Herbal medicine for psoriasis and their molecular targets: A systematic review

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Psoriasis is an incurable, chronic, recurrent immune-mediated inflammatory dermatosis characterized by epidermal hyperplasia and excessive infiltration of inflammatory cells into the dermis and neovascularization. The study aimed to provide a systematic review on the in vitro, in vivo, and clinical studies to support traditional uses of herbal medicine for psoriasis treatment. The systematic review was performed by combining three databases, that is, PubMed, ScienceDirect, and Scopus, using the search terms “Psoriasis” AND “Herbal medicine” AND/OR “Traditional medicine.” Full-text articles included after the screening were further evaluated by applying the predefined eligibility criteria. One hundred and twenty research articles were included in the analysis. The included articles involve 94 herbs used as a single herbal extract (n=58 plants) or isolated compounds (n=54 compounds) or as compositions in traditional medicine formulas (n=24 formulas). Most were related to plants or recipes used in Traditional Chinese Medicine (TCM) (63 articles and 207 plants). Research targeting inflammatory and proliferative processes in disease pathogenesis, development, and progression has been an extensive area. The antipsoriasis activity of most plants was mainly through the effects on inflammatory molecules and signaling pathways and immune cells (T-cells, dendritic cells, monocytes, neutrophils, and macrophages), as well as apoptotic molecules and signaling pathways. Plants targeting other signaling molecules should be further investigated.

Key words: Psoriasis, herbal medicine, inflammation, signaling pathways, immunomodulation.

INTRODUCTION

Psoriasis is an incurable, chronic, recurrent immune-mediated inflammatory dermatosis characterized by epidermal hyperplasia and excessive infiltration of inflammatory cells into the dermis and neovascularization (Mason et al., 2013). Clinical presentation includes erythematous scaly rash patches (itching and flaking skin) that affect the scalp, trunk, extensor surfaces of the limbs, and the genital area. The global prevalence rate is
approximately 2-3% (Parisi et al., 2013). Although the disease seldom leads to death, it significantly impairs the quality of life due to chronic complications, that is, pruritic erythema and thick loose scales, as well as comorbidities such as arthritis, cardiovascular diseases, metabolic disorders, and psychological depression (Scheiba et al., 2011). Multiple factors such as genetics, inflammation, metabolism, autoimmunity, environment, and infection are associated with psoriasis (Ayala-Fontanez et al., 2016).

Current knowledge on the pathogenesis of psoriasis, however, remains incomplete. Although the molecular mechanisms involved are complex, growing evidence suggests that significant pathological changes are abnormal proliferation and differentiation of epidermal keratinocytes, excessive infiltration of the immune/inflammatory cells-- T cells (Th17, Th1, and Th2), dendritic cells (DCs), macrophages and neutrophils and increased skin angiogenesis (Chamian et al., 2004). The sequence of pathological events in psoriasis is thought to start with an initiation phase in which triggering factors (e.g., skin trauma, infection, drugs, strong sunlight, physiological stress, and smoking) lead to activation of the immune system, followed by the maintenance phase consisting of the chronic progression of the disease (Rendon et al., 2019). The premature maturation of keratinocytes induced by an inflammatory cascade in the dermis results in rapid changes in skin cells. The immune cells move from the dermis to the epidermis and secrete pro-inflammatory cytokines such as IL-1β, IL-6, IL-12, IL-22, IL-23, IL-17A, and IFN-γ (Chan et al., 2006). These inflammatory signals then stimulate keratinocytes to proliferate and secrete cytokines such as IL-1, IL-6, and TNF-α, which signal downstream inflammatory cells to arrive at the site of inflammation and stimulate additional inflammation (Albanesi et al., 2018). Besides, a defect in regulatory T cells and regulatory cytokine IL-10 is also suggested to be involved in psoriasis pathogenesis (Owezarczyk-Saczonek et al., 2018).

The current treatment of psoriasis is limited by adverse drug reactions/toxicity, disease recurrence, and drug resistance. There is no satisfactory or effective cure for psoriasis. The available treatments, both local and systemic, which have to some extent, proved effective are coal tar, Dithranol (anthralin), calcipotriol, corticosteroids, photochemotherapy (PUVA, psoralens with long-wave ultraviolet radiation), retinoids, methotrexate, and other cytostatic drugs (e.g., hydroxyurea and cyclosporine). All have limited clinical efficacy with adverse drug reactions. Patients with mild-to-moderate psoriasis are usually treated with topical treatments, while systemic therapy, monoclonal antibodies, or phototherapy is reserved for patients with the moderate-to-severe disease (Martin et al., 2019). Identification of new and effective antipsoriatic agents with few adverse effects, particularly those from herbal medicine remains a research hotspot in dermatology to date.

The study aimed to provide a systematic review and analysis of the evidence-based research (in vitro, in vivo, and clinical studies) of herbal medicine for psoriasis treatment.

MATERIALS AND METHODS

The systematic review was performed by combining three databases, that is, PubMed, ScienceDirect, and Scopus. The search terms applied were "Psoriasis" AND "Herbal medicine" AND/OR "Traditional medicine." All articles were retrieved and downloaded to the EndNote X9 database (Thomson Reuters Company, Canada) for further analysis. They were initially screened by titles and abstracts to exclude irrelevant articles. Full-text articles included after the screening were further evaluated by applying the predefined eligibility criteria. The inclusion criteria were articles (i) published during 2001 and March 2020; (ii) available as full texts in English; and (iii) with in vitro/in vivo/ex vivo clinical studies related to herbal or traditional medicine with antipsoriasis activity. The exclusion criteria were articles: (i) related to other skin diseases; or (ii) duplicated articles; or (iii) with unclear methodology or insufficient information, or (iv) review articles, letters to the editor, editorials, systematic analysis, or meta-analysis.

Two reviewers extracted data independently and resolved the disparity by discussion and suggestion from the third reviewer. The information obtained for analysis were the first author's name and year of publication, name of plant and part used, traditional use for psoriasis or other diseases, and/or pharmacological activity, tested extract/compound/formulation, objective(s) of the study, type of study (in vitro/in vivo/clinical), and key results and conclusions.

RESULTS

A total of 1,822 articles from PubMed, ScienceDirect, and Scopus databases were downloaded to the EndNote database. Five hundred and seventy-four articles were excluded, and further analysis of the titles and abstracts of the remaining 1,248 articles led to the exclusion of 917 articles (excluded, based on title and abstract). Finally, 120 articles were included in the analysis. The flow diagram of the study inclusion and exclusion is presented in Figure 1, and the study summary is provided in Tables 1 and 2.

The included articles involve 94 herbs used as a single herbal extract (n=58 plants) or isolated compounds (n=54 compounds) or as compositions in traditional medicine formulas (n=24 formulas). Table 3 provides detailed information on the herbal composition in traditional medicine formulas or decoction. Most were related to plants or recipes used in Traditional Chinese Medicine (TCM) (63 articles and 207 plants). Most studies were conducted in vitro (n=31), followed by in vivo (n=30) in animals, and clinical studies in patients with different types of psoriasis (n=18).
DISCUSSION

Molecular signaling associated with psoriasis and potential drug targets

A dysregulated crosstalk between epidermal keratinocytes and immune cells leads to inflammation, abnormal proliferation, and differentiation of keratinocytes, the hallmark of psoriasis (Benhadou et al., 2019). The activation of T cells, DCs and their upregulation of pro-inflammatory factors are considered to mainly affect the pathogenic development of psoriasis (Flatz et al., 2013). The pro-inflammatory cytokines IL-6, IL-23, IL-22, IL-17A, IFN-γ and TNF-α, have an essential role in inflammation and also affect hyperproliferation and terminal differentiation of keratinocytes (Kouris et al., 2014). Other inflammatory mediators, psoriasis-associated genes and the signaling molecules/pathways that significantly accelerate the inflammatory processes of psoriasis include growth factors (TGF-β), arachidonic acid-derived lipid mediators (COX-2, LOX-5, LOX-15, and LTB), IL-23/IL-17 axis, IL-23/Th17 axis, the signal transducers and activators of transcription (STAT) signaling pathway, NF-kB signaling pathway, Janus kinase/signal transducer and activator of transcription (JAK/STAT) pathway, toll-like receptor (TLR), MyD88, TLR-NF-κB inflammasome pathway, TLR7/8-MyD88-NF-κB NLRP3 inflammasome pathway, NF-kB, MAPK, PI3K/Akt inflammasome pathway, p38 MAPK/NF-κB p65 pathway, ERK1/2 pathway, IL-22 and p38 MAPK pathway, CDC6 protein, coiled-coil α-helical rod protein 1 (CCHCR1), Yes-associated protein (YAP), steroidogenic acute regulatory protein (STAR), vitamin D receptor (VDR), intercellular adhesion molecule-1 (ICAM-1), and vascular cell adhesion molecule-(VCAM-1) (Chirioozzi et al., 2018). Angiogenesis is the critical pathological process of psoriasis which is associated with disease development (Creamer et al., 2007). Pathological angiogenesis observed in psoriasis promotes and maintains inflammation, while inflammation is an established inducer.
Table 1. Summary of plants and/or isolated compounds that are used or have been investigated for their antipsoriasis potential that modulate inflammation and immune response. (* indicates the compositions of the formulations which are presented in Table 3).

