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Innovative Strategies in Psoriasis Management: The Promise of Green-Synthesized Nanoparticles and Their Therapeutic Implications

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ABSTRACT

Psoriasis is a chronic autoimmune skin disorder characterised by inflammation, keratinocyte hyperproliferation, and immune imbalance. Conventional treatments often have limitations, including side effects and treatment resistance, necessitating the development of targeted and effective therapeutic strategies for this disease. Nanotechnology offers promising solutions for psoriasis management through targeted drug delivery, improved bioavailability, and reduced systemic side effects. The green synthesis of nanoparticles using eco-friendly and sustainable methods has emerged as a novel approach for producing biocompatible nanoparticles. This review explores the potential of green-synthesised nanoparticles for psoriasis treatment, focusing on their synthesis, characterisation, and therapeutic efficacy. Various types of nanoparticles, including metallic, polymeric, and lipid-based nanocarriers, are discussed, highlighting their unique properties and advantages. The mechanisms of action of these nanoparticles in psoriasis management, such as their anti-inflammatory effects, immunomodulatory properties, and keratinocyte regulation, are elucidated. Experimental methods, including in vitro and in vivo studies, are reviewed, providing insights into the efficacy and safety of green-synthesised nanoparticles. The results demonstrate the potential of these nanoparticles to reduce inflammation, modulate immune responses, and regulate keratinocyte proliferation and differentiation. Furthermore, the safety and biocompatibility of these nanoparticles are discussed, emphasising their potential for long-term application.
Keywords: Psoriasis, Inflammation, Nanoparticles, Green synthesis

I. Introduction

Psoriasis is a chronic autoimmune skin condition characterised by inflammation and excessive keratinocyte proliferation, leading to thick, scaly plaques on the skin. This condition can manifest at any age, but it most commonly peaks in the early 30s and early 60s. Psoriasis affects 1-3% of the global population and is considered a moderately prevalent condition. Clinically, psoriasis is characterised by an immune system imbalance, contributing to its inflammatory nature 1. It often involves complications such as psoriatic arthritis, which further complicates the disease burden by adding joint pain and potential joint damage. This immune system imbalance is central to the pathology of psoriasis, resulting in the overproduction of skin cells and the formation of characteristic plaques 2. The impact of psoriasis is not limited to physical symptoms but extends significantly to quality of life and economic aspects. Patients with psoriasis often report a lower quality of life, similar to that of individuals with conditions such as diabetes or cancer. This impact on quality of life is significant due to factors such as social stigmatization 3, physical limitations, and psychological issues such as depression and anxiety. Economically, psoriasis imposes a significant burden on both patients and healthcare systems. Psoriasis management requires lifelong care, often involving expensive treatments and hospitalisations, contributing to high direct medical costs 4. Additionally, indirect costs related to lost productivity and work absenteeism are substantial, as patients may experience difficulties in maintaining employment due to the physical and psychological burdens of the disease.

Psoriasis treatment is fraught with several challenges, primarily due to the limitations of existing therapies, side effects, and treatment resistance 5, 6. Conventional therapies, including topical treatments, phototherapy, and systemic medications such as methotrexate and cyclosporine, are often used to manage psoriasis. However, these treatments may not adequately control the disease in all patients and can be associated with significant adverse effects 7. The use of these treatments is generally limited by their non-specific action and the risk of systemic toxicity, particularly with long-term use (fig.1) 8. The side effects of conventional psoriasis treatments are a major concern. For instance, topical corticosteroids can cause skin atrophy and telangiectasia, whereas systemic agents can lead to liver toxicity and bone

marrow suppression. Moreover, treatments can become less effective over time, and patients may develop resistance, necessitating a switch in therapy 9.

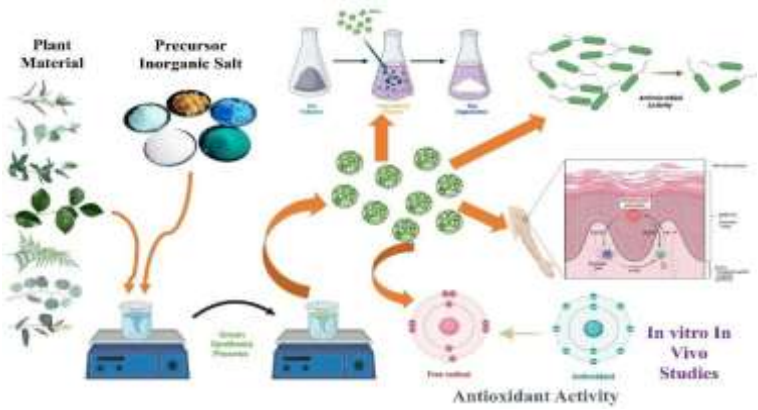

Figure 1 Nano particles Formation

There is a growing need for targeted treatments that offer better efficacy and fewer side effects. Biologics that target specific components of the immune response have transformed the management of moderate-to-severe psoriasis 10. These include therapies targeting TNF-α, IL-17, IL-12/23 and IL-23. Despite their effectiveness, the development of antibodies against biological agents and varying patient responses still pose challenges. Furthermore, biologics are associated with high costs and require ongoing administration 11.

