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NANO-SOLUTIONS: REVOLUTIONISING DERMATOLOGY THROUGH INNOVATIVE SKIN TREATMENTS

Sushma Mahendrakar*[1], Rutuja Pawar[2], Haripriya Nair[2], Raj Patil[2], Sham Pawar[2], Sneha Patil[2]

[1]Department of Pharmaceutical Assistant Professor, SVB's College of Pharmacy and Research, Dombivli-421204 Maharashtra, India.

[2]Students of SVB's College of Pharmacy and Research, Dombivli- Maharashtra, India.

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***Corresponding Author**
Sushma Mahendrakar
Department of Pharmaceutical Assistant Professor, SVB's College of Pharmacy and Research, Dombivli-421204 Maharashtra, India.

ABSTRACT

Nanoparticle technology is transforming the fields of dermatology and cosmetics by improving the efficacy and safety of topical treatments. This review explores how nanoparticles are used in managing various skin conditions, including acne, psoriasis, eczema, fungal infections, wound healing, and skin cancer, as well as cosmeceutical issues, emphasizing their ability to enable controlled release and targeted delivery of therapeutic agents. While these advancements offer significant benefits, concerns regarding safety and toxicity highlight the need for thorough regulatory measures. Looking ahead, emerging innovations like advanced delivery systems and biocompatible scaffolds show promise for further enhancing skin health. Overall, nanoparticles are poised to revolutionize skincare, offering new possibilities for safer and more effective treatments.

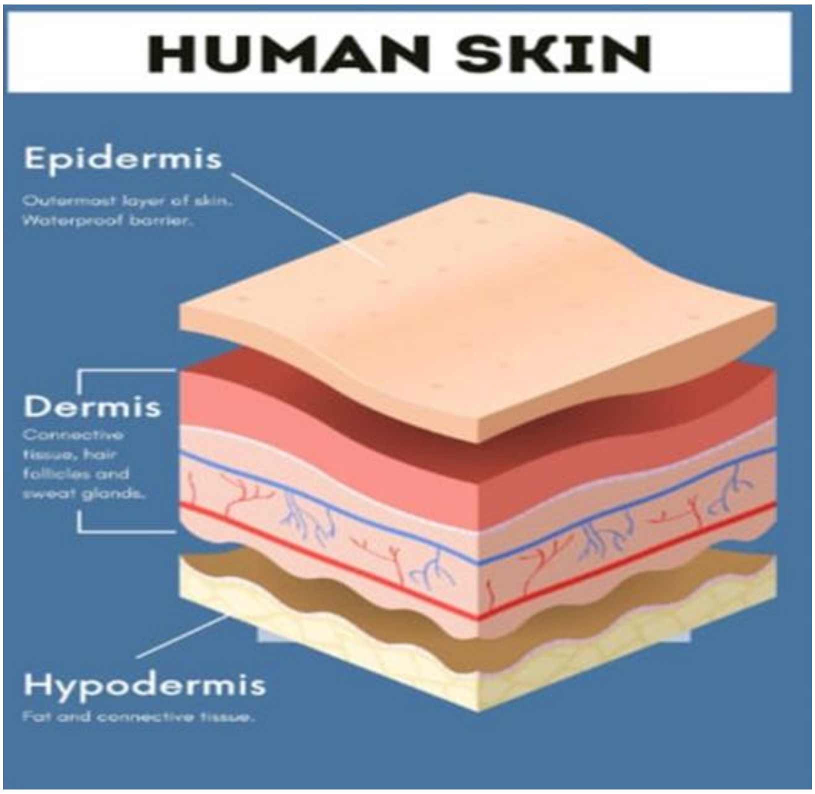
KEYWORDS: Nanoparticles, Topical skin treatments, Dermatological applications of nanoparticles, Skin penetration enhancement, Drug delivery.

INTRODUCTION

The field of dermatology has witnessed significant advancements in recent years, particularly with the integration of nanotechnology in topical skin treatments and cosmetics. Nanoparticles, with their unique size-dependent properties, offer enhanced penetration, improved stability, and targeted delivery of therapeutic agents. This innovation holds promise for addressing various skin conditions, from acne to aging, while also optimizing cosmetic formulations. As the demand for effective and safe skin care solutions continues to grow, the exploration of nanoparticles presents a compelling avenue for research and application. This comprehensive review aims to elucidate the current state of nanoparticle technology in dermatology, examining its mechanisms of action, benefits, and potential challenges, ultimately highlighting its transformative impact on skin health and aesthetics.

OVERVIEW OF THE SKIN

1. **Anatomy and Physiology of the Skin-** The largest organ of the human body is skin, performing essential functions such as acting as a protective barrier against external elements, including chemicals and microorganisms. It also prevents fluid and salt loss and helps regulate body temperature. Human skin varies in structure and thickness, typically measuring about 1.5 mm thick and consisting of three primary layers: the epidermis, dermis, and hypodermis.[1]



- ***Epidermis-*** The outer layer, the epidermis, is composed of two key components: the stratum corneum (SC) and the viable epidermis. The stratum corneum, approximately 10–20 µm thick, plays a critical role in the skin's barrier function by limiting drug absorption. It consists of dehydrated, dead corneocytes (mature keratinocytes) embedded in structured lipid layers. Beneath the SC lies the viable epidermis, which measures around 0.06–0.8 mm thick and contains 4–5 layers of living dermal fibroblasts and keratinocytes.[1] Each keratinocyte in the epidermis measures about 40 μm in diameter and 0.5 μm in thickness, with intercellular spaces not exceeding 0.1 μm. For effective dermal drug delivery, medications must penetrate this intact SC layer. Once a drug crosses the SC, it can accumulate in the adjacent fatty tissues, resulting in higher concentrations over time.[2]

- ***Dermis*****-** Situated beneath the epidermis, the dermis ranges from 0.3 to 5 mm in thickness and contains connective tissue, sweat glands, hair follicles, and a network of capillaries, lymphatic vessels, and nerve endings.[1]
- ***Hypodermis*****-** The hypodermis, the deepest layer of the skin, consists of loose, white, fibrous connective tissue and adipose tissue, providing insulation and cushioning for the body.[1]

