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A SYSTEMATIC REVIEW ON SCALP PSORIASIS: EFFECTIVE THERAPIES AND MANAGEMENT

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ABSTRACT

Psoriasis, characterized by chronic inflammation, has extreme impact on the condition of life of affected individuals due to its early onset, persistent nature, and both physical and psychosocial consequences. Scalp psoriasis, a prevalent and challenging condition, necessitates effective management to enhance patient quality of life. It impacts approximately 80% of individuals with psoriasis and poses treatment difficulties due to hair presence, limited accessibility, and cosmetic issues associated with topical treatments. Scalp involvement is frequent in psoriasis, presenting a particular challenge for treatment due to difficulties in therapeutic delivery. It is crucial to establish effective treatment approaches for scalp psoriasis to enhance the overall well-being of patients. This discussion explores current perspectives on the handling of scalp psoriasis.

KEYWORDS: Psoriasis, Scalp, Special site, Systemic, Topical, Phototherapy.

INTRODUCTION

Psoriasis is a chronic, systemic inflammatory ailment characterized by immune system participation, affecting not only the integumentary system, but also other bodily organ systems. It is a persistent skin condition characterized by the accumulation of skin cells in various areas of the body, resulting in the formation of silvery-red patches that may flake, itch, crack, and bleed.^[1] In the context of psoriasis, there exists a heightened rate of skin cell generation (hyperproliferation) occurring within a matter of days instead of the typical timeframe of weeks. This phenomenon arises as a consequence of erroneous communication from the immune system, thereby stimulating this accelerated process. This leads to the accumulation of excess cells on the skin surface, resulting in the formation of patches and plaques.^[2]

Epidemiology

According to data from the World Psoriasis Day consortium, approximately 125 million individuals globally, constituting around 2–3% of the global population, are affected by psoriasis. The prevalence of psoriasis in children is generally below 1% in all countries, whereas in adults, it ranges from about 0.17% in East Asia to 2.50% in Western Europe. A 2017 research study indicates that in India, the prevalence rate falls within the range of 0.44-28%, predominantly affecting individuals aged 30 or 40 years and older, with males experiencing the condition at a rate twice that of females. [4]

Pathophysiology

There are two primary hypotheses about psoriasis development. The first proposes that psoriasis arises from abnormal skin cell growth and reproduction due to epidermal and keratinocyte faults. The second hypothesis considers psoriasis an immune-mediated disorder, where activated T cells migrate to the dermis, release cytokines (including tumor necrosis factor-alpha [TNF α]), and cause inflammation and rapid skin cell production. The specific trigger for T cell activation remains unidentified. [6,7]

More than 60 susceptibility loci have now been identified using genome-wide association studies.5 Many of the candidate causal genes are involved in antigen presentation (HLA-C and ERAP1), NF-kappa B signalling (TNIP1), type 1 interferon pathway (RNF113 and IFIH1), interleukin (IL)- 23/Th17 axis (IL23R, IL12B and TYK2) and skin barrier function (LCE3). [8] This suggests a complex interplay between T cells, dendritic cells and keratinocytes as the likely underlying the pathophysiology of psoriasis, with the IL-23/Th17 axis being the central driver of immune activation, chronic inflammation and keratinocyte proliferation.6 Environmental triggers have been known to exacerbate psoriasis such as obesity, stress, betablockers, smoking and lithium.7 Although there is a relative paucity of data, pustular psoriasis appears to be genetically distinct, with different susceptibility genes implicated (IL36RN, AP1S3 in those of European descent and CARD14). [9,10]

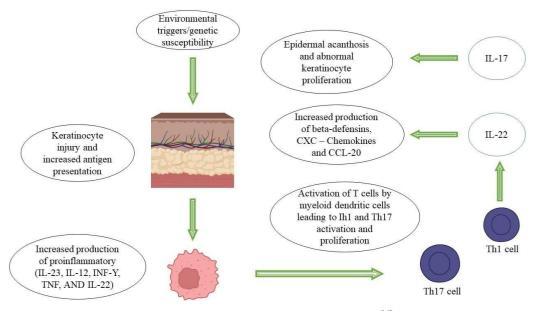


Figure 1: Pathogenesis of psoriasis. [6]

