

## **Incorporating Herbal Nano formulation as Topical Formulation for the Treatment of Skin Infection Like Psoriasis: A Review**

**Soumik Patra<sup>1</sup>, Himalay De<sup>2</sup>, Krishna Pal<sup>3</sup>, Subir Paul<sup>1</sup>, Madhabi Chakraborty<sup>1</sup>, Kiran Mondal<sup>1</sup>, Sourav Bhowmick<sup>1\*</sup>**

<sup>1</sup> School of Pharmacy, Seacom Skills University, Santiniketan, Kendradangal, West Bengal 731236, India.

<sup>2</sup> Department of Pharmaceutics, DEROZIO PHARMA INSTITUE, Gopal Chak, Moyna, Gopal Chak, West Bengal 721629, India.

<sup>3</sup> Department of Pharmaceutical Technology, JIS University, 81 Nilgunj Road, Jagarata Pally, Deshpriya Nagar, Agarpara, Kolkata 700109, West Bengal, India.

**\*Corresponding author: Sourav Bhowmick**

School of Pharmacy, Seacom Skills University, Santiniketan, Kendradangal, West Bengal 731236, India.

### **Abstract**

Skin infections such as psoriasis present persistent therapeutic challenges due to their chronic inflammatory nature, impaired epidermal barrier function, and limited penetration of conventional topical agents. Recent advancements in nanotechnology have enabled the development of herbal nanoformulations that enhance the delivery, stability, and therapeutic performance of plant-derived bioactives. This study explores the potential of incorporating herbal nanoformulations into topical preparations for effective management of psoriasis and related skin infections. Herbal compounds rich in anti-inflammatory, antioxidant, antimicrobial, and immunomodulatory properties-often suffer from poor solubility, low skin permeability, and rapid degradation when applied directly. Nano-encapsulation using systems such as liposomes, nanoemulsions, solid lipid nanoparticles, and polymeric nanoparticles offers improved skin retention, controlled drug release, and targeted delivery to inflamed tissues. These nanosystems enhance therapeutic efficacy while minimizing systemic side effects and irritation. Incorporating herbal nanoformulations into topical creams, gels, or ointments provides a promising strategy for addressing the multifactorial pathology of psoriasis, including keratinocyte hyperproliferation, cytokine overexpression, and oxidative stress. Preliminary findings indicate significant improvements in lesion reduction, erythema

control, and patient comfort compared with conventional formulations. Overall, herbal nano-based topical delivery represents a safe, biocompatible, and highly effective approach for treating psoriasis, offering the potential to transform current dermatological therapies and improve patient outcomes.

**Keywords:** Psoriasis, Nanoparticles, Liposomes, Ethosomes, Nanospheres. Nanoformulations.

## Introduction

Psoriasis, an inflammatory, immune-mediated illness with pathogenic traits linked to autoimmune, impacts the joints (elbows and knees), lower back, scalp, and skin. This is debilitating gruesome, deformity, chronic, along with noncommunicable<sup>1</sup>. There is no recognized treatment. Though most occurrences happen between the ages of 50 and 69, it can develop at any age. Psoriasis prevalence estimates vary from 0.09 to 11.43 percent, affects at least 100 million individuals worldwide. As a result, psoriasis is a significant worldwide health concern<sup>2</sup>. The illness affects 2-4% of people worldwide, with Scandinavians being more affected than both African and Asian populations<sup>3</sup>. The number among other things, such as age, sex, geography, ethnicity, genetics, and environment, contribute to this variance<sup>4</sup>.

Psoriasis is a multifactorial disorder, meaning that several other variables can cause or worsen psoriasis symptoms. Stress, illnesses, and skin traumas are a few examples. Furthermore, a lot number of drugs have been linked to the development of Psoriasis as well as its aggravation (Table 1, Figure 2)<sup>33</sup>. The active components that are most frequently reported to cause Psoriasis include beta-blockers, tetracyclines, lithium, antimalarials, and non-steroidal anti-inflammatory drugs<sup>2</sup>.

Treatment for psoriasis usually focusses on symptom relief, inflammation reduction, and slowing down skin cell proliferation. Treatment options are determined by the type of psoriasis, its severity, and personal characteristics including age and general health<sup>5</sup>. The initial line of treatment for mild to moderate PSO is frequently topically applied active agents. These consist of calcineurin inhibitors, coal tar, retinoids, corticosteroids, vitamin D analogues, and dithranol<sup>2</sup>. The topical therapy does, however, provide several difficulties. For thicker plaques or ones seen on the scalp, palms, or soles, the anti-psoriatic might not be permeable to the skin deeply enough. Both genders both suffer from psoriasis, which is more prevalent in women, with an average age of 33<sup>6</sup>. According to genetic and immunological traits, there are two separate subgroups: early beginning, occurring at age late-onset, and older than 40 years (75 percent of cases), occurring after 40 years old (25 percent of instances). Black individuals are less prone to this sickness than light-skinned people<sup>7</sup>.

Nanoparticles' ability to increase penetration has drawn attention in the dermatology sector, particularly regarding the management of psoriasis. Due to the unique characteristics, they possess-like their small size, wide surface area as well as capacity to encapsulate and distribute medications to specific areas-nanoparticles may help control psoriasis, though research is still underway<sup>8</sup>. Through direct delivery of anti-psoriatic medications towards the afflicted skin, the nanoparticles could improve the permeation of drugs, boost effectiveness, along with lessen systemic absorption-related side effects. Drugs used to treat Psoriasis can have their stability, solubility, and bioavailability increased by adding them to a variety of formulations, such as creams, gels, ointments, and sprays<sup>9</sup>. Both patient comfort and compliance may be improved by these formulations. Numerous liposome varieties, Nanostructured lipid carriers (NLCs), solid lipid nanoparticles (SLNs), and nanoemulsions (NEs), noisome, nano sponges, ectosomes, there has been scientific literature on dendrimers and anti-psoriatic nanocrystals<sup>10</sup>.

### **Research on psoriasis epidemiology**

The highest prevalence of psoriasis is found in wealthy nations such as North America, Central Europe, Western Europe, and Australasia; the United States, India, and China had the largest adult populations with psoriasis, followed closely through France, Germany, Brazil, and the United Kingdom; Between East Asia and Australasia, the prevalence of psoriasis in adults ranged from 0.14% (95% CI 0.05% to 0.40%) to 1.99% (0.64% to 6.60%); rates were considerably higher in Western Europe, central Europe, North America, southern Latin America. With prevalences of 30.3 and 321.0 per 100,000 person-years, respectively, Taiwan and Italy<sup>11</sup>.

### **Etymology of psoriasis**

**Immune Activation Mediates Pathogenesis:** Psoriasis is a T-cell-mediated autoimmune disease in which cytokines are produced by resident skin cells (e.g., melanocytes, keratinocytes, and endothelial cells), adaptive immune cells (T and B cells), and innate immune cells (macrophages, dendritic cells, and neutrophils). It seems that these exchanges exacerbate along with sustain ongoing inflammation<sup>12</sup>. Due to their function as one type of professional antigen-presenting cell is the dendritic cell. After cytokine activation dendritic myeloid cells release 23 and IL-12. IL-12 causes native T cells to develop into TH1 cells. IL-23 is essential for the survival and proliferation of TH 17 and 22 cells. TH1 cells produce TNF-gamma and IFN-gamma; TH22 cells make IL-22; and TH17 cells compound TNF-gamma<sup>13</sup>. It is believed that the most significant of these pathways is the TH17 pathway, which is triggered by IL-23. These

cytokines cause infiltration of immune cells into the skin and dermal blood vessels in lesions and stimulate keratinocyte growth<sup>14</sup>.

### **Pathogenesis By the Involvement of Genetics**

In some instances, a genetic predisposition may be the cause of psoriasis. The HLA genes are regarded as crucial, along PSOR1 on chromosome 6p21.3, PSOR2 on chromosome 17q, PSORS3 & PSORS4 on chromosome 1cenq21, PSORS5 on chromosome 3q21, and PSORS6 on chromosome 19p, together with PSORS9 on chromosome 4q31<sup>15</sup>. Psoriasis outbreaks perhaps caused by fractalkine, or CX3CL1 and CX3CRI genes that are receptors because among the chemotactic actions on monocytes, T cells, NK cells<sup>16</sup>.

### **Pathogenesis that is Mediated by Peptides that Fight Bacteria**

There are antimicrobial peptides in plants, insects, and mammals. There are 12 to 50 amino acids in AMPs which are effective against viruses, bacteria, fungi, and protozoa. Cell cycle regulators, angiogenesis factors, and chemotactic factors are only a few of the many elements that affect inflammatory responses<sup>17</sup>. S100 proteins, cathelicidin, and  $\alpha$ -defensins are all expressed in psoriatic lesions<sup>18</sup>. It has been suggested that these AMPs have a major role in psoriasis. The three classes of defensin peptides are  $\alpha$ ,  $\beta$ , and  $\theta$ . They are cationic. These groups contain triple disulphide bonds inside the molecule<sup>18</sup>. The levels of psoriatic lesions contain peptides of the human neutrophils (HNP) 1–6, which are 6 different types of the  $\alpha$ -defensins. The four types of the  $\kappa$ -defensins are human  $\beta$ -defensins (hBD) 1–4. hBD 2-3 is activated in keratinocytes by TNF- $\alpha$  and IFN- $\gamma$  which are highly expressed regarding psoriatic dimensions<sup>19</sup>. Additionally observed is the actual induction of hBD 2 by IL-17A and IL-22. 100 low molecular weight proteins (9–13 kDa) with two calcium binding sites arranged in helix-loop-helix patterns are called proteins and individual copy counts of  $\kappa$ -defensin are associated with genes influences on psoriasis susceptibility<sup>17</sup>. Thirteen distinct S1 proteins are expressed in the skin of both healthy and psoriatic individuals. The amounts of calgranulin B (S100A9), calgranulin C (S100A12), and calgranulin 15 in the blood rise inside psoriatic lesions, which are identified by S100A7 (psoriasis), and S100A8 (calgranulin A). Interleukin-22, interleukin-17A, and immunoglobulin-17F treatment of keratinocytes resulted in elevated expression of S100A9, S100A7, and S100A8<sup>20</sup>. The AMP-producing cathelicidin LL-37, has been associated to the beginning of psoriasis. It could potentially have a part in inflammation in Figure 2. Both LL-37 and DNA stimulation trigger the type I IFN that is markedly elevated in skin that is psoriatic<sup>21</sup>.

## **Additional Significant Causes**

Air pollution and sun exposure, vaccinations, medications, diabetes mellitus, physical trauma, infections, and obesity, dyslipidaemia, stress, smoking, alcohol, and high blood pressure are a few of the known causes of psoriasis medicines<sup>22</sup>.

Certain drugs been used in clinical linked from the beginning, aggravating and intensifying psoriasis, including imiquimod, a treatment that inhibits the growth of viruses, IFNs, lithium, beta-blockers, and anti-cytokine treatments for psoriasis<sup>7</sup>. Imiquimod, among the many thoroughly researched current triggers for psoriasis, stimulates the interferon type I.<sup>1</sup>

Guttate psoriasis, has existed linked streptococcal throat infections in the past, along with comparable cloned in patients with plaque psoriasis, T-cells have been discovered in their tonsils and skin lesions<sup>23</sup>. The one that fungus the more prevalent form of Candida that causes disease is Candida albicans, and its colonisation boosts anti-fungal immunity, which could contribute to the genesis of psoriasis<sup>5</sup>.

**Trauma:** Alcohol, smoking, stress, and obesity. Even though numerous studies have linked smoking, stress, obesity, and psoriasis. It is commonly believed that emotional stress makes psoriasis worse, and many psoriasis patients and physicians agree<sup>24</sup>. There is a complex relationship between mental discomfort and psoriasis, as demonstrated according to the Dermatology Life Quality Index ratings. A comprehensive review of research (32,537 individuals) comprising 39 trials found that 46% of patients had a stress-related illness<sup>25</sup>. Smoking and alcohol consumption have been connected to psoriasis. Smoking increases the risk of developing pustular psoriasis lesions<sup>26</sup>. A variety of drug-related psoriasis forms, including erythrodermic, pustular, palmoplantar, scalp, nail, and plaque, can develop. Obesity is strongly associated with the onset and exacerbation of psoriasis. Psoriasis and BMI were associated in another study that included a much bigger prospective population<sup>27</sup>.

**Sunshine and air pollution:** Among the atmosphere contaminants which induce ozone causes skin damage and oxidative stress, volatile organic molecules, polycyclic aromatic hydrocarbons, oxides, particulates, ultraviolet (UV) radiation and heavy metals. Cadmium, an air pollutant, is part of the pathophysiology of psoriasis. People with psoriasis have higher amounts of cadmium than people without the condition<sup>28</sup>.

**Vaccination:** Influenza vaccinations can cause psoriasis. As a type of local immunotherapy, BCG injections have been given to patients with bladder cancer, one patient experienced an erythrodermic pustular skin rash because of the treatment<sup>20</sup>. A retrospective analysis found that adenovirus immunisation correlated with a higher prevalence of psoriasis. Analysis

Psoriasis can also result from additional immunizations, for example the pneumococcal polysaccharide and vaccines against tetanus and diphtheria<sup>29</sup>.

**Dyslipidaemia:** Dyslipidaemia is more common in patients with psoriasis, as well as how severe their psoriasis probably as an exacerbate their dyslipidaemia itself. Previously, a study including 70 psoriasis patients discovered that 62.85% of them had dyslipidaemia<sup>30</sup>.

**Hypertension:** A meta-analysis found that the general prevalence and occurrence of high blood pressure were greater in patients with psoriasis. The results of this meta-analysis findings moreover showed one link amid severe psoriasis as well as a higher chance of developing hypertension<sup>31</sup>. Patients with psoriasis are more likely than the general population to have hypertension, according to a multicentre, noninterventional study that included 2210 psoriasis patients, of whom 26% had hypertension<sup>32</sup>. Figure 1 described the pathogenesis of psoriasis.

