Role of Environmental Factors in The Pathogenesis of Psoriasis and its Management

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Abstract

A complex hereditary skin disease with an inflammatory condition, psoriasis can affect people of any age, and is most common in people between the ages of 15 and 60. It also has a negative impact on the emotional, physical, and psychosocial well-being of affected patients. Oxidative stress, innate immunity, and realease of numerous inflammatory cytokines are hypothesized to have a pivotal role in the pathogenesis of psoriasis. The main contributor to these pathological hallamark is formation of reactive oxygen species (ROS) from the skin metabolism and the environmental factors itself, making it prime target for this condition. Intervention targeting these envirnonmetal factors will prevent ROS-mediated prosiatic pathogenesis from causing cell death and malfunction. This review aims to update knowledge about various types of psoriasis, their allied risk factors, and the function of oxidative stress, inflammation, and immunity in psoriatic conditions, along with insights into potential role of herbal medications in the management and treatment of psoriasis. Incorporating shards of knowledge about role inflamation, oxidative stress, and immunity can help fill in the gaps in the picture of psoriasis, and can lead to development of new therapeutic invention for ailment of psoriasis by targeting these factors.

Keywords: Environmental Factors, Herbal Medicine, Herbal Plants, Pathogenesis, Psoriasis, Risk Factors, and Treatment Approaches

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Introduction

Psoriasis is a skin condition that causes chronic inflammation and has a complex etiology. It is a pathological condition with prominent hereditary and autoimmune characteristics. It has been demonstrated that abnormalities in the formation of free radicals, lipid peroxidation, lymphokine secretion, and essential fatty acid metabolism all contribute to skin damage in psoriasis patients. Global prevalence for psoriasis is estimated at 2%, but this varies from place to place (Christophers, 2001). It has a low prevalence in Asian and other African populations and accounts for 11% of Caucasian and Scandinavian populations (Gibbs, 1996). and approximately 5% of the Indian population is affected by this dreadful skin illness. Several microbes e.g., Bacterial species of *Streptococcus, Staphylococcus, Corynebacterium, Pseudomonas, Clostridium,* etc. and fungal species like *Malassezia,Candida* are associated

with worsening psoriasis (Paulino et al., 2006, 2008). Enterotoxin produced by some strains of *Staphylococcus aureus* can cause psoriatic lesions. This enterotoxin is a potent T-cell activator. Staphylococcal antigens are called super antigens because of their ability to activate T cells with high frequency.

Psoriasis is also characterized by an imbalance of reactive oxygen species (ROS) environmental, genetic, and immunological factors which can damage cellular components. The antioxidant system generally protects the body from ROS but disruption of the antioxidant system occurs in Psoriasis (Kadam et al., 2010). People with psoriasis are affected mentally, and physically and are more likely to experience anxiety, depression, cardio-metabolic, and rheumatologic comorbidities (Kimball et al., 2005), all of which can significantly impact the quality of life (Armstrong et al., 2011). In the case of psoriasis, it is common to have swelling and redness around the scalp. Psoriatic scales are usually white-silver and appear dense with red areas. They can appear anywhere on the body, including the hands, feet, neck, scalp, face, nails, mouth, and genitals. These episodes will break and bleed from time to time. However, approximately 80% of those affected have mild to moderate psoriasis body area. Skin cells usually form at the skin base, gradually rise to the surface, and eventually fall. The average life cycle of skin cells is one month and the production process may take a few days to complete. The result of this rapid overproduction leads to skin cell accumulation. An inflammatory immune-mediated condition known as psoriasis has no known long-term treatment. Although there are several ways to manage psoriasis, no single medicine makes an acceptable and comprehensive claim. Numerous synthetic medicinal drugs have also been documented to have side effects for psoriasis. Due to their safety and accessibility, herbal medications may hold promise as possible anti-psoriatic molecules. The essential players in the development of psoriasis, including T-cell trafficking, cytokine inhibition, and T-cell activation should be properly recognized before designing a herbal medication candidate. The immunologically mediated hypothesis of psoriasis postulates that immunosuppressive medications might cure psoriasis, however, the function of the immune system is still unknown (Singh-Manoux et al., 2014). The purpose of this article is to investigate the medicinal plants that are effective in treating skin problems by tageteing various pathological hallmarks of psoraisis.

Types of Psoriasis

Psoriasis affects about 10% of the population. Only about 2-3% of people develop the illness. Psoriasis seems to be passed down to the generations and is clinically classified into two groups:

1) Non-pustular psoriasis, which includes guttate, *Psoriasis vulgaris* (early and late-onset), erythrodermic, inverse psoriasis, and palmoplantar.

