Nanotechnology in psoriasis

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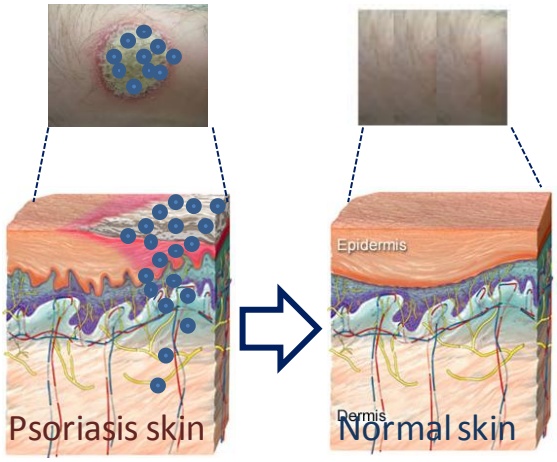
Abstract:

Psoriasis is a chronic autoimmune skin disease with a substantial negative impact on the patient's quality of life. To date, a wide range of treatment options such as topical delivery of corticosteroids, vitamin D derivatives, phototherapy, and administration of immuno-modulators are available. However, these approaches have major limitations such as a plethora of side effects and skin develops resistance to treatments over time. In addition, therapeutic outcome of psoriasis treatments also can be unpredictable. To address these limitations several attempts have been made in recent years using nanotechnology. These nanotherapeutics offer several advantages including reducing non specific targeting, bypassing first passage metabolism, increasing the efficacy of the drugs. However, there are no long-term effective therapies till today, so this remains at the top of the list for unmet needs. Psoriasis is now leading autoimmune disease, and advancements in complex disease biology at molecular level enriched our understanding. Thus, innovative, safer and effective therapeutics and strategies are required to target hyperactive immune elements that target multiple pathways of psoriasis pathogenesis.



Application of nanotherapeutics

In Telugu:

సోరియాసిస్ ఒక ఆటో ఇమ్మ్యూన్ చర్మ వ్యాధి . ఈ వ్యాధి వ్యక్తిగత జీవనశైలిని ఎంతో ప్రభావితం చేస్తుంది. ఈ వ్యాధి నియంత్రణకు కార్టికో స్టెరాయిడ్స్ ,విటమిన్ డి ఉత్పాదకాలు మొదలైన పైపూత ఔషధాలు , ఆంటీబాడీలు మొదలైన జీవౌషధాలు ఉన్నప్పటికీ దీర్ఘకాలిక వాడకం వల్ల వీటి నుంచి వచ్చే దుష్పరిణామాలు అధికంగా ఉన్నాయి. నానో సాంకేతిక పరిజ్ఞానంను ఉపయోగించి చేసే ప్రస్తుత పరిశోధనలు ఈ దుష్పరిణామాల నుంచి రోగిని విముక్తి కలిగించేవిగా ఆశలు రేకేతిస్తున్నాయి. అయితే ఈ నానో ఔషధాలు ఇంకా ప్రయోగాల స్థితిలోనే ఉన్నాయి. భవిష్యత్తులో ఈ ఔషధాలు సోరియాసిస్ ను సమర్థవంతంగా నియంత్రించగలవనే భావిస్తున్నాం.

1. Introduction:

Psoriasis is a chronic autoimmune skin disorder with a substantial negative impact on the patient's quality of life (Figure 1).[1,2,3] Although psoriasis primarily affects the skin and joints (psoriatic arthritis), several co-morbidities including inflammatory bowel disease, lymphoma, obesity and metabolic syndrome are associated with psoriasis.[4,5,6] Psoriatic patients also suffer from significant emotional burden including depression, mood disorders and suicidal thoughts[7] and have an increased risk of cardiovascular disease.[8] A wide range of treatment options such as topical delivery of corticosteroids, retinoids, vitamin D derivatives, phototherapy are available. However, these medications have plethora of side effects. Nanotechnology has the potential to have a revolutionary impact on treatment for autoimmune diseases such as psoriasis, rheumatoid arthritis. The topical applications for psoriasis treatment offer the altering the aberrant immune reactions with minimal to zero toxicity to normal tissue. However, the cutaneous delivery of therapeutics still faces many obstacles. The penetration of macromolecular drugs through the epidermis barrier becomes the predominant major technical challenge in cutaneous delivery.[9] Thus, penetration-enhancing techniques are needed for topical drug delivery. Nanoparticles are found to be the most promising carriers for delivering therapeutics topically. Nanoparticles, such as liposomes and polymer particles and nanocrystalline particles, have already been evaluated as potential drug carrier systems in animal models with encouraging results. In the present review, we will discuss different nanotherapeutic options available for psoriasis.