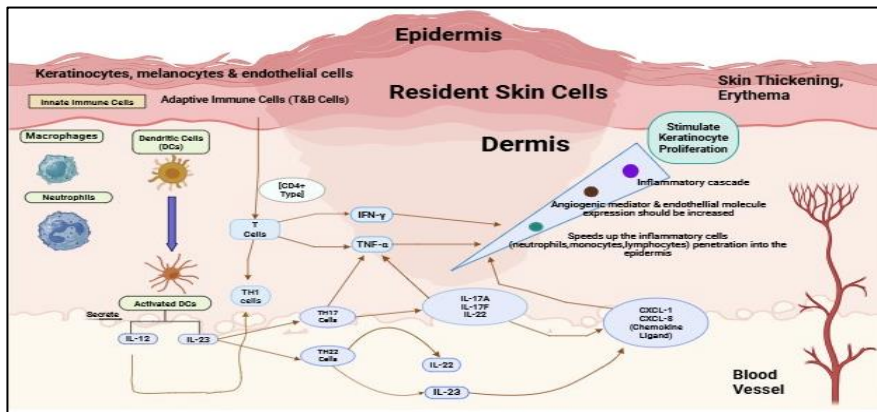


Figure 1. The pathogenesis of psoriasis

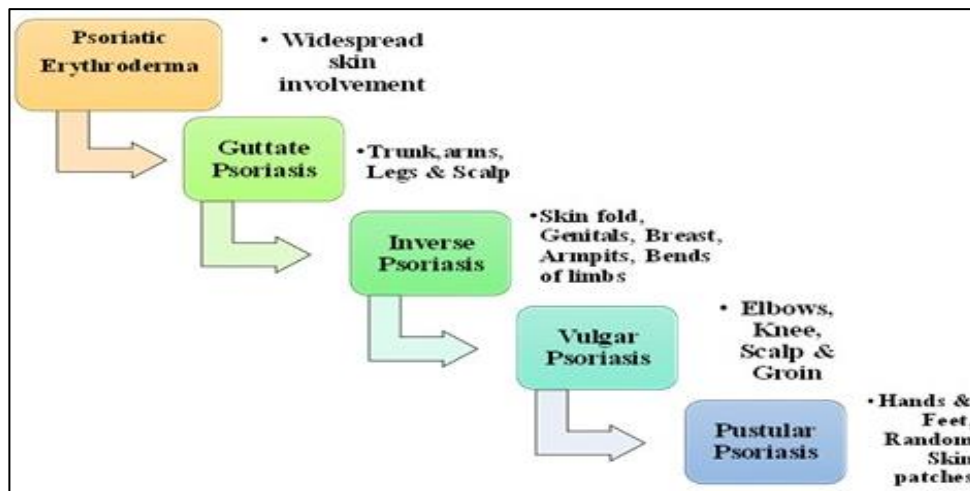
Table 1: A Clinical Classification of Psoriasis That Includes Several Significant Symptom

The kind of psoriasis	Particular traits and expressions
Psoriasis vulgaris or plaque psoriasis	<p>Type that is most common (85% to 90% of patients).</p> <ul style="list-style-type: none"> <li>• Woronoff's ring may be visible on the skin around a psoriatic plaque. Inflammatory red, elevated, erythematous, dry.</li> <li>• Most often, it affects the skin of your face, palms, soles, and gluteal fold; the scalp and behind your ears; and the extensor surfaces of your forearm and knee joints, especially the elbow and knee joints.</li> <li>• Plaques can take on a variety of sizes and shapes, such as: This kind, known as psoriasis gyrate, is more likely to have wavy or curving linear patterns. Annular psoriasis is a type of psoriasis</li> </ul>

	<p>where ring-shaped lesions. The pores of pilosebaceous follicles known as Psoriasis follicularis are lined with tiny, scaly papules.</p>
<p>Inverse psoriasis or flexural psoriasis or intertriginous psoriasis</p>	<p>Impacts 12-26% of all psoriasis cases.</p> <ul style="list-style-type: none"> <li>• It can be confused with candidal, intertrigo, is characterized by flat, well-defined, wet patches or plaques that are deep red or white and scale-free. This condition mostly affects the groyne, gluteal cleft, popliteal fossa, axillae, antecubital fossae, infra- and sub-acromial creases, and umbilicus, among other body folds.</li> </ul>
<p>Guttate psoriasis or droplet psoriasis</p>	<p>This affects 20% of psoriasis types.</p> <ul style="list-style-type: none"> <li>• Mostly impacts children and teenagers and it is characterized by numerous small, scaly, reddish plaques, drop-shaped papules, and plaques that usually affect the arms, legs, and trunk. Prior skin characteristics and streptococcal infection of the UTI (pharynx or tonsils) are linked to set.</li> </ul>
<p>Pustular psoriasis</p>	<p>It's divided into two phenotypic categories.</p> <ol style="list-style-type: none"> <li>1) Generalized pustular psoriasis (GPP), also known as von Zum bush psoriasis.             <ul style="list-style-type: none"> <li>• Although extremely uncommon, it could be lethal. This condition is characterized by sterile cutaneous eruptions and inflammation of the stratum spinosum, which is characterized by diffuse erythema, systemic inflammation, and episodic, widespread skin redness.</li> <li>• Another name for this illness is impetigo herpetiformis, which is the medical term for widespread pustular psoriasis during pregnancy.</li> </ul> </li> <li>2) Psoriasis that is localized or palmoplantar pustulosis (PPP).             <ul style="list-style-type: none"> <li>• Palmoplantar pustulosis is characterized by sterile yellow pustules, which are two types:</li> </ul> </li> </ol>

	<p>Barber's pustular psoriasis: This condition is more common in women and those with a family history of it. The palmoplantar region, especially the erythematous thenar and hypothenar regions, has 2 to 4 mm pustules that are indicative of this illness. Sterile pustular eruptions on the skin of the hands and feet, known as acrodermatitis continua of Hallopeau, cause significant loss of nails and distal phalanx; in extreme cases, amputations may be necessary.</p>
<p>Erythrodermic psoriasis</p>	<ul style="list-style-type: none"> <li>• 0.4% to 7% of all psoriasis cases are affected.</li> <li>• The skin's maximal surface (more than 75%) is extremely red and peeling, the condition is characterized by diffuse erythema, either with or without skin scaling.</li> <li>• The disease's most severe form results in electrolyte imbalances, hypothermia, iron and vitamin B<sub>12</sub> deficiencies, folate deficiencies, heart failure.</li> </ul>
<p>Psoriatic arthritis (PsA)</p>	<p>PsA can also be associated with subclinical intestinal inflammation, cardiovascular disease, osteoporosis, and uveitis.</p> <ul style="list-style-type: none"> <li>• Psoriatic arthritis has a normal incidence of 0.02 to 1.1%, while in psoriatic individuals, its prevalence ranges from 5.4 to 7.0%.</li> <li>• Moll and Wright have categorized psoriatic arthritis into five different clinical groupings.</li> </ul> <ol style="list-style-type: none"> <li>I. <b>Classical PsA:</b> This affects around 10% of the population. It impacts the distal interphalangeal joints of the nail-covered hands and feet.</li> <li>II. <b>Asymmetric oligoarticular arthritis:</b> This type of cooperative cooperation is extremely prevalent. The knee joint is asymmetrically injured.</li> <li>III. <b>Symmetric polyarticular form:</b> Distal interphalangeal joints typically experience impact and are prone to ankylosing when correlated with RA.</li> </ol>

	<p>IV. <b>Arthritis motilins:</b> One of the hallmarks of this disease is osteolysis of the phalangeal and metacarpal bones. Often, sacroiliitis is a contributing component.</p> <p><b>Spondylitis form:</b> Merely 2% to 4% of people have isolated spondylitis. Most often, it is associated with a disorder called peripheral arthritis.</p>
<b>Nail psoriasis</b>	<p>Nail infections with yellow or brownish patches beneath the nails can be identified by capillaries beneath the nail, nail whitening, a pinhead-sized depression, nail breaking, and subungual hyperkeratosis. Patients who suffer from plaque psoriasis are more likely to develop nail psoriasis, which can show up as tiny pits on the nails, onycholysis, oil or salmon stains, or even nail plate cracking (dystrophy).</p>
<b>Scalp psoriasis or Sebo psoriasis</b>	<p>It affects the postauricular and parasternal areas, the scalp, and seborrheic areas of the face, such as the nasolabial folds and eyebrows. The temporary baldness is caused by silvery white scales that resemble dandruff and have itchy.</p>



**Figure 2. Typical Locations for Psoriasis.**

**Psoriasis treatments that are currently available**

Psoriasis is a common condition that cannot be cured, and because of its extremely complex pathophysiology. The degree of psoriasis, its location, and any comorbid illnesses all affect the therapy option<sup>34</sup>. Commonly used therapeutic approaches for the management of psoriasis include immunosuppressive drugs, phototherapies, local therapy, and other systemic treatment

alternatives<sup>35</sup>. Depending on the varied aspects of psoriasis, these therapy options are used in different ways. Depending on the symptoms, psoriasis can be mild, moderate, or severe. Local treatments for mild to severe symptoms typically involve corticosteroids, vitamin D, and its equivalents<sup>30</sup>. Systemic therapies and phototherapy should be tried if local treatment doesn't work or if the problem gets worse. To increase efficacy, local therapy is coupled with UVB and UVA phototherapies. Phototherapy should not be used by patients who have liver or kidney disease, cataracts, or photosensitivity<sup>36</sup>. In addition to adverse effects and unfavourable outcomes like elevated blood pressure or cholesterol, prolonged systemic therapy with synthetic drugs may cause hepatotoxicity and renal failure, which might result in death. Therefore, the best way to reduce side effects is through natural herbal therapy, and the second way to change the dosage form is through cutting-edge drug delivery technology<sup>37</sup>.

### **Traditional topical therapy for psoriasis**

The basis of treating mild to moderate instances of psoriasis is topical corticosteroids, which work by lowering inflammation and delaying the condition's hallmark fast skin cell proliferation. Class I (very strong) treatments are used for severe psoriasis, while Class VII (weak) treatments are used face or skin folds. They come in a variety of forms, including creams, ointments, and sprays<sup>38</sup>. Stronger agents are often used for harder regions, while weaker ones are used for delicate areas. Inflammation and irritation are lessened. They inhibit psoriasis's defining feature, the overgrowth of skin cells<sup>39</sup>.

The seven classes of topical corticosteroids are arranged according to their strength, with Class I being the strongest and Class VII the weakest. The cheeks, creases, and large patches are sensitive regions that are treated with mild corticosteroids<sup>24</sup>. For smaller, less sensitive, or more recalcitrant psoriasis patches, stronger corticosteroids are used. Because they can alter the immune system and have anti-inflammatory properties, topical calcineurin inhibitors are also crucial in the treatment of PSO. Although they are more frequently used to treat atopic dermatitis, or eczema, they can also be used to treat psoriasis in some situations<sup>40</sup>. This is especially true in sensitive areas (like the face and genital PSO), where other treatments are less effective due to their higher risk of side effects and increased percutaneous penetration. Tacrolimus and Pimecrolimus are the two main calcineurin inhibitors used in dermatology<sup>41</sup>. They work by preventing calcineurin, an enzyme involved in T cell activation, from doing its

job. Through the inhibition of T cell activation, these drugs aid in lowering inflammation and the aberrant immunological response that defines PSO<sup>42</sup>.

Their efficacy is increased by combining them with other topical therapies, including corticosteroids, because their methods of action are different but complimentary. Furthermore, some research has shown that vitamin D may help repair the weakened epidermal barrier caused by corticosteroid treatment and lower the risk of steroid-induced skin atrophy<sup>15</sup>. For this reason, topical therapy combining corticosteroids and vitamin D analog can offer more thorough and long-term PSO control<sup>43</sup>. While some studies support the use of dithranol in combination with other topical treatments or ultraviolet radiation B (UVB) phototherapy to improve the body's response in PSO, several studies have suggested that dithranol may be effective at high concentrations for brief skin contact<sup>27</sup>. Salicylic acid is a common topical keratolytic (scaling-softening) agent for psoriasis that works by removing the scales and reducing the thickness of psoriatic plaques. Both prescription and over-the-counter versions are available, and it helps reduce psoriasis's scaly look, itching, and inflammation<sup>15</sup>. It is frequently used either by itself or in conjunction with other therapies, such as topical steroids, to increase their efficacy<sup>19</sup>. Redness and itching may be lessened by its anti-inflammatory qualities (Table 2)<sup>45</sup>. When scales are removed, the skin's absorption of other topical drugs, such calcineurin inhibitors and corticosteroids, is enhanced, increasing their effectiveness. Salicylic acid shampoos and scalp treatments work especially well to lessen scalp scaling<sup>44</sup>. In creams or ointments, it is frequently used to treat the hyperkeratotic (thick, scaly) lesions of plaque psoriasis<sup>1</sup>.

Psoriatic plaques can be softer, and the penetration of topical treatments can be improved by using nonmedical moisturizers and emollients before the topical medications. They may not immediately address the inflammation linked to PSO<sup>8</sup>. PSO may be well managed with traditional topical medication; nevertheless, this approach has drawbacks. Topical drugs have the primary drawback of causing skin irritation, which can manifest as burning, itching, or redness<sup>4</sup>.

