaccumulation.

**Nanohydroxyapatite.**

Nanohydroxyapatite has been used in oral care and cosmetics, is included in many products for tooth sensitivity and enamel remineralization. And is considered a hope and safety for oral care products. Nanohydroxyapatite particles have been incorporated into oral care products such as toothpastes and mouthwashes, and due to their remineralizing and desensitizing properties, nanohydroxyapatite particles have been incorporated into oral care products such as toothpastes and mouthwashes.

**Gold and silver nanoparticles**

Gold and silver nanoparticles have many applications as well as antibacterial and antifungal properties. Gold and silver nanoparticles are used in cosmetics such as deodorants and anti-aging creams. In Europe, the SCCS has not yet decided on the safety of nanocolloidal silver when used in oral and topical applications due to the large number of reports. In the United States, cosmetics cannot be claimed to contain antibiotics because the claim is based on the function of the body, so it can only be used in medicine and not in makeup. It has been reported that silver nanoparticles can be used as effective growth inhibitors of many diseases. Silver and silver-based compounds are widely used to control bacterial growth. The use of silver in cosmetics may be affected due to the gradual precipitation of silver-based elements in solutions and emulsions, and this solution may be the use of silver nanoparticles. Ogura et al. investigated the use of silver nanoparticles as cosmetics and reported that silver nanoparticles remained stable for more than one year and did not precipitate. Additionally, silver nanoparticles can be used as antibiotics against bacteria and fungi and do not penetrate human skin. Plit-

Prosiak et al. studied the use of gold and silver nanoparticles in cosmetics. They report that the difference between silver and gold nanoparticles is incorporated into the cream's formula. The silver nanoparticles entered the cream mixture in a clumped state, but the gold nanoparticles did not clump after entering the cream mixture. They attributed this phenomenon to the larger value of the electrokinetic potential on the surface of gold nanoparticles.

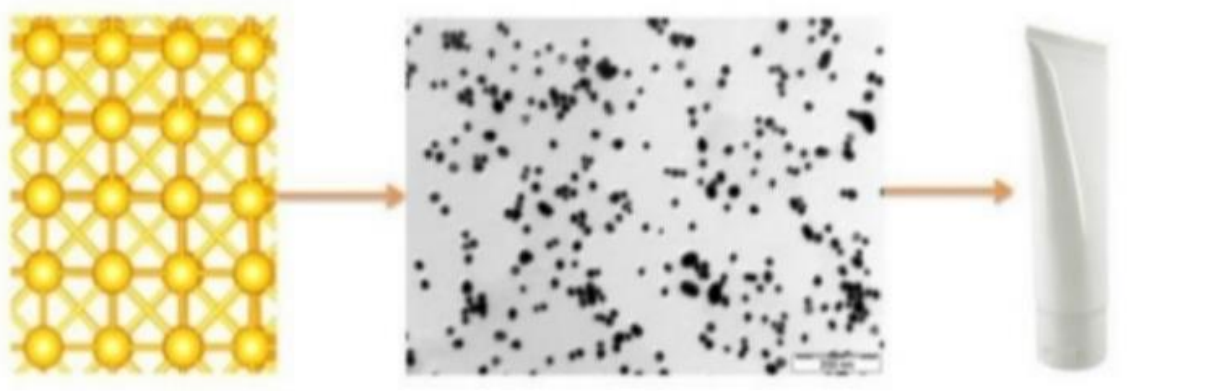

**Fig.no :-1:-** Gold Nanoparticles use in cosmetics.

**Nanoliposomes**

Nanometer scale liposomes are called nanoliposomes. These are concentric bilayer vesicles in which the water content is surrounded by a lipid bilayer composed of phospholipids. Nanoliposomes are biodegradable and biocompatible and represent a versatile class in cosmetics. They are used as protective agents for skin permeability and moisturizing for active ingredients such as vitamins. They can be used to deliver odors in antibiotics, body antibiotics, and lip balm]. Despite its good properties, problems of low drug loading, lack of reproduction, and physical and chemical instability still exist.

