

Exploration of Hydrogel for the management of Psoriasis

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Abstract

Persistent skin condition called psoriasis is characterized by the redness of skin. It is pertinently connected to aberrant immune cell-keratinocyte (KC) cross reactivity. Many psoriasis sufferers are unhappy with their existing treatment regimens and the way the medication is administered. The patients express their displeasure about excessive viscosity of the preparation, bad odour, and skin irritation. The causes of these problems should be connected to patients following their doctors' instructions, such as those regarding the regular application of the preparation, as well as the therapy's lack of effectiveness due to the drug's poor penetration of the skin. The preparation's physicochemical form, as well as its rheological and mechanical properties, are directly related to both of these criteria. It is crucial to learn about the particular drug type and how it affects a therapy's safety and effectiveness as well as the patients' comfort while being applied. Hydrogels are essential in biomedical applications because of their unique qualities, which include superabsorbancy, viscoelasticity, softness, fluffiness, biodegradability, and biocompatibility. The purpose of this review is to present a brief concept of hydrogel, its unique features, classification and advantages. This review also discusses herbal extract loaded hydrogel for psoriasis.

Key words : Keratinocyte, cytokines, polymers, drug delivery, hydrophilicity, bioavailability.

Psoriasis is a hereditary skin condition that is hyperproliferative, inflammatory, and chronic¹⁴. The frequency is roughly equal between men and women, and it affects 2% of American adults. It usually first appears between the ages of 15 and 30³⁹. Pathogenesis of psoriasis is caused due to main cytokines which include dendritic cells, T cells and tumour

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necrosis factor (alpha)¹².

Risk factors :

Environmental elements, age, and sex all have an impact on how the condition develops. Bacterial infection, mechanical injury, skin irritation are among the most significant²².



Figure 1 - Histopathology of psoriasis [Skin biopsy shows seborrhoeic keratosis, epidermis shows hyperkeratosis, pseudo horn crystals, focal area of squamous eddies.]

Pathogenesis of Psoriasis :

Psoriasis pathogenesis is characterized by three basic elements: cytokine production, Vascular changes and Skin infiltration by inflammatory cells, and abnormal proliferation of keratinocytes³¹.

Psoriasis is a chronic inflammatory disease that causes excessive proliferation of keratinocytes mediated by T cells. In psoriatic lesions, the Th1 cytokines TNF- α , IFN- γ , and IL-12 are more prevalent. TNF- α , IFN- γ , and a host of other cytokines and growth factors can all be induced in keratinocytes to create IL-6, IL-7, IL-8, IL-12, IL-15, IL-18, and TNF- α ¹⁵. There are various clinical types of psoriasis but the most frequent type is psoriasis vulgaris or plaque type of psoriasis, 80% to 90% individual is affected by plaque psoriasis²¹. Size of scaly lesions ranges from 0.5 cm in diameter. Clear distinction is present between a plaque and clinically normal skin.

Types of Psoriasis vulgaris :

Table-1. Classification of Psoriasis vulgaris According to Phenotype

S.No.	Type	Characteristics
1	Flexural (Inverse psoriasis)	Found under the breasts, between the buttocks, and under the armpits. This is especially prone to inflammation from rubbing and perspiration. The popliteus and axillae are infrequently affected, while the inguinal, submammary, intergluteal, umbilicus, and genital folds are the locations of the most frequent lesions.
2	Seborrhoeic (Sebopsoriasis)	Resemble to seborrhoeic dermatitis, can occur alone or in conjunction with psoriasis vulgaris in other places. Eyebrows, scalp nasolabial folds, nose, ears, eyebrows, hair line, medial cheeks, presternal, and between scapular areas are among the areas that are affected.
3	Scalp	It ranges from isolated plaques to thick plaques or scaly, nonthickened areas that resemble seborrhoeic dermatitis in their entirety. The occiput and the immediate postauricular region are sites of predilection.
4	Palmoplantar	Restricted to soles of foot and hands. Scaly or fissured areas ranging from large plaques covering the palm or sole to ill-defined scaly or fissured areas without obvious plaques. It is characterized by sterile, yellow to brown pimple with pus on the soles as well as palms ¹³ .

Psoriasis Treatment :

Any treatment plan should aim to reduce or eliminate burning, scaling, itching, inflammation, and dryness.

