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ROLE OF NOVEL NATURAL RESOURCES IN THE TREATMENT OF PSORIASIS

Ravuri Thanuja*, Gudibandi Bhavitha Sree, Uggirala Mounika and Chandu Babu Rao.

Priyadarshini Institute of Pharmaceutical Education and Research, 5th Mile, Pulladigunta, Guntur-522017.Andhra Pradesh, India.

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Abstract

There is no long-term treatment for psoriasis, an inflammatory immune-mediated illness. Elbows, lower back, scalp, knees, and other body parts may become inflamed as a result of this illness. Biologics are now being used to treat psoriasis; however, because of their highly targeted inflammatory mediators, the immune system may be able to go around the blockade and cause a relapse of the illness as well as other clinical and immunological symptoms. Because of their structural diversity and multiple active individuals across ages mechanisms, natural compounds isolated from herbal medications have synergistic actions to treat psoriasis and its comorbidities. Together with certain immunological molecules including TNF, IL-12, IL-23, IL-17, and other molecules that can contribute to the pathogenesis of psoriasis, the properties of natural products have T cells that clearly play a part in the disease's pathogenesis. Because they are readily available and safe, herbal medications may have anti-psoriatic properties. To create a powerful, secure, and dependable treatment, more scientific research on these herbal resources is required.

Keywords: Psoriasis, Immunotherapy, Plaque, Inflammation, Natural Products.

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*Corresponding Author

Ravuri Thanuja

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Introduction

Psoriasis represents an autoimmune, persistent inflammatory disease that affects the skin and has a powerful hereditary component [22]. The name psoriasis is from the Greek language, meaning "roughly itching condition" (psora: "itch", sis: "action"). Among the various inflammatory disease psoriasis is found to be more severe in forms, though is not infectious. The mostly affected parts in psoriasis are skin, nails and joints(1). The characteristics symptoms of psoriasis are erythema with sharp borders and covered with multiple layers of silvery white scales which primarily occur on the scalp and extensor parts of the limb. It is distinguished by persistent inflammation, which results in uncontrolled keratinocyte growth and differentiation. In accordance with the International Psoriasis Day collaboration, psoriasis affects 125 million individuals globally, or around 2-3% of the population (2). According to research, psoriatic arthritis affects 10-30% of psoriasis

suffers. In 2023, the Executive Board of World Health Organization (WHO) recommended a resolution that requests to increase awareness of psoriasis as one of the main health problems worldwide

History of Psoriasis:

Psoriasis is an inflammatory skin disease that the medical community first recognized in the early 19th century. Since then, researchers have learned a lot about psoriasis, although the condition has a long history of misunderstandings. Today, a variety of modern treatments can significantly reduce the severity of psoriasis and even help a person achieve remission. This article provides a concise overview of long history of peoples understanding of psoriasis and its treatments.

Early History: Throughout history, there were many varied beliefs about the cause of psoriasis, including inadequate hygiene, poor nutrition, microbes, blood disorders, allergies and underlying health conditions. As a result, unorthodox treatments used to cure the conditions were used in practice, including feces, urine, onions herbal concoctions and various oils. It was recognized even in ancient times that sunlight seemed to have an effect on the severity of symptoms of psoriasis and, to an extent, this was utilized in the treatment of the condition.

Hippocrates(460-377BC) was the first physician to use coal tar in the treatment of psoriasis to increase

sensitivity to sunlight, but he also supported the use of topical arsenic for the treatment of psoriasis. Galen (133-200AD) was the first person to identify psoriasis as a health condition of the skin and penned the terminology using the Greek word psora, which means “to itch”. In addition to the application of arsenic, he also recommended the application of a broth in which a certain social stigma. (3)

Types of Psoriasis

Historically, the disease has been classified on the basis of clinical appearance. According to morphology and localization, plaque psoriasis is a most common type of psoriasis, covers around 85% of psoriatic population. (4) In this type of psoriasis, scalp, trunk and buttocks are mainly infected but inflammation may occur at anywhere on the body. The degree of severity of disease is classified as mild, moderate, and severe, which is further measured by means of patient's body surface area (BSA) affected by psoriatic lesions. Normally 3-10% BSA is considered to be moderate while more than 10% is considered to be severe. Plaque psoriasis: The most common type of psoriasis, plaque psoriasis causes dry, itchy, raised skin patches covered with scales. There may be few or many. They usually appear on the elbows, knees, lower back and scalp. The patches vary in color, depending on skin color, particularly on brown or Black skin.