2. **Drug Delivery through Skin**- With an extensive surface area of nearly 20 square feet, the skin offers a unique route for drug delivery. Common topical products include antifungal treatments, sunscreens, Olagents, local anaesthetics, antiseptics, and anti-inflammatory medications for conditions like psoriasis.[1] In contrast, transdermal drug delivery targets systemic effects by utilizing the skin as an entry point into the body. Transdermal patches are frequently used to deliver medications such as nicotine for smoking cessation, buprenorphine and fentanyl for chronic pain, and hyoscine (scopolamine) for motion sickness. Both topical and transdermal delivery rely on drug permeation through the stratum corneum, a process governed by Fick's second law.[2] After penetrating the SC, drugs must navigate through various skin layers, encountering both lipophilic and hydrophilic environments before reaching the dermis. Human skin equivalents have been developed to simulate human skin in vitro for studying drug permeation. Generally, small molecules, whether lipophilic or hydrophilic, can penetrate the SC independently or through pathways created by sweat glands and hair follicles. However, delivering larger molecules—such as peptides, proteins, siRNA, or DNA—remains a significant challenge in research.[1] To enhance drug penetration through the SC for topical applications and facilitate the movement of drug molecules into the dermis for transdermal delivery, scientists are exploring various methods. Several strategies involve the use of chemical enhancers such as fatty acids, surfactants, esters, alcohols, polyalcohol's, and phospholipids. These enhancers disrupt the ordered structure of the

SC, solubilize and extract keratin or lipid components from the SC, and fluidize the SC matrix to improve drug penetration.[2]

EMERGENCE OF NANOTECHNOLOGY

1. **Definition and Basic Principles-** Nanotechnology refers to the manipulation and engineering of materials at the nanoscale, typically ranging from 1 to 100 nanometres. This field leverages the unique physicochemical properties of nanosized particles, which differ significantly from their bulk counterparts. The principles of nanotechnology involve controlling materials at the molecular level to enhance their functionality, leading to innovative applications across various domains, including medicine, electronics, and materials science.[3]
2. **Significance of Nanoparticles in Enhancing Treatment Efficacy-** Nanoparticles have emerged as critical tools in enhancing the efficacy of treatments across various medical fields. Their high surface-to-volume ratio allows for increased interaction with biological systems, which can lead to improved drug delivery and therapeutic outcomes. For example, nanoscale drug delivery systems can reduce side effects and enhance the effectiveness of chemotherapy by enabling targeted delivery of drugs to tumour sites.[3] Moreover, innovative methods like hyperthermia and vasculature blocking utilize magnetic nanoparticles to improve therapeutic precision, particularly in cancer treatment.[4] Recent advancements also showcase the potential of nanoparticles in topical administration. Studies have demonstrated that encapsulated formulations significantly enhance cutaneous drug delivery, as seen with Pheroid™ technology, which improves the skin permeability and efficacy of drugs like 5-fluorouracil for melanoma treatment.[2] This approach not only facilitates localized treatment but also opens avenues for delivering larger molecules, such as therapeutic peptides and nucleic acids, which traditionally faced barriers in absorption through the skin.
3. **Rationale for Focusing on Topical Administration:** Topical administration presents several advantages for drug delivery, particularly in treating localized conditions. The skin, with its substantial surface area and accessibility, serves as an ideal route for delivering therapeutic agents directly to affected areas, minimizing systemic exposure and associated side effects. The development of nanocarriers—such as liposomes, nano capsules, and nanostructured lipid carriers—enables controlled release and targeted action, enhancing treatment outcomes for conditions like skin cancer.[21]

Furthermore, the use of nanoparticles in topical formulations can improve the stability and bioavailability of drugs, addressing challenges related to solubility and permeation. Recent innovations in this field, including spherical nucleic acids and cell-penetrating peptides, emphasize the growing potential of nanotechnology to revolutionize drug delivery systems. These advancements highlight a future where customized therapeutic approaches can lead to more effective and safer treatment options for patients.[21,27]

4. **Nanoparticles and their general characteristics-** Nanoparticles are ultrafine particles that typically range in size from 1 to 100 nanometres. They exhibit unique physical and chemical properties due to their small size and high surface area-to-volume ratio. Research over the last two decades has demonstrated the ability of nanoparticles to facilitate drug delivery across the skin barrier. Various types of nanoparticles, including solid lipid nanoparticles, liposomes, polymeric nanoparticles, and metal-based nanoparticles, have shown promise as effective topical drug delivery systems. Moreover, electrospun nanofibers have emerged as a valuable tool in wound healing and antimicrobial applications. Despite these advancements, the clinical impact of these technologies remains limited, as evidenced by the relatively few advanced clinical studies available. The transition from extensive research to clinically utilized products has been slow, highlighting a critical need for quantitative studies that elucidate the relationships between nanoparticle dosage, exposure, penetration, and therapeutic efficacy. Further research is also necessary to address the toxicity of nanoparticles and to compare their penetration efficiency in healthy versus diseased skin. Understanding the mechanisms governing nanoparticle transport through the three main layers of the skin remains an area requiring more exploration. Additionally, many studies fail to utilize commercially relevant controls, often comparing nanoparticle formulations solely with untreated or drug-free samples, rather than established clinical "gold standards".[5]
5. **Types of Nanoparticles Used in dermatology-** Nowadays, several types of nanoparticles and nanomaterials are investigated and approved for clinical use.[6] Nanoparticles are classified into different categories based on their size, shape, and chemical characteristics[7], as follows:

- *Metal-Based Nanoparticles*- Metal nanoparticles are composed entirely of metals and exhibit unique electrical properties due to localized surface plasmon resonance (LSPR). Common examples include:

a) *Gold Nanoparticles*- Gold Nanoparticles (AuNPs) are Nanoparticles made of gold. They have different and unique physical and chemical properties. Gold nanoparticles (AuNPs) have found a prominent place in high-end cosmetic products, including skin creams, lotions, hair treatments, facial masks, lipsticks, and deodorants, over the past several years, offering advantages such as anti-aging effects, hydration, and skin restoration.[8]

b) *Silver Nanoparticles*- Silver nanoparticles (AgNP's) are made of Silver, with a particle size range of 1-100 nm. They have unique physical and chemical properties. Because of their relatively small size and high surface-to-volume ratio, which cause chemical and physical differences in their properties compared to their bulk counterpart, silver nanoparticles may exhibit additional antimicrobial capabilities not exerted by ionic silver.[7]

c) *Zinc Oxide Nanoparticles*- Zinc oxide nanoparticles (ZnONPs) are made of zinc with a particle size range of 1 nm to 100 nm. ZnO NP is synthesized by either the solution method or the hydrothermal method. The applications of ZnO Nanoparticles are gas sensors, chemical and biosensors, light-emitting diodes, photodetectors, and photocatalytic applications. Research is currently examining ZnO nanoparticles (ZnO-NPs) as antibacterial agents in both nanoscale and microscale formulations.[7]

- *Lipid-Based Nanoparticles*- Lipid-based nanoparticles typically range from 10 to 1,000 nm and are often spherical in shape. They usually consist of a solid lipid core surrounded by a matrix of soluble lipophilic molecules, making them suitable for biological applications.

a) *Liposomes*- Liposomes are spherical or multilayered vesicles formed through the self-assembly of diacyl-chain phospholipids in aqueous solutions. The bilayer membrane consists of hydrophobic tails and hydrophilic heads, resulting in an amphiphilic structure. These vesicles can be created from both natural and synthetic phospholipids. The characteristics of liposomes, such as particle size, rigidity, fluidity, stability, and electrical charge, are significantly influenced by their lipid composition.[9]

b) *Niosomes*- The term “niosomes” comes from the fact that the medication is enclosed in a vesicle made of non-ionic surfactants, which are amphiphilic. Similar to liposomes, niosomes possess a bilayer structure, but instead of phospholipids, they utilize non-ionic surfactants. Niosomes are not only biodegradable and non-toxic, but they also have the advantage of delivering both hydrophobic and hydrophilic therapeutic components through their hydrophobic bilayer and aqueous core, respectively.[10]

- *Polymer Based Nanoparticles*- Polymeric nanoparticles (NPs) have attracted considerable interest over recent years due to their properties resulting from their small size. Size range of polymeric nanoparticles is less than 500 nm. Advantages of polymeric NPs as drug carriers include their potential use for controlled release, the ability to protect drug and other molecules with biological activity against the environment, improve their bioavailability and therapeutic index. The term "nanoparticle" comprises both nanocapsules and nanospheres, which differ with respect to their morphology.[11]

a) *Nanocapsule*- Nanocapsules, as characteristic class of nanoparticles, are made up of one or more active materials (core) and a protective matrix (shell) in which the therapeutic substance may be confined. Nanocapsules comprise of an oily or an aqueous core, which is surrounded by a thin polymer membrane. Two technologies have been utilized for obtaining such nanocapsules: the interfacial polymerization for monomer and the interfacial Nano-deposition method for preformed polymer.[12]

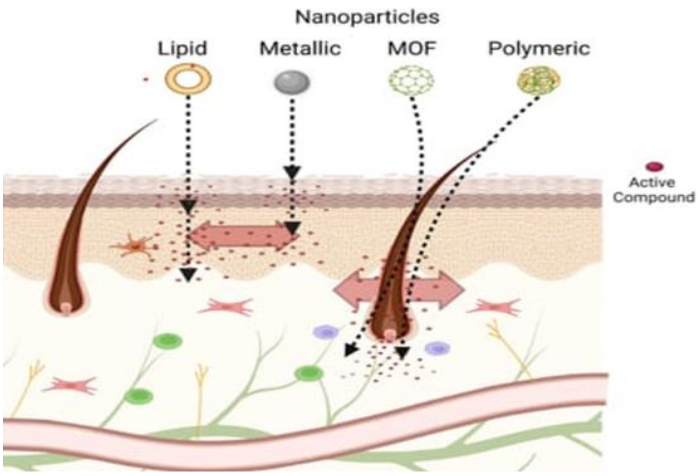
b) *Nanosphere*- These are the division of polymeric nanoparticles. Nanospheres are matrix type structure, which the spherical particulate systems are characterized by a size range between 10-200 nm are widely used as carriers in drug delivery systems in clinical application. They can be amorphous or crystalline in nature, and also, they have protected the drug from enzymatic and chemical degradation. Nanospheres are biodegradable or non- degradable. Nanospheres can be used for the organ targeted release of drug.[13]

6. Mechanisms of Action

- *Nanoparticles interaction with the skin*- Nanoparticles, typically ranging from one to one hundred nanometres, exhibit distinct physicochemical properties that enhance their interaction with the skin. These interactions are vital for effective drug delivery and cosmetic applications, as they allow for improved penetration and targeted delivery of active ingredients. The skin, as the largest organ, acts as a protective barrier against external agents. However, traditional topical formulations often struggle to penetrate this barrier effectively. Nanoparticles, due to their small size, can interact with the skin in several ways, enhancing the delivery of therapeutic and cosmetic agents.
- *Mechanisms such as penetration through the stratum corneum, cellular uptake, and targeted delivery*-a) *Penetration through the Stratum Corneum*- In the skin stratum corneum (SC) is the topmost layer of the skin and act as the primary barrier to absorption. Nanoparticles can penetrate the SC via two main pathways:

- Transcellular Pathway: This involves the diffusion of nanoparticles through the corneocytes. However, this pathway can be limited due to the rigid structure of these cells.