Green synthesis is an eco-friendly approach to producing nanoparticles. Nanotechnology holds significant promise for psoriasis management, particularly for targeted drug delivery 12, 13. Nanotechnology-based drug delivery systems can enhance psoriasis treatment by improving the precision and efficiency of drug delivery to affected sites. This targeted approach allows for increased retention of drugs in the skin, controlled and sustained drug release, and reduced systemic absorption, thereby minimising the side effects 14.

Green synthesis, an eco-friendly technique associated with nanotechnology, integrates the principles of green chemistry and engineering. This approach involves the use of benign and sustainable methods to produce nanoparticles, thereby minimising environmental impact. Green nanotechnology aims to develop drug delivery systems that are effective and environmentally responsible 15.

Key physical methods: ball milling, microwave-assisted heating, hydrothermal processes Green synthesis involves the use of eco-friendly and sustainable methods to produce chemical compounds and nanomaterials 16. This approach aligns with the principles of green chemistry, which focuses on minimising the use and generation of hazardous substances in the design, manufacture, and application of chemical products. The scope of green chemistry extends beyond basic chemical synthesis, emphasising the efficient use of raw materials, energy, and water, and the reduction of waste and emissions throughout the product life cycle 17.

Green synthesis offers several advantages over traditional synthesis methods, particularly in terms of environmental and economic benefits. Traditional methods often involve toxic chemicals and generate significant waste, whereas green synthesis uses renewable resources, such as plant extracts and biocompatible materials, leading to cleaner and safer production processes 18.

The green synthesis of nanoparticles involves the use of biological sources for efficient and eco-friendly production. This method capitalises on natural materials and processes, in contrast to traditional chemical and physical methods, which may be hazardous and costly 19.

- **Plant-Based Materials:** Extracts and Secondary Metabolites **Plant** extracts are popular for the synthesis of nanoparticles because they contain various biomolecules that can act as reducing and stabilising agents. These extracts offer a wide range of biochemical pathways, contributing to the efficient reduction of metal ions to nanoparticles. Plant-based synthesis is advantageous because of its eco-friendliness, availability, and ease of use 20 . Secondary metabolites in plants, such as polyphenols, flavonoids, and alkaloids, play crucial roles in nanoparticle formation, offering antioxidant properties and minimizing toxicity 21 .
- **Microbial Systems:** Bacteria, Fungi, Algae Microorganisms such as bacteria, fungi, and algae are considered excellent biofactories for nanoparticle synthesis. They facilitate the biosynthesis of nanoparticles through their metabolic processes, leading to an environmentally friendly and cost-effective production. Microbial synthesis often involves the use of biomolecules in microbial cells or secretions to reduce metal ions to nanoparticles 22 . Algae, for

instance, provide a renewable and sustainable source, contributing to the synthesis of valuable nanoparticles such as gold, silver, and iron [23].

- **Biomolecules:** Proteins, Enzymes, and Polysaccharides Biomolecules , such as proteins, enzymes, and polysaccharides , from various biological sources can be employed as reducing and capping agents in nanoparticle synthesis. These biomolecules aid in the stabilisation of nanoparticles, preventing agglomeration and enhancing their stability [24]. The use of biosurfactants is one such strategy, employing microbial-origin surfactants composed of sugars and fatty acids to mediate nanoparticle synthesis in a more controlled and environmentally friendly manner.
- The integration of these biological sources into nanoparticle synthesis processes not only reduces their environmental impact but also enhances the overall sustainability of the production methods, aligning with the principles of green chemistry.