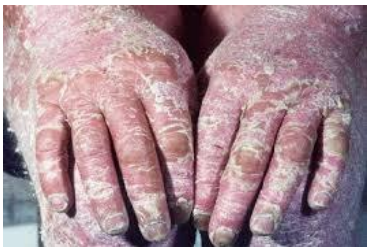


Fig. 1: Psoriatic plaques on hands

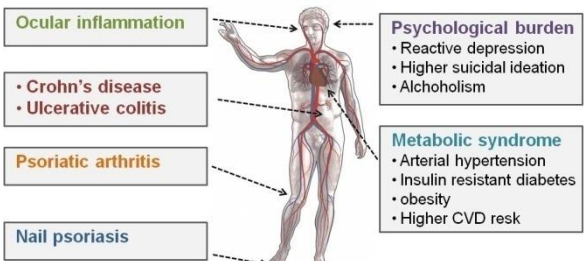


Fig. 2: Co-morbidities associated with psoriasis

2. Therapeutics for psoriasis:

2.1 Corticosteroids:

Corticosteroids, one of the most frequently used classes of drugs in dermatology, have been in practice to treat psoriasis too, either alone or in combination with other drugs.[10,11] Korting *et al*. developed liposomes containing 0.039% betamethasone dipropionate (BDP) (Figure 3) and compared it with a commercial propylene glycol gel containing 0.064% BDP in a double-blind, randomized, paired trial lasting 14 days in 10 patients with psoriasis vulgaris and eczema. This report documented improvement in case of eczema, but not in psoriasis.[12]

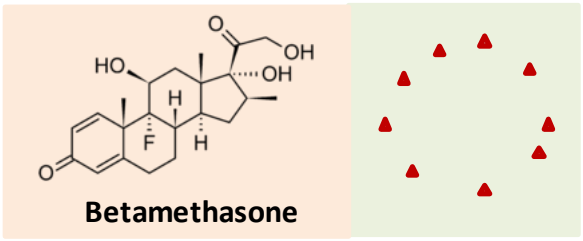


Fig. 3: Betamethasone encapsulated liposomes

2.2 Retinoids:

Retinoid such as tretinoin (TRE) is a widely used drug in the topical treatment psoriasis and other skin disorders but unpleasant side effects often appear in the form of scaling, erythema, burning, and stinging.[13] Rodilf DM et al., developed chitosan based solid lipid nanoparticle system to overcome these limitations (Figure 4). [14]

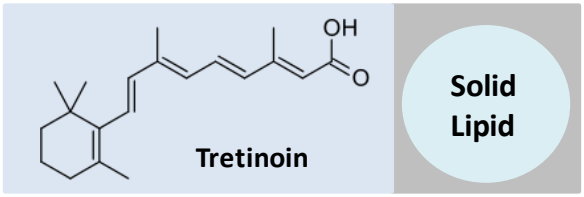


Fig. 4: Tretinoin encapsulated SLNs

2.3 Vitamin D analogues:

Vitamin D_3 analogues such as calcipotriol, maxacalcitol, tacalcitol, and

calcitriol are the mainstay of treatment in mild-to-moderate plaque psoriasis. Local irritation is the most frequently noted side effect, which is managed by combining vitamin D_3 analogues with topical corticosteroids.[15] Lin *et al*. developed nano liquid carriers (NLCs) loaded with both MTX and calcipotriol and reported enhanced drug permeation with limited skin irritation in animal models (Figure 5).[16] Prufer *et al*. incorporated 1, 25-dihydroxyvitamin D_3 in liposomes and reported its superiority over un-encapsulated drug in efficacy as well as safety[17,18] and administration of immuno-modulators are available.[19,20,21]