<table>
<thead>
<tr>
<th>Plant (part)</th>
<th>Note</th>
<th>Tested extract/compound/for modulation</th>
<th>Objective</th>
<th>Type of study</th>
<th>Key results and Conclusion</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acanthus mollis (leaf), Achillea ligustica (leaf), Artemisia arborescens (leaf), Inula viscosa (flowering aerial)</td>
<td>Italian traditional medicine for psoriasis and skin diseases.</td>
<td>Extract (methanol)</td>
<td>To investigate the mechanism underlying antipsoriasis activity (anti-inflammatory activity).</td>
<td><em>In vitro: Human buffy coat</em></td>
<td>Supporting traditional use: inhibition of 5-LOX and COX-1 complemented with an anti-inflammatory activity at the level of NF-κB.</td>
<td>(Bader et al., 2015)</td>
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<tr>
<td>Aloe vera (leaf)</td>
<td>Ayurvedic traditional medicine for psoriasis and others. Antibacterial and wound-healing promoters. Anti-inflammatory, anti-oxidant.</td>
<td>0.5% Hydrophilic cream</td>
<td>To evaluate clinical efficacy and tolerability</td>
<td><em>Clinical: Patients with psoriasis (n=60)</em></td>
<td>Safe and effective alternative treatment for psoriasis (significant clearing of psoriasis plaques- 82.8%, and decreased of PASI score)</td>
<td>(Syed et al., 1996)</td>
</tr>
<tr>
<td>Alpha Oasis (AO) extract consisting of 10 medicinal herbs*</td>
<td>Medicinal herb for anti-inflammatory.</td>
<td>Alpha Oasis extract</td>
<td>To investigate anti-inflammatory activity on inhibition of pro-inflammatory factors TNF-α by macrophage cells.</td>
<td><em>In vivo: Balb/c mice (IMQ-induced psoriasis model)</em></td>
<td>Potential for inflammatory diseases including psoriasis through inhibiting TNF-α secretion of macrophages.</td>
<td>(Ye et al., 2016)</td>
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<tr>
<td>Alpinia galangal (rhizome), Annona squamosa (leaf) Curcuma longa (rhizome)</td>
<td>Thai traditional medicine for skin diseases.</td>
<td>Extracts (ethanol)</td>
<td>To investigate the molecular mechanism of antipsoriasis action through the involvement of NF-κB signaling network biomarkers associated with psoriasis after treatment.</td>
<td><em>In vitro: HaCaT cell</em></td>
<td>Downregulation of NF-κB signaling molecules, reflecting potential use in diseases with inflammation and hyperproliferation. - A. galangal: regulation of NF-κB networks via decreasing expression of CSF-1 and NF-κB2 while increasing TNFAIP3 expression. - C. longa: decrease of expression of CSF-1, IL-8, NF-κB2, NF-κB1 and RelA - A. squamosa: reduction of CD40 and NF-κB expression</td>
<td>(Saeelee et al., 2011)</td>
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<tr>
<td>Amphipterygium adstringens (bark)</td>
<td>Mexican traditional medicine for psoriasis and inflammatory diseases</td>
<td>Pyrolytic oils</td>
<td>To characterize pyrolytic fractions and mechanisms of antipsoriasis action on IL-8 production in IL-17 stimulated HaCaT keratinocytes</td>
<td><em>In vitro: HaCaT cell</em></td>
<td>Inhibitory effects on IL-8 production, suggesting their potential role for treating IL-17 driven dermatological diseases, including psoriasis.</td>
<td>(Esquivel-Garcia et al., 2020)</td>
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<tr>
<td>Andrographis paniculata (leaf, aerial part)</td>
<td>Anti-inflammatory disorders.</td>
<td>Andrographolide compound</td>
<td>To investigate antipsoriasis action through anti-inflammatory activity.</td>
<td><em>In vivo: Male C57/BL6 mice (IMQ-induced psoriasis model)</em></td>
<td>Antipsoriasis action: Inhibition of LPS /IMQ signaling transduction via inducing autophagic proteolysis of myeloid differentiation factor 88 (MyD88), and thus, inhibition of the production of multiple pro-inflammatory cytokines in dendritic cells.</td>
<td>(Shao et al., 2016)</td>
</tr>
</tbody>
</table>
### Table 1. Cont’d

