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A Review on Disease Management and Drug Delivery Aspects in Psoriasis

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Abstract — This review offers insight into disease management of psoriasis and pharmaceutical approach for the effective drug delivery for the treatment of this disease. Several treatment regimens has been tried for psoriasis but rate of success is always limited as for as conventional system is concerned. This review deals in details about topical drug delivery in general and its challenges in designing effective drug delivery against psoriasis.

Keyword — Psoriasis, skin disorder, topical therapy, Antipsoriatic drug

1. INTRODUCTION

Psoriasis is a chronic inflammatory skin disorder that may drastically affect the quality of life of an affected person. Different treatments are available for psoriasis and among this topical therapy are most commonly used in majority of patients. Psoriasis has genetic and life style triggers; the treatment guidelines involve continuous monitoring and lifelong care for the patients. Knowledge of the disease trigger factors and their role in precipitating the psoriasis is quiet important in the disease management. Care should be taken to avoid these psoriasis triggers. In recent years, new biological therapies have been introduced and several existing treatments have been improved giving new hope to people with psoriasis.

Quality of life in a disease whether it's pre-treatment or post-treatment speak a lot about its all round impact on patients. Psoriasis has negatively effects on quality of life. Psoriasis is a lifelong, chronic, and recurrent disease. In a patient surveys conducted by the National Psoriasis Foundation between 2001 and 2008 in the USA, 33% of patients with mild disease and 60% of patients with moderate-to-severe psoriasis reported that their disease significantly affect their everyday life. Psoriasis can be as debilitating as many other serious medical or psychiatric conditions. The physical, psychological and social dimensions of life are negatively affected by the psoriasis and can be greater than those resulting from life-threatening illnesses such as myocardial infarction. Physical and mental rankings of psoriasis and other diseases, from best functioning (1) to worst functioning is (11). Physical rank of psoriasis is (10) just second to congestive heart failure (11) while mental rank is (9) which is third highest after depression (11) and chronic lung disease (10) but overall it has (10+9=19) rank which is highest amongst all disease[1]

The different types of psoriasis based on symptoms is given under:

Plaque Psoriasis
Guttate Psoriasis
Inverse Psoriasis
Erythrodermic Psoriasis
Pustular Psoriasis

According to Ayurveda, psoriasis (Sidhma Kushtam) occurs due to vitiation of doshas of Vata and Kapha. The reasons are use of incompatible food and accumulation of toxins etc.

Psoriasis treatment involves mainly three types of therapy:

Antipsoriatics		
Topical	Tars	Tar
	Antracens	Dithranol
	Psoralens	Trioxysalen – Methoxsalen
	Others	Fumaric acid – vitamina D (Calcipotriol, Tacalcitol, Calcitriol) – Tazarotene
Phototherapy		Artificial or natural light sources
Systemic	Psoralen	Methoxsalen – Bergapten- Trioxysalen
	Retinoids	Etretinate – Acitretin

Different treatment options are available to control and eliminate the symptoms of psoriasis. Nevertheless, most of them cannot be regarded as an ideal drug molecule. This may either be due to their inherent adverse effects or their improper incorporation in the conventional vehicles.

Topical Corticosteroids
Calcipotriene
Sequential Therapy with calcipotriene and super potent corticosteroids
Salicylic Acid
Coal Tar
Goeckerman's Regimen
Tazarotene
Calcineurin Inhibitors

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2. SKIN AS DELIVERY TARGET

The skin, called *cutis* in Latin (term cutaneous derived from it), is the largest organ of the body counting more than 10% of the total body mass. Its large surface area of around two square meters considered essential for the survival as it is in direct contact with the environment providing multifunctional activity against varying conditions. For pharmaceutical technologist's approach skin presents tremendous opportunities for drug delivery and overcoming the barrier function of it has become the essence in the design of topical drug delivery systems. Thus, before going for topical formulations it is necessary to study skin and its barrier function thoroughly.

