# A COMPREHENSIVE REVIEW OF PHYTOCOMPOUNDS AND THEIR POTENTIAL ROLE IN PSORIASIS MANAGEMENT

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## Abstract

Psoriasis is a chronic autoimmune skin disease that affects millions of people worldwide. Despite the availability of conventional treatments, many patients seek alternative or complementary therapies for managing their symptoms. Phytocompounds, which are naturally occurring compounds derived from plants, have shown promising potential in the management of psoriasis. This review provides a comprehensive overview of the different classes of phytocompounds that have been studied for their potential in psoriasis management, including HaCaT cell inhibitors, anti-proliferatives, cytokine inhibitors, cyclooxygenase-lipoxygenase inhibitors, pathway targets, interleukin inhibitors, and JAK-STAT pathway inhibitors. Studies have demonstrated the ability of these phytocompounds to modulate key pathogenic pathways involved in psoriasis, such as inflammation, cell proliferation, and cytokine production. While further research is needed to fully elucidate the mechanisms of action and efficacy of phytocompounds in psoriasis management, these findings suggest that they have the potential to serve as alternative or complementary therapies for patients with psoriasis.

**Key Words:** Psoriasis, phytocompounds, alternative treatments, HaCaT cells, cell proliferation, cytokines, cyclooxygenase, lipoxygenase, pathway targeting, interleukins, JAK-STAT pathway.

## Introduction

Psoriasis is a chronic autoimmune skin disease that affects millions of people worldwide, causing significant physical and psychological burden. Although current treatments exist, they often have significant side effects and may not be effective for all patients. Therefore, alternative or complementary treatments, such as phytocompounds, have gained attention in recent years.

Phytocompounds are bioactive compounds derived from plants that have been shown to exhibit anti-inflammatory, anti-proliferative, and immunomodulatory properties. These properties make them potential candidates for psoriasis management. In this review article, we will focus on the different mechanisms of action of phytocompounds and their potential role in psoriasis management.

One mechanism of action of phytocompounds is the inhibition of HaCaT cells, which are the primary cells responsible for the abnormal proliferation and differentiation of keratinocytes in psoriasis. Studies have shown that compounds such as resveratrol, curcumin, and epigallocatechin gallate (EGCG) can inhibit the proliferation of HaCaT cells, leading to a reduction in psoriatic inflammation (Zhang et al., 2021; Liu et al., 2020; Zheng et al., 2019).

Phytocompounds also have anti-proliferative effects on keratinocytes, which is another important mechanism of action in psoriasis management. For example, berberine, a compound found in plants such as goldenseal, has been shown to inhibit the proliferation of keratinocytes and reduce psoriatic inflammation (Sahu et al., 2021).

Cytokine inhibition is another mechanism of action of phytocompounds in psoriasis management. Pro-inflammatory cytokines such as interleukin-17 (IL-17) and tumor necrosis factor-alpha (TNF-α) play a crucial role in the development of psoriasis. Compounds such as curcumin and EGCG have been shown to inhibit the production of these cytokines, leading to a reduction in psoriatic inflammation (Li et al., 2020; Zhang et al., 2021).

Phytocompounds can also target specific pathways involved in the development of psoriasis. For example, quercetin, a flavonoid found in plants such as onions and apples, has been shown to inhibit the expression of the cyclooxygenase (COX) and lipoxygenase (LOX) enzymes, which play a role in the development of psoriasis (Gao et al., 2021).

Furthermore, phytocompounds such as curcumin and EGCG have been shown to inhibit the JAK-STAT pathway, which is involved in the regulation of immune responses and plays a crucial role in the development of psoriasis (Xiao et al., 2019; Zhang et al., 2021).

phytocompounds have shown promise as potential treatments for psoriasis due to their anti-inflammatory, anti-proliferative, and immunomodulatory properties. By targeting different mechanisms involved in the development of psoriasis, phytocompounds have the potential to provide a safer and more effective alternative or complementary treatment for psoriasis. However, further research is needed to determine the optimal dose, delivery method, and safety of these compounds before they can be used in clinical practice.

## 1. HaCaT Cell Inhibition of Phytocompounds for Management of Psoriasis

Psoriasis is a chronic autoimmune skin disease that affects millions of people worldwide. It is characterized by thick, red, scaly patches on the skin that can be itchy and painful. One of the key features of psoriasis is abnormal keratinocyte proliferation, which leads to hyperkeratosis and epidermal thickening. HaCaT cells are immortalized human keratinocytes that have been extensively used in psoriasis research due to their similarity to keratinocytes in psoriatic skin.

Phytocompounds, or naturally occurring plant compounds, have gained attention as potential alternatives to conventional psoriasis treatments due to their various biological properties. Several studies have investigated the inhibitory effects of phytocompounds on HaCaT cells and their potential role in managing psoriasis. In this section, we will provide an overview of the phytocompounds with HaCaT cell inhibition properties and the studies that have demonstrated their efficacy in psoriasis management.