2) Pustular psoriasis, which includes impetigo herpetiformis, generalized pustular, palmoplantar pustular, and localized pustular.

Plaque Psoriasis: According to the American Academy of Dermatology (AAD), plaque psoriasis affects approximately 80% of total psoriatic patients. Plaques are red spots covered with a white mass in color with dead skin cells. Elbows, scalp, and lower back scars are familiar places to appear. Itching or painful plaques are common. Small red spots appear on the skin with

gutted psoriasis. The most common scenario is to start in infancy or old age. The spots are small, distinct, droop-shaped spots on the trunk, limbs, face, and scalp. Gut psoriasis can be caused by stress, skin injury, infection, or medication.

Psoriasis vulgaris: Psoriasis vulgaris is the most prevalent amongst all types of psoriasis. It manifests itself clinically as erythematous patches with crisp edges and pearly scales. Lesions are symmetrically distributed and are usually located in the knees, elbows, scalp, and sacral regions. *Psoriasis vulgaris* can give rise to several diseases that are phenotypically and genotypically linked yet distinct from one another. Indeed ,there are two variants of *Psoriasis vulgaris* i.e. flexible and serous. Flexural/intertriginous (inverse) psoriasis appears shiny red, without scales, and occurs in the interstitial areas. It most commonly occurs in the skin folds like between the bums, under the breast, and armpits. It is prone to irritation from friction and sweat due to its locality in sensitive areas. Well-divided erythematous plaques with variable degrees of infiltrates, sometimes with a predisposition to cause itching and burning, are the major clinical presentation of inverse psoriasis (Koca, 2016). Serous psoriasis, which can be mistaken for seborrheic dermatitis, has fatty scaling. It gets its name from its shape and anatomical distribution, and it can appear alone or in combination with Psoriasis. The nasolabial fold, the mid cheekbones, the nose, the ears, the eyebrows, the hairline, the scalp, the anterior and internasal regions, and the hairline are all impacted. The lesions are thin, red, and well-divided, similar to intercellular Psoriasis, with varying degrees of intercellular extensionis seen around the eyebrows, nasolabial folds, and in the ventral and prefrontal areas (C. E.M. Griffiths et al., 2007).

Guttate Psoriasis: Guttate psoriasis (also known as teardrop psoriasis, or extrinsic psoriasis) is the second most prevalent psoriasis, meaning "drop" in Latin. Small red scaly patches that appear out of nowhere, mostly on the widely dispersed trunk are its defining feature. Many small, teardrop-shaped red nodules cover a vast skin area as intestinal symptoms. The spots have a wide range of colors. The trunk, arms, legs, and scalp are the most common sites for lesions. Lesions occur abruptly, with droplets and, less typically, scaly psoriatic papules, often after a streptococcal infection (Martin et al., 1996).

Erythrodermic psoriasis: Erythrodermic psoriasis is a type of psoriasis that manifests as an inflammatory condition in the body. Erythrodermic attacks occur very frequently, and the symptoms include extensive red lesions. This prevalent type of psoriasis has lesions that cover roughly 80% of the body's surface (Aghmiuni & Khiavi, 2017).

Palmoplantar psoriasis: The yellow-brown sterile pustules that commonly arise on the palms and soles are classified as palmoplantar psoriasis, a subtype of psoriasis. Chronic palmoplantar psoriasis affects about 25% of persons with plaque psoriasis.(Koca, 2016) Scaly lesions are predominant in palmoplantar prosriasis and their thickening can give rise to keratosis (Bowcock & Barker, 2003).

Impetigo herpetiformis: Psoriasis of pregnancy, also known as generalized pustular psoriasis. Erythematous lesions mark it with pustules that start and spread from areas of flexion and tend to clump together. Mucosal involvement and onychomycosis consequent to sublingual pustules can

be seen as it progresses. The lesions are itchy or painful, and they smell bad. Malaise, fever, chills, nausea, and vomiting may develop in addition to general deterioration.

Nail psoriasis: A clinical indication of psoriatic inflammation on the nail bed and base, approximately half of psoriasis patients acquire specific nail alterations. Pitting and distal stools are the most typical symptoms of nail psoriasis. Pitting, yellow discoloration, and pericardium are signs of subcutaneous hyperkeratosis, onychomycosis, and severe nail dystrophy (Kahl et al., 2012).

Psoriatic arthritis (PSA): A persistent inflammatory joint condition called psoriatic arthritis affects 6% to 39% of patients with psoriasis. In the general population, it affects 0.1-0.25% of people. PSA is categorized as a spondylitis disease based on a variety of clinical and radiological features. This type of arthritis can progress gradually and be mild or quick and severe. PSA is a severe form of arthritis with a prognosis resembling rheumatoid arthritis (Gaydukova et al., 2012; Kane et al., 2003).