Clinical Presentations

Psoriasis, being an autoimmune disease, triggers an overactive response from the body's immune system, leading to various complications. Various other possible mechanisms contributing to psoriasis are family history of the disease, external factors like infections, especially streptococcal and HIV infections, drugs that are used for treating heart disease, malaria, or mental health problems, smoking and obesity. Psoriasis causes rashes which are life-threatening due to some complications like hypothermia. Thick, crimson-colored patches of skin with silvery-white scales that cause itching or a burning sensation are frequently found on the elbows, knees, Scalp, torso, palms, and the soles of the feet. Dry and cracked skin that leads to itching or bleeding may be experienced. The nails may become thick, ridged, or pitted.

Additionally, the disease's symptoms, which include pruritus, erythema, and scaling, among others, have a substantial negative psychological influence on the afflicted patients and significantly lower their quality of life. Psoriasis manifests in various forms such as plaque, flexural, guttate, pustular, or erythrodermic psoriasis. The predominant type of psoriasis is plaque psoriasis, which primarily affects the knees, elbows, and scalp. Patients suffering from guttate psoriasis can develop plaque psoriasis.^[11]

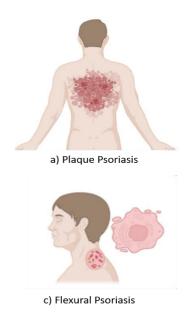
1. Plaque psoriasis: Also known as psoriasis vulgaris, stands out as the predominant form of psoriasis, affecting approximately 80-90% of individuals diagnosed with the condition. It manifests as thick, reddish or purplish skin patches, frequently accompanied by silvery-white or grey scales. These patches commonly emerge on areas such as elbows, knees, lower back,

or the scalp. Ranging in size from 1 to 10 centimetres, the patches can extend to cover larger areas of the body. It's important to note that aggravating the scales through scratching often exacerbates the symptoms.^[9]

- 2. Guttate psoriasis: Characterized by the emergence of small red spots on lighter skin tones, while in darker skin tones, these spots may take on a violet or brown hue. It ranks as the second most prevalent type of psoriasis, affecting approximately 8% of individuals diagnosed with the condition. Typically, guttate psoriasis onset occurs during childhood or young adulthood. The spots, which are small, distinct, and shaped like drops, commonly appear on the torso and limbs, with the possibility of affecting the face and scalp. Although these spots are generally not as thick as those seen in plaque psoriasis, they can evolve into plaque psoriasis over time.
- **3. Flexural or inverse psoriasis:** Commonly manifests in skin folds, such as beneath the breasts, in the armpits, or around the groin. This particular type of psoriasis presents as red or purple patches that are often smooth and shiny. The presence of sweat and moisture in skin folds prevents the shedding of skin scales in this form of psoriasis. Occasionally, it may be misdiagnosed as a fungal or bacterial infection due to its appearance. The discomfort associated with inverse psoriasis is heightened by skin-on-skin contact. It is noteworthy that individuals with inverse psoriasis often concurrently experience a different form of psoriasis in other areas of their body. [12]
- **4. Pustular psoriasis:** At times, can be quite severe. This type of psoriasis has a rapid onset, presenting as numerous white pustules surrounded by red or darkened skin. It may manifest in isolated areas like the hands and feet or extend to cover a significant portion of the skin's surface. The pustules may coalesce, forming scaling areas. In cases where it affects the entire body, as seen in the Von Zumbusch subtype, it can pose a life-threatening risk due to severe systemic effects. Some individuals undergo cyclic phases of pustule formation and remission. [13]
- **5. Psoriatic arthritis:** (PsA) is a painful and physically restrictive condition that impacts approximately 30% to 33% of individuals diagnosed with psoriasis.^[14] This condition comprises five subtypes, each with distinct symptoms. Presently, there is no cure for Psoriatic arthritis.^[10] As an autoimmune disease, psoriasis prompts the body to attack both joints and skin. It can have a significant impact on multiple joints and tends to be particularly severe in

the hands, often affecting the nails. Typically, skin symptoms manifest prior to the onset of joint-related symptoms. [15]

