Psoriasis: A Current Treatment Approach

Dhruba Sankar Goswami¹, Arnab Chakraborty*²

¹Associate Professor, Gitanjali College of Pharmacy, Birbhum, WB.
²Assistant Professor, Adamas University Jagannathpur, 24 Parganas, Kolkata 700126.

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ABSTRACT

Psoriasis is a common immunological problem related to skin, it may occur on skin or mucous membrane, and it possess a difficulty in treatment manifestation. Reviewing the efficiency of existing and marketed herbal and biological treatments in reducing different types of psoriasis lesions along with the types of psoriasis are the target of the current review. The disease psoriasis, most commonly damages on the skin of the elbows, knees, scalp, hips, bony prominences of joint, in between buttock, vulva and penis. Patients of psoriasis may face the physical, mental and socioeconomic harassment in the society. It causes depression which may further worsen the disease. immunological, genetic and environmental factors like cold weather, any kind of trauma to the skin may play role for starting of psoriasis. Some other important such as Streptococcus pneumoniae infection, obesity, smoking, drinking of alcohol and regular use of soap may worsen the situation. Especially in the case of palmoplantar psoriasis the condition of the patient gets very painful because in that case blister filled with pus on palm may be very painful and working with exfoliated skin may be very difficult to work with. As the PSOR gene, TNF alpha and T lymphocytes are mainly responsible for psoriasis it can be the target for future treatment of psoriasis.
INTRODUCTION:
Psoriasis is a dermatological abnormality that can be identified with red, itchy scaly patches which may occur in the knees, elbows, torso, lumber area and frontotemporal area of scalp [1]. Generally, it occurs on the bony prominence like elbow and knee of leg and hand. Psoriasis can be called as a chronic autoimmune condition that causes the rapid building and proliferation of dermal parenchyma. Psoriasis patches having dandruff-like scaling of the horny layer of the skin [2]. If we consider the histology of psoriasis then it is seen that there is accumulation of T lymphocytes, endothelial cells, and vascular dendritic cells [3]. It is seen that there is swelling for some weeks or months, inflammation around the flare. There is no option for complete healing for psoriasis. The immunology of psoriasis is unveiled as, the T cells become hyperactive and destroy the dermal parenchyma by mistake. Thus, the Inflammation happens. To cope up with the reaction the keratinocytes rapidly grow. Hence the responsible factors for psoriasis are major histocompatibility complex (MHC) & T lymphocytes. As per the Genome-wide association studies have identified nine chromosomal loci (PSORS1 through PSORS9) that can be linked to psoriasis. The major genetic determinant seems to be PSORS1, which probably accounts for 35–50% of the hereditary component of psoriasis. HLA-Cw6-positive and HLA-Cw6-negative patients with Psoriasis vulgaris have distinct clinical features [4].

Epidemiology:
The spread of psoriasis varies from 0.14% in eastern Asia, in western Europe (1.92%), central Europe (1.83%) and in southern Latin America (1.1%) [5]. In Northern India, the prevalence of psoriasis in adults varies from 0.44 to 2.8%, with a much lower prevalence in children [6].

Symptoms:
symptoms of Psoriasis vary from individuals [7]. The Common symptoms are as follows:
1. skin scaling with flakes in small child
2. Dry, broken skin from which blood and tissue fluid may leak
3. Swelling in joints with loss of flexibility
4. A firm, swollen finger
5. Itching, burning or soreness on the affected skin
6. Thickening, pit, ridge and crack of nail
7. sacroiliac joint inflammation)
8. Red patchy skin covered with thick, silver scales
9. Pain, redness and swelling to the heel and ankle joint
10. Morning stiffness of muscles that improves during the day [8]. There are many types of psoriasis, including:

a. Plaque psoriasis: This type of psoriasis can be easily and frequently found. It causes dry, raised, red blooded, pruritic plaques covered in whitish scales. Itching may occur to the plaque, and there may be few or many. They usually appear on bony prominence like elbows, knees, lower back and scalp. Dryness, cold weather, UV radiation are the cause of it [9]. It is generally associated with Human Leucocyte Antigen CW6 and happens before 40 years age [10].

b. Nail psoriasis: In case of nail psoriasis, the following observations can be seen -- pitting, leukonychia, grooves and Brittleness of nail plate. The other symptoms are discoloration, separation of the nail plate from the nail bed [11].
c. **Guttate psoriasis:** This type of psoriasis mainly happens in paediatric patients and during adolescence. It's generally occurred by bacteria. It's marked by small, tear shaped, scaling lesions that may occur on the thorax, upper and lower extremities [12].

