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Comprehensive PASS-powered elucidation of phytoconstituent therapeutic profiles for advanced psoriasis intervention strategies

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ABSTRACT: Psoriasis is a chronic inflammatory skin disease marked by immune dysregulation, leading to rapid skin cell turnover and formation of thick, red, scaly plaques, mainly on the scalp, elbows, knees, and lower back. These plaques cause itching, pain, and significant quality-of-life impairment. The most common form, plaque psoriasis, accounts for 80–90% of cases. Although the Th17/IL-23 pathway is known to play a key role in disease pathogenesis, variability in disease progression and response to biologic therapies underlines the need for more personalized treatments. Recently, natural products have gained interest for their anti-inflammatory and immunomodulatory effects in psoriasis management. Compounds like curcumin, quercetin, and naringin have shown beneficial modulation of key inflammatory pathways. Pharmacological studies using computational tools (PASS software) have predicted bioactivities of plant-derived compounds such as quercetin, curcumin, kaempferol, stigmasterol, taraxerol, aloesin, emodin, and mukulol against biological targets linked to psoriasis—including tumor necrosis factor-α, antioxidant enzymes, lipoxygenase, cytochrome P450, and Janus kinase. This integrated investigation supports the therapeutic promise of these natural compounds for psoriasis, suggesting potential for developing more effective and targeted treatments.

1. INTRODUCTION

Over 60 million youngsters and adults worldwide struggle with psoriasis, an inflammatory dermatological condition that can lead to other medical issues, and research on the worldwide burden of psoriasis is prioritized. In 2014, the group declared psoriasis as an ongoing noncommunicable, unsettling, deforming, debilitating illness regardless of treatment. Psoriasis affects both men and women, with an average age of onset of 33 years. The disease usually strikes women between the ages of 16–22 and 55–60. It has two subcategories based on genetic and immunological features: early-onset (75% of cases) and late-onset (after 40) (Bhosle et al. 2006).

The degree of psoriasis progression can range from isolated spots to widespread skin involvement. The scientific literature classifies this disorder into different types based on clinical presentation, severity, and affected body parts. Among the many categories, plaque psoriasis (*Psoriasis vulgaris*) is the most common, accounting for 80–90% of all psoriatic cases (Kumar et al., 2025).

This variation is distinguished by clearly defined, raised crimson plaques coated in a light silvery scale. Plaque often

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occurs on the scalp, elbows, knees, and lower back but can appear anywhere on the body. These plaques can cause substantial itching and pain, and, in rare cases, may develop bleeding fissures (Cannavò et al., 2016; Griffiths et al., 2010).

1.1. Pathophysiology and etiology

Psoriasis results from a complex interplay between immunologic dysfunction and abnormal keratinocyte proliferation, primarily triggered by an exaggerated immune response. Key mediators in this process are T lymphocytes, notably the Th1 and Th17 lineages, which produce pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α), interleukin-17 (IL-17), and IL-23 (Hao et al., 2021). These mediators contribute to the exaggerated proliferation of keratinocytes and the inactivation of normal differentiation, resulting in the formation of thickened, scaly plaques (Arican et al., 2005; Gelfand et al. 2005).

The subsequent inflammatory environment continues the recruitment of additional immune cells and maintains chronic inflammation and hyperproliferation in the epidermis. Genetic predisposition, environmental hits and triggers (e.g., psychological stress or infections), which lead to the exacerbation of the disease activity, are responsible for the classic psoriasis features characterized by erythema, scaling, and dermal thickening (Cannavò et al., 2017; Giannoni et al., 2015).

While there have been remarkable advances in understanding the immune mechanisms involved in psoriasis, especially the pivotal role of the Th17/IL-23 axis, many critical issues remain unexplained by its complex pathophysiology (Griffiths et al., 2010). Differences in patient responses and treatment duration suggest that further research is required. Besides immune pathways, we need to further investigate genetic, environmental, and microbiome interactions to better understand disease onset, progression, and heterogeneity (Boehncke and Schön, 2015).

1.2. Challenges in treatment and future directions

At present, some psoriasis treatments, especially biologic agents, show wide variation in therapeutic response, and many patients are refractory or develop primary or secondary failure (Hao et al., 2021). This disparity underscores the need for a more personalized approach, as not all standard therapies are equally effective across individuals.

To maintain the benefit over time, new biologics and alternative treatments (including botanicals) need to be evaluated for both efficacy and long-term safety in clinical research. This lack underscores the need for further investigation into the pathogenesis of the disease and for more efficient, personalized treatment approaches.