Causes of psoriasis:

Various environmental factors including stress, hypocalcemia infections (e.g. Streptococcal pharyngitis) physical trauma (koebner or isomorphic phenomenon) and some medications including beta blockers, IFNs, antimalarial and systemic corticosteroids are responsible for psoriasis. A part from these some other factors as higher body mass index(BMI) rapid weight changes, alcohol consumption, vitamin D deficiency and habit of tobacco are also associated to increase psoriatic inflammation. [5]

Symptoms:

The general symptoms of this disease includes silvery scales on bright red, pitting on nails, genetic predisposition, well demarcated plaques (usually on the scalp, elbows and knees) and chronic inflammation. People with psoriasis are also have risk of coronary artery disease. The main symptoms are irritation, red and flaky patches of skin. Patches are most often seen on the elbows, knees and middle of the body, but can appear on scalp and elsewhere in the body. The skin may be itchy, dry and covered with raised thick silvery flaky skin pink red in color. Other symptoms include genital sores, joint pains, thickening and browning of nail and severe dandruff on the scalp. This disorder is so severe that it often needs lifelong treatment. Apart from the various predicted reasons for psoriasis to induce the drug induced psoriasis are more common and is explored next to this. (6)

Pathogenesis of Psoriasis:

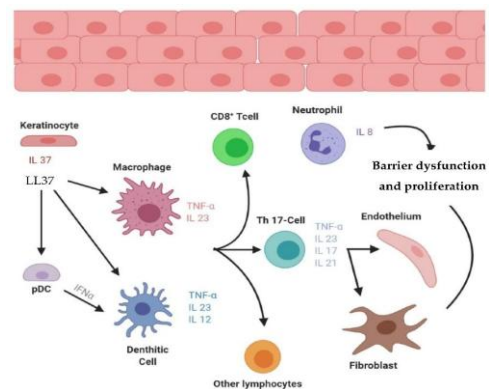
Up to now, research into the pathogenesis of psoriasis has been exploratory. Before 1979, keratinocyte dysregulation, leading to keratinocyte hyper proliferation, was considered to contribute to the disease(7). In 1986, evidence emerged that psoriasis was associated with the activation of lymphocytes, infiltration of lymphocytes, and abnormal proliferation of keratinocytes. Presently, most investigators believe that the activation of immune cells (such as T cells, neutrophils, MCs, and macrophages), which secrete copious amounts of cytokines, eventually leads to the proliferation of keratinocytes, epidermal thickening, and angiogenesis.

The Roles of DCs in psoriasis:

DCs, the professional antigen-presenting cells, comprised myeloid DCs (MDCs) and plasma cell-like DCs (pDCs). DCs are significant contributory factors to the development of psoriasis because of the cytokines secreted by them and their influence on T cells. MDCs are involved in immune regulation through the secretion of cytokines (such as interleukin [IL] 12, IL-cytokines. Moreover, IFN- α enhances the expression of IL-22R on epidermal keratinocytes, which is followed by the inhibition of keratinocyte differentiation, resulting in the thickening of the epidermis. (8)

Roles of T Cells in Psoriasis:

Over the last 2 decades, research has tended to focus on the T cells, primarily including CD4+ T and CD8 T cells, and their vital roles in the pathogenesis of psoriasis. Under the induction of MDCs or macrophages, naïve CD4 T cells can differentiate into Th1, Th2, Th17, or Treg cells, which seems to work primarily by producing cytokines. (9)



Diagnosis of Psoriasis:

To diagnose psoriasis, your doctor usually examines your skin, scalp, and nails for signs of the conditions. They may also ask questions about your health and medical and family history, such as whether you:

- Experience symptoms such as itchy or burning skin
- Had a recent illness or experienced severe stress.
- Take certain medicines
- Have relatives with the disease
- Experience joint tenderness

Natural Products Used in The Treatment of Psoriasis:

Nigella sativa:

Nigella sativa is a popular therapeutic plant that has a long religious and cultural background in Unani, Ayurveda, Arabic, and Chinese medicine. Many bioactive natural agents, including alpha-hederin, alkaloids, thymoquinone, and saponins, are found in *N. sativa* and contribute to its wide spectrum of effects as a bronchodilator, diuretic, antidiabetic, analgesic, antihypertensive, antibacterial, antineoplastic, and anti-inflammatory agent, making it a promising therapeutic for dermatological diseases.(10) Thymoquinone (TQ) is the major bioactive ingredient, accounting for 30–40% of essential oils. TQ's high antioxidant and anti-inflammatory actions have prompted much investigation into its wide spectrum of health benefits. The *N. sativa* treatment has been proven to dramatically decrease inflammation via TQ-mediated secretion of proinflammatory cytokines as well as eosinophils. Several researchers investigated the impact of TQ on attenuating inflammation of the airways in a rat model of allergic asthma. TQ intraperitoneal administration prior to airway challenge showed a significant reduction in eosinophilia in the lung, serum IgG and IgE levels, and IL-13, IL-4, and IL-5 proinflammatory Th2 cytokines. *N. sativa* functions as an antioxidant by enhancing free radical defense by inhibiting elastase, lipid peroxidation, and myeloperoxidase.(11)

Capsicum Annum:

Capsicum annum is considered a plant species endemic to southern North America, northern South America, and the Caribbean.

Aloe Barbadensis Miller:

Aloe barbadensis Miller (also called *Aloe vera* Linnaeus) seems to be a succulent tropical plant of the Liliaceae family. Aloe leaf pulp contains 98.5% water, while gel or mucilage contains 99.5% water. Carbohydrates, proteins, mucopolysaccharides, enzymes, anthraquinones, salicylic acid, chromes vitamins, and minerals also make up the remaining 0.5–1%. Acemannan and Aloeemodin are antibacterial active ingredients that can help with psoriasis. Furthermore, owing to its catalytic activity, salicylic acid eliminates psoriatic plaques. Aloe vera gel is employed to treat psoriasis by reducing redness and scaling. It is employed to make topical creams and lotions. Aloe vera also has immunomodulatory, antioxidant, anti-inflammatory, anti-fungal, and anti-tumor properties. It also promotes skin hydration and wound healing by increasing collagen activity. This aids in the healing of the psoriatic skin's negative consequences.(12)

Angelica sinensis:

Angelica sinensis (Dong Quay, female ginseng) seems to be a biennial or perennial plant in the family Apiaceae. It is also known as Dong Quay. Something has long been utilized in traditional Chinese medicine (TCM). TCM claims that it stimulates and replenishes blood while also correcting insufficiency. Psoralen, a powerful

furocoumarin, is found in *Angelica sinensis* extract. Psoralens are used in the treatment of psoriasis as they behave as photosensitizers when exposed to UV-A. Patients self-administer PUVA therapy by eating *Angelica sinensis* and then exposing themselves to natural sunlight or UV.