<p>| <strong>Antrodia cinnamomea (fruit)</strong> | Taiwanese traditional medicine for diarrhea, food and drug poisoning, hypertension, abdominal pain, pruritus, liver dysfunction, cancer. Anti-inflammatory, anti-oxidant, anticancer, hepatoprotective, antifatigue, vasorelaxation. | Extract (ethanol) | To investigate the effect on suppression of Th17 cell differentiation and anti-psoriasis activity. | In vivo: C57BL/6 &amp; BALB/c mice (IMQ-induced psoriasis model) | The potential role for treatment of psoriasis by acting through inhibition of Th17 cell differentiation by blocking STAT3 activity. | (Li et al., 2015) |
| <strong>Bai Xuan Xia Ta Re Pian</strong> (consisting of 7 herbs)* | TCM for psoriasis, ringworm, tinea vesicolor, atopic dermatitis, shingles, acneembolism. | TCM formula | To investigate potential active constituents and mechanism of antipsoriasis action. | In vitro: HaCaT cell &amp; in vivo: Balb/c mice (IMQ-induced psoriasis model) | Potential for treatment psoriasis by acting on multiple targets and pathways synergistically through inhibition of IL-17- related inflammatory pathways. Eleven out of 75 isolated compounds might be active constituents. | (Pang et al., 2018) |
| <strong>Betulinic acid (pentacyclic triterpenoid from plant species, e.g., birch tree, birch bark oil, and paenoriaceae)</strong> | Anti-inflammatory, anticoagulant, antifibrotic, anti-angiogenesis, anti-oxidant. | 3β-hydroxy-20(29)-en-28-oic acid | To investigate anti psoriasis activity and mechanism of action through the immunosuppressant activity. | In vivo: Balb/c &amp; C57BL/6 mice (IMQ-induced psoriasis model) | Immunosuppressant for psoriasis (NF-κB inhibitor); mainly through suppressing Th17 response by reducing the frequency of IL-17 expressing CD4+ and γδT cells, as well as inhibition of pro-inflammatory cytokines (RORγt, IL-17A, IL-6, and TNF-α), suppression of NF-κB signaling) without cytotoxic effect. | (Lu et al., 2019) |
| <strong>Boswellia carteri</strong> (resin) | TCM for psoriasis, asthma, cancer, inflammation, analgesia, colitis, arthritis. Antioxidant, anti-inflammatory. | Acetyl-11-keto-β-boswellic acid | To investigate antipsoriasis action on activation of dendritic cells | In vivo: Balb/c mice &amp; C57 mice (IMQ-induced psoriasis model) | Potential for treatment of psoriasis by inhibition of the activation of TLR8 and IRF signaling pathways. | (Wang et al., 2018) |
| <strong>Caesalpinia bonduc (leaf)</strong> | Indian traditional medicine for psoriasis | Decoction and hydroalcoholic extract | To investigate antipsoriasis activities | In vitro: HaCaT cell &amp; in vivo: Albino mice (Mouse tail model) | Supporting traditional use in psoriasis. Only hydroalcoholic extract: good activity in vitro and in vivo, and inhibitory effect on lipooxygenase. Others: the varying degree of activity. | (Muruganathan tham et al., 2011) |
| <strong>Chunghyuldan</strong> (consisting of 5 herbs)* | Traditional medicine for hyperlipidemia, ischemia, antioxidant. | Formula Extract (ethanol) | To investigate activity in chronic psoriatic dermatitis through anti-inflammatory activity | In vivo: Balb/c mice (Oxazolone-induced mouse dermatitis model for chronic psoriatic dermatitis) | Improvement of contact dermatitis or psoriasis through regulation of COX-2 produced by macrophage cells and TNF-α and IL-4 produced by Th cells. | (Woo et al., 2005) |
| <strong>Cimicifuga simplex</strong> (root) | TCM for anti-inflammatory, antiviral. | 9,19-Cycloartenol glycoside G3 compound | To investigate antipsoriasis activity through an inhibitory effect on immune response (RORY IL-17 Th17 and CD4 CD25) | In vivo: Mice | Anti-inflammatory effect on suppression of pathogenic CD4+ T cell differentiation and IL-17/RORγt/IL-10/FoxP3 ratio. | (Su et al., 2017) |
| <strong>Citrus plants (fruit peel) and Silkworm Bombyx mori</strong> | TCM for anti-inflammation, anticancer, obesity, hyperglycemia, hyperlipidemia. | Naringin extract, Sericin | To investigate antipsoriasis activity mechanism of action through anti-inflammatory activity | In vitro: Human PBMCs | Potential for use as a complementary therapy with conventional treatment of psoriasis: - each and combination: downregulation of pro-inflammatory cytokines (TNF-α, IL-6, IL-23, IL-12p40) associated with psoriasis. | (Deenonpoe et al., 2019) |
| <strong>Cnidium officinale</strong> (rhizome) | Female genital anti-inflammatory diseases. Anti-anemia, antifungal, sedative, smooth muscle relaxing. | Extract (methanol) and isolated compounds | To investigate protective effects in skin disorder models through anti-inflammatory activity | In vivo: Balb/c mice (IMQ-induced psoriasis model) | Potential for psoriasis treatment by reduction of inflammatory signals including IFN-γ, c-fos, and kB-α. | (Lee et al., 2018) |</p>
<table>
<thead>
<tr>
<th>TCM Name</th>
<th>TCM Formula</th>
<th>TCM Role</th>
<th>Antipsoriasis Activity</th>
<th>References</th>
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<tr>
<td>Conifers (Pinus massoniana Lamb (resin))</td>
<td>Rosin (water-boiled)</td>
<td>To investigate antipsoriasis activity through anti-inflammatory activity</td>
<td>In vivo: Balb/c mice</td>
<td>Antipsoriasis activity through inhibition of differentiation and cytokine expression of the inflammatory cells, in particular, Th17 cell differentiation and cytokine secretion of IL-23, IL-17A, and IL-17F in the IL-23/IL-17. (Li et al., 2019)</td>
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<tr>
<td>Cruciferous vegetables</td>
<td>1-(4-Chloro-3-nitrobenzenesulfonyl)-1H-indol-3-yl-methanol (indole-3-carbinol natural) topical formulation</td>
<td>To investigate the molecular mechanism of antipsoriasis through anti-inflammatory and anti-oxidant activities</td>
<td>In vivo: Balb/c mice (IMQ-induced psoriasis model)</td>
<td>Antipsoriasis through suppression of cytokine expression through inhibition of MAPKs, NF-κB, and AP-1. Advantage: targeting of multiple signaling, facile absorption into the skin, ease of manufacturing, and scale-up. (Weng et al., 2019)</td>
</tr>
<tr>
<td>Curcuma longa (rhizome)</td>
<td>Curcumin compound</td>
<td>To investigate the mechanism of antipsoriasis activity</td>
<td>In vitro: PBMCs</td>
<td>Potential for treatment of psoriasis: - inhibiting hKv1.3 channel - inhibiting the activation of T-cells and reducing the expression of inflammatory cytokines IL-2 and IFN-γ - safe with no toxicity to kidneys (Kang et al., 2016)</td>
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<tr>
<td>Curcuma kwangsiensis (rhizome)</td>
<td>Curcumin-loaded hyaluronan (HA)-modified ethosomes (HA-ES)</td>
<td>To develop HA-modified ethosomes as a novel nano-topical delivery system (to improve permeation of curcumin) targeting CD44 in the inflamed epidermis and evaluate the antipsoriasis activity</td>
<td>In vivo: C57BL6 mice (IMQ-induced psoriasis, Skin retension, and Permeability models)</td>
<td>HA-modified ethosomes with propylene glycol was successfully developed as a novel drug carrier for curcumin. Targeting CD44 protein, which is overexpressed in inflamed psoriatic skin. (Zhang et al., 2019)</td>
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<tr>
<td>Dang-Gui-Liu-Huang Tang (consisting of 7 herbs)*</td>
<td>Diarylheptanoid compound</td>
<td>To investigate the effects on major immunological functions of dendriticcells.</td>
<td>In vivo: Dendritic cells from mouse bone marrow and spleen</td>
<td>Modulation of multiple functions of dendritic cells in the immuno-pathogenesis of psoriasis, including antigen uptake, maturation, migration, pro-inflammatory cytokines production, and finally attenuated the proliferation and differentiation of Th subsets and their effector cytokine production. (Liu et al., 2018)</td>
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<tr>
<td>Berberine (principle compound)</td>
<td>TCM formula and Berberine (principle compound)</td>
<td>To investigate antipsoriasis activity and underlying mechanism of action</td>
<td>In vitro: HaCaT cell</td>
<td>Formula: a possible treatment for psoriasis. Berberine hydrochloride: a useful component of ointment-based treatment: - suppressing the production of Th17 cytokines like IL-22 and the induction of CCL20, a chemokine that regulates Th17 cell migration to skin lesions. - inhibiting the proliferation markers K16 and K17. (Nguyen et al., 2018)</td>
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<tr>
<td>Berberine (principle compound)</td>
<td>To investigate CDC6 (one of the key regulators in DNA replication) expression in psoriatic skin; evaluate its function in the proliferation of human keratinocytes; evaluate the antipsoriasis activity</td>
<td>In vitro: HaCaT cell</td>
<td>CDC6 protein: required for cell proliferation in keratinocytes. Berberine: decrease of CDC6 expression and inhibition of proliferation of keratinocytes via suppressing JAK-STAT3 pathway, and CDC6 upregulation. (Sun et al., 2019)</td>
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<tr>
<td>Plant/Extract</td>
<td>Use</td>
<td>Methodology</td>
<td>In Vivo</td>
<td>Comments</td>
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<td>Datura metel L. (flower)</td>
<td>TCM for pain, asthma, rhematism, coughs, convulsions, etc.</td>
<td>Extract (alcohol)</td>
<td>To investigate antipsoriasis activity and underlying mechanism of anti-inflammatory action.</td>
<td><em>In vivo</em>: C57BL/6 mice (IMQ-induced psoriasis model)</td>
</tr>
<tr>
<td>Witaxanolides compounds</td>
<td>To investigate anti-inflammatory effect mechanism of antipsoriasis</td>
<td><em>In vivo</em>: HaCaT Cell</td>
<td>Withanolides alleviated IMQ-induced epidermal hyperplasia and inflammatory cell infiltration via suppressed the activation of STAT3, ERK1/2 and p38 signaling pathways</td>
<td>(Li et al., 2019)</td>
</tr>
<tr>
<td>Enicostema axillare (whole plant)</td>
<td>Indian traditional medicine for psoriasis.</td>
<td>Extract (methanol)</td>
<td>To investigate antipsoriasis action through the immunomodulatory activity</td>
<td><em>In vivo</em>: Swiss albino &amp; C57BL6 mice</td>
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<tr>
<td>Eucalyptus saligna (rocket seeds)</td>
<td>Anticarcinogenic, anti-inflamatory, anti-proliferative.</td>
<td>4-Methylthiobutylisothiocyanate (MTBI)</td>
<td>To investigate the effects of MTBI and synthesized compounds on the growth and cell cycle of HaCaT keratinocytes and THP-1 monocytes</td>
<td><em>In vitro</em>: HaCaT</td>
</tr>
<tr>
<td>Euphorbia kansui Radix (root)</td>
<td>Edema, ascites, asthma. Antiviral, antiproliferative, immunomodulatory.</td>
<td>Extract (ethanol)</td>
<td>To investigate antipsoriasis activity and underlying mechanism of action through the immunomodulatory activity</td>
<td><em>In vivo</em>: Balb/c mice (IMQ-induced psoriasis model)</td>
</tr>
<tr>
<td>Evodia rutaecarpa (fruit)</td>
<td>TCM for anti-inflammatory, antiallergic and immunosuppressive.</td>
<td>Rutaecarpine compound</td>
<td>To investigate the function and mechanism of antipsoriasis activity</td>
<td><em>In vivo</em>: Balb/c mice (IMQ-induced psoriasis model)</td>
</tr>
<tr>
<td>Glycyrrhiza glabra (licorice plant) (root)</td>
<td>TCM for allergic diseases. Anti-ulcer.</td>
<td>Glycyrrhizin (glycoconjugated triterpene)</td>
<td>To investigate antipsoriasis activity and mechanism of action</td>
<td><em>In vitro</em>: HaCaT cell</td>
</tr>
<tr>
<td>Ilicium verum (fruit)</td>
<td>Spice</td>
<td>Extract (ethanol)</td>
<td>To investigate anti-inflammatory activity and regulatory mechanisms in human keratinocytes.</td>
<td><em>In vitro</em>: HaCaT cell</td>
</tr>
<tr>
<td>Indigo Naturalis (Qing Dai powder from aerial part/stem/leaf of mainly Strobilanthes formosanus Moore or in some cases from Baphicacanthus)</td>
<td>TCM for inflammation including psoriasis infections, inflammatory diseases, leukemia.</td>
<td>Extract (ethanol) and Tryptanthrin (major compound)</td>
<td>To investigate the target genes and pathways involved in antiangiogenesis in psoriasis.</td>
<td><em>In vitro</em>: Chick embryos (Embryonic chick chorioallantoic membrane (CAM) assay)</td>
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<tr>
<td>Topical ointment</td>
<td>To evaluate clinical efficacy in moderate psoriasis</td>
<td>Clinical: Patients with psoriasis (n=16 treated group)</td>
<td>Antipsoriasis activity in moderate psoriasis: through suppression of the IL-17 pathway</td>
<td>(Cheng et al., 2017a)</td>
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<td>Table 1. Cont’d</td>
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<td><strong>Extract (DMSO)</strong></td>
<td><strong>In vitro: HUVEC</strong></td>
<td><strong>Anti-inflammatory activity: suppression of TNF-α-induced VCAM-1 expression via inhibition of AP-1/c-Junactivation.</strong> (Chang et al., 2010)</td>
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<tr>
<td><strong>Topical ointment</strong></td>
<td><strong>Clinical: Patients with psoriasis (plaque-type) (n=51)</strong></td>
<td><strong>A novel, safe, and effective therapy for plaque-type psoriasis.</strong> (Lin et al., 2008)</td>
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| **Extract (methanol)**                                                        | **In vivo: C57BL/6 mice** | **Indole alkaloids: contribution to anti-IL 17 properties of Qing Dai:**  
|                                                                              |                    | - Indigodole C and tryptanthrin: significant inhibition of IL-17 production of Th17 cells  
|                                                                              |                    | - Indigodole A and indirubin: suppressing IL-17 expression (dose dependent) without toxicity toward Th17 and Jurkat cells, respectively.** (Lee et al., 2019) |
| **Extract and its threemajor ingredients (Indirubin, Indigo, Tryptanthrin)** | **In vitro: Human keratinocytes** | **Extract: enhancing claudin-1 expression and tight junction function in HaCaT cell.**  
|                                                                              | **In vitro: Human skin** | **3 compounds: synergistic effect on upregulating tight junction function.** (Lin et al., 2013) |
| **Extract and its threemajor ingredients (Indirubin, Indigo, Tryptanthrin)** | **In vitro: Human neutrophils** | **Indigo Naturalis, indigo, and tryptanthrin inhibited O2− generation and elastase release in FMLP/CB activated human neutrophilic, at least in part mediated by inhibition of MAPK activation and regulation of calcium mobilization.** (Lin et al., 2009) |
| **Lindiol (extract in oil for topical use)**                                 | **Clinical: Patients with nail psoriasis (n=31 for treated arm)** | **Effective and safe for therapy of nail psoriasis:**  
|                                                                              |                    | - reducing NAPSI scores were superior to the control group (olive oil), with no adverse events during the 24 weeks of treatment.** (Lin et al., 2014) |
| **Lindiol (extract in oil for topicaluse)**                                  | **Clinical: Patients with nail psoriasis (n=33)** | **Safe and effective alternative therapy for psoriatic nails, with the greatest efficacy on onycholysis and sublingual hyperkeratosis, which arise from hyperproliferation, hyperkeratosis, and parakeratosis of the nail bed, through:**  
|                                                                              |                    | - regulating proliferation and differentiation of epidermal keratinocytes  
|                                                                              |                    | - restoring the epidermal barrier function  
|                                                                              |                    | - inhibiting of inflammatory reactions** (Lin et al., 2015) |
| **Topical ointment**                                                          | **Clinical: Patients with plaque-type psoriasis (n=14)** | **Topical Indigo Naturalis ointment: a novel, safe and effective therapy for psoriasis, at least in part by modulating the proliferation and differentiation of keratinocytes in the epidermis, as well as inhibiting the infiltration of T-lymphocytes and subsequent down-regulation of IL-17 pathway.** (Lin et al., 2007) |
Table 1. Cont’d

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<tr>
<th>Medicinal plant</th>
<th>TCM for</th>
<th>Formula (water extract)</th>
<th>To investigate the anti-psoriatic activity through anti-inflammatory action on human neutrophils</th>
<th>In vitro: Human neutrophils</th>
<th>Effective modality to improve the treatment of patients with psoriasis through antineutrophilic inflammatory effects.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paeonia lactiflora (root)</td>
<td>TCM for anti-inflammation and immunomodulation</td>
<td>Paeoniflorin (main active ingredient)</td>
<td>To investigate the mechanism of antipsoriatic activity</td>
<td>Balb/c &amp; C57BL/6 mice (IMQ-induced psoriasis model)</td>
<td>Antipsoriasis activity by inhibiting Th17 cell response (STAT3 phosphorylation and RORγt expression) and cytokine secretion.</td>
</tr>
<tr>
<td>PAMs (Chinese natural and folk medicinal plants Consisting of 4 medicinal herbs)*</td>
<td>TCM for prevention of wound infection and festering, cell necrosis, dry gangrene, and blood circulation obstacles</td>
<td>extract (ethanol)</td>
<td>To investigate the underlying mechanism of antipsoriatic action</td>
<td>In vitro: HaCaT cell</td>
<td>A promising candidate for inflammatory skin disorders including psoriasis by inhibition of translocation of NF-κB and production of inflammatory cytokines (IL-8, IL23, TNF-α, and ICAM-1).</td>
</tr>
</tbody>
</table>

of angiogenesis (Costa et al., 2007).