Risk factors

Exacerbations of psoriasis have been linked to acute viral and bacterial infections. A streptococcal infection causes guttate psoriasis in young persons and children. According to several researches, heavy drinkers develop inflammatory skin sores. Psoriasis is now more common than ever in smokers or ex-smokers. even those without a family history of psoriasis can develop drug-induced psoriasis. The mechanism of drug-induced psoriasis remains a mystery. Psoriasis has been discovered to be triggered by physiological stress in 60% of cases (L. Naldi et al., 1992; Luigi Naldi, 2004).

Medications: Researchers have found that many drugs, including antivirals, anti-proliferative (imiquimod), antidepressants (lithium), tumor necrosis factor (TNF-α), interferons (IFN-α), beta-blockers, and many biologics, including anti-cytokine therapies are used to treat psoriasis, have been clinically associated with initiation and exacerbation of the disease (Kim & del Rosso, 2010). It was discovered that the signs and symptoms of psoriasis were made worse by pembrolizumab, a breakthrough cancer immunotherapy drug approved by the Food and Drug Administration (FDA) (Sahuquillo-Torralba et al., 2016). These medicines primarily work by interfering with the immune system, causing psoriasis to develop.

Ultraviolet (UV) radiation exposure: Natural sunshine or artificial UV rays exposure are the one of the leading risk factor that trigger psoriasis. Due to geographical inequalities in UV distributions, the prevalence of psoriasis may vary across regions. The prevalence of absolute latitude varied from 0% (average complete latitude 13.35 in Samoa) to 3.3%, according to a case-control study (in Tanzania, middle absolute latitude 6). The application of sunscreen and ground reflection of UV rays can potentially alter the average UV exposure. Vitamin D synthesis can be increased by UV-B exposure. Vitamin D is a hormone that aids in the treatment of psoriasis and aids in the body's absorption of calcium (Enamandram & Kimball, 2013).

Alcohol intake: It is untrue that drinking alcohol is linked to an increased risk of psoriasis onset and worsening. However, studies have demonstrated that alcohol increases the production of pro-inflammatory cytokines from a variety of cell types. It causes lymphocyte proliferation and

prolonged systemic inflammation. Cyclin D1 and A5 integrin are two examples of keratinocyte proliferation-related genes whose mRNA levels are decreased by alcohol comsumption. Furthermore, acetylcholine has been linked to the development of psoriasis. The likelihood of developing psoriasis in women is directly correlated with increased beer drinking. A similar study also found that alcohol consumption can worsen psoriasis severity (Qureshi et al., 2010). However, more investigation into the precise processes by which drinking alcohol and smoking cigarettes promote psoriasis is required to validate the association (Poikolainen et al., 1990).

Smoking: Smoking or being exposed to secondhand smoke can enhance the chances of developing psoriasis. It is unclear exactly how smoking affects the development of the psoriasis condition. Studies have shown that smoking lowers the quality of life for those who have rheumatoid arthritis and spondyloarthritis (Chung et al., 2012; Poddubnyy et al., 2013; Westhoff et al., 2008).

Diet and obesity: It is frequently asked by patients about what foods they can and cannot consume as well as whether changing their diet can stop a recurrence or make them feel better. Of course, the question here is whether or not losing weight will affect their skin condition. Recent research suggests that a high body mass index score and psoriasis severity are related, suggesting that patients' severity index scores and psoriasis area can be improved by decreasing weight. Additionally, it is inevitable that healthy eating practices will benefit psoriatic patients, including the use of selenium, vitamin D, oral vitamin B12, and omega-3 fatty acids in fish oils (Bardazzi et al., 2010; Millsop et al., 2014).

Pathogenesis associated with psoriasis

The onset and development of psoriasis is a structurally complex process that is regulated by connective tissue and skin epithelium. It is also controlled by various regulatory modulators and cellular components of the adaptive and innate immune systems. Psoriatic skin lesions are caused by trauma, infection, and inflammation. A combination of environmental and genetic factors induces cell death which further initiates the production of antimicrobial peptides. Keratinocytes produce the resulting peptides, as illustrated in Figure 1. It is still unknown which cell in psoriasis targets the major (core) abnormality. Keratinocytes have been suggested as one of the candidates. Endothelial cells and fibroblasts raised, red psoriatic papules or plaques demonstrate aberrant keratinocyte differentiation, proliferation, and infiltration of inflammatory components into the skin on histological inspection. The first two key pathogenic features of psoriasis, aberrant keratinocyte proliferation and keratinocyte differentiation, are caused by slow growth and maturation kinetics. In a typical epidermis, basal keratinocytes divide every 13 days and spend the majority of their time in the G1 phase of the cell cycle. It takes roughly 26 days for a new keratinocyte to mature and shed. On the other hand, proliferating psoriatic keratinocytes had their cell cycle shortened to around 15 days, and their maturation and secretion phases were shortened to about four days. Psoriatic keratinocytes divide quickly, and this is followed by a rise in the expression of maturation markers for keratinocytes similar to what has been observed after injury to the epidermis. This demonstrates the connection between psoriatic lesions and normal healing (Baker & Fry, 1992; Christopher E.M. Griffiths et al., 1989).