1.3. Natural products as therapeutics

Medicinal plants are being studied as potential treatments for psoriasis due to their anti-inflammatory, antioxidant, and immunomodulatory properties. Among these, quercetin, a flavonoid-rich component of fruits and vegetables, has demonstrated impressive potential to ameliorate psoriatic symptoms. It operates by reducing levels of pro-inflammatory cytokines TNF-α, IL-6, and IL-17 (Kashani et al., 2021; Masson et al., 2020). The drug primarily functions by suppressing the NF-κB signaling cascade, a master mediator of inflammation (Mehta et al., 2011). In addition to improving skin lesions, quercetin increases antioxidant enzyme activity and reduces oxidative stress in psoriasis (Chen et al., 2017; Griffiths et al., 2015).

Curcumin, a polyphenolic natural compound derived from turmeric, has been demonstrated to have potent anti-inflammatory effects by influencing the expression of several inflammatory sites and reducing cytokines. Clinical trials have suggested that curcumin can reduce psoriasis symptoms and enhance the efficacy of standard therapeutic options, without significant side effects. This renders it a potential adjunctive treatment for psoriasis (Zhang et al., 2022; Aodah et al., 2023).

Kaempferol, a flavonol distributed in many plant resources, also showed anti-inflammatory activity. It damps the proinflammatory cytokine expression and T cell infiltration into psoriatic lesions. It also increases regulatory T cells, restoring the immune balance in psoriasis (Lee et al., 2024).

Citrus fruit-derived naringin has demonstrated both anti-inflammatory and antioxidants effects. It has not been well studied specific to psoriasis, but limited early reports suggest potential therapeutic effects (Ramadass et al., 2020). Also, the plant sterols squalene and stigmasterol have strong antioxidant properties; they might help protect the skin barrier and reduce inflammation. Taraxerol, a triterpene, has been shown to have anti-inflammatory effects, and aloesin, an active compound found in aloe vera, is associated with soothing and wound-healing applications (Li et al., 2025).

Other compounds of interest include emodin, which can inhibit the production of pro-inflammatory cytokines and induce apoptosis in activated T cells, thereby exerting an immunomodulatory effect. Mukulol, isolated from Guggul resin, has also been reported to exhibit anti-inflammatory activities (Nallasamy et al., 2021; Chiu and Kuo, 2018; Ghosh et al. 2018).

Although the promise is great, most available evidence is based on preclinical data or limited to small series. Well-designed clinical trials are required to establish their therapeutic efficacy, optimal dosage, long-term safety, and enhance their bioavailability. Progress in formulation technologies will also be required to improve their PK profiles and clinical potential for psoriasis therapy.

1.4. Role of PASS in evaluating phytoconstituents

Prediction of activity spectra for substances (PASS) is a computer-aided method that describes and predicts the biological activity profiles of chemical compounds. It returns two major probabilities of activity (Pa) and inactivity (Pi). A higher value of Pa implies that the probability of exhibiting a particular biological effect is relatively high.

In the present study, the PASS tool was used to assess the drug-likeness of some phytochemicals, i.e., quercetin, curcumin, kaempferol, stigmasterol, taraxerol, aloesin, emodin, and mukulol, against psoriasis. The current study allows identification of compounds with an interesting cellular activity profile and to orient further experimental research and prospective therapeutic development (Bhushan and Sindhu, 2024).

2. METHOD

To evaluate the pharmacological properties of the selected phytochemicals for psoriasis treatment, we employed PASS. Compounds were chosen based on previous in vitro and in vivo studies that implicated them as potential therapeutic agents. The detailed structures of these analogues were drawn in their corresponding Simplified Molecular Input Line Entry System (SMILES) notation and have been obtained from the PubChem database.

These SMILES notations were used for analysis by the PASS software program, which provides predictions of an extended set of biological activities based on probabilities to specific pharmacological targets. This workflow offers a rationalized strategy for identifying natural compounds with potential therapeutic activity, and initial results may provide clues for managing psoriasis, which requires further experimental and clinical validation.

3. RESULT

The most promising phytochemical was quercetin, which showed high predicted activity against several targets involved in psoriasis. It also displayed the highest antioxidant capacity (Pa = 0.872), but also high activities of JAK inhibition (Pa = 0.787) and TNF-α inhibition (Pa = 0.501). These activities suggest that quercetin could serve as a source for new drugs against oxidative stress and the regulation of key inflammatory pathways involved in the psoriasis process.

Curcumin also had significant pharmacological effects, including its ability to inhibit TNF-α (Pa = 0.764). Nevertheless, both its antioxidant (Pa = 0.610) and JAK inhibitory potency (Pa = 0.369) were lower than those of quercetin.

This compound exhibited good predicted JAK inhibition (Pa = 0.745) and moderate lipoxygenase inhibition (Pa = 0.443), indicating the possibility of association with immune and oxygenative pathways, respectively, correlating with disease.