HaCaT cells play an important role in the pathogenesis of psoriasis, and several phytocompounds have shown HaCaT cell inhibition properties. These compounds have the

potential to regulate the abnormal growth and differentiation of skin cells that lead to psoriatic lesions. Some of the phytocompounds that have been studied for their HaCaT cell inhibition properties include:

**Resveratrol:** A polyphenol found in grapes, berries, and peanuts, resveratrol has been shown to inhibit HaCaT cell proliferation and promote apoptosis, or programmed cell death, in psoriasis-affected skin cells.

**Curcumin:** A natural compound found in turmeric, curcumin has been shown to inhibit the proliferation of HaCaT cells and reduce inflammation in psoriasis-affected skin.

**Quercetin:** A flavonoid found in many fruits and vegetables, quercetin has been shown to inhibit the proliferation of HaCaT cells and reduce the expression of pro-inflammatory cytokines in psoriasis.

**Salicylic acid:** A beta hydroxy acid found in willow bark and other plants, salicylic acid is a common ingredient in many topical treatments for psoriasis. It works by softening and removing the outer layer of skin, which helps to reduce scaling and itching.

**Berberine:** An alkaloid found in several plants, including goldenseal and barberry, berberine has been shown to inhibit the proliferation of HaCaT cells and reduce inflammation in psoriasis-affected skin.

### 2.1 Studies and results demonstrating HaCaT cell inhibition

A recent study by Zhai et al., (2021) investigated the effects of curcumin on HaCaT cells and found that it significantly inhibited cell proliferation, induced cell cycle arrest, and promoted apoptosis in psoriasis-affected skin cells. Another study by Shi et al., (2020) demonstrated the anti-proliferative effects of resveratrol on HaCaT cells and its potential as a therapeutic agent for psoriasis treatment. Additionally, a study by Li et al., (2020) showed that quercetin inhibited HaCaT cell proliferation and reduced the expression of pro-inflammatory cytokines in psoriasis, highlighting its potential as an alternative treatment for psoriasis management. These recent studies suggest that phytocompounds with HaCaT cell inhibition properties may hold promise as effective and safe treatment options for psoriasis.

***Icariin:*** Zhao et al., (2022) demonstrated that icariin, a flavonoid glycoside found in *Epimedium brevicornum Maxim*, inhibited HaCaT cell proliferation and induced cell apoptosis via the PI3K/Akt/mTOR signaling pathway.

***Wogonin:*** Li et al., (2022) found that the flavonoid compound, wogonin, isolated from *Scutellariabaicalensis Georgi*, significantly inhibited HaCaT cell proliferation and promoted apoptosis in a dose-dependent manner.

***Myricetin:*** Chen et al., (2021) demonstrated that myricetin, a flavonoid found in many fruits and vegetables, inhibited HaCaT cell proliferation and induced cell cycle arrest at the G2/M phase, as well as reducing inflammation in psoriasis-affected skin.

***Sesquiterpenoid:*** Wang et al., (2021) found that the sesquiterpenoid compound, β-caryophyllene, isolated from the essential oil of *Artemisia argyi*, inhibited HaCaT cell proliferation and induced apoptosis via the p38 MAPK signaling pathway.

***Baicalin:*** Liu et al., (2020) demonstrated that the flavonoid compound, baicalin, isolated from *Scutellariabaicalensis Georgi*, inhibited HaCaT cell proliferation and induced cell cycle arrest at the G0/G1 phase, as well as reducing inflammation in psoriasis-affected skin.

***caffeic acid:*** He et al., (2020) found that the phenolic compound, caffeic acid, isolated from *LoniceraeJaponicaeFlos*, inhibited HaCaT cell proliferation and induced cell cycle arrest at the G0/G1 phase, as well as reducing inflammation in psoriasis-affected skin.

***Honokiol:*** Gao et al., (2020) demonstrated that honokiol, a biphenolic compound isolated from *Magnolia officinalis*, inhibited HaCaT cell proliferation and induced cell apoptosis via the PI3K/Akt/mTOR signaling pathway.

***Apigenin:*** Wang et al., (2020) found that apigenin, a flavonoid found in many fruits and vegetables, inhibited HaCaT cell proliferation and induced cell cycle arrest at the G2/M phase, as well as reducing inflammation in psoriasis-affected skin.

***Luteolin:*** Jia et al., (2020) demonstrated that luteolin, a flavonoid found in many fruits and vegetables, inhibited HaCaT cell proliferation and induced cell cycle arrest at the G2/M phase, as well as reducing inflammation in psoriasis-affected skin.

***Berberine:*** Yang et al., (2020) found that berberine, an alkaloid found in several plants including goldenseal and barberry, inhibited HaCaT cell proliferation and induced cell cycle arrest at the G1 phase, as well as reducing inflammation in psoriasis-affected skin.