Infiltration of inflammatory components into the skin: Indeed biology has made enormous progress in understanding the complex etiology of psoriasis. Cytokines such as interleukin (IL)-17, IL-23, and TNF- α are important for developing and managing skin abnormalities in psoriasis. Due to the significant production of IL-2 and IFNγ in skin lesions and the absence of IL-4 in skin lesions, psoriasis is thought to be characterized by a type 1 cytoskeletal cytokine pattern from T-helper cells. A variety of cytokines are released by activated keratinocytes that affect themselves and other cell types, including T-lymphocytes. Several ILs (IL1, IL6, and IL8), transforming growth factors (TGF), and TNF-α. Intercellular adhesion molecule (ICAM-1) is an adhesion molecule, also triggers leukocyte infiltration in psoriatic lesions. T cell activation, proliferation, and chemotaxis in skin infiltration can be enhanced by IL-6 and IL-8 (Baker & Fry, 1992; Christopher E.M. Griffiths et al., 1989). The IL-23 / Th-17 signaling pathway indicates the sequence of biological events is also involved in pathogenesis of psoriasis (Di Cesare et al., 2009).

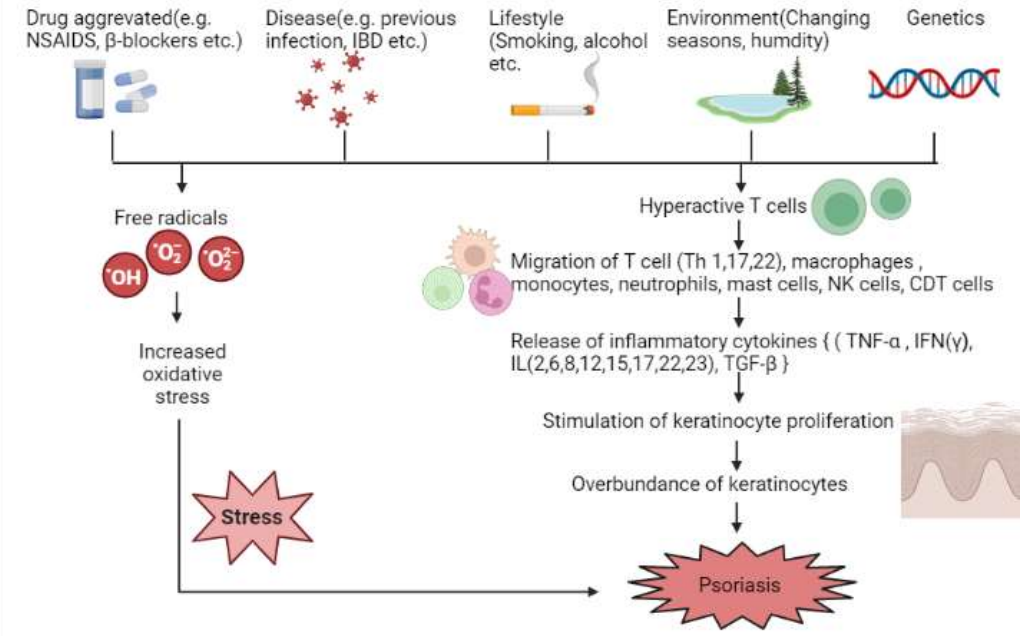

Figure 1: Role of various risk factors and their associated pathogenesis in the occurrence of psoriasis