d. **Inverse psoriasis:** This mainly occurs on vagina, penis, armpit and hips. Inverse psoriasis causes smooth patches of red skin but there are no scales that worsen with friction and sweating. Bacterial and fungal infections may trigger this type of psoriasis [13][14].

e. **Pustular psoriasis:** In this type of psoriasis causes pus-filled lesions that occur in the palms or the soles. Further infection can also occur [15][16].

f. **Erythrodermic psoriasis:** erythrodermic psoriasis affects the whole torso with a red-blooded rash. The rash is very itchy and inflames badly. The trigger factors are cortisones, lithium salts, quinine [17].

g. **Psoriatic arthritis:** Psoriatic arthritis causes swollen, inflamed joints that are typical of arthritis. In this case mild to severe type of rheumatoid arthritis can occur and it can affect any articulation especially the interphalangeal one. It may change the anatomy of the articulation permanently [18].

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**Trigger Factors of Psoriasis:**
Many people who are predisposed to psoriasis may be symptomless for ever till the psoriasis is triggered by some factors like allergens. Common psoriasis triggers include:

1. **Cold and dry weather**
2. **Trauma to the skin** (the normal healing gets hampered)
3. **Beta blockers, atorvastatin and primaquine**
4. **Tolnaphate, calcium channel blockers, enalapril, GMCSF, ILs, INFs, fibric acid derivatives like clofibrate, gemfibrozil and tumour necrosis factors antagonists like adalimumab.**

**Complications:**
Psoriasis can also increase the chance of developing other conditions, including:

1) **Psoriatic arthritis,** which exacerbate, rigidity with excrescences to the articulation

2) **Inflammatory problems of eye** such as conjunctivitis, blepharitis and uveitis in eye.

3) **As the psoriasis is related to the Autoimmune diseases,** such as celiac disease, multiple sclerosis and the IBS also affect along with psoriasis [19].
**Pathophysiology of Psoriasis:**

CD+ T cells in the epidermis and a combination of CD4+ and CD8+ cells to dermis are responsible for psoriasis. The immune-therapy of psoriasis is based on the role of IL-23. IL-23 is released from dendritic cells, which helps to stimulate Th17, thus, IL-17 and IL-22 release leading to local inflammation and keratinocyte formation on dermis\(^\text{[20]}\).

**Fig. No.: 1 Immunological Cascade of Psoriasis**

- **Upregulation**
  - Th1 cytokines (interferon-gamma [IFN-] and interleukin [IL-]2), IL-1, IL-6, and tumour necrosis factor-alpha (TNF-alpha)

- **Downregulation**
  - Th2 cytokines (IL-10)

**Table no. 1: Upregulation and downregulation of cytokines**

<table>
<thead>
<tr>
<th>Upregulation</th>
<th>Downregulation</th>
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<td>Th1 cytokines (interferon-gamma [IFN-] and interleukin [IL-]2), IL-1, IL-6, and tumour necrosis factor-alpha (TNF-alpha)</td>
<td>Th2 cytokines (IL-10)</td>
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**Treatment:**

**Traditional treatment by herbal drugs:**

- *Mahonia aquifolium* is also called barberry. Oregon grape has anti-inflammatory properties. The stem and leaves of the plant can be ground into a powder or distilled into an extract that is then used to make a topical skin cream. It’s been found to reduce redness in psoriatic flares when used with ointment\(^\text{[21]}\). *Indigo naturalis* extract can treat nail psoriasis. It was found that using the oil on nail psoriasis every day for several weeks improves the result rapidly\(^\text{[22]}\). *Aloe vera* is a plant known for its soothing and cooling properties. Aloe vera may also help regenerate skin cells and heal irritated skin. Psoriasis can be treated with aloe vera gel and 0.5% aloe vera containing cream. Applying the cream topically up to 3 times per day for 15 days
could decrease inflammatory response and helps to treat mild psoriasis [23]. Turmeric or Curcuma longa Family gingiberaceae is a good ayurvedic medicine and its active medicinal agent is curcumin. Turmeric has powerful anti-inflammatory and antibacterial properties, hence can be used in psoriasis. Poison oak works via inhibition of the keratinocyte hyperproliferation and inducing apoptosis, inhibition of immune-inflammatory reaction, suppression of phosphorylase kinase (PhK) activity, and inhibition of the hedgehog (Hh) signalling pathway. The oral or topical administration of Psoralea corylifolia L. (Leguminosae) with exposure to ultraviolet A (UVA) light can control psoriasis.

There is no cure is available for psoriasis [24].