- Intercellular Pathway: More favourable for nanoparticles, this route allows substances to move along the lipid matrix that fills the spaces between corneocytes. This pathway offers higher diffusivity and is crucial for enhancing penetration efficacy.[14]



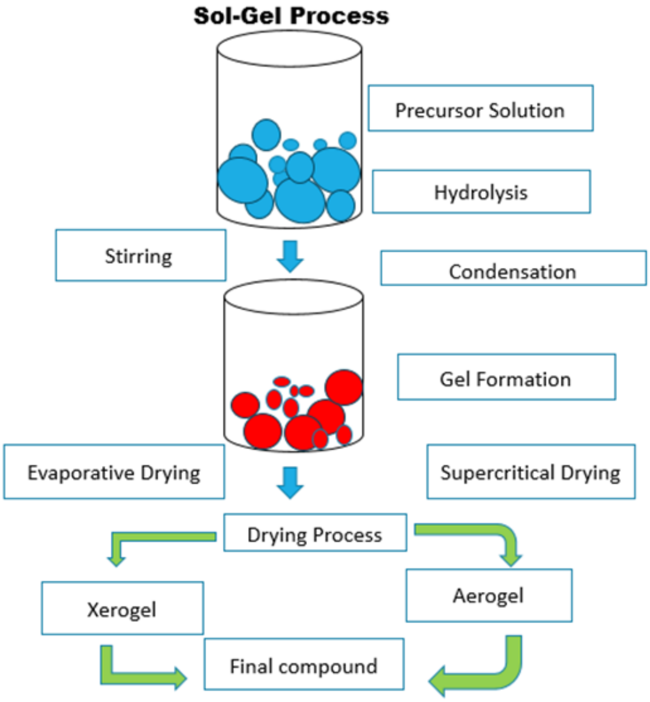
a) Role of Skin Appendages: Skin appendages, such as hair follicles and sweat glands, also provide routes for nanoparticle absorption. Although they constitute a small portion of the skin's surface, they can facilitate targeted delivery by allowing nanoparticles to access deeper layers of the skin.[14] Accumulation within these appendages may enhance the uptake of therapeutic agents, particularly when the barrier morphology is altered.
b) *Cellular Uptake*- Once nanoparticles penetrate the skin, they can be taken up by skin cells through mechanisms such as endocytosis. This cellular uptake enhances the delivery of active compounds directly into the cells, increasing the efficacy of treatments and improving overall skin health.
c) *Targeted Delivery*- The ability of nanoparticles to encapsulate active ingredients ensures precise delivery to specific skin layers or cells. This targeted approach minimizes side effects and enhances the effectiveness of the treatment.[15] For example, nanoparticles can deliver anti-aging agents directly to the dermis, where they can exert their beneficial effects.

7. Methods of preparation of nanoparticles

a) *Physical Methods/ Top-Down Approaches*- Nano-structured materials formed by the breaking down of bulk substances using top-down techniques. Physical approaches combine a number of methods that can be utilized in different phases to obtain nanoscale architectures. There are numerous different methods in the top-down paradigm available, each bringing its specific advantages to this process of transforming bigger materials into those with nanoscale dimensions.[7]

- *Milling and Grinding*- Mechanical milling is a technique that typically utilizes high-energy impact processes to generate strong localized heating forces within planetary or shaker mills. These mills contain balls that work to convert bulk materials into nanoscale structures. Atomization is another versatile method that produces various nanostructured materials, such as aluminium alloys for strengthening, wear-resistant coatings, and nanocomposites. This process is particularly relevant for ball-milled chemical vapor deposition (CVD) graphene, which stands out as a promising class of nanoparticles with potential applications in energy and environmental fields.[7]
- *Sputtering*- Sputtering is a process in which microparticles are ejected from a solid surface due to bombardment by energetic ions from a plasma or gas. The energy of these ions causes tiny clusters of atoms to be sputtered from the target material. This method is advantageous because it is more cost-effective than electron beam lithography, and the resulting nanomaterials closely match the composition of the target material, with minimal contamination.[7]
- *Lithography*- Lithography involves using a high-energy beam of light or electrons to create nanoparticles. There are two primary types of lithography: masked and maskless. Maskless lithography offers the significant advantage of enabling arbitrary nanopattern printing without the need for masks or plates, making it a cost-effective and adaptable technology.[7]
- *Laser Ablation*- Laser ablation is a technique that employs a focused laser beam to vaporize material, producing micro features. In laser-induced synthesis, nanoparticles are generated by applying an intense laser beam to a target material. The generation of nanoparticles is primarily related to the intensity of the laser, which vaporizes the precursor material during the ablation process. This method is environmentally friendly, as it produces noble metal nanoparticles that can serve as catalysts in the production of various nanomaterials, including metal nanoparticles, carbon nanostructures, oxide composites, and ceramics.[7]

b) *Bottom-up approach /Chemical methods*- Bottom-up methods involve assembling tiny atoms and molecules to form nano-structured particles. These approaches encompass both chemical and biological techniques.[7]



Sol gel process- The sol-gel method is a widely recognized and frequently used technique for synthesizing nanomaterials. This process begins with metal alkoxides or metal precursors in solution, which undergo hydrolysis and thermal treatments to concentrate. The result is a stable sol, often referred to as a sol-gel. Through hydrolysis and condensation, the viscosity of the sol increases, leading to its transformation into a gel. The particle size can be controlled by adjusting parameters such as the concentration, temperature, and pH of the precursor solution. Additionally, there is a crucial period for the evaporation of the solvent, as well as for processes such as dissolution or agglomeration, which facilitate the transition from liquid to solid and enable the formation of a solid mass. To create unstable nanoparticles, any chemical precursors or templates must be removed. Compared to other synthesis techniques, the sol-gel method is environmentally friendly and offers numerous advantages. Notably, it allows for the production of materials at low working temperatures, simplifies the creation of composites, and enables the formation of complex nanostructures. Overall, the sol-gel technique presents a sophisticated approach to nanomaterial fabrication.[7]

- *Chemical Vapor Deposition (CVD)*- Chemical Vapor Deposition (CVD) is a technique make use for the deposition of thin films through chemical reactions involving vapor-phase precursors. For effective CVD processes, the selected precursors must exhibit adequate volatility, high chemical purity, strong evaporation stability, low toxicity, and a long shelf life. It is also crucial that any residual precursors are completely removed due to their potential toxicity. CVD encompasses various techniques, including vapor phase epitaxy, metal-organic CVD, and atomic layer deposition. Additionally, modifications such as oxygen plasma-enhanced CVD can further refine the process. These methods help address concerns regarding the production of colloids that are uniformly sized and delicately dispersed. CVD is an excellent approach for ensuring the high quality of nanomaterials and is particularly well-known for synthesizing various two-dimensional nanoparticles.[7]