Psoriasis is a condition that is mostly mediated by T cells. T-cell subsets and macrophages, dendritic cells, keratinocytes, and neutrophils are all part of this pathway. It is unclear what specifically caused this abnormal immunological response. Although early genetics and external stressors such as bacterial, viral infections, and stress have been indicated as crucial causes of psoriasis. The pathophysiology of psoriasis has traditionally been divided into two stages: initiation and management. Release of antimicrobial peptide LL-37 catholysidine by blocking keratinocytes in the epidermis is key pathgentic hallmark of psoriasis. Pathogen-derived DNA, along with auto-DNA, form complex with LL-37. The plasmacytoid in the dermis binds to the nine complexes of receptor-like tolls on dendritic cells. Type 1 interferons, IL-6 and IL-1, are

secreted by these plasmacytoid dendritic cells, which stimulate local myeloid dendritic cells to move to the drying lymph nodes. When exposed to resting T-cells, cytokines like IL-12 and IL-23 divide T-cells turn into mature Th-1, Th-17, and Th-22 cells and these T-cell lineages release IFN, TNF-α, IL-17A, and IL-22 which consequently promotes keratinocyte proliferation and alters differentiation, when they return to the skin (Harrington et al., 2005). After skin injury, keratocytes emit a variety of cytokines, immunomodulators and inflammatory chemicals. The pro-inflammatory nature of IL1-, IL-6, IL-8, and TNF explains the main pathogenic aspect of psoriasis: the penetration of inflammatory components into the skin.(Mansbridge & Knapp, 1987) Angiogenesis causes erythema of the dermal papilla, dilated and torn vessels, scaling due to skin hardening by keratinocyte proliferation, and altered differentiation (Harrington et al., 2005).

Oxidative stress and inflammatory signaling pathways in psoriasis: : Oxidative stress, an imbalance between endogenous antioxidants and oxidants, also favors psoriasis. Reduced antioxidant levels/activity, formation of reactive oxygen and nitrogen species (ROS/RNS) influence the etiopathogenesis of psoriasis. ROS/RNS-induced stress affects transcription factors and upregulates several protein kinase pathways that are responsible for autophagy and autophagic associated regulation pathways. Various transcription factors in inflammatory signalling pathways may be influenced by ROS, which can function as a secondary messenger. The Nuclear factor kappa B (NF-kB), Mitogen-activated protein kinase (MAPK) and Janus kinase-Signal transducers and activators of transcription (JAK-STAT) signaling pathways are related inflammatory mechanisms that are altered by ROS generation and later on promote psoriasis (Lin & Huang, 2016).

Innate immunity in the pathogenesis of Psoriasis: Invading pathogens can be completely eliminated by a large number of innate immune cells. The natural immune system is essential for the host's defense against viruses because it recognizes infections and activates an adaptive immune response. The body's innate immune system serves as its first line of defense against infection in psoriasis, followed by adaptive immune response. Macrophages, neutrophils, monocytes, mast cells, cytotoxic T cells and natural killer (NK) cells are components of the innate immune system. By producing cytokines and chemokines, innate immune cells stimulate the migration of more leukocytes to the inflammation site. When the innate immune system is activated, it triggers a cascade of inflammatory responses that can lead to chronic inflammation and autoimmune disease. According to genetic, experimental, and pharmacological studies, the innate immune system plays a significant role in the progression of psoriasis. The use of IL4 to induce a switch from a Th1 to a Th2 phenotype was an early attempt to redirect the immune reaction toward a more anti-inflammatory phenotype, however this method hasn't worked effectively in clinical practice (Ghoreschi et al., 2003). The differentiation of regulatory T cells has been the subject of recent research. However, regulatory T cells can transform into IL-17-producing cells in an inflammatory setting. The micro immunological milieu of the dermis and the plasticity of the regulatory T cells must be considered when creating therapies to control the immune system in psoriasis. Certain cytokines might have anti-inflammatory or

supportive effects on the autoimmune process, depending on the disease's stage. A unique technique is needed to gain a deeper knowledge of the function of specific innate immune system components in disease and to pinpoint possible therapeutic targets for psoriasis (Sweeney et al., 2011).

Treatment approaches for Psoriasis

Psoriasis is a common autoimmune skin condition characterized by erythematous patches, mostly thick, silvery-white scales. Although the clinical cycles of psoriasis vary widely from person to person, the lesions continue to recur but no curative treatments exist to date. Plaque psoriasis is the most prevalent form of clinical psoriasis, and it typically affects the flexed areas of the skin like the knees and elbows. Still, lesions on the scalp, navel and interstitial skin regions can also occur. The second most common clinical pattern is the gout phenotype closely associated with previous or concurrent streptococcal infection. Psoriatic intestinal lesions flare up and spread to virtually all major areas of the trunk and extremities, usually one to two weeks after a strep infection. Intestinal psoriasis has a more acute clinical course and may resolve independently (Mallbris et al., 2005). However, it can eventually develop into a plaque phenotype. Dermatologic psoriasis is the most complete clinical disease, with more than 90% of the skin surface affected. Pustular psoriasis is confined to the palms and soles or is generalized. As in erythrodermic psoriasis, the recent phenotype can be life-threatening. Although psoriasis most commonly affects the skin, but involvement of the nails and joints is also common (Monteiro-Riviere, 2020).