**Table 2. Categorized Corticosteroid.**

<b>Potency Category</b>	<b>Corticosteroid</b>	<b>Kind of Vehicle</b>
Extra-Strong Potency (Class 1)	Dipropionate of betamethasone, Propionate of clobetasol, Valerate of Diflucortolone, Fluocinonide,	Ointment, Cream, Gel, Lotion, Shampoo, Foam, Aerosol, Ointment, Solution Ointment, Oily Cream, Cream Tape Lotion.
Strong Potency (Class 2)	Amcinonide, Betamethasone dipropionate, Clobetasol propionate, Desoximetasone , Fluocinonide.	Ointment Ointment Cream Cream Cream, Ointment, Gel Ointment, Cream Gel, Cream, Solution,
Strong Potency (Class 3)	Amcinonide, Betamethasone dipropionate, Betamethasone valerate, Diflorasone diacetate, Diflucortolone valerate, Fluocinonide, Mometasone furoate, Triamcinolone acetonide	Cream, Lotion Cream Ointment, Foam Ointment, Cream Cream Ointment, Cream Ointment Ointment Ointment, Cream
Moderate Potency (Class 4)	Betamethasone dipropionate, Clo cortolone pivalate, Fluocinolone acetonide, Flurandrenolide, Fluticasone propionate, Hydrocortisone valerate, Mometasone furoate, Triamcinolone acetonide	Spray Cream Ointment Ointment Cream Ointment Cream, Lotion, Solution Cream, Aerosol Spray, Dental Paste
Potency in the lower to midrange (Class 5)	Betamethasone dipropionate, Betamethasone valerate, Desonide, Fluocinolone acetonide, Flurandrenolide, Fluticasone propionate, Hydrocortisone butyrate, Hydrocortisone probutate, Hydrocortisone valerate, Prednicarbate Triamcinolone acetonide	Lotion Cream Ointment, Gel Cream Lotion, Cream Lotion Cream, Ointment Cream Cream Cream Lotion, Ointment

Minimal Potency (Class 6)	Alclometasone dipropionate, Betamethasone valerate, Desonide, Fluocinolone acetonide, Triamcinolone acetonide	Cream, Ointment Lotion Cream, Lotion, Foam Cream, Shampoo, Oil Cream
Least Potent (Class 7)	Hydrocortisone (base, $\geq 2\%$ ), Hydrocortisone (base, $< 2\%$ ), Hydrocortisone acetate	Cream, Ointment, Lotion, Solution Ointment, Cream, Gel, Lotion, Spray, Solution Cream, Lotion

### Difficulties with topical anti-psoriatics administration

Drug penetration is restricted by the skin's natural barrier, which presents difficulties for topical anti-psoriasis treatments, particularly in thick psoriatic plaques. Regular, time-consuming applications and other adverse effects often make patient adherence challenging<sup>46</sup>. Managing comorbidities, treating high-impact regions (such as the scalp, face, and genitalia), the requirement for long-term therapy to sustain remission, and formulation limits are additional challenges. Effective penetration of active substances is hindered by the stratum corneum, the outermost layer of skin, which serves as a physical barrier. The thick, flaky, hyperkeratotic nature of psoriatic plaques itself makes it more difficult for drugs to be absorbed<sup>40</sup>. Drug distribution and effectiveness are difficult to achieve with traditional topical formulations because they are unable to overcome these obstacles.

Topical treatments can be inconvenient to apply frequently and over an extended period, which can lower patient adherence. Patients discontinue treatment when using certain topicals, such as corticosteroids, for an extended period of time because they may experience localized irritation, dryness, or itching<sup>34</sup>. A lot of patients are not happy with how slowly their treatments start to work<sup>47</sup>.

Comorbidities, or the presence of additional medical disorders, can complicate therapy decisions for psoriasis patients. Stress, some infections, and lifestyle choices are some of the things that can make psoriasis worse and make therapy more difficult. As a barrier, the stratum corneum, the skin's outermost layer, restricts how quickly the active substances can penetrate the skin<sup>48</sup>. The thicker and hyperkeratotic plaques that are frequently associated with psoriasis further impede drug penetration, making traditional treatments ineffective in terms of delivery and efficacy. It is challenging for topical medications to penetrate the skin's outermost layer using the traditional medicine formulation method<sup>30</sup>. Extreme disease-related symptoms like

itchiness and hyperkeratosis make this issue much more difficult. It may be more difficult for the active substances to penetrate the deeper layers of the skin due to the elevated cholesterol and decreased ceramide content of psoriasis skin features. Furthermore, the admission of relatively significant amounts of the medicine is limited by the insufficiency of hydrating stimuli such skin water<sup>49</sup>. However, the skin is typically not sufficiently hydrated, which restricts the anti-psoriatic' ability to penetrate the skin to a comparatively high degree. Additionally, different body parts have variable levels of skin permeability. The skin of the face and genitalia, for instance, is more porous than the skin on the palms and soles. When selecting a distribution system, the unique features of the impacted area must be considered<sup>33</sup>. Tacrolimus, dithranol, and calcipotriene are examples of anti-psoriatic medications that fall under the Biopharmaceutical Classification System (BCS) Class II, which indicates that they have poor water solubility, which may impact their absorption and bioavailability. For this reason, it is frequently necessary to use formulations that improve medication solubility<sup>56</sup>. Usually, topical psoriasis therapies need to be applied consistently over an extended period. The inconvenient nature of frequent application, the lengthy course of treatment, and possible adverse effects can all make patient compliance difficult. As was already noted, long-term usage of anti-psoriatics, particularly powerful corticosteroids, can result in skin irritation, dryness, or itching<sup>35</sup>. This might drive patients to stop taking their medication. Drugs applied topically may also enter the bloodstream if they are applied to significant portions of the body or to patients whose skin integrity is compromised. The likelihood of systemic side effects may rise as a result<sup>50</sup>.

### **Herbal-nanomedicines for psoriasis**

The cutaneous condition known as psoriasis can be successfully managed with topical drugs. To treat psoriasis more effectively, researchers created localized medication delivery devices. Natural bioactive chemicals have low solubility, poor skin penetration, skin irritation, and photosensitivity, which restrict their clinical relevance and render patients uncooperative, despite their potential therapeutic impact<sup>52</sup>. Nanostructured systems like the ethosome, which attaches to the polar functional group of skin's lecithin molecules to reduce the melting range of lipids in the SC and increase lipid fluidity and membrane permeability, and the liposome, which combines epidermal keratinocytes and lipids to enhance drug accumulation (Table 3)<sup>33</sup>, were developed by researchers. the lipid milieu provided by the liposphere, which may facilitate the bioactive's ability to alleviate psoriasis while minimizing adverse effects<sup>29</sup>. To

overcome the limitations of plant bioactives for increased activity, the next section describes the potential plant bioactive, their anti-psoriasis mechanism, and the nano-formulations used<sup>20</sup>.

***Psoralea corylifolia*:** Psoralen, the main bioactive component of *Psoralea corylifolia* (Babchi), a traditional medicinal plant, has antibacterial, antioxidant, anti-inflammatory, and anti-psoriatic properties. However, oxidation, degradation, skin irritation, toxicity, and poor skin permeability limit the clinical use of psoralen. To address these problems, delivery systems based on nanocarriers have been developed<sup>35</sup>. Psoralen-loaded liposomes made via thin-film hydration enhanced the toxicity-free penetration, skin adhesion, and retention of PUVA therapy. Cationic and anionic lipid-based liposomes decreased inflammatory markers (IL-17, IL-22), improved medication penetration beyond the stratum corneum, and more successfully decreased PASI score. Ethosomes that contained ethanol increased the buildup of psoralen skin (6.56 times greater than tincture), boosted membrane permeability, and offered improved therapeutic efficacy with less cytotoxicity<sup>53</sup>. In contrast to tincture, in vivo investigations verified greater bioavailability (C<sub>max</sub> and AUC). Babchi oil (BO) encapsulated in  $\beta$ -cyclodextrin nanostructures provided sustained release, enhanced stability, decreased irritation, and antioxidative benefits against psoriatic pathways linked to ROS. Liposomes, ethosomes, and  $\beta$ -cyclodextrin nanogels are examples of nanocarriers that, when combined, greatly improve psoralen distribution, increase therapeutic efficacy, reduce side effects, and have promise for managing psoriasis<sup>55</sup>.

***Nigella sativa*:** In *Nigella sativa* (black cumin, Ranunculaceae), the main bioactive component is thymoquinone (TQ), which has potent anti-inflammatory, anti-psoriatic, and antioxidant properties. Although recurrence was observed in certain patients after treatment, clinical investigations have documented therapeutic effects for psoriasis. The hydrophobicity, low stability, low bioavailability, and limited skin penetration of TQ limit its therapeutic usage<sup>40</sup>. Formulations based on nanocarriers have been investigated as a means of overcoming these constraints. With their ideal particle size (~84 nm), high drug entrapment (~81%), and better dermal flow, Ali et al. created TQ-loaded lipid nanoparticles (TQNPs), which showed improved drug delivery and decreased skin irritation. Similarly, Jain et al<sup>15</sup>. demonstrated improved clinical efficacy, prolonged retention, and higher biocompatibility by encapsulating TQ in lipospheres (~70 nm). In vitro investigations employing a model of imiquimod (IMQ)-induced psoriasis shown notable decreases in TNF- $\alpha$  and IL-17 expression in addition to improvements in lesion shape<sup>20</sup>. Nanocarriers' lipidic environment enhances TQ absorption, retention, and anti-inflammatory properties, which in turn lowers cytokine release and

keratinocyte proliferation. All these results point to the potential of nanocarrier-based TQ formulations as psoriasis treatment approaches<sup>23</sup>.

**Curcumin longa:** By reducing cytokines (IL-2, IL-12, IL-17, IL-22, IL-23, TNF- $\alpha$ , and IFN- $\gamma$ ) and phosphorylase kinase activity in keratinocytes and T-cells, curcumin (Cur), the primary bioactive of *Curcuma longa*, has potent anti-inflammatory, anti-proliferative, and anti-psoriatic actions. Its low skin permeability, photosensitivity, and poor water solubility, however, limit its therapeutic use<sup>17</sup>. Numerous tactics based on nanocarriers have been devised to get around these obstacles: Alginate/chitosan nanoparticles (Cur-CS/Alg NPs): TNF- $\alpha$ -induced HaCaT cells exhibit enhanced photostability and cooperative anti-proliferative effects when exposed to blue light. Hyaluronic acid-modified ethosomes (HA-ES) decreased pro-inflammatory cytokines significantly in psoriatic animals, improved skin-targeted distribution, and increased Cur retention<sup>54</sup>. High encapsulation efficiency, prolonged release, and effective dermal penetration are characteristics of PLGA nanoparticles (Cur-PLGA NPs, 50–150 nm), which lower inflammatory indicators and alleviate clinical symptoms. Superior clinical improvements (scaling, redness, thickness) were demonstrated by the curcumin-tacrolimus liposphere gel, which increased skin permeability and decreased keratinocyte proliferation<sup>25</sup>. Comparing imiquimod-curcumin nanoemulgel (IMQ-Cur-NEG) to IMQ alone, the latter showed improved drug retention and penetration, regulated immune responses, and postponed the onset of psoriasis-like symptoms. Overall, curcumin-based nanocarriers enhance therapeutic efficacy, stability, solubility, and epidermal penetration, making them viable options for the treatment of psoriasis<sup>17</sup>.

**Capsicum annuum:** One of the main alkaloids found in *Capsicum annuum*, capsaicin (CAP), targets several inflammatory pathways to produce potent anti-psoriatic actions. Through TRPV1-mediated mechanisms, CAP depletes Substance-P (SP) in the skin microvasculature, lowering angiogenesis, inflammation, keratinocyte hyperproliferation, and vasodilation<sup>20</sup>. Its therapeutic success in psoriasis is also attributed to its inhibition of TNF- $\alpha$ , which suppresses NF- $\kappa$ B activation. Low skin permeability and low solubility are problems for CAP. Furthermore, local discomfort (burning and stinging) limits its topical usage and lowers patient compliance<sup>55</sup>.

Emulsions, liposomes, and niosomes: Using a thin-film hydration technique, Gupta et al. (2014) created emulsified gel formulations of CAP with cholesterol, span 80, and soy phosphatidylcholine. These nano-systems demonstrated a high encapsulation efficiency (~83.8%), better penetration (~20.36  $\mu$ g/cm<sup>2</sup>/h), and significantly increased stratum corneum (SC) retention (almost 4-fold)<sup>23</sup>. At hyperproliferative skin areas, this promoted increased CAP

accumulation while reducing adverse consequences. Nanostructured lipid carriers (NLCs) and solid lipid nanoparticles (SLNs) made by solvent diffusion were contrasted<sup>19</sup>. With an encapsulation efficiency of approximately 87.4% compared to 79.7% for SLNs, a significantly higher drug loading capacity ( $7.5 \times$  vs  $6.2 \times$ ), a smaller size ( $\sim 145$  nm), improved skin permeation and retention, a lower water content (which improves occlusion), and improved occlusive effects—which allow for better localization at the drug–SC interface—NLCs outperformed SLNs<sup>45</sup>.

***Smilax china***: The Liliaceae family includes *Smilax china*. Quercetin is a flavonoid that has anti-inflammatory, anti-psoriatic, and antioxidant qualities and is present in the plant part's meth-anolic extract<sup>49</sup>. Quercetin's anti-psoriatic properties result from 16/10 necrosis factor (TNF) downregulating NF-kB transcriptional activation on proinflammatory gene promoters<sup>36</sup>. The primary disadvantage that restricts its therapeutic potential is photosensitivity and limited penetrability, despite its possible anti-psoriatic properties. Liposomes, lipid nanocapsules (LNC), and smart crystals were the three methods Hatahet et al. (2018) employed to manufacture nano-formulations<sup>40</sup>. A monocyte cell line (TPH-1) and a keratinocyte cell line (HaCaT) were used to analyse and compare the effects. The related investigation found that quercetin, at a dosage of 5 g/ml, had the highest cellular viability on HaCaT cells<sup>56</sup>. While quercetin smart crystals showed a high degree of skin deposition retention in the upper outer part of SC, indicating that they could be used as sunscreen, LNC was able to penetrate the viable epidermis and help treat autoimmune diseases like psoriasis<sup>10</sup>.

***Woodfordia fruticosa***: The Lythraceae family includes the leafy shrub *Woodfordia fruticosa* (*W. fruticosa*, WF), which is well-known for its potent bioactive components (flavonoids, glycosides, tannins, and phenolics) that aid in the treatment of psoriasis. Nevertheless, a higher PASI score and erythema and scales diminish the therapeutic benefit<sup>9</sup>. The flower extract of WF was utilized by Raghuwanshi and associates (2019) to target HSP70-1 (heat shock protein 70-1), which can reduce psoriasis. The scientists produced biogenic gold nanoparticles of WF extract (WFAuNPs) and concluded that the biogenic nanostructured formulation they produced might be a useful substitute for treating psoriasis<sup>18</sup>. When WFAuNPs in the 10–20 nm size range are added to the Carbopol 934 gel, they significantly reduce epidermal thickness, parakeratosis, and keratinocyte hyperproliferation, minimize TNF- $\alpha$ , IL-22, and IL-23 serum cytokines, and lower the mean DAI (disease activity index) score of  $0.63 \pm 0.08$  and PSI (psoriasis symptom inventory) score<sup>20</sup>.