**Nanocapsules**

Nanocapsules are polymeric NM capsules surrounded by an oil phase or water phase.Nanocapsules are used in cosmetics to protect ingredients, reduce odor and solve incompatibility problems of formula ingredients . Polymer nanocapsule suspensions can be used directly on the skin as a final product or

Incorporated as an ingredient in semisolid products. The level of skin penetration of ingredients can be varied depending on the polymers and surfactants used as raw materials . Stable poly-L-lactic acid nanocapsules with a diameter of 115 nm were prepared by the nanoprecipitation method, and perfume release was achieved by trapping perfume molecules in polymer nanocarriers .This technology, which encapsulates molecules in biocompatible nanocapsules, may play an important role in the future.

**Skin Structure.**

Skin is the largest organ of the human body, accounts for approximately 15% of body weight and has an area of approximately 2 square meters. It represents the main barrier between the body and the external environment. Its role is to protect the body from other factors, maintain homeostasis and provide positive results. The skin system consists of three layers: epidermis, dermis, and hypodermis and associated tissues including hair follicles, sebaceous glands, sweat glands, and nails. Epidermis is the uppermost 50-100 micron thick skin layer that separates the inside of the human body from the external environment. It consists of keratinocytes.process of F

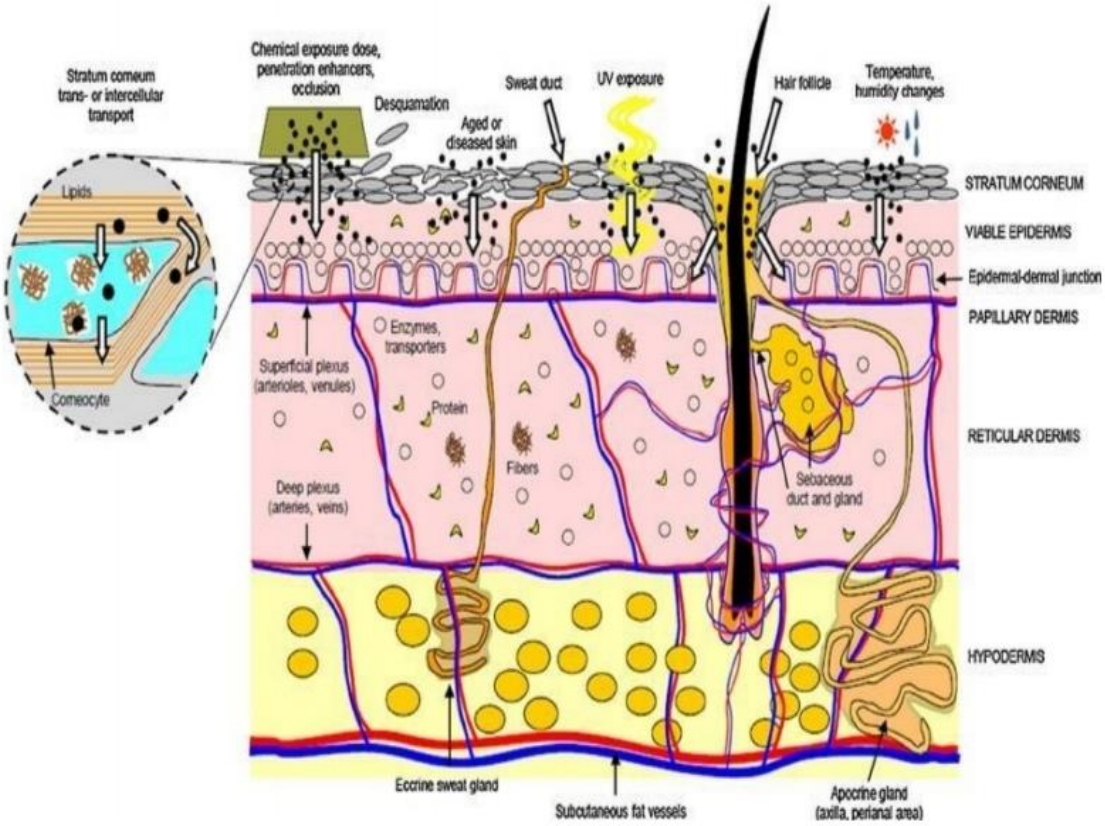


**Fig.no:-2:-** Skin Structure.

stratum corneum, stratum lucidum, stratum granulosum, stratum spinosum and stratum basale. These layers show distinct keratinocyte differentiation. Keratinocytes in the basal layer are single-layered, columnar and mitotically active, while the uppermost 15-20 layers are polygonal, all distinct, dead and nucleated keratinocytes (now called keratinocytes). It is the least permeable “stratum corneum” of the skin Keratinocytes are embedded in a bilayer lipid

## Factors affecting the delivery of lipid nanoparticles to the skin

Size of lipid nanoparticles, nature and content of surfactant, particle surface charge. And state of lipids on the basis of nanoparticles. Parameters can affect the penetration of the drug into the skin. The penetration of lipid nanoparticles into the skin is based on the occlusive effect of lipid membrane formation through permeation. Smaller particles lead to stronger adhesion and clogging compared to larger particles, increasing the skin permeability of drugs. In one study, increasing size from 123 nm to 173 nm. Led to a decrease in permeate flux from 3.1 µg/cm3/h to 1.9 µg/cm3/h. The surface charge of lipid nanoparticles also affects the penetration of drugs into the skin system. The price of stratum corneum is low; Therefore, the use of good lipid nanoparticles ensures that they interact with the skin layer and prevent it from penetrating into deeper layers. Additionally,