- *Co-Precipitation Methods*- Co-precipitation is a wet chemical technique, also known as consolidation. This method utilizes solvents such as non-solvent polymers, ethanol, acetone, and hexane. It can incorporate either synthetic or natural polymeric phases. During this process, the polymer mass traps excess solvent, leading to the diffusion of the polymer-solvent into the non-solvent phase. The interphase stress created between these two phases results in the generation of nanoparticles. One of the primary advantages of co-precipitation is its ability to produce large quantities of water-soluble nanocarriers with minimal use of potentially harmful reagents. Many commercially available iron oxide nanoparticle-based MRI contrast agents, such as Feridex, Resovist, and Combidex, have been developed using this technique.[7]

c) *Biological Methods*- Green or biological nanoparticle synthesis uses bioactive agents like plant materials, microbes, and biowaste. This eco-friendly method is simple, cost-effective, produces stable nanoparticles, and generates non-toxic byproducts. It is also scalable and helps avoid harmful byproducts.[7]

- *Biological Synthesis Using Microorganism*- Microbial-mediated synthesis of nanoparticles has gained recognition as a cost-effective and efficient alternative to traditional physical and chemical methods. This process can occur through two primary pathways: biosynthesis in aqueous solutions, both inside and outside cellular compartments. Certain microbes, such as *Pseudomonas stutzeri* Ag295, found in silver mines, can precipitate metal ions by enveloping silver either within or on the surface of their cell membranes. These cells utilize various reductases to sequester and neutralize toxic metals. For example, *Klebsiella pneumoniae*, a large and small coccus, is capable of synthesizing cadmium sulfide (CdS) nanoparticles.[16]
- *Synthesis Using Plant Extracts*- Plant extracts play a significant role in the biosynthesis of nanoparticles, often referred to as green synthesis. For instance, leaves of the geranium herb (*Pelargonium graveolens*) are employed in the production of gold nanoparticles.

Silver nanoparticles can also be synthesized using plant extracts; this is achieved by mixing 1 ml of a 1 mmol aqueous solution of silver nitrate with 5 ml of the plant extract. This process can also be adapted for alcoholic extracts by combining the plant extract and silver nitrate and then placing the mixture in a shaker at 150 rpm while avoiding light exposure.[16]

8. Applications of nanoparticles

Applications in Topical Skin Treatments- Nanoparticles are becoming a pivotal component in dermatology, significantly improving the effectiveness and safety of topical therapies and cosmetic products. In dermatological uses, nanoparticles can encapsulate active ingredients, which enhances their stability and bioavailability while reducing potential side effects. Additionally, the integration of nanoparticles into skincare formulations not only improves treatment outcomes for various skin disorders but also introduces innovative approaches to anti-aging and sun protection. As research progresses in this area, the potential for nanoparticles to transform dermatological practices becomes increasingly evident, offering new therapeutic strategies and better patient outcomes.

- **Acne Treatment**

a) Acne vulgaris: With an excessive sebum secretion in skin leading to inflammatory lesions on the face, chest, and back. Severity varies from mild to severe, and treatments traditionally include topical antibiotics and retinoids, which can cause side effects like skin irritation, dryness, peeling, increased sensitivity to sunlight, and even hyperpigmentation. Prolonged antibiotic use also risks bacterial resistance.[17]

b) Innovations by nanoparticles: - Nanoparticles offer controlled and sustained drug release, minimising side effects and enhancing treatment effectiveness. They allow for precise delivery of active ingredients such as benzoyl peroxide and salicylic acid directly to affected areas, reducing irritation and improving treatment outcomes.[17] Solid lipid nanoparticles (SLN) have demonstrated improved efficacy in topical delivery of antiandrogens for acne treatment.[18] Commercial acne products now incorporate nanoparticle technology for more targeted and controlled delivery of key ingredients like benzoyl peroxide and retinoids.[17,18]

- **Psoriasis**

a) Psoriasis: Psoriasis is a chronic inflammatory skin condition marked by the accelerated growth of skin cells, resulting in thick, red, and scaly plaques. It affects 2-3% of the global population and is caused by a combination of genetic, immune, and environmental factors. Psoriasis typically appears on areas like the elbows, knees, scalp, and lower back, significantly impacting the quality of life. While there is no cure, treatments such as topical medications, systemic drugs, and biologic therapies aim to manage symptoms and reduce flare-ups.[19]

b) Innovations by nanoparticles- Nanoparticles offer targeted delivery of anti-inflammatory drugs directly to the affected areas, reducing symptoms like redness and scaling more effectively than traditional treatments.[19] Lipid-based nanoparticles, such as solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs), enhance skin permeability and drug retention, improving the efficacy of treatments like acitretin (Vitamin A derivative) and calcipotriol (synthetic Vitamin D3)[20,21] Nanoparticle formulations also improve the delivery of psoralens in Psoralen plus ultraviolet light A (PUVA) therapy, minimizing side effects associated with systemic administration.[20] TyroSpheres have demonstrated the ability to deliver antiproliferative drugs like paclitaxel directly to the epidermis, further reducing systemic exposure and improving treatment outcomes.[17] Nanoparticles in combination with biologics, such as Secukinumab, are being investigated to enhance drug absorption and therapeutic efficacy in moderate to severe psoriasis cases.[19,21]

- **Eczema**

a) Eczema (Atopic Dermatitis): Eczema is a chronic inflammatory skin disorder characterized by dry, itchy, and irritated skin. Though it predominantly affects children, individuals of all ages may experience it, leading to significant discomfort and reduced quality of life. The condition stems from a complex combination of genetic factors, environmental triggers, and immune system irregularities. Flare-ups are often triggered by allergens, irritants, stress, and changes in temperature or humidity. Treatment involves skin care practices, topical therapies, and lifestyle modifications to manage symptoms and inflammation.[18]

b) Innovations by nanoparticles: Nanoparticles enhance the delivery of moisturizers and anti-inflammatory agents, improving symptom relief (itching and redness) and boosting the skin's moisture retention.[20] Liposome formulations of betamethasone dipropionate have shown superior efficacy compared to conventional formulations, even at lower drug concentrations.[18] Solid lipid nanoparticles (SLNs) with clobetasol propionate have been more effective than standard creams for treating eczema, providing better drug delivery to the skin while reducing the risk of side effects like skin atrophy.[18,20] Nanostructured lipid carriers (NLCs) loaded with betamethasone dipropionate and clobetasol propionate are promising new formulations for topical eczema treatments, improving drug delivery and skin sensitivity management.[20]