The role of herbal medicine in psoriasis

Complementary and alternative medicine is a common option in self-medicating patients who have psoriasis, with 30-40% of patients using or having used these remedies in combination with conventional psoriasis therapy (Jensen et al., 1990). Herbs used in traditional medicines for psoriasis include mainly those from Asia, particularly China (traditional Chinese medicine: TCM), India (Ayurveda), and Thailand. Some are also used in traditional medicines in European countries and Mexico (Shenefelt, 2011). Nevertheless, their traditional use was, in most cases, arbitrary, without scientific proof of their
Table 2. Summary of plants and/or isolated compounds that are used or have been investigated for their antipsoriasis potential that action on apoptosis, cell differentiation, angiogenesis and anti-oxidative stress. (* indicates the compositions of the formulations which are presented in Table 3).

<table>
<thead>
<tr>
<th>Plant (part)</th>
<th>Note</th>
<th>Tested extract/compound/formulation</th>
<th>Objective</th>
<th>Type of study</th>
<th>Key results and Conclusion</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angelica dahlia (root), Angelica pubescens (root), Angelica sinensis (stem), Astragalus membranaceus (root), Atractyloides macrocephala (root), Codonopsis pilosula (root), Coptis chinensis (root), Curcuma aromatica (rhizome), Forsythia suspensa (fruit), Lentinus edodes (fruiting body), Paeonia lactiflora (root), Phellodendron amurense (root bark), Poria cocos (sclerotia), Rehmannia glutinosa (root), Scutellaria baicalensis (root)</td>
<td>TCM for inflammation.</td>
<td>Extract (water, methanol, or ethanol)</td>
<td>To investigate anti-inflammatory activities to support antipsoriasis activity.</td>
<td>In vitro: Human buffy coat</td>
<td>Potential for treatment of psoriasis with anti-inflammatory activity.</td>
<td>(Prieto et al., 2003)</td>
</tr>
<tr>
<td>Artemisia anomala S. (aerial part)</td>
<td>TCM for wound healing, pain, bacterial infections.</td>
<td>Extract (suspended in acetone: 15:1), and sonicated with ultrasound for 30 min to yield the extracts.)</td>
<td>To investigate anti-proliferative and anti-oxidative activities to support antipsoriasis activity and mechanism of action</td>
<td>In vitro: HaCaT cell</td>
<td>A promising candidate for psoriasis: - increasing cell viability and antioxidant capacity via activation of AMPK pathway. - inhibiting cell apoptosis via activation of caspase pathways.</td>
<td>(Gao et al., 2016)</td>
</tr>
<tr>
<td>Averrhoa carambola L. (leaf)</td>
<td>Headaches, vomiting, coughing, hangovers, appetite stimulant, diuretic, antidiarrheal, anti-eczemas, anti-diabetes.</td>
<td>Extract (ethanol) &amp; its n-butanol, ethyl acetate fractions</td>
<td>To investigate the potential anti-inflammatory activity to support antipsoriasis activity.</td>
<td>In vivo: Swiss male mice (Croton oil-induced ear edema model)</td>
<td>All: effective in reducing edema and cellular migration of polymorphonuclear leukocytes, supporting the use in inflammatory skin disorders, including psoriasis.</td>
<td>(Cabrini et al., 2011)</td>
</tr>
<tr>
<td>Caesalpinia bonduc (leaf)</td>
<td>Indian traditional medicine for psoriasis</td>
<td>Decoction and hydroalcoholic extract</td>
<td>To investigate antipsoriasis activities</td>
<td>In vitro: HaCaT cell</td>
<td>Supporting traditional use in psoriasis. Only hydroalcoholic extract: good activity in vitro and in vivo, and inhibitory effect on lipoxygenase. Others: the varying degree of activity.</td>
<td>(Murugan antham et al., 2011)</td>
</tr>
</tbody>
</table>
### Table 2. Cont’d

<table>
<thead>
<tr>
<th>Plant Species</th>
<th>Medicinal Use</th>
<th>Extracts</th>
<th>Method</th>
<th>Activity/Model</th>
<th>Supporting Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cassia angustifolia (leaf), Corpis chinensis (root), Phellodendron amurense (root bark), Rhem palmatum (root), Scutellaria baicalensis (root)</td>
<td>Asian traditional medicine for skin diseases.</td>
<td>Extracts (ethanol)</td>
<td>To investigate anti-inflammatory activities</td>
<td>In vivo: Swiss mice (TPA-induced ear edema model, Arachidonic acid-induced ear edema model, Oxazolone-induced contact-delayed type hypersensitivity model, DTH-induced ear edema model)</td>
<td>Supporting inflamed skin diseases: All: anti-inflammatory activities and activities on edema with different degrees and spectrum. None: activity on Phospholipase A2. (Cuellar et al., 2001)</td>
</tr>
<tr>
<td>Celastrus orbiculatus (leaf)</td>
<td>TCM for psoriasis.</td>
<td>Celastrol Compound</td>
<td>To evaluate the mechanism of antiproliferative activity</td>
<td>In vitro: HaCaT cell</td>
<td>Induction of apoptosis of keratinocytes via both death receptor (inhibition of NF-κB activity) and mitochondrial pathway. (Zhou et al., 2011)</td>
</tr>
<tr>
<td>Centella asiatica (leaf), and psoralen-containing seeds of Psoralea corylifolia and synthetic compound dithranol</td>
<td>Ayurvedic medicine &amp; TCM for skin diseases including psoriasis and vitiligo.</td>
<td>Extracts (water)</td>
<td>To investigate antipsoriasis activity</td>
<td>In vitro: SVK-14 keratinocyte cell</td>
<td>Topical antipsoriasis: worthy of further investigation. Antipsoriasis activity: interpenoid glycosides madecassoside and asiaticoside rather than phenolic compounds. (Sampson et al., 2001)</td>
</tr>
<tr>
<td>Celastrus paniculatus (seed)</td>
<td>Ayurvedic medicine for psoriasis.</td>
<td>Extract (Soxhlet apparatus using petroleum ether as a solvent)</td>
<td>To investigate preventive role against psoriasis-like dermatitis</td>
<td>In vivo: Balb/c mice (IMQ-induced psoriasis model)</td>
<td>Marked attenuation of symptoms and processes underlying psoriasis-like dermatitis. (Arora et al., 2016)</td>
</tr>
<tr>
<td>Citrus reticulate (Tangerine, peels)</td>
<td>TCM for anti-inflammation, anticancer, obesity, hyperglycemia, hyperlipidemia.</td>
<td>Hesperidin compound</td>
<td>To investigate antipsoriatic activity</td>
<td>In vivo: Balb/c mice (IMQ-induced psoriasis model)</td>
<td>Therapeutic value for the prevention and treatment of psoriasis: improvement of psoriasis-like skin lesion, reduced epidermal thickness, decreased proliferation, and differentiation of epidermal cells, inhibited expression of inflammatory factors, reduced local skin lesions and serum insulin and glucose levels, modulated signaling pathway and regulates keratinocyte metabolism. (Li et al., 2019)</td>
</tr>
<tr>
<td>Convallaria majalis (seed)</td>
<td>Slowing and regulating heart rate.</td>
<td>Convallatoxin (98%)</td>
<td>To investigate the mechanism of antipsoriasis action</td>
<td>In vitro: HaCaT cell</td>
<td>Potential for treatment of psoriasis by suppression of keratinocyte hyper-proliferation through ROS-mediated necroptosis. Antipsoriasis activity on both mouse models. (Jiang et al., 2020)</td>
</tr>
<tr>
<td>Gloriosa superba (root) and Catharanthus roseus (leaf)</td>
<td>TCM: G. superba for intestinal worms, bruises, infertility, joint pain, cancer. Kapha and Vata conditions, skin problems. C. roseus for menorrhagia, diabetes, hypertension, cancer.</td>
<td>Extract (ethanol)</td>
<td>To investigate the mechanism of antipsoriasis action through the effect on the expression of the psoriatic marker, keratin17 (K17)</td>
<td>In vitro: HaCaT cells</td>
<td>Antipsoriasis activity of both extracts through suppression of K17 and p-STAT3 expression (G. superba, more active). (Pattarachotanant et al., 2014)</td>
</tr>
<tr>
<td>Gynura pseudochina DC hispida Thv (leaf)</td>
<td>Herpes zoster, abscesses, thermal burn.</td>
<td>Extract (methanol)</td>
<td>To investigate clinical efficacy and safety</td>
<td>Clinical: Patients with mild-to-moderate chronic plaque psoriasis (n=25)</td>
<td>Improvement of psoriasis lesions, similarly to 0.1% TA cream, with minimal short-term side effects. (Rerknimitr et al., 2016)</td>
</tr>
</tbody>
</table>
### Table 2. Cont’d

