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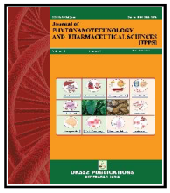

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Phytotherapeutic advances in psoriasis: A natural approach to treatment

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Abstract

Psoriasis is a chronic autoimmune skin disorder, characterized by hyperproliferation of keratinocytes and excessive inflammation, leading to the formation of psoriatic plaques. Conventional treatments, including corticosteroids, immunosuppressants, and biologics, offer symptomatic relief but often pose challenges such as adverse effects, drug resistance, and recurrence. In recent years, plant-derived therapies have gained attention as potential alternative or complementary treatments due to their immunomodulatory, anti-inflammatory, and antioxidant properties. Various phytochemicals, including polyphenols, flavonoids, alkaloids, and carotenoids, have demonstrated efficacy in alleviating psoriasis symptoms by modulating immune responses, inhibiting inflammatory cytokines, and reducing oxidative stress. Notable medicinal plants such as *Aloe vera*, *Artemisia capillaris*, St. John's Wort, *Rehmannia glutinosa*, and *Salvia miltiorrhiza* have shown promising results in preclinical and limited clinical studies. These natural compounds act through multiple mechanisms, including NF-κB, MAPK, and JAK-STAT pathway inhibition, suppression of pro-inflammatory cytokines (IL-17, IL-23, TNF-α), and regulation of keratinocyte differentiation. While these findings highlight the therapeutic potential of phytochemicals, further clinical trials are essential to validate their efficacy, optimize dosages, and ensure safety. This review explores the current advancements in plant-based treatments for psoriasis, emphasizing their mechanisms of action, therapeutic potential, and the need for further research to establish them as viable treatment options in dermatology.

1. Introduction

Psoriasis is a chronic autoimmune disease that has been known since ancient times. It is the most common genetic skin disorder, characterized by the gradual formation of psoriatic plaques thick, scaly patches of skin, accompanied by pustules and spots. The disease begins in the upper layer of the dermis, where blood vessels become enlarged and twisted. As immune cells like lymphocytes and granulocytes move into the epidermis, an abnormal cycle of skin cell growth begins. Keratinocytes, which are the main cells of the epidermis, start multiplying too quickly and fail to mature properly. This results in the thickening of the skin and the loss of structural layers, leading to the development of parakeratosis (a condition where keratinocytes retain their nuclei). As psoriasis progresses, skin cells continue to overgrow, disrupting the normal structure of the epidermis. The stratum corneum (the outermost layer of the skin) disappears entirely, and immune cells accumulate, forming Munro's microabscesses. The condition often appears as red, inflamed patches covered with silvery-white scales, typically arranged in a symmetrical pattern (Gudjonsson *et al*., 2021). Psoriasis is caused by an overactive immune system, particularly involving T cells, dendritic cells, and inflammatory molecules such as interleukin-23, interleukin-17, and tumour necrosis factor (TNF). It is also linked with an increased risk of metabolic syndrome and cardiovascular disease. People with severe psoriasis are more likely to develop conditions like obesity, cholesterol, diabetes, and high blood pressure (Boada *et al.,* 2018). While existing treatments can help manage psoriasis symptoms, there is no permanent cure discovered till date. Many conventional therapies often have side effects such as skin thinning, organ damage, immune suppression, infections, and even an increased risk of cancer, making long-term treatment difficult. As a result, there is a growing need for safer, more effective, and affordable treatment options. One promising approach is the use of plant-based compounds. Research has shown that herbal medicines have immunoregulatory and antioxidant properties that may help control psoriasis. Studies highlight the potential of natural substances to reduce inflammation and oxidative stress, which are the key factors in the progression of the disease. Various plant-derived compounds have been tested in laboratory settings (*in vitro*), animal studies (*in vivo*), and even clinical trials have been performed. These studies suggest that natural substances can influence immune system responses, help reduce inflammation, and improve psoriasis symptoms (Karakas *et al*., 2020). This emerging research provides a deeper understanding of how phytochemicals interact with the immune system and oxidative stress pathways. By exploring the effects of plant-derived compounds at a molecular level, scientists hope to develop alternative therapies that are both effective and safe for long-term use (Zouboulis *et al*., 2018).