***Tripterygium wilfordii***: "Lei Gong Teng," or *Tripterygium wilfordii*, is a member of the Celastraceae family of herbs. One pentacy-clic triterpene in the herb, celastrol (Cel), is thought

to have anti-inflammatory, antioxidant, and anti-tumor properties. Based on its ability to suppress Th17 cell growth through pSTAT3 activation and induce macrophage death through the NF-kB mechanism, Cel is believed to have anti-inflammatory characteristics<sup>19</sup>. Its low permeability and poor water solubility, however, limit its therapeutic potential. The application of a topical delivery approach based on nano carriers could enhance the solubility and biocompatibility of cells. Using the thin-film hydration technique, Meng et al. (2019) produced niosomes with cholesterol, span 20, and 60 in a 3:1:1 ratio and evaluated the essential characteristics<sup>57</sup>. An outstanding outcome in conquering the difficulties of plain Cel was indicated by the particle size of  $147.4 \text{ nm} \pm 5.6 \text{ nm}$ , the zeta potential of  $-48.9 \pm 1.1 \text{ mV}$ , and the PDI of  $0.258 \pm 0.02$ . Additionally, the hydrogel served as a core carrier to keep SC hydrated and prolong the topical medication's time on the skin. According to a study on in vitro penetration, the drug content of Cel Nio gel in the skin was almost 13 times greater than that of Cel hydrogel<sup>18</sup>. Moreover, because it can enhance Cel solubility and reduce erythema and scaling on the dorsal skin, Cel Nio gel has an in vitro penetration of  $465.3 \pm 84.1 \text{ ng/cm}^2$ . Niosomes have the potential to adsorb to keratin filaments and promote lipid fluidity, which in turn increases Cel permeability. Through the inhibition of keratinocyte growth, the Cel may decrease the amounts of IL-22, IL-23, and IL-17 in the epidermis, hence reducing the creation of chemokines and the aggregation of inflammatory cells<sup>58</sup>.

**Table 3: Natural plant-based products' anti-psoriatic properties**

<b>The Plant's Name with Significant Traits</b>	<b>Mechanism of Work</b>	<b>Medication Administration Methods Regarding Treating Psoriasis</b>
<i>Aloe Vera</i> Phytochemical <i>Aloe-emodin, Barbaloin</i>	Inhibiting specific enzymes that contribute to inflammation, cell division, mitochondrial damage from redox reactions, lipid degradation in psoriatic epidermal membranes, etc.	Emulgel, barbaloin gel and hydrophilic lotion, and chitin nanogel with aloe emodin
<i>Longa curcuma</i> the plant compound curcumin	• Disintegrated nucleus of cells became more numerous. Caspases 9 and 8 are stimulated,	Systems of liquid crystals, Liposomal gel, a nanoparticle with collagen

	<p>mitochondria release cytochrome c, Inhibit extracellular regulated kinases 1/2 and suppress the activity of protein kinase B and NF-κB.</p> <ul style="list-style-type: none"> <li>•Cut down on Akt and ERK phosphorylation levels.</li> </ul> <p>Lower the extent to which TNF-α, mRNA for IL-17A, 22, 17F, 6, 1, and TNF-α while raising those of involucrin and filaggrin. R1/R2 TRAIL expression should be increased in HaCaT cells while inhibiting the generation that TNF-α causes IL-6/8.</p>	<p>patches that are porous, Curcumin-Loaded Hyaluronan-Modified Ethosomes, Topical Gel Loaded with Nano sponge, Nanostructured Lipid Carriers (NLC), Hydrogel made from silk fibroin and polymeric nanoparticles, cellulose nanofiber (CNF), nanogel, nanoemugel, and polymeric hydrogel Curumin Nanoparticles, Liposphere Gel, Turmeric Microemulgel, and Nanoemulsion Gel</p>
<p><i>Capsaicin</i> annually Plant-based capsaicin</p>	<p>Decrease in the amount of substance P present in the local sensory nerve terminals. One neuropeptide with strong vasodilator properties is substance P. It's possible that capsaicin inhibits its vasodilatory effects.</p>	<p>Carbopol gel, emulsomes, niosomes, and liposomes are vesicular systems filled with capsaicin, lipidic nanoparticles, Nanoparticles of Silver Loaded with Capsaicin, Cubosomes, Namomemgel, hypermerized lipid-polymer nanoparticles loaded with capsaicin albumin nanoparticles, packed with capsaicin nanolipoidal carriers.</p>
<p><i>Sativa</i> <i>nigella</i> Kaempferol and</p>	<p>Quercetin inhibits the synthesis of IL-1, 6, 8, and TNF-α by UV in human keratinocytes, the activation</p>	<p>Liposphere Gel Loaded with Quercetin and Commiphora Mukul</p>

<p>quercetin are phytochemicals.</p>	<p>of BV-2 microglia by IFN-<math>\gamma</math>, and the expression of NF-kB, STAT-1, and iNOS by LPS. While increasing psoriasis, kaempferol reduced erythema, scaling, and thickness, PASI scores, Th17 development, IL-17A, 6, and TNF-mRNA levels in mice. Expression of the genes CD4 + FoxP3 + Tregs and FoxP3 and IL-10. In addition to inhibiting Multiplication of T cells and mTOR signaling, kaempferol decreases psoriatic NF-B signalling.</p>	
<p>Rutin, Luteolin, and Kaempferol are phytochemicals found in <i>Givotia rottleriformis</i>.</p>	<p>Prevent the split of keratinocytes.</p>	<p>Rich in Gallic Acid and Rutin Herbal Gel.</p>
<p><i>Ginkgo biloba</i>, <i>Selaginella nipponica</i>, <i>Selaginella tamariscina</i>, and <i>Selaginella pachystachys</i> phytochemical amyoflavone (AMF)</p>	<p>In M5-treated HaCaT cells, inhibiting expression of mRNA reduced thickness of the skinfold, dropped growth of cells, sped up apoptotic, furthermore inhibited the synthesis of IL-17A, 22 and cyclin D1 and E. Additionally, AMF reduced the overexpression of p65 NFKB in psoriasis.</p>	<p>TPGS/soluplus mixed nanomicelles loaded with amenoflavones</p>
<p><i>Magnesium chamomilla</i> with <i>Hypericum perforatum</i> Flavonoids and</p>	<p>The flavonoid inhibits NF-kB along with lowers IL-8 and E-selectin levels. Human mast cells (HMC-1) produce cytokines that cause inflammation (GM-CSF,</p>	<p>Cream and Ointment</p>

Apigenin (Biapigenin) are phytochemicals	TNF- $\alpha$ , and IL-6 & 8) in response to apigenin's.	
<i>Capillaries of Artemisia</i> and <i>Artemisia annua</i> Artesunate and essential oils are phytochemicals.	Restrain the thickness of the epidermis, immune-regulatory mechanisms, apoptosis, differentiation, and proliferation.	Cream
<i>Hydrocotylasiatica</i> , also known as <i>Centella Asiatica</i> Asiaticoside and Madecassoside are phytochemicals	It is necessary to prevent keratinocytes from replicating.	Extract in water, silver nanoparticles
<i>Smilax glabra</i> The phytochemicals luteolin and astebin	Reduced TNF-driven activation of HaCaT along with enhanced keratinolytic growth of TNF- $\alpha$ , IL-2, IFN- $\alpha$ , and 6, 17A production by CD4 CD81 T cells. (138) Aspirin prevents Th17 cell development, isolates T cells' IL-17 release, and stops Th17 cells' Jak/Stat3 signalling.	Microemulsion, Liposomes
<i>Scutellaria baicalensis</i> Phytochemical Baicalin	Baicalein increased the expression of the K1/K10 keratins 1 and 10 and inhibited the development of keratinocytes while causing morphological differentiation.	-
<i>Mahonia aquifolium</i> Plant-based chemicals Jatrorrhizine, corytuberine, oxyberberine, berberine (isoquinoline	Berberine suppresses cellular development by intercalating into DNA, inhibits autoreactive Th1 and Th17 cells, and inhibits keratinocyte growth inhibitor. It also reduces dermal and epidermal T cell invasion.	Herbal ointment, gel

<i>alkaloid), and columbamine</i>		
<i>KBA, also known as 11-ketob-boswellic acid, and AKBA, also known as acetyl-11-ketob-boswellic acid, are phytochemical boswellic acids found in Boswellia serrate.</i>	Leukotriene synthesis is prevented (5-LO) via blocking 5-lipoxygenase.	Nano Gel, cream, and Bosexil
<i>Coffea Arabica, Cola acuminata, and Camellia sinensis are phytochemicals that contain caffeine.</i>	Psoriasis progresses more slowly when caffeine is consumed because it lowers the activation of inflammatory pathways.	Topical gel coated with nanosponge, both nanostructured lipid carriers (NLCs) and solid-lipid nanoparticles (SLNPs) respectively.
<i>Camptotheca acuminata</i> <i>Phytochemical Camptothecin, isocamptothecin</i>	Keratinocytes and antiproliferative apoptosis are caused by downregulating telomerase activity.	Extract, tincture, and ointment
<i>Δ9-Tetrahydrocannabinol, cannabis sativa</i> <i>phytochemicals, cannabinol, cannabidiol, and cannabigerol</i>	HPV-16 E6/E7 transformed human skin keratinocytes, or hyperproliferating human keratinocytes were less likely to proliferate.	Transdermal patches, hydrophilic gel, and ointment
<i>Deltanidin is a phytochemical found in the blue-berry Vaccinium sect. Cyanococcus</i>	Pathological markers of the psoriasiform lesions have decreased, along with inflammation-causing cell infiltrationPI3K/Akt, mTOR	The solution

	inhibition, and the expression of inflammatory cytokines in both mRNA and protein.	
<i>Burm from Embelia Ribes Plant The emblem</i>	By directly affecting pro-inflammatory cytokines, it reduces skin thickness and weight and inhibits the generation of IL-1, TNF- $\alpha$ , and neutrophil-mediated myeloperoxidase activity.	Extract
<i>The phytochemical Toddacoumalone is found in Toddalia asiatica (L.) Lam. (T.aculeata Pers.).</i>	Moderately potently prevent PDE4, and The lipopolysaccharide-induced RAW264. Seven cells also exhibit inhibition of the production of cytokines that cause inflammation (TNF- $\alpha$ and IL-6).	Ointment

### Treatments for psoriasis using herbal and polyherbal nano-formulations

The loss of skin ceramide and barrier functions causes poor water absorption and hydration capacity when the skin is affected by psoriasis, which is why traditional dosage forms like gels, ointments, creams, tinctures, and lotions have poor or acceptable therapeutic efficacy for natural drug products<sup>40</sup>. Therefore, the drugs themselves must have the appropriate degree of permeability and water-holding capacity to provide the greatest therapeutic benefit when used to treat psoriasis (Table 4)<sup>51</sup>. Furthermore, new drug delivery technologies like liposomes, lipospheres, NE, crystals, spheres, niosomes, ethosomes, microneedles, and foams can be used to increase skin penetrability, have hydration power, and target inflammatory cells or cytokines with natural drug products<sup>46</sup>. Figure 3 outline the treatments for psoriasis using herbal nano formulations.

**Table 4. The Function of Herbal-Based Medication Delivery Method in the Management of Psoriasis.**

Sl. No.	Extract and Plant-Based Substances	Nanoparticle	Method	Extract and Plant-Based Substances	Nanoparticle
01.	255 µg/m is the IC50 value for ethanolic seed extract, babchi oil (Psoralea), and <i>Psoralea carylifolia</i>	Gel-based liposomes	Hydration of thin films	Male BALB/c mice weighing 20–25 g and 8–11 weeks of age	<ul style="list-style-type: none"> <li>• 100 nm particle size.</li> <li>• Cationic liposomes have a zeta potential of 75.12%, anionic liposomes have a -28.5 mV, and 60.08%.</li> <li>• Exhibits a five-fold increase in permeability and a decrease in tumor necrosis factor-<math>\alpha</math>, IL-17, and IL-22.</li> </ul>
02.	<i>Colchicum autumnale</i> , or colchicine	Liposomes	Sounding	Wistar rats weighing between 150 and 200 g	<ul style="list-style-type: none"> <li>• Continuous supply.</li> <li>• Increased epidermal deposition (12.5 times) in</li> </ul>

					<p>comparison to the medication solution alone.</p> <ul style="list-style-type: none"> <li>• Enhance long-term medication administration, skin absorption, and site-specificity.</li> </ul>
03.	<p>IC<sub>50</sub> = 254 +/- 28 nM for capsaicin (CAP) and <i>Capsicum annum</i></p>	<p>Studying the differences between niosomes, liposomes, and emulsions</p>	<p>Hydration of thin films</p>	<p>In albino rats, the dorsal skin</p>	<ul style="list-style-type: none"> <li>• Limits the production of NF-kb, which inhibits TNF-<math>\alpha</math>. Plain medication versus lipogel.</li> <li>• After 24 hours, it entered via the epidermis (mg/cm<sup>2</sup>) (19.67 <math>\pm</math> 1.65 vs. (7.34 <math>\pm</math> 1.04).</li> <li>• Comparing the ordinary medication (8.26 <math>\pm</math> 1.02) with the skin</li> </ul>