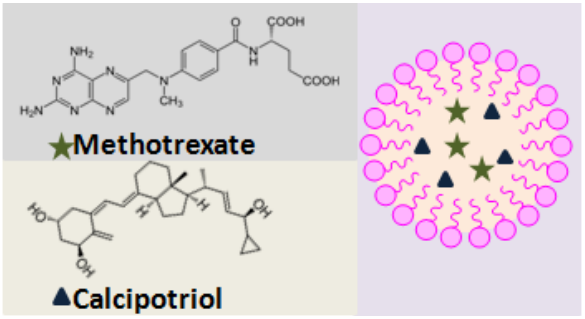


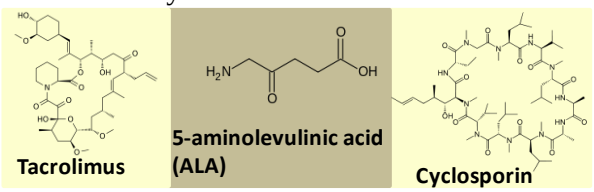
Fig. 5: Therapeutics encapsulated NLCs

2.4 Phototherapy:

If psoriasis can't be controlled by topical treatments, phototherapy, or light therapy are the optional. Ultraviolet light is emitted from the sun can dramatically slow the growth of skin cells, reducing the symptoms of psoriasis. But artificial ultraviolet lamps and lasers are a more targeted way of treating the condition.[22,23] Topical photodynamic therapy (PDT) with 5-aminolevulinic acid (ALA), a second-generation photosensitizer is a treatment option for psoriasis covering large area.[24] The major limitation of this strategy, however, is the poor penetration of ALA into the skin lesions.

2.5 Immune suppressants:

Tacrolimus (FK506), an effective and well-tolerated immunosuppressant, has also found its importance in the treatment of chronic plaque-psoriasis. Various clinical trials of tacrolimus in chronic plaque-psoriasis have been conducted with the conventional topical formulations.[25,26] Cyclosporin A (CsA) is used in the treatment of psoriasis by oral as well as topical route. Its high molecular weight (more than 500 Da) and limited cutaneous permeation are the key challenges for topical delivery.[27] Many attempts have been made to achieve localized site-specific immunosuppression using conventional topical formulations of CsA, e.g., at Novartis Research Centre (Vienna, Austria), but off without any avail.[28]



2.6 Biological agents:

Recently, many biological agents including Ustekinumab, Alefacept, Efalizumab, Etanercept, Infliximab and Adalimumab[29,30] have been developed to target the hyperactive immune reaction. The main barriers in psoriasis therapy are the potential severe adverse effects of long-term treatment with systemic immune suppressive agents.[31,32] In addition, the cost of these biological agents is $20,000 to $30,000 per year, which is a big hurdle for their extensive use in clinic.[33] Also, these approaches have major limitations and setbacks including the fact that skin develops resistance to treatments over time. In addition, therapeutic outcome of psoriasis treatments also can be unpredictable.[31,32,34,35,36]

3. <u>National Status:</u>

Towards developing therapeutics for psoriasis Agarwal *et al*. developed dithranol entrapped in liposomal and niosomal vesicles (0.5%) and found both of them superior to conventional formulation, while liposomes showed better results than niosomes employing mice skin. They found both of them superior to conventional formulation, while liposomes showed better results than niosomes.[37] Gidwani *et al*. in their patent application revealed the usefulness of mixed vesicular systems of dithranol with and without salicylic acid. The formulations, when tested on more than 12 patients for 4 weeks, proved to be effective and devoid of irritation and staining.[38] This product when tested clinically in an open label[39] as well as randomized double blind trials[40] showed that dithranol in greatly reduced doses (0.5%) in liposomes could clear the

psoriasis plaques to match that of 1.15% commercially available dithranol ointment.[40] The advantages of liposomal dithranol in terms of efficacy and compliance (no irritancy and non staining) have been attributed to the ability of strategic liposomal formulation design. Katare *et al*. developed TAM liposomes of multilamellar nature, which exhibited appreciably enhanced skin permeation as well as retention of drug molecules in the skin to treat psoriasis.[41,42] Agarwal et al delivered capsaicin through lipid nanoparticle for treating psoriasis.[43] There is lacuna of developing nucleic acid therapeutics of skin diseases in India.

4. Future directions:

There was considerable advance in the field of nanotherapeutics for psoriasis. However, there are no long-term effective therapies, so this remains at the top of the list for unmet needs. Psoriasis is now leading autoimmune disease, and advancements in complex disease biology at molecular level enriched our understanding. Thus, innovative, safer and effective therapeutics and strategies are required to target hyperactive immune elements that target multiple pathways of psoriasis pathogenesis.

Acknowledgements:

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