II. Characterization techniques

Spectroscopic methods: UV-Vis, FTIR, XRD, Microscopic techniques: SEM, TEM Other analytical methods: EDX, DLS Characterization techniques play a crucial role in determining the properties and functionalities of nanoparticles-

- **Spectroscopic Methods:**
  - **Ultraviolet–visible (UV-Vis) Spectroscopy:** This technique is used to determine the optical properties of nanoparticles by measuring the absorbance or reflectance of UV and visible light, providing insights into the electronic transitions within the material [27].
  - **Fourier Transform Infrared (FTIR) Spectroscopy:** FTIR helps in identifying functional groups and chemical bonds present in nanoparticles. It is used to investigate the molecular bonding and interactions between the components of the nanoparticles [28].
  - **X-Ray Diffraction (XRD):** XRD is crucial for determining the crystalline structure and phase identification of nanoparticles. It provides information on the crystalline size, orientation, and strain within the nanoparticle lattice [29].
- **Microscopic Techniques:**
  - **Scanning Electron Microscopy (SEM):** SEM allows high-resolution imaging of nanoparticles, providing detailed information about their surface morphology and composition. It is often used in combination with EDX for elemental analysis [28].
  - **Transmission Electron Microscopy (TEM):** TEM provides high-resolution images of the internal structure and morphology of nanoparticles at the atomic level. It is invaluable for assessing the size, shape, and detailed internal structure of nanoparticles [30].
- **Other Analytical Methods:**
  - **Energy-Dispersive X-ray Spectroscopy (EDX):** EDX is often coupled with electron microscopy techniques to provide elemental analysis and chemical characterisation of nanoparticles [28].
  - **Dynamic Light Scattering (DLS):** DLS is used to measure the size distribution and stability of nanoparticle suspensions in liquid environments. This determines the hydrodynamic diameter, offering insights into the particle size and distribution within a colloid [30].

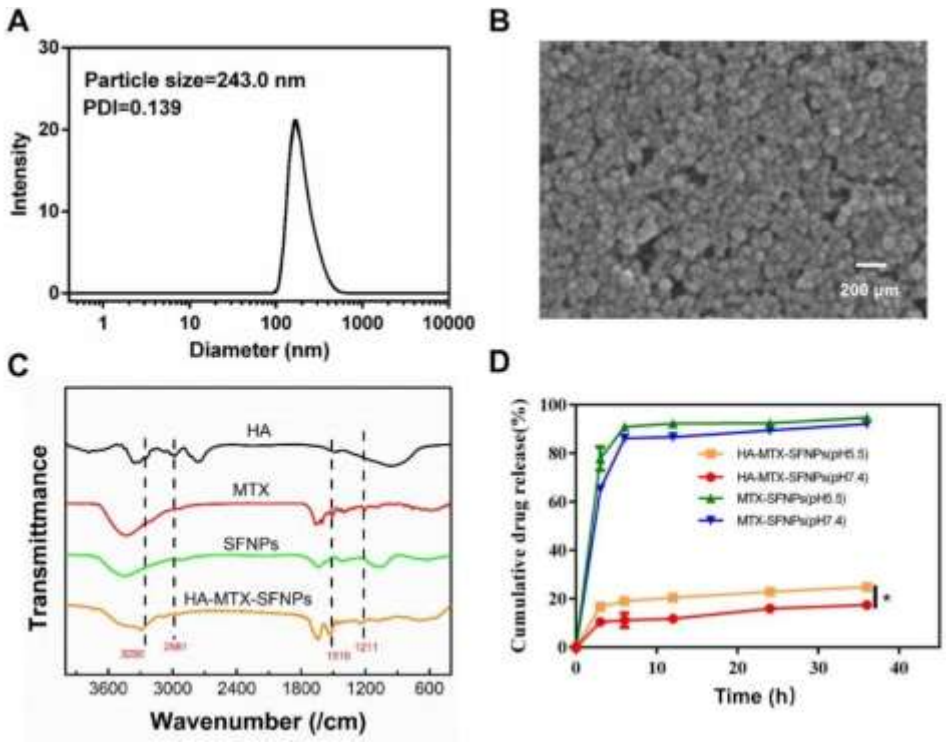

Figure 2. Physicochemical characterization of NPs. (A) The particle size distribution of HA-MTX-SFNPs. (B) SEM diagram of HA-MTX-SFNPs. (C) FITR characterization of NPs. (D) MTX-SFNPs and HA-MTX-SFNPs drug release curves under pH 7.4 and pH 5.5 conditions. Each point represents the average value ± S.E.M (n = 3, *P< 0.05)

These techniques collectively enable a comprehensive understanding of the physical, chemical, and structural properties of nanoparticles, which is essential for their application in various fields.

The green synthesis of metallic nanoparticles offers a sustainable alternative to conventional methods for producing nanoparticles with potential applications in psoriasis treatment owing to their significant antimicrobial and anti-inflammatory properties.

