© 2026 Journal of Pharmacy & Pharmacognosy Research, 14 (2), 2405, 2026
ISSN 0719-4250
https://jppres.com

DOI: https://doi.org/10.56499/jppres_14.2.2405

Review

Adverse events and potential herb-drug interactions of plants used for psoriasis: A systematic review

[Eventos adversos y posibles interacciones entre plantas utilizadas para la psoriasis: una revisión sistemática]

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Abstract

Context: Medicinal plants have been widely used for psoriasis management for centuries. However, their safety profiles remain insufficiently documented.

Aims: To systematically evaluate adverse events (AEs) and potential pharmacokinetic interactions of antipsoriatic herbal treatments.

Methods: A PRISMA-compliant review was conducted using PubMed, Cochrane, Google Scholar, Web of Science, and Scopus databases (January 2015-December 2022). Clinical trials, case reports, and ethnomedicinal studies reporting AEs of single plant antipsoriatic preparations were included. CONSORT criteria for herbal medicines were applied to assess study quality.

Results: Eleven studies covering nine herbal treatments were included. While most of reported AEs were mild, severe cases involving *Indigo naturalis*, *Psoralea corylifolia*, and *Ranunculus arvensis* were documented. Several herbal metabolites (indirubin, psoralen, curcumin, triptolide) showed potential pharmacokinetic interactions with conventional drugs.

Conclusions: While generally well tolerated, antipsoriatic herbal therapies can induce mild to severe AEs and may alter drug metabolism. Long-term, high-quality randomized trials are needed to establish their safety profile.

Keywords: adverse events; complementary medicine; herb-drug interactions; medicinal plants; pharmacovigilance; psoriasis.

Resumen

Contexto: Las plantas medicinales se han utilizado ampliamente para tratar la psoriasis durante siglos. Sin embargo, sus perfiles de seguridad siguen insuficientemente documentados.

Objetivos: Evaluar sistematicamente los eventos adversos (EA) y las posibles interacciones farmacocinéticas asociadas a los tratamientos herbales antipsoriásicos.

Métodos: Se realizó una revisión según PRISMA utilizando las bases de datos PubMed, Cochrane, Google Scholar, Web of Science y Scopus (enero de 2015 a diciembre de 2022). Se incluyeron ensayos clínicos, informes de casos y estudios etnomedicinales que informaron EA de preparaciones antipsoriásicas de una sola planta. Se aplicaron los criterios CONSORT a los estudios sobre medicamentos herbales para evaluar la calidad de los estudios.

Resultados: Se incluyeron once estudios que abarcaban nueve tratamientos herbales. Si bien la mayoría de los EA notificados fueron leves, se documentaron casos graves relacionados con *Indigo naturalis*, *Psoralea corylifolia* y *Ranunculus arvensis*. Varios metabolitos herbales (indirrubina, psoraleno, curcumina, triptolida) presentaron posibles interacciones farmacocinéticas con fármacos convencionales.

Conclusiones: Si bien generalmente se toleran bien, las terapias herbales antipsoriásicas pueden inducir EA de leves a graves y alterar el metabolismo de los fármacos. Se necesitan ensayos aleatorizados a largo plazo y de alta calidad para establecer su perfil de seguridad.

Palabras Clave: eventos adversos; farmacovigilancia; interacciones entre hierbas y fármacos; medicina complementaria; plantas medicinales; psoriasis.

ARTICLE INFO
Received: February 18, 2025.
Accepted: February 19, 2026.
Available Online: March 5, 2026.

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INTRODUCTION

Psoriasis is a complex, chronic immunoinflammatory skin condition that impacts approximately 125 million people globally (Armstrong et al., 2021). This condition frequently coexists with various comorbidities, including cardiovascular diseases, chronic kidney disease, uveitis, mental health disorders, metabolic syndrome, inflammatory bowel disease, and psoriatic arthritis, which substantially increase disease burden and therapeutic complexity (Fu et al., 2018).

Current therapeutic options for psoriasis include topical agents, systemic therapies, phototherapy, and biologic treatments, which are frequently used in combination to optimize disease control (Damiani et al., 2022). In parallel, the use of complementary and alternative medicine (CAM) is widespread among psoriasis patients, with reported prevalence ranging from 2% to 70% globally (Díaz-Murillo et al., 2016; Talbott & Duffy, 2015). CAM approaches encompass mind-body interventions and natural products such as herbs, vitamins, and dietary supplements, with herbal therapies being the most commonly used modality (Gamret et al., 2018; Talbott & Duffy, 2015; Wnuk-Kłosińska et al., 2021). Motivations for CAM use include preference for natural treatments, perceived lower toxicity, dissatisfaction with conventional therapies, curiosity, and positive online information (Murphy et al., 2019; Talbott & Duffy, 2015; Wnuk-Kłosińska et al., 2021).

CAM modalities are typically combined with conventional antipsoriatic therapies, yet patients often fail to disclose their use to clinicians (Damevska et al., 2014; Wnuk-Kłosińska et al., 2021). Although commonly perceived as safe, herbal preparations can cause adverse events (AEs) and clinically relevant interactions, particularly in patients with comorbidities or in paediatric populations (Wnuk-Kłosińska et al., 2021). The concomitant use of medicinal plants and conventional drugs may result in reduced therapeutic efficacy or increased toxicity, potentially leading to treatment discontinuation and complicating clinical management. Therefore, there is a need to document the safety of plants used for psoriasis to promote their responsible use.

Herb-drug interactions may occur through pharmacokinetic (PK) or pharmacodynamic (PD) mechanisms. PK interactions, which alter drug absorption, metabolism, or elimination, may affect systemic drug exposure and are sometimes manageable through dose adjustment (Asher et al., 2017). In contrast, PD interactions are less predictable, are not associated with changes in plasma concentrations, and cannot be mitigated by dosage modifications (Asher et al., 2017). Herb-drug PK interactions can be predicted more readily than PD interactions once the pharmacokinetic characteristics of both the drugs and the plant constituents are known (Showande et al., 2019). This knowledge is essential for preventing clinically significant herb-drug interactions (Wang et al., 2015). In psoriasis, identifying such interactions is particularly challenging because patients with comorbidities often use multiple conventional medications alongside herbal products, thereby increasing the risk of clinically relevant interactions (Fu et al., 2018). This complexity is further compounded by underreporting of herbal use and the limited number of clinical studies specifically designed to assess herb–drug interactions, underscoring the need for a critical appraisal of the available evidence in this context (Wnuk-Kłosińska et al., 2021).

Despite the widespread use of herbal therapies in psoriasis management, existing systematic and narrative reviews have focused on evaluating therapeutic efficacy, either alone or in combination with conventional treatments (Dabholkar et al., 2021; Elkhawaga et al., 2023; Gonçalves et al., 2023; Kasemnitichok et al., 2022; Nowak-Perlak et al., 2022). In contrast, safety-related aspects, such as side effects and herb-drug interactions, have received limited and fragmented attention. This lack of consolidated evidence makes risk assessment and informed clinical decision-making difficult. Therefore, the aim of this review was to critically evaluate evidence from clinical trials, case reports, and ethnomedicinal studies on adverse events associated with plants commonly used for psoriasis, to bridge this existing knowledge gap. Additionally, the potential of relevant plant metabolites to contribute to herb-drug interactions was examined, providing a more comprehensive assessment of their safety.

MATERIAL AND METHODS

Review methodology

This review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations (Page et al., 2021). However, because protocol registration could not be performed retrospectively, the study lacks an international registry record, which represents a limitation.

Eligibility criteria

This study established the eligibility criteria utilizing the PICO framework, encompassing Population, Intervention, Control, and Outcomes. The population under consideration consisted of psoriasis patients, while the intervention focused on using medicinal plants in clinical trials, case reports, or ethnomedicinal studies. The control group included psoriasis patients who received no herbal treatment, placebo, or

standard therapies. The outcomes pertained to documenting side effects associated with medicinal plant intervention. A structured summary of the inclusion and exclusion criteria according to the PICO framework is provided in Table 1.

The inclusion criteria were as follows: a) clinical trials, case reports, and ethnomedicinal studies reporting the use of plants for psoriasis, including whole plants, specific plant parts (leaves, stems, heartwood, and flowers, among others), oils or their extracts; b) articles written in English or Spanish; c) studies published between 2015 and 2022.

Studies were excepted if they met the following exclusion criteria: a) preclinical studies; b) clinical trials including participants not diagnosed with psoriasis; c) use of chemical compounds isolated from plants; d) multiple plant preparations; e) co-interventions with antipsoriatic drugs, phototherapy, homeopathy, vitamins, diets and/or dietary supplements, f) ethnomedical studies that did not use plants recognized for its antipsoriatic use; g) unpublished manuscripts, preprints, and conference abstracts; h) clinical studies, case reports or ethnopharmacological research using medicinal plants for psoriasis without reports of AEs; i) studies outside the established search date.