Curcuma longa L:

Curcuma longa (Zingiberaceae) is a perennial plant with characteristic odour and slightly pungent bitter in taste. The rhizome contains three main curcuminoids, namely curcumin, desmethoxycurcumin, and bisdemethoxycurcumin, as well as volatile oils (tumerone, atlantone, and zingiberone). *C. longa* is largely used in traditional medicine especially in Ayurvedic medicine for its analgesic, antibacterial, antioxidant, expectorant, and anti-inflammatory properties. Curcumin demonstrated to be a highly pleiotropic molecule able to interact with numerous molecular targets involved in inflammation (13)

Matricaria recutita L:

Matricaria chamomile, or *Matricaria recutita*, is a part of the Asteraceae family. It has traditionally been employed to alleviate digestive issues. Chamazulene seems to be the primary phytochemical accountable for antipsoriatic action. It's a derivative of the oil extraction matrix derived from flower. Chamazulene exerts anti-inflammatory action by suppressing lipoxygenase, which inhibits leukotriene B₄ synthesis (LTB₄). LTB₄ production then increases, resulting in psoriatic plaque. Therefore, Chamazulene's positive impact will be demonstrated by inhibiting LTB₄. Quercetin is an anti-inflammatory, anti-tumor, antiviral, and antibacterial flavones. It inhibits both IFN-induced STAT-1 stimulation and NF- κ B activation. It reduces the generation of histamine and IgE.(14) It inhibits the enzymes nitric oxide synthase (iNOS), TNF-, and IL. Quercetin works through many processes and might be used to treat

psoriasis. Apigenin is indeed a flavone with anti-inflammatory and antioxidant properties. It inhibits NF- κ B activation and decreases TNF-induced luciferase reporter gene transactivation. It also lowers TNF-, suppresses COX-2, IL-6, and IL-8 expression, and inhibits TNF-induced luciferase reporter gene transactivation. It also protects against fungal infections. Chamomile essential oil inhibits NF-, TNF-, IL-1, IL-6, iNOS, and COX-2. (15)

Indigo (Baphicacanthus cusia, Brem.):

Melaleuca alternifolia:

The *Melaleuca* plant is endemic to Oceania and is utilized in traditional medicine in Australia. terpinene, -terpineol, terpinen-4-ol, 1,8-cineol, -pinene, terpinolene, sabinene, and limonene are all found in tea plant oil. Sesquiterpenes and aromatic chemicals make up the remainder of the oil. In vivo, tea tree oil also has substantial antibacterial and antifungal properties. Methyl eugenol, terpinen-4-ol, and 1,8-cineol all play important roles in

antibacterial action. Terpinen-4-ol has been shown to reduce TNF-, IL-1, IL-8, and PGE2 production. It can also influence vasodilation and plasma extravasation. In a trial of 27 patients to assess the impact of tea oil on weeping or flare induced by histamine, the volume of mean weeping decreased significantly after 10 min of treatment. Human and rodent investigations had similar findings. Tea plant oil reduced the susceptibility to flared and wheal histamines. Tea tree oil, on the other hand, has been linked to contact allergies in a small number of people. Freshly extracted oil is a mild to the moderate sensitizer, while oxidation elevates the oil's allergenic action. The oil contains sensitizers such as -terpinene, ascaridole, -phellandrene, limonene, and trihydroxymenthane. The majority of the responses are caused by direct tea tree oil application, Tea tree oil taken orally can ultimately cause systemic contact dermatitis, cognitive confusion, and coma. (16)

Silybum marianum:

It is commonly known as Milk Thistle. This plant is very well known for its hepatoprotective activity. Numerous changes have been detected in the liver of patients with psoriasis, including steatosis, periportal inflammation, fibrosis, necrosis and cirrhosis. A multifactorial etiology of liver disease in patients with psoriasis includes changes due to alcohol use, nutritional factors, anti - psoriatic medications and a direct effect of the psoriasis itself. Abnormally high levels of CAMP and leukotrienes have been observed in psoriatic patients and normalization of these levels may improve the condition. The importance of silymarin in the treatment of psoriasis may be due to its ability to improve endotoxin removal by the liver, inhibit CAMP phosphodiesterase and inhibit leukotriene synthesis. (17)

Antipsoriatic Activity of Herbal plants:

A number of herbal formulations are being used in market around the globe for treatment of psoriasis. The medicinal plants play a vital role in pharmacological research and drug

development, since medicinal plants have many advantages over other medicines including various side effects, ease of availability at lower cost and patient compliance. Therefore, researchers are seeking for potential herbal products as an alternative to synthetic drugs in psoriasis therapy. Some of the herbal plants used in psoriasis along with their active constitute and mechanisms of action. A number of herbal formulations are being used in market around the globe for treatment of psoriasis. The medicinal plants play a vital role in pharmacological research and drug development, since medicinal plants have many advantages over other medicines including various side effects, ease of availability at lower cost and patient compliance. Therefore, researchers are seeking for potential herbal products as an alternative to synthetic drugs in psoriasis therapy. Some of the herbal plants used in psoriasis along with their active constitute and mechanisms of action.(18)

Future Challenges of Herbal Remedy for Psoriasis Treatment:

The herbal sources are currently getting more reliability due to their safety and easy availability. For herbal remedy and screening of plant extracts for anti-psoriatic activity the

main targets to consider is the T-cell activation, T-cell trafficking, Cytokine inhibition and Counter offensive strategies. Anti-inflammatory and next generation immunosuppressant ideally would be able to treat psoriasis effectively. Future challenges are several folds and include the caring and monitoring of patient and biologic monitoring of the historical background, chronic inflammatory mediators. The specific trigger identified for initial production of TNF- α cytokines may also impact TNF- α production include HMG- B1, IL- 15 and IL-23. Elucidation of the basic mechanism by which the disease is transmitted from one generation to another is another facet of the research which must be investigated to explore some more herbal drugs for the treatment of psoriasis.(19)

Herbal Nanotechnology for Psoriasis Treatment:

Most of the herbal drugs from herbal origin are poorly water soluble due to presence of hydrophobic active ingredients which results in low bioavailability and increased systemic clearance. Therefore, increased or repeated dose is requiring, that leads to limited clinical used of herbal medicines. An alternative option is required to increase water solubility of herbal drugs as well as to localize the drug in particular site for improved patient compliance and better efficacy. In recent years, nanoparticles and micro particles have been used widely for herbal medicines and have gained unique position for delivery of various bio actives, proteins, peptides and drugs for treatment of various skin diseases and considered to be an important one as they improve the selectivity, increase patient compliance, effectiveness and The authors concluded on the basis of these results that microemulgel may be considered as an alternative therapeutic option for plaque psoriasis. Topical Nano gel formulation of Acitretin and Aloe emodin was prepared by using natural polymer chitin for the treatment of psoriasis. The formulated Nano gel was optimized on the basis of amplitude, particle size, drug release and time of probing. Non-fickian release pattern was observed during in-vitro drug release at pH 5.5 suggesting prolonged release nature of the drug. It was also observed that retention of drug was high at the inner layer of skin, which is essential to treat disease like psoriasis. Biocompatibility of the drug was confirmed during the histopathological investigation after in vivo skin irritation study on Perry's mouse tail model (20).

Conclusion

This review has made it abundantly evident that substances produced from nature have the potential to play a significant role in psoriasis treatments in the future. This article has provided an overview of some of the

substances and plants that have been investigated thus far for potential anti-psoriasis benefits. But nature still has a lot more undiscovered riches. There is several health benefits associated with phytochemicals, and research into their physiological impacts is still being done. Due to the accessibility of plants and the ease of manufacture of the products, the traditional use of natural compounds in the treatment of psoriasis is comparatively inexpensive. Many plants have been shown to have anti-psoriatic properties; these are covered in this review. Conversely, only a specific proportion of psoriasis sufferers can now get herbal therapy. Herbal extracts can be used to treat psoriasis in addition to synthetic drugs. Combining the two uses could result in a lower dosage of synthetic drugs and a return of side effects. The standardization of herbal medicines requires quality control procedures and regulatory regulations in order to ensure the safety and efficacy of psoriasis treatment. Further research with a bigger sample size are required to evaluate the therapeutic efficacy of these natural compounds. This area needs to look into fresh plant resources as well.

Author contributions

All authors are contributed equally.

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Declaration of Competing Interest

The authors have no conflicts of interest to declare.

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