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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

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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).

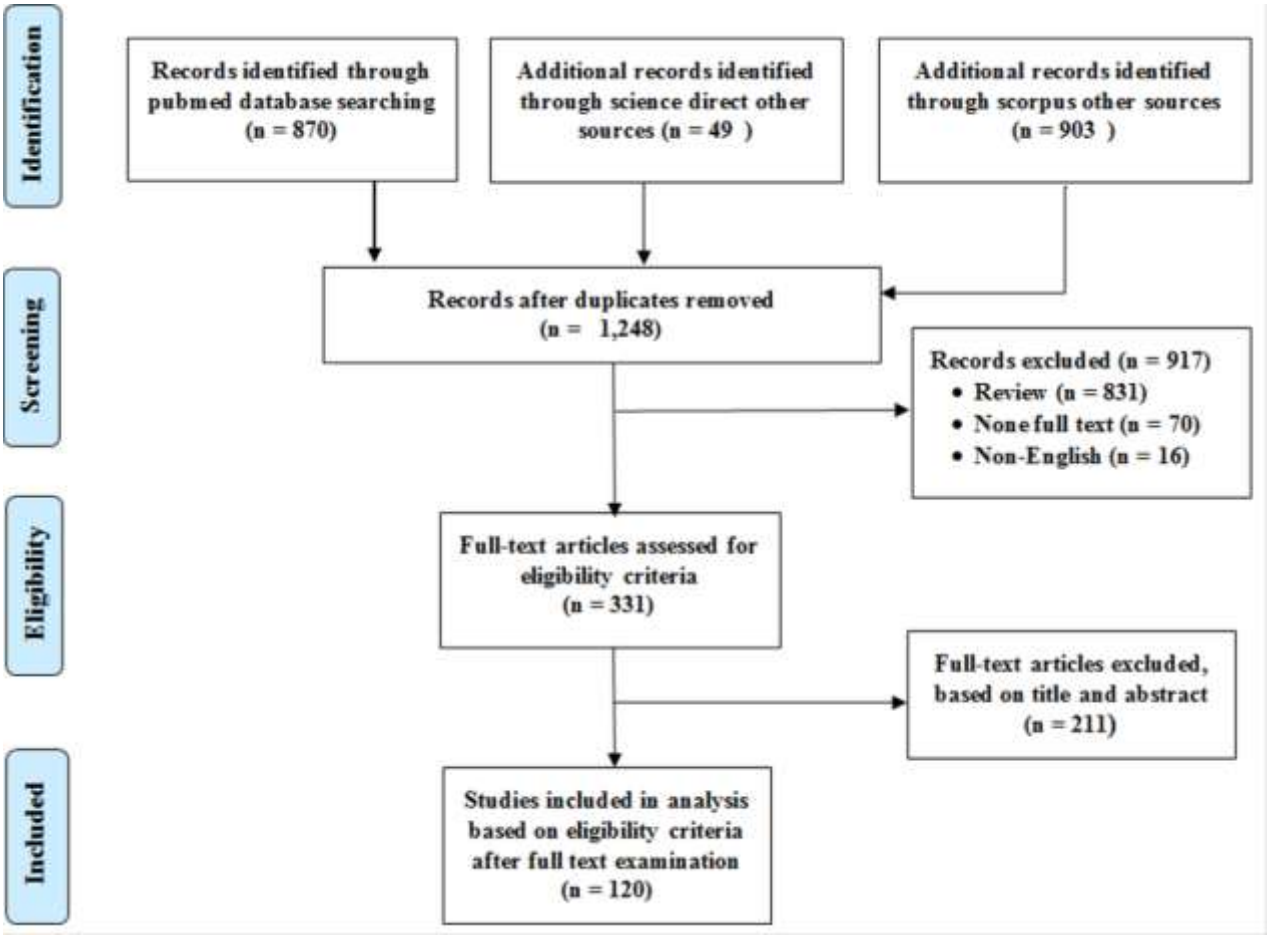

Figure 1. Flow chart of article selection process.

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).

Plant (part)	Note	Tested extract/compound/formulation	Objective	Type of study	Key results and Conclusion	Reference
Acanthus mollis (leaf), *Achillea ligustica* (leaf), *Artemisia arborescens* (leaf), *Inula viscosa* (flowering arial)	Italian traditional medicine for psoriasisand skin diseases.	Extract (methanol)	To investigate the mechanism underlying antipsoriasis activity (anti-inflammatory activity).	*In vitro:* Human buffy coat	Supporting traditional use: inhibition of 5-LOX and COX-1 complemented with an anti-inflammatory activity at the level of NF-κB.	(Bader et al., 2015)
Aloe vera (leaf)	Ayurvedic traditional medicine forpsoriasis and others. Antibacterial and wound-healingpromoters. Anti-inflammatory, anti-oxidant.	0.5% Hydrophilic cream	To evaluate clinical efficacy and tolerability	Clinical: Patients with psoriasis (n=60)	Safe and effective alternative treatment for psoriasis (significant clearing of psoriasis plaques- 82.8%, and decreased of PASI score)	(Syed et al., 1996)
		Aloe polysaccharide	To investigate the mechanism underlying antipsoriasis activity	*In vitro:* HaCaT cell	Potential candidate for psoriasis through anti-inflammatory activity (inhibition of TNF17α induced proliferation of keratinocytes and over activation of the NF-κB signaling pathway.	(Leng et al., 2018)
		Extract (aqueous)	To investigate preventive role against psoriasis-like dermatitis	*In vivo:* Balb/c mice (IMQ-induced psoriasis model)	Marked attenuation of symptoms and processes underlying psoriasis-like dermatitis.	(Arora et al., 2016)
Alpha Oasis (AO) extract consisting of 10 medicinal herbs*	Medicinal herb for anti-inflammatory.	Alpha Oasis extract	To investigate anti-inflammatory activity on inhibition of pro-inflammatory factors TNF-α by macrophage cells.	*In vivo:* Balb/c mice (oxazolone-induced inflammation)	Potential for inflammatory diseases including psoriasis through inhibiting TNF-α secretion of macrophages.	(Ye et al., 2016)
				In vitro: Macrophage cells		
Alpinia galangal (rhizome), *Annona squamosal* (leaf) *Curcuma longa (*rhizome)	Thai traditional medicine for skindiseases.	Extracts (ethanol)	To investigate the molecular mechanism of antipsoriasis action through the involvement of NF-κB signaling network biomarkers associated with psoriasis after treatment.	*In vitro:* HaCaT cell	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. squamosal:* reduction of CD40 and NF-κB expression	(Saelee et al., 2011)
Amphipterygium adstringens (bark)	Mexican traditional medicine forpsoriasis and inflammatory diseases	Pyrolytic oils	To characterize pyrolytic fractions and mechanisms of antipsoriasis action on IL-8 production in IL-17 stimulated HaCaT keratinocytes	*In vitro*: HaCaT cell	Inhibitory effects on IL-8 production, suggesting their potential role for treating IL-17 driven dermatological diseases, including psoriasis.	(Esquivel-García et al., 2020)
Andrographis paniculata (leaf, aerial part)	Anti-inflammatory disorders.	Andrographolide compound	To investigate antipsoriasis action through anti-inflammatory activity.	*In vivo:* Male C57/BL6 mice (IMQ–induced psoriasis model)	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.	(Shao et al., 2016)

Table 1. Cont'd

Antrodia cinnamomea (fruit)	Taiwanese traditional medicine for diarrhea, food and drug poisoning, hypertension, abdominal pain, pruritus, liver dysfunction, cancer. Anti-inflammatory, anti-oxidant, anticancer, hepatoprotective, antifatigue, vasorelaxation.	Extra ct (etha nol)	To investigate the effect on suppression of Th17 cell differentiation and anti-psoriasis activity.	*In vivo:* C57BL/6 & BALB/c mice (IMQ-induced psoriasis model)	The potential role for treatment of psoriasis.by acting through inhibition of Th17 cell differentiation byblocking STAT3 activity.	(Li et al., 2015)
Bai Xuan Xia Ta Re Pian (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 *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)
Betulinic acid (pentacyclic triterpenoid from plant species, *e.g.,* birch tree, birch bark oil, and paeoniaceae)	Anti-inflammatory, antica ncer, antifibrotic, anti-angiogenesis, anti- oxidant.	3β-hydroxy-lup-20(29)-en-28-oic acid	To investigate anti psoriasis activity and mechanism of action through the immunosuppressant activity.	*In vivo:* Balb/c & 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 cytotoxiceffect.	(Liu et al., 2019)
Boswellia carterii (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 & C57 mice (IMQ-induced psoriasismodel)	Potential for treatment of psoriasis by inhibition of the activation of TLR8 and IRF signaling pathways.	(Wang et al., 2018)
Caesalpinia bonduc (leaf)	Indian traditional medicine for psoriasis	Decoction and hydroalcoholic extract	To investigate antipsoriasis activities	*In vitro:* HaCaT cell *In vivo:* Albino mice (Mouse tail model)	Supporting traditional use in psoriasis. Only hydroalchoholic extract: good activity *in vitro* and *in vivo*, and inhibitory effect on lipoxygenase. Others: the varying degree of activity.	(Muruganantham et al., 2011)
Chunghyuldan (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.	(Wee et al., 2005)
Cimicifuga simplex (root)	TCM for anti-inflammatory, antiviral.	9,19-Cycloartenol glycoside G3 compound	To investigate antipsoriasis activity through an inhibitory effect on immune response (RORϒ 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)
Citrus plants (fruit peel) and Silkworm *Bombyx mori*	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)
Cnidium officinale (rhizome)	Female genital anti-inflammatorydiseases. Anti-anemia, antifungal, sedative, smooth muscle relaxing.	Extract (methanol) andisolated 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 IκB-α.	(Lee et al., 2018)