<table>
<thead>
<tr>
<th>Herbal Anti-inflammatory Treatment (HAT1: consisting of 25 plants)*</th>
<th>Herbal extracts for inflammation</th>
<th>Topical spray formulation (20% extract in a 5% ethanol solution)</th>
<th>To investigate relative safety and efficacy in comparison to calcipotriol</th>
<th>Clinical: Adult patients with mild-to-moderate psoriasis (n=28)</th>
<th>Effective and safe topical therapy for psoriasis.</th>
<th>(Alex et al., 2019)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hippophae rhamnoides</strong> (Sea buckthorn) (fruit)</td>
<td>Anti-atherogenic, hypoglycemic, anti-aggregant, antioxidant, antibacterial, anti-ulcer, anti-inflammatory, antihypertensive, anticancer. Beneficial effects in hepatic disease wound healing, atopic dermatitis and radiation protection.</td>
<td>Extract (topical oil)</td>
<td>To evaluate the effect on psoriasis lesions in previously untreated patients</td>
<td>Clinical: Patients with mild-to-moderate psoriasis (n=10)</td>
<td>Improvement of psoriasis area severity index (PASI) score.</td>
<td>(Boca et al., 2019)</td>
</tr>
<tr>
<td><strong>Jueyin</strong> (consisting of 8 herbs)*</td>
<td>TCM for psoriasis</td>
<td>Formula (water extract-alcohol)</td>
<td>To investigate the mechanism of antipsoriasis activity</td>
<td><em>In vivo</em>: C57BL/6 (IMQ-induced psoriasis model)</td>
<td>Effective antipsoriasis through inhibition of keratinocyte proliferation and reduction of NO and MDA expression. Further study required to identify the main functional composition, clarify molecular mechanisms responsible for antiproliferation and anti-inflammation.</td>
<td>(Ma et al., 2014)</td>
</tr>
<tr>
<td><strong>Leguminous plants</strong> <em>Sophora flavescens</em> Ait (root), <em>Sophora alopecuroides</em> L (seed), <em>Sophora subprostrata</em> (root).</td>
<td>Oxymatrine: Cancer, hepatitis, cirrhosis. Anti-inflammatory, anti-oxidant, anti-proliferative.</td>
<td>Oxymatrine compound</td>
<td>To investigate underlying mechanisms of antipsoriasis action on cell proliferation and apoptosis.</td>
<td>Clinical: Patients with psoriasis patients (n=79)</td>
<td>Regulation of mitosis and inhibition of the excessive expression of proliferating cell nuclear antigen (PCNA) and Ki-67 in the skin lesions and promotion of the restoration of apoptotic Bcl-2 expression (recovery of the balance between skin cell proliferation, differentiation, and apoptosis).</td>
<td>(Shi et al., 2019b)</td>
</tr>
<tr>
<td><strong>Luteolin flavonoid from Bryophyta, Pteridophyta, Pinophyta, Magnoliophyta</strong></td>
<td>Antioxidant, anti-inflammatory, antimicrobial, anticancer, antiangiogenesis.</td>
<td>Luteolin compound</td>
<td>To evaluate clinical efficacy and potential in treating psoriasis and to explore the mechanism of action (anti-inflammatory action)</td>
<td><em>In vitro</em>: HaCaT cell</td>
<td>Reduction of lesions and symptoms through reversing the effects of IFN-y, inhibition of expression and exosome secretion of HSP90, and regulation of the proportion of immunocytes.</td>
<td>(Lv et al., 2020)</td>
</tr>
<tr>
<td><strong>Mahonia aquifolium</strong> (root and wood)</td>
<td>American traditional medicine for inflammatory skin diseases including psoriasis; berberine is an active principle.</td>
<td>Extract (topical cream)</td>
<td>To investigate the efficacy and safety</td>
<td>Clinical: Patients with mild-to-moderate psoriasis (n=200)</td>
<td>Effective and safe in mild-to-moderate psoriasis.</td>
<td>(Bernstein et al., 2006)</td>
</tr>
</tbody>
</table>
Table 2. Cont’d

<table>
<thead>
<tr>
<th>TCM Formula (decoction)</th>
<th>Health Condition/Treatment</th>
<th>TCM Formula (decoction)</th>
<th>TCM Formula (decoction)</th>
<th>TCM Formula (decoction)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melissa officinalis L. (lemon balm)</td>
<td>Greece traditional medicine for several diseases/conditions including tracheobronchitis, hysteria, epilepsy, heart arrhythmia, hypnotic, skin diseases.</td>
<td>Decoction and fractions</td>
<td>To investigate potential antipsoriatic activity and chemical profile</td>
<td>In vivo: Balb/c mice (IMQ-induced psoriasis model)</td>
</tr>
<tr>
<td>Psoralea corylifolia (seed)</td>
<td>Psoriasis, vitiligo, eczema, alopecia. Cytotoxic, anticancer, antimicrobial, immunomodulatory.</td>
<td>8-Methoxypsoralen (MOP), Psoralen, Isopisoralen, Psoraladin, and Bakuchiol</td>
<td>To find alternative compounds in P. corylifolia and assess percutaneous absorption, antiproliferative activity, and ability to improve psoriasis-like lesions for PUVA (ultraviolet A) therapy</td>
<td>In vitro: HaCaT cell</td>
</tr>
<tr>
<td>Psor p27 (consisting of 11 herbs for systematic treatment and consisting of 3 for herbal bath)*</td>
<td>TCM for psoriasis</td>
<td>Formula (decoction) and Topical ointment</td>
<td>To investigate the effect on the expression of the psoriasis-associated antigen Psor p27 (associated with acute-phase psoriasis)</td>
<td>Clinical: Patients with psoriasis (n=15)</td>
</tr>
<tr>
<td>Pulian ointment (NPLO: consisting of 2 herbs)*</td>
<td>TCM for psoriasis</td>
<td>Topical ointment</td>
<td>To evaluate clinical efficacy and safety in psoriasis Vulgaris of the blood-heat syndrome</td>
<td>Clinical: Patients with psoriasis Vulgaris of blood-heat syndrome (n=300)</td>
</tr>
<tr>
<td>QoolSkin* (Consisting of 4 herbs)*</td>
<td>TCM formula for psoriasis.</td>
<td>The topical formulation for psoriasis</td>
<td>To investigate the clinical efficacy</td>
<td>Clinical: Patients with chronic plaque psoriasis (n=150)</td>
</tr>
<tr>
<td>Radix rubiae (root and rhizome)</td>
<td>TCM for psoriasis. Antiproliferative.</td>
<td>Extract (ethanol)</td>
<td>To investigate anti-proliferative activity</td>
<td>In vitro: HaCaT cell</td>
</tr>
<tr>
<td>Rubia cordifolia L. (root)</td>
<td>TCM for psoriasis</td>
<td>1,4-dihydroxy-2-naphthoic acid</td>
<td>To investigate antipsoriatic activity</td>
<td>In vitro: HaCaT cell</td>
</tr>
</tbody>
</table>
Table 2. Cont’d

<table>
<thead>
<tr>
<th>Herbal Medicine</th>
<th>Formulation</th>
<th>Characteristics</th>
<th>Activities</th>
<th>Study Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salvia miltiorrhiza Bunge (Danshen) (root)</td>
<td>Cryptotanshinone: anti-inflammatory, antibacterial, anticancer.</td>
<td>Danshenso (major component of Danshen)</td>
<td>To investigate effects on cell proliferation, cell cycle, and apoptosis, including the effect on YAP (yeast-associated protein) expression</td>
<td>In vitro: HaCaT cell</td>
</tr>
<tr>
<td>-</td>
<td>Cryptotanshinone compound</td>
<td>To investigate antipsoriasis activity and mechanism of action</td>
<td>In vivo: C57BL/6J mice (IMQ-induced psoriasis model)</td>
<td>Potential for treatment of psoriasis: mainly through modulating STAT3 and inducing G0/G1 arrest.</td>
</tr>
<tr>
<td>Salvia miltiorrhiza Radix (root)</td>
<td>-</td>
<td>Tanshinone IIA</td>
<td>To investigate the cellular mechanism that leads to cell cycle arrest and apoptosis in psoriasis</td>
<td>In vitro: Primary mouse keratinocytes</td>
</tr>
<tr>
<td>-</td>
<td>Soratinex® Herbal complex (consisting of 22 herbs)**</td>
<td>German topical products</td>
<td>Scalp and body cleansing gel, scalp and body ointment, skin conditioner</td>
<td>To evaluate clinical efficacy and safety</td>
</tr>
<tr>
<td>-</td>
<td>Scutellaria baicalensis (root)</td>
<td>-</td>
<td>Baicalin (5% cream)</td>
<td>To investigate anti-inflammatory activity and keratinocyte differentiation-inducing activity</td>
</tr>
<tr>
<td>-</td>
<td>Shi Du Ruan Gao (consisting of 5 herbs)*</td>
<td>TCM for psoriasis</td>
<td>Formula</td>
<td>To evaluate the efficacy and safety</td>
</tr>
<tr>
<td>-</td>
<td>Sinapis Alba Linn (mustard seed for spice and TCM)</td>
<td>Respiratory and GI diseases</td>
<td>Mustard seed was ground using a mechanical blender and added to the normal forage at the desired concentration of 5%. Forage pellets were then made and stored in a dry and strictly sanitary condition at room temperature.</td>
<td>To investigate antipsoriasis activity</td>
</tr>
<tr>
<td>-</td>
<td>Stellera chamaejasme L. (flower)</td>
<td>-</td>
<td>Extract (ethanol) and its constituents</td>
<td>To investigate the effect on cutaneous wound healing</td>
</tr>
<tr>
<td>-</td>
<td>Taodan granules (consisting of 9 herbs)*</td>
<td>TCM for psoriasis</td>
<td>Formulation</td>
<td>To investigate clinical efficacy, safety, and control of disease recurrence</td>
</tr>
</tbody>
</table>
Table 2. Cont’d