Information sources

A comprehensive search was conducted across five academic search systems: PubMed, Cochrane Library, Google Scholar, Web of Science, and Scopus. The search terms applied were consistent across all five search systems. Boolean operators, specifically OR and AND, were used to expand and refine search results, ensuring thorough coverage of relevant literature. On July 29, 2022, the reviewers reached consensus. They conducted a final review of the databases in September 2022, focusing specifically on reports published in English or Spanish within the established period and limiting the search to clinical trials, case reports, and ethnopharmacological studies.

Search strategy

A preliminary Google search was conducted to define the search terms, focusing on "plants" and "psoriasis." From the results, potential search terms were identified. A search strategy was formulated using these terms, and additional relevant terms were identified. All authors approved the search strategy. The outcomes of each search and the corresponding search terms were forwarded to five reviewers (MG, REG, MEVH, ARRO, MEGP) for validation. These reviewers also identified relevant studies.

More details on the search terms used in this study are provided in Table 2. The bibliographies of all manuscripts pertinent to this study were reviewed to uncover any publications that might have been overlooked.

Table 1. Inclusion and exclusion criteria, structured according to the PICO framework.

PICO element	Description	Inclusion criteria	Exclusion criteria
P-Population	Patients with psoriasis	Individuals clinically diagnosed with psoriasis	Patients without a confirmed diagnosis of psoriasis. Animal studies or *in vitro* models. Studies combining psoriasis with other diseases without a separate analysis
I-Intervention	Medicinal plants in clinical trials, case reports, or ethnomedicinal studies	Use of medicinal plants, including whole plants, specific plant parts (leaves, stems, heartwood, flowers), oils, or extracts, administered orally or topically	Interventions not related to medicinal plants. Use of isolated chemical compounds. Studies evaluating combinations in which the plant's effect cannot be defined. Co-interventions with antipsoriatic drugs, phototherapy, homeopathy, vitamins, diets, and/or dietary supplements
C – Comparator	Control or comparator	Placebo, standard therapy, or no herbal treatment used as a comparator	Comparators that are not clinically relevant. Studies without a comparator group, despite the design requiring a comparison group
O-Outcomes	Safety outcomes	Reported adverse events (AEs) associated with medicinal plant use	Studies that only report efficacy without providing safety data. Clinical studies, case reports, or ethnopharmacological research using medicinal plants to treat psoriasis that do not report any adverse events
Language	Publication language	Articles published in English or Spanish	Articles published in other languages
Time frame	Publication period	Studies published between January 2015 and September 2022	Studies outside the predefined period

Table 2. Terms utilized for the search in this study.

Academic search systems/ search dates	Search term	Filters
PubMed/July 2022-Sept 2022	(Psoriasis OR Plaque psoriasis) AND (Herbal therapy OR Phytotherapy OR Herbal remedies OR Plant extract OR Plant) AND (Ethnomedicine OR Ethnopharmacology) AND (Adverse events OR Adverse effects OR Side effects OR Toxicity OR Safety)	2015-2022; clinical trials; case reports; clinical study; controlled clinical trial; randomized controlled trial; English and Spanish language; humans; exclude preprints
Cochrane Library/July 2022-Sept 2022	(Psoriasis OR Plaque psoriasis) AND (Herbal therapy OR Phytotherapy OR Herbal remedies OR Plant extract OR Plant) AND (Ethnomedicine OR Ethnopharmacology) AND (Adverse events OR Adverse effects OR Side effects OR Toxicity OR Safety)	January 2015-September 2022; Trials, "Complementary Medicine" in Cochrane groups
Google Scholar/July 2022-Sept 2022	(Psoriasis OR Plaque psoriasis) AND (Herbal therapy OR Phytotherapy OR Herbal remedies OR Plant extract OR Plant) AND (Ethnomedicine OR Ethnopharmacology) AND (Adverse events OR Adverse effects OR Side effects OR Toxicity OR Safety)	2015-2022; English and Spanish language
Web of Science/July 2022-Sept 2022	(Psoriasis OR Plaque psoriasis) AND (Herbal therapy OR Phytotherapy OR Herbal remedies OR Plant extract OR Plant) AND (Ethnomedicine OR Ethnopharmacology) AND (Adverse events OR Adverse effects OR Side effects OR Toxicity OR Safety)	2015-2022; Human studies; English language; "Life Sciences & Biomedicine"
Scopus/July 2022-Sept 2022	(Psoriasis OR Plaque psoriasis) AND (Herbal therapy OR Phytotherapy OR Herbal remedies OR Plant extract OR Plant) AND (Ethnomedicine OR Ethnopharmacology) AND (Adverse events OR Adverse effects OR Side effects OR Toxicity OR Safety)	2015-2022; English language

Selection process

Five independent reviewers (MG, REG, MEVH, ARRO, MEGP) conducted a title screening of the initial 228 records. Incomplete or ambiguous information related to herbal intervention or psoriasis treatment was categorized as "not relevant texts". Subsequently, it was excluded (n = 164), following discussion and agreement among the reviewers to ensure alignment with the scope of the review. Subsequently, MG, REG, MEVH, and MEGP reviewed the abstracts of the remaining articles (n = 64) to remove duplicates (n = 39) and to evaluate eligibility against the predefined selection criteria. Any discrepancies, particularly those related to the study selection criteria, were addressed through discussions among the reviewers (IBBC, IRH, MGP) until consensus was reached. The articles that were ultimately selected (n = 23) underwent further exhaustive examination by ARRO, IBBC, IRH, MG, and MEGP to ensure adherence to the selection criteria. Disagreements were again resolved through discussions with REG, MEVH, and MGP. The selection process concluded with the inclusion of 11 articles.

Data collection process

A data collection form was created using Microsoft Word with the approval of all authors. MG, REG, MEVH, ARRO, and MEGP independently gathered data from the eligible studies utilizing this form. The data extracted by the five authors were compared, and any discrepancies were addressed through discussions with IRH, IBBC, and MGP until consensus was reached.

Following the comprehensive review of each selected article, the subsequent data were extracted: publication date, manuscript title, databases where the article can be accessed, details of the intervention (name of the herbal preparation and part of the plant), route of administration, severity and type of psoriasis, study type (clinical trial, ethnomedicinal, case reports), number of participants (in the case of clinical studies), and a description of any reported safety event.

Data items

The data extracted from the reviews encompassed information regarding the study population, the characteristics of the herbal intervention, the study design, and the authors' conclusions. This study did not conduct heterogeneity assessments among the study results, nor were sensitivity analyses performed due to substantial clinical and methodological heterogeneity across studies. Accordingly, a narrative synthesis was undertaken as the most appropriate approach to summarize the available evidence.

Study quality assessment

The quality assessment of clinical trials included in the systematic review was performed considering the Consolidated Standards of Reporting Trials (CONSORT) statement for herbal medicine interventions (Gagnier et al., 2006). This tool addresses six specific domains considered crucial when medicinal plants are used in randomized controlled clinical studies: (1) herbal medicine product name; (2) characteristics of the herbal product; (3) dosage regimen and quantitative description; (4) qualitative testing; (5) placebo/control group; (6) practitioner.

The domain concerning the herbal medicinal name (domain #1) considers the description of the Latin binomial plant name together with botanical authority and family name for each herbal ingredient, the proprietary product designation (i.e., brand name), and the licensing authorization of the herbal product being examined (Gagnier et al., 2006). The characteristics of the herbal products (domain #2) relate to the description of the parts of the plant used, the type of raw material (fresh or dried), the solvent for extraction, the plant/solvent ratio, and the method of authentication of the plant material, including botanical analysis (Gagnier et al., 2006). The dosage regimen and quantitative description (domain #3) refers to the specification of the dosage of the medicinal plant, the duration of its administration, and the concentration of the constituents within each dosage unit of the herbal formulation. In the case of standardized products, it is also required to inform about the amount of active metabolite present in each dosage unit (Gagnier et al., 2006).

Qualitative testing (domain #4), conversely, emphasizes the importance of documenting the product's chemical fingerprint and the methodologies employed. It also involves incorporating details regarding specialized testing or purity assessments, such as tests for heavy metals or contaminants (Gagnier et al., 2006). The placebo/control group (domain #5) underscores the need to provide a rationale for the type of control or placebo used in clinical trials. The practitioner (domain #6) accentuates the importance of giving a detailed account of the practitioners involved in the herbal intervention, including their training and practical experience. This domain was deemed acceptable if the trial included the name of the health institution (hospital, clinic), research centre, or university where the study was conducted.