- **Gold Nanoparticles (AuNPs):** AuNPs are known for their unique optical and chemical properties, which make them suitable for biomedical applications. Green synthesis methods utilise plant extracts and other natural resources for the bioreduction of gold ions to nanoparticles. These methods not only minimise environmental impact but also enhance the biocompatibility of nanoparticles, making them suitable candidates for therapeutic applications, including potential chronic skin disorders such as psoriasis [32,33].
- **Silver Nanoparticles (AgNPs):** Silver nanoparticles exhibit potent antimicrobial properties, which have been explored in various medical applications. They are synthesised through green methods using plant extracts, which act as reducing and stabilising agents, making the process eco-friendly and cost-effective. AgNPs are appreciated for their broad-spectrum antibacterial and anti-inflammatory effects, which can be beneficial for managing skin conditions such as psoriasis [34,35].
- **Zinc Oxide Nanoparticles (ZnO-NPs)** are commonly used because of their excellent biocompatibility and low toxicity. The green synthesis of ZnO-NPs often involves plant extracts that facilitate the formation of nanoparticles without the use of harsh chemicals. ZnO-NPs are known for their antimicrobial activity and ability to promote skin health, making them suitable for treating inflammatory skin diseases , such as psoriasis. These nanoparticles can also boost reactive oxygen species (ROS) production, which contributes to their therapeutic efficacy in skin applications [36,37].

III. Chitosan-Based Nanoparticles

Chitosan, derived from chitin, is a cationic polysaccharide with outstanding properties, such as biocompatibility, biodegradability, and mucoadhesive properties, making it a promising material for drug delivery systems. Chitosan-based nanoparticles are highly effective drug carriers, allowing for the controlled release and targeted delivery of therapeutic agents. Nanoparticles can encapsulate a wide range of drugs and have demonstrated applications in cancer treatment, antimicrobial applications, and drug delivery to non-parenteral areas, such as the brain and eyes. Chemical

modifications of chitosan enhance these properties, facilitating better solubility and specific targeting abilities through functionalization with groups such as folic acid for cancer cell targeting.

PLGA Nanoparticles: Poly(lactic-co-glycolic acid) (PLGA) is a biodegradable synthetic polymer extensively used in the pharmaceutical industry because of its biocompatibility and controlled degradation profiles. PLGA nanoparticles have been widely researched for drug delivery applications, offering benefits such as reduced side effects, lower dosing frequency, and improved bioavailability. They are particularly effective in transdermal drug delivery systems. The versatility of the polymer allows for modifications that enhance drug targeting and release. PLGA-based formulations are employed in various therapeutic areas, including dental applications, cancer therapy, and as carriers for the sustained release of proteins and other macromolecules.

Dendrimers: Dendrimers are hyperbranched, monodisperse, three-dimensional macromolecules with numerous surface functional groups that enhance solubility and reactivity. They are considered ideal nanocarriers for drug delivery because of their high loading capacity, ability to enhance the solubility of hydrophobic drugs, and controlled release profiles. Dendrimers have been utilised in various biomedical applications, including as vectors for gene delivery, cancer therapy, and brain targeting. Their architecture allows for the detailed manipulation of their physical and chemical properties, making them highly versatile for drug and gene delivery.

Collectively, these polymeric nanoparticles offer various advantages depending on their composition and structure, expanding the possibilities for drug delivery systems and therapeutic interventions in diverse medical fields. Although I cannot generate a full essay, I can provide information on chitosan-based nanoparticles, PLGA nanoparticles, and dendrimers based on the available literature.

Lipid-based nanocarriers, including liposomes, solid lipid nanoparticles (SLNs), and nanostructured lipid carriers (NLCs), are pivotal in drug delivery systems because of their diverse applications and inherent properties.

Liposomes are spherical vesicles composed of one or more phospholipid bilayers and are known for their biocompatibility and versatility. Liposomes can encapsulate both hydrophilic and hydrophobic drugs, protecting them from degradation. They are used in various fields, including pharmaceuticals, cosmetics, and food industries. Their applications in drug delivery extend to cancer therapy, where they are modified to target specific tumour markers, thereby reducing side effects and improving drug delivery efficacy. Liposomes can also deliver vaccines and genetic material, demonstrating their significant potential in theranostic applications that combine therapy and diagnostics.

Solid Lipid Nanoparticles (SLNs) were developed to overcome the limitations of traditional liposomes and polymeric nanoparticles. They offer controlled drug release, enhanced stability, and the possibility of improved bioavailability owing to their solid lipid matrix. SLNs are primarily composed of biocompatible and biodegradable lipids, providing a suitable platform for drug delivery across various administration routes, including oral, topical, and parenteral routes. They serve as carriers for both hydrophilic and lipophilic drugs, with benefits such as improved pharmacokinetic profiles and targeted delivery capabilities.