The human skin is organized into two distinct layers, namely the outermost epidermis and the layer below epidermis is called dermis (Figure 1.1). Beneath the dermis are subcutaneous fatty tissues. Bulbs of hair embedded in to these fatty tissues. The highly vascular dermis is made up of a connective tissue containing network of blood vessels, hair follicles, pilosebaceous units and sweat glands. The epidermis is avascular in nature and has five numbers of different layers, which, from outermost to bottom, are stratum corneum (also called Horny layer), stratum lucidum presents only in thick skins, stratum granulosum (Granular layer), stratum spinosum (Prickly cell layer) and stratum germinativum (Growing layer). The stratum corneum consists of corneocytes which is dead epidermal cells rich in keratin and surrounded by crystalline intercellular lipid domains. In addition to the almost impermeable corneocytes, the barrier function of stratum corneum is offered by the presence of a unique mixture of lipids in the intercellular spaces of it. These lipids, though acting as barriers, can provide a passage for permeation of exogenous chemicals, including drugs[2]. Therfore, drug delivery across the stratum corneum has become the real challenge in the design of topical drug delivery systems[3].

Absorption through skin generally takes place either by transepidermal route or by transfollicular route. Transepidermal pathway can be described as diffusion across the skin. Stratum corneum is the major resistance encountered along this pathway. Transepidermal permeation pathway first involves partitioning into the stratum corneum followed by diffusion across this tissue. Most of the drugs and substances diffuse across the stratum corneum via the intercellular lipoidal route. Transfollicular absorption takes place through skin appendages. Hair follicle and associated sebaceous gland present in skin collectively referred to as skin appendages. This is a secondary route of absorption.

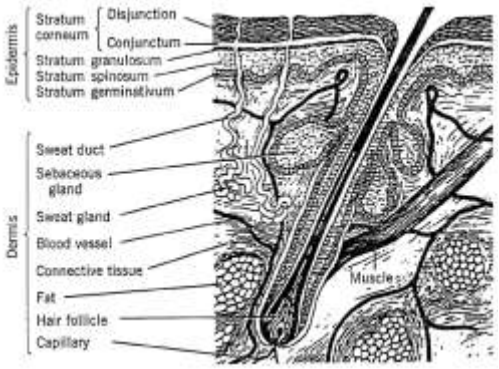

Fig.1.1. Structure of human skin

After getting insight into skin and its barrier function it is imperative to develop drug delivery systems instead of applying drug molecules alone in a conventional manner to overcome the epidermal barrier for effective topical drug delivery. Drug delivery systems with modifications at both physical and chemical level can be effective against barrier function of the skin[4].

Drug delivery systems found effective in topical delivery:

Nanostructured lipid carriers and Solid lipid nanoparticles (so called NLC and SLN)

Other colloidal carriers such as liposomes, niosomes and polymeric nanoparticles

Other approaches such as Iontophoresis, Sonophoresis, Electroporation, Local thermal treatment, Micro-needles arrays and Mechanical perforation of stratum corneum by high velocity particles[5, 6] are also developed.

With an eye on improving the topical delivery of drugs with drug delivery systems certain chemical enhancement methods has been applied such as (1) occlusion: to prevent trans-epidermal water loss from stratum corneum by the use of hydrogels, ointment bases [7, 8], (2) increasing the hydration of stratum corneum by high water content in the formulation, (3) addition of chemical enhances in the formulation to disrupt the lipid organization in the stratum corneum such as azone, terpenes, fatty acids, dimethylsulphoxide (DMSO) and alcohols[09], (4) addition of compounds in the formulation that are able to alter the protein organization in the stratum corneum, such as DMSO or urea, (5) use of penetration enhancers in the formulations such as Transcutol P[10], (6) Modifying the thermodynamic activity of the drug in the formulation at the moment of the application, e.g. ethanol[11], (7) For poorly soluble substances, solubilization of the drugs in the donor e.g. surfactants[12].

Topical drug delivery is often intended for the local treatment of disorder by direct application of a formulation containing the appropriate drug. The disorder can be of cutaneous origin such as bacterial skin infections and dermatitis, cutaneous manifestations of a general disease (e.g. psoriasis) as well as diseases associated with mucosal surfaces such as candidiasis and periodontitis. The drug should ideally be confined to the surface or within the site of application to effectively treat

the disorder without appreciable systemic drug absorption. This unintended drug absorption occurs, is of sub therapeutics quantities. Thus, the site of application forms the target of topical drug delivery systems. The most commonly employed vehicles to achieve topical drug delivery are semisolids such as ointments, creams and gels. Semi-solid formulation in all their diversity dominate the system for dermal delivery, but medicated powders, spray, foams, and even medicated adhesive systems are also in use[13].