Table 1. Cont'd

Conifers (*Pinus massnlana Lamb* (resin))	Traditional medicines in Egypt, Nordic countries, and Turkey for inflammation skin diseases, such as ulcer, punctured abscesses, and/or burns.	Rosin (water-boiled)	To investigate antipsoriasis activitythrough anti-inflammatory activity	*In vivo:* Balb/c mice	Antipsoriasis activity through inhibition of differentiation and cytokine expression of the inflammatory cells, in particular, Th17cell differentiation and cytokine secretion of IL-23, IL17A, and IL-17F in the IL-23/IL-17.	(Li et al., 2019)
Cortex mountan (root bark)	TCM for inflammatory diseases.	Paeonol compound	To investigate antipsoriasis activity and mechanism of action through anti-inflammatory activity.	*In vivo:* Balb/c mice (IMQ-induced psoriasis model)	Potent antipsoriasis activity through suppression of the maturation and activation of dendritic cells by decreasing MyD88 and TLR8 proteins in the TLR7/8 signaling pathway.	(Meng et al., 2019)
Cruciferous vegetables	Anticancer.	1-(4-Chloro-3-nitrobenzenesulfonyl)- 1H-indol-3-yl-methanol (indole-3-carbinol natural) topical formulation	To investigate the molecular mechanism of antipsoriasis through anti-inflammatory and anti-oxidant activities	*In vivo:* Balb/c mice (IMQ-induced psoriasis model)	Antipsoriasis through suppression of cytokine expression through inhibition of MAPKs, NF-κB, andAP-1). Advantage: targeting of multiple signaling, facile absorption into the skin, ease of manufacturing, and scale-up.	(Weng et al., 2019)
Curcuma longa (rhizome)	Ayurvedic medicine for psoriasis, abdominal pain, liver disorders, diabetic wounds, rheumatism, anorexia, menstrual difficulties. Anticancer.	Curcumin compound	To investigate the mechanism of antipsoriasis activity	*In vitro:* PBMCs *In vivo:* Mice (Keratin 14-VEGF transgenic mouse model)	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)
		Curcumin-loaded hyaluronan (HA)-modified ethosomes(HA-ES)	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	*In vivo:* C57BL/6 mice (IMQ-induced psoriasis,Skin retention, and Permeability models) *In vitro:* HaCaT	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)
		Extract (aqueous)	To investigate preventive role against psoriasis-like dermatitis	*In vivo:* Balb/c mice (IMQ-induced psoriasismodel)	Marked attenuation of symptoms and processes underlying psoriasis-like dermatitis.	(Arora et al., 2016)
Curcuma kwangsiensis (rhizome)	TCM for Blood Stasis Syndrome(BSS).	Diarylheptanoid compound	To investigate the effects on major immunological functions of dendriticcells.	*In vitro:* Dendritic cells from mouse bone marrowand spleen *In vivo:* C57BL/6 malemice	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)
Dang-Gui-Liu-Huang Tang (consisting of 7 herbs)*	TCM for psoriasis Berberine: GI disorders, bacterial diarrhea. Antihyperglycemic, anticancer, antidepression.	TCM formula and Berberine (principlecompound)	To investigate antipsoriasis activity and underlying mechanism of action	*In vitro:* HaCaT cell *In vivo:* Balb/c mice (IMQ-induced psoriasis model)	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)
		Berberine (principle compound)	To investigate CDC6 (one of the key regulators in DNA replication) expression in psoriatic skin; evaluate itsfunction in the proliferation of human keratinocytes; evaluate theantipsoriasis activity	*In vitro:* HaCaT cell	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)

Table 1. Cont'd

Datura metel L. (flower)	TCM for pain, asthma, rheumatism,coughs, convulsions, etc.	Extract (alcohol)	To investigate antipsoriasis activity and underlying mechanism of anti-inflammatory action.	*In vivo:* C57BL/6 mice(IMQ-induced psoriasis model)	Psoriasis protective effect by inhibiting the inflammatory response *via* inhibition of TLR7/8–MyD88–NF-κB NLRP3 inflammasome pathway.	(Yang et al., 2019)
		Withanolides compounds	To investigate anti-inflammatory effect mechanism of antipsoriasis	*In vitro:* HaCaT Cell *In vivo:* Balb/c & C57BL/6mice (IMQ-induced psoriasismodel)	Withanolides alleviated IMQ-induced epidermal hyperplasia and inflammatory cell infiltration *via* suppressed the activation of STAT3, ERK1/2 and p38 signaling pathways	(Li et al., 2019)
Enicostema axillare (whole plant)	Indian traditional medicine for psoriasis.	Extract (methanol)	To investigate antipsoriasis actionthrough the immunomodulatory activity	*In vivo:* Swiss albino &C57/BL6 mice *In vivo:* Sheep peritoneal macrophages, and RBCs	Action on both humoral and cell-mediated immune functions and decrease of the release of pro-inflammatory cytokines.	(Saravanan et al., 2012)
Eruca sativa (rocket seeds)	Anticarcinogenic, anti -inflammatory, antiproliferative.	4-Methylthiobutylisothiocyanate (MTBI)	To investigate the effects of MTB1 and synthesized compounds on the growth and cell cycle of HaCaT keratinocytes and THP-1 monocytes	*In vitro:* HaCaT	Antipsoriasis activity through suppression of cell proliferation ofactivated monocytes, downregulating TNF-α and IL-12/23p40 in LPS-activated monocytes and affecting monocyte activation.	(Yehuda et al., 2009)
Euphorbia kansui Radix (root)	Edema, ascites, asthma. Antiviral, a ntiproliferative, immunomodulatory.	Extract (ethanol)	To investigate antipsoriasis activity and underlying mechanism of action through the immunomodulatory activity	*In vivo:* Balb/c mice (IMQ-induced psoriasis model)	Antipsoriasis activity through the suppression of Th17 differentiation and the activation of dendritic cells.	(Kim et al., 2017)
Evodia rutaecarpa (fruit)	TCM for anti-inflammatory, antiallergic and immunosuppressive.	Rutaecarpine compound	To investigate the function and mechanism of antipsoriasis activity	*In vivo:* Balb/c mice (IMQ-induced psoriasis model)	Improvement of psoriasis-like dermatitis through effectson pDC-and Th17-associated cytokines *via* modulation of NF-κB and TLR7 signaling.	(Li et al., 2019)
Glycyrrhiza glabra (licoriceplant) (root)	TCM for allergic diseases. Anti-ulcer.	Glycyrrhizin (glycoconjugated triterpene)	To investigate antipsoriasis activity and mechanism of action	*In vitro:* HaCaT cell *In vivo:* Balb/ c mice (IMQ-induced psoriasis model)	Amelioration of skin inflammation by inhibiting ICAM-1 (intracellular adhesion molecule 1) expression *via* interference with TNF-α-induced activation of NF-κB and phosphorylation of ERK/p38 MAPK to activate protein kinase cascade in keratinocytes	(Xiong et al., 2015)
Illicium verum (fruit)	Spice	Extract (ethanol)	To investigate anti-inflammatory activity and regulatory mechanisms in human keratinocytes.	*In vitro:* HaCaT cell	Potential preventive and/or therapeutic agent for inflammatory skin diseases including psoriasis: - Anti-inflammatory activity: blocking activation of JAK/STAT1 pathway	(Sung et al., 2013)
Indigo Naturalis (Qing Dai powder from aerial part/stem/leave of mainly *Strobilanthes formosanus* Moore or in some cases from *Baphicacanthus*	TCM for inflammation including psoriasis Infections, inflammatory diseases, leukemia.	Extract (ethanol) and Tryptanthrin (major compound)	To investigate the target genes and pathways involved in antiangiogenesis in psoriasis.	*In vitro:* Chick embryos (Embryonic chick chorioallantoic membrane(CAM) assay) *In vitro:* Human vascular endothelial cell (HUVEC)	Both: anti-angiogenesis activity. Antiangiogenesis activity of tryptanthrin: G2/M phase arrest, suppression of migration and tube formation through inhibition of Akt and FAK pathway.	(Chang et al., 2015)
		Topical ointment	To evaluate clinical efficacy in moderate psoriasis	Clinical: Patients with psoriasis (n=16 treated group)	Antipsorosis activity in moderate psoriasis: through suppression of the IL-17 pathway	(Cheng et al., 2017a)

Table 1. Cont'd

		Extract (DMSO)	To investigate anti-inflammatory activityin psoriasis (effects on TNF-α- stimulated human umbilical vein endothelial cells and TNF-α activatedtranscription factor)	*In vitro:* HUVEC	Anti-inflammatory activity: suppression of TNF-α induced VCAM-1 expression *via* inhibition of AP-1/c-Junactivation.	(Chang et al., 2010)
		Topical ointment	To evaluate safety and efficacy inpsoriasis	Clinical: Patients with psoriasis (plaque-type) (n=51)	A novel, safe, and effective therapy for plaque-type psoriasis.	(Lin et al., 2008)
		Extract (methanol)	To investigate antipsoriasis activity and underlying mechanism of action through anti-inflammatory activity	*In vivo:* C57BL/6 mice	Indole alkaloids: contribution to anti-IL 17 properties of Qing Dai: - Indigodole C and trypthanthrin: 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)	To investigate the antipsoriasis effecton TJs function and expression of claudin-1 (role as a barrier in human epidermal cells) in psoriatic plaque	*In vitro:* Human keratinocytes *In vitro:* Human skin	Extract: enhancing claudin-1 expression and tightjunction function in HaCaT cell. 3 compounds: synergistic effect on upregulating tight junction function.	(Lin et al., 2013)
		Extract and its threemajor ingredients (Indirubin, Indigo, Tryptanthrin)	To investigate the effect on superoxide anion generation and elastase release and signaling pathways involved in its anti-inflammatory activity	*In vitro:* Human neutrophils	Indigo Naturalis, indigo, and trypthanthrin inhibited O_2 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)
		Lindioil (extract in oil for topical use)	To evaluate clinical efficacy and safety in nail psoriasis	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)
		Lindioil (extract in oil for topicaluse)	To compare efficacy and safety with standard current topical medication calcipotriol solution	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	To evaluate clinical efficacy and safety on treating plaque-type psoriasis and to analyze the histological change in skin tissues	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

		Tryptanthrin (major component)	To investigate the anti-angiogenicmechanisms	*In vitro:* HUVEC	Anti-angiogenesis through: - downregulating apelin expression through suppressing apelin promotor activity and shortened mRNA half-life. - MAPK/ERK & PI3K/Akt: important in apelin signaling of angiogenesis.	(Chang etal., 2019)
		Indirubin (bisindole compound)	To investigate immunoregulatory activity and underlying mechanisms of antipsoriasis-related inflammation through regulating γδ T cell-mediated immune response	*In vivo:* Balb/c mice (IMQ-induced psoriasis model)	Alleviation of IMQ-induced psoriasis mainly by inhibiting γδ T cell-mediated inflammatory responses involving IL-17 secretion and JAK3/STAT3 activation.	(Xie et al., 2018)
Kan-Lu-Hsiao-Tu-Tan (consisting of 11 herbs)*	TCM for warm diseases.	Formula (water extract)	To investigate antipsoriasis activity through anti-inflammatory action on human neutrophils	*In vitro:* Human neutrophils *In vivo:* Mice (IMQ-induced psoriasis model)	Effective modality to improve the treatment of patients with psoriasis through antineutrophilic inflammatory effects.	(Chiang etal., 2020)
Lithospermum erythrorhizon (root)	TCM for antibacterial, anti-inflammatory, anticancer, contraceptive, antithyroid, anti-immunosuppressive, hypoglycemic effects, protection of liver.	Beta-dimethylacryloyl alkannin compound	To investigate antipsoriasis activity on the activation of dendritic cells (anti-inflammatory action)	*In vivo:* Balb/c mice (IMQ-induced psoriasis model) *In vitro:* PBMCs	Antipsoriasis activity through suppression of thefunction of activated dendritic cells: - decreasing IL-23 expression - suppressing the expression and secretion of IL-6, IL-12 p40, IL-23, IL-1β, tumor necrosis factor-α Mrna and proteins.	(Wang etal., 2015)
Paeonia lactiflora (root)	TCM for anti-inflammation and immunomodulation Paeoniflorin: inflammatory diseases, including rheumatoid arthritis, hepatic fibrosis, and colitis.	Paeoniflorin (main active ingredient)	To investigate the mechanism of antipsoriasis activity	*Balb/c & C57BL/6 mice (IMQ-induced psoriasis model)*	Antipsorosis activity by inhibiting Th17 cell response (STAT3 phosphorylation and RORγt expression) and cytokine secretion.	(Zhao et al., 2016a)
				In vitro: Mouse spleen cells		
PAMs (Chinese natural and folk medicinal plants Consisting of 4 medicinalherbs)*	TCM for prevention of wound infection and festering, cell necrosis, dry gangrene, and blood circulation obstacles	extract (ethanol)	To investigate the underlyingmechanism of antipsoriasis action	*In vitro:* HaCaT cell	A promising candidate for inflammatory skin disordersincluding psoriasis by inhibition of translocation of NF-κB and production of inflammatory cytokines (IL-8,IL23, TNF-α, and ICAM-1).	(Dou et al.,2017)

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).