Nanostructured Lipid Carriers (NLCs) represent the second generation of lipid nanoparticles, improving SLNs by incorporating both solid and liquid lipids. This structural modification enhances the drug loading capacity and stability, overcoming the limitations of SLNs. NLCs offer controlled release, improved drug entrapment efficiency and prolonged drug retention time. They have broad applications in the pharmaceutical and cosmetic industries, including transdermal delivery, which benefits from their ability to penetrate deeper into the skin layers. NLCs demonstrate enhanced targeting capabilities, making them suitable carriers for treating diseases such as cancer, infections, and neurodegenerative disorders.

These lipid-based nanoparticles are crucial for developing advanced delivery systems, offering improved stability, biocompatibility, and efficiency in delivering therapeutic agents across various applications. Their evolving innovations continue to expand their potential to enhance drug delivery and therapeutic outcomes.

IV. Mechanism of Action in Psoriasis Management

Reduction of inflammatory mediator production In the management of psoriasis, various mechanisms of action target the inflammatory processes underlying this chronic skin disorder. Key strategies focus on modulating pro-inflammatory cytokines, inhibiting transcription factors, and reducing the production of inflammatory mediators.

- **Modulation of Pro-inflammatory Cytokines**: In psoriasis, cytokines such as tumour necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-17 (IL-17) play critical roles in driving the inflammatory process. Therapies targeting these cytokines can effectively reduce inflammation and ameliorate psoriatic symptoms. TNF-α

inhibitors, for instance, have shown significant efficacy in reducing the inflammatory response by blocking the activity of TNF-α, a central cytokine involved in the inflammatory cascade associated with psoriasis.

- **Inhibition of NF-κB and Other Transcription Factors** : The Nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) is a crucial transcription factor involved in regulation ting of genes responsible for inflammation, immunity, and cell proliferation. In psoriasis, NF-κB is often aberrantly activated, contributing to the inflammatory milieu and keratinocyte proliferation characteristic of the disease. Therapeutic strategies that inhibit NF-κB signalling can attenuate these processes, offering a means to control psoriasis. For example, methotrexate acts by suppressing NF-κB activation, thereby reducing psoriatic inflammation 58–60 .
- **Reduction of Inflammatory Mediator Production** : Psoriasis management also involves the reduction of inflammatory mediators. NF-κB activation leads to the production of various inflammatory mediators , such as nitric oxide and prostaglandins, which exacerbate the condition. Agents that block NF-κB activity consequently reduce the production of these mediators, alleviating inflammation. Anti-inflammatory agents, such as chelidonine, effectively suppress these pathways , thereby mitigating psoriasis inflammation 59,61 .

V. Immune Response

Control of neutrophil infiltration Immunomodulation involves various mechanisms that regulate the activity of immune cells, such as T-cells, dendritic cells, and neutrophils, each playing crucial roles in maintaining immune homeostasis and effective immune responses.

- **Regulation of T-Cell Activity** : T-cells are central to the adaptive immune response, and their activity is tightly controlled to prevent inappropriate immune responses. Dendritic cells (DCs) are pivotal in priming naïve T cells and modulating their differentiation into effector cells , such as Th1, Th2, Th17, and regulatory T cells (Tregs). This regulation is achieved through the presentation of antigens and the expression of co-stimulatory molecules which influence T-cell activation and proliferation. Additionally, T-cells can modulate DC function, enhancing their ability to present antigens effectively through interactions known as "licensing" or "education ", which are mediated by cytokines and surface molecule interactions 62,63 .
- **Modulation of Dendritic Cell Function** : Dendritic cells serve as the primary antigen-presenting cells that bridge innate and adaptive immunity. They modulate T cell responses by processing and presenting antigens, expressing co-stimulatory molecules, and secreting cytokines. DCs can be influenced by other immune cells , including granulocytes. For example, neutrophils can affect DC function through direct interaction or the release of cytokines and chemokines, thereby influencing T-cell responses and DC's antigen-presenting capacity of DCs 64,65 .
- **Control of Neutrophil Infiltration** : Neutrophils play a crucial role in the rapid response to infection and tissue injury as part of the innate immune system. Beyond their direct antimicrobial functions, they can modulate adaptive immune responses by interacting with DCs and T cells . Neutrophils can present antigens to T-cells and influence T-cell differentiation towards Th1 and Th17 responses. Furthermore, interactions between neutrophils and dendritic cells can enhance DC's ability of DCs to activate T-cells, thereby influencing the magnitude and direction of the immune response 66,67 .

These mechanisms highlight the complex intercellular communication and regulatory processes that modulate immune responses, ensuring effective defense against pathogens while maintaining immune tolerance.

