Review Article

Therapeutic potential of flavonoids in the management of psoriasis

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Received: 3 January 2024 Revised: 18 February 2024 Accepted: 22 February 2024

Abstract

Psoriasis is a common inflammatory skin disorder, caused by the various environmental, genetical factors. Plaques formation, itching, redness of skin are the common symptoms in the long run. there are several types of diseases based on the types of puples present on the skin like plaque, postular, guttate, inverse and erythrodermic. Around 125 million population throughout the world suffering with this disease with several comorbidities like psoriatic arthritis, cardiovascular diseases. Treatment available based on severity of the disease. topical, oral, systemic and phototherapy are available and the current treatment is boosted for the usage of biologics manufactured based on the mab's to regulate psoriasis some extent. But, these therapies cause serious life threatening side effects like hypersensitivity reactions, upper urinary tract infections and several neurological diseases. The present study was aimed to usage of plant products in the treatment of psoriasis like Flavanoids. These natural compounds are already proved for their anti oxidant, anti inflammatory and anti proliferative properties, which are very much useful in the psoriasis treatment. Flavonoids are secondary metabolites derived from the plants and used to improve the defense mechanism in plants. Psoriasis is a life time disease with no permanent treatment. Usage of natural compounds may improve the quality of life and reduce the side effects caused by the chemical compounds.

Keywords: Phototheraphy, psoriasis, comorbidities, flavonoids, nutraceuticals, inflammatory

Introduction

The family of naturally occurring polyphenolic chemicals known as flavonoids has garnered a growing amount of attention. They are intrigued by many scientific domains because of their ubiquitous nature as well as their variety of biological activity (Liga et al., 2023). Plants synthesize flavonoids, which are secondary metabolites with a benzo-γ-pyrone skeleton, by different synthesis pathways, including the phenylpropanoid, shikimate, and flavonoid pathways (Rehan, 2021). Over 5,000 hydroxylated polyphenolic compounds, known as flavonoids, are a vast family of chemicals that have several vital roles in plants. These roles include controlling cell development, battling microbial infections, and luring pollinating insects (Kumar et al., 2013). More than 10,000 flavonoid compounds have been discovered and isolated thus far (Ullah et al., 2020). Flavonoids have 15 carbon atoms organized in three rings (C6–C3–C6), designated A, B, and C. They are produced by the phenylpropanoid metabolic pathway (Do Nascimento et al., 2022). Soy isoflavones, flavonols, and flavones are the most common flavonoids in the human diet. Catechin levels in fruits and legumes range from 4.5–610 mg/kg (Karak, 2019). Humans have ingested flavonoids since the beginning of human life on Earth, or approximately 4 million years. They have numerous biological features that improve human health and help to lower the risk of disease. The oxidative alteration of LDL cholesterol is expected to have a significant role in atherosclerosis. Galfridian, a significant polyphenolic substance discovered in Glycyrrhiza glabra (Fabaceae), reduces LDL oxidation through free radical scavenging (Fuhrman et al., 1997).

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Classification of flavonoids

Plant cell vacuoles are the primary source of flavonoids, which are mostly found there as C- or O-glycosides. The fundamental C6–C3–C6 skeleton of flavonoids (designated A, B, and C) determines their fundamental molecular structure. Based on changes to their fundamental skeletons,

DOI: https://doi.org/10.31024/ajpp.2024.10.1.2

flavonoids are divided into seven subclasses: flavones, flavanones, isoflavones, flavonols, chalcones, and anthocyanins (Hussain et al., 2020, Chen, 2023, Zakaryan, 2017).

Flavanones

Medicinal plants and the everyday food of humans both include flavanones, which are a class of flavonoid molecules commonly found in plants (Cao, 2021). Many major plant groups, including the Compositae, Leguminosae, and Rutaceae, have a broad distribution of flavanones. The entire plant, including the vegetative and generative portions, including the branches, bark, stem, leaves, roots, flowers, fruits, seeds, rhizomes, peels, and other sections, might contain flavanones, depending on the kind of plant. Erythridin and naringenin aglycones are well distributed flavanones found in food. The antioxidant, antiviral, anti-inflammatory, anticancer, and radical scavenging properties of flavanones are their pharmacological actions (Denaro et al., 2021). The quantity and arrangement of phenolic OH groups determine the antioxidant activity of flavanones. Higher antioxidant activity is demonstrated by flavanones in hydrophilic environments. Certain flavanones, like hesperidin and neo hesperidin, lose part of their antioxidant activity in this environment, while others, including narirutin, naringin, and naringenin, become pro-oxidants.