Three independent reviewers conducted this assessment (IBBC, IRH, MEGP). The discrepancies were discussed with two other reviewers (REG, MEVH) and resolved by consensus. Studies that satisfactorily met at least four of the six items were considered high-quality clinical studies.

Potential herb-drug interactions of selected plants

Previous studies indicate that patients frequently utilize herbal remedies alongside conventional treatments without disclosing these practices to their healthcare providers (Damevska et al., 2014; Wnuk-Kłosińska et al., 2021). Considering that the plants highlighted in the systematic review are recognized for their antipsoriatic properties and can be administered via various routes in conjunction with conventional drugs, an additional non-systematic review was conducted focusing on *in vitro* and *in vivo* preclinical and clinical pharmacokinetic studies related to enzyme induction or drug interactions of their primary metabolites. Three reviewers (IRH, IBBC, and MEGP) used Google Scholar to provide a more comprehensive, critical overview of the safety of these plants.

RESULTS

Study selection

This review identified 228 records from the search process. Following the removal of irrelevant topics (n = 164), which the reviewers eliminated due to their ambiguous or incomplete information on the use of herbal treatments for psoriasis, a more detailed screening was conducted of the remaining 64 articles' titles and abstracts. This evaluation excluded 39 records because they were duplicates in the databases. After this stage, 25 publications were considered for inclusion. However, two of them were excluded because, although they met the inclusion criteria, they used plants alongside conventional treatments, specifically acitretin and methotrexate (Gönül et al., 2016; Yu et al., 2017).

Following this process, 23 studies were assessed for eligibility. Of these publications, 12 were excluded because, although they were studies that included medicinal plants to treat psoriasis, no adverse effects associated with their therapeutic use were reported, thus compromising the outcome assessment. Finally, 11 studies were included in the systematic review. Fig. 1 illustrates an overview of the search and selection process.

Study characteristics

The overall characteristics of the 11 studies included in the systematic review are summarized in Table 3. Nine antipsoriatic herbal treatments (*Indigo naturalis*, *Psoralea corylifolia* L., *Ranunculus arvensis* L., *Santulum album* L., *Aloe vera* (L.) Burm.f., *Anthemis cotula* L., *Gynura pseudochina* var. hispida (Thwaites) Hook.f., *Curcuma longa* L., and *Tripterygium wilfordii* Hook.f (TwHF) associated with AEs were identified and utilized in eight clinical trials, two case reports, and one ethnopharmacological study. The herbal treatment

with the highest adverse event reports was *Indigo naturalis* (*Baphicacanthus cusia* (Nees) Bremek). Topical administration was used in 91% of studies, while 9% used the oral route. The most frequently reported AEs were itching or pruritus (4 studies), erythema (3 studies), dermatitis (3 studies), and pain (3 studies). While most of the reported AEs were classified as mild or moderate, severe AEs were found to be associated with the use of *Indigo naturalis*, *P. corylifolia*, and *R. arvensis*. In six studies, herbal treatments were used for mild-to-moderate psoriasis, whereas *T. wilfordii* was the sole herbal intervention administered for severe psoriasis. Plaque psoriasis emerged as the clinical subtype most frequently treated through herbal therapies, whereas two studies reported AEs associated with herbal remedies for palmoplantar and nail psoriasis.

Study quality assessment

A quality assessment was conducted to evaluate the data sources used in this review, to enhance the reliability of the information presented. Eight eligible clinical trials were evaluated for quality. Details of this assessment are mentioned in Table 4.

Six studies were identified as high-quality, with minimal risk of bias (Cheng et al., 2017; Lin et al., 2018; Rerknimitr et al., 2016; Sarafian et al., 2015; Wu et al., 2015; Yazdanpanah et al., 2021). However, only the research conducted by Lin et al. (2018) met all the criteria outlined in the Consolidated Standards of Reporting Trials (CONSORT) statement for herbal medicine interventions (Gagnier et al., 2006). The domain identified as having the greatest potential for bias among these six studies was qualitative testing (domain #4), as most randomized clinical trials failed to provide details on the chemical analysis of the herbal product. Furthermore, the sole randomized clinical trial, deemed low-quality and high-risk of bias, was conducted by Lin et al. (2015).

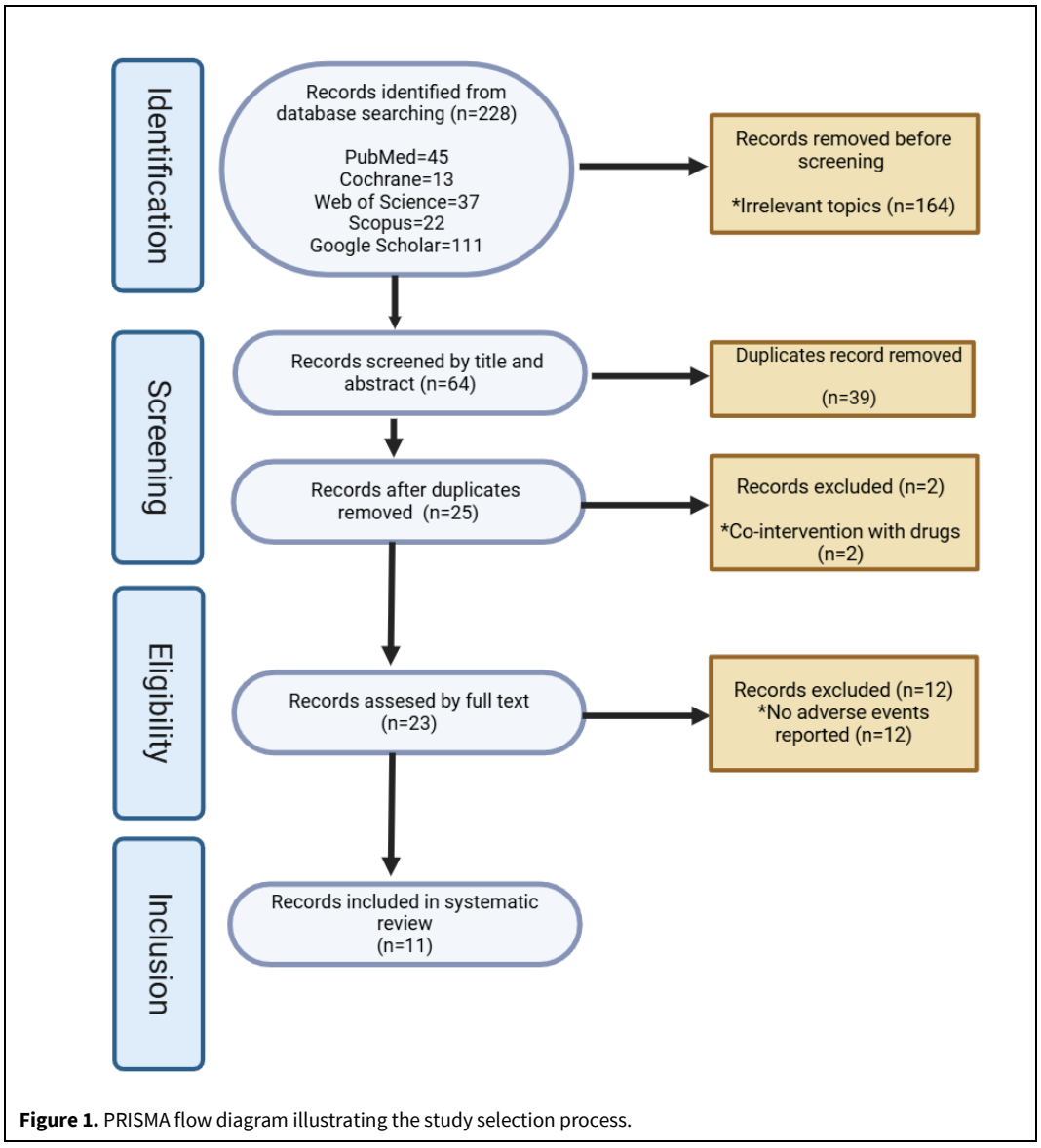


Figure 1. PRISMA flow diagram illustrating the study selection process.

Table 3. Characteristics of the selected studies.