2. Epidemiology and pathophysiology of psoriasis

Psoriasis is a chronic skin condition affecting around 2% of the global population. It is more prevalent among Caucasians, less common in Asians, and least common in Black individuals. The disease is also more frequently observed in colder northern regions,

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whereas it occurs less often in tropical climates. In Europe, the prevalence of psoriasis varies between 0.6% and 6.5%, with higher rates in northern countries (Lindberg *et al.*, 2019). Psoriasis can develop at any age, making it difficult to predict an average onset. Many cases go undiagnosed for years due to delayed medical visits. However, research suggests that the disease commonly appears between the ages of 15 and 20 at the earliest, and between 55 and 60 at the latest (Menter *et al.*, 2020). The complexity of psoriasis lies in its impact on various parts of the body, including the skin, nails, and joints, as well as its connection to both the adaptive and innate immune systems. It can occur in different forms depending on the underlying biological mechanisms. Today, it is widely accepted that psoriasis is an autoimmune condition driven by immune system cells and inflammatory cytokines, which are the primary targets for treatment (Nestle *et al.*, 2009). Another factor contributing to psoriasis is the skin's microbiota. The bacteria residing on the skin play a vital role in regulating immune responses, and researchers believe that an abnormal immune reaction triggered by these microorganisms may contribute to the development of autoimmune diseases (Belkaid and Segre, 2014). Genetics also play an important role in psoriasis. Certain genetic mutations affecting immune cell regulation can alter cytokine levels, influencing the growth and differentiation of skin cells (keratinocytes). These genetic variations can result in different disease patterns and severity (Tsoi *et al.*, 2012). More recent research has linked psoriasis to epigenetic modifications, such as DNA methylation, histone modifications, and non-coding RNAs (including microRNAs and long non-coding RNAs). These chemical changes affect gene expression by altering chromatin structure, which in turn influences the activity of transcription factors that regulate various genes. Understanding these genetic and epigenetic factors may provide new insights into the disease and potential treatment strategies (Boehncke *et al.,* 2019).

3. Immune system responses in psoriasis

The cause of psoriasis is complex, mainly due to an abnormal immune response in the skin. This response is influenced by genetic factors and various environmental triggers, such as skin injuries, infections, and certain medications (Kim *et al.,* 2019). A key feature of psoriasis is chronic inflammation, which leads to the excessive growth and abnormal development of keratinocytes (skin cells). When examining psoriatic plaques under a microscope, they show a thickened epidermis (hyperplasia) and an inflammatory environment filled with immune cells like dendritic cells, macrophages, T cells, and neutrophils (Liu *et al.*, 2018). Psoriatic plaques involve two main types of cells: keratinocytes (from the epidermis) and immune cells known as mononuclear leukocytes. The interaction between these cells is regulated by genes associated with psoriasis. Keratinocytes play a direct role in activating immune cells, particularly leukocytes, which further contribute to inflammation. The disease disrupts the balance between the innate and adaptive immune systems, affecting factors that influence T cells and dendritic cells (Jiang *et al.,* 2020). Several immune cells are involved in psoriasis. Neutrophils, which are part of the body's first line of defence, are short-lived and must be continuously produced in the bone marrow. They migrate to the epidermis in response to chemokines like interleukin-8 (IL-8) and CXCL1, as well as proteins such as S100A7/A8/A9, which are produced by keratinocytes. Another key immune cell type is plasmacytoid dendritic cells (pDCs), which express BDCA-2+ and CD123+ antigens and release high levels of interferon-alpha (IFN-α) upon activation, playing a critical role in triggering psoriasis (Gottlieb *et al.,* 2020). In psoriasis, the interaction between immune cells and skin cells leads to persistent inflammation. Large numbers of T-cells and mature dendritic cells (DCs) accumulate in the skin, where they interact with chemokines like CCL19, CCL21, CXCL12, and CCL18. These chemical signals help activate T cells directly at the site of inflammation (Lowes *et al.,* 2007). T cells in psoriasis are mainly classified into two groups: helper T cells (TH) and cytotoxic T-cells (TC). Some of these T cells express CD161 and other receptors typically found on natural killer cells, suggesting that natural killer-like T cells may play a role in psoriasis development. The immune response is further sustained by keratinocytes, which release molecules that stimulate immune cells. In turn, the activated immune cells influence keratinocyte behavior, causing them to express adhesive molecules that attract more T cells (Nograles *et al.,* 2008). Dendritic cells also play a crucial role in psoriasis by detecting danger signals through Toll-like receptors (TLRs). These signals, which may come from heat shock proteins (HSPs) or S100A12 proteins, trigger DC activation and maturation. Peptide antigens can further stimulate the immune system, leading to the activation of T cells and the formation of specific T-cell populations in psoriatic skin (Guthrie e*t al.,* 2012). Chronic immune activation in psoriasis is believed to be linked to persistent antigen stimulation, leading to uncontrolled T-cell activity. Developing effective treatments for psoriasis depends on understanding the molecular pathways that drive this inflammation. One model suggests that cytokines like IL-23 and IL-12 initiate a chain reaction, leading to the production of IFN-γ and TNF, which then activate numerous genes involved in inflammation (Batalla *et al.*, 2019). Key cytokines that drive psoriasis include TNF-α, lymphotoxin-α (LT-α), IL-1, IL-17, IL-20, IL-22, and interferons. These molecules activate transcription factors such as STAT and NF-κB, which further amplify the inflammatory response. Dendritic cells work in coordination with IFN-α, IL-20, IL-12, and IL-23 to sustain this cycle of inflammation. IL-12 and IL-23, in particular, stimulate T cells to release more inflammatory cytokines, while heat shock proteins and cell interaction further trigger the immune response (Griffiths *et al.,* 2017). Other cytokines, such as TGF-β, IL-1, IL-6, and IL-20, influence keratinocyte growth and contribute to the thickening of psoriatic skin. Additionally, a complex network of chemokines regulates immune cell movement, with more than a dozen different chemokines showing increased activity in psoriasis. This highlights the numerous pathways involved in the disease, making it a highly intricate condition to treat (Rojas *et al.*, 2019).