Promotion of normal cell differentiation Keratinocytes are crucial for maintaining skin health by controlling processes such as cell proliferation, differentiation, and establishment of the skin barrier. The mechanisms involved in the regulation of keratinocytes are as follows:

- **Inhibition of Keratinocyte Hyperproliferation** : Hyperproliferation of keratinocytes is a hallmark of certain skin disorders , such as psoriasis. Signalling pathways , such as PI3K/Akt , are implicated in promoting keratinocyte proliferation. Modulating these pathways can help control excessive cell proliferation. For instance, Epidermal Growth Factor Receptor (EGFR) signalling has been shown to play a role in keratinocyte proliferation. EGFR activation suppresses keratinocyte differentiation, exacerbating conditions that lead to proliferation, which can be targeted to inhibit hyperproliferation .
- **Enhancement of Skin Barrier Function** : The skin barrier function is maintained by keratinocyte differentiation and the formation of tight junctions, which are essential for preventing transepidermal water loss and protecting against pathogens. Integrins play a significant role in keratinocyte adhesion and signalling, which are necessary for barrier function. Dysregulation of integrins can disrupt the barrier ; thus, enhancing proper integrin

function can support barrier integrity. Moreover, fibroblast growth factors (FGFs) regulate epidermal barrier function by maintaining keratinocyte proliferation and barrier protein expression, thereby preventing inflammation and maintaining cutaneous homeostasis 70,71 .

- **Promotion of Normal Cell Differentiation**: Keratinocyte differentiation is essential for creating a protective, cornified layer in the skin. Differentiation involves a series of signalling pathways, including the Wnt and BMP pathways, which regulate the expression of differentiation markers , such as filaggrin and loricrin. An imbalance in these pathways can lead to skin diseases due to poor differentiation. Calcium-induced differentiation is another mechanism in which increased intracellular calcium levels instigate the differentiation process through pathways such as ER stress and autophagy, facilitating normal keratinocyte differentiation 72,73 .

Stability and scalability assessments In the field of nanotechnology, the green synthesis of nanoparticles offers an environmentally friendly and sustainable alternative to traditional chemical methods. This approach utilises natural resources, such as plant extracts, which act as reducing, stabilising, and capping agents. An overview of the experimental methods involved in nanoparticle synthesis and characterisation is provided below.

- **Green Synthesis Protocols** : Green synthesis involves using biological components , such as plants, fungi, and bacteria , to produce nanoparticles, minimising environmental impact. Plant extracts, for example, offer phytochemicals such as phenolic compounds, terpenoids, and proteins that play crucial roles in reducing and stabilising nanoparticles (NPs) . This method is noted for its cost-effectiveness, simplicity, and ability to produce uniform nanoparticles with enhanced stability and biocompatibility. Examples include silver nanoparticles synthesised using Ocimum sanctum leaf extract and gold nanoparticles produced using Sargassum muticum algae extract, emphasising the efficacy of green routes in nanoparticle synthesis 74–76 .
- **Physicochemical Characterisation Techniques** : Accurate characterisation of nanoparticles is essential to confirm their synthesis, stability, and suitability for various applications. Techniques include:
  - **UV-Vis Spectroscopy** : Used to monitor nanoparticle formation by detecting specific absorption peaks (e.g. gold nanoparticles exhibit a peak at approximately 550 nm).
  - **Fourier-transform infrared spectroscopy (FTIR)** : assesses chemical bonding and functional groups on nanoparticle surfaces.
  - **Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM)** provide detailed information on the morphology, size, and structure of nanoparticles.
  - **X-ray Diffraction (XRD)** : identifies crystalline structures and phase compositions .
  - **Dynamic Light Scattering (DLS)** : Measures particle size distribution and zeta potential, which are indicators of stability.
- **Stability and Scalability Assessments** : Ensuring the stability and scalability of nanoparticles is critical for their practical application and commercialisation . Green-synthesised nanoparticles often demonstrate enhanced stability owing to their biogenic capping agents. Furthermore, large-scale production techniques involve optimising conditions , such as pH, temperature, and reactant concentrations , to maintain consistency. Assessments also focus on maintaining nanoparticle size, shape, and functional properties during scale-up production processes 75,76,78 .

Gene expression and protein analysis In vitro studies employ sophisticated techniques and models to investigate cellular processes, cytotoxic effects, and molecular dynamics. These studies are integral to understanding the interactions between cells and materials, particularly in fields such as toxicology and drug development. Here's an overview:

- **Cell Culture Models** :
  - **Keratinocytes and Immune Cells** : These commonly used in vitro to study skin biology and immune responses. For example, keratinocytes are used to model skin responses in drug screening and can be cultivated in both 2D and 3D environments. 3D cultures, such as those using AlgiMatrix, better mimic in vivo conditions by maintaining cell-cell interactions and extracellular matrix components, improving the relevance of anticancer drug testing.
  - **Immune Cell Models**: Often used to assess immune responses to nanoparticles and other agents, specifically looking at pathways like endocytosis and immune activation in cells such as macrophages .
- **Cytotoxicity and Cellular Uptake Assays** :
  - These assays are essential for evaluating the safety and efficacy of nanoparticles and drug. For example, cytotoxicity can be assessed using the MTT assay, which measures the cell viability. Cellular uptake is often

studied using methods such as flow cytometry or inductively coupled plasma mass spectrometry to quantify nanoparticle accumulation within cells 82,83 .