Psoriasis is a skin condition with no recognized cause. There is currently no known cure for psoriasis, however there are numerous therapies that can help to minimize the signs and symptoms of the condition. In general, psoriasis patients have three treatment options: systemic. biological, and topical. Detailed mechanism of all three treatment options are described in Table 1, Table 2, and Table 3 respectively. Often, a mix of therapy is suggested, and phototherapy is also a treatment option. Combining topical, systemic, and light treatments can typically result in lower doses of each, as well as enhanced efficacy.

Table 1: Systemic medication for treatment of psoriasis

S.No	Treatment	Mechanism of action	Ref.
1	Phototherapy UVB PUVA	They suppress the skin's immune reaction, which depresses the series of immunological alterations.	(Aghmiuni & Khiavi, 2017)
2	Methotrexate	Act as an immunosuppressant.	(Reich et al., 2011)
3	Cyclosporine	A calcineurin inhibitor that inhibits T-lymphocyte activation and so provides a therapeutic advantage.	(Gottlieb et al., 1992)

4	Retinoids Etretinate Acitretin Liarozole	Hydrophilic and consequently migrate to bind intracellular retinoid receptor all-trans retinoic acid receptor, 9–cis retinoic acid receptor (RXR, RAR), the molecule migrates to the nucleus and regulates gene transcription, modifying epidermal proliferation and differentiation.	(Fredriksson & Pettersson, 1978)
5	Fumaric Acid Esters (Fumaderm)	Inhibitor of NFkB and induce apoptosis of T cells	(Hoefnagel et al., 2003; Treumer et al., 2003)
6	Apremilast	Inhibitor of phosphodiesterase 4 (PDE4)	(Afra et al., 2019)
7	BMS-582949	MAPK inhibitors	(Afra et al., 2019)
8	Tofacitinib Ruxolitinib	Jak-STAT inhibitors	(Bachelez et al., 2015)
10	CT327	Tyrosine kinase Inhibitors	(Roblin et al., 2015)
11	CF101	Adenosine A3 receptor agonist, de-regulation of the NF-κB signaling pathway	(Fishman et al., 2012)

Table 2: Biologics treatment for psoriasis

S.no	**Biologics**	**Route of administration**	**Mechanism of action**	**Ref.**
1	Biologics Alefacept	Intramuscular	Inhibit activation of T-cells.	(Jenneck & Novak, 2007)
2	Efalizumab	Subcutaneous	Interacts with activated T-cells with keratinocytes.	(Jullien et al., 2004)
3	Etanercept	Subcutaneous	It binds to the TNF-α molecule. It acts as a competitive inhibitor of TNF-α.	(Scheinfeld, 2004; Tyring et al., 2006)
4	Infliximab	Intarvenous	By interacting with both membrane-bound and soluble TNF-α, it binds to both molecules and inhibits their biological action.	(Rønholt & Iversen, 2017)
5	Adalimumab	Subcutaneous	Same as Infliximab.	(Rønholt & Iversen, 2017)

6	Ustekinumab	Subcutaneous	Inhibit activation of T-cells.	(Tsai et al., 2011)
7	Ixekizumab	Subcutaneous	Neutralizes IL-17A.	(Teraki et al., 2018)
8	Brodalumab	Subcutaneous	It can inhibit the actions of other IL-17 cytokines linked to psoriasis.	(Wade et al., 2019)

Table 3: Topical treatment for Psoriasis

S.no	Medication	Mechanism of action	Ref.
1	Calcipotriol	It interacts with and modulates epidermal proliferative, inflammatory, and keratinization genes.	(Laws & Young, 2010)
2	Dithranol	Keratinocyte proliferation is inhibited, T-cell activation is prevented, and cell differentiation is restored, most likely due to mitochondrial malfunction.	(McGill et al., 2005)
3	Tazarotene	It interacts to and modulates epidermal proliferative, inflammatory, and keratinization genes.	(Duvic et al., 1998)
4	Coal tar	Same mechanism as Dithranol.	(Arbiser et al., 2006)
5	Corticosteroid	It regulates gene transcription particularly for pro-inflammatory cytokines, by binding to the intracellular corticosteroid receptor.	(Torsekar & Gautam, 2017)