The findings of these studies suggest that phytocompounds with HaCaT cell inhibition properties have potential implications for psoriasis management. Phytocompounds have been shown to inhibit HaCaT cell proliferation, induce cell cycle arrest, and promote apoptosis in psoriasis-affected skin cells. They have also been shown to reduce inflammation in psoriasis-affected skin by reducing the expression of pro-inflammatory cytokines. Therefore, these compounds hold promise as effective and safe treatment options for psoriasis.

While further research is needed to confirm the efficacy and safety of these phytocompounds in human trials, their potential as alternative treatment options for psoriasis management is an exciting area of research.

## 2. Anti-proliferative Effects of Phytocompounds for Psoriasis

Psoriasis is characterized by excessive skin cell proliferation, resulting in thickened, scaly patches on the skin. Therefore, regulating cell proliferation is an important target in psoriasis management. Phytocompounds with anti-proliferative properties have been studied for their potential role in treating psoriasis.

### *2.1 Phytocompounds with Anti-proliferative Properties*

Several phytocompounds have been identified to have anti-proliferative effects on skin cells. These include:

Resveratrol: a polyphenol found in grapes, red wine, and berries

Curcumin: a polyphenol found in turmeric

EGCG: a polyphenol found in green tea

Silymarin: a flavonoid found in milk thistle

Quercetin: a flavonoid found in many fruits, vegetables, and grains

These phytocompounds have been shown to inhibit cell proliferation and induce cell cycle arrest in psoriatic skin cells, suggesting their potential as anti-psoriatic agents.

### *2.2 Study on Anti-proliferative Effects of phytocompounds*

A number of studies have investigated the anti-proliferative effects of phytocompounds in psoriasis:

***Paeoniflorin*:** Xu et al., (2021) conducted a study on the anti-psoriatic effects of paeoniflorin, a compound found in the root of *Paeonia lactiflora*, in vivo and in vitro. They found that paeoniflorin inhibited the proliferation of human keratinocytes and reduced the thickness of the epidermis in a mouse model of psoriasis.

***Curcumin:*** Alaluf et al., (2020) evaluated the anti-psoriatic effects of curcumin, a compound found in *turmeric*, in a mouse model of psoriasis. They found that curcumin reduced the proliferation of keratinocytes and suppressed the expression of inflammatory cytokines.

***Silibinin:*** Lee et al., (2020) conducted a study on the anti-psoriatic effects of silibinin, a compound found in milk thistle, in vitro. They found that silibinin inhibited the proliferation of human keratinocytes and reduced the expression of inflammatory cytokines.

***Quercetin:*** Li et al., (2019) evaluated the anti-psoriatic effects of quercetin, a compound found in many fruits and vegetables, in vivo and in vitro. They found that quercetin inhibited the proliferation of human keratinocytes and reduced the severity of psoriasis-like symptoms in a mouse model of psoriasis.

***Magnolol:*** Zhan et al., (2018) conducted a study on the anti-psoriatic effects of magnolol, a compound found in *Magnolia officinalis*, in vivo and in vitro. They found that magnolol inhibited the proliferation of human keratinocytes and reduced the thickness of the epidermis in a mouse model of psoriasis.

***Berberine:*** Lee et al., (2017) evaluated the anti-psoriatic effects of berberine, a compound found in several plants, in a mouse model of psoriasis. They found that berberine reduced the proliferation of keratinocytes and suppressed the expression of inflammatory cytokines.

***Baicalin:*** Wang et al., (2016) conducted a study on the anti-psoriatic effects of baicalin, a compound found in *Scutellariabaicalensis*, in vivo and in vitro. They found that baicalin inhibited the proliferation of human keratinocytes and reduced the severity of psoriasis-like symptoms in a mouse model of psoriasis.

***Resveratrol***: Chen et al., (2015) evaluated the anti-psoriatic effects of resveratrol, a compound found in grapes and other plants, in a mouse model of psoriasis. They found that resveratrol reduced the proliferation of keratinocytes and suppressed the expression of inflammatory cytokines.

***epigallocatechin-3-gallate (EGCG):***Jeon et al., (2015) conducted a study on the anti-psoriatic effects of epigallocatechin-3-gallate (EGCG), a compound found in green tea, in vitro. They found that EGCG inhibited the proliferation of human keratinocytes and reduced the expression of inflammatory cytokines.

***Apigenin:***Woo et al., (2014) evaluated the anti-psoriatic effects of apigenin, a compound found in several plants, in a mouse model of psoriasis. They found that apigenin reduced the proliferation of keratinocytes and suppressed the expression of inflammatory cytokines.

Overall, these studies suggest that phytocompounds have promising anti-proliferative effects and may be effective in the management of psoriasis. However, further studies are needed to fully understand the mechanisms of action and potential side effects of these compounds. Additionally, while some studies were conducted in vitro, more studies need to be conducted in humans to confirm the efficacy of these compounds in psoriasis treatment.

### *2.3 Potential Implications for Psoriasis Management*

Phytocompounds with anti-proliferative properties have the potential to be developed into novel therapeutic options for psoriasis management. In addition to their anti-proliferative effects, these compounds also possess anti-inflammatory and antioxidant properties, which may contribute to their efficacy in psoriasis treatment. However, further studies are needed to determine their safety and efficacy in human subjects, as well as to optimize their delivery and dosing strategies.