Some of the other compounds tested had low to moderate activity (lower Pa) against most targets, such as stigmasterol, taraxerol, squalene, and emodin. Moderate ability as a JAK inhibitor was predicted for stigmasterol (Pa = 0.490), while squalene and taraxerol showed the same level of predicted JAK-inhibitory potential, with Pa values of 0.679 and 0.675, respectively. But their whole therapeutic profile was less rich than that of quercetin.

This may suggest that its action is also taking place in the kinases, oxidative stress, and inflammation pathways simultaneously. This indicates that quercetin might be used as a natural therapy for psoriasis, but to date, it needs more preclinical and clinical studies. Table 1 presents the predicted activity values (Pa) for the selected compounds, calculated using PASS software.

The profile of antioxidant activity (Figure 1) also demonstrates greater overall effectiveness of quercetin compared to the other tested DBs, with an approximate score of 0.872. Kaempferol (0.856) and naringin (0.851), which are also highly efficient antioxidants, followed in the same order. Curcumin showed moderate (0.61) antioxidant activity, while compounds such as stigmasterol (0.215), taraxerol (0.32), and mukulol (0.171) exhibited only weak activity Intermediate values were found for squalene (0.657), aloesin (0.589), and emodin (0.407).

The results above suggest that quercetin, kaempferol, and naringin could be used as potential candidates for the treatment of oxidative stress, which plays a crucial role in keratinocyte hyperproliferation associated with the inflammatory cascade of psoriasis. Stigmasterol, taraxerol, and mukulol had lower values than the other compounds, indicating that their role in healing should not be predominantly through an antioxidant mechanism. They would thus either function through the supercluster or, more likely, through specific signaling pathways, as suggested by their other activity scores.

Table 1
Predicted activity values (Pa) of the selected compounds as calculated by PASS software.

Target for psoriasis	Quercitin	Curcumin	Kaempferol	Naringin	Stigmasterol	Squalene	Taraxerol	Aloesin	Emodin	Mukulol
Antioxidant	0.872	0.61	0.856	0.851	0.215	0.657	0.32	0.589	0.407	0.171
Lipoxygenase inhibitor	0.407	0.319	0.443	0.077	–	0.102	0.086	–	0.337	–
Cytochrome P450 inhibitor	0.396	–	0.397	–	–	0.212	–	–	0.181	0.247
TNF-α inhibitor	0.501	0.764	–	–	–	–	–	–	–	–
Janus kinase (JAK) inhibition	0.787	0.369	0.745	–	0.49	0.679	0.675	–	0.741	0.521

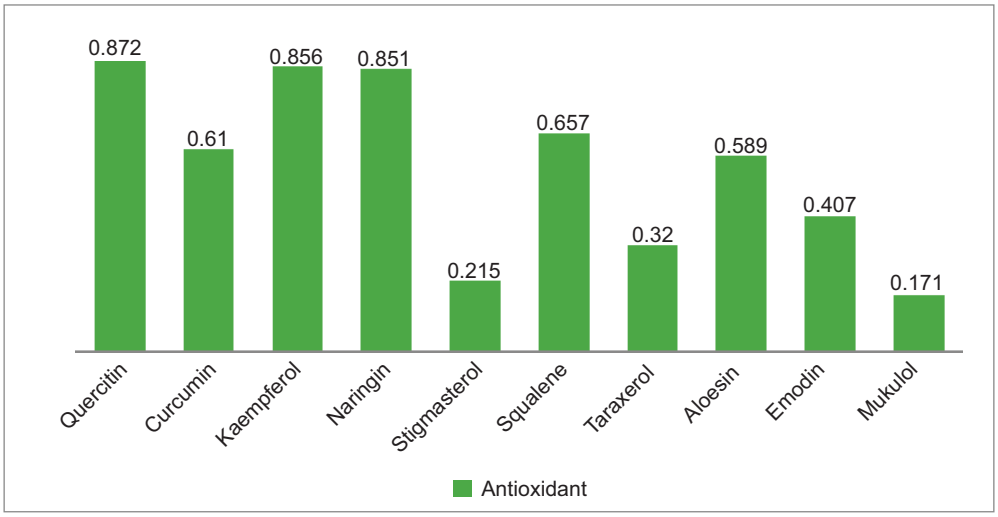

Figure 1. Predicted antioxidant activity (Pa values) of selected phytocompounds relevant to psoriasis, as calculated by PASS software. Quercetin demonstrated the highest antioxidant potential (Pa = 0.872), followed closely by kaempferol (Pa = 0.856) and naringin (Pa = 0.851). Curcumin showed moderate activity (Pa = 0.61), whereas compounds such as stigmasterol, taraxerol, and mukulol exhibited comparatively weak antioxidant properties. Intermediate values were observed for squalene, aloesin, and emodin. The results showed quercetin's superior antioxidant profile, supporting its potential as a leading compound for alleviating oxidative stress in psoriasis.