Plant (part)	Note	Tested extract/compound/formulation	Objective	Type of study	Key results and Conclusion	Reference
Angelica dahulica (root), *Angelica pubescens* (root), *Angelica sinensis* (stem), *Astragalus membranace* (root), *Atractyodes macrocephala* (root), *Codonopsis pilosula* (root), *Coptis chinensis* (root), *Curcuma aromatica* (rhizome), *Forsylthia suspensa* (fruit), *Lentinus edodes* (fruiting body), *Paeonia lactiflora* (root), *Phellodendron amurense* (root bark), *Poria cocos* (sclerotia), *Rehmannia glutinosa* (root), *Scutellaria baicalens* (root)	TCM for inflammation.	Extract (water, methanol, or ethanol)	To investigate anti-inflammatory activities to support antipsoriasis activity.	*In vitro:* Human buffy coat *In vivo:* Wistar rats	Potential for treatment of psoriasis with anti-inflammatory activity: Most potent: *A. membranaceus*, *F. suspensa* & *P. coco* (inhibition of LTB4). *F. susepensa & P. cocos*: inhibitory activity on human leukocyte esterase.	(Prieto et al., 2003)
Artemisia anomala S. (arial part)	TCM for wound healing, pain, bacterial infections.	Extract (suspended in acetone: (15:1), and sonicated with ultrasound for 30 min to yield the extracts.)	To investigate anti-proliferative and anti-oxidative activities to support antipsoriasis activity and mechanism of action	*In vitro:* HaCaT cell	A promising candidate for psoriasis: - increasing cell viability and antioxidant capacity *via* activation of AMPK pathway. - inhibiting cell apoptosis *via* activation of caspase pathways.	(Gao et al., 2016)
Averrhoa carambola L. (leaf)	Headaches, vomiting, coughing, hangovers, appetite stimulant, diuretic, antidiarrheal, anti-eczemas, antidiabetes.	Extract (ethanol) & its n-butanol, ethyl acetate fractions	To investigate the potential anti-inflammatory activity to support antipsoriasis activity.	*In vivo:* Swiss male mice (Croton oil-induced ear edema model)	All: effective in reducing edema and cellular migration of polymorphonuclear leukocytes, supporting the use in inflammatory skin disorders, including psoriasis.	(Cabrini et al., 2011)
Berberis aristata (root)	Ayurvedic medicine for skin diseases.	Extract loaded transferosomal gel	To investigate antipsoriasis activity through anti-inflammatory action.	*In vitro:* Franz diffusion cell *In vivo:* Mice, Wistar rats (IMQ-induced psoriasis and Carrageenan-induced paw edema models)	Potential anti-inflammatory and antipsoriasis formulation.	(Nimisha et al., 2017)
Caesalpinia bonduc (leaf)	Indian traditional medicine for psoriasis	Decoction and hydroalcoholic extract	To investigate antipsoriasis activities	*In vitro:* HaCaT cell *In vivo:* Albino mice (Mouse tail model)	Supporting traditional use in psoriasis. Only hydroalchoholic extract: good activity *in vitro* and *in vivo*, and inhibitory effect on lipoxygenase. Others: the varying degree of activity.	(Murugan antham et al., 2011)

Table 2. Cont'd

Cassia angustifolia (leaf), *Corpis chinensis* (root), *Phellodendron amurense* (root bark), *Rhem palmatum* (root), *Scutellaria baicalensis* (root)	Asian traditional medicine for skin diseases.	Extracts (ethanol)	To investigate anti-inflammatory activities	*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)	Supporting inflamed skin diseases: All: anti-inflammatory activities and activities on edema with different degrees and spectrum. None: activity on Phospholipase A_2.	(Cuéllar et al., 2001)
Celastrus orbiculatus (leaf)	Celastrol (TCM for psoriasis).	Celastrol Compound	To evaluate the mechanism of antiproliferative activity	*In vitro:* HaCaT cell	Induction of apoptosis of keratinocytes *via* both death receptor (inhibition of NF-κB activity) and mitochondrial pathway.	(Zhou et al., 2011)
Centella asiatica (leaf), and psoralen-containing seeds of *Psoralea corylifolia* and synthetic compound dithranol	Ayurvedic medicine & TCM for skin diseases including psoriasis and vitiligo.	Extracts (water)	To investigate antipsoriasis activity	*In vitro:* SVK-14 keratinocyte cell	Topical antipsoriasis: worthy of further investigation. Antipsorosis activity: triterpenoid glycosides madecassoside and asiaticoside rather than phenolic compounds.	(Sampson et al., 2001)
Celastrus paniculatus (seed)	Ayurvedic medicine for psoriasis.	Extract (Soxhlet apparatus using petroleum ether as a solvent)	To investigate preventive role against psoriasis-like dermatitis	*In vivo:* Balb/c mice (IMQ-induced psoriasis model)	Marked attenuation of symptoms and processes underlying psoriasis-like dermatitis.	(Arora et al., 2016)
Citrus reticulate (Tangerine, peels)	TCM for anti-inflammation, anticancer, obesity, hyperglycemia, hyperlipidemia.	Hesperidin compound	To investigate antipsoriatic activity	*In vivo:* Balb/c mice (IMQ-induced psoriasis model)	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)
Convallaria majalis (seed)	Slowing and regulating heart rate.	Convallatoxin (98%)	To investigate the mechanism of antipsoriasis action	*In vitro:* HaCaT cell *In vivo:* Balb/c mice (IMQ- and TPA-induced psoriasis models)	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)
Gloriosa superba (root) and *Catharanthus roseus* (leaf)	TCM: *G. superba* for intestinal worms, bruises, infertility, joint pain, cancer. Kapha and Vata conditions, skin problems. *C. roseus* for menorrhagia, diabetes, hypertension, cancer.	Extract (ethanol)	To investigate the mechanism of antipsoriasis action through the effect on the expression of the psoriatic marker, keratin17 (K17)	*In vitro:* HaCaT cells	Antipsoriais activity of both extracts through suppression of K17 and p-STAT3 expression (*G. superba*, more active).	(Pattarachotanant et al., 2014)]
Gynura pseudochina DC (leaf) *hispida Thv* (leaf)	Herpes zoster, abscesses, thermal burn.	Extract (methanol)	To investigate clinical efficacy and safety	Clinical: Patients with mild-to-moderate chronic plaque psoriasis (n=25)	Improvement of psoriasis lesions, similarly to 0.1% TA cream, with minimal short-term side effects.	(Rerknimitr et al., 2016)]

Table 2. Cont'd

Herbal Anti-inflammatory Treatment (HAT1: consisting of 25 plants) *	Herbal extracts for inflammation	Topical spray formulation (20% extract in a 5% ethanol solution)	To investigate relative safety and efficacy in comparison to calcipotriol	Clinical: Adult patients with mild-to-moderate psoriasis (n=28)	Effective and safe topical therapy for psoriasis.	(Alex et al., 2019)
Hippophae rhamnoides (Sea buckthorn) (fruit)	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.	Extract (topical oil)	To evaluate the effect on psoriasis lesions in previously untreated patients	Clinical: Patients with mild-to-moderate psoriasis (n=10)	Improvement of psoriasis area severity index (PASI) score.	(Boca et al., 2019)
Jueyin (consisting of 8 herbs)*	TCM for psoriasis	Formula (water extract-alcohol)	To investigate the mechanism of antipsoriasis activity	*In vivo:* C57BL/6 (IMQ-induced psoriasis model)	Effective antipsoriais 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 an anti-inflammation.	(Ma et al., 2014)
Leguminous plants *Sophora flavescens Ait* (root), *Sophora alopecuroides L* (seed), *Sophora subprostrata* (root),	Oxymatrine: Cancer, hepatitis, cirrhosis. Anti-inflammatory, anti-oxidant, antiproloferative.	Oxymatrine compound	To investigate underlying mechanisms of antipsoriasis action on cell proliferation and apoptosis.	Clinical: Patients with psoriasis patients (n=79)	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).	(Shi et al., 2019b)
Luteolin flavonoid from *Bryophyta, Pteridophyta, Pinophyta, Magnoliophyta*	Antioxidant, anti-inflammatory, antimicrobial, anticancer, antiangiogenesis.	Luteolin compound	To evaluate clinical efficacy and potential in treating psoriasis and to explore the mechanism of action (anti-inflammatory action)	*In vitro:* HaCaT cell *In vivo:* Balb/c mice (IMQ)-induced psoriasis model)	Reduction of lesions and symptoms through reversing the effects of IFN-γ, inhibition of expression and exosome secretion of HSP90, and regulation of the proportion of immunocytes.	(Lv et al., 2020)
Mahonia aquifolium (root and wood)	American traditional medicine for inflammatory skin diseases including psoriasis; berberine is an active principle.	Extract (topical cream)	To investigate the efficacy and safety	Clinical: Patients with mild-to-moderate psoriasis (n=200)	Effective and safe in mild-to-moderate psoriasis.	(Bernstein et al., 2006)