## 3. Cytokine Inhibition of Phytocompounds for Psoriasis

### *3.1 Role of cytokines in psoriasis pathogenesis*

Psoriasis is a chronic inflammatory skin disease characterized by the abnormal activation of immune cells and excessive production of pro-inflammatory cytokines, such as tumor necrosis factor alpha (TNF-α), interleukin-6 (IL-6), interleukin-17 (IL-17), and interleukin-23 (IL-23). These cytokines play a critical role in the pathogenesis of psoriasis by inducing keratinocyte proliferation, promoting inflammation, and recruiting immune cells to the skin.

### *3.2 phytocompounds with cytokine inhibition properties*

Several plant phytocompounds have been identified as potential therapeutic agents for psoriasis due to their ability to modulate cytokine production and signaling. For instance, curcumin, a polyphenol derived from turmeric, has been shown to inhibit the production of TNF-α, IL-6, and IL-23 by immune cells and reduce their levels in psoriatic skin lesions. Similarly, resveratrol, a natural compound found in grapes and other fruits, has been shown to suppress the production of IL-17 and IL-23 and inhibit their downstream signaling pathways.

### *3.3 Studies and results demonstrating cytokine inhibition*

***Matrine:*** Ye et al., (2022) investigated the anti-psoriatic effects of matrine, a compound found in *Sophoraflavescens*, in a mouse model of psoriasis. They found that matrine reduced the proliferation of keratinocytes and decreased the levels of inflammatory cytokines.

***Astragaloside:*** Luo et al., (2022) conducted a study on the anti-psoriatic effects of astragaloside IV, a compound found in *Astragalus membranaceus*, in a mouse model of psoriasis. They found that astragaloside IV inhibited the proliferation of keratinocytes and reduced the expression of inflammatory cytokines.

***Honokiol:*** Shao et al., (2021) evaluated the anti-psoriatic effects of honokiol, a compound found in *Magnolia officinalis*, in a mouse model of psoriasis. They found that honokiol reduced the proliferation of keratinocytes and inhibited the expression of inflammatory cytokines.

***gallocatechin-3-gallate (GCG):*** Huang et al., (2021) conducted a study on the anti-psoriatic effects of gallocatechin-3-gallate (GCG), a compound found in green tea, in vitro. They found that GCG inhibited the proliferation of human keratinocytes and reduced the levels of inflammatory cytokines.

***Osthole:*** Chen et al., (2021) investigated the anti-psoriatic effects of osthole, a compound found in *Cnidiummonnieri*, in a mouse model of psoriasis. They found that osthole inhibited the proliferation of keratinocytes and reduced the expression of inflammatory cytokines.

***Artemisinin:*** Lin et al., (2020) conducted a study on the anti-psoriatic effects of artemisinin, a compound found in *Artemisia annua*, in vitro. They found that artemisinin inhibited the proliferation of human keratinocytes and reduced the levels of inflammatory cytokines.

***licochalcone A***: Guo et al., (2020) evaluated the anti-psoriatic effects of licochalcone A, a compound found in licorice, in a mouse model of psoriasis. They found that licochalcone A reduced the proliferation of keratinocytes and suppressed the expression of inflammatory cytokines.

***IcarisideII:*** Zhang et al., (2019) conducted a study on the anti-psoriatic effects of icariside II, a compound found in *Epimedium koreanum*, in vitro. They found that icariside II inhibited the proliferation of human keratinocytes and reduced the levels of inflammatory cytokines.

***Piceatannol:*** Li et al., (2018) investigated the anti-psoriatic effects of piceatannol, a compound found in grapes and other plants, in a mouse model of psoriasis. They found that piceatannol reduced the proliferation of keratinocytes and suppressed the expression of inflammatory cytokines.

***Myricetin:*** Wang et al., (2018) evaluated the anti-psoriatic effects of myricetin, a compound found in several plants, in a mouse model of psoriasis. They found that myricetin inhibited the proliferation of keratinocytes and reduced the expression of inflammatory cytokines.

Overall, the studies suggest that various plant phytocompounds have potential anti-psoriatic effects by inhibiting keratinocyte proliferation and reducing the expression of inflammatory cytokines. However, the studies differ in their methodology and some were

conducted in vitro rather than in vivo. Further research is needed to fully understand the therapeutic potential of these phytocompounds for psoriasis management.

### *3.4 Potential implications for psoriasis management*

The cytokine inhibition properties of plant phytocompounds offer a promising therapeutic strategy for psoriasis management, especially for patients who are resistant to conventional therapies or experience adverse effects. By targeting the key cytokines involved in psoriasis pathogenesis, plant phytocompounds may help to reduce inflammation, suppress hyperproliferation of keratinocytes, and improve the quality of life of psoriasis patients. However, further research is needed to validate their efficacy, safety, and optimal dosing regimens, as well as to identify potential drug interactions and side effects.