Herbal intervention	Study type	Psoriasis type/number of patients/ duration	Route of adm.	Part of plant	Adverse events	Ref.
Indigo naturalis (Beijing Tong Ren Tang Pharmaceutical Company, from China) *vs. Indigo naturalis* (*Indigofera tinctoria* L., from Iran)	Randomized double-blind clinical trial	Mild to moderate plaque psoriasis/54/8 weeks	Topical	Not described (plant powder)	Moderate dermatitis (7 patients in the Iranian herbal group and 5 in the Chinese group) Severe dermatitis (1 patient in the Chinese group and one in the Iranian herbal group) Severe pruritus and erythema (1 patient in the Chinese group and 1 patient in the Iranian group) Mild increase in alkaline phosphatase	(Yazdanpanah et al., 2021)
Psoralea corylifolia L.	Case report	Psoriasis (severity not described)	Topical	Not described (oil from the plant)	Photodermatitis Severe pain Erythema	(Faulkner et al., 2021)
Ranunculus arvensis L.	Case report	Palmoplantar psoriasis (severity not described)	Topical	Whole plant	Severe pain, itching, and presence of eroded bullous lesions with crust and ulcerated areas	(An et al., 2018)
Indigo naturalis Baphicacanthus cusia (Nees) Bremek	Randomized double-blind, parallel-group, four-arm, dosage-controlled phase 2a clinical trial	Mild to moderate plaque psoriasis/100/8 weeks	Topical	Oil from leaves	Nasopharyngitis (17 patients) Upper respiratory tract infection (8 patients) Erythema (8 patients) Allergic contact dermatitis (one patient)	(Lin et al., 2018)
Indigo naturalis Baphicacanthus cusia (Nees) Bremek	Randomized double-blinded, placebo-controlled clinical trial	Mild to moderate plaque psoriasis/24/9 weeks	Topical	Extract from the aerial parts of the plant	Pruritus (4 patients) Rash (2 patients) Nasopharyngitis (2 patients) Abdominal distension (1 patient) Constipation (1 patient) Cough (1 patient) Dizziness (1 patient) Oropharyngeal pain (1 patient)	(Cheng et al., 2017)
Santulum album L.	Single-center open-label proof of concept phase 2 clinical trial	Mild to moderate plaque psoriasis/11/28 days	Topical	Essential oil from the heartwood	Mild skin irritation (1 patient)	(Sharma et al., 2017)
Aloe vera (L.) Burm.f.	Ethnopharmacology survey	-	Topical	Gel from leaves	Dryness Stinging Soreness Fissures Erythema Contact urticaria	(Shawahna & Jaradat, 2017)
Anthemis cotula L.	Ethnopharmacology survey	-	Topical	Paste from flowers	Contact sensitization	(Shawahna & Jaradat 2017)
Gynura pseudochina var. hispida (Thwaites) Hook.f.	Randomized controlled clinical trial using left-to-right comparisons	Mild to moderate psoriasis/25/8 weeks	Topical	Extract from leaves	Yellowish staining (24 patients) Stinging sensation (3 patients) Itch (7 patients)	(Rerknimitr et al., 2016)
Indigo naturalis	Randomized observer-blind, active-controlled, intra-subject clinical trial	Nail psoriasis/28/24 weeks	Topical	Not described (oil extract)	Skin irritation (2 patients)	(Lin et al., 2015)
Curcuma longa L.	Randomized prospective intra-individual, right–left comparative, placebo-controlled, double-blind clinical trial	Mild to moderate plaque psoriasis/34/9 weeks	Topical	Hydroalcoholic turmeric extract	Burning (6% of patients) Irritation (3% of patients) Dryness (6% of patients)	(Sarafian et al., 2015)
Tripterygium wilfordii Hook.f (TwHF)	Randomized, double-blind, double-dummy, parallel-group clinical trial	Moderate to severe plaque psoriasis/115/8 weeks	Oral	Not described (chloroform–methanolic extract of TwHF)	Menstrual disorders Dry mouth Gastrointestinal complaints Swelling of the lower limbs Increase levels of Aspartate transaminase and triglycerides	(Wu et al., 2015)

Table 4. Quality of clinical trials using herbal therapies for psoriasis.

ID	Herbal medicine product name	Characteristics of the herbal product	Dosage regimen and quantitative description	Qualitative testing	Placebo/control group	Practitioner
(Yazdanpanah et al., 2021)	YES	YES	YES	NO	YES	YES
(Lin et al., 2018)	YES	YES	YES	YES	YES	YES
(Cheng et al., 2017)	YES	YES	YES	NO	YES	YES
(Sharma et al., 2017)	YES	YES	YES	NO	NO	YES
(Rerknimitr et al., 2016)	YES	NO	YES	NO	YES	YES
(Lin et al., 2015)	NO	NO	YES	NO	NO	YES
(Sarafian et al., 2015)	YES	NO	YES	YES	YES	YES
(Wu et al., 2015)	YES	NO	YES	NO	YES	YES

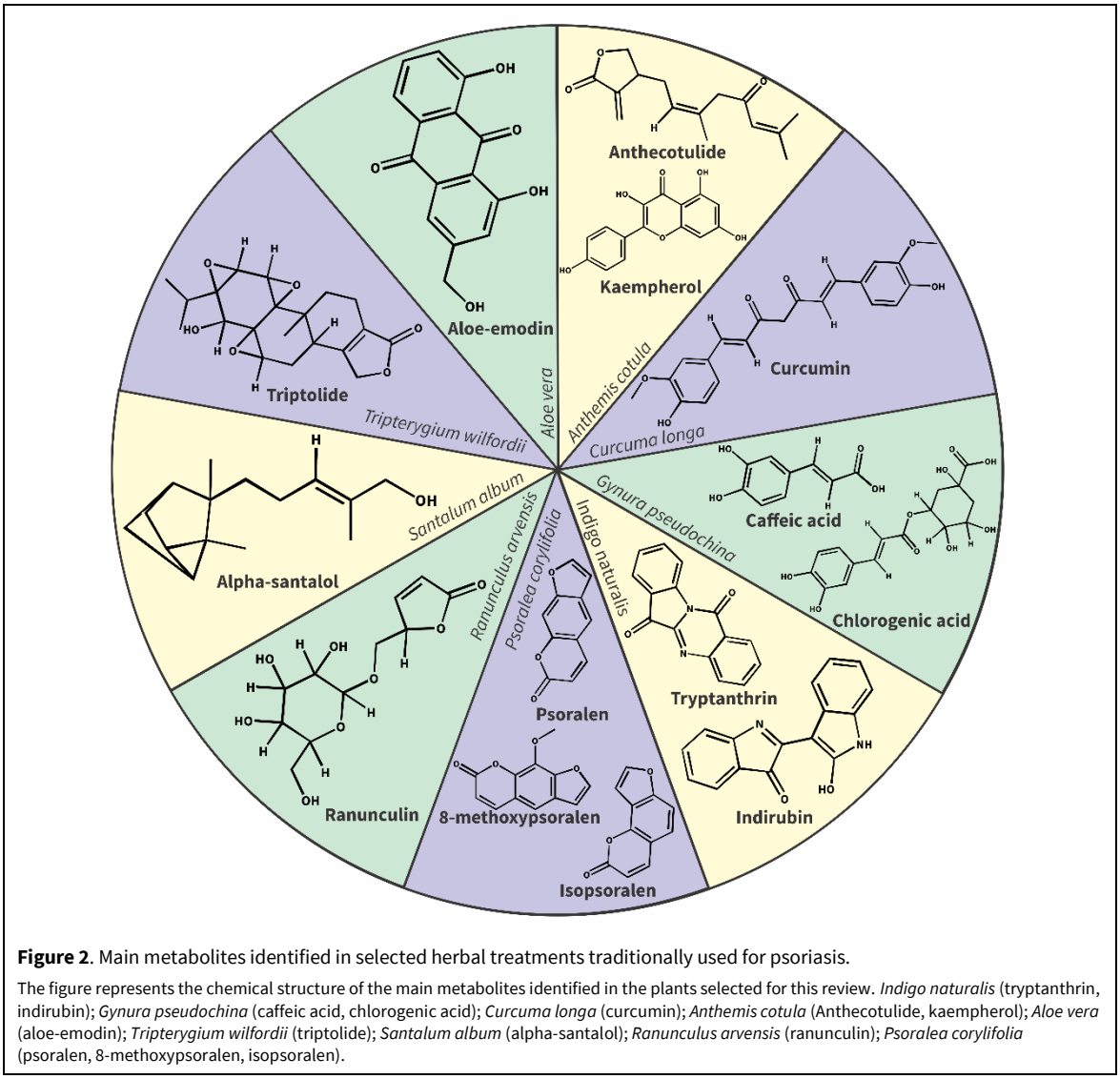


Figure 2. Main metabolites identified in selected herbal treatments traditionally used for psoriasis.

The figure represents the chemical structure of the main metabolites identified in the plants selected for this review. *Indigo naturalis* (tryptanthrin, indirubin); *Gynura pseudochina* (caffeic acid, chlorogenic acid); *Curcuma longa* (curcumin); *Anthemis cotula* (Anthecotulide, kaempherol); *Aloe vera* (aloe-emodin); *Tripterygium wilfordii* (triptolide); *Santalum album* (alpha-santalol); *Ranunculus arvensis* (ranunculin); *Psoralea corylifolia* (psoralen, 8-methoxypsoralen, isopsoralen).

