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# Understanding the prospective of nano-formulations towards the treatment of psoriasis

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ABSTRACT

Psoriasis is a consistently recurring, inflammatory, autoimmune disorder of the skin, affecting about 2–5% of the world population. Abundant therapeutic agents are accessible for the treatment of psoriasis. Nevertheless, none of them are entirely secure and effective to treat the disease without compromising patient compliance. Furthermore, already existing drugs are supposed to restrain the ailment and alleviate the sign and symptoms with no complete cure. However, they focus on restraining the disease and alleviating the symptoms without providing an absolute cure. Therefore there remains a vital challenge, to explore a new drug moiety or delivery system which could safely and effectively manage psoriasis without compromising patient compliance. Furthermore, conventional formulations offer reduced benefit/risk ratio of anti-psoriatic drugs, which limits the use of existing conventional formulations.

Novel formulations based on nanocarriers are a promising prospect to overcome the limitation of conventional formulations by offering a reduction in dose, dosing frequency, dose-dependent, side effects with enhanced efficacy. Presently nano-formulations have gained widespread application for effective and safe treatment of psoriasis.

The present review primarily focuses on conventional therapeutic strategy and recent advances in lipid-based, polymer-based and metallic nano-formulations of a variety of anti-psoriatic drugs. The practicability of various nanocarrier systems including liposomes, nanostructured lipid carriers, ethosomes, solid lipid nanoparticles, nanocapsules, micelles, dendrimers, gold nanoparticles and silver nanoparticles have been discussed in detail. The review also traces related patents to exemplify the role of various nanoparticles in psoriasis treatment. In a nutshell, nano-formulations remain established as a promising modality for treating psoriasis treatment as they propose better penetration, targeted delivery, enhanced safety, and efficacy.

## 1. Introduction

Psoriasis is a consistently recurring, inflammatory, autoimmune disorder of the skin, affecting about2–5% of the population globally. The disease is usually expressed as highly inflamed red erythematous plaques supported by silvery scales [1]. The presence of scaly patches is an outcome of the unusual excessive proliferation of epidermis, incomplete cornification and preservation of nuclei in cells of stratum corneum, unlike normal skin. Histopathological features observed in the psoriatic skin include hyperplasia of epidermis with significant differentiation of keratinocyte, increased angiogenesis and presence of prominent inflammatory infiltrate. Disease etiology is multi-factorial with an amalgamation of hereditary factor (family background) and environmental factor (alcohol, contagion, drugs, stress) triggering the immuno-histological changes observed in the skin [2,3].

Patients who have psoriasis are associated with physical stigmatization which adds to augment the psychological difficulties in their socio-professional and emotional life. Topical therapy, phototherapy, and systemic therapy are the primary therapeutic alternative for treatment of psoriasis. For mild disease generally, topical treatment is recommended as a first-line treatment. However, for a severe condition, systemic treatment or phototherapy is indicated [4]. Though many treatment options currently exist to lessen the sign and symptoms of psoriasis none of them are competent enough to cure the disease

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completely.

Topical therapies with conventional formulations offer several limitations like limited drug penetration, increased dosing frequency, adverse toxicity and decreased patient compliance [5]. Furthermore, phototherapy and systemic drugs display many side effects including liver toxicity, renal toxicity, skin cancer and high blood pressure. All such issues limit the use of already available conventional therapeutics for psoriasis.

Therefore there remains a momentous confront for global health organization and pharmaceutical company to explore a new drug moiety or delivery system which could safely and effectively manage psoriasis without compromising patient compliance [6]. However, recognition of the pathophysiological mechanism of psoriasis and identification of different triggering factors are always major concerns. Furthermore, these observations would lead to the establishment of novel therapeutic for psoriasis. In last decades, most of the new anti-psoriatic drugs approved in the market are monoclonal antibodies, targeting various pathophysiological events concerned in development and progression of the disease. However, this antibody-based therapy is costly for individuals in poor and emerging economies [1]. Therefore, in present scenario research is being focused towards the development of a novel delivery system to resolve skin penetration issues concerned with conventional drugs. Also, the novel delivery system (nanocarrier based drug delivery systems) possess the potential to overcome the problems linked with conventional drug delivery systems such as high dose requirement and dose-dependent side effects [7].

In recent years, a novel drug delivery system based on nano-formulation has been extensively explored by the researchers to accomplish a safe and effective therapy for an apathetic disease like psoriasis. In this regards, success has been achieved to a great extent, and numerous patents are also granted.

Present review emphasizes the pathogenesis of psoriasis, available treatment options, need and applications of nano-formulations in psoriasis therapy, recent patents related to conventional and novel nano-formulations for psoriasis and prospects in the therapy.