<table>
<thead>
<tr>
<th>Formula</th>
<th>TCM consisting of 11 herbs*</th>
<th>TCM for clearing heat, cooling blood and removing toxic substances combined with acitretin capsule.</th>
<th>To evaluate clinical efficacy and safety in psoriasis of the blood-heat syndrome</th>
<th>Clinical: Patients with psoriasis (n=80)</th>
<th>The combined use of TCM with acitretin capsule: a safe and effective therapy for psoriasis, and worthy of application in clinical practice. (Zhang et al., 2009)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tinospora cordifolia (root, stem, leaf)</td>
<td>Ayurvedic medicine for psoriasis</td>
<td>Extract (aqueous)</td>
<td>To investigate preventive role against psoriasis-like dermatitis</td>
<td>In vivo: Balb/c mice (IMQ-induced psoriasis model)</td>
<td>Marked attenuation of symptoms and processes underlying psoriasis-like dermatitis (Arota et al., 2016)</td>
</tr>
<tr>
<td>Tuhuai formulation (mainly consisting of 6 herbs)*</td>
<td>TCM for psoriasis</td>
<td>Topical extract (ethanol)</td>
<td>To investigate antiproliferative and anti-inflammatory activities and mechanisms of action</td>
<td>In vivo: Female hairless mice (hr/hr) &amp; Male CD-1 mice (TPA-induced epidermal hyperproliferative and Oxazolone-induced ear inflammation models)</td>
<td>Clinically useful in the treatment of psoriasis and other inflammatory dermatoses: - inhibiting epidermal proliferation in an epidermal hyperproliferative model - reducing the development of ear thickness (Man et al., 2008)</td>
</tr>
<tr>
<td>Vernonia anthelmintica Wildt. (fruit)</td>
<td>Indian traditional medicine for skin diseases. Various parts with different activities: anti-inflammatory, anti-oxidant, antimicrobial, anti-diabetic, antivertigo, anticancer.</td>
<td>Extract (methanol) and fatty acid-enriched fractions</td>
<td>To investigate antipsoriasis activity and characterize bioactive fraction(s)</td>
<td>In vitro: HaCaT cell</td>
<td>Antipsoriasis activity: essential fatty acids, primarily linoleic acid, palmitic acid, oleic acid, and stearic acid. (Dogra et al., 2018)</td>
</tr>
<tr>
<td>Wen-tong-hua-yu (consisting of 16 herbs)*</td>
<td>TCM for psoriasis</td>
<td>Formula</td>
<td>To evaluate clinical efficacy, safety, and quality of life in psoriasis compared with methotrexate</td>
<td>Clinical: Patients with psoriasis (n=21 for treated arm)</td>
<td>Antipsoriasis efficacy: not confirmed despite widespread belief and use in TCM for the treatment of psoriasis. Methotrexate: more effective than TCM or placebo throughout 6 months (Ho et al., 2010)</td>
</tr>
<tr>
<td>White mange mixture (consisting of 10 herbs)*</td>
<td>TCM</td>
<td>Formula</td>
<td>To investigate antipsoriasis activity in vaginal psoriasis</td>
<td>In vivo: Mice (Murine model of vaginal psoriasis)</td>
<td>Significant inhibition of vaginal psoriasis by decreasing the amount of epithelium KC (epidermal keratinocyte) cell PCNA (proliferating cell nuclear antigen) and production of inflammatory cytokines GM-CSF in serum (Guo et al., 2019)</td>
</tr>
<tr>
<td>Zhuhuang granule (consisting of 10 herbs)*</td>
<td>TCM modified formulation of Zhuhuang Decotion for psoriasis.</td>
<td>The modified formulation of Zhuhuang Decotion</td>
<td>To evaluate clinical efficacy and safety</td>
<td>Clinical: Psoriasis patients (n=15)</td>
<td>Effective antipsoriasis: reduction of PASI scores. miR-146a and miR-99a: potential biomarkers for disease activity and clinical efficacy in psoriasis patients treated with Zhuhuang (Yang et al., 2016)</td>
</tr>
<tr>
<td>Zanthoxylum nitidum (root)</td>
<td>Anti-inflammatory, antimalarial, antifungal, antiangiogenesis, anticancer.</td>
<td>Nitridine chloride</td>
<td>To investigate antipsoriasis activity and mechanism of action</td>
<td>In vitro: HaCaT</td>
<td>Antipsoriasis activity through inhibition of HaCaT cell proliferation, induction of apoptosis (S phase) through JNK signaling pathway. (Yang et al., 2019)</td>
</tr>
</tbody>
</table>

IMQ-induced psoriasis and TPA-induced epidermal hyperplasia models.
<table>
<thead>
<tr>
<th>Traditional medicine formula</th>
<th>Herbal composition</th>
</tr>
</thead>
<tbody>
<tr>
<td>AO herbal</td>
<td>Consists of 10 herbs Japanese creeper, Chinese honey locust spine, Wooly datchman's pipe, Pubescent angelica, Garden balsam, Cantonese buttercup, Giant typhoniun tuber, Euphorbia, semen hyoscyami and sesame oil</td>
</tr>
<tr>
<td>Bai Xuan Xia Ta Re Pian</td>
<td>Consists of 6 herbs <em>Euphorbiae Humifusae Herba, Chebulae Fructu, Terminalia Belliricae Fructus, Chebulae Fructus Immaturus, Aloe and Resina Scammoniae</em></td>
</tr>
<tr>
<td>Dang-Gui-Liu-Huang Tang</td>
<td>Compose of 7 herbs <em>Angelicae Gigantis Radix, Rehmanniae Radix, Rehmanniae Radix Preparat, Scutellariae Radix, Astragali Radix, Coptidis Rhizoma, and Phellodendri Cortex</em></td>
</tr>
<tr>
<td>HAT1</td>
<td>Consists of 25 herbs <em>Achillea millefolium, Aesculus hippocastanum, Althaea officinalis, Avena sativa, Berberis vulgaris, Cochlearia officinalis, Conium maculatum, Ervum lens, Hamamelis virginiana, Hydrastis canadensis, Malva sylvestris, Matricaria chamomilla, Nasturtium officinale, Phytolacca decandra, Pimpinella saxifraga, Populus alba, Populus tremuloides, Rhus toxicodendron, Sambucus nigra, Sanguinaria canadensis, Scrophularia nodosa, Smilax medica, Tussilago farfara, Veronica officinalis and Vincetoxicum officinale</em></td>
</tr>
<tr>
<td>Kan-Lu-Hsiao-Tu-Tan (KLHTT)</td>
<td>Consists of 11 herbs Soapstone, Artemisia capillaris, Scutellaria baicalensis, Acorus gramineus, Clematis armandii, Fritillaria cimbrica, Forsythia suspensa, Amomum kravanh, Mentha haplocalyx and Belamcanda chinensis</td>
</tr>
<tr>
<td>Jueyin granules</td>
<td>Consists of 8 herbs <em>Haliotis diversicolor, Flos Lonicerae japonicae, Radix Rehmanniae exsiccata, Cortex Moutan, Herba Hedysotisdiffusae, Folium isatidis, Smilax china L and Radix Curcumae</em></td>
</tr>
<tr>
<td>PAMs</td>
<td>Consists of 4 herbs <em>Carthamust inctorius, Lithospermum erythrorhizon, Solanum indicum, and Cymbopogon distans</em></td>
</tr>
<tr>
<td>Psoriasis 1</td>
<td>Consists of 13 herbs <em>rhizoma Smilacis glabrae, Folium isatidis, Radix isatidis, Angelica sinensis, Hedyotis diffusa, Sichuan lovage rhizome, Plantain herb, Fructus kochiae, Chinese lobelia, Nidus vespea, rhizoma alismatis, cortex dictamni and Radix glycyrrhiza</em></td>
</tr>
<tr>
<td>PSORI-CM01</td>
<td>Consists of 7 herbs: <em>Radix Paeonias Rubra, Rhizoma Cucumbra, Sarcandra glabra, Rhizoma Smilacis Glabras, Fructus Mume, Radix arnebias and Radix Glycyrrhizas.</em></td>
</tr>
<tr>
<td>PSORI-CM02</td>
<td>Consists of 5 herbs: <em>Rhizoma curcumae, Radix paeonias rubra, Sarcandra glabra, Rhizoma smilacis glabrae, and Fructus mume</em></td>
</tr>
<tr>
<td>The herbal compounds used for systemic treatment Pso p27</td>
<td>Herbal decoction consists of 11 herbs <em>Rhizoma Smilacis Glabrae, Foliun Isatidis, Rhizoma Menispermi, Oldenlandia, Rhizoma Curcumae, Rhizoma Polygoni Cuspidati, Corru Saigae Tataricae, Gypsum Fibrosum, Herba Solani Lyrat, Herba Duchesneae Indicae, Cornu Saigae Tataricae</em> herbal bath <em>Cacumen Platycladi, Rhizoma Curcumae, Nepal dock root</em></td>
</tr>
<tr>
<td>Pulian ointment</td>
<td>Consists of 2 herbs <em>Phellodendron amurense and Scutellaria baicalensis</em></td>
</tr>
<tr>
<td>QoolSkin (topical)</td>
<td>Consists of: riboflavin, citrus medica limonum (lemon) juice, vinegar, taraxacum officinalis (danadelon) extract, cereus grandiflorus (cactus) flower extract and opuntia coccinellifera fruit extract, ascorbic acid, calcium ascorbate, sodium ascorbate, and tartaric acid</td>
</tr>
<tr>
<td><strong>Table 3. Cont’d</strong></td>
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</tr>
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</tbody>
</table>
| **Soratinex®** | Consists of 25 herbs  
*Prunus amygdalus dulcis*, *Simmondsia chinensis*, *Persea gratissima*, *Daucus carota*, *Calendula officinalis*, *Citrus sinensis*, *Triticum vulgare germ*, *Prunus armeniaca kernel*, *Lavendula augustifolia*, *Santalum album*, *Pogostemon cablin*, *Pelargonium graveolens*, *Rosemary officinalis*, *Dromiceius*, *Citrus ursiumssp bergamia oil*, *Pinus sylvestris leaf oil*, *Chamomilla recutita oil*, *Commiphora myrrha oil*, and *Citrus aurantium amara flower* |
| **Shi Du Ruan Gao** | Consists of 5 herbs  
*Indigo naturalis*, *Cortex Phellodendri*, *Gypsum fibrosum preparatum*, *Calamine*, and *Galla chinensis* |
| **Taodan granules** | Consists of 9 herbs  
*Astragalus adscens Pall*, *Glycyrrhiza glabra*, *Angelica sinensis radix*, *Ligusticum wallichii*, *Prunus persica (L.) Batsch*, *Salvia miltiorrhiza Bunge*, *Curcuma zedoaria (Christm.) Rosc.*, *Achyranthes bidentata Blume*, *Smilax china (L.)* |
| **Tuhuai** | Consists of 6 herbs  
soaking flos sophorae, *smilax glabra roxb*, *Paeonia lactiflora*, *radix scutellariae*, flos  
lonicerate and glycyrrhiza uralensis |
| **Wannachawee Recipe** | Consists of 8 herbs  
*Alpinia galanga (L.) Willd*, *Smilax glabra Wall.exRoxb*, *Smilax corbularia Kunth*, *Smilax sp.*, *Stemonainvoluta Inthachub Stemona collinsiae Craib*, *Rhinacanthus nasutus*, *Acanthus silicifolius L* |
| **Wen-tong-hua-yu** | Consists of 16 herbs  
*Ephedra sinica*, *Acrornitum napellus*, *Sinapis alpa*, *Cinnamomum cassia*, *Zingiber officinale*, *Rehmannia glutinosa*, *Smilax glabra*, *Dictamus dasyacarpus*, *Imperata cylindrica*, *Salvia miltiorrhiza*, *Spatholobus subcactus Dunn*, *Lithospermum officinale*, *Sophora japonica L*, *Glycyrrhiza glabra L.*, *Glycyrrhiza uralensis Fisch*, *Indigofera testacea* |
| **White mange mixture** | Consists of:  
10 g of Fructus amomi, 20 g Figwort, 20 g Chinese Angelica, 20 g *Scutellaria baicalensis*, 20 g Madder, 15 g *Radix Arnebiae*, 25 g *Rhizoma imperatae*, 15 g Honeysuckle, 20 g Cortex Moutan, and 15 g Licorice |
| **Xiaoyin Granules** | Consists of 18 herbs  
| **Yinxieling decoction** | Consists of 7 herbs  
*Radix rehmanniae recen*, *Angelica sinensis*, *Radix paeoniae rubra*, *Ligusticum wallichii*, *Radices lithospermi*, *Curcumza zedoary*, *Chloranthus spica* |
| **Zhuhuang granule** | Consists of 10 herbs  
*Radix Rhapontici (Rhaponticum uniflorum (L.) DC.*), *Gypsum Fibrosum (natural calcium sulfate CaSO4 H2O)*, *Radix Scutellaria (Scutellaria baicalensis Georgi)*, *Rhizoma Coptidis (Coptidis chinensis Franch)*, *Cortex Phellodendri (Phellodendron amurense Rupr)*, *Fructus Gardenia (Gardenia jasminoides Ellis)*, *Radix Bupleuri (Bupleurum chinense DC.)*, *Radix Paeoniae Alba (Paeonia lactiflora Pall.)*, *Radix Ophiopogonis (Ophiopogon japonicus (Thunb.)), and Lophatherus gracile* |
| **TCM consisting of 11 herbs** | Consists of 11 herbs  
10 g dandelion, 12 g forsythia fruit, 30 g isatis root, 15 g isatis leaf, 30 g imperata rhizome, 15 g honeysuckle flower, 15 g prunella spike, 15 g moutan bark, 15 g red and white peony root each, 15 g rehmannia root, and 15 g figwort root |
effectiveness and safety. Besides, their traditional applications vary from country to country without standardization. Further research is needed to clarify their effects and, hopefully, provide new options to psoriasis patients. Interestingly, the results of the systematic review indicate that research on herbal medicine as an alternative treatment for psoriasis is an intensive research area. Various in vitro, in vivo, and clinical study approaches were applied to support their potential clinical uses for psoriasis. For the in vitro study, Spontaneously Transformed Human Keratinocyte Cell Culture (HaCaT) has extensively been used to study the epidermal homeostasis and pathophysiology of psoriasis. Due to their highly similar physiological characteristics to those of normal human keratinocytes, HaCaT cell is a widely used model to study the proliferation and differentiation of human epidermal cells and the pharmacological activity of psoriasis treatment (Deyrieux et al., 2007). The principal model for in vivo studies is the imiquimod (IMQ)-induced psoriasis-like model in mice. IMQ is a toll-like receptor (TLR7/8) agonist which is a potent immune activator that causes activation and maturation of DCs when applied to the skin of mice (Kim, 2009). IMQ-induced psoriasis-like mouse model has been widely used to mimic inflammation-type psoriasis critically dependent on the IL-17 and IL-23 cytokine axis, and these models are of benefit for facilitating research on the mechanisms of potential treatments for psoriasis (Rodriguez et al., 2017). Clinical studies to evaluate the clinical efficacy of herbal medicines in patients with different types of psoriasis are usually based on the primary efficacy parameters, including Psoriasis Area and Severity Index (PASI), DAS28 score, and Disease Activity in Psoriatic Arthritis (DAPSA) (Feldean and Krueger, 2005; Tucker et al., 2019).