Collectively, the plot indicates that quercetin possesses excellent antioxidant properties and ranks it as a leading natural compound in fighting oxidative damage, alongside its anti-inflammatory and kinase-inactivating profile.

The lipoxygenase-inhibitory activity pattern (Figure 2) showed kaempferol (Pa = 0.443) to be the most active, followed by quercetin (Pa = 0.407), and emodin (Pa = 0.337). Now, lipoxygenase enzymes can lead to the generation of leukotrienes, which are critical mediators of inflammation in psoriasis, and thus these results are indeed relevant. These compounds could thus contribute to lower leukocyte recruitment and skin inflammation by inhibiting this pathway.

Enzyme inhibition assay: Curcumin showed moderate activity (Pa = 0.319), as did other compounds, such as naringin (Pa = 0.077), stigmasterol (Pa = 0.102), taraxerol (Pa = 0.086), and aloesin, which exhibited weak potential as lipoxygenase inhibitors. No significant mukulol activity was observed via this pathway.

On the whole, the graph emphasizes that many of the tested phytocompounds possess promising lipoxygenase inhibitory activity, where kaempferol, quercetin, and emodin showed the highest inhibitory activity against the enzyme, while supporting their antioxidant and kinase inhibitory profiles. This implies their potential role in regulating lipid-based proinflammatory mediators that promote psoriatic lesions.

Cytochrome P450 inhibition profile (Figure 3) showed both kaempferol (Pa = 0.397) and quercetin (Pa = 0.396) as leading compounds, where the two compound hits exhibited almost similar predicted activity. Conversely, these regulatory trends suggest that both flavonoids might also play a role in drug-metabolizing enzymes, which is relevant for therapeutic response and the occurrence of concomitant drug-drug interactions during antipsoriatic treatment.

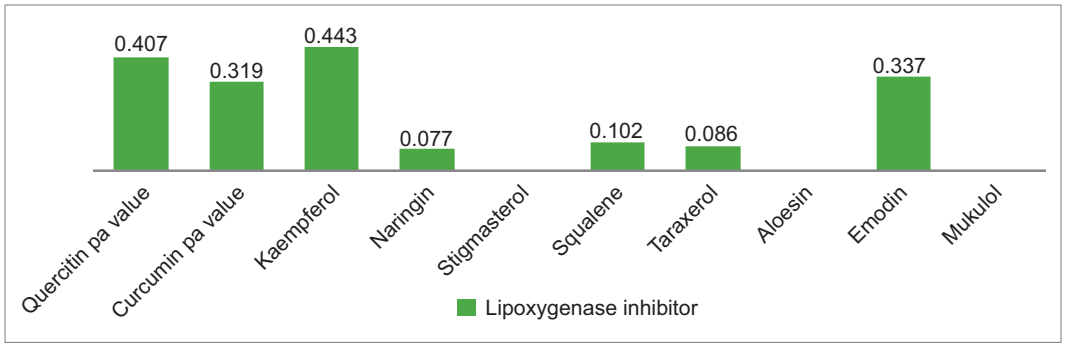

Figure 2. Predicted lipoxygenase inhibitory activity (Pa values) of selected phytocompounds relevant to psoriasis, as calculated by PASS software. Kaempferol exhibited the highest inhibitory activity (Pa = 0.443), followed by quercetin (Pa = 0.407) and emodin (Pa = 0.337). Curcumin showed moderate inhibition (Pa = 0.319), whereas naringin, stigmasterol, squalene, taraxerol, and aloesin displayed minimal activity. Mukulol showed a negligible effect in this pathway. These results suggest that kaempferol, quercetin, and emodin may play a complementary role in attenuating lipid-mediated inflammatory responses in psoriasis.