4. Oxidative stress in psoriasis

Recent studies have shown that reactive oxygen species (ROS) and nitric oxide synthase (NOS) play a significant role in the development of psoriasis. An imbalance in redox levels, along with increased inducible nitric oxide synthase (iNOS), contributes to oxidative stress, making it important to understand the underlying molecular mechanisms. This knowledge can help identify natural antioxidant-rich substances that may offer potential treatment options for psoriasis (Mocan *et al.,* 2017).

4.1 Reactive oxygen species (ROS)

ROS are oxygen-containing molecules that react with other substances in the body. They include radicals such as hydrogen superoxide (HO_2-), superoxide (O_2-), hydroxyl (OH•), and peroxyl radicals (RO_2•), as well as non-radicals like ozone (O_3), hydrogen peroxide

(H_2O_2), and hypochlorous acid (HOCl). These molecules are produced naturally within cells through enzyme-controlled metabolic processes, radiation exposure, and environmental factors. One of the primary sources of ROS is cellular respiration, where oxygen is gradually reduced in the electron transport chain to form water. However, during this process, ROS can also be released from the mitochondria. Another significant source is peroxisomal metabolism, where hydrogen is removed from biomolecules, producing hydrogen peroxide. Additionally, immune cells, particularly leukocytes, produce ROS through the enzyme NADPH oxidase during an "oxidative burst," which plays a key role in immune defence. External factors such as ultraviolet radiation can also trigger ROS formation in the skin (Ali *et al.,* 2016).

4.2 Nitric oxide synthases (NOS)

NOS enzymes catalyze the production of nitric oxide (NO) in the body. There are three main types of NOS: eNOS (endothelial NOS) - found in blood vessel linings, regulating vascular function, nNOS (neuronal NOS) present in nerve cells, involved in neural signaling, and iNOS (inducible NOS) - produced in response to inflammation, and its overactivity is linked to psoriasis. Unlike eNOS and nNOS, which are always present and calcium-dependent, iNOS is only produced when triggered by inflammatory signals. In psoriasis, keratinocytes and other skin cells produce excessive iNOS, leading to oxidative stress. When active, NOS uses oxygen, NADPH, and L-arginine to generate nitric oxide, which can further react with superoxide to form peroxynitrite (ONOO-), a highly reactive compound that causes significant cellular damage (Ormerod *et al.,* 1998).