Common dietary flavanones without a catechol nucleus are often categorized as poor antioxidants, and their metabolites are thought to be even less potent. Therefore, their antioxidant activity must not be connected to the most significant processes underlying their health impacts (Cai et al., 2016).

Flavones

The most significant flavonoid subclass is flavones. Fruits, leaves, and flowers are rich sources of flavones, which are present as glucosides. Red peppers, chamomile, mint, celery, parsley, and ginkgo biloba are all sources of flavones. Lutein, apigenin, and tangerine make up this group of flavonoids. Peels from citrus fruits are rich in polymethoxylated flavones such as tartrate, nobiletin, and sinensetin (Manach and Donovan, 2004).

Isoflavones

The distinct different subclasses of flavonoids are called isoflavonoids. Isoflavonoids occur primarily in soybeans and other leguminous plants, and they are only widely distributed in the kingdom of plants. Microbes have also been discovered to contain certain isoflavonoids (Mathies et al., 2008). Additionally, it has been discovered that they are crucial as precursors for the synthesis of phytoalexins during interactions between plants and microbes (Aoki et al., 2006; Jaiswal et al., 2019). Isoflavonoids show great promise in the treatment of several illnesses. Isoflavones with oestrogenic action in specific animal models, such as genistein and daidzein, are widely considered to be phyto-oestrogens. Szkudelska and Nogowski examined how genistein causes changes in hormones and metabolism, which might impact several disease pathways (Szkudelska and Nogowski, 2007).

Flavonols

Ketone groups on flavonoids are called flavonols. They serve as proanthocyanidins' building components.

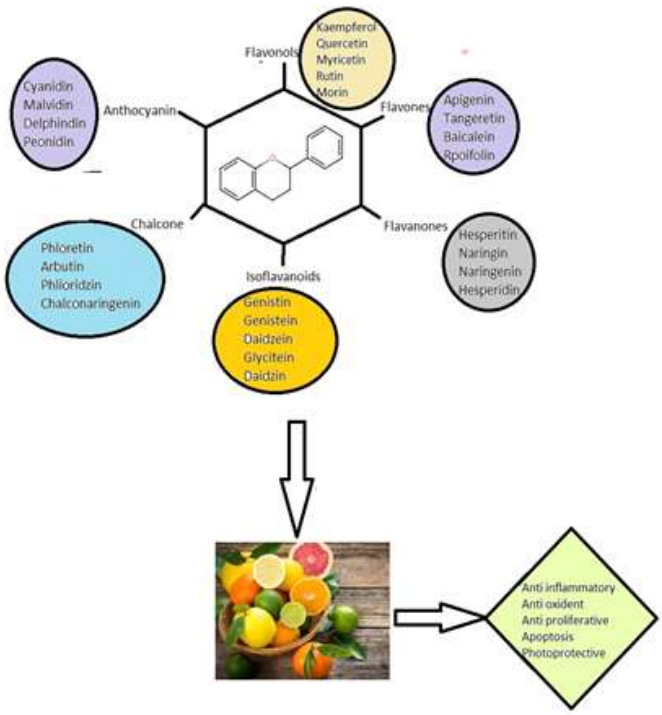

Figure 1. Flavonoid sub- classes with their source of material and its activities (Shen et al., 2022)

Numerous fruits and vegetables are rich in flavonols. Kaempferol, quercetin, myricetin, and fisetin are the flavonols that have been studied the most. Flavonol-rich foods include onions, kale, lettuce, tomatoes, apples, grapes, and berries. In addition to fruits and vegetables, flavonols can also be found in tea and red wine. Consuming flavonols has been linked to several health advantages, such as the ability to act as an antioxidant and a lower risk of cardiovascular disease (Panche et al., 2016).