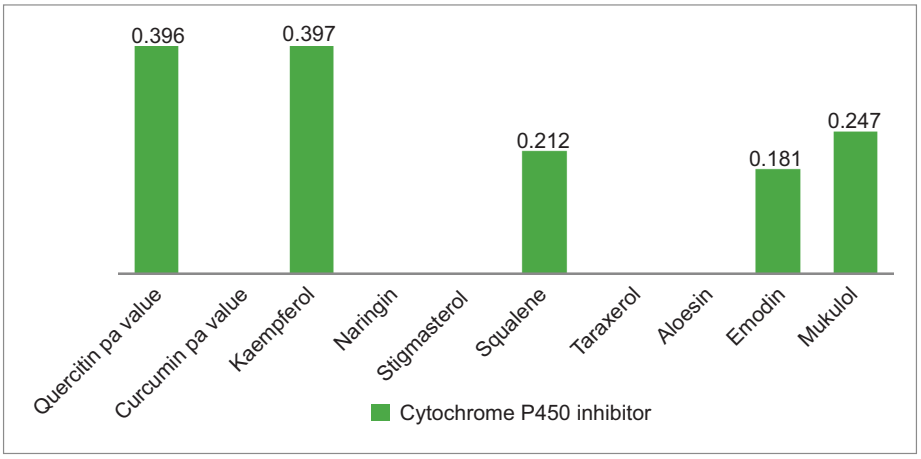

Figure 3. Pa values (predicted CYP-450 inhibitory activity) of some selected phytocompounds that are related to psoriasis, as described by PASS software. The estimated activities were highest for kaempferol (Pa = 0.397) and quercetin (Pa = 0.396), indicating that these flavonoids might be involved in the modulation of drug-metabolizing enzymes. The lowest parasite activities were observed with naringin and stigmasterol, while mukulol (Pa = 0.247), squalene (Pa = 0.212), and emodin (Pa = 0.181) showed moderate inhibition of the parasites. These findings suggest that quercetin and kaempferol, in addition to their antioxidant/anti-inflammatory effects, may affect xenobiotic metabolism, underscoring their potential therapeutic relevance and the necessity of considering herb–drug interactions.

Other compounds showed quite moderate activity, with Pa of 0.247 for mukulol, 0.212 for squalene, and 0.181 for emodin; as for the remaining phytoconstituents, inhibition is marginal. Neither naringin nor stigmasterol was predicted to be active in this class.

These findings suggest that quercetin and kaempferol affect xenobiotic metabolism by CYP450s, as well as anti-inflammatory and antioxidative actions. While this may be a beneficial trait in reducing pro-oxidant metabolites, it also serves as an important reminder that herb–drug interactions should be studied when using these compounds therapeutically.

The best among the class of compounds, as predicted by inhibition Pa, was curcumin (Pa = 0.764) and Iso-curcumin for TNFα inhibition profile (Figure 4). Which makes sense-when you consider its known anti-inflammatory, especially in the reduction of pro-inflammatory cytokines. Thus, quercetin also exhibited a mild effect (Pa = 0.501) and presented further proof of its ability to mediate inflammation signaling.

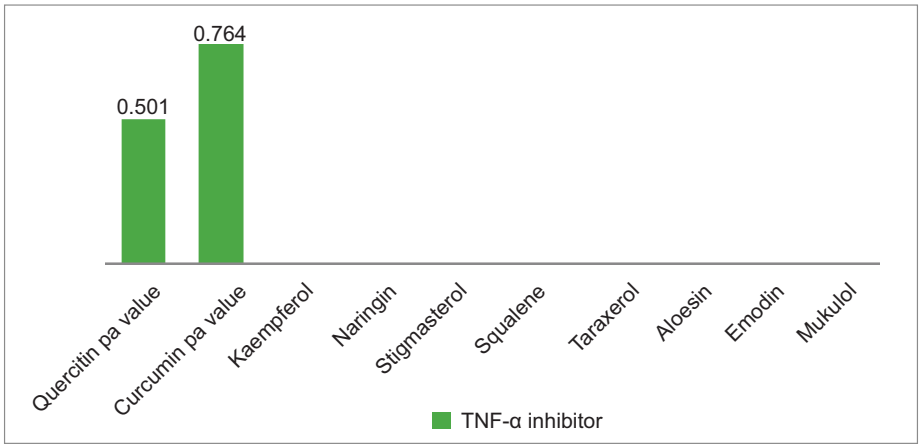

Figure 4. Predicted Pa values of TNF-α inhibitory activity of the chosen psoriasis-related phytocompounds estimated using PASS software. Among these compounds, curcumin showed the highest activity of TNF-α inhibition (Pa = 0.764), followed by quercetin with medium activity (Pa = 0.501). All other compounds had only minor activity in this pathway. These results demonstrate a more robust anti-inflammatory influence of curcumin, particularly on TNF-α–induced pathways, and modest cytokine-modulating activity by quercetin.

As a matter of interest, none of the other tested compounds revealed a potential predicted TNF-α inhibitory activity, suggesting a more selective action of curcumin and quercetin. Because TNF-α is a key player in psoriasis inflammation and an important target for biologic treatment, the results implicate curcumin and quercetin as natural agents that may be able to inhibit cytokine-associated inflammation.

Taken together, the findings indicate that although quercetin has a multifaceted nature (antioxidant kinase/cytokine modulation), curcumin appears to have a predominant role in TNF-α inhibition, validating its selection as an effective natural anti-inflammatory mediator for psoriasis intervention.