- **6.** Scalp psoriasis: It is a prevalent occurrence among individuals with plaque psoriasis. It can manifest as severe dandruff for some, while others may experience pain, itchiness, and noticeable effects along the hairline. [16] Scalp psoriasis has the potential to spread to the neck, face, and ears, forming either one substantial patch or several smaller patches. Managing regular hair hygiene can become challenging in some instances, as excessive scratching may lead to hair loss and scalp infections. Additionally, this condition can evoke feelings of social stress.[17]
- 7. Erythrodermic psoriasis: Also known as exfoliative psoriasis, is an uncommon psoriasis variant that appears bright red on lighter skin tones or takes on a dark purplish hue in individuals with darker skin tones. This condition involves significant skin shedding and is considered a medical emergency. Hospitalization may be necessary, as the body may struggle to regulate its temperature. Erythrodermic psoriasis is characterized by widespread red or purple skin covered with silvery scales, often affecting extensive areas of the body. The shedding of skin in this form tends to occur in larger pieces compared to the smaller scales typically associated with most types of psoriasis. [18]
- **8.** Nail psoriasis: While not formally categorized as a distinct "type" of psoriasis, nail psoriasis frequently occurs as a common expression of the condition. It is frequently mistaken for fungal infections and other nail-related infections. [19]





d) Pustular Psoriasis

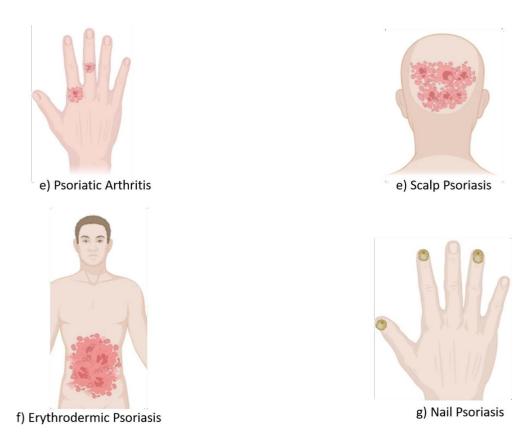


Figure 2: Showing different types of Psoriasis; (a) Plaque Psoriasis, (b) Guttate Psoriasis, (c) Flexural Psoriasis, (d) Pustular Psoriasis, (e) Psoriatic Arthritis, (f) Scalp Psoriasis, (g) Erythrodermic Psoriasis, (h) Nail Psoriasis.

Scalp Psoriasis

In the current review, more focus is given on scalp psoriasis because about 80% of psoriasis cases involve the scalp, making it the most frequently affected area of the body. Because of its severity and disproportionate influence on quality of life, psoriasis of the scalp necessitates special attention. It can be identified by the presence of red, thicker areas or plaques on the scalp, surrounded by silvery-white scales. These affected areas can occur in a specific region or cover the entire scalp. While it may be confined within the hairline, it often extends to the back of the head, forehead (facial psoriasis), ears, or neck. Despite being partially hidden by hair; scalp psoriasis can cause discomfort and emotional distress due to persistent itching and flaking resembling dandruff. Sleep is disrupted, scratching leads to skin infections and damage to the skin barrier, hair loss cannot be reversed (alopecia). In some cases, chronic and recurring scalp psoriasis can lead to scarring alopecia. Scalp psoriasis may be linked to psoriatic arthritis (PsA). The condition may occur independently or alongside other types of psoriasis, typically following a chronic, relapsing-remitting course. [20]