Medicinal Plants used in the Treatment of Psoriasis: Nowadays psoriatic patients utilize a variety of complementary and alternative medicine (CAM) (Aghmiuni & Khiavi, 2017; Hashem Hashempur et al., 2014; Muzaffer et al., 2019; Pazyar & Yaghoobi, 2016; Shawahna & Jaradat, 2017). In many societies around the world, the usage of medicinal plants has grown to be one of the most well-liked therapeutic interventions. Some therapeutic herbs are applied topically, while others are taken to get systemic benefits. The traditionally utilization of medicinal plants for ailment of various skin related disorders has been seen as a viable approach as supported by numerous evidence (Wadhwa et al., 2022). Prominent academic institutions and regulatory organizations are increasingly establishing guidelines to enable the methodologically rigorous conduct of randomized clinical trials utilizing a variety of CAM techniques, which includes the use of medicinal plants. Several medicinal plants have been undergone numerous randomized controlled clinical trials to treat the signs and symptoms of psoriasis. Some medicinal herbs have been shown to treat psoriasis signs and symptoms, while others have not shown any significant change (Seville, 1964). A few probable natural sources and their unique phytoconstituents utilized in psoriasis treatment have been summarized in Table 4.

Table 4: Medicinal plant possessing Anti-psoriasis activity

S.No	Botanical name	Common name	Part used	Active constituent
1	*Aloe vera*	Aloe	Leaves	Anthraquinone,

				acemannan, and salicylic acid
2	*Catharanthus roseus*	Vinca	Entire Plant	Alkaloids
3	*Anthemis cotula*	Chamomile	Flowers	Flavanoids
4	*Linum usitatissimum*	Flax	Seeds	α-Linoleic Acid
5	*Simmondsia chinensis*	Jojoba	Seeds	Waxes
6	*Capsicum annuum*	Red pepper	Fruits	Capsaicin
7	*Glycyrrhiza glabra*	Liquorice	Roots	Glycyrrhezinic acid
8	*Persea Americana*	Avocado	Fruits	β-sitsterol, lecithin, and monounsaturated fatty acids
9	*Ficus carica*	Fig	Fruits	Flavonoids and tannins
10	*Olea europaea*	Olive	Fruit Oil	Flavonoids and isoflavones
11	*Nigella sativa*	Black cumin	Oil	Flavanoids
12	*Ammi visnaga*	Khella	Fruits	Khellin
13	*Curcuma longa*	Turmeric	Rhizomes	Curcumin
14	*Pinus halepensis*	Pine	Wood	Flavanoids
15	*Juglans regia*	Walnut	Fruits (Peels)	Palmitic acid and oleic acid
16	*Prunus amygdalus*	Bitter almonds	*Seeds*	Oleic acidand α-linoleic acid,
17	*Malva sylvestris*	Common mallow	*Leaves*	Flavonoids
18	*Salvia fruticosa*	Sage	Leaves	Rutin and quercetin
19	*Paronychia argentea*	Algerian	Entire Plant	Flavanoids
20	*Lawsonia inermis*	Henna	Leaves	Terpenoids and naphthoquinones
21	*Urtica urens*	Stinging nettles	*Leaves*	Phenolic and flavanoids
22	*Senna alexandrina*	Senna	Leaves	Sennosoids
23	*Inula viscosa*	Inula	Leaves	Gallic acid and flavanoids
24	*Origanum jordanicum*	Thyme	Leaves	Terpenoids and flavanoids
25	*Allium sativum*	Garlic	Bulb	Flavanoids and sulfides
26	*Citrus limon*	Lemon	Fruit	Flavanoids
27	*Zingiber officinale*	Ginger	Rhizome	Phenolic compounds and flavonoids
28	*Musa paradisiaca*	Banana	Fruits	Flavanoids
29	*Ricinus communis*	Castor	Seeds	Flavanoids
30	*Vitis vinifera*	Grape	Fruits	Flavanoids and anthocyanins

31	*Teucrium capitatum*	Germander	Leaves	Terpenoids, flavanoids, and phenolic compounds
32	*Silybum marianum*	Milk thistle	Seeds	α-linolenic acid
33	*Harpagophytum procumbens*	Devil's claw	Roots	Iridoids
34	*Melaleuca alternifolia*	Tea tree	Leaves	Terpinens
35	*Calendula officinalis*	Calendula	Flowers	Triterpenoids and flavanoids
36	*Mahonia aquifolium*	Oregon grape	Fruits	Berberine
37	*Angelica sinensis*	Chinese angelica	Root	Furocoumarin
38	*Cassia fistula*	Amaltas	Fruit pulp	Flavonoids
39	*Cassia tora*	Sickle senna	Leaves	Luteolin, quercetin, and formononetin
40	*Givotia* Rottleriformis	White catamaran tree	Bark	Rutin, luteolin, and kampferol
41	*Psoralea corylifolia*	Psoralea	Seeds	Psoralen
42	*Pongamia pinnata*	Pongam tree	Seeds	Karanjin
43	*Rubia cordifolia*	Indian madder	Roots	Triterpene
44	*Smilax china*	China root	Rhizome	Quercetin
45	*Thespesia populnea*	Indian tulip	Bark	Flavonoids and triterpenoids
46	*Wrightia tinctoria*	Sweet indraja	Leaves	Quercetin 3o-rhamnoside
47	*Trigoneslla arabica*	*Fenugreek*	Seeds	Luteolin and quercetin