**Topical agents:**

Two months of application of dermal corticosteroids like halobetasol, clobetasol, mometasone furoate can mollify the condition. Tritenoin and isotretinoin and tar are also used but can sooth slowly [25]. Combination therapy with vitamin D and synthetic corticosteroids as mometasone furoate, clobetasol, halobetasol were in combination form for chronic plaque psoriasis [26]. Single corticosteroid like mometasone alone can sometimes be used for the initial treatment [27]. Both o/w and w/o type of protective substance and emollients such as yellow and white paraffin, liquid paraffin and complex triphasic emulsions are used to clear of psoriatic plaques. salicylic acid damages the keratinocytes thus reduce the flares of psoriasis. Coconut oil, olive oil when used as an emollient in psoriasis [28].

methotrexate, an anticancer drug which is available as oral gel on mucous membrane can be consider as an example of dermal therapy. The immunity of the affected tissues gets lowered hence lower the exacerbation [29].

It is recommended by some dermatologist that medications used in streptococcal infections may improve guttate and chronic plaque psoriasis; but no certain established data are available [30].

**Modern medicines:**

It was seen that the monoclonal antibodies like: ixekizumab, secukinumab, brodalumab, guselkumab, certolizumab, and ustekinumab are very important and effective medication for treatment of psoriasis [31][32], as the target of treatment should be IL17, IL12/23, IL23, and TNF alpha. As the immunological pathways of psoriasis involve Th9, Th17, Th1 lymphocytes, and IL-22. Another treatment of severe erythrodermic psoriasis is fumaric acid and folate inhibitor like methotrexate or trimetrexate [33].

**Non-biologic systemic treatments:**

Non-biologic systemic treatments frequently used for psoriasis are some anticancer drugs and other molecules include methotrexate, ciclosporin, hydroxycarbamide, dimethyl fumarate, and retinoids [32]. In case of the erythrodermic type, Methotrexate and ciclosporin are anticancer that destroy the hyperimmune cells and immunosuppressant medications that suppress the immune system; retinoids like isotretinoin and tritenoin are derived from vitamin A can used. Hydrocortisone and betamethasone are not used here in the case, as they can produce and relapse flare after withdrawal [33].

Mabs are synthetic to semisynthetic drugs that alter and suppress the immunological cascade in psoriasis. They target the specific protein and specific pathways
of immune action. For the treatment of different types of psoriasis like plaque psoriasis the biologics are very popular now a day [34], as it is well known that immunosuppressant can increases the chance of infection it was found that fungal infection may occur with long term immunosuppressant treatment.

Mabs and other biologicals are used as ideal therapeutic substance as all other substances are nonresponsive in the case of plaque psoriasis [34]. ustekinumab is a fully human monoclonal antibody that directly inhibits IL-12 and IL-23 by binding their shared p40 subunit. So, it should be carefully given to the pregnant mother as the proper reactions are not yet reported. Infliximab like drugs which targets the TNF are not used for the patient suffering from hepatitis or HIV.

infliximab, adalimumab, golimumab and certolizumab are the monoclonal antibodies that developed to block the TNF alpha signalling. Other monoclonal antibodies, such as ixekizumab, [35] have been identified against inflammatory cytokines [36] and inhibit the inflammatory pathway. It is a humanized IL 17 monoclonal antibody.

ustekinumab targets the IL12 and IL 23 [33] Gusekumab is a fully human IL-23p19 monoclonal antibody. In 2017 the US FDA approved gusekumab for plaque types of psoriasis. One clinical trial done on the efficacy of anti TNFs on children suggested that 90 days of etanercept treatment retard the severity of the disease. [34] now a days the monoclonal antibodies have developed due to their selective and target specific action. The CD11a subunit can be a great site for nullifying the adhesion of T-lymphocytes thus the T lymphocyte-based inflammation can be prevented. Efalizumab can be the good choice for showing such kind of action. But it was banned due to its side effects. Alefacept also helps to reduce the number of T cell by activating the NK cells. [35] Apremilast may also be used. Sometimes due to immune tolerance antidrug antibody doesn’t react with TNF alpha and binds with wrong binding site of antigen then the monoclonal antibody does not inhibit the inflammatory mechanism of psoriasis [36].

CONCLUSION:
Psoriasis is a common immunological problem, it may occur with or without cutaneous involvement anywhere, and it possess a difficulty in treatment manifestation. Reviewing the efficiency of existing and marketed herbal and biological treatments in reducing different types of psoriasis lesions was the target of the current review. As per the review it was found that the disease specific immunotherapy is much better than using topical corticosteroids and anticancer drugs [38][39]. It was found that the TNF alpha and T lymphocytes should be main target for reducing inflammation as well as the PSORS1 to PSORS9 gene can be the target for gene therapy for psoriasis [37].

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