The antipsoriasis activities of herbs/herbal medicine were screened or confirmed to support the traditional uses in vitro (Arora et al., 2016; Jiang et al., 2020; Nimisha et al., 2017; Sampson et al., 2001), in vivo (Cabrini et al., 2011; Cuéllar et al., 2001; Jiang et al., 2020; Li et al., 2019; Man et al., 2008; Nishima et al., 2017; Zhang et al., 2019), and clinical studies (Alex et al., 2020; Bernstein et al., 2006; Boca et al., 2019; Cohen et al., 2007; Duan et al., 2019; Ho et al., 2010; Li et al., 2017; Lin et al., 2011; Lin et al., 2014; Lin et al., 2015; Ru et al., 2019; Syed et al., 1996; Wollina et al., 2018; Yan et al., 2015; Yang et al., 2016; Yu et al., 2017; Zhang et al., 2009). TCM plays an important contribution to the research of natural products for psoriasis, followed by Indian traditional medicine (Ayurved). Herbs that have been reported to exert antipsoriasis activities include Angelica spps (Dai et al., 2014), Artemisia anomala (Gao et al., 2019), Astragalus membranace (Deng et al., 2019), Atractyloides macrocephala (Prieto et al., 2003), Bowswellia carteri (Majee et al., 2014), Catharanthus (Pattarachotanant et al., 2014), Cellulastrorobiculatus (Zhang et al., 2018), Cimicifuga simplex (Su et al., 2017), Citrus reticulate (Weng et al., 2016), Codonopsis pilosula (Tang et al., 2012), Coptis chinensis (Tse et al., 2006), Cortex mountan (Na Takauhung et al., 2018; Meng et al., 2019), Curcuma aromatic (Li et al., 2020), Curcuma kwangsinensis (Sarafian et al., 2015), Curcuma longa (Saelee et al., 2011), Datura metel (Yang et al., 2019), Evodia rutaecarpa (Li et al., 2019), Forsythia suspense (Sung et al., 2016), Gloriosa superba (Pattarachotanant et al., 2014), Glycyrrhiza glabra (Xiong et al., 2015), Indigo naturalis (Lin et al., 2015), Lentinus elodes (Prieto et al., 2003), Lithospermum erythrhorizon (Yan et al., 2015), Paeonia lactiflora (Sun et al., 2015), Panax ginseng (Lee et al., 2011), Phellodendron amurenese (Li et al., 2017), Poria cocos (Prieto et al., 2003), Radix rubiae (Tse et al., 2007), Rehmannia tinos (Iliev et al., 2003), Rhododendron brachycarpum (Jeon et al., 2017), Rubia cordifolia (Mok et al., 2013), Ruanunclaceae (Iliev et al., 2003), Salvia mitiorrhiza (Li et al., 2012), Scutellaria baicalensis (Hung et al., 2018), Sinapis alba (Ho et al., 2010), Smilax glabra (Di et al., 2016), and Tripterygium wilfordii (Wu et al., 2015). Most of the investigated plants were those used in TCM directly for psoriasis or inflammatory diseases. Apart from single plants, several TCM formulas for psoriasis were investigated for their antipsoriasis potential and underlying mechanisms of action. These include Bai Xuan Xia Ta Re Pian (7 herbs) (Pang et al., 2018), Dang-Gui-Liu-Huang Tang (7 herbs) (Nguyen et al., 2018), Herbal Anti-inflammatory Treatment (HAT1, 25 herbs) (Alex et al., 2020), Jueyin (8 herbs) (Ma et al., 2018), Kan-Lu-Hsiao-Tu-Tan (11 herbs) (Chiang et al., 2020), PAMs (4 herbs) (Dou et al., 2017), Psoriasis 1 (13 herbs) (Sun et al., 2018), PSORI-CM01 (7 herbs) (Han et al., 2017; Wei et al., 2016), PSORI-CM02 (5 herbs) (Chen et al., 2017a; Li et al., 2020), Pso p27 (10 herbs) (Song et al., 2010), Pulain ointments (4 herbs) (Li et al., 2015; Zhou et al., 2019), QoolSkin (4 herbs) (Cohen et al., 2007), Shi Du Ruan Gao (5 herbs) (Yan et al., 2015), Taodan granules (9 herbs) (Ru et al., 2019), Tuhuai (6 herbs) (Man et al., 2008), Wen-tong-hua-yu (6 herbs) (Ho et al., 2010), and White mange mixture (10 herbs) (Gao et al., 2019).

The investigations of antipsoriasis potential of herbal medicine have also been reported from Thailand (Wanachawee Recipe consisting of 8 herbs) (Na Takauhung et al., 2017; Na Takauhung et al., 2018) and Germany (Soratinex Herbal Complex consisting of 22 herbs) (Wollina et al., 2018). Most herbs or herbal formulas produce antipsoriasis by acting on inflammatory signaling molecules/pathways. The antipsoriasis activity was investigated mainly through the effects on inflammatory molecules and signaling pathways and immune cells (T-cells, dendritic cells, monocytes,
neutrophils, and macrophages) (Bader et al., 2016a; Bader et al., 2016b; Brieva et al., 2001; Chang et al., 2010; Cheng et al., 2017a; Chen et al., 2017c; Cuella et al., 2001; Dai et al., 2014; Deenonpoe et al., 2019; Di et al., 2016; Esquivel-Garcia et al., 2020; Jeon et al., 2013; Jeon et al., 2017; Kang et al., 2016; Lee et al., 2019; Leng et al., 2018; Li et al., 2019a; Li et al., 2019b; Li et al., 2019c; Li et al., 2019d; Liu et al., 2018; Liu et al., 2019; Lv et al., 2020; Na Takuathung et al., 2017; Na Takuathung et al., 2018 Nguyen et al., 2018; Pang et al., 2018a; Pang et al., 2018b; Suravanan et al., 2012; Wang et al., 2015; Wang et al., 2018; Wang et al., 2019; Wee et al., 2005; Xie et al., 2018; Ye et al., 2016; Yehuda et al., 2009; Yu et al., 2017; Su et al., 2017; Zhao et al., 2016b), as well as apoptotic molecules and signaling pathways (Brieva et al., 2001; Cuellar et al., 2001; Gao et al., 2019; Han et al., 2017; Jiang et al., 2020; Li et al., 2012; Li et al., 2019b; Mok et al., 2013; Na Takuathung et al., 2017; Na Takuathung et al., 2018; Pattarachotanant et al., 2014; Shi et al., 2019; Sun et al., 2019; Sung et al., 2013; Tang et al., 2018; Tse et al., 2007; Wang et al., 2019; Wee et al., 2005; Xie et al., 2018; Yang et al., 2019; Zhao et al., 2016a, and the oxidative system (Chen et al., 2017a; Pang et al., 2018; Shi et al., 2019; Weng et al., 2019). Few studies investigated the effects of herbal medicines on the angiogenesis process (Chang et al., 2015; Chang et al., 2019; Iliev et al., 2003) and other molecular targets/signaling pathways. Figure 2 summarizes key signaling molecules involved in the pathogenesis of psoriasis including key herbal medicines. Tables 2 and 3 summarize herbs/herbal medicine that has been reported for their antipsoriasis potential in vitro, in vivo, and clinical studies.