Quercetin (Pa = 0.787) was determined to be the most potent compound in terms of its Janus kinase inhibition profile (Figure 5) with similar efficiency rates for kaempferol (Pa = 0.745) and emodin (Pa = 0.741). The findings are of particular interest, as the JAK–STAT signaling cascade is central to psoriasis because it mediates cytokine-driven inflammation and keratinocyte hyperproliferation. Blocking this pathway is the mechanism of action of several modern small-molecule treatments for psoriasis, including JAK inhibitors now used in the clinic.

Squalene (Pa = 0.679) and taraxerol (Pa = 0.675), with moderate activity, and mukulol (Pa = 0.521) and stigmasterol (Pa = 0.49), with intermediate reactivity, showed the lowest efficiency but substantial inhibition. Curcumin (Pa = 0.369) was lowest active tested compound in this group.

The results indicate that quercetin, kaempferol, and emodin are potent natural JAK inhibitors that may be used to modulate abnormal immune signalling leading to psoriasis. Their inhibitory activity on this pathway adds to their antioxidant and anti-inflammatory activities, making them potential cross-target agents for the treatment of chronic inflammatory dermatoses.

Comparative multiple targeting profile (Figure 6) reflects the overall predicted therapeutic potentials of the experimentally tested phytocompounds. Quercetin was identified as the most versatile molecule, showing relatively high activity in all the major pathways (antioxidant defense Pa = 0.872; JAK inhibitor Pa =0.787; TNF-α inhibitor Pa = 0.501). This spectrum of activities indicates its potential to tackle oxidative stress, control cytokine release, and dampen immune signaling, which are critical for maintaining a disease state like psoriasis.

The high activity of curcumin-like inhibitor of TNF-α (Pa = 0.764), moderate activity in JAK, and poorer antioxidant activity could mean that its potential effect is more specific, but at the same time sufficient to blood cytokine-driven inflammation. Both kaempferol and emodin showed broad-spectrum properties mainly via strong JAK inhibitory effect (Pa = 0.745 and 0.741) alongside remarkable antioxidant, implying their potential as adjuvants.

Molecules, on the other hand, such as stigmasterol, squalene, taraxerol, and mukulol, look interesting for specific target activity (mostly JAK or cytochrome P450 inhibition), but they do not have the pan-efficacy of quercetin. An interesting compound, naringin, due to its antioxidant potential, showed little involvement in inflammatory target pathways.

In conclusion, the integrated profile indicates quercetin as the lead compound, closely followed by kaempferol, emodin, and curcumin, with supportive effects. Such a multitarget approach supports the concept of combination therapy or the

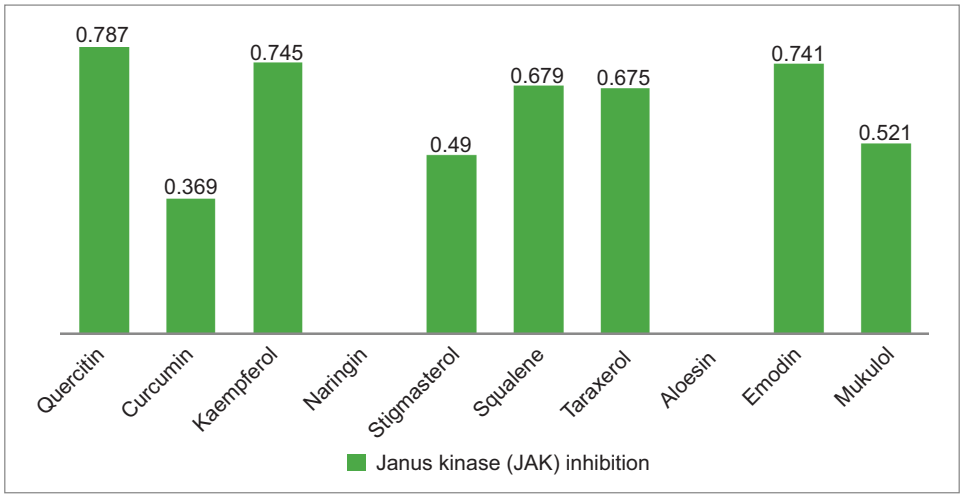

Figure 5. Predicted (PA) values of Janus kinase (JAK) inhibitory activity for the chosen phytocompounds based on psoriasis, calculated by PASS software. Quercetin presented the best JAK inhibitory capacity (Pa = 0.787) as well as kaempferol (Pa = 0.745), and emodin was next (Pa = 0.741). Squalene (Pa = 0.679), taraxerol (Pa = 0.675), and mukulol (Pa = 0.521) exhibited moderate inhibition, whereas stigmasterol (Pa = 0.49) showed relatively weaker inhibition. The weakest JAK inhibition was observed in case of curcumin (Pa = 0.369). These findings suggest that quercetin, kaempferol, and emodin are potential candidates for regulating the JAK–STAT pathway, an important contributor to psoriatic inflammation.