- **Fungal Infections**

a) Fungal infections: These are common skin conditions caused by fungi such as dermatophytes, yeasts, and molds, affecting the skin, nails, and mucous membranes. Examples include athlete's foot, ringworm, and candidiasis. Though often not severe, fungal infections can lead to discomfort, irritation, and inflammation, especially in individuals with weakened immune systems. Fungal infections impact 20-25% of the global population, with conditions like onychomycosis and tinea being particularly prevalent. Conventional oral antifungals may cause side effects like liver toxicity and gastrointestinal issues.[22,23]

b) Innovations by nanoparticles- Nanoparticles improve antifungal treatment by delivering drugs more efficiently to infected areas, enhancing treatment efficacy and reducing drug resistance.[24] Solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs) have been effective in encapsulating antifungal agents such as clotrimazole and ketoconazole, improving skin penetration and controlled drug release.[24] Silver nanoparticles (AgNPs) and gold nanoparticles (AuNPs) show significant antifungal activity, with AgNPs disrupting fungal cell membranes, proving effective against fungi like Candida albicans and Trichophyton mentagrophytes.[25,26] Liposomal formulations, such as those for econazole, can increase drug concentration in the epidermis, reduce skin irritation, and improve patient adherence to treatment.[18] Biodegradable polymeric nanoparticles, particularly chitosan-based, enhance the efficacy of existing antifungal treatments and offer targeted therapy.[23] Nanoparticle-based antifungal treatments have shown superior effectiveness compared to traditional creams and ointments, especially for conditions like athlete's foot and yeast infections, while offering safer alternatives for immunocompromised patients.[22,25]

- **Wound healing and scar treatment**

a) Wounds: A wound refers to any break in the skin’s surface, caused by injury, surgery, or disease, disrupting the skin’s protective barrier. Wounds can range from minor abrasions to severe deep tissue injuries. The healing process involves tissue repair and regeneration, resulting in scar formation. While scars restore the skin's structure, they often differ in appearance and texture from the surrounding skin, potentially causing aesthetic or functional concerns.[7]

b) Innovations by nanoparticles: Silver nanoparticles (AgNPs): AgNPs have strong antimicrobial activity and are used in wound dressings, burn treatments, and diabetic ulcers. They prevent infections, reduce inflammation, stimulate collagen production, and promote faster healing[7,27,28] Copper nanoparticles (CuNPs): CuNPs show antioxidant, antifungal, and antibacterial properties, enhancing wound healing by promoting fibrocyte production and collagen formation, aiding in tissue repair and wound closure.[29] Gold nanoparticles (AuNPs): AuNPs are used in chronic wound treatment, especially diabetic ulcers. When combined with photothermal therapy, they kill bacteria and promote healing by preventing bacterial colonization. Curcumin-loaded AuNPs show enhanced wound healing and antimicrobial effects[17,28] Solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs): SLNs and NLCs improve the delivery of healing agents, offering controlled release and increased antimicrobial activity. These systems, often combined with essential oils or antibiotics, accelerate wound healing.[20] Zinc oxide nanoparticles (ZnONPs): ZnONPs exhibit antioxidant and anti-inflammatory properties, making them effective in treating chronic wounds, diabetic ulcers, and burns. They reduce oxidative stress, promote collagen production, and protect against bacterial infections.[3,28] Electrospun fibre mats: These mats release growth factors (EGF, VEGF, bFGF) and provide a porous structure for gas and liquid exchange while protecting wounds from bacteria. They also serve as drug delivery systems, accelerating wound closure and tissue regeneration.[17] Custom-designed nanomaterial dressings: These dressings can be tailored with biomolecules, growth factors, and antibiotics to overcome traditional wound care limitations, promoting faster and more efficient healing.[30] Lipid-based nanoparticles: These nanoparticles allow for the sustained release of hydrophilic and hydrophobic drugs, enhancing localization at the wound site. Liposomes and hydrogels are used for prolonged delivery of therapeutic agents, improving wound healing outcomes.[28]

- **Skin cancer**

a) Skin Cancer: It is the n which most occurring cancer, usually occurred by exposure to ultraviolet (UV) radiation from the sun or artificial sources. It commonly occurs on sunexposed areas such as the face, neck, and hands. The three main types are basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and melanoma, with melanoma being the most dangerous. Early detection is critical for successful treatment, and recent advancements in topical therapies are providing new avenues for skin cancer management.[2,17]

b) Innovations by nanoparticles- Zinc oxide nanoparticles (ZnONPs): ZnONPs are being explored for their ability to selectively target cancer cells, minimizing damage to healthy tissues and improving treatment efficacy.[7] Gold nanoparticles (AuNPs): Gold nanoparticles are used in cancer therapy due to their unique properties, such as surface plasmon resonance, which enhances drug delivery by concentrating chemotherapeutic agents at the tumor site, reducing side effects.[31] Nanocomposite hydrogels: These hydrogels, such as the rGO-5FU-CMARX nanocomposite, encapsulate and gradually release chemotherapy drugs specifically at melanoma tumor sites, significantly improving treatment outcomes.[26] Titanium nanoparticle-based preventive gel: A titanium dioxide (TiO2) and quercetin (Qu)-based nanogel has been developed as a chemopreventive strategy against UVB-induced skin cancer, enhancing skin deposition and drug release in experimental models.[26] Hybrid nanoparticles: Nanoparticles combining ceramide and hyaluronic acid have been designed for intravenous delivery of docetaxel, improving circulation time and drug targeting in tumors.[26] Pheroid™ technology: This colloidal drug delivery system enhances skin permeability and the anti-melanoma activity of 5-fluorouracil, representing a significant advancement in nanoparticle-based treatments for skin cancer.[2]

Applications in Cosmetics- Cosmeceuticals are products that blend cosmetic and pharmaceutical properties. These items offer cosmetic benefits while also providing therapeutic effects due to their active ingredients, which can improve skin health. Common components include antioxidants, peptides, and vitamins. Cosmeceuticals are designed to tackle specific skin concerns such as aging, pigmentation, and acne, making them more effective than standard cosmetic products. The use of nanoparticles in cosmetics and cosmeceuticals is becoming increasingly prevalent, thanks to several key advantages such as Improved Ingredient Delivery, Enhanced Stability, Targeted Effects, Better Product Texture, Effective UV Protection, etc.