Chalcones

Chalcones belong to the flavonoid subclass. They are distinguished by the lack of "ring C" from the fundamental flavonoid skeleton structure. For this reason, they may also be called open-chain flavonoids. Chalcones include, among others, phlorizin, arbutin, phloretin, and chalco naringenin. Tomatoes, pears, strawberries, bearberries, and some wheat products have high concentrations of chalcones. Due to their many nutritional and biological advantages, chalcones and their derivatives have attracted a lot of interest (Sahu et al., 2014; Liu, 2013; Edwards et al., 1990). The easiest and safest method of preventing illness and regulating activity may be to consume flavonoids through diet. (Panche et al., 2016).

Anthocyanins

Plant, floral, and fruit colors are attributed to pigments called anthocyanins. The anthocyanins that are most often researched are cyanidin, delphinidin, malvidin, pelargonidin, and peonidin. The outer cell layers of a variety of fruits, including raspberries, strawberries, blueberries, bilberries, blackberries, cranberries, and red and merlot grapes, are where they are mostly found. These chemicals are employed in the food sector for a number of purposes due to their stability and health advantages (Giusti and Wrolstad, 2003). Anthocyanin color is influenced by pH levels as well as methylation or acylation at the hydroxyl groups on the A and B rings (Iwashina, 2015).

Psoriasis

Psoriasis is a debilitating, painful, and disfiguring skin disease that is immune-mediated and persistent. Although the exact cause of psoriasis is unknown, oxidative stress and an imbalance of genetic, immunological, and environmental variables are the main culprits (Cannao et al., 2019; Khan et al., 2022; Michalek et al., 2016). Numerous investigations have shown that keratinocyte destruction can be caused by psoriasis triggers such as minor trauma, sunburn, infections, systemic medications, stress, cigarette smoking, air pollution, physical damage, and biological agents (viruses, bacteria) (Nowak et al., 2022). Furthermore, it has been shown that ROS and NOS have a role in the pathophysiology of psoriasis; as a result, oxidative stress is caused by a redox imbalance and high levels of inducible NOS (Narendra et al., 2023). Although it can strike at any age, psoriasis often strikes between the ages of 50 and 69. Over 125 million people worldwide suffer from psoriasis, which has a 2-3% prevalence worldwide (Guarneri et al., 2021; Mizgała-Izworska, 2022).

Psoriasis vulgaris, the most prevalent type of psoriasis, is typified by nearly symmetrical red, scaly plaques and papules coated in white or silver scales, particularly on the scalp, lumbosacral area, and extensor surfaces (Pleńkowska et al., 2020). In the histological findings of psoriasis, keratinocytes exhibit hyperproliferation, abnormal differentiation, and infiltration by inflammatory cells (Weng et al., 2016).

Treatments for generalized psoriasis are photochemotherapy, immunosuppressive medications (cyclosporine and methotrexate), and phototherapy. Retinoids are prescribed for pustular psoriasis. Salicylic acid, urea, tar, glucocorticosteroids, and vitamin D3 derivatives are ingredients in local treatments used to treat psoriasis (Gamret et al., 2018). Additionally, research supports the beneficial effects of flavonoids in the management of psoriasis. Particularly when it comes to skin damage, current treatments, a healthy lifestyle, and the incorporation of an antioxidant-rich diet appear to be promising in mitigating the oxidative stress damage produced by psoriasis (Naguyen et al., 2019). Increased expression of vascular endothelial growth factor (VEGF) and tumor necrosis factor (TNF) is linked to the hyperproliferation of keratinocytes and persistent inflammation in psoriasis (Yamanaka et al., 2021).

Pathophysiology of psoriasis

The epidermis is penetrated by activated T lymphocytes in the pathophysiology of psoriasis, which promotes keratinocyte growth. Thick plaques are the outcome of this keratinocyte turnover imbalance. Parakeratosis and epidermal hyperplasia are two more related characteristics. Furthermore, lipids are not secreted by the epidermal cells, causing the characteristic dry and scaly skin of psoriasis (Singh et al., 2021).