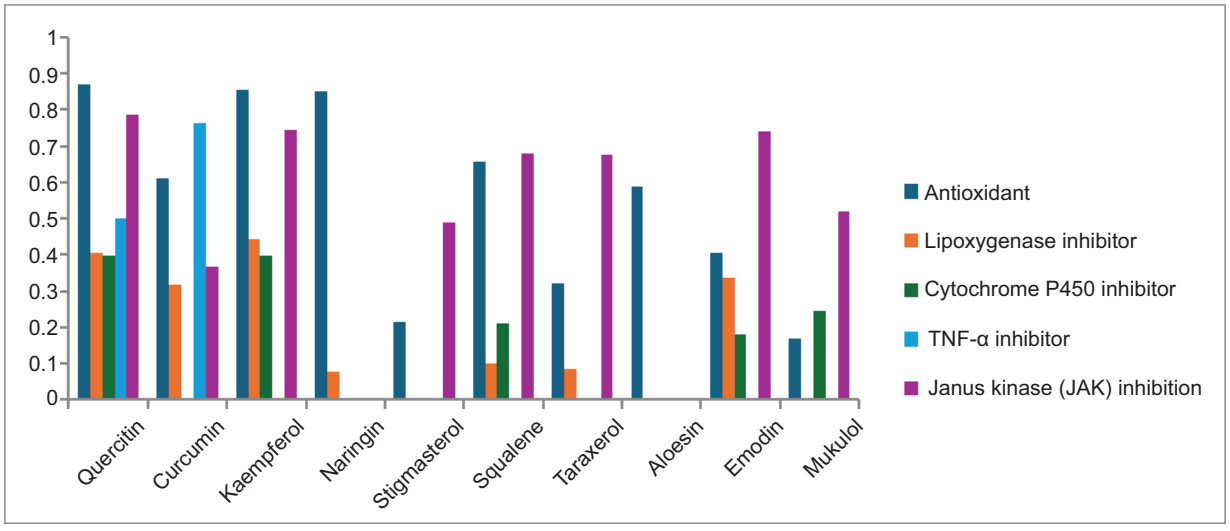

Figure 6. Comparative multitarget activity profile of phytocompounds on psoriasis-related pathway. The graph shows Pa values for antioxidant potential, lipoxygenase inhibition, cytochrome P450 inhibition, TNF-α inhibitor, and Janus kinase (JAK) Inhibition as a function of distance. Among bioactive compounds, quercetin was the most promising, showing broad-spectrum activity as a strong antioxidant and JAK inhibitor, along with TNF-α modulation. Kaempferol, emodin, and curcumin also showed multitarget activities, whereas stigmasterol, squalene, taraxerol, and mukulol showed moderate but selective actions. This collective profile also indicated that quercetin, kaempferol, emodin, and curcumin may be potential leads or supportive agents for the further exploration of multitargeted drugs for psoriasis therapy.

establishment of these phytoconstituents as natural multitarget therapeutics against psoriasis.

Evaluation of various psoriasis-related activities revealed key pharmacological activities, including antioxidant activity, lipoxygenase inhibition, cytochrome P450 inhibition, tumor necrosis factor alpha (TNF-α) inhibition, and Janus kinase (JAK) inhibition. Phytoconstituents such as quercetin, curcumin, kaempferol, and sterols like stigmasterol, taraxerol, aloesin, emodin, and mukulol were explored for their medicinal role as represented in Figure 6.

All compounds showed good antioxidant potential quercetin (QUE) and kaempferol (KAEM) were predicted to have the highest expected activities. Also, naringin, squalene, curcumin, aloesin, emodin, taraxerol, and mukulol were observed to exhibit different types of antioxidant activities among the phytoconstituents included in the study.

Kaempferol was the most active compound against lipoxygenase, followed by Curcumin and Quercetin in that order. Emodin and naringin revealed partial activities, while squalene showed an intermediate inhibitory effect among the test compounds.

Inhibition of cytochrome P450 Quercetin was the most common potent inhibitor, followed by kaempferol, squalene, mukulol, and emodin. The other compounds had no inhibitory effects in this regard. In the context of TNF-α blockade, only curcumin and quercetin showed appreciable activity, with no other investigated compounds showing a marked effect on this major pro-inflammatory cytokine.

A wide variety of compounds, except for naringin and aloesin, had activity against JAK. Quercetin proved to be the most powerful JAK inhibitor and was followed by kaempferol, emodin, taraxerol, squalene, stigmasterol, mukulol, and curcumin, suggesting that these phytochemicals probably have significant medicinal value in treating psoriasis.

Overall, this review demonstrates that the pharmacological effects of these compounds in psoriasis indicate their potential as potent drug candidates for highly specific therapies.