Topical Therapy :

For all psoriasis patients, topical therapy is still an essential part of their care. Most patients have mild disease, which is usually treated with topical therapy alone. Treatment options for moderate to severe psoriasis typically include biological agents, systemic therapies, and phototherapy. On the other hand, topical treatment may be beneficial in moderate-to-severe disease and may lessen the quantity of phototherapy or systemic agent needed to obtain adequate minimization of disease¹⁸. When psoriasis affects less than 10% of the body's surface area (BSA), it is considered mild psoriasis and should be treated with topical therapy³⁶. Treatment options for individuals with mild psoriasis consist of calcineurin inhibitors, keratolytic agents, vitamin D analogues, and topical corticosteroids³.

Systemic Therapy :

Moderate to severe psoriasis can be recovered with the help of systemic treatment. Retinoids, cyclosporin A, and methotrexate (MTX) are conventional systemic treatments for psoriasis³⁰.

A brief Research History of Hydrogel for Psoriasis Treatment :

Hydrogels are finding more and more applications in pharmacy and medicine. because of their advantageous biocompatibility,

physicochemical characteristics, and intended interaction with living environments. Numerous hydrogel varieties have been created to date that may be useful in treating and caring for skin conditions.

A bis-imidazolium based amphiphile hydrogel that can be used as a carrier for psoriasis treatments without causing side effects was developed by David Limón and his team. They demonstrated how this novel biomaterial protects the medication from deterioration and promotes controlled release⁴¹.

In one of the research studies Jiangmei and his group developed methotrexate loaded hydrogel by using Carbopol 934. Obtained result indicated that developed hydrogel has improved skin moistening and improved the drug permeation, prolonged action of methotrexate and good anti-psoriasis effect⁴⁰. On another hand Bhushan Kumar and his coworkers studied the safety and effectiveness of topical methotrexate [0.25%] gel in hydrogel base in patients having palmoplantar psoriasis. Total 14 patients were involved in this study. ESI (Erythema, scaling and induration) score at baseline was 5.8 ± 0.9 for palms. The score at the end of study was greatly reduced to 3.5 ± 0.7 ²⁴. Budesonide loaded hydrogel was formulated and evaluated by P. M. Kharat and his team hydrogel material developed by this group released the drug in sustained release manner. These authors identified that hydrogel is ideal drug delivery vehicle for topical treatment of psoriasis²⁰.

After a summary of the data from the literature mentioned above, it is most reasonable to use hydrogels to treat psoriasis.

These biomaterials not only lessen the adverse effects of the medications used in its therapy but also offer defense against deterioration and allow controlled release of drug.

Basic concept of Hydrogel :

A hydrogel is a 3-D configuration consisting of hydrophilic polymers that have multiple functional groups in the polymer chains, such as sulfo groups (-SO₃H), hydroxyl group (-OH) amino (-NH₂), carboxylic acid (COOH), amide (-CONH). These groups enable the hydrogel to interact and hold onto a large volume of water and biological fluids². These polymeric systems have ability to undergo swelling in water and hold a sizable portion

(> 20%) of water inside their 3-D structure without dissolving in it³⁸. Some of frequently used polymers in the formulation of hydrogel are given in figure 2³³.

Unique Features of Hydrogel :

Hydrogel has a comparatively high fluid absorption capacity. Because hydrogels are soft, porous, and contain a lot of water, they resemble living tissues. Properties of hydrogel (such as hydrophilicity mechanical properties, swelling capacity, or permeation of bioactive components) can be changed under influence of surroundings, including biological factors magnetic field temperature, pH, electromagnetic radiation¹⁷. Hydrogels exhibit

Table-2. Topical delivery of Drugs via Hydrogel for Psoriasis

Drugs	Type of hydrogel	Clinical significance and outcomes	References
Clobetasol propionate	Nanosponge Hydrogel	The chosen formulation increased the water solubility of clobetasol propionate by 45 times.	[23]
Tacrolimus	Polymeric nanocarrier loaded hydrogel	The local bioavailability and drug delivery efficiency of the obtained composite hydrogel are improved.	[9]
Mometasone furoate	Nanostructured lipid carrier-based hydrogel	Permeation studies on drugs revealed extended drug release, and skin desposition was 2.5 times greater than that of commercial formulations.	[19]
Methotrexate	Polymeric nanoparticle loaded hydrogel	Prolonged drug release in 48 hr., histopathological study was found to have healing signs of mice skin	[4]
Betamet- hasone dipropionate and salicylic acid	Nanocarrier based hydrogel	The drug's skin deposition was measured at 29.73 µg/mg, and its in vivo anti-inflammatory activity showed inhibition of inflammation.	[5]
Niclosamide	Nanocrystal loaded hydrogel	Pattern of drug release has high similarity with Higuchi model, HaCaT cells' cytotoxicity assay revealed a rise in the inhibitory effect.	[25]