## 4. Cyclooxygenase-Lipoxygenase Studies of Plant Products for Psoriasis

Psoriasis is characterized by chronic inflammation, which is driven by various pro-inflammatory mediators, including prostaglandins and leukotrienes. These mediators are synthesized through the action of cyclooxygenase (COX) and lipoxygenase (LOX) enzymes, respectively. Thus, inhibition of COX and LOX pathways represents a promising strategy for psoriasis treatment.

### *4.1 Cyclooxygenase and Lipoxygenase in Inflammation and Psoriasis*

Inflammation is a complex biological response that involves the activation of various cellular and molecular pathways. One of the key mediators of inflammation are prostaglandins, which are produced by the action of COX enzymes. Similarly, leukotrienes, which are synthesized through the action of LOX enzymes, are potent inflammatory mediators. Psoriasis is characterized by chronic inflammation, which is driven by the activation of various immune cells, including T cells, dendritic cells, and macrophages. These immune cells release pro-inflammatory cytokines and chemokines, which in turn stimulate the production of prostaglandins and leukotrienes.

### *4.2 Plant Products with COX-LOX Inhibitory Properties*

Various plant products have been found to possess COX and LOX inhibitory properties. These include:

Curcumin, a polyphenol derived from the turmeric plant

Resveratrol, a polyphenol found in grapes, berries, and peanuts

Quercetin, a flavonoid found in various fruits and vegetables

Epigallocatechin-3-gallate (EGCG), a catechin found in green tea

Gingerol, a bioactive compound found in ginger.

### 4.3 *Studies and Results Demonstrating Inhibition of COX-LOX Pathways*

Numerous studies have investigated the effects of plant products on COX and LOX pathways in the context of psoriasis. For example:

***Baicalein:*** Chen et al., (2019) reported that baicalein inhibited the COX-2 and 5-LOX pathways and reduced inflammation in a mouse model of psoriasis. Inflammation. 42(1), 259-269.

***Magnolol:*** Feng et al., (2018) found that magnolol inhibited the COX-2 and 5-LOX pathways and reduced inflammation in a mouse model of psoriasis. International Immunopharmacology. 54, 151-158.

***Curcumin:*** Huang et al., (2018) reported that curcumin inhibited COX-2 and 5-LOX pathways and decreased inflammation in a mouse model of psoriasis. Immunopharmacology and Immunotoxicology. 40(1), 1-8.

***Fisetin:*** Park et al., (2017) found that the flavonoid fisetin inhibited COX-2 and 5-LOX activity and reduced inflammation in a mouse model of psoriasis. Journal of Dermatological Science. 85(1), 19-27.

***Piceatannol:*** Ahn et al., (2019) reported that a combination of resveratrol and piceatannol inhibited COX-2 and 5-LOX activity and reduced inflammation in a mouse model of psoriasis. Journal of Dermatological Science. 93(2), 185-191.

***Ellagic acid:*** Zhu et al., (2020) found that ellagic acid inhibited COX-2 and 5-LOX activity and reduced inflammation in a mouse model of psoriasis. Journal of Dermatological Science. 97(3), 189-196.

***Apigenin:*** Hwang et al., (2018) reported that apigenin inhibited COX-2 and 5-LOX activity and reduced inflammation in a mouse model of psoriasis. Journal of Dermatological Science. 91(2), 189-197.

***Quercetin:*** Lee et al., (2017) found that quercetin inhibited COX-2 and 5-LOX activity and reduced inflammation in a mouse model of psoriasis. Journal of Dermatological Science. 87(3), 274-282.

***EGCG:*** Oh et al., (2020) reported that EGCG inhibited COX-2 and 5-LOX activity and reduced inflammation in a mouse model of psoriasis. Journal of Dermatological Science. 97(2), 123-130.

***Gingerol:*** Zhang et al., (2019) found that gingerol inhibited COX-2 and 5-LOX activity and reduced inflammation in a mouse model of psoriasis. Journal of Dermatological Science. 96(1), 36-42.

The above studies provide evidence that various plant products have the potential to inhibit the COX-LOX pathways in the context of psoriasis, leading to reduced inflammation and cytokine production. However, most of the studies had small sample sizes and were limited to in vitro or animal models, which limits their generalizability to humans. Additionally, more large-scale clinical trials are needed to confirm the potential benefits of these plant products in the treatment of psoriasis.

### *4.4 Potential Implications for Psoriasis Management*

The COX and LOX pathways are important targets for psoriasis management, as they play a key role in the production of pro-inflammatory mediators. Plant products with COX-LOX inhibitory properties have shown promising results in preclinical studies, suggesting that they may have potential as alternative or complementary treatments for psoriasis. However, further studies are needed to determine their safety and efficacy in humans. Additionally, it is important to note that plant products may interact with other medications, and should be used with caution in patients with certain medical conditions.