Epidermal hyperproliferation, aberrant differentiation of epidermal keratinocytes, inflammation, and immunologic changes in the skin are all part of the complex pathophysiology of psoriasis. The hyperproliferation is typified by elevated DNA synthesis and a notably reduced rate of epidermal turnover. A delay in the expression of some keratins that are expressed in typically developing skin and an increase in the expression of others are signs of abnormal keratinocyte differentiation. Based on current developments in biological treatment, the pathophysiology of psoriasis is primarily dependent on skin-resident immune

Table 1. Flavanoids and their treatment in Psoriasis

S. No	Compounds	Pathway	References
1	Hesperidin	Hesperidine reduced serum levels of leptin, adiponectin, and resistin while inhibiting the IRS-1/ERK1/2 signaling pathway. Furthermore, Hesperidine significantly lowered PASI scores, epidermal thickness, epidermal cell proliferation and differentiation, inflammatory factor mRNA expression, local skin lesions, and blood insulin and glucose levels.	Di meglio and Nestle, 2017
2	Naringenin	This study evaluates the effectiveness of Naringenin (NRG) and Sericin as TNF-α blockers. Spray-drying was used to manufacture Sericin (SMs) and (R/S) NRG-loaded Sericin (SNRGMs) microparticles, which were then studied in terms of shape and particle size distribution, as well as encapsulation efficiency.This study shows that sericin-based microspheres containing TNF-α-blockers can reduce cytokine levels, paving the way for new topical treatments for middle-stage psoriasis.	Liu et al., 2019
3	Naringin	Naringin reduces lipopolysaccharide-induced inflammation in HaCaT cells and helps to treat psoriasis. The mechanism could be connected to the suppression of the P38 MAPK/NF-κB signaling pathway.	Chlapanidas et al., 2014
4	Eriodictyol	Th17 cells are important in inflammatory diseases like multiple sclerosis (MS) and its zoonotic equivalent, experimental autoimmune encephalomyelitis (EAE). Th17 cells are the source of IL-17. Since they are essential for cell differentiation, the retinoic acid receptor-related orphan receptors γt (RORγt) are a prospective target for the treatment of Th17-related illnesses. In this work, we discovered that eriodictyol (EDT), a naturally occurring flavonoid that is widely distributed in citrus fruits and peanuts, was situated exactly in the binding pocket of RORγt. By inducing a conformational shift, EDT effectively suppressed the activity of the receptor. This provides information on the transcriptional inhibition of genes reliant on RORγt.	Guan et al., 2020
5	Hesperetin	These AOs inhibited mRNA expression, possibly due to decreased NF-κB activation, as seen by lower IκB-α mRNA levels. In conclusion, the AOs Phloretin, Silymarin, Hesperetin, and Resveratrol effectively suppress PBMCs' inflammatory response to LPS.	Yang et al., 2020
6	Apigenin	Apigenin inhibits IMQ-induced aberrant immune activation by blocking the IL23/STAT3/IL17A signaling axis. Apigenin inhibits IMQ-induced inflammation via deactivating NF-κB. Apigenin suppresses cell hyperproliferation by reducing ERK1/2 activation.	Fordham et al., 2014
7	Tangeretin	PMA enhanced the interaction between HIF-1α and NF-κB through the PKCα-ERK1/2-NF-κB pathway. TAN treatment, however, significantly decreased this activation. Lastly, we discovered that TAN decreased NF-κB p65 and HIF-1α nuclear translocation. By altering the epidermal microenvironment, TAN treatment as a whole reduced the malignant inflammatory response brought on by PMA. Immortalized human keratinocytes (HaCaT) treated with PMA showed a significant increase in inflammation after 4 hours and a decrease in cell survival at 24 hours. In parallel, we replicated a skin inflammation that is exactly the same as PMA-induced psoriasis in humans. Here, the inflammatory response was inhibited by using tangeretin (TAN) as an antagonist.	Meng et al., 2024
8	Baicalein	In mice treated with baicalin, the erythema, scaling, and thickness of the epidermal layer all showed significant improvements. The levels of tumor necrosis factor, interleukin-17A, interleukin-22, and interleukin-23 in the skin significantly decreased after baicalin treatment. In skin-draining lymph node cells, baicalin also inhibited the generation of interleukin-17A produced by imiquimod.	Dey et al., 2020
9	Rhoifolin	The study aimed to assess rhoifolin's anti-inflammatory properties and identify potential mechanisms behind this effect. Rhoifolin reduced carrageenin-induced rat paw oedema in a time and reverse dose-dependent manner. After 4 hours of treatment, rhoifolin at dosages of 2.5, 25, and 250 mg/kg significantly reduced rat paw edema volume by 14, 25, and 45%, compared to the control group (74%). Increasing rhoifolin dosages reduced TNF-α release in inflammatory exudates while also drastically lowering prostaglandin E2 levels.	Wang et al., 2020
10	Quercetin	QC effectively treated psoriasis in IMQ-induced mice, perhaps by improving antioxidant and anti-inflammatory status and inhibiting NF-κB signaling. As a result, QC, a naturally occurring flavone with significant anti-psoriatic properties, has the potential to be developed further as a therapy for psoriasis.	Eldahshan and Azab, 2012
11	Kaempferol	In vitro, kaempferol reduced T cell growth and mTOR signaling. Thus, our data indicate that kaempferol might be a therapeutic medication for human psoriasis in the near future.	Zhang et al., 2021
12	Rutin	In HaCaT cells, rutin decreased TNF-α and IL-6 levels as well as cell growth. The AGE-RAGE signaling cascade is involved in the kernel pathways, while APP, INS, and TNF are the hub genes. Rutin alleviated skin lesions and inhibited cell development in rats with psoriasis-like reactions to IMQ. Rutin may lessen inflammation by blocking the cascade of AGE-RAGE signals.	Liu et al., 2019