**Plants that modulate inflammation and immune response**

Plants that interfere with the production or activity of pro-inflammatory cytokines/mediators through various signaling pathways and steps in the immune cells and/or keratinocytes include *Acanthus mollis* (Bader et al., 2016a), *Artemisia arborescens* (Bader et al., 2016a), *Aloe vera* (Leng et al., 2018), alpha oasis (Ye et al., 2016).
Plants that act on apoptosis, cell differentiation, and angiogenesis processes and oxidative stress

Apart from anti-inflammatory activities, antiproliferative including activities on cell apoptosis and cell differentiation activities were reported for Artemisia anomala (Gao et al., 2019), Celastrus orbiculatus (Zhou et al., 2011), Prunus and soybean (Wang et al., 2019), Gloriosa superba and Catharanthus roseus (Pattarakchatanant et al., 2014), Leguminous plants Sophora flavescens, S. alopecuroides, S. subprostrata (Shi et al., 2019), Radix rubiae (Tse et al., 2007), Rubia cordifolia (Mok et al., 2013), Salvia miltiorrhiza Bunge (Jia et al., 2020; Tang et al., 2018), Salvia miltiorrhiza Radix (Li et al., 2012), Scutellaria baicalensis (Wu et al., 2015), Zanthoxylum nitidum (Yang et al., 2019), as well as Dang-Gui-Liu-Huang Tang (Sun et al., 2019), PSORICM01 (Han et al., 2017; Wei et al., 2016), PSORICM02 (Chen et al., 2017a), and Wannachawee (Na Takuathung et al., 2018) formulas. Anti-oxidative activities were demonstrated for Artemisia anomala S. (Gao et al., 2019), Cruciferous vegetables (Weng et al., 2019), Indigo Naturalis (Lin et al., 2013), Melissa officinalis (lemon balm) (Dimitris et al., 2020), Lagenaria sicera (Zhang et al., 2016), quercetin compound (Chen et al., 2017b) and Sinapis alba (Yang et al., 2013). Studies on anti-angiogenesis activities were limited to only a few herbs, that is, Indigo Naturalis (Chang et al., 2015; Chang et al., 2019) and Panax ginseng Radix (Zhou et al., 2015). Flavonoid from Bryophyta, Pteridophyta, Pinophyta, Magnoliophyta (Lv et al., 2020) reverses the effects of IFN-γ, inhibition of expression and exosome secretion of HSP90, and regulation of the proportion of immunocytes. Melissa officinalis (Dimitris et al., 2020) and Vernonia anthelmintica (Dogra et al., 2018), act on essential fatty acids, primarily linoleic acid palmitic acid, oleic acid, and stearic acid.

Key herbal medicine used in psoriasis

The most well-studied plants were Indigo Naturalis
(Chang et al., 2015; Chang et al., 2019; Chang et al., 2010; Cheng et al., 2017a; Lee et al., 2019; Lin et al.,
2007; Lin et al., 2008; Lin et al., 2009; Lin et al., 2011; Lin et al., 2013; Lin et al., 2014; Lin et al., 2015,
Ruanunculaceae (Pang et al., 2018; Yu et al., 2017),
Aloe vera (Arora et al., 2016; Leng et al., 2018; Syed et
al., 1996), and C. longa (Arora et al., 2016; Kang et al.,
2016; Zhang et al., 2019), Indigo Naturalis or Qing Dai is
obtained from the aerial part/stem/leaf mainly of
Strobilanthes formosanus Moore or, in some cases,
Baphicacanthus cusia, Polygonum tincyorium, and Isatis
indigotica. It is widely used in TCM for psoriasis,
inflammatory diseases, and leukemia. Topical Indigo
Naturalis ointment has proved safe and effective for
plaque-type psoriasis (Cheng et al., 2017a) and nail
psoriasis (Lin et al., 2014; Lin et al., 2015), at least in part
by modulating the proliferation and differentiation of
keratinocytes in the epidermis and inhibiting the
infiltration of T-lymphocytes and subsequent inflamma
tory reactions. Its three major active compounds, indirubin,
indigo, and tryptanthrin, act on multi-targets of various
key pathogenesis processes of psoriasis, particularly
inflammation, apoptosis, and angiogenesis. The anti-
inflammatory activity was shown to be through
inhibition of TNF-α-induced VCAM-1 expression via
inhibition of AP-1/c-Jun activation (Chang et al., 2010),
inhibition of y6 T cell-mediated inflammatory responses
involving IL-17 secretion, and JAK3/STAT3 activation
(Lee et al., 2019; Xie et al., 2018). Indigodole A, C,
trypthanthrin, and indirubin significantly inhibit IL-17
production of Th17 cells both in vitro and psoriasis
patients (Lin et al., 2007). The antiproliferative activity
of plant extract and tryptanthrin was shown to be through
G2/M phase arrest, suppression of migration, and tube
formation through inhibition of Akt and FAK pathway
(Chang et al., 2015). The anti-angiogenesis was
demonstrated to be mainly through suppression of apelin
expression through MAPK/ERK and PI3K/Akt signaling
(Chang et al., 2019). Other underlying mechanisms of
antipsoriasis activity include inhibition of O2
generation and elastase release activity in neutrophils (at
least in part mediated by inhibition of MAPK activation
and regulation of calcium mobilization) and enhancement
of claudin-1 expression and tight junction function in
keratinocytes (Mason et al., 2013). Ruanunculaceae
(root) is used in TCM for immunomodulatory activity.

Paeony is its total glycosides that exert the activity. It
was proved safe and effective when used in combination
with acitretin in patients with moderate-to-severe
psoriasis by reducing liver damage due to acitretin (Yu et
al., 2017). The antipsoriasis activity of paeony was shown
to be via p38 MAPK/NF-κB p65 pathway (downregulation
of proinflammatory cytokines IL-22 and VEGF) (Pang et
al., 2018). In addition, it decreased serum pro-
inflammatory factor IL-6 and Th1 cytokine levels and
circulating Treg and Th1 percentages (Bader et al.,
2016). The main component, paeoniflorin suppressed IL-
22 and P38 MAPK pathways (Yu et al., 2017). Aloe vera
(leave) and C. longa (rhizome) have been used in TCM,
traditional Ayurvedic medicine, and traditional medicine in
other countries for psoriasis, bacterial infections,
inflammation, as well as for anti-oxidant activities and
wound-healing promoters (Shedoeva et al., 2019).
The topical application of the extract or cream was shown to
be a potential candidate for psoriasis both in
experimental or clinical studies through anti-inflammatory
activity (inhibition of TNF-α induced proliferation of
keratinocytes and over activation of the NFκB signaling
pathway) (Arora et al., 2016; Syed et al., 1996). C. longa
has been used for psoriasis, abdominal pain, liver
disorders, diabetic wounds, rheumatism, anorexia,
menstrual difficulties, and cancer. The active compound
curcumin was shown to act on psoriasis through inhibiting
hKv1.3 channel, activation of T-cells, and expression of
inflammatory cytokines IL-2 and IFNγ (Kang et al.,
2016).

Curcumin-loaded hyaluronic (HA)-modified ethosomes
(HA-ES) was successfully developed with propylene
glycol as a novel drug carrier for curcumin to targeting
CD44 protein in the inflamed psoriasis cells (Zhang et al.,
2019). Tripterygium willfordii Hook f. has been used in
TCM for psoriasis, as well as dermatitis, asthma, systemic
lupus erythematosus, rheumatoid arthritis, nephritis,
Behcet's disease, and for prevention of transplant
rejection. The plant contains multiglycosides which exert
antipsoriasis activity through down-regulation of the
function of Th17 cells (via inhibition of STAT3
phosphorylation) (Zhao et al., 2016b). Triptolide
compound was shown to regulate IL-12/IL-23 production
in LPS stimulated mouse peritoneal macrophage and
inhibit p40 expression and IL12p40 transcription (Zhang
et al., 2010).

Conclusion

Herbal medicines have a potential role in the treatment of
psoriasis. Bioactive natural products are considered to be
promising prototypes for the development of new
therapeutic agents for psoriasis. The antipsoriasis
activities of several plants used in traditional medicine for
psoriasis have been confirmed in different experimental
models in conjunction with their underlying mechanisms
of action at the molecular and cellular levels. Research
targeting inflammatory and proliferative processes in
disease pathogenesis, development, and progression
has been an extensive area. Blocking the generation of
an inflammatory infiltrate by interfering with critical
molecules of the adhesion process is an attractive
strategy to treat psoriasis (for example, the approved
drug efalizumab) (Parisi et al., 2013). Controlling these
pro-inflammatory cytokines in DCs would be a
breakthrough for psoriasis treatment. Investigation of anti-angiogenesis activities remains attractive to researchers. Herbs/herbal medicine targeting other signaling molecules should be further investigated.

ABBREVIATIONS

5-LOX; 5-lipoxygenase, AMPK; AMP-activated protein kinase, AP-1; Activator protein 1, CB; Cytochalasin B, COX; Cyclooxygenase, CSF-1; Colony stimulating factor 1, DAS-28; Disease Activity Score-28, DC; Dendritic cells, EAT; Experimental autoimmune thyroiditis model, FAK; Focal adhesion kinase, FMLP; N-formyl-methionyl-leucyl-phenylalanine, GM-CSF; Granulocyte-macrophage colony-stimulating factor, HSP90: Heat shock protein 90, ICAM-1; Intracellular adhesion molecule 1, IFN-γ; Interferon gamma, IL; Interleukin, IMQ; Imiquimod, JNK; The c-Jun NH2-terminal kinase, LPS; Lipopolysaccharide, LTB4; Leukotriene B4, MAPK; Mitogen-activated protein kinase, MyD88; Myeloid differentiation factor 88, NF-κB; Nuclear factor-kB, NO; Nitric oxide, NPSI; Nail psoriasis severity index, PASI; Psoriasis Area Severity Index, PBMC; Peripheral blood mononuclear cell, PCNA; Proliferating cell nuclear antigen, PGE2; Prostaglandin E2, RORyt; Retinoic-acid-receptor-related orphan nuclear receptor gamma, ROS; Reactive oxygen species, STAT3; Signal transducer and activator of transcription 3, TA; Triaminocline acetone, TCM; Traditional Chinese medicine, Th; T helper cell, TLR; Toll-like receptor, TNF-α; Tumor necrosis factor-alpha, TNFAP3; Tumor necrosis factor, alpha- TPA; 12-O-Tetradecanoylphorbol-13-acetate, VCAM; Vascular cell adhesion molecule, VEGF; Vascular endothelial growth factor, YAP; Yeast-associated protein.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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