❖ The concept of the protein corona, where proteins adsorbed on nanoparticles alter their interaction with cells, provides crucial insights into mitigating potential cytotoxic effects by reducing cell membrane penetration . [84]

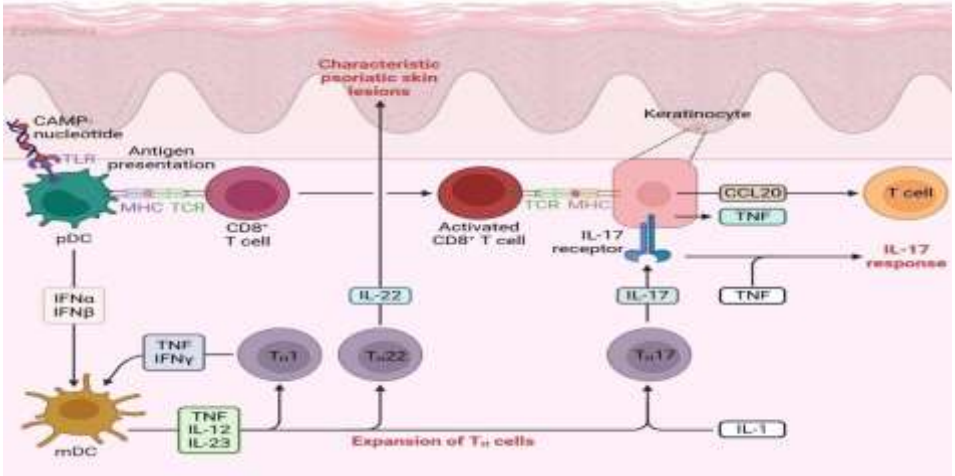

Figure 3. Diagrammatic representation of mechanism of action Psoriasis

VI- Gene Expression and Pr otein Analysis :

These analyses provide deep insights into the cellular responses to treatment at the molecular level. Gene expression can be profiled using microarrays or RNA sequencing, which allows the detection of changes in mRNA levels. Proteomic approaches can complement these data by revealing protein expression and interactions through techniques such as mass spectrometry. These approaches are instrumental in distinguishing different cellular responses, such as those induced by nanoparticle exposure, revealing pathways such as the oxidative stress response which are crucial for understanding cytotoxic mechanisms and informing safer nanoparticle design.

By integrating these methodologies, in vitro studies not only enhance our understanding of cellular behaviors and interactions but also inform the development and testing of new pharmaceuticals and nanoparticles, contributing to advances in biomedical research and applications.

In vivo studies are crucial for understanding psoriasis pathophysiology and evaluating new treatments. Here is a summary of the key aspects regarding the use of animal models, administration routes, and efficacy and safety evaluations in psoriasis research.

➢ **Animal Models of Psoriasis**

❖ Animal models are invaluable for studying psoriasis, although no single model perfectly replicates psoriasis in humans . Common models include imiquimod-induced psoriasiform dermatitis in mice, which is frequently used because of its ability to mimic psoriasis-like inflammation and hyperplasia.

❖ Xenotransplantation, in which human skin is transplanted onto immunocompromised mice, is another method that allows the study of human-specific immune responses and the testing of therapeutic compounds on human tissues.

➢ **Topical and Systemic Administration Routes**

❖ Topical administration is commonly used in psoriasis treatment to directly deliver drugs to the affected skin areas. Studies have shown that drug penetration and efficacy can vary based on disease stage and skin condition. For instance, increased skin thickness and hyperkeratosis in later disease stages can hinder drug penetration, affecting treatment outcomes.

❖ Systemic routes, including oral and injectable biologics or small molecules, are used for moderate-to-severe cases. These treatments often target specific immune pathways implicated in psoriasis pathogenesis, such as T-cell activity and cytokine production.

➢ **Efficacy and Safety Evaluations**

❖ In vivo studies assess the efficacy of treatments by measuring outcomes such as lesion clearance, reduction in inflammatory markers, and improvement in skin barrier function. The efficacy of biologic agents

such as etanercept and infliximab in moderate-to-severe psoriasis is well documented , although long-term efficacy data are still limited.