Potential herb-drug interactions of selected plants

The systematic review revealed side effects related to the use of *Indigo naturalis*, *Psoralea corylifolia* L., *Ranunculus arvensis* L., *Santulum album* L., and *Aloe vera* (L.). Burm.f., *Anthemis cotula* L., *Gynura pseudochina* var. hispida (Thwaites) Hook.f., *Curcuma longa* L., and *Tripterygium wilfordii* Hook.f (TwHF). Primary metabolites of the herbal treatments are presented in Fig. 2.

These plants are widely used in the management of psoriasis and associated comorbidities, predominantly through topical and oral administration (Lv et al., 2018; Mahajan et al., 2022; Sukadeetad et al., 2018). Such patterns of use increase the potential for interactions between plant-derived metabolites and conventional drugs. Accordingly, Table 5 summarizes the effects of key phytochemicals on drug-metabolizing enzymes and their potential to cause pharmacokinetic herb-drug interactions.

Table 5. Impact of the primary metabolites of selected plants on drug-metabolizing enzymes and potential to cause herb-drug interactions.

Herbal treatment	Major metabolite	Model	Effects on drug-metabolizing enzymes/ metabolite-drug PK interactions	Ref.
Indigo naturalis	Indirubin	HepG2cells	Induction of CYP3A4 gene reporter activity and CYP3A4 mRNA expression	(Kumagai et al., 2016)
		HepG2 cells	Increase the UGT activities	(Donato et al., 2010)
		C57BL/6JJcl mice	Increase 3-fold the CYP1A2 protein	(Sugihara et al., 2004)
Psoralea corylifolia	Psoralen	IRC mice	Inhibition of the activities of CYP2D6, CYP3A4, GST-α, and GST-μ enzymes CYP3A4 metabolizes antipsoriatic drugs (cyclosporine, acitretin, roflumilast, and apremilast, among others)	(Jiang et al., 2022)
		Recombinant human enzyme	Inactivation of the CYP2B6 enzyme As CYP2B6 metabolizes more than 4% of drugs (bupropion, methadone, cyclophosphamide, etc.), there is a risk of toxicity	(Ji et al., 2015)
		Sprague-Dawley rats	Psoralen + Anastrozole Psoralen significantly increases systemic exposure of anastrozole	(Zhang et al., 2018b)
	Isopsoralen	Sprague Dawley rats	Isopsoralen + Tofacitinib Isopsoralen markedly decreases the metabolism of tofacitinib through competitive inhibition of CYP3A4	(Wang et al., 2024)
	8-MOP	Human liver microsomes	8-MOP is an irreversible inhibitor of human CYP1A2 Caution should be exercised in co-administration with drugs acting as CYP1A2 substrates (such as theophylline, lidocaine, caffeine, etc.), as there is a potential for toxicity	(Alehaideb et al., 2021)
		C57BL/6 mice	8-MOP + acetaminophen 8-MOP significantly inhibits acetaminophen metabolism by competitively inhibiting CYP2E1	(Liu et al., 2023)
Aloe vera	Aloe-emodin	Recombinant human CYP1B1 enzyme	Aloe-emodin inhibits the activity of the human CYP1B1 enzyme	(Meng et al., 2022)
		Human recombinant enzymes and liver microsomes	Aloe-emodin inhibited CYP1A2 and CYP2C19 activity	(Liu et al., 2021)

Table 5. Impact of the primary metabolites of selected plants on drug-metabolizing enzymes and potential to cause herb-drug interactions (continued...)

Herbal treatment	Major metabolite	Model	Effects on drug-metabolizing enzymes/ metabolite-drug PK interactions	Ref.
Curcuma longa	Curcumin	Healthy male volunteers	Curcumin + Sulphasalazine Curcumin significantly increased plasma sulphasalazine levels, resulting in a 1.8-fold increase in AUC_{0-24}	(Kusuhara et al., 2012)
		Healthy male volunteers	Curcumin + Talinolol After 2 weeks of co-administration, the AUC_{0-48} and AUC_0—of talinolol increased by 67 and 80%, respectively. The C_{max} of Talinolol was significantly higher after curcumin administration	(He et al., 2012)
		Healthy male volunteers	Following the administration of curcumin, CYP1A2 activity decreased by 28.6%, whereas CYP2A6 activity increased by 48.9% Because CYP1A2 metabolizes theophylline, clozapine, and acetaminophen, herb-drug interactions should be considered in clinical practice	(Chen et al., 2010)
		Wistar rats	Curcumin + Tramadol Curcumin significantly reduces tramadol concentrations	(Dibaei et al., 2024)
		Sprague-Dawley rats	Curcumin + Everolimus Curcumin consumption notably reduced the bioavailability of everolimus by activating CYP3A4	(Hsieh et al., 2014; Joo et al., 2024)
Tripterygium wilfordii	Tripterygium glycosides	Sprague-Dawley rats	TGT + Leflunomide TGT significantly decreases the formation of teriflunomide, the only active metabolite of leflunomide	(Boucetta et al., 2022)
		Sprague-Dawley rats	TGT + Losartan TGT decreased the losartan metabolism	(Hu et al., 2017)
	Triptolide	Sprague-Dawley rats	Triptolide + Amlodipine The systemic exposure of amlodipine increased	(Zhang et al., 2018a)
		Sprague-Dawley rats	Triptolide + Fenofibrate Triptolide may enhance the systemic exposure of fenofibric acid by inhibiting the fenofibrate metabolism.	(Li et al., 2019)
		Sprague-Dawley rats	Triptolide + Atorvastatine Triptolide inhibits CYP3A4 expression, thereby impairing both its own detoxification and that of atorvastatin, leading to hepatotoxicity	(Zheng et al., 2021)

UGT: UDP-glucuronsyltransferases; GST: glutathione-S-transferases; CYP: cytochrome P450; TGT: tripterygium glycosides; AUC: area under the curve; 8-MOP: 8-methoxypsoralen.

DISCUSSION

Interpretation

Globally, it is estimated that approximately 2-70% of psoriasis patients use medicinal plants, either as standalone treatments or in combination with conventional therapies (Díaz-Murillo et al., 2016; Keseroglu et al., 2015; Landis et al., 2014; Weng et al., 2016). The utilization of complementary therapies, particularly medicinal plants for psoriasis, varies considerably across geographical regions, cultural contexts, and healthcare systems. In the present review, the included studies originated from diverse regions, including Iran, China, the United Kingdom, Turkey, Taiwan, Canada,

Palestine, and Thailand, reflecting heterogeneous patterns of herbal use and clinical practice.

Psoriasis patients commonly perceive medicinal plants as inherently safe, believe that disclosure to healthcare professionals is unnecessary, and assume that herbal products can be safely combined with conventional drugs or administered through both oral and topical routes (Keseroglu et al., 2015; Talbott & Duffy, 2015; Wnuk-Kłosińska et al., 2021). These perceptions, together with cultural traditions, regulatory differences, and variability in plant preparation and dosing practices, may influence exposure patterns and the reporting of adverse events. The situation becomes more complex when herbal treatments are administered to patients with comorbidities, increasing the potential for interactions.

Despite the widespread use of medicinal plants for psoriasis, only a limited number of narrative or systematic reviews have explicitly addressed safety concerns and AEs associated with these therapies (Deng et al., 2014; Herman & Herman, 2016). Previous reviews have primarily focused on efficacy, mechanisms of action, or topical formulations, reporting mostly mild adverse effects, while providing limited analysis of serious adverse events or potential herb-drug interactions. This gap may be partly explained by the short duration and small sample sizes of clinical studies, as well as the frequent combination of herbal and conventional therapies, which complicates AE attribution and leads to underreporting of clinically relevant safety outcomes.

In this context, the present review is novel as it systematically synthesizes available evidence on AEs and safety concerns associated with medicinal plants used for psoriasis, rather than focusing on therapeutic efficacy. While the limited number of studies and heterogeneous data constrain definitive conclusions, this safety-oriented approach addresses a critical gap in the literature and provides a foundation for improved pharmacovigilance and future hypothesis-driven clinical investigations.

Among the investigations included in this systematic review, the research by Sharma et al. warrants specific examination, as the herbal treatment intervention was not assessed against a control treatment. Instead, safety outcomes were assessed by evaluating AEs reported by participants after the therapy (Sharma et al., 2017). This research is a single-center, open-label trial evaluating the safety, tolerability, and efficacy of an herbal treatment in a small cohort of psoriasis patients. Despite potential biases, the decision to include this study in the systematic review was based on three key factors: a) adherence to the established inclusion criteria; b) the design characteristics, which prioritized the assessment of treatment safety; c) publication in a reputable pharmacological journal.