4.3 The role of oxidative stress in psoriasis

Oxidative stress occurs when the balance between ROS and antioxidants is disrupted, leading to molecular damage. Excessive ROS levels contribute to DNA modifications, lipid peroxidation, and the release of pro-inflammatory cytokines. While low levels of ROS are necessary for normal cellular functions, high levels drive inflammation and tissue damage in psoriasis (Koguchi *et al*., 2015). Research has shown a link between oxidative stress markers and psoriasis severity, with increased total oxidative stress (TOS) and malondialdehyde (MDA) levels correlating with disease progression. At the same time, antioxidant markers such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) tend to decrease. Additionally, non-enzymatic antioxidants like vitamins E and C, as well as glutathione (GSH), are often found at lower levels in psoriasis patients (Baccarelli *et al*., 2012). Oxidative stress activates multiple inflammatory pathways, including NF-κB (nuclear factor kappa-light-chain-enhancer of activated B cells), a key regulator of the immune response, MAPK (mitogen-activated protein kinases), which are involved in cell signaling and inflammation, and JAK-STAT (Janus kinase/signal transducer and activator of transcription), which influences immune cell activation and cytokine release. These pathways stimulate T-helper cells (Th1 and Th17), leading to inflammation, abnormal keratinocyte growth, immune cell infiltration in the skin, and disrupted blood vessel formation. Additionally, ROS drives lipid peroxidation, leading to an imbalance in cellular signaling molecules like cGMP and cAMP, which contributes to excessive skin cell proliferation. High levels of oxidized LDL (ox-LDL) and phospholipase A2(PLA2) activity further promote inflammation (Min *et al*., 2018). Another effect of oxidative stress is increased cytosolic calcium (Ca^{2+}) levels, which interfere with keratinocyte differentiation and proliferation, potentially causing cell death. Moreover, oxidative stress enhances the function of myeloid dendritic cells (mDCs), which release IL-8 and TNF-α, further stimulating T-cell activation. The Th1 immune response is particularly affected, leading to higher levels of IFN-γ and IL-2 in psoriatic skin (Muller *et al*., 2019). ROS also influences blood vessel formation (angiogenesis) by stimulating vascular endothelial growth factor (VEGF), which contributes to the development of new blood vessels in psoriasis. This factor aids leukocyte migration into the skin, worsening inflammation. Moreover, ROS activates specific MAPK pathways, including ERKs, JNKs, and p38 MAPKs, which are involved in psoriasis development. Depending on the situation, ROS can either activate or inhibit NF-κB signaling, making them a crucial factor in the disease's progression (Duan *et al*., 2018). Substances of natural origin - plants and phytochemicals with potential therapeutic significance in reducing ROS and iNOS. Recently, during the pursuit of novel therapies, natural compounds have gained significant attention due to their vast diversity, safety, and availability. Several clinical studies have shown that some of the following natural-origin substances can attenuate psoriasis through numerous molecular mechanisms associated with apoptosis, inhibition of angiogenesis, and overexpression of inducible-nitric oxide synthases (He *et al*., 2017).

5. Plants and phytochemicals with potential therapeutic significance in reducing ROS and iNOS

Recently, natural compounds have garnered considerable attention in the development of novel therapies due to their diversity, safety, and accessibility. Several clinical studies have demonstrated that various substances of natural origin have the potential to mitigate psoriasis through several molecular mechanisms. These mechanisms include the induction of apoptosis, inhibition of angiogenesis, and modulation of inducible nitric oxide synthase (iNOS) overexpression. For instance, compounds such as curcumin and resveratrol have been shown to exert anti-inflammatory effects, reduce oxidative stress, and promote the resolution of inflammation (Choi *et al*., 2014; Gupta *et al*., 2016). Additionally, the suppression of angiogenesis by natural agents like flavonoids has been highlighted as a critical factor in psoriasis management (Kumar *et al*., 2015). These findings suggest that natural products could provide promising adjunctive therapies for psoriasis, with further clinical studies necessary to explore their full therapeutic potential.

5.1 Medicinal plants for psoriasis treatment

5.1.1 *Aloe barbadensis* Miller

A. vera, a succulent plant widely recognized for its medicinal properties, is commonly used to treat various ailments, particularly skin conditions. The gel extracted from its leaves is a key ingredient in cosmetics, pharmaceuticals, and dietary supplements due to its rich composition of bioactive compounds such as anthraquinones, polysaccharides, vitamins, salicylic acid, carotenoids, and flavonoids. These components have anti-inflammatory properties that can help alleviate psoriasis symptoms by reducing skin irritation and inflammation. Laboratory studies indicate that A. vera extract (from both gel and leaves) can modulate inflammatory pathways by inhibiting NF-κB, MAPK, and PI3K signaling, suppressing the production of inflammatory mediators like iNOS, IL-6, and IL-1β,

and reducing prostaglandin E2 through COX blockade. Research on HaCaT cells, a psoriatic skin model stimulated with TNF-α, demonstrated that *A. vera* extract at concentrations of 20, 40, and 80 µg/ml for 24 h could improve cell viability (Lee *et al*., 2016).