Treatment for scalp psoriasis

Scalp psoriasis is usually treated through a combination of medical interventions and lifestyle management in order to alleviate symptoms and enhance the overall condition.^[21] Here are various approaches to treating scalp psoriasis.^[22,23]

Topical Treatments: Topical treatments are the preferred initial option for mild-to-moderate scalp disease. [24]

- **A) Corticosteroids:** When it comes to scalp psoriasis, topical corticosteroids remain the primary and well-established treatment in terms of both safety and effectiveness. These anti-inflammatory medications are available in various forms, including creams, ointments, foams, and shampoos, and are applied directly to the scalp.^[25] Moreover, the inclusion of alternative topical solutions such as vitamin D analogues and keratolytic agents can serve as a beneficial complement to the therapeutic strategy for the management of scalp psoriasis.^[26]
- B) Combination Corticosteroid and Vitamin D Analog Topical Therapy: While moderate, high, and super-potent corticosteroids prove effective in managing scalp psoriasis, there is limited information on the long-term safety of corticosteroid monotherapy specifically on the scalp. Consequently, vitamin D analogues emerge as a valuable option for maintenance therapy and long-term control. Combining topical corticosteroids with vitamin D analogues appears to be at least as effective as corticosteroid monotherapy, and recent research suggests it may offer additional benefits in certain cases. [27] A systematic review indicates that combination topicals comprising corticosteroids and vitamin D analogues demonstrate greater efficacy compared to both topical corticosteroid and vitamin D monotherapy for treating scalp psoriasis, albeit with a marginal additional benefit over corticosteroid monotherapy. Furthermore, combination therapy results in fewer withdrawals from treatment due to adverse events when compared with vitamin D monotherapy.
- **C) Topical Calcineurin Inhibitors:** Drugs like tacrolimus and pimecrolimus can be effective in reducing inflammation and scaling.^[29]
- **D) Keratolytic:** Keratolytic agents can be used as an adjunctive treatment to reduce psoriatic scale. They are proposed to increase the absorption of topical corticosteroids, which may lead to increased efficacy and clearance.^[30]
- 2. Medicated Shampoos: The presence of hair adds complexity to the treatment of scalp

psoriasis, presenting a unique set of challenges. The formulation of treatment vehicles significantly influences patient satisfaction and adherence to the prescribed regimen. Shampoos offer a convenient, clean treatment option for patients, whether used independently or in conjunction with other therapies. However, limited research has assessed the actual effectiveness of these preparations. Existing studies suggest that shampoos, at most, have a modest impact on treating scalp psoriasis.^[31]

- A) Coal Tar Shampoos: Coal tar is effective in inhibiting the proliferation of skin cells and alleviating inflammation. Due to its potent anti-inflammatory, anti-proliferative, and anti-itch properties, this substance has been used as a treatment for psoriasis for many years. While crude coal tar is the most effective tar for psoriasis, it can be challenging to apply to the scalp. As a result, coal tar solution or liquor carbonic detergents, ranging from 5% to 20%, are often recommended. This formulation is usually presented as a lotion or incorporated into a corticosteroid preparation. However, the use of coal tar has decreased in Favor of newer topical medications due to challenges associated with its malodour, adverse effects like hair staining and drying, and concerns about carcinogenicity. Despite recent studies challenging some of these findings, Canada and the European Union have banned the use of coal tar in cosmetic preparations due to concerns about its potential to cause cancer. [33]
- B) Salicylic Acid Shampoos: Salicylic acid can aid in the removal of scales and promote the effectiveness of other treatments. Ranging from 5% to 10%, exhibits a robust keratolytic effect. Usually included in ointments or mineral oil blends, this substance is used over a prolonged period to reduce the thick, scaly patches linked to plaque psoriasis. By removing the scales, it helps other medications penetrate the skin. However, patients may struggle to wash the product out of their hair because of how it's made. To solve this, they can use a clarifying shampoo on their hair before showering to help remove the salicylic acid product effectively. [35]
- C) Ketoconazole Shampoos: Ketoconazole shampoos are sometimes included in the treatment regimen for scalp psoriasis. Ketoconazole shampoos are typically used as directed by a healthcare professional. The process involves applying the shampoo to wet hair, creating lather, and allowing it to remain on the scalp for a few minutes before rinsing. The frequency of use will depend on the severity of the condition and the specific product prescribed. Although ketoconazole is primarily an antifungal medication used to treat fungal infections, it may also provide benefits in managing certain scalp conditions, including psoriasis. Because