4. DISCUSSION

The therapeutic effects of phytochemicals have been particularly studied in psoriasis, and one such compound is quercetin. Of the chemicals assessed, quercetin showed consistently high predicted activity against a number of pharmacological targets across all PASS analyses and was therefore regarded as broadly effective. The functions investigated (antioxidant activity, lipoxygenase inhibition, cytochrome P450 inhibition, TNF-α inhibition, and Janus kinase (JAK) inhibition) are all important in psoriasis pathogenesis or therapy.

Given that psoriasis is typically driven by oxidative stress, quercetin's potent antioxidant activity is highly relevant. Although kaempferol showed good antioxidant activity as well, it was predicted that quercetin would have been more potent. This discrepancy suggests that quercetin may protect against cellular damage caused by oxidation and inflammation, effects that can help prevent some of the phenomena observed in psoriatic lesions. Furthermore, the suppression of cytochrome P450 enzymatic activity by quercetin enhances its medicinal value by minimizing potential toxic effects on psoriasis patients through drug-drug interactions, thereby making TNF-α combined therapy for psoriasis treatment feasible.

Regarding the inflammatory pathways, only quercetin and curcumin showed a significant inhibition of TNF-α, which is central in driving inflammation in psoriasis. The fact that quercetin can downregulate this cytokine will likely provide significant clinical advantages. Further, potent JAK inhibition makes it an attractive immunomodulator. As JAK pathways function in multiple inflammatory responses, quercetin's dual roles in regulating TNF-α and JAK make it a potentially versatile drug for psoriasis therapy.

These results indicate that quercetin is not only pharmacologically versatile, but the compound also specifically targets crucial pathways related to the pathophysiology of psoriasis. Other phytochemicals (e.g., curcumin and kaempferol) are conditionally promising; however, quercetin is of particular interest given its higher predicted activity across more targets. This evidence strongly supports further development of it as a new, natural, multitargeted therapy for psoriasis.

These predictions have been further supported by recent experimental studies. Quercetin treatment significantly decreased the Psoriasis Area and Severity Index (PASI) scores and alleviated histopathological changes in imiquimod-induced psoriasis-like mice. The treated animals exhibited decreased release of serum TNF-α, IL-6, and IL-17, as well as increased antioxidant enzyme activity in skin tissue and decreased oxidative stress indicators. Mechanistic investigations indicated that these activities may be, in part, associated with the regulation of the NF-κB signaling pathway. Quercetin, in particular, downregulated pro-inflammatory proteins and upregulated protective factors, thereby promoting a more balanced inflammatory response and skin health.

Altogether, the computational and experimental data underscore quercetin as one of the top natural compounds for psoriasis. The extensive pharmacological action and dual modulation of oxidative stress and immune-mediated inflammation suggested its potential clinical application. More studies of its mechanism of action and clinical effectiveness will be needed to delineate quercetin as an effective, safe therapeutic

modality for R. phaseolus–induced chronic inflammatory skin disorder.

5. CONCLUSION

Phytochemicals, as potential candidates for psoriasis therapy, have a promising role, and the study of quercetin for the treatment of psoriasis has gained interest due to its excellent pharmacological activity. In this commentary, we have mainly focused on quercetin's more general therapeutic effects, including its antioxidant activity, inhibition of lipoxygenase and cytochrome P450 enzymes, and its action at very early points in the TNF-α and JAK pathways. These properties underscore quercetin's potential for successful treatment of psoriasis at the root cause.

Corroborative data from computational and experimental investigations also reinforce quercetin as a promising therapeutic. Its strong antioxidant activity even exceeds that of kaempferol, making it especially useful in fighting oxidative damage, a major aspect of psoriasis pathophysiology. Moreover, the combined inhibition of cytochrome P450 and modulation of inflammatory cytokines by quercetin contribute to its therapeutic potential, with a minimised risk of drug interactions. The capability of sCRT to attenuate TNF-α release, as well as its impact on NF-κB signalling, provides important evidence for its potent anti-inflammatory action and thus its potential for targeted psoriasis treatment.

Strong support for quercetin's clinical potential is available from preclinical studies, particularly in the imiquimod-induced psoriasis model. It could markedly decrease the PASI scores, reduce pro-inflammatory cytokine levels, and increase antioxidant defenses, indicating a potent therapeutic action. Furthermore, quercetin's protective effects against external stimuli, such as UV-induced oxidative damage, suggest broader dermatological applications beyond psoriasis.

Finally, quercetin acts not only as an adjunct but also as a chemopreventive agent in the natural therapy of psoriasis. Its pharmacological properties and empirical evidence suggest that it warrants further study and clinical trials. As more studies emerge, quercetin could prove to be a vital player in integrative dermatology, providing a powerful and natural alternative for psoriasis (and possibly other chronic skin disorders).

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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