Table 2. Cont'd

Melissa officinalis L. (lemon balm)	Greece traditional medicine for several diseases/ conditions including tracheobronchitis, hysteria, epilepsy, heart arrhythmia, hypnotic, skin diseases.	Decoction and fractions	To investigate potential antipsoriatic activity and chemical profile	*In vivo:* Balb/c mice (IMQ-induced psoriasis model)	Decoction: primary and dichloromethane extract secondary to significantly contribute to antipsoriais activity. Decoction: reestablish skin physiology by decreasing dryness and enhancing skin barrier functions with the best anti-oxidant activity.	(Dimitri et al., 2020)
Lagenaria siceraria (fruits)	Increase of pulmonary blood circulation.	Periplogenin (topical)	To investigate antipsoriasis activity and underlying mechanism of action	*In vitro:* HaCat cell *In vivo:* Balb/c mice (IMQ-induced and TPA-induced psoriasis models) *In vitro:* Human PBMCs	Antipsoriasis action through induction of ROS-miediated necroptosis. Potential utilize of inducing ROS-mediated necroptosis as a novel therapeutic strategy for psoriasis treatment.	(Zhang et al., 2016)
Psoralea corylifolia (seed)	Psoriasis, vitiligo, eczema, alopecia. Cytotoxic, anticancer, antimicrobial, immunomodulatory.	8-Methoxypsoralen (MOP), Psoralen, Isopsoralen, Psoralidin, and Bakuchiol	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	*In vitro:* HaCaT cell	Different natures of compounds in penetrating into and across the skin. Antipsoriasis activity of all compounds: through suppression of keratinocyte proliferation. 8-MOP & Isopsoralen: significant reduction of psoriatic lesions via reduction of epidermal thickening, cytokine release, and barrier defect in the presence of UVA.	(Alalaiwe et al., 2018)
Pso p27 (consisting of 11 herbs for systematic treatment and consisting of 3 for herbal bath)*	TCM for psoriasis	Formula (decoction) and Topical ointment	To investigate the effect on the expression of the psoriasis-associated antigen Pso p27 (associated with acute-phase psoriasis)	Clinical: Patients with psoriasis (n=15)	Pso p27: probably participates in the immune reactions in psoriasis (study on the mechanism of action required).	(Song et al., 2010)
Pulian ointment (NPLO: consisting of 2 herbs)*	TCM for psoriasis	Topical ointment	To evaluate clinical efficacy and safety in psoriasis Vulgaris of the blood-heat syndrome	Clinical: Patients with psoriasis Vulgaris of blood-heat syndrome (n=300)	Effective, well-tolerated, and convenient remedy for psoriasis Vulgaris (decrease of PASI score, improvement of erythema, infiltration, and size of psoriasis).	(Zhou et al., 2019)
		Topical ointment	To investigate clinical efficacy and safety in psoriasis Vulgaris of the blood-heat syndrome	Clinical: Patients with psoriasis Vulgaris of the blood-heat syndrome (n=51 in the test arm)	Safe and effective for external treatment of psoriasis of the blood-heat syndrome: total effective rate = 84.31%, improvement of PSAI score of the lesions, and scores on erythema, infiltration, size of the lesion, itching. No adverse event.	(Li et al., 2017)
QoolSkin* (Consisting of 4 herbs)*	TCM formula for psoriasis.	The topical formulation for psoriasis	To investigate the clinical efficacy	Clinical: Patients with chronic plaque psoriasis (n=100)	Reduction of psoriasis severity; better efficacy with 3 times-daily regimens for a long period.	(Cohen et al., 2007)
Radix rubiae (root and rhizome)	TCM for psoriasis. Antiproliferative.	Extract (ethanol)	To investigate anti-proliferative activity	*In vitro:* HaCaT cell	Antiproliferative activity on keratinocyte through induction of apoptosis *via* activation of caspase-3 and cell cycle arrest at G1	(Tse et al., 2007)
Rubia cordifolia L. (root)	TCM for psoriasis	1,4-dihydroxy-2-naphthoicacid	To investigate antipsoriasis activity	*In vitro:* HaCaT cell	Potential for treatment of psoriasis by induction of apoptosis of keratinocytes through G0/G1 arrest, as well as inhibition of caspase-dependent and -independent pathways of apoptosis.	(Mok et al., 2013)

Table 2. Cont'd

Salvia miltiorrhiza Bunge (Danshen) (root)	Cryptotanshinone: anti-inflammatory, antibacterial, anticancer.	Danshensu (major component of Danshen)	To investigate effects on cell proliferation, cell cycle, and apoptosis, including the effect on YAP (yeast-associated protein) expression	*In vitro:* HaCaT cell	Potential for treatment of psoriasis: - inhibition of cell proliferation, apoptosis, and cell cycle arrest (G0/1) - prevention of abnormal epidermis proliferation by modulating YAP expression	(Jia et al., 2020)
		Cryptotanshinone compound	To investigate antipsoriasis activity and mechanism of action	*In vivo:* C57BL/6J mice (IMQ-induced psoriasis model)	Potential for treatment of psoriasis: mainly through modulating STAT3 and inducing G0/G1 arrest.	(Tang et al., 2018)
Salvia miltiorrhiza Radix (root) -	TCM for prevention of psoriasis)	Tanshinone IIA	To investigate the cellular mechanism that leads to cell cycle arrest and apoptosis in psoriasis	*In vitro:* Primary mouse keratinocytes	Supporting traditional use in psoriasis:- - inhibition of mouse keratinocyte proliferation (dose- & time-dependent) - induction of apoptosis (mainly through caspase pathway)	(Li et al., 2012)
Soratinex® Herbal complex (consisting of 22 herbs)**	German topical products	Scalp and body cleansing gel, scalp and body ointment, skin conditioner	To evaluate clinical efficacy and safety	Clinical: Patients with mild to moderate plaque psoriasis (n=18)	Efficacy and safety profile: recommendation for self-treatment in the out-patient setting	(Wollina et al., 2018)
Scutellaria baicalensis (root)	TCM for psoriasis liver protection, anti-inflammation, anti-allergy anticancer.	Baicalin (5% cream)	To investigate anti-inflammatory activity and keratinocyte differentiation-inducing activity	*In vivo:* Balb/c mice 2,4-dinitrofluorobenzene (DNFB)-induced contacthypersensitivity (CHS) model, Mouse tail model)	Promising agent for psoriasis: - inhibition of DNFB-induced CHS reaction - keratinocyte differentiation-inducing activity	(Wu et al., 2015)
Shi Du Ruan Gao (consisting of 5 herbs)*	TCM for psoriasis	Formula	To evaluate the efficacy and safety	Clinical: Patients with stable mild-to-moderate chronic plaque-type psoriasis (n=149)	Safe and effective therapy for plaque-type psoriasis	(Yan et al., 2015)
Sinapis Alba Linn (mustard seed for spice and TCM)	Respiratory and GI diseases	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.	To investigate antipsoriasis activity	*In vivo:* Mice (IMQ-induced psoriasis model) *In vivo:* Mouse spleens and Blood	Antipsoriasis activity through alterations of anti-xidantion status, expression of NF-κB, IFN-γ, IL-17 and IL-22 and the compositions of immunocytes.	(Yang et al., 2013)
Stellera chamaejasme L. (flower)	Stubborn skin ulcers. Antiviral, anticancer, antibacterial, immunomodulatory, insecticidal.	Extract (ethanol) and its constituents	To investigate the effect on cutaneous wound healing	*In vitro:* HaCaT & RAW 264.7 cells *In vivo:* Sprague-Dawley (SD) rats	Potential use for psoriasis treatment for wound healing effect: - increasing phosphorylation of ERK and Akt - inhibiting NO and PGE2 release and mRNA expression of inflammatory mediators - enhancing motility of keratinocytes - improving cutaneous wound healing in SD rats	(Kim et al., 2017)
Taodan granules (consisting of 9 herbs)*	TCM for psoriasis	Formulation	To investigate clinical efficacy, safety, and control of disease recurrence	Clinical: Patients with mild-to-moderate psoriasis Vulgaris (n=216)	Improvement of PASI score and recurrence rate after 8 weeks of treatment.	(Ru et al., 2019)

Table 2. Cont'd

TCM consisting of 11 herbs*	TCM for clearing heat, cooling blood and removing toxic substances) combined with acitretin capsule.	Formula	To evaluate clinical efficacy and safety in psoriasis of the blood-heat syndrome	Clinical: Patients with psoriasis (n=80)	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)
Tinospora cordifolia (root, stem, leaf)	Ayurvedic medicine for psoriasis	Extract (aqueous)	To investigate preventive role against psoriasis-like dermatitis	*In vivo:* Balb/c mice (IMQ-induced psoriasis model)	Marked attenuation of symptoms and processes underlying psoriasis-like dermatitis	(Arora et al., 2016)
Tuhuai formulation (mainly consisting of 6 herbs)*	TCM for psoriasis	Topical extract (ethanol)	To investigate antiproliferative and anti-inflammatory activities and mechanisms of action	*In vivo:* Female hairless mice (hr/hr) & Male CD-1 mice (TPA-induced epidermal hyperproliferative and Oxazolone-induced ear inflammation models)	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)
Vernonia anthelmintica Willd. (fruit)	Indian traditional medicine for skin diseases. Various parts with different activities: anti-inflammatory, anti-oxidant, antimicrobial, antidiabetic, antivertigo, anticancer.	Extract (methanol) and fatty acid-enriched fractions	To investigate antipsoriasis activity and characterize bioactive fraction(s)	*In vitro:* HaCaT cell *In vivo:* Laca mice (Psoriasis tail model)	Antipsorosis activity: essential fatty acids, primarily linoleic acid, palmitic acid, oleic acid, and stearic acid.	(Dogra et al., 2018)
Wen-tong-hua-yu (consisting of 16 herbs)*	TCM for psoriasis	Formula	To evaluate clinical efficacy, safety, and quality of life in psoriasis compared with methotrexate	Clinical: Patients with psoriasis (n=21 for treated arm)	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)
White mange mixture (consisting of 10 herbs)*	TCM	Formula	To investigate antipsoriasis activity in vaginal psoriasis	*In vivo:* Mice (Murine model of vaginal psoriasis)	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)
Zhuhuang granule (consisting of 10 herbs)*	TCM modified formulation of Zhuhuang. Decoction for psoriasis.	The modified formulation of Zhuhuang Decoction	To evaluate clinical efficacy and safety	Clinical: Psoriasis patients (n=15) *In vitro:* Human PBMCs	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)
Zanthoxylum nitidum (root)	Anti-inflammatory, antimalarial, antifungal, antiangiogenesis, anticancer.	Nitidine chloride	To investigate antipsoriasis activity and mechanism of action	*In vitro:* HaCaT	Antipsorosis activity through inhibition of HaCaT cell proliferation, induction of apoptosis (S phase) through JNK signaling pathway.	(Yang et al., 2019)
				In vivo: Balb/c mice *IMQ-induced psoriasis and TPA-induced epidermal hyperplasia models)*		

Table 3. Compositions of the traditional medicine formulas used for psoriasis treatment.