Table 1. Continue .....

13	Morin	Overall, our data imply that morin might effectively enhance the p53-specific ligasing capacity of MDM2 in UVB-induced p53 activation.	Wang et al., 2023
14	Myricetin	Based on its ability to reduce inflammation and restore skin barrier integrity, myricetin may offer protection against obesity-related Alzheimer's disease. As well as preventing CD4+T cell infiltration and lowering immunoglobulin E and histamine levels, myricetin also changed the production of pro-inflammatory factors (CCL17, CCL22, IL-1β, TGF-β) and Th1, Th2, and Th17 and Th22 cytokines. Myricetin also improved lamellar body secretion, decreased transepidermal water loss, and increased the production of the protein and mRNA for filaggrin. These actions helped to repair the compromised barrier function.	Lee et al., 2014
15	Genistin	Genistein inhibits NF-κB, PGs, pro-inflammatory cytokines, iNOS, ROS, and free radicals, contributing to its anti-inflammatory effect.	Gao et al., 2023
16	Genistein	In IMQ mice's dorsal skin and TNF-induced HaCaT cells, genistein can significantly lower the expression of phosphorylated STAT3 (pSAT3). The effect of genistein in reducing the production of TNF-α, IL-6, and IL-23 in HaCaT cells was diminished by Stat3 siRNA. Genistein has the ability to inhibit TNF-α-induced NF-κB nuclear translocation and I-kBα phosphorylation (pI-kBα). In conjunction with the NF-κB inhibitor BAY 11-7082, the effects of genistein. In HaCaT cells, there was a decrease in the expression of TNF-α and VEGFA. According to the results, genistein may be created to treat psoriasis lesions.	Goh et al., 2022
17	Daidzein	Psoriasis, acne, photoaging, and skin cancer are just a few of the skin disorders that have been treated using topical and systemic retinoid therapy. Three isoforms of RARs and RXRs—α, β, and γ—are involved in the action of retinoidoids. After ligands attach to RAR and RXR, coactivators like CBP/p300 are brought in to boost the transcription of genes that have retinoic acid response elements (RARE) in their promoter regions. It has never been demonstrated before that the isoflavone daidzein acts as an agonistic ligand of RAR.	Wang et al., 2019
18	Glycitein	Topical and systemic retinoid treatment has been used to treat psoriasis, acne, photoaging, and skin cancer, to name a few. The actions of retinoidoids include three isoforms of RARs and RXRs: α, β, and γ. Coactivators such as CBP/p300 are introduced to enhance the transcription of genes containing retinoic acid response elements (RARE) in their promoter regions when ligands connect to RAR and RXR. The isoflavone daidzein has never before been shown to function as an agonistic ligand of RAR.	Oh et al., 2013
19	Daidzin	Soybean produces genistein and daizyin in the cytoplasm, which are then malonylated into malonyldaidzin/genistein by malonyl-CoA:isoflavone 7-O-glucoside 6-O-malonyltransferase, or glycosylated into daizin and genistin by UDP-glucose:isoflavone 7-O-glucosyltransferase.	Nagula and Wairkar, 2019
20	Cyanidin	By inhibiting the inflammatory response and lowering oxidative damage—most likely via STAT3/PI3K inactivation and HO-1 activation—PCs lessen the symptoms of psoriasis. In vitro studies involving the use of PI3K, STAT3, and HO-1 inhibitors are planned in order to better understand the processes behind PC activity. Our results shed information on a potentially effective psoriasis treatment and offer an experimental framework for mechanistic exploration of PCs' antipsoriatic qualities.	Kim, 2022
21	Delphinidin-3-gluco side	At a dosage of 80 μM, Dp inhibits the growth of NHEK and induces apoptosis. At doses ranging from 10 to 40 μM, Dp did not affect the expression of apoptotic genes. A 3D epidermal comparable model demonstrated that Dp therapy increased the production of caspase 14 and keratin 1.	Zhu et al., 2022
22	Malvidin	The potential therapeutic use of malvidin 3-O-glucoside (M3G) in reducing inflammation generated by inflammasomes has been investigated. In microglia and the brain, M3G suppresses caspase-1 and IL-1β proteins by specifically targeting inflammasomes such as NLRP3, NLRC4, and AIM2. In addition to reducing stress-induced inflammasome-mediated innate reactions and bacterial-mediated inflammation, M3G also helps with feelings of anxiety and depression.	Husain et al., 2022
23	Peonidin	Specific black rice fractions rich in cyanidin 3-O-glucoside and peonidin 3-O-glucoside have anti-inflammatory properties. In A549 and THP-1 cells, this fraction significantly reduced the expression of inflammatory genes (NLRP3, IL-1β, and IL-18) and the secretion of cytokines (IL-6, IL-1β, and IL-18) produced by the spike glycoprotein S1 component of SARS-CoV-2.	Ijinu et al., 2023