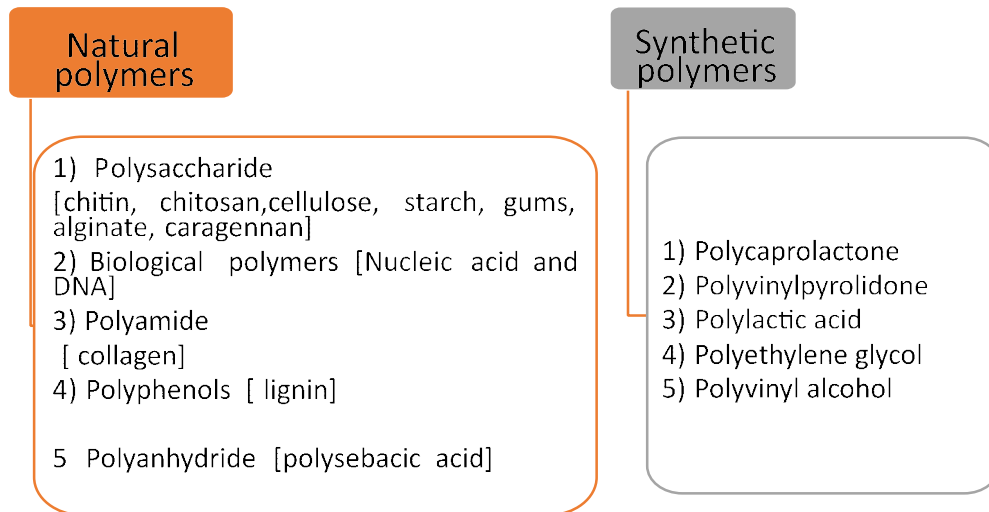


Figure 2. Flow chart of Common Polymers Used in Hydrogel

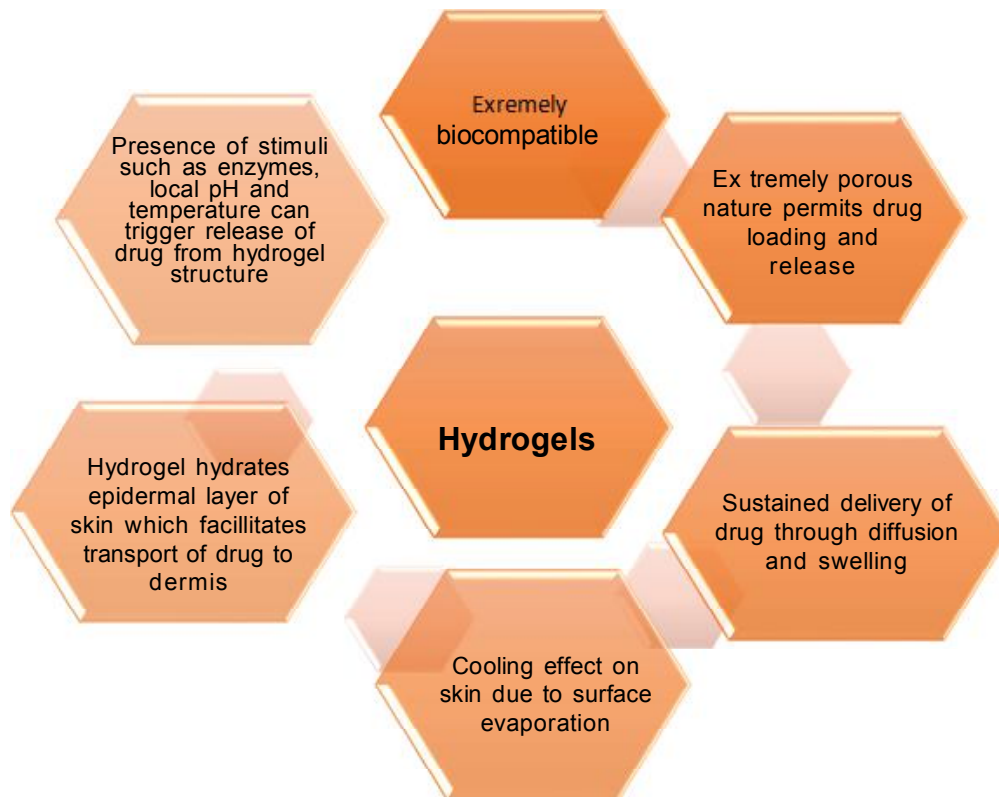


Figure 3. Advantages of Hydrogel

viscoelastic mechanical behaviour, which is related to water and the flow of polymer networks in fluid. Hydrogels primarily experience specific hydrolytic and/or enzymatic degradation over time²⁷. Hydrophilic functional groups attached to the backbone of polymer give hydrogels their ability to absorb water, while cross-links between organization of chains give them resistance against dissolution¹.