On the other hand, although the study by Lin et al. (2015) was considered low quality, it was included after a thorough analysis. This study appeared in the "Letters" section. Thus, likely due to the brevity typical of such publications, specific information was omitted, including the Latin binomial name of the plant, details of herbal product preparation, the chemical fingerprint chromatographic analysis, and the rationale for the controls employed. Despite these limitations, its inclusion in this review was justified, as it met the predefined inclusion criteria. Moreover, the study was published in a reputable journal, supporting the consideration of its findings.

Due to the scarcity of studies specifically designed to evaluate the safety of herbal treatments, only a limited number of studies (11 studies covering 9 herbal treatments) met the predefined inclusion criteria. Although these studies provide preliminary evidence regarding safety, the small sample sizes limit the external validity and generalizability of the findings. Therefore, the results should be interpreted with caution, and larger, well-designed clinical studies are needed to confirm these safety outcomes. A comprehensive assessment of the selected plants, considering their use in psoriasis and associated comorbidities, as well as their potential to induce plant–drug interactions, provides further evidence to strengthen the overall understanding of their safety.

Herbal treatments inducing serious AEs

Psoralea corylifolia

P. corylifolia (PC) is used in Indian (Ayurveda), Chinese, and Korean folk medicine. Its antipsoriatic activity is related to the presence of furocoumarins, mainly psoralen, isopsoralen, and 8-methoxypsoralen (8-MOP) (Alalaiwe et al., 2018) (Fig. 2). Topical or oral psoralens followed by UVA radiation (PUVA) have been widely used for the treatment of psoriasis, with 8-methoxypsoralen (8-MOP) being the principal psoralen approved by the Food and Drug Administration (FDA) for photochemotherapy. Compounds present in PC have been reported to induce hepatotoxicity (Fig. 3). Higher serum levels of 25-hydroxyvitamin D appear to confer protection against 8-MOP-induced hepatotoxicity, suggesting caution when using PUVA therapy in psoriasis patients with low vitamin D levels (Zhao et al., 2019).

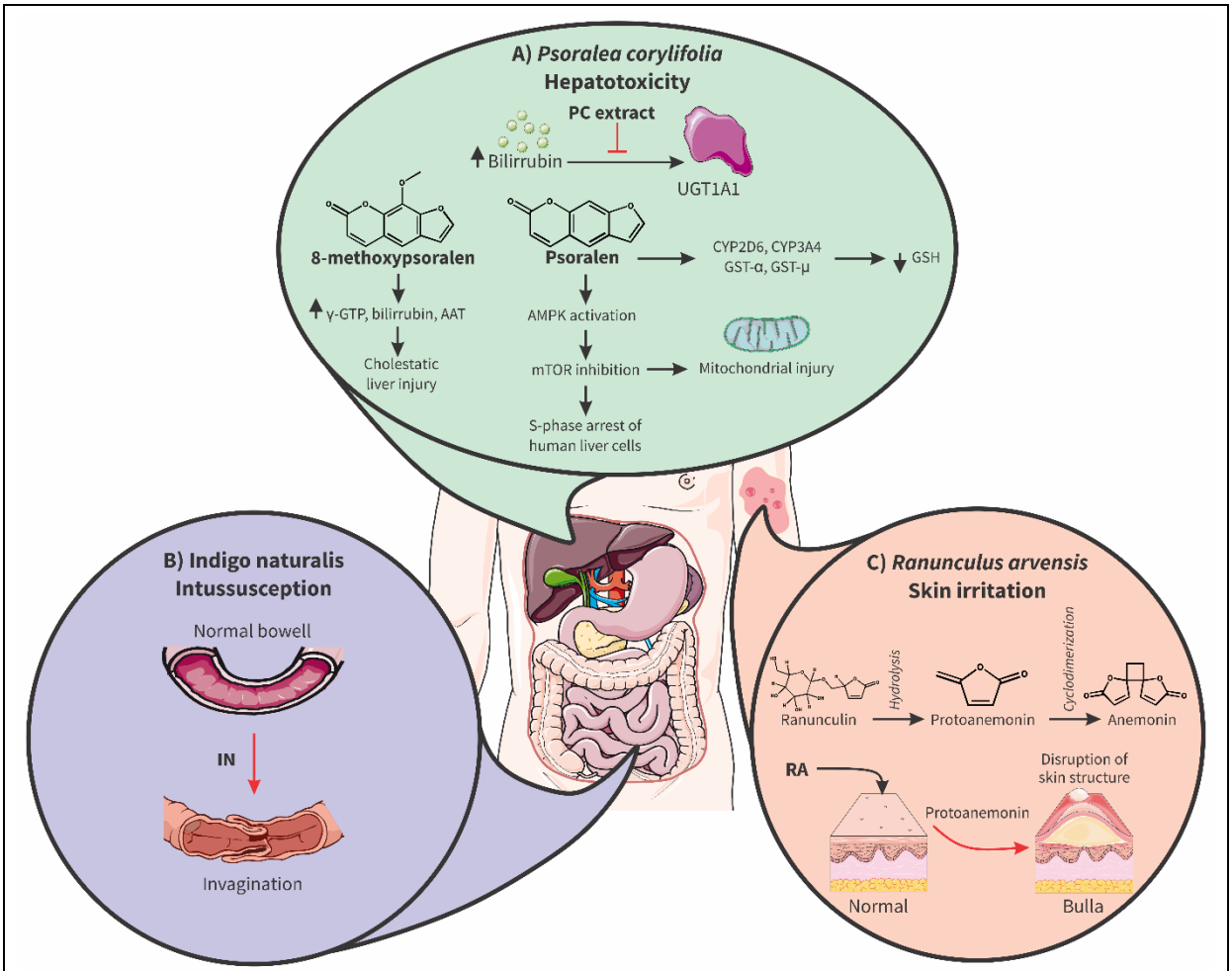


Figure 3. Clinically important adverse events of *Indigo naturalis*, *Psoralea corylifolia, and Ranunculus arvensis*.

***Psoralea corylifolia* (PC) can induce hepatotoxicity (A).** Multiple mechanisms have been proposed to explain PC hepatotoxicity. Psoralen, one of its main constituents, can inhibit drug-metabolizing enzymes such as CYP2D6, CYP3A4, and glutathione-S-transferases (GST), leading to glutathione depletion and subsequent liver injury (Jiang et al., 2022). Psoralen has also been shown to reduce the viability of normal human liver cells by inducing cell cycle arrest, inhibiting the mTOR signalling pathway, and causing mitochondrial damage (Zhou et al., 2018). PC extracts can inhibit human uridine 5-diphosphoglucuronyltransferase A1 (UGT1A1), an enzyme involved in bilirubin metabolism, leading to elevated bilirubin levels and liver toxicity (Wang et al., 2015). 8-methoxypsoralen (8-MOP) induces cholestatic liver injury by increasing serum γ-glutamyl transpeptidase (γ-GTP), total bilirubin, and alanine aminotransferase (AAT) levels (Zhao et al., 2019).

***Indigo naturalis* (IN) can provoke intussusception (B).** IN can damage the intestinal wall, disrupt normal peristalsis, and facilitate the invagination of one segment of the bowel into an adjacent segment. The interval between the initiation of IN consumption and the onset of intussusception appears to be relatively short. (8 weeks) (Naganuma et al., 2019).

***Ranunculus arvensis* (RA) can induce severe skin irritation (C).** RA contains ranunculin. Upon plant crushing, ranunculin is hydrolyzed into protoanemonin. This compound irritates the skin, as it can disrupt disulfide bonds, leading to skin structure and bulla formation disturbance. Because protoanemonin rapidly polymerizes to the non-irritant anemonin, only freshly damaged plants cause this severe skin injury.

Psoriasis patients, particularly children, have a higher likelihood of developing epilepsy (Amanat et al., 2018; Kelati et al., 2017). Special caution is advised when combining 8-MOP with pregabalin, as their concomitant use impairs motor coordination in mice (Zagaja et al., 2016). The concomitant use of psoralen and metoprolol may induce hepatic dysfunction due to psoralen-mediated inhibition of CYP2D6 (Jiang et al., 2022).

Indigo naturalis

Indigo naturalis (IN) has long been recognized as an important herbal remedy for psoriasis. It is derived from several plant species, including *Baphicacanthus cusia* (Nees) Bremek (*Acanthaceae*), *Polygonum tinctorium* W.T. Aiton (*Polygonaceae*), *Indigofera tinctoria* L. (*Fabaceae*), and *Isatis indigotica* Fort. (*Brassicaceae*). The antipsoriatic activity of IN has been mainly attributed to the presence of tryptanthrin (TYP) (Cheng et al.,

2017), indirubin (IND) (Cheng et al., 2017; Lin et al., 2012; 2018), and their synergistic action (Lin et al., 2013) (Fig. 2).