## 2. Pathophysiology

Psoriasis is a T-cell mediated disease which generally arises due to the mistaken signal processing of the self-immune system. It is supposed that in psoriasis keratinocytes multiply and reaches the skin surface very quickly from the basal layer within 6–8 days unlike normal skin [8,9]. Usually, keratinocytes mature and shed off every 35–40 day but in case of psoriasis, keratinocytes mature and move to epidermis within a week, and instead of being shedding off, they gather on epidermis resulting non-evident lesions. Difference between the standard and psoriatic epidermal skin has been shown in Fig. 1. There are many hypotheses explaining the pathogenesis of psoriasis but most accepted hypothesis states that pathogenesis of psoriasis rely on the activation of wounded and/or flowing immunocytes such as T cells, neutrophils, dendritic cells, macrophages and a variety of products secreted by them which eventually leads to hyperproliferation, thickened epidermis, and angiogenesis of keratinocytes [10,11].

Molecular events taking place during the pathogenesis of psoriasis has been further elaborated in this section and depicted in Fig. 2. Psoriasis originates when unidentified autoantigen binds with major histocompatibility complex (MHC) of antigen-presenting cells (APCs) of skin. Following the recognition of autoantigen, APCs such as Langerhans cells present in the skin migrates towards regional lymph nodes, where these cells reversibly link with naïve T cells with the subsequent interaction of surface molecules present on both the cells [12]. After that, the MHC of APCs presents the antigen to a receptor of T-lymphocyte to start activation of the T cells. The subsequent signal for activation of T-lymphocyte activation is a cell-cell interaction called as co-stimulation [13]. In the absence of co-stimulation, T lymphocyte will either endure apoptosis or turn into impassive. Co-stimulation engrosses coupling of T cell ligand with the receptor of APCs. The pairs comprise lymphocyte functional antigen (LFA)-3 pairing with CD2, B7 pairing with CD28, and ICAM-1 pairing with LFA-1 [3].

Following co-stimulation activated T lymphocytes experience clonal selection which leads to the production of antigen-recognizing T-lymphocytes and memory T cells. Next, the activated T lymphocytes go into the circulatory system followed by migration to inflamed skin. Once activated T lymphocyte arrives at the inflamed site of skin, it encounters beginning autoantigen and releases T-helper type-1 (TH1) cytokines such as tumor necrosis factor alpha (TNFA), interleukin-1 (IL-1) and gamma interferon (INFG) [14,15]. These cytokines contribute a vital function in the phenotypic expression of disease such as inflammation, epidermal hyper-proliferation, etc. Moreover, TH1 cytokines lead to the production of a cascade of cytokines from other cells that mostly influence the distinguishing features of psoriatic lesions [16,17].

## 3. Treatment options for psoriasis

Topical therapy, phototherapy, and systemic therapy are the existing therapeutic alternative for psoriasis [18]. In order choose active therapy patients are needed to divide into mild-to-moderate and moderate-to-severe disease categories. Moderate-to-severe psoriasis is usually defined as the participation of more than 5–10 percent of the body surface area (the entire surface of the palm, together with fingers of one hand constitutes about 1 percent of the body surface area) or engagement of the palm, sole or face. However, patients having involvement of less than 5 percent body surface area fall under the category of mild to moderate psoriasis [19,20].

For the management of limited or mild-to-moderate psoriasis, topical agents are considered, while for moderate-to-severe disease phototherapy or systemic therapy is taken into account. Nevertheless, patients on systemic therapy would also need to keep on some topical agents [21]. Detail about the treatment options for psoriasis has been depicted in Fig. 3.

## 4. Challenges in the Treatment of psoriasis

### 4.1. Psychosocial aspect

Chronic nature of psoriasis drastically deteriorates the quality of life of psoriasis patient as they experience great psychological, financial and social burdens [22]. Therefore before the initiation of any psoriasis treatment, addressing patients' psychosocial needs is a great challenge. Psoriasis patients probably experience 1.5 times more depression than those lacking the disease. Evidence suggests that clinical outcome especially adherence concern could be optimized if the patients' emotional needs are dealt wisely. Furthermore, the execution of depression screening into medical practice might facilitate the detection and management of the disease [23,24].

### 4.2. Therapeutic aspect

Presently, many therapeutic options are available for psoriasis treatment, but getting a harmless and effectual therapy is still a significant challenge [25].

Topical therapy remains a widely employed option for psoriasis, and about 80% of the psoriasis population depends on topical therapy. However, topical therapy using conventional formulation possesses its limitation of poor drug penetration and absorption due to barrier properties of skin. This barrier results in slow penetration rates and restricted uptake of therapeutic moiety [26]. Furthermore, in psoriasis, skin becomes very tough and rigid owing to epidermal hyperplasia, hyperkeratosis and lack of common moisturizing elements like water. All these phenotypic changes over skin also limit sufficient drug penetration across the psoriatic skin. Thus the therapeutic effectiveness of