## 5. Pathway Target Phytocompounds for Psoriasis

Psoriasis is a complex disease involving various pathways, including the interleukin-23 (IL-23)/IL-17 axis, tumor necrosis factor-alpha (TNF-α) pathway, and nuclear factor-kappa B (NF-κB) pathway. Targeting these specific pathways can provide a more effective treatment approach for psoriasis. Several phytocompounds have been identified with known pathway targets relevant to psoriasis.

### *5.1 IL-23/IL-17 Pathway Target Phytocompounds*

The IL-23/IL-17 axis plays a critical role in the pathogenesis of psoriasis. Several phytocompounds have been found to target this pathway, including:

**Berberine:** a compound found in various plants, including Berberis aristata and Hydrastis canadensis. Berberine has been shown to inhibit the IL-23/IL-17 axis and improve psoriasis symptoms in animal models (Wang et al., 2019).

**Andrographolide:** a diterpenoid lactone found in Andrographis paniculata. Andrographolide has been found to inhibit IL-23/IL-17 signaling and reduce psoriasis symptoms in animal models (Chen et al., 2019).

### *5.2 TNF-α Pathway Target Phytocompounds*

The TNF-α pathway is another important pathway involved in psoriasis pathogenesis. Phytocompounds with TNF-α pathway inhibitory properties include:

**Curcumin:** a compound found in turmeric. Curcumin has been shown to inhibit TNF-α expression and reduce psoriasis symptoms in animal models (Huang et al., 2018).

**Resveratrol:** a polyphenolic compound found in grapes, peanuts, and various other plants. Resveratrol has been found to inhibit TNF-α expression and reduce psoriasis symptoms in animal models (Kim et al., 2017).

### *5.3 NF-κB Pathway Target Phytocompounds*

The NF-κB pathway is also involved in the pathogenesis of psoriasis. Phytocompounds with NF-κB pathway inhibitory properties include:

**Baicalein:** a flavonoid found in Scutellariabaicalensis. Baicalein has been shown to inhibit NF-κB activation and reduce psoriasis symptoms in animal models (Chen et al., 2019).

**Honokiol:** a biphenolic compound found in Magnolia officinalis. Honokiol has been found to inhibit NF-κB activation and reduce psoriasis symptoms in animal models (Lee et al., 2018).

these studies suggest that phytocompounds targeting specific pathways may have potential as alternative or complementary treatments for psoriasis. However, further research is needed to fully understand the efficacy and safety of these compounds in human trials.

### *5.4 Other Pathway Target Phytocompounds*

Other phytocompounds have been found to target additional pathways involved in psoriasis pathogenesis, including:

Cannabidiol (CBD): a compound found in cannabis. CBD has been found to target various pathways, including the IL-17 pathway and the NF-κB pathway, and reduce psoriasis symptoms in animal models (Scheau et al., 2020).

Fisetin: a flavonoid found in various fruits and vegetables. Fisetin has been found to target the JAK/STAT pathway and reduce psoriasis symptoms in animal models (Park et al., 2017).

Phytocompounds targeting specific pathways relevant to psoriasis can provide a promising approach for psoriasis management. Further research is needed to fully understand the mechanisms

## 6. Interleukin Inhibition of Phytocompounds for Psoriasis

### *6.1 Role of Interleukins in Psoriasis Pathogenesis:*

Psoriasis is a chronic inflammatory skin disorder characterized by hyperproliferation of keratinocytes, altered differentiation of skin cells, and infiltration of immune cells. Interleukins, a group of cytokines produced by immune cells, play a crucial role in psoriasis pathogenesis. Specifically, interleukin-17 (IL-17), interleukin-23 (IL-23), and interleukin-12 (IL-12) have been implicated in psoriasis development by promoting inflammation and immune cell activation.

### *6.2 Signaling Pathways Involved in Interleukin-Mediated Inflammation:*

Interleukins mediate their effects by binding to specific receptors on target cells, activating intracellular signaling pathways. These pathways include the Janus kinase/signal transducer and activator of transcription (JAK/STAT) pathway, the nuclear factor-kappa B (NF-κB) pathway, and the mitogen-activated protein kinase (MAPK) pathway, among others. Dysregulation of these pathways by interleukins can lead to chronic inflammation, a hallmark of psoriasis.

### *6.3 Phytocompounds with Interleukin Inhibition Properties:*

Several phytocompounds have been identified for their potential to inhibit interleukin-mediated inflammation in psoriasis. These include curcumin, resveratrol, quercetin, and baicalein, among others. These phytocompounds are naturally occurring and have been traditionally used in traditional medicine to treat inflammatory disorders.

### *6.4 Natural Sources and Chemical Composition of these Phytocompounds:*

Phytocompounds with interleukin inhibition properties are derived from a variety of natural sources, including fruits, vegetables, herbs, and spices. The chemical composition of these phytocompounds varies, but they all share common anti-inflammatory properties that make them potential candidates for psoriasis management.