Traditional medicine formula	Herbal composition
AO herbal	Consists of 10 herbs Japanese creeper, Chinese honey locust spine, Wooly datchman's pipe, Pubescent angelica, Garden balsam, Cantonese buttercup, Giant typhonium tuber, Euphorbia, semen hyoscyami and sesame oil
Bai Xuan Xia Ta Re Pian	Consists of 6 herbs *Euphorbiae Humifusae Herba, Chebulae Fructu, Terminalia Belliricae Fructus, Chebulae Fructus Immaturus,* Aloe and *Resina Scammoniae*
Dang-Gui-Liu-Huang Tang Compose of 7 herbs	Compose of 7 herbs *Angelicae Gigantis Radix, Rehmanniae Radix, Rehmanniae Radix Preparat, Scutellariae Radix, Astragali Radix, Coptidis Rhizoma,* and *Phellodendri Cortex*
HAT1	Consists of 25 herbs *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*
Kan-Lu-Hsiao-Tu-Tan (KLHTT)	Consists of 11 herbs Soapstone, *Artemisia capillaris, Scutellaria baicalensis, Acorus gramineus, Clematis armandii, Fritillaria cirrhosa, Pogostemon cablin, Forsythia suspensa, Amomum kravanh, Mentha haplocalyx* and *Belamcanda chinensis*
Jueyin granules	Consists of 8 herbs *Haliotis diversicolor, Flos Lonicerae japonicae, Radix Rehmanniae exsiccata, Cortex Moutan, Herba Hedyotisdiffusae, Folium isatidis, Smilax china L* and *Radix Curcumae*
PAMs	Consists of 4 herbs *Carthamust inctorius, Lithospermum erythrorhizon, Solanum indicum,* and *Cymbopogon distans*
Psoriasis 1	Consists of 13 herbs *rhizoma Smilacis glabrae , Folium isatidis , Radix isatidis , Angelica sinensis , Hedyotis diffusa , Sichuan lovage rhizome , Plantain herb , Fructus kochiae , Chinese lobelia , Nidus vespae, rhizoma alismatis, cortex dictamni* and *Radix glycyrrhizae .*
PSORI-CM01	Consists of 7 herbs*:* *Radix PaeoniasRubra, Rhizoma Cucumas, Saracandraglabra, Rhizoma Smilacis Glabras, FructusMume, Radix arnebias* and *Radix Glycyrrhizas.*
PSORI-CM02	Consists of 5 herbs: *Rhizoma curcumae, Radix paeoniae rubra, Sarcandra glabra, Rhizoma smilacis glabrae,* and *Fructus mume*
The herbal compounds used for systemic treatment Pso p27	Herbal decoction consists of 11 herbs *Rhizoma Smilacis Glabrae, Folium Isatidis, Rhizoma Menispermi, Oldenlandia, Rhizoma Curcumae, Rhizoma Polygoni Cuspidati, Cornu Saigae Tataricae, Gypsum Fibrosum, Herba Solani Lyrat, Herba Duchesneae Indicae, Cornu Saigae Tataricae* herbal bath *Cacumen Platycladi, Rhizoma Curcumae,* Nepal dock root
Pulian ointment	Consists of 2 herbs *Phellodendron amurense* and *Scutellaria baicalensis,*
QoolSkin (topical)	Consists of: riboflavin, citrus medica limonum (lemon) juice, vinegar, taraxacum oficinalis (danadelion) extract, cereus grandiflorus (cactus) flower extract and opuntia coccinellifera fruit extract, ascorbic acid, calcium ascorbate, sodium ascorbate, and tartaric acid

Table 3. Cont'd

Soratinex®	Conisists 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* , *Ctrus urantium ssp 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 adsurgens 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 *Alpiniagalanga(L.)Willd, SmilaxglabraWall.exRoxb, Smilax corbularia Kunth, Smilax sp, StemonainvolutaInthachub Stemona collinsae Craib, Rhinacanthus nasutus, Acanthu silicifolius L*
Wen-tong-hua-yu	Consists of 16 herbs *Ephedra sinica, Acronitum napellus, Sinapis alpa, Cinnamomum cassia, Zingiber officinale, Rehmannia glutinosa, Smilax glabra, Dictamus dasycarpus, Imperata cylindrica, Salvia miltiorrhiza, Spatholobus suberectus Dunn, Lithospermum officinale, Sophora japonica L, Glycyrrhia glabra L., Glycyrrhiza uralensis Fisch, Indigofera tentoria*
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 *Salvia miltiorrhiza Bge., Isatis indigotica Fort.,Coix lacryma-jobi L. var. mayuen (Roman.) Stapf, Scutellaria baicalensis Georgi, Saposhnikovia divaricata (Turcz.) Schischk., Artemisia capillaris Thunb., Cremastra appendiculataMakino (Appendiculate Cremastra Pseudobulb), Sophora flavescens Ait., Alisma orientalis (Sam.) Juzep., Angelica sinensis (Oliv.) Diels. (Chinese Angelica), Paeonia lactiflora Pall. (White Peony Alba), Poria cocos (Schw.) Wolf (Indian Bread), Polyporus umbellatus (Pers.) Fries (Chuling), Notopterygium incisum Ting ex H.T.Chang, Stephania terandra S. Moore,Anemarrhena asphodeloides Bge., Glycyrrhiza uralensis Fisch., Rheum officinale Baill. (Rhubarb)*
Yinxieling decoction	Consists of 7 herbs *Radix rehmanniae recen, Angelica sinensis, Radix paeoniae rubra, Ligusticum wallichii, Radices lithospermi, Curcuma 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 Lophatherum 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) (Feldman 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), *Atractylodes macrocepphala* (Prieto et al., 2003), *Bowswellia carterit* (Majeed et al., 2014), *Catharanthus* (Pattarachotanant et al., 2014), *Cellastrus orbiculatus* (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 Takuathung 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), *Forsylthia 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 erythrorhizon* (Yan et al., 2015), *Paeonia lactiflora* (Sun et al., 2015), *Panax ginseng* (Lee et al., 2011), *Phellodendron amurense* (Li et al., 2017), *Poria cocus* (Prieto et al., 2003), *Radix rubiae* (Tse et al., 2007), *Rehmannia tinosa* (Iliev et al., 2003), *Rhododendron brachycarpum* (Jeon et al., 2017), *Rubia cordifolia* (Mok et al., 2013), *Ruanunculaceae* (Iliev et al., 2003), *Salvia miltiorrhiza* (Li et al., 2012), *Scutellaria baicalensis* (Hung et al., 2018), *Sinapsis 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-Hsiaso-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., 2017; 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 Takuathung et al., 2017; Na Takuathung 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,

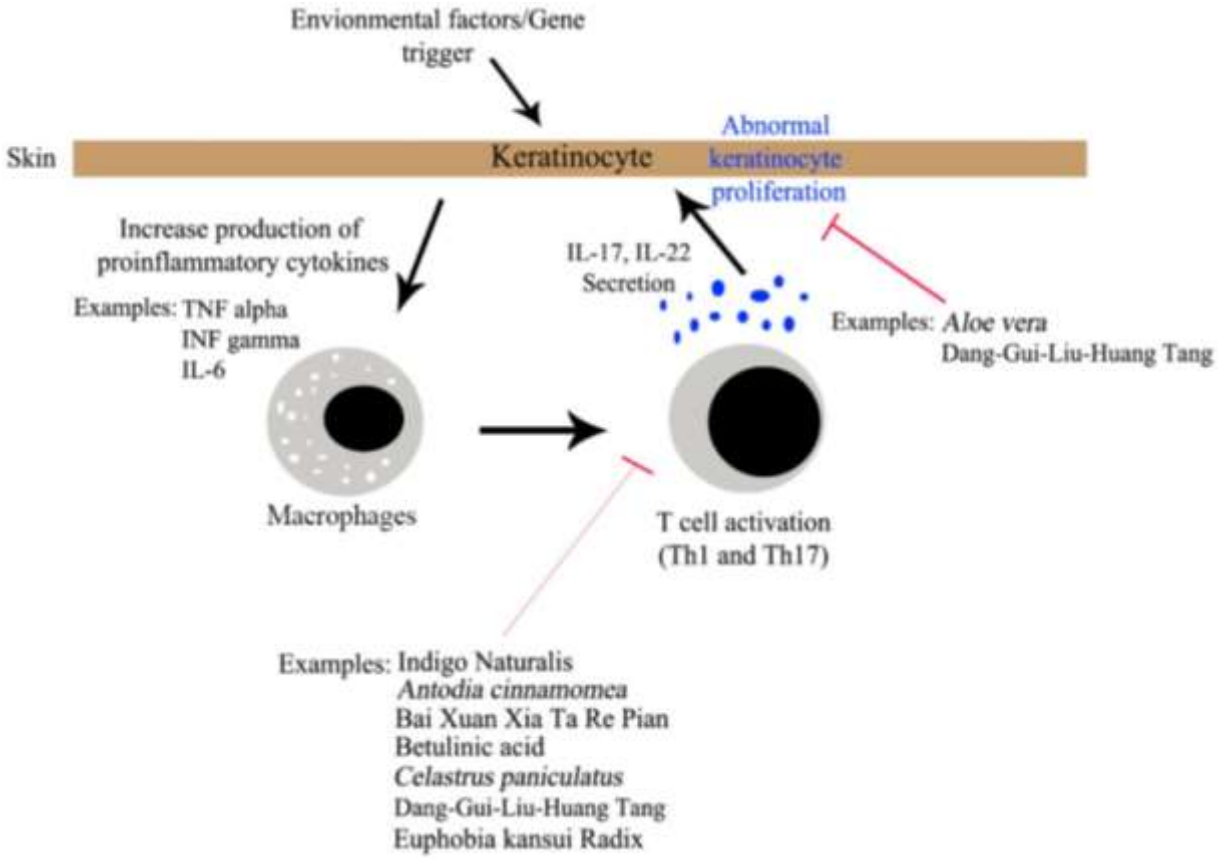

Figure 2. Summarizing the pathogenesis of psoriasis or signaling molecules/pathways with representative natural products.