- **Anti-Aging and Wrinkle Reduction**

a) Anti-Aging and Wrinkle Reduction: Aging skin is characterized by a loss of elasticity, reduced collagen production, and the appearance of wrinkles. Environmental factors, such as UV radiation and oxidative stress, exacerbate these changes. The anti-aging skincare industry has increasingly turned to nanoparticle-based treatments to address these concerns.[20,26]

b) Innovations by nanoparticles- Gold nanoparticles (AuNPs): AuNPs are prized for their antioxidant and moisturizing effects, helping to protect the skin from UVA-induced oxidative stress, supporting elasticity, and minimizing wrinkle formation.[26] Polymersomes: These nanoparticles allow for the controlled release of active ingredients, improving skin elasticity and cell function, which reduces visible aging signs.[26] Lipid-based nanocarriers: Nanoemulsions (NEs) and nanostructured lipid carriers (NLCs) are effective in delivering anti-aging ingredients like Coenzyme Q10 (CoQ10), increasing their stability and skin absorption. Products formulated with NLCs, such as Cutan Voa Nano Repair Q10 cream, have demonstrated superior hydration and wrinkle reduction compared to traditional creams.[20] Solid lipid nanoparticles (SLNs): SLNs are used to encapsulate antioxidants like resveratrol and ellagic acid, enhancing their penetration into the skin and allowing for more effective reduction of oxidative stress.[20] Nanopeptides: Nanopeptides help to reduce oxidative stress and prevent collagen breakdown, which are key factors in skin aging. Their small size allows them to target specific skin concerns effectively, and they improve moisture retention, resulting in a more hydrated and youthful appearance.[32] Nanocapsules: One of the earliest uses of nanoparticles in anti-aging was the encapsulation of vitamin A in nanocapsules, which allowed for gradual release and prolonged skin benefits, improving hydration and reducing wrinkles.[18]

- **Sun Protection**

a) Sun Damage (Photodamage): Sun damage occurs due to prolonged exposure to ultraviolet (UV) radiation from the sun, leading to premature aging (wrinkles, fine lines), reduced skin elasticity, uneven skin tone, dark spots, and an increased risk of skin cancers like melanoma. Preventive measures include sunscreen, protective clothing, and minimizing sun exposure.[20,33]

b) Innovations by nanoparticles: Titanium Dioxide (TiO_2) and Zinc Oxide (ZnO) nanoparticles: These nanoparticles are key ingredients in sunscreens, improving UV light scattering and providing robust protection against both UVA and UVB radiation. They are nearly invisible on the skin, addressing cosmetic concerns and enhancing consumer acceptance.[33] Amorphous Silica: Used in sunscreens to enhance the dispersion of TiO_2 and ZnO nanoparticles, improving the formulation's effectiveness.[33] Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs): These nanoparticles enhance the sun protection factor (SPF) and allow for the use of lower concentrations of active ingredients, reducing potential side effects while improving sunscreen performance.[26] Lipid-based Nanocarriers: These enhance UV scattering and improve sunscreen stability, providing a smoother application experience and increased SPF.[20] Liposomes and Niosomes: These specialized delivery systems encapsulate both lipid-soluble and water-soluble active ingredients, enhancing the effectiveness and penetration of skincare products, including sunscreens. They protect ingredients from degradation and deliver them efficiently to target areas.[32]

- **Moisturizers and Hydration**

a) Hydration: Hydration refers to the process of adding moisture to the skin to keep it plump and healthy. This is achieved through the use of humectants like hyaluronic acid or glycerin that draw water into the skin and moisturizers that lock in moisture using ingredients like emollients and occlusives.[24]

b) Innovations by nanoparticles- Solid Lipid Nanoparticles (SLNs): Known for their occlusive properties and UV-blocking potential, SLNs help prevent moisture loss, improve hydration, and protect the skin from environmental stressors[24] Liposomes: Composed of phosphatidylcholine, liposomes are widely used in moisturizers and creams to enhance hydration. Their smoothening and conditioning properties improve overall skin texture and moisture retention. They are also effective in hair care products like shampoos and conditioners. Polymeric Nanoparticles: These nanoparticles improve the delivery of hydrating agents by enabling deeper penetration into the skin and providing a prolonged release of moisturising ingredients, resulting in better skin hydration and moisture retention.[26]

9. Safety, toxicology and stability of nanoparticles

a) Toxicity of Nanoparticles- Nanoparticles, due to their small size, facilitate the transport of active chemical agents across biological barriers, such as the skin, lungs, and various tissues and organs. These particles primarily enter the human body through inhalation or skin contact, with additional routes including injection or ingestion via medications or food. Their specific composition can lead to significant health issues, including irreversible oxidative stress, organelle damage, asthma, and even cancer. Acute toxicity from exposure to nanoparticles and nanostructured materials often manifests as the production of reactive oxygen species, protein denaturation, mitochondrial dysfunction, and disruption of phagocytic activity. In the long term, chronic toxicity may involve uptake by the reticuloendothelial system and neuronal tissues, along with the formation of neoantigens, potentially resulting in organ enlargement and dysfunction. Nanotoxicology is a multidisciplinary field focused on assessing the risks that nanomaterials pose to human health and the environment. This area of study considers various factors, including the physicochemical characteristics of nanomaterials, exposure routes, distribution within biological systems, molecular interactions, toxic effects, and relevant regulatory issues. By thoroughly investigating the toxicological properties of these materials, scientists can gather valuable data to inform future safety evaluations and risk assessments for both the nanomaterials themselves and the products that incorporate them. The potential toxicity of various nanoparticles includes:

- Gold: Liver damage, activation of hepatic macrophages.
- Silver: Kidney damage, inflammation, and mineralization.
- Zinc Oxide: Cytotoxicity, cell membrane damage, and increased oxidative stress.
- Iron Oxide: Oxidative stress and DNA damage.
- Liposomes: Inflammation.
- Quantum Dots: Inflammation and liver damage.[34]

Many uncertainties exist regarding whether the unique properties of engineered nanomaterials pose health risks. The potential health risks associated with exposure to such substances are generally linked to several factors:

- The magnitude and duration of exposure.
- The persistence of the material within the body.
- The inherent toxicity of the material.
- The susceptibility or health status of the individual.