the negative value of the stratum corneum prevents the diffusion of negative lipid nanoparticles into the skin. For these reasons, it is recommended to use intermediate nanoparticles in order to work well compared to its positive or negative results. The type and concentration of surfactants in lipid nanoparticle formulations play an important role in skin penetration. In one study, different concentrations of Tween 80 and soy lecithin were used as surfactant and co-surfactant. The results showed that skin absorption of lipid nanoparticles increased with increasing Tween 80 concentration, while skin permeability decreased with increasing lecithin concentration. It is also suggested to improve the integration of drugs into lipid nanoparticles to improve skin permeability and reduce skin irritation. Nanostructured lipid carrier (NLC) containing a solid lipid core (SLN) or a core consisting of a binary mixture of solid and liquid lipids also affects the skin permeability of lipid nanoparticles. Gels packed with NLCS and NNLC Have been reported to accumulate more cyclosporine and calcipotriol in pig ears compared to SLN gels. Additionally, drug-loaded NLC reduced the severity of inflammation in serum cytokine levels and skin morphology compared with SLN in a mouse model of psoriasis.

## NANOMATERIALS IN COSMETICS.

Nanoparticles used in drug delivery systems have attracted the attention of the cosmetic industry. For example, nanoencapsulated vesicle delivery systems, nanoemulsions and nnanocrystals. Lipids Plastids and Niosomes, Nicells, polymer nanocapsules, products. Lipid nanoparticles etc. With the widespread use of nanotechnology in cosmetics, the risks of nanotechnology to health and the environment become more important.

### Products on the market

The first nanocosmetic formula contains lipid spheres with a size of 10 to 100 nanometers. The first product was created by Shiseido in Japan in 1991, before Lancôme made it a must-have product in 1999. Since then, many brands have also developed nano formulas: Then nanocarriers appear in cream jars. Sponge- or small-shell-shaped reservoirs contain compounds such as beta-carotene and vitamin E.

### Liposomes.

Liposomes have a lipid bilayer, so products made with it are cream. ; It was created by the house of Dior in 1986. Although liposomes are unstable and contain additional antioxidants, they are used in cosmetics. 15 Liposomes were first-in-class nanocarriers developed for use in drug delivery in the early 1970s. Liposomes are biocompatible, biodegradable, harmless, flexible vesicles that easily encapsulate active ingredients and are suitable for the delivery of hydrophobic and hydrophilic 43 compounds. Liposomes can improve the absorption of active ingredients through the skin, thus increase concentration.