In traditional Chinese medicine, IN is administered both orally and topically for treating psoriasis (Sun et al., 2021) and is also used to manage comorbid conditions such as ulcerative colitis (Naganuma et al., 2019). Patients with psoriasis have a 1.71-fold increased risk of developing ulcerative colitis (Fu et al., 2018). Consequently, this plant may be taken orally not only for psoriasis but also for the management of this coexisting condition, thereby increasing the likelihood of clinically relevant AEs or herb-drug interactions.

A nationwide survey in Japan investigated the incidence of AEs linked to IN in ulcerative colitis. A total of 91 patients reported 107 AEs. The most frequent were liver dysfunction (40 cases), gastrointestinal symptoms (21 cases), headache (13 cases), pulmonary arterial hypertension (11 cases), intussusceptions (10 cases), colitis not related to ulcerative colitis (8 cases), and mild dyspnea (3 cases) (Naganuma et al., 2019).

Mild and reversible liver dysfunction was reported in 10–20% of patients receiving 0.5–2.0 g/day oral IN according to a prospective, multicentred, randomized, double-blind, placebo-controlled trial for ulcerative colitis. The effect was attributed to CYP1A1 induction via the activation of the hepatic aryl hydrocarbon receptor (AhR) (Naganuma et al., 2018).

Although most AEs reported for IN are reversible, intussusception is considered a serious AE as it causes ischemic injury and intestinal obstruction requiring surgical treatment. The mechanism proposed for IN-driven intussusception is shown in Fig. 3. Clinicians should remain vigilant when encountering uncommon intussusception in psoriasis patients and inquire about the use of IN for psoriasis or co-morbid diseases.

Ranunculus arvensis

R. arvensis is widely used in Turkish medicine to treat arthritis, rheumatism, and psoriasis (Bhatti et al., 2015). The ranunculin in this plant can provoke erythematous, eroded bullous lesions on the skin (An et al., 2018), whose mechanism is shown in Fig. 3. Given this serious toxic skin effect, the topical use of the freshly crushed plant is not recommended.

Herbal treatments inducing mild-to-moderate AEs

Santulum album

S. album is a sandalwood species used in Ayurvedic, Unani, Siddha, and Chinese traditional medicine (Moy & Levenson, 2017). Sandalwood album oil (SAO) is an essential oil distilled from the *S. album,* which can reduce the levels of IL-17, a key target cytokine involved in psoriasis (Sharma et al., 2019). Over 125 chemical compounds have been identified in SAO. However, its primary active ingredients are (Z)-α-santalol and (Z)-β-santalol, which constitute roughly 55% and 24% of the composition, respectively (Sharma et al., 2019) (Fig. 2). SAO is commercially available as an acne product manufactured by Galderma (Fort Worth, Texas) under the Benzac® name.

Patients with psoriasis appear to have a slightly increased risk of cancer (Vaengebjerg et al., 2020). SAO has been used to alleviate mucositis induced by chemoradiotherapy in head and neck cancer; however, its use may cause adverse effects such as nausea, vomiting, and irritation (Ha et al., 2020). Although SAO is primarily applied as a topical dermatological product, a small proportion of individuals (0.1–2.4%) exhibit allergic reactions to this oil (de Groot & Schmidt, 2017). Studies on the transdermal delivery of α-santalol have shown no accumulation of this compound in the blood, indicating minimal systemic exposure during topical administration (Dave et al., 2017). Consequently, topical use of SAO is associated with a low likelihood of systemic side effects.

Aloe vera

A. vera is one of the most popular plants for treating dermatological conditions (Long, 2016), and it can be administered orally or topically. *A. vera* contains multiple bioactive compounds, but the antipsoriatic action is mediated, at least partially, by the presence of aloe-emodin (Fig. 2) (Divya et al., 2016). The impact of this metabolite on drug-metabolizing enzymes is presented in Table 5.

The Pharmacovigilance Program of India identified two non-serious AEs of topical contact dermatitis and itching induced by *A. vera* (Kalaiselvan et al., 2015), whereas oral use of this plant can cause hepatotoxicity (Gill et al., 2020; Parlati et al., 2017; Rabe et al., 2005; Yang et al., 2010). The underlying mechanisms of *A. vera*-induced hepatotoxicity are idiosyncratic and dose-independent, with an unpredictable prognosis (Parlati et al., 2017).

Intake of aloe juice activates the efflux transporter P-glycoprotein and CYP3A4, thereby decreasing the systemic exposure of cyclosporin, a drug used for psoriasis (Yang et al., 2017). Given the central role of CYP3A4 in the metabolism of antipsoriatic drugs such as tacrolimus, apremilast, and acitretin, among others, it is essential to carefully evaluate the potential risks associated with the concomitant use of aloe preparations with these medications.

Anthemis cotula

A. cotula, known as mayweed chamomile, treats psoriasis by topical application (Shawahna & Jaradat, 2017). It is also used orally to treat gastrointestinal problems, gouty arthritis, dysentery, and fever (Shawahna & Jaradat, 2017; Sut et al., 2019). Anthecotulide, one of its main constituents, has irritant topical activity (Schmidt, 1986). Thus, this plant can cause contact dermatitis (Aberer, 2008; Salapovic et al., 2013).

Gynura pseudochina

G. pseudochina is a medicinal plant found in Southeast Asia and Africa used to treat psoriasis, herpes zoster infection, abscesses, and thermal burn by topical administration (Rerknimitr et al., 2016). It is also used orally for inflammation, hemorrhage, and dysentery (Sukadeetad et al., 2018). Among their primary metabolites, caffeic acid (CA) has been regarded as the most effective antipsoriatic compound (Fig. 2) (Sukadeetad et al., 2018). The topical use of this plant can provoke a stinging sensation and itch, whereas its oral administration at high doses requires special precautions due to hepatotoxic pyrrolizidine alkaloids (Sukadeetad et al., 2018).

Curcuma longa

C. longa, known as turmeric, is a plant native to Southeast Asia. Curcumin, one of its primary constituents, has garnered substantial interest for psoriasis (Sarafian et al., 2015), both orally and topically (Zhang et al., 2022). Antipsoriatic turmeric-derived preparations are generally consumed as monotherapy but can be combined with antipsoriatic drugs (Bilia et al., 2018; Draelos, 2022).

Table 5 presents the curcumin-drug interactions. Clinicians should consider the potential impact of turmeric-derived preparations on drug metabolism when prescribing medications such as clarithromycin or sedative hypnotics, which are P-glycoprotein substrates (He et al., 2012). As curcumin increases CYP2A6 activity, and elevated CYP2A6 activity has been associated with an increased risk of colorectal cancer, a comorbidity related to psoriasis (Fu et al., 2021), caution should be exercised when administering high doses of curcumin to patients who overexpress CYP2A6 (Chen et al., 2010).

Tripterygium wilfordii

T. wilfordii (TwHF) is a traditional Chinese herbal medicine and is used for psoriasis via topical and oral administration, as monotherapy or in combination with conventional drugs (Lv et al., 2018). The primary antipsoriatic metabolites are triptolide, celastrol, and demethylzeylasteral (Ru et al., 2020). However, triptolide is the most extensively studied (Fig. 2). Side effects on the liver, kidney, spleen, gastrointestinal tract, and heart have been associated with the oral use of TwHF and triptolide (Xi et al., 2017).

The incidence of TwHF-related nephrotoxicity is 5.81% (Feng et al., 2019). Oral TwHF (20 mg, 3 times a day) for 8 weeks increased transaminase and triglyceride levels in patients with psoriasis (Wu et al., 2015). Oral administration of 18 g/day of a TwHF extract can provoke moderate to severe gastrointestinal reactions (Han et al., 2012).

Given that CYP3A4 is primarily involved in triptolide metabolism (Table 4), and considering that P-glycoprotein mediates the hepatic and biliary clearance of triptolide, it is essential to exercise caution when administering triptolide concurrently with CYP3A4 (ketoconazole, erythromycin, tamoxifen, etc.) and P-glycoprotein (cyclosporin A, verapamil, quinidine, etc.) inhibitors to prevent an increase in its exposition and toxicity (Deng et al., 2020; Xu et al., 2018).

Overall, the analysis of the medicinal plants evaluated in this review highlights key priorities for future research. Further studies should focus on rigorously designed clinical trials using standardized herbal products, an adequate number of participants, and longer follow-up periods to better characterize safety outcomes in psoriasis. Particular attention should be given to herb-drug interactions and the safety of herbal preparations in patients with comorbidities and polypharmacy, as these areas remain insufficiently explored.

Limitations of evidence

Currently, a restricted number of reviews document AEs and potential herb-drug interactions associated with antipsoriatic herbal remedies (Deng et al., 2014; Jo et al., 2023; Radu et al., 2024). Acquiring relevant information regarding the safety of antipsoriatic herbal interventions has been notably difficult. Much of the research has focused on demonstrating the benefits of medicinal plants, often neglecting their safety. This oversight can be partially attributed to the tendency for studies yielding positive outcomes to be more readily published.