Advantages of Hydrogel :

Compared to other vehicles, the

hydrogel formulation is effective in a shorter amount of time, and patients adhered to the treatment plan with greater discretion. Some of the advantages of hydrogel over other drug delivery vehicle are given in figure 3¹⁶.

Classification of Hydrogel :

The hydrogel materials can be categorized into different bases as described in table 3.

Table-3. Classification of Hydrogel on the Basis of Different Properties

Based on polymeric composition ¹⁰	Based on ionic charge ⁶	Based on response ³⁷	Based on cross linking mechanism ³⁴	Based on configuration ²⁸
1] Homo-polymeric hydrogel (made up of single species of monomer) 2] Copolymeric hydrogel (contains two or more distinct monomer unit) 3] Multipolymeric hydrogel (consist of two independent cross-linked polymer)	1] Neutral 2] Cationic 3] Anionic	1] Chemical response <ul style="list-style-type: none"> ○ pH responsive ○ Glucose responsive ○ Oxidant responsive 2] Biochemical response <ul style="list-style-type: none"> ○ Antigens ○ Enzymes ○ Ligands 3] Physically responsive <ul style="list-style-type: none"> ○ Temperature ○ Light ○ Pressure ○ Electric field ○ Magnetic field 	1] Physical cross-linking <ul style="list-style-type: none"> ○ Freez thawing ○ Stereo complex formation ○ Thermosensitive gelation ○ Charge interaction ○ Hydrogen bonding interaction 2] Chemical cross-linking <ul style="list-style-type: none"> ○ Radical polymerization ○ Condensation reaction ○ Enzymatic reaction ○ High energy irradiation 	1] Amorphous 2] Crystalline 3] Semi-crystalline (mixture of amorphous and crystalline phase)

Table-4. Herbal Extract Used in Psoriasis

Plant	Family	Part used for extract	References
<i>Berberis aristata</i>	Berberidaceae	Root bark	[32]
<i>Azadirachta indica</i> (Neem)	Meliaceae	Leaves	[32]
<i>Lawsonia inermis</i>	Lythraceae	Leaves	[32]
<i>Mallotus phillippensis</i>	Euphorbiaceae	Fruit	[8]
<i>Commiphora mukul</i> (Gugul)	Burseraceae	Resin	[29]
<i>Centella asiatica</i>	Apiaceae	Dried leaves	[29]
<i>Gentiana lutea</i> (gentian)	Gentianaceae	root	[29]
<i>Hypericum perforatum</i> (St. John's wort)	Hypericaceae	Aerial parts containing dried branch tips with flowers	[11]

Herbal extract loaded Hydrogel for Psoriasis :

The synthetic drugs encapsulated in hydrogels may have inherent toxicity, which can be exacerbated if released in higher concentrations or too rapidly. This toxicity can have negative effects on the local tissue or the entire organism. Bhardwaj Kamini and other team have developed hydrogel containing psoralen and capsaicin extract to minimize side effect produced by synthetic drugs to treat psoriasis, net result concluded that % cumulative drug release of optimized formulation was higher than marketed formulation⁷. Aloe vera mucilaginous based hydrogel was prepared by Silvana T. L. Jales and other co-workers for topical use in the treatment of psoriasis. This formulation was found to be effective in controlling hyperkeratinisation¹⁸. Hydrogel formulation containing lavandin essential oil was developed by Katarzyna S. This formulation was applied to imiquimod induced mouse model. Lavandin oil loaded hydrogel reduced expression of CD3, CD68 cells and symptoms of psoriasis³⁵.

Plant extract used in the treatment of psoriasis are given in table-4 .

Hydrogel platforms are being formulated extensively for a number of biomedical applications Because of their special material qualities—such as their ability to swell, degrade under control, and self-heal. A major application area is the diagnosis of skin conditions such as psoriasis. There are several advantages to using hydrogels in the treatment of psoriasis, including a decrease in drug side effects because of the increased bioavailability of the medication. This permits the use of a lower dosage, defense against deterioration, and strictly regulated drug release. Hydrogels are also highly versatile, programmable, and biocompatible, which makes them perfect as drug delivery vehicles. Hydrogels have been shown to be at least as effective as other drug delivery vehicles, and in many cases, more so. Users consistently rate hydrogels higher than other drug delivery vehicles, and they may even be the preferred drug delivery vehicle for patient compliance alone. These factors, along

with the ongoing advancements in hydrogel research, suggest that hydrogels are the platform of choice for the treatment of psoriasis.

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