❖ Safety evaluations focus on identifying potential adverse effects and understanding the long-term safety profiles of treatments. Agents are evaluated for their ability to manage symptoms without causing significant adverse effects . For example, new topical agents , such as tapinarof and roflumilast , have shown promising safety profiles with manageable side effects in treating mild-to-moderate psoriasis.

The integration of various animal models, administration routes, and comprehensive evaluations in in vivo studies provides essential insights into the development of safe and effective psoriasis therapies.

VII. Results and Discussion.

➢ **Nanoparticle Characterizationa:** Size, shape, and surface properties, Analysis of nanoparticle dimensions using dynamic light scattering and electron microscopy, Evaluation of morphology and surface characteristics through scanning electron microscopy, Assessment of surface charge and zeta potential measurements

➢ **Therapeutic Efficacya**: Anti-inflammatory and immunomodulatory effects of the extracts were quantified by measuring the reduction of pro-inflammatory cytokines (such as TNF-α, IL-6, and IL-17) in cell culture models. Assessment of NF-κB pathway inhibition and inflammatory mediator production. Evaluation of T-cell activity modulation and dendritic cell function in vitro

Impact on keratinocyte proliferation and differentiation, Analysis of keratinocyte growth rates and cell cycle progression, Measurement of differentiation markers expression (e.g., involucrin, loricrin), Assessment of skin barrier function through trans epidermal water loss measurements.

Comparison with standard psoriasis treatments, Side-by-side efficacy comparison with topical corticosteroids and systemic therapies, Evaluation of onset of action and duration of therapeutic effects, Analysis of combination therapy potential with existing psoriasis treatments.

Nanoparticles synthesized through green methods, especially silver nanoparticles (AgNPs), have exhibited notable antibacterial effects. These particles compromise bacterial cell membranes, deactivate respiratory enzymes, and produce reactive oxygen species (ROS) that harm cellular structures. 1 Antifungal Activity: AgNPs have shown antifungal capabilities against resistant fungi like Candida albicans and Candida tropicalis. They disrupt membrane integrity, cause osmotic imbalance, and prevent fungal budding. 2 Antiviral Effects: Nanoparticles, particularly those composed of silver and gold, have demonstrated potential against enveloped DNA/RNA viruses. They impede viral attachment and entry by blocking interactions between viral surface mechanisms and host cell receptors. 3 Antiparasitic Activity: Green-synthesized AgNPs have been effective against mosquito larvae and malarial parasites. For example, AgNPs created using Bacillus safensis achieved complete mortality against Anopheles gambiae larvae. 4 Anti-inflammatory and Anticoagulant Properties: Nanoparticles have shown promise as carriers for anti-inflammatory drugs, especially in treating autoimmune diseases like rheumatoid arthritis. They have also displayed anticoagulant properties, with heparin-stabilized ferrimagnetic iron oxide nanoparticles (Hep-SPIONs) showing potential for use in haemodialysis. 5 Anticancer Applications: Various nanoparticles have exhibited anticancer properties. For instance, titanium oxide nanotubes coated with selenium nanoparticles have been found to inhibit the growth of MG-63 cancer cells. 6 Biosensing and Imaging: Green-synthesized nanoparticles have applications in biosensing for pathogen detection and nanoimaging for medical diagnostics. For example, carbon nanoparticles derived from honey have been used for sentinel lymph node imaging in cancer diagnosis.

VIII. Conclusion and future prospective

Psoriasis remains a significant healthcare challenge due to its complex autoimmune nature and the limitations of current treatments, which often cause systemic side effects, are costly, and offer limited therapeutic efficacy. Nanotechnology presents a promising alternative, enabling precise drug delivery with enhanced therapeutic potential. Biosynthesized nanoparticles produced through green synthesis, using biological materials like plant extracts and microbial organisms, offer eco- friendly and non-toxic solutions. These nanoparticles exhibit anti-inflammatory, antioxidant, and immunomodulatory properties while improving skin penetration and controlled drug delivery. Their nanoscale dimensions make them more effective than conventional treatments. Despite their advantages, challenges such as scalability, long- term stability, and economic viability should be addressed. Further research is needed to optimize nanoparticle

interactions with psoriatic tissues and achieve optimal therapeutic outcomes. Advanced analytical techniques, computational modelling, and artificial intelligence can help address synthesis limitations and improve nanoparticle design. The integration of multimodal nanoparticles with personalized medicine offers new possibilities for psoriasis treatment, enhancing both nanomedicine and dermatological therapeutics. Breakthroughs in green synthesis, biomaterials, and catalytic systems will drive future developments. Machine learning and AI are advancing customized pharmaceutical drugs tailored to individual patient needs. A bioinspired, green synthesis approach provides a sustainable and effective strategy to overcome current therapeutic barriers, ensuring continued progress in psoriasis treatment and nano-medicine.

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