Table 1. Continue .....

24	Phloretin	Phloretin shown a stronger anti-inflammatory effect in tests conducted using several animal and cellular models. Phloretin has an impact on a number of inflammatory signaling pathways, such as AMPK, Nrf2, MAPK, and NF-κB. It enhances the production of prostaglandins, nitric oxide, adhesion molecules, chemokines, and proinflammatory cytokines.	Dubey, 2023
25	Arbutin	Due to its anti-arthritic properties, arbutin decreased the activity of SOD, GSH, and CAT antioxidant enzymes and raised IL-4 and IL-10 levels, while decreasing IL-17. The amounts of COX-2, 5-LOX, TNF-α, IL-1β, IL-6, and NF-κB were also reduced. These data lead one to believe that arbutin is a feasible anti-arthritic drug due to its numerous anti-arthritic capabilities. Our results are further supported by a computational docking investigation.	Habtemariam, 2023
26	Phloridzin	Phloretin shown stronger anti-inflammatory properties in a range of cellular and animal studies. Numerous inflammatory signaling pathways, such as NF-κB, MAPK, Nrf2, and AMPK, are impacted by phenotretin. Proinflammatory cytokines, adhesion molecules, chemokines, prostaglandins, and nitric oxide are all enhanced by it.	Malik et al., 2023
27	Chalconaringenin	Antioxidant, antibacterial, anticancer, anti-inflammatory, antihypertensive, antidiabetic, anti-obesity, neuroprotective, and hepatoprotective qualities are among the biological activities that have been noted. Moreover, several clinical studies conducted on humans and animals have demonstrated that these chalcones have a positive food safety profile by not being harmful to normal cells. The overall positive effects of chalcones showed that these compounds are safe to ingest, very nutritious, and very promising as lead chemicals for the development of alternative pharmaceuticals to treat a variety of illnesses.	Slimestad, and Verheul, 2011

cells, important signal transduction pathways, tumor necrosis factor-α, interleukin (IL)-23p19, and the IL-17A axis. Along with T helper17 cells that secrete IL-17, innate lymphoid cell (ILC3) induces psoriasis rashes directly without T-cell/antigen interaction in response to antimicrobial peptides generated by activated keratinocytes and inflammatory cytokines. Upon proliferation in the presence of IL-7 and IL-23, ILC3 typically expresses the mutant receptor gamma t linked to retinoic acid in the nucleus and produces IL-17 and IL-22. Psoriasis rash, blood, and even non-rashing areas of psoriatic skin have all been linked to elevated ILC3s (Rendon and Schakel, 2019).