Topical drug delivery has the capacity to achieve controlled and sustained drug delivery to provide predictable and extended duration of drug activity that many conventional modes of drug administration fail to achieve. The principal advantage of topical drug delivery lies in targeting the drug action directly to the site of disorder by allowing accumulation of high local drug concentration within the tissue and around its vicinity for enhanced drug action this is more effective when drugs with short biological half-life, narrow therapeutic window are applied with topical route. Such targeted drug action is unlikely to be attainable if drug is delivered via systemic pathway or from oral route. The major systemic and oral side effects as well as variable drug bioavailability associated with first-pass metabolism for drugs administered systemically can be avoided. Other advantages include ease of administration which will improve patient compliance, easy termination of drug delivery by prompt removal of the applied formulation in the case of any adverse event, and relatively large area of application in comparison with buccal or nasal cavity. Although topical drug delivery offers certain advantages over systemic delivery for selected drugs and conditions, the resistance against drug transport across skin barrier remains a major challenge to efficient drug delivery by this route. There is also potential of skin irritation or contact dermatitis arising from one or more components in the topical formulation. Solvent evaporation after exposure of a formulation to the environment may render inconsistencies in the formulation composition. In some cases poor permeability of some drugs through the skin leads to poor pharmacological response. Possibility of allergic reactions and degradation of drug by the enzymes present in epidermis may create problems[14].

The success of topical drug delivery is dependent on the interplay among various factors; such as physiological factors of skin, physicochemical nature of the drug, formulation components and their interactions with each other, are among those to look for the success of this therapy[13, 2]. These factors are:

Physicochemical nature of active substances

- Partition coefficient
- pH-condition
- Drug solubility
- Concentration
- Particle size
- Polymorphism
- Molecular weight

Dermatological conditions

- Moisture content of skin
- Thickness of the skin treated
- Skin age
- Species variations
- Condition of the skin (intact/injured)
- Skin temperature

Formulation content of topical product

- Vehicles
- Permeation enhancers
- Other additives

Thus, one can say that treatment of skin disorders through topical drug delivery has distinct advantages as compared to oral and parenteral administration but topical drug delivery is still a daunting task for formulators due to difficulties in controlling and determining the amount of drug reached at different skin layers. Physicochemical properties of drug and formulation components and their interaction are the factors which influence this distribution of drug among skin layers[15]. A suitable colloidal delivery system for topical application may be prepared using physiological lipids which have good acceptance by the host body and cost effective too.

A general criterion for the selection of optimal formulation parameters when developing a topical drug delivery system

Factor	**Preference**
Drug	Preferentially lipophilic
Vector type	Lipidic in nature in nanonized form
Carrier size	Lowest as possible to facilitate uptake and passage
pH	Close to physiological pH to avoid irritation
Vehicle	Semisolid consistency preferred

Psoriatic skin conditions and challenges for topical drug delivery

Rigidization of psoriatic skin has been attributed to a rise in the levels of cholesterol and fall in the levels of ceramides. Apart from this, normal moisturizing factors (NMFs) like water are almost absent in the psoriatic skin of a patient. As a result of these factors, targeting drug molecule in a vehicle to the psoriatic tissues using topical route poses a big challenge.

Common skin changes in psoriasis

Skin lesions covered with scales having thickened inflammation.

Dry skin due to deficient natural moisturizing factor

Imbalanced skin lipids

Skin having tethered hair

Skin sensitivity

Corneocytes have excessive growth and aberrant differentiation

Topical delivery into the psoriatic skin have lately been proposed to be addressed by the colloidal carrier systems, such as liposomes[16, 17], niosomes and mixed miceller system[18], silica aerogel[19] and ethosomes[20], lipid

microemulsion[21]. The application of lipids in particular in these formulations resolves the problem of lipid imbalance and lack of moisture content. Thus, these lipoidal and allied carriers can result in an effective delivery of drugs across psoriatic skin[22].

3. Conclusion

Psoriasis is a topical disorder with unknown etiology and still after advancement in medical science complete cure of this disease is not yet established. Thus quality of life after disease identification is definitely compromised in a big way and requires a conscious efforts and protocols as disease management is an important tool to keep this disease under control. Topical therapy whether it is conventional or novel is always choice of delivery system for pharmaceutical technocrats. Psoriatic skin pose a stiff challenge in designing a viable topical delivery system for delivery of antipsoriatic drugs and combining advantages of novel drug delivery system precisely colloidal drug delivery approaches provides a better drug delivery regime to the psoriasis treatment.

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5. Conflict of Interest:

None declared