Future prospective

Although there are still many unanswered problems, it has been discovered how to better understand the etiology and pathogenesis of psoriasis as well as its therapeutic approaches. Herbal sources are gaining in popularity as a result of their safety and accessibility. T-cell activation, cytokines inhibition, counter-offensive techniques, and T-cell trafficking are the major targets to address while developing herbal remedies and screening plant extracts for anti-psoriatic effectiveness. Anti-inflammatory and next-generation immunosuppressive drugs would be perfect for efficiently treating psoriasis. Future concerns include patient care and monitoring, as well as biological surveillance of the patient's historical background and chronic inflammatory mediators. High-mobility group protein B1 (HMGB1), IL-15, and IL-23, which have been identified as triggers for the early synthesis of TNF-cytokines, may potentially have an impact on TNF production. Clarifying the basic mechanism by which the condition is passed on from one generation to the next is another area of research that has to be looked at to investigate new herbal treatments for psoriasis. Herbal medications are increasingly being used to treat skin illnesses such as psoriasis. Some of them have been shown to inhibit epidermal hyperplasia

and/or inflammation, making them useful in the treatment of psoriasis. Unfortunately, there is little information available on the effectiveness and safety of using herbal products topically to treat psoriasis. To support herbal psoriasis treatment, additional scientific documentation and evidence are required, which needs to be supported by reliable clinical trials that make use of standardized formulations and materials.

Understanding the systemic symptoms of psoriasis requires elucidating several layers of omic data. Different omic levels such as transcriptome, proteome, metabolism, lipidome, glycome, and epigenome, that are of a complex and holistic nature, can provide significant volumes of data, allowing researchers to explore this objective in greater depth and connect the dots between each level. Advances in knowledge of the etiology and pathogenesis of psoriasis will emphasize the potential for novel and customized treatment approaches. The identification of psoriasis susceptibility genes will result in the identification of biochemical pathways involved in the etiology of the condition, allowing for the development of targeted treatments. Furthermore, immune-based treatments, such as those that immunize T cells with doses of non-pathogenic T cells or target appropriate T-cell receptors on auto- or antigen-reactive T cells, may also be successful in preventing the progression of the disease.

Conclusion

Data suggests that current pharmacological therapy, a healthy lifestyle, and the inclusion of an antioxidant-rich diet can help lessen the damage produced by oxidative stress in psoriasis. Future research should, however, look into the application of novel medicinal, genetic, and molecular techniques. Investigating the relationship between antioxidants, the immune system, and psoriasis could lead to a better understanding of the disease's onset, severity, and relapse, as well as diagnostic and therapeutic applications. Perhaps oxidative stress treatment can provide an opportunity for psoriasis patients to live healthier lives. More research into oxidative stress in psoriasis can likely help us get closer to understanding the disease's pathogenesis. ROS are molecules that play a role in both pathological and normal epidermal physiology. Various redox-sensitive cellular signal transduction pathways, such as JAK–STAT, NF-κB, and MAPK/AP-1, up-regulate the expression of proinflammmatory cytokines and chemokines and are involved in the progression of psoriasis. The regulation of these signal transduction cascades by ROS is thought to be the cause of psoriasis. On the other hand, the majority of the molecular mechanism guiding the modulation of ROS-mediated signaling pathways is yet unclear. There are still many unsolved questions regarding the health consequences of ROS, the molecular mechanism, and the recognition of specific ROS engaged in skin conditions like psoriasis. Finally, there is evidence that substances that trigger antioxidative reactions are successful treatments for psoriasis and other disorders where oxidative stress plays a significant role. Synthetic medications used to treat it have side effects, and some of them have been shown to cause psoriasis with an undesirable effects. In that instance, natural herbal medicine is the logical choice, as it is both safe and effective as a synthetic drug.

List of abbreviations

CAM Complementary and alternative medicine

HMGB1	*High-mobility group protein B1*
ICAM	Intercellular adhesion molecule
IFN	Interferons
IL	Interleukins
JAK-STAT	Janus kinase-Signal transducers and activators of transcription
MAPK	Mitogen-activated protein kinase
NF-κB	Nuclear factor kappa B
PDE	Phosphodiesterase
PSA	Psoriatic arthritis
ROS	Reactive oxygen species
TNF-α	Tumor necrosis factor alpha

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