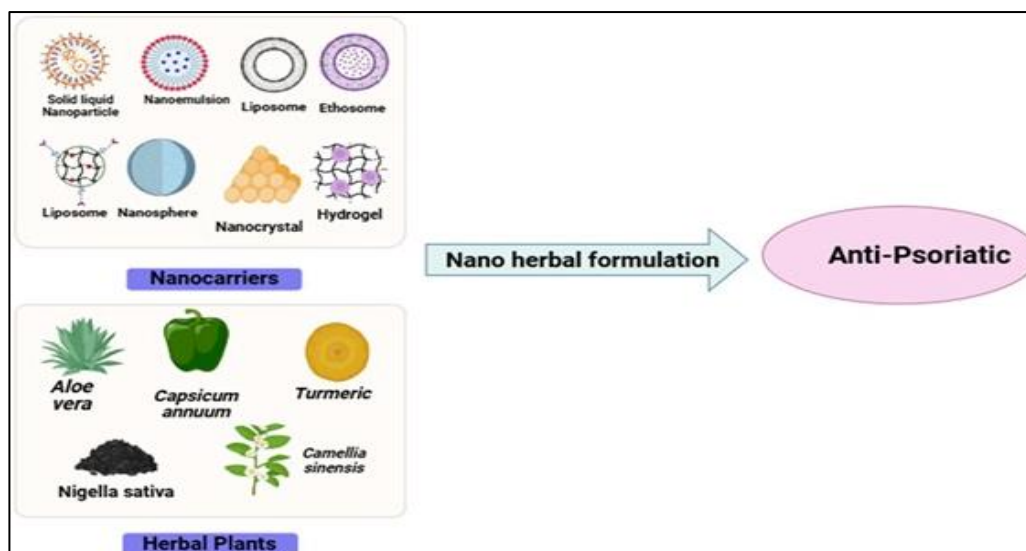
					<p>accumulation lipo gel (23.02 ± 2.39).</p> <ul style="list-style-type: none"> <li>• Size, PDI, and %EE (70.98 ± 2.36, 0.136 ± 0.024, and 368.5 ± 43 nm, respectively).</li> </ul>
04.	IC50 value of 255 µg/ml for ethanolic seed extract of Psoralen- <i>Psoralea carylifolia</i>	Ethosomes	Straightforwardly altered injection	Sprague-Dawley male rats weighing 180–220 g	<ul style="list-style-type: none"> <li>• Increased skin psoralen deposition (6.56-fold).</li> <li>• Skin deposition, penetration, effectiveness, and toxicity.</li> </ul>
05.	255 µg/ml is the IC50 value for ethanolic seed extract of Psoralen and <i>Psoralea carylifolia</i> .	An analysis that compares liposomes with ethersomes	The work of Touitou	Male Sprague-Dawley rats weighing 180–220 grams	<ul style="list-style-type: none"> <li>• ↑ Psoralen is effectively delivered to human immortalized epidermal cells using liposomes.</li> <li>• Ethamome's ability to effectively transport to human</li> </ul>

					embryonic skin fibroblast cells is demonstrated.
06.	Celastrol, or <i>Tripterygium wilfordii</i>	Niosomes	Hydration of thin films	Women C57/BL6 mice (18~22 g and ages 7-9 weeks).	<ul style="list-style-type: none"> <li>• Comparing in vitro permeability to drug-alone.</li> <li>• ↓Cytokine levels (IL-22, 23, and 17) with erythema and scaling.</li> </ul>
07.	Ammonium glycyrrhizinate	Niosome	Thick-layer evaporation	CD-1 male mice weighing 25–30 g.	8- Safety and good skin tolerance. The anti-inflammatory of 9.
08.	The IC50 value for thymoquinone (TQ) is 23.9 µg/ml.	EVs (ethosomal vesicles)	Cold technique	Swiss albino mice weighing 20–25 grams	According to TQ EV and TQ, cumulative drug skin penetration was 36.62 ± 2.01% and 11.60 ± 1.07, respectively, and the quantity

					retained in the skin was $88.71 \pm 3.02 \mu\text{g}/\text{cm}^2$ and $72.86 \pm 3.01$ .
09.	IC50 values for tea tree oil, <i>Melaleuca alternifolia</i> , and terpinen-4-ol	Microemulsion	-	Swiss albino mice weighing 25–35 grams.	Improved absorption of medications - Tea tree oil (5%) is harmless for the skin.
10.	Oil of Turmeric	Microemulsion	Titration	Carrageenan from murine. Male (150–180 g) Spaghe-Dawley rats.	Non-irritating and steady during the research period.
11.	Both caffeine and curcumin	Nano-structured lipid transporter	Hot homogenization, as well as ultrasonography.	Both sexes of healthy BALB/c mice (8–11 weeks).	<ul style="list-style-type: none"> <li>• Inhibited thickness in both epidermal and subcutaneous tissues is revealed by histopathology investigations. -</li> <li>↓ Key psoriasis symptoms and treatments -</li> <li>Indicate compatibility and non-irritability.</li> </ul>

					<ul style="list-style-type: none"> <li>• <math>40\% \pm 1.72\%</math>– <math>63.92\% \pm</math> <math>1.06\%</math> %EE.</li> </ul>
12.	Capsaicin	A comparison analysis of NLCs and SLNs	Diffusion method of solvents	The albino rat's dorsum	<ul style="list-style-type: none"> <li>• Reduce inflammation of the skin.</li> <li>• Due to their larger flaws, NLCs have a 7.5-fold higher drug loading capacity with fewer drug expulsions than SLNs and simple drug solutions (6.2-fold).</li> </ul>
13.	<i>Woodfordia fruticosa</i>	AuNPs, or gold	The in-silico straining technique.	Swiss albino mice, 15–16 weeks old, weighing 20–30 grams.	<ul style="list-style-type: none"> <li>• <math>\downarrow</math> IL-22, IL-23, and TNF<math>\alpha</math>.</li> <li>• <math>\downarrow</math> Parakeratosis, thicker epidermis, and increased keratinocyte proliferation.</li> </ul>
14.	European black elder berry	AgNPs, or silver nanoparticles	Green synthesis technique	Wistar male rat, 3 months old, weighing	<ul style="list-style-type: none"> <li>• The IC<sub>50</sub> value for cell viability was 79.4 <math>\mu</math>g/ml.</li> <li>• Cytokine production has</li> </ul>

				110–130 grams.	<p>an in vitro anti-inflammatory impact, although keratinocytes' IL-1 gene is.</p> <ul style="list-style-type: none"> <li>• There is a lowering of IL-1,6 in vivo that has a stable protective effect.</li> </ul>
15.	The extract of <i>Cornus mas</i> with chloroauric acid	Silver and Gold NPs	Green synthesis technique	Human epidermis	<ul style="list-style-type: none"> <li>• NO, IL-12, and TNF-<math>\alpha</math> are released.</li> <li>• Minimally harmful effects on culturing cell lines.</li> <li>• When it comes to penetration, Au-NPs outperform Ag-NPs.</li> </ul>



**Figure 3. Treatments For Psoriasis Using Herbal Nano Formulations**

### Boost the permeability of the skin

**Liposomes:** Liposomes could let medications penetrate through the stratum corneum, the skin's barrier, and more effectively reach the afflicted tissues. Drugs can be better absorbed via the skin and shielded against deterioration by liposomes. Liposomes have the potential to reduce systemic adverse effects linked to oral or injectable treatments by delivering chemicals directly to the afflicted location<sup>39</sup>. Multiple anti-psoriatic drugs can be delivered via liposomes, which could improve the therapeutic efficacy and target various facets of the condition. To maximize medication transport and targeting, liposomes can be modified with a variety of elements, including as surface alterations and the addition of permeation enhancers<sup>26</sup>.

Thus, Doppalapudi created liposomal nanocarriers with psoralen, which entails attaching the nanocarrier to gels to improve skin adherence and water-holding ability. While liposomal gels were able to penetrate the SC barrier, the psoralen solution remained restricted to the upper SC. In SC, intracellular lipids may be integrated into the liposome bilayer structure during skin interaction, enhancing the diffusion of liposomal molecules into skin cells while preserving the multi-bilayer structure<sup>59</sup>.

In the liposomal formulation, dithranol is enclosed in phospholipid liposomes. It has been demonstrated in early experiments that this formulation leaves very little discoloration on skin or clothing and causes very little physical irritation. With nearly no local side effects, 0.5 percent liposomal dithranol gel was found to be just as effective as 1.15 percent dithranol cream in treating stable plaque psoriasis. Due to its ease of washing and little staining of skin and fabric, dithranol lipogel is more palatable to patients and physicians than currently available formulations<sup>17</sup>.

Engineering marvels, liposome and micelle-based formulations aim to increase the solubility and stability quotient of herbal ingredients. Herbal agents are made more bioavailable and easier to penetrate the skin thanks to liposomes, which are encased in lipid bilayers, and micelles, which are made of amphiphilic molecules. These cutting-edge compositions are excellent at delivering herbal antioxidants and anti-aging elixirs, combating oxidative stress and improving the health of the skin<sup>60</sup>.

**Ethosomes:** Ethosomes are flexible vesicles composed of phospholipids (usually in concentrations between 0.5 and 10%), water, and ethanol (usually in concentrations between about 20 and 50 percent of ethanol content). Unlike regular liposomes, ethersomes target the deeper layers of the skin, causing more long-term deposition but less initial skin deposition<sup>61</sup>. Since the ethanol in ethersomes may create an ionic link with the water-soluble functional group of the skin's lecithin molecules, the lipids' melting point is lowered in the subcutaneous layer (SC), increasing their fluidity and ability to traverse cell membranes. Since ethersomes are highly elastic and deformable, they might be able to pass through skin channels that are smaller than the vesicle's diameter<sup>20</sup>.

Psoralen-loaded ethosomes showed 6.56 times greater skin deposition than tincture, suggesting enhanced skin penetration and deposition for lower toxicity and longer-term efficacy. The drug concentration in the dermis was higher with this formulation than with a tincture. The use of ethosomal vesicular systems may enhance drug solubility, retention, and penetration<sup>62</sup>. This is why thymoquinone (TQ) ethosomal gel has demonstrated encouraging outcomes in psoriasis treatment. Given curcumin's poor water solubility and HA's ability to target the CD44 protein in inflammatory epidermis, it's a good organic ligand<sup>12</sup>. Targeting the CD44 protein found in the inflammatory epidermis, HA Ethosomes is the newest topical delivery technology. As a result, the therapy of psoriasis has seen a rise in therapeutic action and a decrease in harmful effects<sup>10</sup>.

Anthralin-loaded ethosomal preparations were created utilizing a straightforward procedure to improve the drug's safety and effectiveness, and they were subsequently contrasted with liposomes. Ex-vivo permeability assays revealed that the anthralin ethosomal gel penetrated the rat abdominal skin significantly more than the drug liposomal gel<sup>21</sup>. The PASI ratings indicated that ethosomes were more effective than liposomes. The findings indicate that the anthralin ethosomal gel developed by the researchers may enhance the medication's efficacy and safety in psoriasis sufferers<sup>4</sup>.

With the "modification-encapsulation" process, multifunctional ethosomes modified with curcumin-loaded glycyrrhetic acid-D-a-tocopherol acid polyethylene glycol succinate (GA-

TPGS) was successfully produced. When multifunctionalized ethosomes are used as permeation enhancers and solubilizers, curcumin and glycyrrhetic acid absorption and loading are enhanced<sup>27</sup>. IL-6-stimulated HaCaT cells and mice showed mild anti-inflammatory and antioxidative effects in both in vitro and in vivo experiments. In summary, multifunctionalized ethosomes based on the "modification-encapsulation" technique may be able to treat psoriasis in combination, offering a novel idea for therapies that combine synergistic therapy and benefit from the system's efficient co-delivery of Cur and glycyrrhetic acid<sup>3</sup>.

**Niosomes:** A thicker stratum corneum, a characteristic of psoriasis, can restrict the effectiveness of topical therapies. Given their size and shape, niosomes may be able to get past this barrier and more efficiently carry medications to the skin's deeper layers. When skin enzymes or other environmental variables are present, herbal extracts may degrade. These active substances may be protected by niosomes, maintaining their activity and enhancing their therapeutic effectiveness<sup>1</sup>. It is possible to build niosomes to target skin layers, like the dermis or epidermis. This can help to maximize the medication's effectiveness at the location of inflammation while lowering the total dosage required. Because they are big or poorly soluble in lipids, many herbal chemicals are poorly absorbed via the skin. These substances' bioavailability can be greatly enhanced by encapsulating them in niosomes, which will raise concentrations at the site of action<sup>16</sup>. To provide a long-lasting effect, niosomes can be engineered to release their contents gradually. For the treatment of psoriasis's chronic inflammation, this can be especially helpful. By preventing the active ingredients from degrading and lowering the possibility of precipitation or sedimentation, niosomes can increase the stability of polyherbal compositions<sup>2</sup>.

Niosome formulations with a Box-Behnken design (3-factor, 3-level) have demonstrated that topically applied niosomes may provide a customized diacerein dosage for enhanced psoriasis therapy, potentially eliminating the adverse side effects associated with systemic exposure<sup>15</sup>. Encapsulating celastrol in niosomes increased the drug's polarity and epidermal penetration in mice, significantly improving its efficacy in treating psoriasis. Treatment for psoriasis can be achieved effectively by incorporating acitretin into niosomes for topical delivery. The amount of medication that would be absorbed through injured skin would be controlled by this method<sup>63</sup>.

**Nanohydrogel:** An IMQ-induced psoriasis model was used to demonstrate the effective anti-psoriasis properties of a nanohydrogel made by the micellar Choline-Calix [4] arene (CALIX and CUR) and curcumin (CUR) with no toxicity. Curcumin's anti-inflammatory properties are

maintained when it is trapped in a calixarene-based hydrogel due to the nanohydrogel's capacity to solubilize it and shield it from rapid degradation<sup>64</sup>. When opposed to conventional medicines, curcumin's usual properties-such as skin dispersibility, stickiness, and perforation-may provide a novel administration route for the anti-psoriatic strategy that enhances patient satisfaction while simultaneously increasing effectiveness and comfort<sup>5</sup>.

**Nanogel:** A topical nanogel containing two distinct anti-psoriatic medications-Acitraetin (Act) and Aloe-emodin (AE)-is developed in this work. Using basic regeneration chemistry, Chitin Nanogel Systems (CNGs) were developed. In the in vitro hemolysis assay, all of the Nanogel systems-control chitin (CNGs), acitraetin-loaded (Act CNGs), and aloe-emodin-loaded (AECNGs)-were compatible with blood. System release and edema are increased by an acidic PH<sup>65</sup>. System accumulation at the epidermal and dermal layers was elevated, according to fluorescence imaging and ex-vivo pig skin penetration tests. In psoriasis skin safety studies and Perry's mouse tail model, acitraetin and aloe-emodin proved to be helpful<sup>6</sup>.