in some cases, scalp psoriasis can be exacerbated by the presence of a yeast-like fungus called Malassezia. Ketoconazole can help reduce the growth of this fungus on the scalp. Further, ketoconazole shampoos can aid in reducing scaling and itching associated with scalp psoriasis. By addressing the underlying fungal component, these shampoos may contribute to a decrease in symptoms. In addition, ketoconazole shampoos are often used in combination with other treatments for scalp psoriasis. They may be recommended as part of a comprehensive approach that includes corticosteroid shampoos, salicylic acid preparations, or other medicated shampoos. Some individuals with scalp psoriasis use ketoconazole shampoos as a maintenance therapy to prevent flare-ups and manage symptoms over the long term. [36]

- **3. Phototherapy** (**Light Therapy**): Conventional ultraviolet (UV) therapies like narrowband UVB or Psoralen UVA (PUVA) are not practical for treating scalp psoriasis. However, methods to enhance delivery, such as the UVB comb, have been developed and tested. Exposure to ultraviolet B (UVB) light under controlled conditions has the potential to decelerate the proliferation of impacted skin cells and alleviate inflammation. ^[37] In a study involving 14 participants, the fiber-optic UVB comb was used three times a week for 12 weeks, with a specific area of the scalp serving as a control site. The results of this study showed a mean improvement in the modified Psoriasis Area and Severity Index (PASI) score of 3.6 for the treatment sites. There was a significant difference in the mean modified PASI between the treatment and control sites of 3.9 (P<0.0001). ^[38,39]
- **4. Oral/Systemic Medications:** Systemic therapy is generally not the first-line approach for treating scalp psoriasis unless it becomes necessary for cases that are resistant or severe. Although there is limited evidence supporting the effectiveness of traditional treatments such as acitretin, methotrexate, and cyclosporine for scalp psoriasis, some clinical trials have looked into how scalp psoriasis responds to biologic therapy and newer medications. These trials have been reported either through sub-analyses or as pre-planned endpoints. Overall, the improvement of scalp psoriasis typically corresponds to the overall improvement of body psoriasis, when systemic therapies are used. In more serious instance, the immune response can be regulated by prescribing oral medications like methotrexate, cyclosporine, or acitretin. [40]
- I) TNF-Alpha Inhibitors: TNF- α inhibitors are biologic drugs that treat psoriasis by blocking TNF- α , a key inflammatory molecule. This action reduces inflammation and immune cell activation, leading to improved skin symptoms. Common TNF- α inhibitors

include adalimumab (Humira), etanercept (Enbrel), and infliximab (Remicade).