5.1.2 *Artemisia capillaris* var. *acaulis* Pamp.

A. capillaris, a traditional herbal remedy in East Asia, is known for its effectiveness in treating fever and liver disorders. This plant contains chlorogenic acids, coumarins, and flavonoids, which have shown potential benefits in treating conditions such as cancer, hepatitis, malaria, obesity, and infections. (Banu *et al*., 2020). In psoriasis, *A. capillaris* extract has been found to limit excessive keratinocyte proliferation and promote apoptosis. Furthermore, it may reduce leukocyte infiltration by suppressing ICAM-1 expression and lowering nitric oxide production through iNOS inhibition. *In vitro* studies using HaCaT cells treated with varying concentrations (1 to 100 µg/ml) of *A. capillaris*, for 72 h demonstrated improved cell viability. Additional *in vivo* experiments on mice, where psoriasis was induced using IMQ, further validated its potential benefits (Kim *et al*., 2017).

5.1.3 St. John's wort (*Hypericum perforatum* L.)

St. John's wort has been traditionally used for treating burns, wounds, diarrhea, ulcers, sunburns, keloid scars, and hemorrhoids. A clinical study involving 20 psoriasis patients who applied St. John's wort ointment showed significant reductions in skin redness, scaling, and thickness compared to a placebo group. Another clinical trial on plaque-type psoriasis confirmed that areas treated with this herbal ointment exhibited reduced inflammation and improved skin texture (Bauer *et al*., 2018).

5.1.4 *Rehmannia glutinosa* (Gaetrn.) Libosch. Ex DC.

R. glutinosa extract is known for its strong antioxidant properties, which help neutralize free radicals and suppress inflammatory responses by inhibiting iNOS expression. Additionally, this herb has been shown to reduce the levels of proinflammatory cytokines such as TNF-α, IL-6, IL-17A, and IL-23, as well as lower prostaglandin E2 production by blocking COX2. Its effects are likely mediated through JAK-STAT pathway inhibition. *In vivo,* studies on mice treated with *R. glutinosa* extract at doses of 100 and 200 mg/kg body weight for seven days, and *in vitro* studies on THP-1 and RAW264.7 cells demonstrated its effectiveness in reducing psoriasis-like skin inflammation (Zhang *et al*., 2015).

5.1.5 *Salvia miltiorrhiza* var. *miltiorrhiza*

S. miltiorrhiza is widely studied for its anti-inflammatory, antioxidant, and antiproliferative properties. Research suggests that this herb may also have antipsoriatic effects. *In vitro* studies on HaCaT cells stimulated with IL-1, IL-17, IL-22, and oncostatin M, as well as *in vivo* studies on IMQ-stimulated mice, indicate that *S. miltiorrhiza* root extracts can alleviate inflammation by scavenging free radicals and inhibiting Akt and ERK1/2 phosphorylation. The extract also thins skin lesions, reduces scaling, and suppresses keratinocyte proliferation while promoting apoptosis. Although, the exact mechanism remains unclear, researchers suggest that the inhibition of YAP and STAT3 activation may play a role (Li *et al*., 2019).

5.2 Alkaloids

5.2.1 Capsaicin

Capsaicin, the active compound found in chilli peppers, interacts with vanilloid receptors, leading to the depletion of substance P from sensory neurons. This action helps reduce local vasodilation, angiogenesis, and keratinocyte overgrowth. Additionally, capsaicin inhibits NF-κB and AP-1 signaling pathways, thereby reducing inflammation, redness, and itching in psoriasis patients. However, its topical use is limited due to the burning sensation it causes. These findings were supported by in vitro experiments on human promyelocytic leukemia (HL-60) cells stimulated with TPA (Chen *et al*., 2015).

5.3 Polyphenols

5.3.1 Resveratrol

Resveratrol, a polyphenol found in grapes, berries, and the plant *Polygonum cuspidatum*, is known for its antioxidant, anti-inflammatory, anticancer, and antidiabetic properties. Animal studies on imiquimod-induced psoriasis models have demonstrated that resveratrol reduces proinflammatory cytokine production (IL-17A, IL-19, IL-23) and promotes keratinocyte apoptosis. This effect is likely due to SIRT1 activation and Akt inhibition. *In vitro* studies on normal human epidermal keratinocytes (NHEK) further support its potential to decrease excessive keratinocyte proliferation. Additionally, resveratrol inhibits aquaporin 3 (AQP3), which plays a role in skin hydration and inflammation (Cai *et al.*, 2017).