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., 2017b; 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), *Amphipterygium adstringens* (Na Takuathung et al., 2018), Bai Xuan Xia Ta Re Pian formula (Pang et al., 2018) *Caesalpinia bonduc* (Murunganantham et al., 2011), Chunghuldan (Wee et al., 2005), citrus plants (Deenonpoe et al., 2019), *Cnidium officinale* (Lee et al., 2018), Conifers Li et al., 2019), *Curcuma longa (*Kang et al., 2016), *Curcuma kwangsiensis* (Liu et al., 2018), *Enicostema axillare* (Saravanan et al., 2012), *Eruca sativa* (Vehuda et al., 2009), *Euphorbia kansui* Radix (Kim et al., 2017), *Evodia rutaecarpa* (Li et al., 2019), Prunus and soybean (Wang et al., 2019), *Illicium verum* Sung et al., 2013), Indigo Naturalis (Chang et al., 2010; Cheng et al., 2017a; Lee et al., 2019; Lin et al., 2017), *Lithospermum erytrorhizon* (Wang et al., 2015), Ruanunculaceae (Bader et al., 2016; Leng et al., 2018; Pang et al., 2018), *Viola tricolor* (Hellinger et al., 2014), as well as Dan-Gui-Liu-Huang Tang (Nguyen et al., 2018), PSOI-CM01 (Han et al., 2017; Wei et al., 2016), PSORI-CM02 (Chen et al., 2017a) and Yinxieling formulas (Dai et al., 2014). The contribution of various immune cells was confirmed with several herbs or herbal medicines. The effects on T cells (Th17, Th1, and Threg) were reported with *Cimicifuga simplex* (Su et al., 2017), Conifers (Li et al., 2019), *Curcuma longa* (Zhang et al., 2019; Kang et al., 2016), *Datura metel* (Li et al., 2019), *Euphorbia kansui* Radix (Hellinger et al., 2014), *Evodia rutaecarpa* (Li et al., 2019), Indigo Naturalis (Lee et al., 2019), *Paeonia lactiflora* (Zhao et al., 2016a), *Polypodium leucotomos* (Brieva et al., 2001), PSORI-CM-02 (Li et al., 2020), Ruanunculacea (Bader et al., 2016), *Smilax glabra* (Di et al., 2016), *Triprerygium wilfordii* (Zhao et al., 2016b), as well as Dang-Gui-Liu-Huang Tang (Nguyen et al., 2018), Xiaoyin (Xu et al., 2012), and Wanchawee (Na Takuathung et al., 2017), Kan-Lu-Hsiaso-Tu-Tan formula (Chiang et al., 2020), and PSORI-CM02 formula (Li et al., 2020). Associated signaling molecules/pathways involve (i) NF-kB: *Acanthus mollis* (Bader et al., 2016), *Achillea ligustica* (Bader et al., 2016), *Alpinia* galangal (Saelee et al., 2011), *Annona squamosal* (Saelee et al., 2011), *Artemisia arborescens* (Bader et al., 2016), Betulinic acid (Liu et al., 2019), Cruciferous vegetables (Weng et al., 2019), *C. longa* (Saelee et al., 2011), *Evodia rutaecarpa* (Li et al., 2019), *Inula viscosa* (Bader et al., 2016), PAMs (Dou et al., 2017), *Panax ginseng* Radix (Shi et al., 2019), Prunus and soybean (Wng et al., 2019), Quercetin compound (Chen et al., 2017b), Psoriasis 1 formula (Sun et al., 2018), PSORI-CM01 formula (Han et al., 2017; Wei et al., 2016), PSORI-CM02 formula (Chen et al., 2017a); (ii) STAT signaling: *Antrodia cinnamomea* (Li et al., 2015), Prunus, and soybean (Wang et al., 2019), *Tripterygium wilfordii* (Zhao et al., 2016b), and Psoriasis 1 formula (Sun et al., 2018); (iii) JAK/STAT pathway: *Illicium verum* (Sung et al., 2013), Indigo Naturalis (Xie et al., 2013), and PSORI-CM02 formula (Li et al., 2020); (iv) TLR: *Boswellia carterii* (Wang et al., 2018), *Cortex mountan* (Na Takuathung et al., 2018), and *Evodia rutaecarpa* (Li et al., 2019); (v) TLR7-NF-κB inflammasome pathway: *Rhododendron brachycarpum* (Jeon et al., 2013); (vi) MyD88: *Andrographis paniculate* (Shao et al., 2016); and *Cortex mountan* (Meng et al., 2017); (vii) TLR7/8–MyD88–NF-κB NLRP3 inflammasome pathway: *Datura metel* L. (Yang et al., 2019); (viii) NF-κB, MAPK, PI3K/Akt inflammasome pathway: *Rhododendron brachycarpum* (Jeon et al., 2017); (ix) p38 MAPK/NK-kB p65 pathway: Ruanunculaceae (Pang et al., 2018); (x) IL-22 and P38 MAPK pathways: Ruanunculaceae (Yu et al., 2017); (xi) IL-23/IL-17 Axis: *Vanilla planifolia* [143]; (xii) ICAM-1: *Glycyrrhiza glabra* (Xiong et al., 2015); (xiii) and VCAM-1: Indigo Naturalis (Chang et al., 2010).

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* (Pattarachotanant 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), PSORI-CM01 (Han et al., 2017; Wei et al., 2016), PSORI-CM02 (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 siceraria* (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 indigotoca.* 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 inflammatory 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 suppression of TNF-α-induced VCAM-1 expression via inhibition of AP-1/c-Jun activation (Chang et al., 2010), inhibition of γδ 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 O_2 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/NK-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 NF-□B 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 IFN-γ (Kang et al., 2016).

Curcumin-loaded hyaluronan (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 wilfordii* Hook f. has been used in TCM for psoriasis, as well as dermatitis, asthma, systemic lupus erythematosus, rheumatoid arthritis, nephritis, Bechet'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-κB, **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, **RORγt;** Retineic-acid-receptor-related orphan nuclear receptor gamma, **ROS;** Reactive oxygen species, **STAT3;** Signal transducer and activator of transcription 3, **TA;** Triamcinolone acetonide, **TCM;** Traditional Chinese medicine, **Th;** T helper cell**, TLR;** Toll-like receptor, **TNF-α;** Tumor necrosis factor-alpha, TNFAIP3; 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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REFERENCES

Alalaiwe A, Hung CF, Leu YL (2018). The active compounds derived from *Psoralea corylifolia* for photochemotherapy against psoriasis-like lesions: The relationship between structure and percutaneous absorption. European Journal of Pharmacological Science 124:114-126.

Albanesi C, Madonna S, Gisondi P, Girolomoni G (2018). The interplay between keratinocytes and immune cells in the pathogenesis of psoriasis. Frontier in Immunology 9:1549-1563.

Alex P, Williams S, Sutton L, Yesudas T, Sutton C, Thomas S, Centola M (2020). Efficacy and safety of HAT1 compared with calcipotriol in the treatment of patients with mild to moderate chronic plaque psoriasis: results from an open-label randomized comparative pilot clinical study. Clinical and Experimental Dermatology 45(3):318-322.

Arora N, Shah K, Pandey-Rai S (2016). Inhibition of imiquimod-induced psoriasis-like dermatitis in mice by herbal extracts from some Indian medicinal plants. Protoplasma 253(2):503-515.

Ayala-Fontánez N, Soler DC, McCormick TS (2016). Current knowledge on psoriasis and autoimmune diseases. Psoriasis (Auckl) 6:7-32.

Bader A, Martini F, Schinella GR (2016). Modulation of Cox-1, 5-, 12- and 15-Lox by popular herbal remedies used in southern Italy against psoriasis and other skin diseases. Phytotherapy Research 29(1):108-113.

Benhadou F, Mintoff D, Marmol DE (2019). Psoriasis: keratinocytes or immune cells - which is the trigger? Dermatology 235(2):91-100.

Bernstein S, Donsky H, Gulliver W, Hamilton D, Nobel S, Norman R (2006). Treatment of mild to moderate psoriasis with Reliéva, a *Mahonia aquifolium* extract--a double-blind, placebo-controlled study. American journal of therapeutics 13(2):121-126.

Boca AN, Ilies RF, Saccomanno J, Pop R, Vesa S, Tataru AD, Buzoianu AD (2019). Sea buckthorn extract in the treatment of psoriasis. Experimental Therapy and Medicine 17(2):1020-1023.

Brieva A, Guerrero A, Pivel JP (2001). Immunomodulatory properties of a hydrophilic extract of *Polypodium leucotomos.* Inflammation and Pharmacology 9(1):361-371.

Cabrini DA, Moresco HH, Imazu P (2011). Analysis of the potential topical anti-inflammatory activity of *Averrhoa carambola* L. in Mice. Evidence-Based Complementary and Alternative Medicine 908059.

Chamian F, Krueger JG (2004). Psoriasis vulgaris: an interplay of T lymphocytes, dendritic cells, and inflammatory cytokines in pathogenesis. Current Opinion in Rheumatology 16(1):331-337.

Chan JR, Blumenschein W, Murphy E (2006). IL-23 stimulates epidermal hyperplasia via TNF and IL-20R2-dependent mechanisms with implications for psoriasis pathogenesis. Journal of Experimental Medicine 203(2):2577-2587.

Chang HN, Pang JH, Yang SH (2010). Inhibitory effect of indigo naturalis on tumor necrosis factor-α-induced vascular cell adhesion molecule-1 expression in human umbilical vein endothelial cells. Molecules 15(3):6423-6435.

Chang HN, Huang ST, Yeh YC (2015). Indigo naturalis and its component tryptanthrin exert anti-angiogenic effect by arresting cell cycle and inhibiting Akt and FAK signaling in human vascular endothelial cells. Journal of Ethnopharmacology 174(1):474-481.

Chang HN, Yeh YC, Chueh HY (2019). The anti-angiogenic effect of tryptanthrin is mediated by the inhibition of apelin promoter activity and shortened mRNA half-life in human vascular endothelial cells Phytomedicine 58:152879.

Chen H, Liu H, Lu C (2017a). PSORI-CM02 Formula Increases CD4+ Foxp3+ Regulatory T Cell Frequency and Ameliorates Imiquimod-Induced Psoriasis in Mice. Frontier in Immunology 8:1767.

Chen H, Lu C, Liu H (2017b). Quercetin ameliorates imiquimod-induced psoriasis-like skin inflammation in mice via the NF-κB pathway. International Immunopharmacology 48(1):110-117.

Cheng HM, Wu YC, Wang Q (2017a). Clinical efficacy and IL-17 targeting mechanism of Indigo naturalis as a topical agent in moderate psoriasis. BMC Complementary and Alternative Medicine 17:439.

Cheng HM, Chen FY, Li CC (2017b). Oral administration of vanillin improves imiquimod-induced psoriatic skin inflammation in mice. Journal of Agricultural Food and Chemistry 65(4):10233-10242.

Chiricozzi A, Romanelli P, Volpe E (2018). Scanning the immunopathogenesis of psoriasis. International Journal of Molecular Science 19(1):21-32.