**Liquid crystalline nano reservoir:** This work created Berberine Oleate (Brb-OL) loaded Liquid Crystal Nanoparticles (LCNPs) using the hydrotrope technique (Brb-OL-LCNPs). The amount of Brb collected in the skin of rats treated with Brb-OL-LCNPs was three times greater than that of pure Brb. When Brb-OL-LCNPs hydrogel was applied to the skin in an in vitro model of psoriasis, the disease's symptoms and inflammatory cytokines were reduced<sup>66</sup>.

**Metallic nanoparticles:** Silver and gold nanoparticles complexed with the plant extract *Cornus mas* (AgNPsCM and AuNPsCM, respectively) were used topically to regulate the inflammatory reactions associated with the skin. Nanoparticle exposure caused proinflammatory macrophages to generate NO, TNF- $\alpha$ , and IL-12; AuNPsCM was more effective than AgNPsCM. Their smaller size, which permits higher cell penetration and activity, may be the reason for Au-NPs' differing efficacy (13-52 nm) compared to Ag-NPs (9-82 nm)<sup>67</sup>.

**Liposphere:** Unlike traditional creams, Liposphere can more deeply penetrate the skin to more efficiently reach the afflicted areas. Their construction ensures a long-lasting therapeutic impact by allowing the encapsulated herbal components to release gradually and continuously. Psoriasis is a chronic ailment that needs regular treatment to control its symptoms; therefore, this prolonged release can be especially helpful. The bioavailability and absorption of herbal extracts can be improved by lipospheres, resulting in a stronger and more efficient treatment<sup>7</sup>. Because the encapsulated herbal ingredients are shielded from deterioration, their stability and efficacy upon skin contact are guaranteed. The likelihood of irritation or negative reactions is reduced because lipospheres are often well-tolerated by the skin. Better integration and

compatibility are promoted by their ability to replicate the skin's natural lipid layers thanks to their lipid-based nature<sup>68</sup>. The results demonstrated that the liposphere gel loaded with quercetin and Commiphora mukul enhanced the retention of both drugs in the dermal layer when compared to conventional cream. According to these results, a liposphere gel that contains a combination of quercetin and Commiphora mukul may be a successful and efficient treatment for psoriasis<sup>22</sup>. Though thymoquinone (TMQ) has anti-psoriatic capabilities, its hydrophobicity, limited water solubility, and sensitivity to light or pH make it hard to come by. A potential remedy for these delivery problems was thought to be lipospheres. Lipospheres offer a great, scalable, and reliable penetration technique when applied topically<sup>8</sup>. TMQ lipospheres were prepared and tested using particles with a diameter of less than 70 nm. These lipospheres enabled skin compatibility, slower absorption, and deeper skin penetration. In an in vitro model of psoriasis, lipospheres have demonstrated anti-inflammatory and anti-psoriatic qualities<sup>49</sup>. Cell line studies showed decreased levels of IL-2, 6, 1, TNF-a, and Nitric Oxygen; nevertheless, animal models with psoriatic skin showed improvements in phenotypic and histological features as well as decreased levels of TNF-a and Interlukin-17. Low solubility, inability to penetrate skin, and inconsistent absorption are issues with topical treatment of tacrolimus and curcumin<sup>69</sup>. To address these problems, tacrolimus and curcumin lipospheres, each with a particle size of around 50 nm, were created and mixed into a gel for topical application. The medications and the shear thinning behaviours were observed when the liposphere gel entered the epidermal layers. The phenotypic and histological features of psoriasis are improved by liposphere gel containing tacrolimus and curcumin<sup>9</sup>.

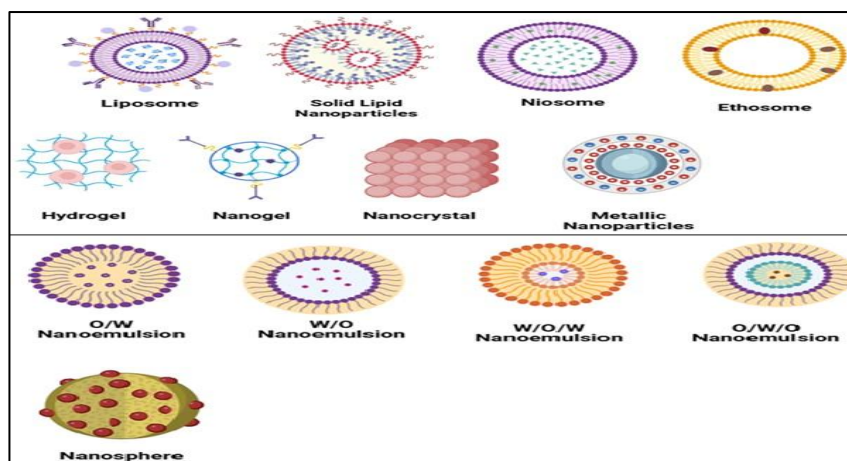
**Nano emulsion:** Since nano emulsions are kinetically stable, the active components will be delivered consistently over time since they are less likely to separate or degrade<sup>70</sup>. Because of the increased surface area of nano emulsion droplets, more active substances can be encapsulated. By enhancing distribution and decreasing the requirement for larger dosages, nano emulsions can lessen the systemic adverse effects linked to conventional therapies<sup>10</sup>. Good spread ability and a steady (biphasic) release pattern were characteristics of NE gel. In vitro results were favourable, and skin bioavailability increased 4.33 times<sup>71</sup>. The formulation proved to be more successful than the commercial formulation since in-vivo studies have demonstrated that NE reduces serum cytokines and improves psoriasis conditions<sup>10</sup>. A NE including curcumin, resveratrol, and thymoquinone was created to treat psoriasis. In experiments with Balb/c mice, an enhanced anti-psoriatic effect was demonstrated, where nanoemulgel formulation is effective in treating psoriasis<sup>23</sup>.

**Nanosphere:** Nanospheres are essential for improving the effectiveness of polyherbal psoriasis therapy formulations. Improved drug penetration, less adverse effects, and tailored administration to the skin are all benefits of using them. To ensure that the active components reach the intended location while reducing systemic absorption, they are encapsulated and protected<sup>72</sup>. Human immortalized keratinocyte (HaCaT) cells were used to examine the effectiveness of E/DMSN. The pore diameters ranging from 3.5 nm to 4.6 nm (DMSN2). The anti-proliferative and pro-tumor effects of these E/DMSNs were noticeably greater than those of free erianin<sup>73</sup>. Because tyrosine-derived nanospheres facilitate the transport of lipophilic substances into the skin through deeper layers, they may be useful for topical delivery applications. The tyrospheric transport of paclitaxel at concentrations more than 100 ng/cm<sup>2</sup> of skin surface area and an increase in the cytotoxicity of paclitaxel to keratinocytes may help treat psoriasis<sup>11</sup>.

**Foams:** As opposed to conventional ointments or creams, foams might enhance the way medications are absorbed into the skin. This is because a supersaturated solution produced by the quick evaporation of propellants in foams might boost the drug's thermodynamic activity and facilitate penetration<sup>13</sup>. By modifying foam-based drug delivery systems to include nanotechnology and other cutting-edge methods, drugs can be delivered more precisely to skin layers or even to inflammatory cells. Treatment for psoriasis can be made more natural and holistic by using foams as a delivery vehicle for polyherbal formulations. Patient preference for foams is frequently based on their quick onset of effect, simplicity of application, and aesthetic appeal<sup>74,12</sup>. The PSO-LONG trial was the first to demonstrate that Cal/DB foam therapy was both safe and effective over an extended period of time in a study for the management of psoriasis<sup>24</sup>. All patients with mild to severe psoriasis can benefit from Cal/BD aerosol foam's effectiveness and good tolerance. Due to its greater effectiveness and quicker effect on itching symptoms compared to other preparations, patients prefer this Cal/BD formulation. Consequently, Cal/BD aerosol foam is a great first-choice treatment for psoriasis sufferers, regardless of how severe their condition is<sup>75</sup>.

**Solid Lipid Nanoparticles and Nanostructured Lipid Carriers:** A plethora of benefits are offered by SLNs include improved skin penetrating capabilities, increased stability, and prudent drug release kinetics. When it comes to skin conditions like acne<sup>50</sup>. By encapsulating and delivering a variety of active herbal ingredients, these nanocarriers can produce synergistic effects and possibly lower the total dosage needed. With no risk of skin irritation or increased

skin deposition, the SLN-based gel formulation of Acitretin provides a safe and efficient method for topical administration<sup>40</sup>. Tetrahydro curcumin (THC)-containing lipidic nanoparticles (LNs) have been included into the base of an ointment that researchers have created using an animal model of psoriasis. This is why the novel THC-LNs ointment has depigmenting properties and is a safe and effective alternative to psoriasis therapies that are currently<sup>76</sup>. Thymoquinone (TQ) lipid nanoparticles (NPs) gave psoriasis patients a higher cutaneous flow ( $5.77 \mu\text{g}/\text{cm}^2/\text{h}$ ) and a delayed medication release ( $57.55\% \pm 5.38\%$ ). All three of these symptoms were shown to have decreased in the toxic control group's psoriatic model, as indicated by the PASI score and the primary irritation index score of 1.4, both of which were detected in the skin irritation inquiry<sup>77</sup>. NLCs with polydispersity index (PDI)  $<0.3$ , 100% entrapment efficiency, and particle sizes less than 300 nm were developed. In comparison to the negative control, the developed method decreased disease, severity, and the release of the cytokines ILs-17, 22, 23, and TNF- $\alpha$ . Nanostructured lipid carriers with caffeine and curcumin in a topical gel are more effective than commercially available formulations at treating psoriasis<sup>78</sup>. A 12-hour sustained medication release was offered via a topical gel based on an improved NLC-based formulation. NLC-based gel can lessen psoriasis more than previously believed, according to in-vivo studies and ex-vivo permeation tests. Those who suffer from psoriasis could find that a gel containing NLC provides a better and more efficient local treatment<sup>79</sup>. Figure 4 illustrates the kinds of distinct nanocarriers.



**Figure 4. Kinds of Distinct Nanocarriers**

### **Enhance the moisture power of skin**

**Microemulsions:** Microemulsions are essential in polyherbal psoriasis formulations because they improve the active components' bioavailability and skin penetration. A promising therapeutic technique, they enhance formulation stability, effectively deliver medications, and may lower cytokine and inflammatory levels(80). A microemulsion that contained salvianolic

acid B reduced the degree of acanthosis, inhibited the cytokines both interleukin-17 and interleukin-23, and diminished the severity of the illness (Figure 5)<sup>60</sup>.

### **Enhance ability to goal**

**Nanofibers:** In polyherbal formulations regarding the management of psoriasis, nanofibers increase medication penetration, goal the damaged skin, and achieve controlled release, which improves medication delivery, efficacy, and minimizes adverse effects. The use of nanofiber technology can enhance the therapeutic potential of polyherbal formulations that combine natural components to treat psoriasis<sup>40</sup>.

Nano-TQ formulations have demonstrated potential in preclinical research, successfully reducing cytokine levels, inflammation, erythema, and scaling in psoriatic lesions. Using a mouse model, curcumin-loaded cellulose nanofiber (CNF) films have been shown to treat dermatitis by lowering pro-inflammatory cytokines and hydrating the skin. To improve their therapeutic effects and lessen their negative effects, nanofibers have been employed to carry various plant extracts, such as cinnamon aldehyde and antimicrobial peptides<sup>66</sup>.

**Microemulsion Gel:** To improve epidermal localization and boost anti-psoriatic efficacy, a topical formulation of methoxsalen is made in this work applying babchi oil. This composition can be administered topically for longer release and enhanced penetration. Both natural babchi oil and synthetic methoxsalen have been combined to make nanoemulgels. Tween 80 was the surfactant, and babchi oil was the oil phase<sup>81</sup>. Homogenization under high force was used to create four distinct nanoemulsion formulations. To create a nanoemulgel the optimal nanoemulsion formulation or formulations, based on the results of characterisation exist combined with the foundation of the carbopol gel. When compared as a plain gel in skin that has been removed from living penetration, the nanoemulgel (NG2) demonstrated better infiltration as well as targeted the accumulation of methoxsalen throughout the outermost layer<sup>29</sup>. According to the encouraging results, nanoemulgel is an appropriate carrier for topical administration regarding methoxsalen-babchi oil<sup>50</sup>.

**Liposomal Gel:** Polyherbal compositions using liposomal gels can improve the topical distribution and effectiveness of herbal compounds used to treat psoriasis. As nano-carriers, liposomes-small, spherical vesicles-encapsulate and shield herbal extracts, enhancing their skin absorption. Therefore, in comparison to traditional herbal formulations, this can result in better anti-psoriatic action and fewer adverse effects<sup>21</sup>. It has been demonstrated that liposomes containing Ibrutinib and Curcumin can improve skin thickness and reduce inflammation in psoriasis. Liposomes that carry the psoriasis medication anthralin have been demonstrated to improve the medication's effectiveness and lessen its adverse effects. Betamethasone and all-

trans retinoic acid liposomes have demonstrated stronger anti-psoriatic effects than single drug formulations<sup>60</sup>.

**Nanoemulgel:** Babchi oil is utilized in this study to develop a topical version of methoxsalen that could potentially administered topically for longer-lasting release and improved skin penetration, which improves location of the epides and boosts anti-inflammatory effectiveness. Their produced nanoemulgels in which blend natural Babchi oil with synthetic methoxsalen<sup>21</sup>. High-pressure homogenization was employed to create four distinct nanoemulsion formulations, with oil of Babchi serving like the phase of oil and the surfactant Tween 80. Comparing the nanoemulgel (NG2) to plain gel within ex-vivo skin penetration, the latter displayed better permeation as well as methoxsalen throughout the outermost layer. The encouraging results show that topical distribution of methoxsalen-babchi oil can be accomplished with nanoemulgel<sup>27</sup>.

**Sirbal (SIRB)-001: Innovative Herbal Mixture:** A unique aqueous polyherbal formulation (SIRB-001) was created by the researchers by combining A 1:1:3 ratio of *Rehmannia glutinosa Libosch*, *Lonicera Japonica*, and *Rheum palmatum L*<sup>21</sup>. In the treatment of psoriasis, SIRB-001 has demonstrated promising outcomes. There is evidence from in vitro studies that SIRB-001's anti-psoriatic effects including Pro-apoptotic, anti-inflammatory, anti-angiogenic, and antiproliferative in patients<sup>57</sup>.