5.3.2 Curcumin

Curcumin, the bioactive compound in turmeric, has been used for centuries as a traditional remedy in Southeast Asia. It is well-known for its antioxidant, anti-inflammatory, antimicrobial, and anticancer properties. Research suggests that curcumin may be beneficial for psoriasis treatment by directly interacting with TNF-α at its receptor-binding sites, thereby disrupting signal transduction and suppressing inflammation. Molecular docking studies have confirmed this interaction, revealing that curcumin binds to key TNF-α residues, thereby modulating immune responses (Shao *et al*., 2016).

5.3.3 Rottlerin

Rottlerin, a natural polyphenolic compound extracted from Mallotus philippinensis, has been investigated for its antihypertensive, antifertility, and antiallergic properties. *In vitro* studies on HaCaT cells indicate that rottlerin effectively suppresses keratinocyte hyperproliferation, making it a potential therapeutic agent for psoriasis treatment (Choi *et al*., 2011).

5.4 Flavonoids

Flavonoids are natural compounds found in plants that have significant health benefits, particularly in reducing inflammation and oxidative stress (Banu *et al.,* 2016). Many flavonoids have been studied for their potential in treating psoriasis due to their anti-inflammatory and immunomodulatory properties (Hertog *et al*., 1993).

5.4.1 Quercetin

Quercetin is a flavonoid commonly found in plants like *Ginkgo biloba* and St. John's wort. It has various biological effects, including anti-inflammatory, antioxidant, cardioprotective, and anticancer properties. Studies have shown that quercetin helps regulate inflammation by modulating key signaling pathways, such as the MAPK and NF-κB pathways. Research on rats has demonstrated that administering quercetin significantly reduces levels of

inflammatory cytokines like TNF-α, IL-6, and IL-17 (Sanchez *et al.*, 2016).

5.4.2 Apigenin

Apigenin is widely present in foods like sweet peppers, parsley, thyme, celery, onions, and tea. It is known for its antibacterial, anti-inflammatory, and antioxidant properties. This flavonoid is particularly effective in suppressing NF-κB activation in autoimmune cells, which plays a critical role in inflammatory diseases like psoriasis. Studies on mice have shown that apigenin reduces cytokine levels, such as IL-6 and IL-12, which are elevated in psoriasis (Yang *et al.*, 2012).

Figure 1: Different plants used in the treatment of psoriasis.

5.4.3 Kaempferol

Kaempferol is found in tea, broccoli, apples, strawberries, and beans. It has strong anti-inflammatory effects, making it beneficial for psoriasis treatment. Research has shown that kaempferol reduces inflammation in psoriatic skin by suppressing the phosphorylation of NF-κB and inhibiting Th17 levels, both of which are involved in psoriasis pathogenesis (Zhao *et al.*, 2017).

5.4.4 Genistein

Genistein, a flavonoid present in soybeans and fava beans, exhibits antioxidant and anti-inflammatory effects. Studies on mice have shown that genistein reduces the expression of inflammatory cytokines like IL-1β, IL-6, TNF-α, and IL-17. It also inhibits STAT3 phosphorylation and NF-κB activation, key pathways involved in inflammation and psoriasis development (Wu *et al.*, 2018).

5.4.5 Rutin

Rutin is found in citrus fruits, apples, tea, and buckwheat. It has strong antioxidant and anti-inflammatory properties. Researchers studied the antipsoriatic activity of rutin and found that while it showed promising results in animal models, its effectiveness in in-vitro tests was limited. However, traditional medicine practitioners have long used rutin-containing plants for treating skin conditions (Mao *et al.*, 2007).

5.4.6 Naringenin

Naringenin, present in grapefruit, lemon, tangerine, and oranges, has multiple pharmacological benefits, including antioxidant and anti-inflammatory effects. Studies on psoriasis models have shown that naringenin significantly reduces inflammatory cytokines like TNF-α, IL-1β, and IL-6, leading to reduced skin inflammation (Chung *et al.*, 2016).

5.4.7 Naringin

Naringin is found in citrus fruits like grapefruit, oranges, and tomatoes. Clinical trials on psoriasis patients have demonstrated that naringin inhibits TNF-α and IL-6 production, both of which are elevated in psoriasis and contribute to immune system dysfunction (Baek *et al.*, 2015).