It is believed that the TH17 pathway is most activated by IL-23 among these pathways. IL-23 signaling is intracellularly mediated by STAT3, Tyk2, and Jank2, which triggers the transcription of important inflammatory mediators. These cytokines cause keratinocyte proliferation downstream, increased production of endothelial adhesion molecules and angiogenic mediators, and immune cell infiltration into the skin lesions.

Diagnosis of Psoriasis

Psoriasis is a skin disorder; upon clinical manifestations we can identify and confirm the disease by the histological studies.

The above mentioned methods are the currently available clinical diagnosis methods by checking the body surface area, erythema and thickness of skin layers. PASI score indicating the reduction in psoriatic symptoms in clinical trials settings (Mah, 2021).

Genetic intervention in Psoriasis

Psoriasis is an autoimmune disease and it may have the genetic intervention in their pathophysiology. So far 25 genes are identified by the researchers which may initiate the psoriasis mechanism, biological pathways are playing a key role in propagating the genetical polymorphism is termed as the pathobiological mechanisms PSORS1 (Psoriasis susceptibility loci 01) are identified as the major genetical interventions present in this disease (Greb et al., 2016).

Table 2. Psoriasis diagnosis methods

Diagnosis method	Score	Clinical manifestations	Remarks
PGA (Physician global assessment)	0-5	Erythema, thickening of skin.	accepted for clinical practice.
BSA (body surface area assessment)	0-3%	mild	accepted for clinical practice.
	3-10%	moderate	
	>10%	severe	
PASI(Psoriasis area severity index)	0-72	Erythema, thickening, Surface area involved	Its use is limited to clinical trials.

Current treatment based on severity of psoriasis:

IL- interleukin; PDE- Phosphodiesterase; PUVA- Psoralen + UV; TNF-Alpha- Tumor necrosis factor- TYK- Tyrosine kinase; JAK- Janus kinase.

Over the past centuries the treatment for psoriasis was advanced and more specific than the earlier treatment. Initially psoriasis was treated with the Coal tar to reduce the itching symptoms and inflammation, later on the treatment was modified to Cyclosporine drug which is used in cancer therapy. Retinoic acids and vitamin D therapies are adjuvant to the main course. In the 20th century treatment was advanced by using biologics with high specificity. Moreover all the therapies are having more number of side effects with lesser specificity. Phototherapy is the treatment procedure to reduce the propagation of the disease and it may cause the skin layer damage up to some extent.

Mild psoriasis

Mild psoriasis often affects less than 3% to 5% of the skin's surface. There are several treatment options for mild psoriasis, including calcineurin inhibitors, keratolytics, topical corticosteroids, and phototherapy. A variety of factors influence treatment options, including patient preferences, comorbidities, and the location and severity of the lesions (Claire et al., 2020).

Moderate-to-Severe Psoriasis

Usually, 10% or more of the body's surface area is covered with severe psoriasis. Systemic medications are the primary treatment for moderate to severe psoriasis, although they can also be utilized for localized illness or when topical therapies fail. Biologics, oral medicines, and phototherapy should be