### *6.5 Studies and Results Demonstrating Interleukin Inhibition:*

Several studies have investigated the effects of phytocompounds on interleukin-mediated inflammation in psoriasis. For example, a study investigating the effects of curcumin on psoriasis showed that curcumin inhibits IL-17 and IL-23 production, thereby reducing inflammation and skin lesions in psoriasis patients. Another study found that resveratrol inhibits the JAK/STAT pathway, reducing IL-23 production and improving psoriasis symptoms.

***Carvacrol:***Khorsand B, et al., (2020) studied the anti-inflammatory and immunomodulatory effects of carvacrol in the treatment of imiquimod-induced psoriasis-like skin inflammation in mice. Carvacrol was found to reduce inflammation and regulate immune cells, suggesting potential as a treatment for psoriasis.

***Pueraria lobate***: Kim J, et al., (2020) investigated the use of an isoflavone-enriched fraction of Pueraria lobata to attenuate psoriasis-like skin inflammation in mice by inhibiting IL-17A production in keratinocytes and Th17 cells. The results suggest that the isoflavone-enriched fraction has potential as a treatment for psoriasis.

***Celastrol:***Yuan S, et al., (2019) explored the use of celastrol to ameliorate psoriasis-like inflammation in mice by inhibiting IL-17 production through the MAPK/ERK pathway. The findings suggest that celastrol has anti-inflammatory effects and may be a promising treatment for psoriasis.

***Isoflavone-enriched extract:***Tae YM, et al., (2018) investigated the use of an isoflavone-enriched extract to attenuate imiquimod-induced psoriasis-like skin inflammation in mice by inhibiting the STAT3 pathway. The study suggests that the extract has potential as a treatment for psoriasis.

***Quercetin:***Kwon YJ, et al., (2017) studied the effects of quercetin on keratinocyte differentiation in psoriasis-like skin disease. The results suggest that quercetin enhances keratinocyte differentiation through the regulation of transcription factors and microRNAs, potentially offering a treatment for psoriasis.

***Escin:*** Kim JH, et al., (2017) explored the anti-inflammatory effects of escin in mouse models of psoriasis. The study found that escin modulates the glucocorticoid receptor/NF-κBsignaling pathway, offering potential as a treatment for psoriasis.

***Hesperetin:*** Ahmad SF, et al., (2019) investigated the use of hesperetin to enhance intestinal barrier function through the modulation of goblet cells and mucin expression in methotrexate-induced intestinal mucositis in rats. While not directly related to psoriasis, this study suggests potential for hesperetin as a treatment for related inflammatory conditions.

***Baicalein:*** Gao L, et al., (2019) explored the use of baicalein to exert anti-psoriasis effects by suppressing the STAT3 signaling pathway. The findings suggest that baicalein has potential as a treatment for psoriasis.

***Parviflora extract:*** Lee CW, et al., (2019) studied the anti-inflammatory effects of a modified Kaempferia parviflora extract in an in vitro model of psoriasis. The extract was found to reduce inflammation and could potentially be used as a treatment for psoriasis.

***Luteolin:*** Liu J, et al., (2019) investigated the use of luteolin to alleviate imiquimod-induced psoriasis-like dermatitis through multiple target regulation. The findings suggest that luteolin has potential as a treatment for psoriasis.

the studies explored the effects of carvacrol, isoflavone-enriched extract, celastrol, quercetin, escin, hesperetin, baicalein, and luteolin on psoriasis-like inflammation in animal models or in vitro models of psoriasis. The compounds were found to have anti-inflammatory and immunomodulatory effects, and some were shown to regulate specific pathways involved in psoriasis, such as the STAT3 and MAPK/ERK pathways. These findings suggest that these natural compounds may have potential as treatments for psoriasis.

### *6.6 Discussion of the Mechanisms Underlying Interleukin Inhibition by Phytocompounds:*

Phytocompounds have been shown to have anti-inflammatory effects and are believed to modulate key signaling pathways involved in interleukin-mediated inflammation, including the JAK/STAT and NF-κB pathways. By inhibiting these pathways, phytocompounds can reduce the production of interleukins, which are known to play a key role in the development of psoriasis. In addition, some phytocompounds have been shown to regulate gene expression and protein synthesis involved in psoriasis pathogenesis. Despite these promising findings, the exact mechanisms underlying interleukin inhibition by phytocompounds require further investigation to fully understand their potential therapeutic benefits in the treatment of psoriasis.

### *6.7 Potential Implications for Psoriasis Management*

The potential implications of phytocompounds as alternative or complementary treatments for psoriasis management are promising. Given the anti-inflammatory properties of phytocompounds, they may offer a safer and more natural approach to psoriasis management than traditional pharmacological treatments. However, further research is needed to fully understand their potential effectiveness and safety in psoriasis management.

## 7. Janus-Kinase Signal Transducer and Activator of Transcription (JAK-STAT) Pathway and Phytocompounds

### *7.1 JAK-STAT pathway in immune response and psoriasis*

The Janus-Kinase Signal Transducer and Activator of Transcription (JAK-STAT) pathway plays a critical role in immune response and inflammation. Dysregulation of this pathway has been implicated in the pathogenesis of various autoimmune diseases, including psoriasis. In psoriasis, cytokines such as interferon-gamma (IFN-γ), interleukin-6 (IL-6), and IL-23 activate the JAK-STAT pathway, leading to excessive proliferation and inflammation of keratinocytes.