Including peer-reviewed publications in this review may introduce selection bias, potentially excluding pertinent unpublished gray literature. Excluding references published in languages other than English and Spanish may have introduced selection bias. As a result, relevant evidence on the safety of plant-based treatments may have been missed, especially studies related to well-established traditional medical systems such as Traditional Chinese Medicine and Ayurvedic Medicine. However, limiting inclusion to studies

published in English and Spanish allowed for accurate evaluation, interpretation, and synthesis of the data, as the authors are fully proficient in these languages. This approach avoided reliance on automated translation tools, thereby enhancing data reliability and optimizing resources and timelines without compromising the methodological rigor of the review.

Although this systematic review identified studies with a low risk of bias and considerable evidence (Cheng et al., 2017; Lin et al., 2018; Rerknimitr et al., 2016; Sarafian et al., 2015; Wu et al., 2015; Yazdanpanah et al., 2021). Some of them are limited by a small sample size (Cheng et al., 2017; Rerknimitr et al., 2016; Sarafian et al., 2015) and a short time (average 8-9 weeks) (Cheng et al., 2017; Lin et al., 2018; Rerknimitr et al., 2016; Sarafian et al., 2015; Sharma et al., 2017; Wu et al., 2015; Yazdanpanah et al., 2021). These constraints limit the ability to adequately assess long-term safety outcomes and the generalizability of findings on the safety of antipsoriatic herbal treatments.

One important limitation that should not be overlooked, and that restricts the generalizability of the safety-related findings of this systematic review, is the absence of chromatographic analyses in most of the included studies (Cheng et al., 2017; Lin et al., 2015; Rerknimitr et al., 2016; Sharma et al., 2017; Wu et al., 2015; Yazdanpanah et al., 2021). These analyses are essential for characterizing the chemical fingerprint of the medicinal plants. The chemical composition of herbal products is influenced by various factors, including their geographic origin, climatic conditions, and harvest timing, leading to variability in constituent profiles and concentrations across batches and manufacturers (Gagnier et al., 2006). Such discrepancies can lead to variations in bioavailability and toxicological characteristics.

Given the paucity of research on the safety of commonly used herbal treatments for psoriasis, two case reports (An et al., 2018; Faulkner et al., 2021) and one ethnopharmacological investigation (Shawahna & Jaradat, 2017) were included in this systematic review. Case reports play an important role in identifying safety concerns that may lead to drug withdrawal from the market (Lavertu et al., 2021) and have also been used in earlier reviews assessing plant safety (Di Lorenzo et al., 2015; Wendt et al., 2022). On the other hand, ethnopharmacological studies have been proposed as valuable tools for documenting the safety profiles of herbal medicines (Rodrigues & Barnes, 2013). While both types of investigations offer advantages for evaluating safety outcomes, they should mainly be regarded as hypothesis-generating studies that require further validation through randomized clinical trials. These approaches have inherent limitations, including limited generalizability, an inability to establish causal relationships, and a risk of over-interpretation.

Moreover, it is essential to acknowledge that the studies selected to document potential herb-drug interactions possess certain limitations that warrant attention. Most pharmacokinetic investigations are derived from preclinical models and evaluate the effects of individual plant-derived metabolites rather than herbal preparations as a whole. While these data are useful for assessing the potential to cause herb-drug interactions, their clinical relevance remains uncertain, as they may not accurately reflect real-world scenarios in which herbal products are consumed as complex mixtures and where further biotransformation of these metabolites may mitigate the predicted interactions. Although cytochrome P-450 and other phase-II metabolizing enzymes are critical for xenobiotic metabolism, inferring clinical relevance solely from enzyme activity data represents a simplistic approach. The clinical significance of herb–drug interactions depends on multiple factors, including dose, frequency of intake, route of administration, therapeutic range, and the relative contribution of the affected enzyme in the clinical context. As the relevance of pharmacokinetic interactions can only be confirmed through well-designed, large-scale randomized clinical trials or pharmacovigilance studies, further investigation is warranted.

Finally, the absence of a formal meta-analysis, including statistical heterogeneity and sensitivity analyses, represents a methodological limitation of this review. Substantial clinical, methodological, and outcome heterogeneity across studies precluded meaningful quantitative synthesis, thereby limiting the generalizability and precision of the findings. Consequently, a narrative synthesis was adopted as the most appropriate methodological approach to summarize the available evidence.

Implications

Pharmacovigilance practices and tools have largely evolved within the framework of conventional medicine and have only partially addressed the complex challenges associated with monitoring the safety of herb-derived treatments. Regulatory authorities increasingly recognize these limitations. In Europe, the European Medicines Agency (EMA), through the Committee on Herbal Medicinal Products (HMPC), has emphasized the need to strengthen signal detection, post-marketing surveillance, and the integration of safety data specific to herbal medicines, acknowledging their chemical complexity and variability (European Medicines Agency, 2025). Similarly, the World Health Organization (WHO) and the International Society of Pharmacovigilance have recognized persistent challenges, including underreporting of AEs,

heterogeneous product composition, and frequent concomitant use with conventional medicines (Skalli et al., 2024; World Health Organization, 2004). Together, these observations underscore the need for harmonized global regulatory approaches to improve consistency and effectiveness in safety reporting systems (Sethi et al., 2025). Within this global context, systematic and narrative safety reviews play a critical role in consolidating fragmented evidence and supporting early signal generation for herbal medicinal products.

Given the widespread use of medicinal plants for psoriasis, these findings reinforce the need for strengthened regulatory oversight and for integrating herbal medicine safety into existing pharmacovigilance frameworks through evidence-informed health policies. Addressing these gaps requires structured communication between healthcare providers and patients, including routine assessment of herbal use, as well as the development of practical tools to capture relevant information on commonly used plants systematically, routes of administration (oral/topical), therapeutic indications (psoriasis/comorbidities), concomitant treatments, and duration of use.

Building on these regulatory and pharmacovigilance considerations, the evidence compiled in this review may support policymakers in developing targeted educational initiatives on medicinal plant safety and inform training programs for healthcare professionals on the challenges of integrating herbal therapies into psoriasis management, thereby improving risk recognition and patient engagement.

In addition, these findings highlight the need for coordinated efforts among clinicians, researchers, patients, and policymakers to strengthen the evidence base through mechanistic studies, pharmacovigilance research, and well-designed multicenter clinical trials using standardized, chemically characterized herbal preparations. Such collaboration is essential to developing evidence-based guidelines that ensure the safe and effective integration of herbal treatments into clinical practice.

CONCLUSION

Although numerous studies have investigated herbal treatments for psoriasis, adverse events associated with medicinal plants are infrequently reported, and their actual incidence may be underestimated in real-world settings. Misconceptions regarding the safety of herbal products and underreporting by patients may contribute to this gap.

Medicinal plants used for psoriasis can cause mild to severe side effects and may interact with conventional therapies, underscoring the need for cautious use, health education, and improved pharmacovigilance. Given the small sample sizes and limited follow-up of most clinical studies, well-designed, long-term, large-scale randomized controlled trials using standardized herbal preparations, alone or in combination with antipsoriatic drugs, are required to adequately assess their safety in realistic clinical practice.

CONFLICT OF INTEREST

The research was conducted entirely free from any involvement in commercial, financial, or personal matters that might be perceived as a possible conflict of interest or that could have influenced the outcomes or interpretation of the study. No human/animal research was conducted in this review.

ACKNOWLEDGMENTS

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

GENERATIVE ARTIFICIAL INTELLIGENCE (AI)

The authors used Grammarly Pro (Superhuman Platform Inc., San Francisco, USA) to improve the language and readability of the manuscript. The authors reviewed and edited the content and take full responsibility for its accuracy. No images were generated or manipulated using AI tools.

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Concepts or ideas	x	x	x	x	x	x	x	x
Design	x	x			x			
Definition of intellectual content	x						x	x
Literature search	x	x	x	x	x	x	x	x
Experimental studies								
Data acquisition	x	x	x	x	x	x	x	x
Data analysis	x	x		x			x	x
Statistical analysis								
Manuscript preparation	x	x	x	x	x	x	x	x
Manuscript editing	x	x					x	x
Manuscript review	x	x	x	x	x	x	x	x

Citation Format: Gagaa M, Esquivel-García R, Velázquez-Hernández ME, Bermúdez-Camps IB, García-Pérez M, Rodríguez-Orozco AR, Reyes-Hernández I, García-Pérez ME (2026) Adverse events and potential herb-drug interactions of plants used for psoriasis: A systematic review. J Pharm Pharmacogn Res 14(2): 2405. https://doi.org/10.56499/jppres_14.2.2405

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