5.4.8 Epigallocatechin-3-gallate (EGCG)

EGCG, a major component of green and black tea, has been widely studied for its anti-inflammatory, antioxidant, and antitumor properties. Research on psoriasis models suggests that EGCG can inhibit abnormal epidermal cell proliferation and regulate antioxidant factors, improving psoriasis symptoms (Sharma *et al.*, 2015).

5.4.9 Anthocyanidins

Anthocyanins, responsible for the red, purple, and blue colours in fruits and vegetables, have strong antioxidant and anti-inflammatory properties. Found in berries, grapes, eggplant, and red cabbage, these flavonoids help regulate inflammation. Studies have shown that delphinidin, a type of anthocyanin, suppresses inflammation and promotes skin differentiation, making it beneficial for psoriasis management (An *et al.*, 2019).

5.5 Carotenoids and their role in inflammation

5.5.1 Lycopene

Lycopene, abundant in tomatoes, watermelons, red grapefruits, and papayas, has been studied for its anti-inflammatory and skin-protective effects. Research has shown that topical and oral administration of lycopene can reduce inflammation and improve psoriasis symptoms by decreasing immune cell adhesion and cytokine expression (Choi *et al.*, 2013).

5.6 Anthraquinones and their therapeutic potential

5.6.1 Emodin

Emodin is derived from traditional Chinese medicinal herbs such as *Rheum palmatum* and *A. vera*. It has a wide range of biological activities, including anti-inflammatory and antioxidant effects. Studies indicate that emodin can reduce the proliferation of psoriasis-related skin cells and relieve inflammation when applied topically (Zhang *et al.*, 2014).

Table 1: Different medicinal plant species, distribution, and therapeutic uses

Medicinal plant/ bioactive compound	Category	Distribution/source	Therapeutic uses
A. vera	Vegetal medicinal species	Found in tropical and subtropical regions	Used for skin healing, anti-inflammatory, and antimicrobial effects.
A. capillaris	Vegetal medicinal species	Found in various regions, particularly in East Asia	Known for its antimicrobial, anti-inflammatory, and liver-protective properties.
St. John's Wort	Vegetal medicinal species	Commonly found in Europe, Asia, and North America	Used for depression, anxiety, and wound healing.
R. glutinosa	Vegetal medicinal species	Native to China and other East Asian regions	Used in Traditional Chinese Medicine for tonifying the kidney and liver.
S. miltiorrhiza	Vegetal Medicinal Species	Native to East Asia, particularly China	Used for cardiovascular health, anti-inflammatory, and antioxidant effects.
Capsaicin	Alkaloid	Found in chili peppers	Used for pain relief, weight management, and digestive health

Resveratrol	Polyphenol	Found in red grapes, peanuts, and berries	Known for its antioxidant, anti-aging, and anti-inflammatory properties.
Curcumin	Polyphenol	Found in turmeric	Known for its anti-inflammatory, antioxidant, and anticancer properties.
Rottlerin	Polyphenol	Found in various plant species	Known for its anticancer and antioxidant properties.
Quercetin	Polyphenol, flavonoid	Found in onions, apples, broccoli, citrus fruits, cherries, green tea, coffee, red wine, capers	Known for its anti-inflammatory, antioxidant, and anticancer properties.
Apigenin	Polyphenol, flavonoid	Found in sweet pepper, parsley, thyme, celery, onions, tea	Known for its anti-inflammatory, antioxidant, and anticancer properties.
Kaempferol	Polyphenol, flavonoid	Tea, broccoli, apples, strawberries, beans	Known for its antioxidant, anti-inflammatory, and anticancer properties.
Genistein	Polyphenol, flavonoid	Soybeans, fava beans	Known for its antioxidant, anti-cancer, and estrogenic effects.
Rutin	Polyphenol, flavonoid	Citrus, apples, Betula leaves, buckwheat, black tea, green tea	Known for its anti-inflammatory, antioxidant, and cardiovascular benefits.
Naringenin	Polyphenol, flavonoid	Grapefruit, lemon, tangerine, orange	Known for its antioxidant, anti-inflammatory, and anti-cancer properties.
Naringin	Polyphenol, flavonoid	Citrus, cooked tomato paste, cherries, beans, oregano	Known for its antioxidant, anti-inflammatory, and anticancer properties.
Epigallocatechin-3-gallate (EGCG)	Polyphenol, flavonoid	Green tea, black tea	Known for its antioxidant, anti-inflammatory, and potential cancer-fighting properties.
Anthocyanin	Polyphenol, flavonoid	Berries, strawberries, currants, grapes, tropical fruits, aubergine skin, red cabbage	Known for its antioxidant and anti-inflammatory properties.
Lycopene	Carotenoid	Tomatoes, rosehips, watermelons, red grapefruits, papayas, apricots, pink guavas	Known for its antioxidant and potential cancer-fighting properties.
Emodin	Anthraquinone	Rhubarb, water pepper	Known for its anti-inflammatory, antimicrobial, and anticancer properties.