### Vesicles

Vesicles are defined as vesicles that are biodegradable. Non-ionic surfactants and help deliver drugs by focusing them on the area that needs to be treated. “It is similar to liposomes, but has hydrophilic and hydrophobic ends and is stable. So in 1987 the first product was L’Oréal’s Lancôme. Niosomes are used as amphiphile Carriers in lipophilic and lipophilic medicine.

### Nanocapsules

Nanocapsules are made from a liquid/solid core in which the active ingredient is placed in a cavity surrounded by a polymer membrane made of natural or synthetic polymers. Nanocapsules are used to make hydrogels and emulsion gels. Hydrogels are also used in the production of many personal care products. “Nano capsules have sensory properties. With the development of the cosmetics industry, it has become clear that some companies are turning to increasing efficiency and effectiveness by changing the properties of their products. For this purpose, psychological analysis is carried out. This is nothing; determining the effect of the use of these products is only a human reaction. Psychological analysis, cosmetics industry has proven to be a powerful analytical tool in skin aging prevention research. Nanocapsule encapsulation can improve the physical and chemical stability of lipoic acid and prevent product degradation. Cosmetics containing lipoic acid are better than other drugs in many respects.

**Dendrimers**

Dendrimers are symmetrical entities with a tree-like .Configuration, with clear structures and regular branches, and the ends of the branches are equipped with a ddense Action work It is used in many cosmetics due to its size and molecular weight. Like mascara, nail polish. Due to their innovative properties, they are used in artificial products, hair, skin care and nails. They can be used as an anti-acne treatment.

**Fullerene**

Fullerene is a new material that uses nanotechnology like carbon. Fullerenes are also called “buckyballs”. Fullerene has super antioxidant activity that is at least twice as high as vitamins. Fullerene also has a shiny appearance. It shows its brightening effect by eliminating free radicals from UV rays and preventing excess melanin production. Fullerenes are used in many cosmetics due to their antioxidant properties. Therefore, their use in skin rejuvenation cosmeceutical product formulations is accepted. They were used to create healthy creams and were later used to lighten dark spots.

## CONCLUSION.

Nanotechnology as drug delivery aims to improve the pharmacological and therapeutic properties of traditional drugs. Nanoparticles are used to non-invasively deliver potent, low-toxicity chemicals to the target. Nanotechnology increases the bioavailability, efficiency and selectivity of the drug and reduces side effects and toxicity. Reducing changes in plasma and increasing solubility also play an important role in drug delivery. A variety of nanoparticles are used to deliver drugs, such as polymer complexes, polymer nanoparticles, polymer drug conjugates, dendrimers, nanocrystals, and lipid-based nanoparticles such as body lipids. Inorganic nanoparticles such as metal nanoparticles (gold, silver, metal, platinum, quantum dots) and silica nanoparticles (mesoporous, xerogel). The drug is incorporated into nanoparticles through various binding methods, such as encapsulation and non-covalent binding, and is complexed and conjugated with the polymer carried by reliable linkers. When the polymer surface is coated with a copolymer such as PEG, protection against the body’s immune system is provided. Ligands antibodies, proteins, Bind proteins, carbohydrates and aptamers to achieve high specificity for the target side. Drug conjugate NPs enter cells through a non-functional or targeted mechanism. Finally, nanoparticles can release drugs in a controlled manner in response to changes in enzymes or pH. NP-based drug delivery is also being developed to treat diseases such as cancer, diabetes, heart disease, and central nervous system disease. Nanoparticle-based drug delivery can be further developed in the future

for the treatment of many difficult diseases such as AIDS. In the future, nanotechnology will treat all kinds of human diseases simultaneously by creating multifunctional nanoparticles.

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