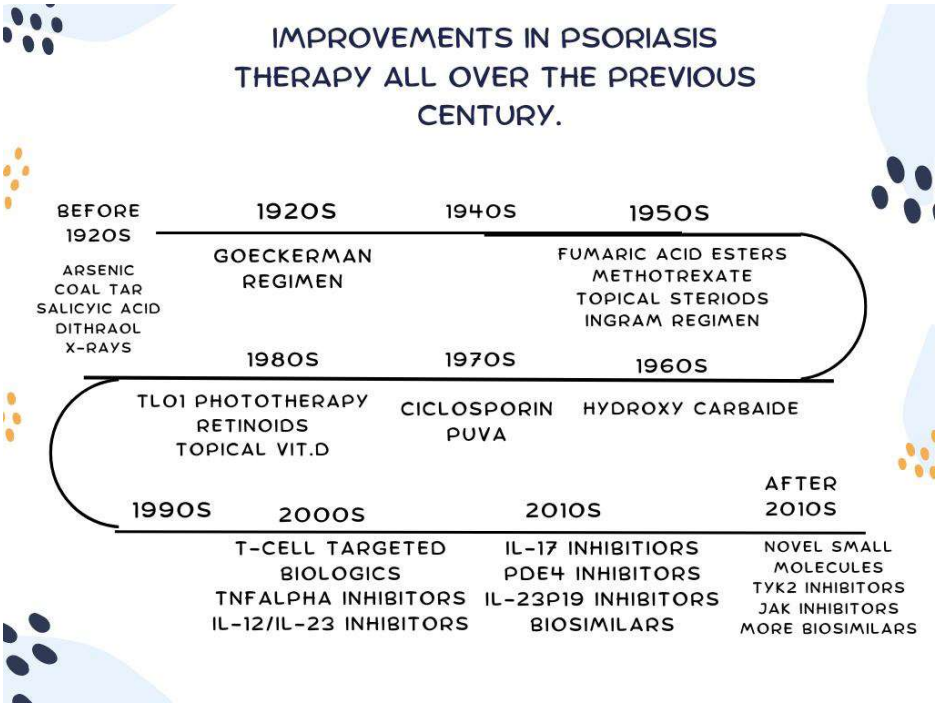

Figure 2. Timeline illustrates the milestones in treatments of Psoriasis in the 19th & 20th century (Claire et al., 2020)

Table 3. Psoriasis treatment and mechanism of action with several side effects (Lee and Kim, 2023)

Drugs	Mechanism of action	Side effects
Methotrexate	Dihydrofolate reductase inhibition blocks purine biosynthesis;	gastrointestinal (nausea) serious liver disease.
Fumaric acid esters	Glutathione inside the cell, adjustments to Nrf2, NF-κB, and HIF-1α; these factors facilitate the transition from a Th1/Th17 pro-inflammatory response to an anti-inflammatory/regulatory Th2 response.	diarrhea, nausea and stomach ache, facial flushing
Ciclosporin	IL-2 is reduced when calcineurin is inhibited.	tingling, numbness, headaches and painful joints, muscle twitching, and high blood pressure.
Acitretin	binding of retinoid receptors to regulate keratinocyte differentiation and proliferation	dry skin, dry lips and dryness of the mucous membranes lining the mouth

used in combination for these individuals, according to both US and European standards. Biologics have demonstrated more effectiveness than oral medicines or phototherapy. Systemic treatment should be explored for individuals with significant psoriasis (i.e., >3% BSA involvement), those whose daily functioning is negatively impacted by psoriasis, those with PsA, and/or those whose QOL is compromised owing to the condition (Bergboer et al., 2012). Topical therapies can be used as supplementary treatments but not as standalone therapy for moderate-to-severe psoriasis (Martin et al., 2019).

Biologics therapy

A biologic usually works better if taken consistently. Biologics may become less effective and have specific adverse effects if they are stopped and started repeatedly. Additionally, after taking a biologic for a while, it may cease to function. If this occurs, a different biologic could function. Studies indicate that while a biologic may lose its efficacy with time, for many patients it might continue to be a safe and effective medication for years. Every biologic has a unique set of potential adverse effects. Most are not severe enough to prevent people from continuing to take the biologic. Among the most typical adverse effects are:

- Upper respiratory tract infection
- Skin reaction where the biologic is injected
- Flu-like symptoms
- Urinary tract infection (Campanati et al., 2016)

Conclusion

In this context, natural compound food promise is still being searched for agents with a low profile of side effects and reasonable cost for the treatment of psoriasis. Several classes have been found, particularly flavonoids, which primarily offer intriguing and potential anti-inflammatory and antioxidant properties. In general, the researchers presented brief but important biological characteristics of the plant, arrival, flavonoids, in vitro, and in vivo, with a focus on its anti-inflammatory action, which may be helpful for psoriasis therapy as well as prevention. Flavonoids have the ability to directly and indirectly affect the generation and activity of inflammatory mediators by influencing the actions of other molecules. The right combination of these phytochemicals might make them interesting candidates for the creation of topical and systemic treatments for psoriasis and other inflammatory skin conditions. But more research ought to concentrate on comprehending the efficacy of flavonoid in humans and advancing their use in the therapy of human illnesses like psoriasis.

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