Chiang CC, Cheng WJ, Lin CY (2020). Kan-Lu-Hsiao-Tu-Tan, a

traditional Chinese medicine formula, inhibits human neutrophil activation and ameliorates imiquimod-induced psoriasis-like skin inflammation. Journal of Ethnopharmacology 246:112246.
Cohen AD, Shalev R, Yaniv R (2007). An open-label study of an herbal topical medication (QoolSkin) for patients with chronic plaque psoriasis. Scientific World Journal 7(2):1063-1069.
Costa C, Incio J (2007). Angiogenesis and chronic inflammation: cause or consequence?. Angiogenesis 10(1):149-166.
Creamer D, Sullivan D, Bicknell R (2007). Angiogenesis in psoriasis. Angiogenesis 5(4):231-236.
Cuéllar MJ, Giner RM, Recio MC (2001). Topical anti-inflammatory activity of some Asian medicinal plants used in dermatological disorders. Fitoterapia 72(1):221-229.
Dai YJ, Li YY, Zeng HM (2014). Effect of Yinxieling decoction on PASI, TNF-α and IL-8 in patients with psoriasis vulgaris. Asian Pacific Journal of Tropical Medicine 7(1):668-670.
Deng G, Chen W, Wang P (2019). Inhibition of NLRP3 inflammasome-mediated pyroptosis in macrophage by cycloastragenol contributes to amelioration of imiquimod-induced psoriasis-like skin inflammation in mice. International Immunopharmacology 74:105682.
Deenonpoe R, Prayong P, Thippamom N (2019). Anti-inflammatory effect of naringin and sericin combination on human peripheral blood mononuclear cells (hPBMCs) from patient with psoriasis. BMC Complementary and Alternative Medicine 19(1): 168-179.
Deyrieux AF, Wilsonm VG (2007). *In vitro* culture conditions to study keratinocyte differentiation using the HaCaT cell line. Cytotechnology 54(1):77-83.
Di TT, Ruan ZT, Zhao JX (2016). Astilbin inhibits Th17 cell differentiation and ameliorates imiquimod-induced psoriasis-like skin lesions in BALB/c mice via Jak3/Stat3 signaling pathway. International Immunopharmacology 32(1):32-38.
Dimitris D, Ekaterina-Michaela T, Christina K (2020). *Melissa officinalis* ssp. altissima extracts: A therapeutic approach targeting psoriasis in mice. Journal of Ethnopharmacology 246:112208.
Dogra NK, Kumar S, Thakur K (2018). Antipsoriatic effect of fatty acid enriched fraction of *Vernonia anthelmintica* Willd. fruits. Journal of Ethnopharmacology 224(1):85-90.
Dou R, Liu Z, Yuan X (2017). PAMs ameliorates the imiquimod-induced psoriasis-like skin disease in mice by inhibition of translocation of NF-kappaB and production of inflammatory cytokines. PLoS One12: e0176823.
Duan Y, Zou J, Mao J (2019). Plasma miR-126 expression correlates with risk and severity of psoriasis and its high level at baseline predicts worse response to *Tripterygium wilfordii* Hook F in combination with acitretin. Biomedical Pharmacotherapy 115:108761.
Esquivel-García R, Ayiania M, Abu-Lail N, López-Meza JE, Rosa E, García-Pérez M, Ochoa-Zarzosa A, García-Pérez ME (2020). Pyrolytic oils from *Amphipterygium astringent bark* inhibit IL-8 production of IL-17-stimulated HaCaT keratinocytes. Annal of Applied Pyrolysis 145: 104749.
Feldman SR, Krueger GG (2005). Psoriasis assessment tools in clinical trials. Annal of Rheumatoid Diseases 64(Suppl 2):ii65-8.
Flatz L, Conrad C (2013). Role of T-cell-mediated inflammation in psoriasis: Pathogenesis and targeted therapy. Psoriasis: Targets Therapy 1(3):1-10.
Gao Y, Yuan J, Liang X, He Y, Li P, Yang M (2019). *Artemisia anomala* extracts enhance the viability and antioxidation capacity of human keratinocytes. Tropical Journal of Pharmacology Research 18(1):61-70.
Guo J, Liu J (2019). Effect of white mange mixture in a murine model of psoriasis. Experimental Therapy and Medicine 18:881-887.
Han L, Sun J, Lu CJ. (2017). Formula PSORI-CM01 inhibits the inflammatory cytokine and chemokine release in keratinocytes *via* NF-κB expression. International Immunopharmacology 44(1):226-233.
Hellinger R, Koehbach J, Fedchuk H. (2014). Immunosuppressive activity of an aqueous *Viola tricolor* herbal extract. Journal of Ethnopharmacology 151(1):299-306.
Ho SG, Yeung CK, Chan HH (2010). Methotrexate versus traditional Chinese medicine in psoriasis: a randomized, placebo-controlled trial to determine efficacy, safety and quality of life. Clinical and Experimental Dermatology 35(2):717-722.
Hung CH, Wang CN, Cheng HH (2018). Baicalin ameliorates imiquimod-induced psoriasis-like inflammation in mice. Planta Medica 84(2):1110-1117.
Iliev E, Broshtilova V (2003). Traditional Chinese medicine principles in the pathogenesis and treatment of psoriasis vulgaris. Seminar International Medicine 1(1):145-150.
Jensen P (1990). Alternative therapy for atopic dermatitis and psoriasis: patient-reported motivation, information source and effect. Acta Dermato-Venereologica 70(1):425-428.
Jeon YJ, Sah SK, Yang HS (2017). Rhododendrin inhibits toll-like receptor-7-mediated psoriasis-like skin inflammation in mice. Experimental Molecular Medicine 49:e349.
Jeon YJ, Kim BH, Kim S. (2013). Rhododendrin ameliorates skin inflammation through inhibition of NF-κB, MAPK, and PI3K/Akt signaling. European Journal of Pharmacology 714(2):7-14.
Jia J, Mo X, Liu J (2020). Mechanism of danshensu-induced inhibition of abnormal epidermal proliferation in psoriasis. European Journal of Pharmacology 868:172881.
Jiang BW, Zhang WJ, Wang Y (2020). Convallatoxin induces HaCaT cell necroptosis and ameliorates skin lesions in psoriasis-like mouse models. Biomedicine and Pharmacotherapy 121:109615.
Kang D, Li B, Luo L. (2016). Curcumin shows excellent therapeutic effect on psoriasis in mouse model. Biochimie 123(1):73-80.
Kim SJ, Jang YW, Hyung KE (2017). Therapeutic effects of methanol extract from *Euphorbia kansui* Radix on imiquimod-induced psoriasis. Journal of Immunological Research 7052560.
Kim M, Lee HJ, Randy A. (2017). *Stellera chamaejasme* and its constituents induce cutaneous wound healing and anti-inflammatory activities. Scienctific Reports 7:42490.
Kim, J (2009). The imiquimod induced psoriatic animal model: scientific implications. Biomedical Journal of Science and Technology Research 13(4):9722-97274.
Kouris A, Pistiki A, Katoulis A. (2014). Proinflammatory cytokine responses in patients with psoriasis. European Cytokine Network 25(1):63-68.
Lee KG, Son SW (2011). Efficacy of Korean red ginseng in the treatment of atopic dermatitis. Journal of Ginseng Research 35(1):149-154.
Lee YJ, Hong IK, Kim H (2018). The amelioration effect of the ethanolic extract of *Cnidium officinale* in mice with imiquimod-induced psoriasis-like skin lesion. Natural Products Science 24(1):21-27.
Lee CL, Wang CM, Hu HC (2019). Indole alkaloids indigodoles A-C from aerial parts of *Strobilanthes cusia* in the traditional Chinese medicine Qing Dai have anti-IL-17 properties. Phytochemistry 162(1):39-46.
Leng H, Pu L, Xu L. (2018). Effects of aloe polysaccharide, a polysaccharide extracted from *Aloe vera*, on TNF‑α‑induced HaCaT cell proliferation and the underlying mechanism in psoriasis. Molecular Medicine Reports 18(4):3537-3543.
Li T, Wei Z, Sun Y (2019). Withanolides, extracted from *Datura metel* L. inhibit keratinocyte proliferation and imiquimod-induced psoriasis-like dermatitis via the STAT3/P38/ERK1/2 pathway. Molecules 24(1):24-43.
Li FL, Xu R, Zeng QC. (2012). Tanshinone IIA inhibits growth of keratinocytes through cell cycle arrest and apoptosis: underlying treatment mechanism of psoriasis. Evidence-Based Complementary and Alternative Medicine 927658.
Li MH, Wu HC, Yao HJ (2015). *Antrodia cinnamomea* Extract Inhibits Th17 Cell Differentiation and Ameliorates Imiquimod-Induced Psoriasiform Skin Inflammation. American Journal of Chinese Medicine 43(3):1401-1417.
Li X, Xie X, Zhang L (2019). Hesperidin inhibits keratinocyte proliferation and imiquimod-induced psoriasis-like dermatitis via the IRS-1/ERK1/2 pathway. Life Science 219(1):311-321.
Li Y, Zhang G, Chen M (2019). Rutaecarpine inhibited imiquimod-induced psoriasis-like dermatitis *via* inhibiting the NF-κB and TLR7 pathways in mice. Biomedicine and Pharmacotherapy 109(4):1876-1883.