As a multidisciplinary field, nanotoxicology focuses on assessing the potential hazards of nanomaterials to human health and the environment. This field examines various aspects, including physicochemical properties, exposure routes, biodistribution, molecular factors, toxicity, and regulatory considerations. By investigating the toxicological potential of nanomaterials, researchers can collect data to support future safety and risk assessments for these innovative substances and their applications. It is crucial to strike a balance between advancing nanomaterials and conducting the necessary research to identify potential health risks, ensuring that critical data is available for future safety evaluations.[34] Despite the potential advantages of nanoparticles in cosmetics, concerns regarding safety and efficacy persist. Consumers are often apprehensive about the long-term health effects of nanoparticles, particularly their potential toxicity and environmental impact. The lack of comprehensive regulatory frameworks in many regions further exacerbates these concerns, leading to calls for clearer guidelines on the safe use of nanomaterials in consumer products.[35]

b) Stability and Shelf Life of Nanoparticle-Based Products- The stability of nanoparticle-based products is critical for maintaining their efficacy and safety. Factors such as temperature, light exposure, and the presence of oxygen can lead to degradation of nanoparticles, which in turn can affect their therapeutic potential. Unstable formulations may lose their intended effects over time and can even pose risks of toxicity. The stability of nanoparticle-based products is a critical factor influencing their efficacy and safety. Nanoparticles are inherently thermodynamically unstable compared to their bulk counterparts, leading to concerns about their aggregation, reactivity, and overall behavior in formulations.[36] Key factors that impact stability include:

Aggregation State: Aggregation affects the effective size and surface area of nanoparticles, directly influencing their reactivity and performance in solutions. The stability of nanoparticles is governed by principles such as the DLVO (Derjaguin-Landau-Verwey-Overbeek) theory, which describes the balance of attractive and repulsive forces acting on them.[35]

Core Composition: The chemical makeup of the nanoparticle core plays a significant role in stability. Different materials, such as metals and metal oxides, exhibit varying stability profiles based on their elemental composition and crystalline structure[35]

Shape and Size: The geometric configuration and size of nanoparticles affect their surface energy, which can influence aggregation and dissolution behavior. Smaller nanoparticles may require different stabilization mechanisms compared to larger ones due to their higher surface area-to-volume ratio.[35]

The lack of stability in nanoparticle formulations can lead to decreased efficacy, increased toxicity, and compromised safety, highlighting the importance of understanding and managing these factors. Several approaches can be employed to improve the stability and shelf life of nanoparticle-based products:

- Controlled Storage Conditions: Storing products in cool, dark environments can help minimize degradation. Using opaque containers can also protect formulations from light exposure.
- Lyophilization: Freeze-drying nanoparticles can significantly enhance their stability. This process removes moisture, thereby reducing the likelihood of agglomeration and degradation during storage.
- Incorporation of Antioxidants: Adding antioxidants to formulations can help mitigate oxidative stress that may lead to nanoparticle degradation, thus extending shelf life.
- Steric Stabilization: The use of polymers or surfactants can create a physical barrier around nanoparticles, preventing them from coming into close contact and aggregating.
- Electrostatic Stabilization: Modifying the surface charge of nanoparticles can create repulsive forces, thereby maintaining separation and stability within the formulation.
- Core Composition Adjustment: Tailoring the core material of nanoparticles can enhance stability under specific environmental conditions, addressing concerns related to composition and crystallinity.
- Incorporation of Stabilizers: Adding stabilizing agents, such as antioxidants, can help mitigate oxidative degradation, thereby extending the shelf life of formulation.[35]

10. Future Directions and Innovations in Nanoparticle Technology

Emerging technologies in nanoparticle science hold significant promise for advancing skin treatments and cosmetic applications. For instance, solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs) are increasingly utilized in sunscreens and as carriers for molecular sunscreens and UV blockers, demonstrating effective controlled release properties for topical applications. Notably, glyceryl behenate SLNs have shown superior localization of vitamin A in the upper skin layers compared to traditional formulations.[37] Advancements in nanotechnology have also introduced innovative therapeutic delivery methods, such as hyperthermia, vasculature blocking, and targeted drug delivery. Magnetic nanoparticles, utilizing superparamagnetic iron oxide, can enhance imaging techniques and facilitate precise drug delivery by targeting specific cells or disease states.[4] Moreover, nanoparticles are being explored for their potential in tissue repair, particularly through the development of biocompatible scaffolds that could significantly enhance therapeutic outcomes.[4] Silver nanoparticles (AgNPs), in particular, have emerged as a promising option for wound care due to their excellent antibacterial activity and anti-inflammatory properties. Their nanometric size allows for enhanced antimicrobial efficacy and targeted delivery, positioning them as ideal candidates for treating chronic diabetic wounds.[38] However, as with all nanoparticle applications, it is essential to address potential health concerns associated with their use, necessitating extensive clinical trials to ensure safety and efficacy.

CONCLUSION

The application of nanoparticles in dermatology and cosmetics marks a significant breakthrough in effective skin treatment and enhancement. Research over the past two decades highlights nanoparticles' ability to navigate the skin barrier, enabling the delivery of therapeutic agents that typically struggle due to size and lipophilicity constraints.[17] By utilizing advanced lipid-based delivery systems such as niosomes, transfersomes, and ethosomes, researchers are achieving improved drug diffusion, targeted effects, and enhanced skin hydration while reducing systemic absorption.[39] Although challenges like high production costs and safety concerns persist, the integration of innovative technologies—such as nanoneedle patches and stimuli-responsive delivery systems—offers exciting potential for overcoming these hurdles.[21] As we refine these methods and focus on creating user-friendly formulations, the prospects for superior skincare products grow ever more promising. Ultimately, the future of nanoparticles in this field is set to transform both therapeutic and cosmetic applications, paving the way for more effective and personalized skincare solutions.

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