- a) Etanercept: It has emerged as one of the initial biologic medications that have been proven effective in treating moderate-to-severe scalp psoriasis. This was demonstrated in a 2012 randomized, double-blind, placebo-controlled study. The study found that after 12 weeks, 86% of patients in the etanercept group achieved PSSI 75, compared to only 11% in the placebo group [p < 0.0001]. Furthermore, at week 12, patients receiving etanercept showed a significantly greater mean PSSI improvement compared to those on placebo (86.8% versus 20.4%, respectively [p < 0.0001]). [41]
- **b) Adalimumab:** A post hoc analysis of the BELIEVE phase III study evaluated the efficacy of adalimumab in treating scalp psoriasis. The enrolled patients had a mean Psoriasis Scalp Severity Index (PSSI) score of 17.9 ± 14.1 at baseline³¹. After 16 weeks of adalimumab treatment, 77.8% of patients achieved a PSSI score of ≤ 4 . Among all adalimumab recipients, including those with both scalp and nail involvement, 61.8% reported experiencing an adverse event. The majority of these events were categorized as mild or moderate, with headache and nasopharyngitis being the two most commonly reported occurrences. [42]
- c) Infliximab: Formal studies specifically focusing on the effectiveness of the anti-TNF chimeric monoclonal antibody infliximab in treating scalp psoriasis are not available. However, a summary of findings from three Phase 3 clinical trials (EXPRESS 1, EXPRESS 2, and SPIRIT) revealed significant enhancement in head and neck psoriasis (≥75% and ≥90% improvement) for both infliximab doses (3 mg/kg and 5 mg/kg) compared to placebo. The observed progress was consistent with the overall responses of the Psoriasis Area and Severity Index (PASI) across all body regions. [44]
- II) IL-12/23 Inhibition: IL-12/23 inhibitors are biologic drugs that treat psoriasis by blocking the cytokines IL-12 and IL-23, which are involved in the inflammatory process. This reduces inflammation and immune cell activation, improving skin symptoms.
- a) Ustekinumab: Formal studies specifically investigating the effectiveness of Ustekinumab, an inhibitor of IL-12/23, in treating scalp psoriasis are not available. [45] However, there are case reports that emphasize the favorable results of this biologic agent in managing challenging cases of scalp psoriasis. Di Cesare.et.al and Papadavid.et.al each present two cases of stubborn scalp psoriasis that exhibited notable improvement, with

clearance observed after 8 weeks of Ustekinumab treatment. [46]

- **III) IL-17a Inhibition:** IL-17A inhibitors are biologic drugs that treat psoriasis by blocking IL-17A, a pro-inflammatory cytokine. This reduces inflammation and immune cell activation, improving skin symptoms.
- a) Ixekizumab: A monoclonal antibody that targets IL-17a was the subject of a post hoc analysis of its Phase 2 trial to evaluate its effects on scalp psoriasis. Out of the 142 patients in the Phase 2 program, 105 (74%) had scalp involvement, with an average baseline Psoriasis Scalp Severity Index (PSSI) of 18.7 (SD 14.1). [48,49] At week 12, there was a significant percentage improvement in PSSI from baseline: 87.1% (25 mg), 94.8% (75 mg), and 84.8% (150 mg), compared to 30.5% for the placebo group. By week 20, a PSSI of 0 (clear) was achieved in 58.3%, 66.7%, and 86.4% of patients receiving ixekizumab (25 mg, 75 mg, and 150 mg, respectively), in contrast to only 10% in the placebo group. At the end of the openlabel period at week 48, all patients were on ixekizumab 120 mg every 4 weeks, and 78% of them achieved a PSSI of 0.55. [50]
- **b) Secukinumab:** An additional monoclonal antibody targeting IL-17a, received approval for treating plaque psoriasis in 2014. Currently, a Phase 3b trial is underway to evaluate its efficacy in patients with scalp psoriasis. The study includes approximately 94 subjects with a PSSI (Psoriasis Scalp Severity Index) of \geq 12, a modified Investigators Global Assessment of \geq 3, and \geq 30% scalp area affected. The 24-week trial consists of a 12-week placebocontrolled period, comparing secukinumab 300 mg to placebo in a 1:1 ratio. The eagerly anticipated results of this study will provide valuable insights into the effectiveness of secukinumab for scalp psoriasis treatment.