**Gel Nanoemulsion:** Thymoquinone, Curcumin, and Resveratrol, which are poorly water-soluble drugs, are delivered through this drug-loaded nanoemulsion at the nano range size of NE through the skin, which uses Tween 20 is the surfactant while oleic acid is the oil phase<sup>79</sup>. Since the mucoadhesive of the gel properties as anticipated during psoriatic skin treatment the investigator discovered which the clear and homogeneous the hydrogel created an improved NE formulation was superior for topical administration based on our textural study along with showed better antipsoriatic outcomes in contrast to the other groups<sup>77</sup>. The findings show that DLNE gel is efficacious and impermeable, suggesting that it could be utilized to treat topical psoriasis<sup>74</sup>.

### **Mechanisms of action of natural medications included using herbal and polyherbal nano-formulations to treat psoriasis:**

**Liposomal nanocarriers loaded with psoralen:** UVA-containing psoralen liposomal nanocarriers, or PUVA's reduces the symptoms of psoriasis by reversing the cytokine description that is frequently associated with psoriasis, which causes the autoimmune response to shift between the counter-regulatory Th2 axis and the inflammatory Th1/Th17 axis<sup>64</sup>.

Through reduction IL-17, IL-22, and TNF- $\alpha$  concentrations, PUVA lessens keratinocyte proliferation and inflammation. DNA is typically intercalated by psoralen<sup>2</sup>. Figure 5 describe distribution of nanocarrier in topical route.

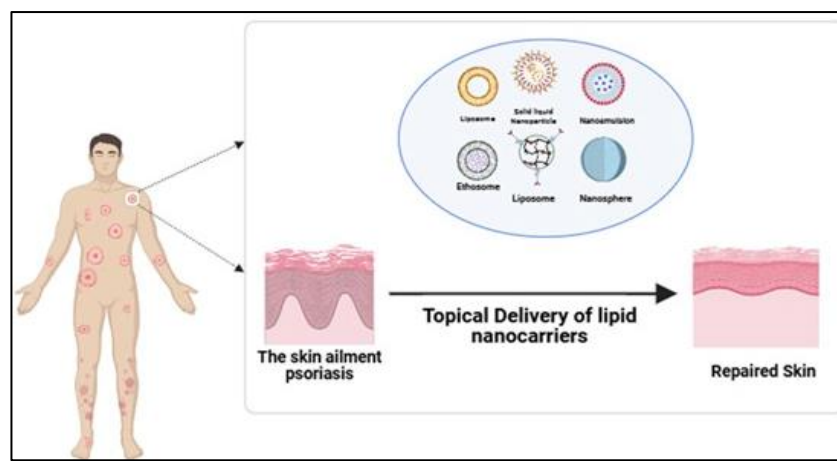
**Liposomal Dithranol Gel and Anthralin Ethosomal Gel are examples of dithranol or anthralin:** The dithranol inhibits the cycle of TCA by lowering the TCA intermediates citrate and malate, which are part of the C1 correlation group. Dithranol changes the amounts of intermediate metabolites created by glycolysis. Increased levels between 0.3 and 0.5  $\mu\text{g mL}^{-1}$  of dithranol caused lactate, pyruvate, glucose, and glucose-6-phosphate to accumulate<sup>15</sup>. Dithranol's impact on central metabolism in HaCaT cells is thus strongly suggested by the existence of these metabolites. Exposure to dithranol also affects the amounts of amino acids within cells<sup>16</sup>.

**Diacerein (Diacerein Rich Niosomes Loaded with Cholesterol):** Reduce the anti-inflammatory consequences of TNF- $\alpha$ , Interlukin-1A, Oncostatin M, IL-17A, and IL-22 on primary human keratinocytes. By reversing the pro-inflammatory controlling the expression of genes in keratinocytes and endothelial cells by IL-1, diacerein prevents both skin inflammation and inflammation-induced atherosclerosis<sup>25</sup>.

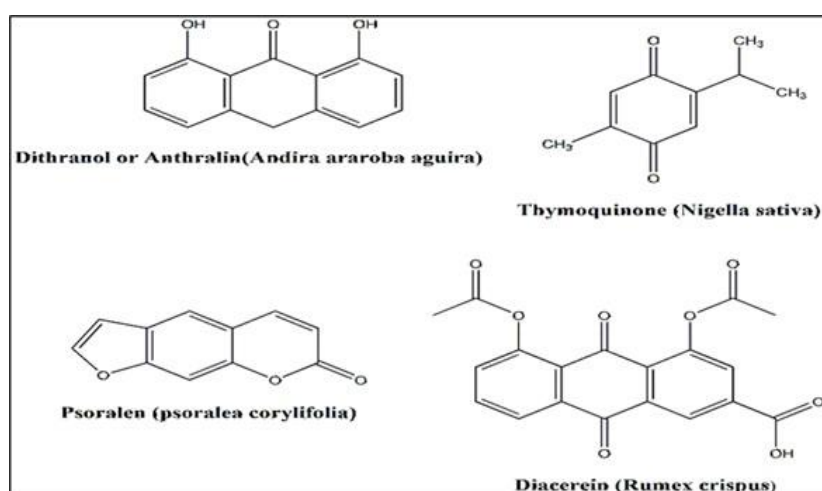
**Alpinia Galanga (Nanoemulsion):** While TNFAIP3 (the NF- $\kappa\text{B}$  gene) showed increased expression, Alpinia galanga inhibited the transcription of CSF-1 and NF- $\kappa\text{B}$  (nuclear factor- $\kappa\text{B}$ ) mRNA transcripts<sup>80</sup>.

**Thymoquinone (TMQ) (Lipospheres):** Thymoquinone decreases the levels of TNF- $\alpha$ , INF-1 $\beta$ , IL-6, IL-17, and IL-2. The biological origin along with chemical structure of the herbal plants listed<sup>82</sup>.

**Liposphere Gel: Tacrolimus and Curcumin:** Cut down on the cytokines such as IL-17 and IL-22, as well as TNF- $\alpha$ <sup>53</sup>. Figure 6. explain some anti-psoriatic herbs' chemical makeup and biological origins.



**Figure 5. Distribution Of Lipid Nanocarriers Topically**



**Figure 6. Some Anti-psoriatic Herbs' Chemical Makeup and Biological Origins**

## Conclusion

People worldwide suffer from psoriasis, a persistent autoimmune skin disorder, is difficult to cure. Although several tactics are used to lessen its intensity, a safe, efficient, and comprehensive solution is still elusive. Topical therapy is still a mainstay of treatment because of its decreased toxicity and enhanced patient compliance. However, due to their drawbacks, including poor medication penetration and dose-related toxicity, standard topical medicines must be used in novel ways to treat this difficult skin condition. Because they get around the problems with traditional approaches, novel medication delivery technologies present a possible answer. The emergence of nanotechnology, which has the potential to be a treatment for skin conditions as well, has been one of the most exciting scientific advances of the last century. Drug delivery topically for psoriasis has grown in popularity thanks to nanocarriers such as Solid lipid nanoparticles (SLNs), liposomes, dendrimers, ethosomes, nanoemulsions, nanostructured lipid carriers (NLCs), and nanocrystals. These nanocarriers also possess the

potential to address a couple of the issues together with traditional medication administration techniques. The one that difficulty in addressing conditions related to the skin, such as acne, psoriasis, and atopic dermatitis, is to minimize drug absorption into the bloodstream while maximizing epidermal penetration and retention to prevent severe adverse effects. Since psoriasis thickens the corneum stratum, it creates one significant obstacle about active ingredients. Throughout the previous few decades, a significant quantity of research has examined this problem, concentrating about lipidic and polymeric nanoparticles. Numerous research groups have reported that nanocarriers may be created to strive for certain either tissues or cells, increase the rate at which drugs are adopted, and release medications within a regulated and sustained manner, enabling precise drug administration. But even with these benefits, nanoparticles are still in their infancy and face obstacles including exorbitant prices, issues with long-term stability, and possible toxicity. Efficient clinical translation and resolution of these problems require thorough preclinical models to comprehend how these nanocarriers interact with the skin.

### **Conflict of interest**

The authors have no conflicts of interest regarding this investigation.

### **Acknowledgments**

The authors acknowledge the support of Seacom Skills University, Santiniketan, Bolpur, West Bengal, India for the present work.

### **References**

1. Amiri D, Willy Schwarz C, Gether L, Skov L. Safety and Efficacy of Topical Calcineurin Inhibitors in the Treatment of Facial and Genital Psoriasis: A Systematic Review. *Acta Derm Venereol.* 2023;103(17):1–7.
2. Kumar S, Jangir BL, Rao R. A new perspective for psoriasis: Dithranol nanosponge loaded hydrogels. *Appl Surf Sci Adv.* 2022:100347.
3. Alhelal HM, Mehta S, Kadian V, Kakkar V, Tanwar H, Rao R, et al. Solid Lipid Nanoparticles Embedded Hydrogels as a Promising Carrier for Retarding Irritation of Leflunomide. *Gels.* 2023;9(7).
4. Yaghoubi A, Ghojzadeh M, Abolhasani S, Alikhah H, Khaki-Khatibi F. Correlation of Serum Levels of Vitronectin, Malondialdehyde and Hs-CRP With Disease Severity in Coronary Artery Disease. *J Cardiovasc Thorac Res.* 2015;7(3):113–7.
5. Maiti D, Naseeruddin Inamdar M, Almuqbil M, Suresh S, Mohammed Basheeruddin Asdaq S, Alshehri S, et al. Evaluation of solid-lipid nanoparticles formulation of methotrexate for anti-psoriatic activity. *Saudi Pharm J.* 2023;31(6):834–44.
6. Rahmanian-Devin P, Askari VR, Sanei-Far Z, Baradaran Rahimi V, Kamali H, Jaafari MR, et al.

- Preparation and characterization of solid lipid nanoparticles encapsulated noscapine and evaluation of its protective effects against imiquimod-induced psoriasis-like skin lesions. *Biomed Pharmacother.* 2023;168(October):115823.
7. Senthamarai R, Kirubha TSV, Velumani AN. Herbal niosomal gel for psoriasis. 2023;(October):3–7.
  8. Lamichhane N, Udayakumar TS, D’Souza WD, Simone CB, Raghavan SR, Polf J, et al. Liposomes: Clinical applications and potential for image-guided drug delivery. *Molecules.* 2018;23(2):1–17.
  9. Ahmad A, Husain A, Mujeeb M, Khan SA, Najmi AK, Siddique NA, et al. A review on therapeutic potential of *Nigella sativa*: A miracle herb. *Asian Pac J Trop Biomed.* 2013;3(5):337–52.
  10. Verma P, Pathak K. Therapeutic and cosmeceutical potential of ethosomes: An overview. *J Adv Pharm Technol Res.* 2010;1(3):274–82.
  11. Kadian V, Dalal P, Kumar S, Kapoor A, Rao R. Comparative evaluation of dithranol-loaded nanosponges fabricated by solvent evaporation technique and melt method. *Futur J Pharm Sci.* 2023;9(1).
  12. Negi P, Sharma I, Hemrajani C, Rathore C, Bisht A, Raza K, et al. Thymoquinone-loaded lipid vesicles: A promising nanomedicine for psoriasis. *BMC Complement Altern Med.* 2019;19(1):1–9.
  13. Wang W, Shu GF, Lu KJ, Xu XL, Sun MC, Qi J, et al. Flexible liposomal gel dual-loaded with all-trans retinoic acid and betamethasone for enhanced therapeutic efficiency of psoriasis. *J Nanobiotechnology.* 2020;18(1):1–14.
  14. World Health Organization psoriasis. Global report on. *Glob Rep Psoriasis.* 2016; 978:1–26.
  15. Sani A, Cao C, Cui D. Toxicity of gold nanoparticles (AuNPs): A review. *Biochem Biophys Reports.* 2021;26.
  16. Kousalová J, Etrych T. Polymeric nanogels as drug delivery systems. *Physiol Res.* 2018;67:s305–17.
  17. Chat VS, Kearns DG, Uppal SK, Han G, Wu JJ. Management of Psoriasis With Topicals: Applying the 2020 AAD-NPF Guidelines of Care to Clinical Practice. *Cutis.* 2022;110(2):8–14.
  18. Sindrilaru A, Filip A, Scharffetter-Kochanek K, Crisan D. How can nanoparticle-based technologies revolutionize the topical therapy in psoriasis? *Exp Dermatol.* 2020;29(11):1097–103.
  19. Khan R, Mirza MA, Aqil M, Hassan N, Zakir F, Ansari MJ, et al. A Pharmaco-Technical Investigation of Thymoquinone and Peat-Sourced Fulvic Acid Nanoemulgel: A Combination Therapy. *Gels.* 2022;8(11):1–24.
  20. Raza H, Shah SU, Ali Z, Khan AU, Rajput IB, Farid A, et al. In Vitro and Ex Vivo Evaluation of Fluocinolone Acetonide–Acitretin-Coloaded Nanostructured Lipid Carriers for Topical Treatment of Psoriasis. *Gels.* 2022;8(11).
  21. Rashid SA, Bashir S, Naseem F, Farid A, Rather IA, Hakeem KR. Olive oil-based methotrexate loaded topical nanoemulsion gel for the treatment of imiquimod induced psoriasis-like skin inflammation in an animal model. *Biology (Basel).* 2021;10(11).
  22. Elkordy AA, Hill D, Attia M, Chaw CS. Liposomes and Their Therapeutic Applications in Enhancing Psoriasis and Breast Cancer Treatments. *Nanomaterials.* 2024;14(21):1–24.
  23. Fereig SA, El-Zaafarany GM, Arafa MG, Abdel-Mottaleb MMA. Tackling the various classes of nano-therapeutics employed in topical therapy of psoriasis. *Drug Deliv.* 2020;27(1):662–80.
  24. Shetty K, Sherje AP. Nano intervention in topical delivery of corticosteroid for psoriasis and atopic dermatitis-a systematic review. *J Mater Sci Mater Med.* 2021;32(8).