7. Discussion

Psoriasis remains a challenging skin disorder with no definitive cure, and current treatments often come with significant drawbacks, such as side effects, limited effectiveness, and patient dissatisfaction. While conventional medications can help manage symptoms by suppressing immune responses, they may also lead to adverse effects like mood swings, diarrhea, and vomiting. This highlights the urgent need for safer, long-term therapeutic options that provide relief without compromising patient well-being. In recent years, researchers have increasingly turned to natural compounds derived from medicinal plants as potential alternatives or complementary therapies for psoriasis. These plant-based treatments offer several advantages, including anti-inflammatory, antioxidant, and antiproliferative properties that can help manage the disease more holistically. Extracts from *A. vera, A. capillaris*, St. John's Wort, *R. glutinosa*, and *S. miltiorrhiza* have demonstrated promising effects in laboratory studies. They have been shown to reduce keratinocyte proliferation, alleviate inflammation, and modulate immune responses, all of which are key factors in psoriasis progression. Unlike conventional drugs, these natural remedies do not appear to cause severe side effects, making them a more appealing option for long-term management. However, despite their potential, most studies on plant-derived treatments have been conducted in laboratory settings or on animal models. While the results are encouraging, more extensive clinical trials on human subjects are needed to confirm their safety, efficacy, and optimal dosage. Furthermore, combining natural compounds with existing psoriasis treatments could lead to more effective outcomes. By integrating these plant-based therapies with immunosuppressants or biologics, patients might experience enhanced symptom relief while reducing their reliance on medications with harsh side effects. Future research should focus on developing standardized formulations, understanding the precise mechanisms of action, and ensuring consistency in treatment results. Overall,

this review underscores the potential of medicinal plants in psoriasis treatment. With further investigation, these natural solutions could provide a much-needed breakthrough in dermatological care, offering patients safer and more effective alternatives to conventional therapies.

8. Conclusion

Despite advancements in medical research, psoriasis remains a chronic and challenging condition to manage. Current treatments, such as corticosteroids, immunosuppressants, and biologics, often provide temporary relief but come with significant limitations. Many patients experience frustration due to drug resistance, recurrence of symptoms, and adverse effects like nausea, fatigue, and increased susceptibility to infections. Given these challenges, there is a growing need for safer and more sustainable treatment options that not only alleviate symptoms but also improve patients' overall well-being. In recent years, natural plant-based compounds have gained attention as potential alternatives for psoriasis treatment. Extracts from medicinal plants have shown promising results in laboratory and animal studies, demonstrating their ability to regulate inflammatory responses, reduce excessive skin cell proliferation, and soothe irritation. Unlike synthetic drugs, these natural compounds generally have fewer side effects, making them an appealing option for long-term management. Several studies have highlighted the benefits of specific plant extracts, such as *A. vera*, *A. capillaris*, St. John's wort, *R. glutinosa*, and *S. miltiorrhiza*, in reducing psoriasis symptoms. These plants contain bioactive compounds that can interfere with inflammatory pathways, decrease oxidative stress, and promote skin healing. Early research suggests that some of these extracts may work by inhibiting key signaling molecules involved in psoriasis progressions, such as NF-êB, MAPK, and JAK-STAT pathways. While these findings are encouraging, most studies have been conducted in controlled laboratory settings or animal models. Clinical trials on human patients are still limited, and further research is needed to confirm the safety, efficacy, and optimal dosage of these natural compounds. If proven effective, plant-based therapies could serve as a complementary or even standalone approach in psoriasis treatment, offering patients a more holistic and less invasive option. Additionally, incorporating natural treatments into conventional therapy could provide a dual approach-enhancing the effectiveness of existing medications while minimizing their side effects. The anti-inflammatory, antioxidant, and immune-modulating properties of these natural substances could help patients achieve better long-term disease management. Ultimately, the future of psoriasis treatment lies in exploring innovative and patient-friendly solutions. With ongoing research, plant-based therapies may soon play a crucial role in improving the quality of life for individuals suffering from this chronic skin condition.

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Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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