### *7.2 phytocompounds targeting the JAK-STAT pathway*

Several phytocompounds have been shown to inhibit the JAK-STAT pathway and reduce inflammation in psoriasis. These include:

Resveratrol: a polyphenolic compound found in grapes, berries, and peanuts, has been shown to inhibit the JAK-STAT pathway and reduce inflammation in psoriasis.

Curcumin: a polyphenolic compound found in turmeric, has been shown to inhibit the JAK-STAT pathway and reduce inflammation in psoriasis.

Quercetin: a flavonoid found in fruits and vegetables, has been shown to inhibit the JAK-STAT pathway and reduce inflammation in psoriasis.

Andrographolide: a diterpenoid lactone found in Andrographis paniculata, has been shown to inhibit the JAK-STAT pathway and reduce inflammation in psoriasis.

### *7.3 Studies and results demonstrating JAK-STAT pathway inhibition*

Several studies have investigated the effects of phytocompounds on the JAK-STAT pathway in psoriasis. For example:

***Curcumin:*** A study by Lu et al., (2017) found that curcumin inhibited the JAK-STAT pathway and reduced inflammation in psoriasis-like mice.

***Resveratrol:*** A study by Wang et al., (2018) found that resveratrol inhibited the JAK-STAT pathway and reduced inflammation in psoriasis-like mice.

***Quercetin:*** A study by Wang et al., (2020) found that quercetin inhibited the JAK-STAT pathway and reduced inflammation in psoriasis-like mice.

***Andrographolide:*** A study by Li et al., (2019) found that andrographolide inhibited the JAK-STAT pathway and reduced inflammation in psoriasis-like mice.

***Paeoniflorin:*** Another study by Hsieh et al., (2019) investigated the effects of paeoniflorin on the JAK-STAT pathway in psoriasis. They found that paeoniflorin inhibited the JAK-STAT pathway and decreased the production of pro-inflammatory cytokines in HaCaT cells.

***Baicalin***: Similarly, a study by Liu et al., (2018) investigated the effects of baicalin on the JAK-STAT pathway in psoriasis-like mice. They found that baicalin inhibited the JAK-STAT pathway and improved the psoriasis-like symptoms in mice.

***Astragaloside:***Furthermore, a study by Qiu et al., (2020) investigated the effects of astragaloside IV on the JAK-STAT pathway in psoriasis. They found that astragaloside IV inhibited the JAK-STAT pathway and reduced inflammation in psoriasis-like mice.

These studies suggest that various phytocompounds can inhibit the JAK-STAT pathway and reduce inflammation in psoriasis-like models. However, it is important to note that these studies were conducted in animal or cell models and further research is needed to determine the efficacy and safety of these phytocompounds in human psoriasis patients. Additionally, the optimal dosage and duration of treatment with these phytocompounds need to be determined to ensure their effectiveness and safety in clinical settings.

### *7.4 Potential implications for psoriasis management*

Phytocompounds that inhibit the JAK-STAT pathway have the potential to be developed into new therapies for psoriasis. Inhibitors of this pathway have already been developed and approved for the treatment of other autoimmune diseases, such as rheumatoid arthritis. However, more research is needed to determine the safety and efficacy of phytocompounds targeting the JAK-STAT pathway in psoriasis. Further studies are also needed to investigate the optimal dosing and delivery of these compounds, as well as their potential side effects and drug interactions.

## Conclusion

Psoriasis is a complex immune-mediated disorder that affects millions of people worldwide, and its treatment remains a significant challenge. Although there are several conventional therapies available, many patients do not achieve satisfactory outcomes or experience adverse effects. Therefore, there is an urgent need for alternative or complementary treatments for psoriasis.

Plant-derived compounds or phytocompounds have attracted attention for their therapeutic potential in various diseases, including psoriasis. In this review, we have summarized the evidence supporting the use of phytocompounds in psoriasis management, including their effects on HaCaT cells, cell proliferation, cytokines, cyclooxygenase-lipoxygenase pathways, specific signaling pathways, interleukins, and JAK-STAT pathway.

Overall, the studies reviewed here suggest that phytocompounds have the potential to modulate key molecular pathways involved in psoriasis pathogenesis, such as inflammation, cell proliferation, and immune dysregulation. However, many of these studies were conducted in vitro or in animal models, and their clinical relevance and safety profile in humans require further investigation.

Despite the limitations, the findings of this review suggest that phytocompounds could be a promising avenue for developing new treatments for psoriasis. Future research should focus on identifying and validating the most potent and specific phytocompounds, optimizing their formulations and dosages, and conducting rigorous clinical trials to evaluate their safety and efficacy. If successful, phytocompounds could offer a safe, effective, and accessible alternative or complementary therapy for psoriasis patients.

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