25. Nsairat H, Khater D, Sayed U, Odeh F, Al Bawab A, Alshaer W. Liposomes: structure, composition, types, and clinical applications. *Heliyon*. 2022;8(5):e09394.
26. Elmets CA, Korman NJ, Prater EF, Wong EB, Rupani RN, Kivelevitch D, et al. Joint AAD–NPF Guidelines of care for the management and treatment of psoriasis with topical therapy and alternative medicine modalities for psoriasis severity measures. *J Am Acad Dermatol*. 2021;84(2):432–70.
27. Morakul B, Junyaprasert VB, Sakehaisri K, Teeranachaideekul V. Cannabidiol-Loaded Nanostructured Lipid Carriers (NLCs) for Dermal Delivery: Enhancement of Photostability, Cell Viability, and Anti-Inflammatory Activity. *Pharmaceutics*. 2023;15(2).
28. Hassan AS, Soliman GM. Rutin Nanocrystals with Enhanced Anti-Inflammatory Activity: Preparation and Ex Vivo/In Vivo Evaluation in an Inflammatory Rat Model. *Pharmaceutics*. 2022;14(12).
29. Fathalla D, Youssef EMK, Soliman GM. Liposomal and ethosomal gels for the topical delivery of anthralin: Preparation, comparative evaluation and clinical assessment in psoriatic patients. *Pharmaceutics*. 2020;12(5).
30. Zhu B, Jing M, Yu Q, Ge X, Yuan F, Shi L. Treatments in psoriasis: from standard pharmacotherapy to nanotechnology therapy. *Postep Dermatologii i Alergol*. 2022;39(3):460–71.
31. Ramez SA, Soliman MM, Fadel M, Nour El-Deen F, Nasr M, Youness ER, et al. Novel methotrexate soft nanocarrier/fractional erbium YAG laser combination for clinical treatment of plaque psoriasis. *Artif Cells, Nanomedicine Biotechnol*. 2018;46(sup1):996–1002.
32. Dadwal A, Baldi A, Kumar Narang R. Nanoparticles as carriers for drug delivery in cancer. *Artif Cells, Nanomedicine Biotechnol*. 2018;46(sup2):295–305.
33. Mashinchian O, Johari-Ahar M, Ghaemi B, Rashidi M, Barar J, Omidi Y. Impacts of quantum dots in molecular detection and bioimaging of cancer. *BioImpacts*. 2014;4(3):149–66.
34. Asad MI, Khan D, Rehman AU, Elaissari A, Ahmed N. Development and in vitro/in vivo evaluation of pH-sensitive polymeric nanoparticles loaded hydrogel for the management of psoriasis. *Nanomaterials*. 2021;11(12).
35. Begines B, Ortiz T, Pérez-Aranda M, Martínez G, Merinero M, Argüelles-Arias F, et al. Polymeric nanoparticles for drug delivery: Recent developments and future prospects. *Nanomaterials*. 2020;10(7):1–41.
36. Essaghraoui A, Belfkira A, Hamdaoui B, Nunes C, Costa Lima SA, Reis S. Improved dermal delivery of cyclosporine a loaded in solid lipid nanoparticles. *Nanomaterials*. 2019;9(9).
37. Chuang SY, Lin CH, Huang TH, Fang JY. Lipid-Based nanoparticles as a potential delivery approach in the treatment of rheumatoid arthritis. *Nanomaterials*. 2018;8(1):1–16.
38. Gavra DI, Endres L, Pető Á, Józsa L, Fehér P, Ujhelyi Z, et al. In Vitro and Human Pilot Studies of Different Topical Formulations Containing Rosa Species for the Treatment of Psoriasis. *Molecules*. 2022;27(17):1–22.
39. Liu P, Chen G, Zhang J. A Review of Liposomes as a Drug Delivery System: Current. *Molecules*. 2022;27(4):1372.
40. Trombino S, Servidio C, Laganà AS, Conforti F, Marrelli M, Cassano R. Viscosified solid lipidic nanoparticles based on naringenin and linolenic acid for the release of cyclosporine a on the skin. *Molecules*. 2020;25(15).

41. Starón A, Dlugosz O, Pulit-Prociak J, Banach M. Analysis of the exposure of organisms to the action of nanomaterials. *Materials (Basel)*. 2020;13(2):1–18.
42. Bacha K, Chemotti C, Mbakidi JP, Deleu M, Bouquillon S. Dendrimers: Synthesis, Encapsulation Applications and Specific Interaction with the Stratum Corneum-A Review. *Macromol*. 2023;3(2):343–70.
43. Lu Y, Cheng L, Ren L, Chen D, Guan S, Zhu S, et al. Therapeutic Effect and Mechanism of Glabridin Liposome on Imiquimod-induced Mice Psoriasis. *Pharmacogn Mag*. 2024;20(1):72–80.
44. Parkash V, Maan S, Chaudhary V, Jogpal V, Mittal G, Jain V. Implementation of Design of Experiments in Development and Optimization of Transfersomal Carrier system of Tacrolimus for the Dermal Management of Psoriasis in Albino Wistar Rat. *J Bioequiv Availab*. 2018;10(5):99–106.
45. Bodnar K, Fehér P, Ujhelyi Z, Bacskay I, Józsa L. Recent Approaches for the Topical Treatment of Psoriasis Using Nanoparticles. *Pharmaceutics*. 2024;16(4).
46. Gisondi P, Bellinato F, Girolomoni G. Topographic differential diagnosis of chronic plaque psoriasis: Challenges and tricks. *J Clin Med*. 2020;9(11).
47. Pu H, Huang J, Gui B, Chen Y, Guo Y, Lian Y, et al. Ultrasound-Responsive Nanobubbles for Breast Cancer: Synergistic Sonodynamic, Chemotherapy, and Immune Activation through the cGAS-STING Pathway. *ACS Appl Mater Interfaces*. 2025;17(13):19317–34.
48. Agrawal YO, Mahajan UB, Mahajan HS, Ojha S. Methotrexate-loaded nanostructured lipid carrier gel alleviates imiquimod-induced psoriasis by moderating inflammation: Formulation, optimization, characterization, in-vitro and in-vivo studies. *Int J Nanomedicine*. 2020;15:4763–78.
49. Mestry M, Rane M, Bajaj A. Commiphora mukul and quercetin loaded liposphere gel: Potential treatment for psoriasis. *Indian J Pharm Educ Res*. 2020;54(3):654–67.
50. Orsmond A, Bereza-Malcolm L, Lynch T, March L, Xue M. Skin barrier dysregulation in psoriasis. *Int J Mol Sci*. 2021;22(19):1–27.
51. Biswasroy P, Pradhan D, Haldar J, Kar B, Ghosh G, Rath G. Recent Advancements in Herbal Bioactive-based Nanoformulations for the Treatment of Psoriasis. *Curr Bioact Compd*. 2022;19(4).
52. Alam M, Mir SR, Amin S. Co-Loaded Nanostructured Lipid Carriers Gel for Improved. 2023.
54. Sabourian P, Yazdani G, Ashraf SS, Frounchi M, Mashayekhan S, Kiani S, et al. Effect of physico-chemical properties of nanoparticles on their intracellular uptake. *Int J Mol Sci*. 2020;21(21):1–20.
55. Khan R, Mirza MA, Aqil M, Alex TS, Raj N, Manzoor N, et al. In Vitro and In Vivo Investigation of a Dual-Targeted Nanoemulsion Gel for the Amelioration of Psoriasis. *Gels*. 2023;9(2).
56. Alam A, Alqarni MH, Foudah AI, Raish M, Salkini MA. Babchi Oil-Based Nanoemulsion Hydrogel for the Management of Psoriasis: A Novel Energy Economic Approach Employing Biosurfactants. *Gels*. 2022;8(12).
57. Hua S, de Matos MBC, Metselaar JM, Storm G. Current trends and challenges in the clinical translation of nanoparticulate nanomedicines: Pathways for translational development and commercialization. *Front Pharmacol*. 2018;9(JUL):1-14.
58. Leung AKC, Barankin B, Lam JM, Leong KF. Childhood guttate psoriasis: an updated review. *Drugs Context*. 2023;12(July).
59. Mohd Nordin UU, Ahmad N, Salim N, Mohd Yusof NS. Lipid-based nanoparticles for psoriasis

- treatment: a review on conventional treatments, recent works, and future prospects. *RSC Adv.* 2021;11(46):29080–101.
60. Fereig S, El-Zaafarany GM, Arafa M, Abdel-Mottaleb MMA. Boosting the anti-inflammatory effect of self-assembled hybrid lecithin–chitosan nanoparticles via hybridization with gold nanoparticles for the treatment of psoriasis: elemental mapping and in vivo modeling. *Drug Deliv [Internet]*. 2022;29(1):1726–42. Available from: <https://doi.org/10.1080/10717544.2022.2081383>
  61. Thirumal D, Sindhu RK, Goyal S, Sehgal A, Kumar A, Babu MA, et al. Pathology and Treatment of Psoriasis Using Nanoformulations. *Biomedicines*. 2023;11(6):1–19.
  62. Bhalani D V., Nutan B, Kumar A, Singh Chandel AK. Bioavailability Enhancement Techniques for Poorly Aqueous Soluble Drugs and Therapeutics. *Biomedicines*. 2022;10(9).
  63. Alam M, Rizwanullah M, Mir SR, Amin S. Promising prospects of lipid-based topical nanocarriers for the treatment of psoriasis. *OpenNano*. 2023; 10:100123.
  64. Xi L, Lin Z, Qiu F, Chen S, Li P, Chen X, et al. Enhanced uptake and anti-maturation effect of celastrol-loaded mannosylated liposomes on dendritic cells for psoriasis treatment. *Acta Pharm Sin B*. 2022;12(1):339–52.
  65. Kumar S, Prasad M, Rao R. Topical delivery of clobetasol propionate loaded nanosponge hydrogel for effective treatment of psoriasis: Formulation, physicochemical characterization, antipsoriatic potential and biochemical estimation. *Mater Sci Eng C*. 2021;119 (August 2020):111605.
  66. Huang C, Gou K, Yue X, Zhao S, Zeng R, Qu Y, et al. A novel hyaluronic acid-based dissolving microneedle patch loaded with ginsenoside Rg3 liposome for effectively alleviate psoriasis. *Mater Des*. 2022; 224:111363
  67. Pushparajah D, Jimenez S, Wong S, Alattas H, Nafissi N, Slavcev RA. Advances in gene-based vaccine platforms to address the COVID-19 pandemic. *Adv Drug Deliv Rev*. 2021;170:113–41.
  68. Yadav T, Yadav HKS, Raizaday A, Alam S. The treatment of psoriasis via herbal formulation and nanopolyherbal formulation: A new approach. *BioImpacts*. 2025;15:30341.
  69. Fadaei MS, Fadaei MR, Kheirieh AE, Rahmanian-Devin P, Dabbaghi MM, Tavallaei KN, et al. Niosome As a Promising Tool for Increasing the Effectiveness of Anti-Inflammatory Compounds. Vol. 23, *EXCLI Journal*. 2024. 212–263 p.
  70. Patil TP, Vibhute AA, Patil SL, Dongale TD, Tiwari AP. Green synthesis of gold nanoparticles via *Capsicum annum* fruit extract: Characterization, antiangiogenic, antioxidant and anti-inflammatory activities. *Appl Surf Sci Adv*. 2023; 13:100372.
  71. Nirmal GR, Liao CC, Lin ZC, Alshetaili A, Hwang E, Yang SC, et al. Topically applied pH-responsive nanogels for alkyl radical-based therapy against psoriasisiform hyperplasia. *Drug Deliv*. 2023;30(1).
  72. Ghasemiyeh P, Mohammadi-Samani S. Solid lipid nanoparticles and nanostructured lipid carriers as novel drug delivery systems: Applications, advantages and disadvantages. *Res Pharm Sci*. 2018;13(4):288–303.
  73. Singh S, Khurana K, Chauhan SB, Singh I. Emulsomes: new lipidic carriers for drug delivery with special mention to brain drug transport. *Futur J Pharm Sci*. 2023;9(1).
  74. Zhao T, Zhou M, Wu R, Wang H, Zouboulis CC, Zhu M, et al. Dendrimer-conjugated isotretinoin for controlled transdermal drug delivery. *J Nanobiotechnology*. 2023;21(1):1–9.
  75. Shahine Y, El-Aal SAA, Reda AM, Sheta E, Atia NM, Abdallah OY, et al. Diosmin nanocrystal gel

- alleviates imiquimod-induced psoriasis in rats via modulating TLR7,8/NF- $\kappa$ B/micro RNA-31, AKT/mTOR/P70S6K milieu, and Tregs/Th17 balance. *Inflammopharmacology*. 2023;31(3):1341–59.
76. Raina N, Rani R, Thakur VK, Gupta M. New Insights in Topical Drug Delivery for Skin Disorders: From a Nanotechnological Perspective. *ACS Omega*. 2023;8(22):19145–67.
77. Elmowafy M, Shalaby K, Elkomy MH, Alsaidan OA, Gomaa HAM, Abdelgawad MA, et al. Polymeric Nanoparticles for Delivery of Natural Bioactive Agents: Recent Advances and Challenges. *Polymers (Basel)*. 2023;15(5):1–34.
78. Pasarin D, Ghizdareanu AI, Enascuta CE, Matei CB, Bilbie C, Paraschiv-Palada L, et al. Coating Materials to Increase the Stability of Liposomes. *Polymers (Basel)*. 2023;15(3):1–30.
79. Papagiannopoulos A, Sotiropoulos K. Current Advances of Polysaccharide-Based Nanogels and Microgels in Food and Biomedical Sciences. *Polymers (Basel)*. 2022;14(4).
80. Montero N, Alhaji MJ, Sierra M, Oñate-Garzon J, Yarce CJ, Salamanca CH. Development of polyelectrolyte complex nanoparticles-PECNs loaded with ampicillin by means of polyelectrolyte complexation and ultra-high pressure homogenization (UHPH). *Polymers (Basel)*. 2020;12(5).
81. Stefanov Stefan R., Andonova Velichka Y. Lipid nanoparticulate drug delivery systems: Recent advances in the treatment of skin disorders. *Pharmaceuticals*. 2021;14(11):1–29.
82. Tripathi PK, Gorain B, Choudhury H, Srivastava A, Kesharwani P. Dendrimer entrapped micro sponge gel of dithranol for effective topical treatment. *Heliyon*. 2019;5(3):e01343.