IV)Oral PDE4 Inhibitors: Oral PDE4 inhibitors, such as apremilast (Otezla), are medications that treat psoriasis by blocking the enzyme phosphodiesterase 4 (PDE4). This action increases levels of cyclic AMP (cAMP), which helps reduce inflammation and improve skin symptoms.

a) Apremilast: The oral phosphodiesterase four inhibitor, apremilast, underwent evaluation in two phase III randomized controlled trials, ESTEEM 1 and ESTEEM 2, to assess its efficacy in treating a subgroup of patients with scalp psoriasis. Treatment with apremilast resulted in a significantly higher proportion of patients achieving scPGA 0/1 (46.5% in ESTEEM 1, 40.9% in ESTEEM 2) at week 16 compared to the placebo group (17.5% in ESTEEM 1, 17.2% in

ESTEEM 2 [p < 0.0001 for both studies]).^[53] The proportion of patients with scPGA 0/1 at week 32 in those treated with apremilast was sustained at 37.4% and 32.4% in ESTEEM1 and ESTEEM 2, respectively. Most adverse events were reported to be of mild or moderate severity.^[54,55]

- **5. Biologics:** These medications are more recent and focus on specific elements of the immune system. They might be suggested for cases that are more severe.^[56] Biologic includes tumour necrosis factor (TNF), interleukin (IL-17 and IL-23) inhibitors or small molecule inhibitor (dimethyl fumarate and apremilast) therapies.^[47]
- **6. Intralesional Therapy:** Complementary therapies, although not considered standard treatment, can be beneficial for patients with difficult-to-treat scalp psoriasis. Intralesional corticosteroids have been used in clinical practice to treat localized scalp disease with good effect. However, there are currently no studies regarding the efficacy of this modality in the scalp.^[57,58]

Table 1: Systemic therapies including biological agents with their formulation types.

Type of Formulation	Biological agents	References
	incorporated	References
Injections / infusions		[59]
	i. Infliximab	[60]
	ii. Adalimumab	[61]
	iii.Etanercept	
	iv.Ustekinumab	[45]
	v. Ixekizumab	[50]
	vi.Secukinumab	[62]
	vii. Tildrakizumab	[63]
	viii. Guselkumab	[64]
	ix. Risankizumab	[65]
Tablets	. Mada at manada	[66]
	i. Methotrexateii. Cyclosporin	[67]
	iii.Acitretin	[68]
	iv. Apremilast	[55]
Liposomal gels	i. Methotrexate	[69]
	ii. Tazarotene	[70]
	iii. Diflorasone diacetate	[,]
Microemulsion gel	i. Betamethasone	[71]
	Dipropionate and salicylic acid	[72]
	ii. Clobetasol propionate	[,2]

7. Home Remedies and Lifestyle Management

- Moisturizing: Maintaining proper moisture levels on the scalp can aid in minimizing dryness and itchiness.
- Avoiding Triggers: Identifying and avoiding triggers such as stress, certain hair products, or environmental factors.
- Regular Shampooing: Using a gentle, medicated shampoo regularly to manage symptoms.
- Healthy Lifestyle: Maintaining a nutritious diet, effectively managing stress, and refraining from smoking and excessive alcohol consumption can potentially lead to a holistic enhancement.^[59]
- **8. Regular Follow-up with a Dermatologist:** Regular and effective communication with a healthcare professional is of utmost importance in order to closely monitor the condition, make necessary adjustments to treatment plans, and address any concerns that may arise. It is imperative for individuals suffering from scalp psoriasis to collaborate closely with their healthcare providers in order to establish the most suitable and effective treatment plan, taking into consideration the severity of their condition and individual factors.

CONCLUSION

Psoriasis, encompassing scalp involvement, is a persistent and recurrent inflammatory condition with a substantial effect on the quality of life of those affected. Patients often express distress concerning their physical appearance, accompanied by symptoms like itching, scaling, and, in certain instances, alopecia. Managing scalp psoriasis poses considerable challenges for both patients and healthcare providers. Furthermore, psoriasis on the scalp significantly adds to the overall burden on the quality of life for patients. It is important to counsel individuals that various treatment options, including biologics, are available for addressing this challenging area.

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