Li L, Zhang HY, Zhong XQ, Lu Y, Wei J, Li L, Chen H, Lu C, Han L (2020). PSORI-CM02 formula alleviates imiquimod-induced psoriasis via affecting macrophage infiltration and polarization. Life Science 243:117231.
Li S, Zhang C, Zhang HY (2020). Efficacy and safety of Jueyin Granules for patients with mild-to-moderate psoriasis vulgaris: protocol for a multicenter randomized placebo-controlled trial. Evidence- Based Complementary and Alternative Medicine 8942301.
Li XQ, Chen Y, Zhou HM (2019). Anti-psoriasis effect of water-processed rosin in mice. Journal of Ethnopharmacology 242:112073
Li N, Zhao W, Xing J (2017). Chinese herbal Pulian ointment in treating psoriasis vulgaris of blood-heat syndrome: a multi-center, double-blind, randomized, placebo-controlled trial. BMC Complementary and Alternative Medicine 17:264.
Lin YK, Chang YC, Hui RC (2015). A Chinese herb, Indigo naturalis, extracted in oil (Lindioil) used topically to treat psoriatic nails: A randomized clinical trial. JAMA Dermatology 151(6):672-674.
Lin YK, See LC, Huang YH (2014). Efficacy and safety of Indigo naturalis extract in oil (Lindioil) in treating nail psoriasis: a randomized, observer-blind, vehicle-controlled trial. Phytomedicine 21(2):1015-1020.
Lin YK, See LC, Chang YC (2011). Treatment of psoriatic nails with indigo naturalis oil extract: a non-controlled pilot study. Dermatology 223(1):239-243.
Lin YK, Chang CJ, Chang YC (2008). Clinical assessment of patients with recalcitrant psoriasis in a randomized, observer-blind, vehicle-controlled trial using indigo naturalis. Archive of Dermatology 144(2):1457-1464.
Lin YK, Wong WR, Chang YC (2007). The efficacy and safety of topically applied indigo naturalis ointment in patients with plaque-type psoriasis. Dermatology 214(1):155-161.
Lin YK, Leu YL, Huang TH (2009). Anti-inflammatory effects of the extract of indigo naturalis in human neutrophils. Journal of Ethnopharmacology 125(1):51-58.
Lin YK, Chen HW, Leu YL, Yang YL, Fang Y, Hwang TL (2013). Indigo naturalis upregulates claudin-1 expression in human keratinocytes and psoriatic lesions. Journal of Ethnopharmacology 145(2):614-620.
Lowes MA, Bowcock AM, Krueger JG (2007). Pathogenesis and therapy of psoriasis. Nature 445(2):866-873.
Liu Q, Yin W, Han L (2018). Diarylheptanoid from rhizomes of *Curcuma kwangsiensis* (DCK) inhibited imiquimod-induced dendritic cells activation and Th1/Th17 differentiation. International Immunopharmacology 56(1):339-348.
Liu C, Chen Y, Lu C (2019). Betulinic acid suppresses Th17 response and ameliorates psoriasis-like murine skin inflammation. International Immunopharmacology 73(1):343-352.
Lu CJ, Xiang Y, Xie XL (2012). A randomized controlled single-blind clinical trial on 84 outpatients with psoriasis vulgaris by auricular therapy combined with optimized Yinxieling Formula. Chinese Journal of Integrative Medicine 18(1):186-191.
Lv J, Zhou D, Wang Y (2020). Effects of luteolin on treatment of psoriasis by repressing HSP90. International Immunopharmacology 79:106070.
Ma T, Jiang WC, Li X (2018). Effects of Chinese formula jueyin granules on psoriasis in an animal model. Evidence-Based Complementary and Alternative Medicine 512562.
Man, M.Q., Shi, Y., Man, M (2008). Chinese herbal medicine (Tuhuai extract) exhibits topical anti-proliferative and anti-inflammatory activity in murine disease models. Experimental Dermatolpgy 17(2): 681-687.
Majeed M, Nagabhushanam K, Natarajan S (2014). Clinical evaluation of AKBBA in the management of psoriasis. Clinical Dermatology 2(1):17-24.
Martin G, Young M, Aldredge L (2019). Recommendations for initiating systemic therapy in patients with psoriasis. Journal of Clinical Aesthetic Dermatology 12(1):13-26.
Mason AR, Mason J, Cork M (2013). Topical treatments for chronic plaque psoriasis. Cochrane Database Systematic Review 3:Cd005028
Meng Y, Liu Z, Zhai C (2019). Paeonol inhibits the development of 1-chloro-2,4-dinitrobenzene -induced atopic dermatitis via mast and T cells in BALB/c mice. Molecular Medicine Reports 19(4):3217-29.
Mok CF, Xie CM, Sham KW (2013). 1,4-dihydroxy-2-naphthoic acid induces apoptosis in human keratinocyte: potential application for psoriasis treatment. Evidence-Based Complementary and Alternative Medicine 792840.
Muruganantham N, Basavaraj KH, Dhanabal SP (2011). Screening of *Caesalpinia bonduc* leaves for antipsoriatic activity. Journal of Ethnopharmacology 133(2): 897-901.
Na Takuathung M, Wongnoppavich A, Pitchakarn P (2017). Effects of Wannachawee recipe with antipsoriatic activity on suppressing inflammatory cytokine production in HaCaT human keratinocytes. Evidence-Based Complementary and Alternative Medicine 5906539.
Na Takuathung M, Wongnoppavich A, Panthong A (2018). Antipsoriatic effects of Wannachawee recipe on imiquimod-induced psoriasis-like dermatitis in BALB/c Mice. Evidence-Based Complementary and Alternative Medicine 7931031.
Na Takuathung M, Wongnoppavich A, Panthong A, Khonsung P, Chiranthanut N, Soonthornchareonnon N, Sireeratawong S (2018). Antipsoriatic effects of Wannachawee recipe on imiquimod-induced psoriasis-like dermatitis in BALB/c Mice. Evidence- Based Complementary and Alternative Medicine 7931031.
Nguyen LTH, Ahn SH, Nguyen UT (2018). Dang-Gui-Liu-Huang Tang a traditional herbal formula, ameliorates imiquimod-induced psoriasis-like skin inflammation in mice by inhibiting IL-22 production. Phytomedicine 47(1):48-57.
Nimisha V, Rizvi DA, Fatima Z (2017). Antipsoriatic and anti-inflammatory studies of Berberis aristata extract loaded nanovesicular gels. Pharmacogenomics Magazine 13(Suppl 3):S587-S594.
Owczarczyk-Saczonek A, Czerwińska J, Placek W (2018). The role of regulatory T cells and anti-inflammatory cytokines in psoriasis. Acta Dermatovenerology and Alpa Pannonica Adria 27:17-23.
Pang W, Qi X, Cao C (2018). Inhibitory effects of TGP on KGF-induced hyperproliferation of HaCaT cells *via* suppression of the p38 MAPK/NF-κB p65 pathway. Molecular Medicine and Reports 8(3): 2207-2215.
Pang X, Zhang K, Huang J (2018). Decryption of active constituents and action mechanism of the traditional uighur prescription (BXXTR) alleviating IMQ-induced psoriasis-like skin inflammation in BALB/c Mice. International Journal of Molecular Science19:1822.
Parisi R, Symmons DP, Griffiths CE (2013). Global epidemiology of psoriasis: a systematic review of incidence and prevalence. Journal of Investigated Dermatology 133(1):377-385.
Pattarachotanant N, Rakkhitawatthana V, Tencomnao T (2014). Effectof *Gloriosa superba* and *Catharanthus roseus* extracts on IFN-γ-induced keratin 17 expression in HaCaT human keratinocytes. Evidence-Based Complementary and Alternative Medicine 249367.
Prieto JM, Recio MC, Giner RM (2003). Influence of traditional Chinese anti-inflammatory medicinal plants on leukocyte and platelet functions. Journal of Pharmacy and Pharmacology 55(9): 1275-1282.
Rerknimitr P, Nitinawarat J, Weschawalit S (2016). The efficacy of *Gynura pseudochina* DC. var. hispida Thv. ointment in treating chronic plaque psoriasis: A randomized controlled trial. Journal of Alternative and Complementary Medicine 22(8): 669-675.
Rendon A, Schäkel K (2019). Psoriasis pathogenesis and treatment. International Journal of Molecular Science 1475.
Rodriguez S, Cancino-Diaz J, Torrez I (2017). Psoriatic animal models developed for the study of the disease, in: Chiriac A, (Ed), An Interdisciplinary Approach to Psoriasis: IntechOpen, London, 75-90.
Ru Y, Yan XN, Yang SQ (2019). Oral Taodan granules for mild-to-moderate psoriasis vulgaris: protocol for a randomized, double-blind, multicenter clinical trial. Annals of Translational Medicine 18:488.
Sampson JH, Raman A, Karlsen G (2001). *In vitro* keratinocyte antiproliferant effect of Centella asiatica extract and triterpenoid saponins. Phytomedicine 8(1):230-235
Saravanan S, Prakash BN, Pandikumar P (2012). Immunomodulatory potential of *Enicostema axillare* (Lam.) A. Raynal, a traditional medicinal plant. Journal of Ethnopharmacology 140(1): 239-246.
Saelee C, Thongrakard V, Tencomnao T (2011). Effects of Thai medicinal herb extracts with anti-psoriatic activity on the expression on NF-κB signaling biomarkers in HaCaT keratinocytes. Molecules

16(5):3908-3932.
Sarafian G, Afshar M, Mansouri P (2015). Topical turmeric microemulgel in the management of plaque psoriasis; a clinical evaluation. Iranian Journal of Pharmacological Research 14(3):865-876.
Scheiba N, Andrulis M, Helmbold P (2011). Treatment of shiitake dermatitis by balneo PUVA therapy. Journal of American Academy of Dermatology 65(33):453-455.
Shao F, Tan T, Tan Y (2016). Andrographolide alleviates imiquimod-induced psoriasis in mice via inducing autophagic proteolysis of MyD88. Biochemical Pharmacology 115(1):94-103.
Shedoeva A, Leavesley D, Upton Z (2019). Wound healing and the use of medicinal plants. Evidence- Based Complementary and Alternative Medicine 2684108.
Shenefelt PD (2011). Herbal Treatment for Dermatologic Disorders, in: Benzie IFF, Wachtel-Galor S, (Eds.), Herbal Medicine: Biomolecular and Clinical Aspects. Boca Raton (FL): CRC Press/Taylor & Francis, Florida pp. 383-404.
Shi Q, He Q, Chen W (2019). Ginsenoside Rg1 abolish imiquimod-induced psoriasis-like dermatitis in BALB/c mice *via* downregulating NF-kappaB signaling pathway. Journal of Food and Biochemistry 43:e13032.
Shi HJ, Zhou H, Ma AL (2019). Oxymatrine therapy inhibited epidermal cell proliferation and apoptosis in severe plaque psoriasis. British Journal of Dermatology 181(5):1028-1037.
Song P, Lysvand H, Yuhe Y (2020). Expression of the psoriasis-associated antigen, Pso p27, is inhibited by traditional Chinese medicine. Journal of Ethnopharmacology 127:171-174.
Su Y, Wu L, Mu G (2017). 9,19-Cycloartenol glycoside G3 from Cimicifuga simplex regulates immune responses by modulating Th17/Treg ratio. Bioorganic and Medicinal Chemistry 25(17):4917-4923.
Su Y, Wang Q, Yang B, Wu L, Cheng G, Kuang H (2017). Withasteroid B from D. metel L. regulates immune responses by modulating the JAK/STAT pathway and the IL-17+RORγt+/IL-10+FoxP3+ ratio. Clinical and Experimental Immunology 190(1):40-53.
Sun S, Zhang X, Xu M (2019). Berberine downregulates CDC6 and inhibits proliferation *via* targeting JAK-STAT3 signaling in keratinocytes. Cell Death and Diseases 10(4):274-280.
Sun Y, Zhang J, Huo R, Zhai T, Li H, Wu P, Zhu X, Zhou Z, Shen B, Li N (2015). Paeoniflorin inhibits skin lesions in imiquimod-induced psoriasis-like mice by downregulating inflammation. International Immunopharmacology 24(2):392-329.
Sun W, Gao Y, Yu X (2018). 'Psoriasis 1' reduces psoriasis‑like skin inflammation by inhibiting the VDR‑mediated nuclear NF‑κB and STAT signaling pathways. Molecular Medicine Reports 18(3):2733-2743.
Sung YY, Yoon T, Jang S (2016). *Forsythia suspensa* suppresses house dust mite extract-induced atopic dermatitis in NC/Nga Mice. PLoS One 11:e0167687.
Sung YY, Kim HK (2013). *Illicium verum* extract suppresses IFN-γ-induced ICAM-1 expression via blockade of JAK/STAT pathway in HaCaT human keratinocytes. Journal of Ethnopharmacology 149(1):626-632.
Syed TA, Ahmad SA, Holt AH (1996). Management of psoriasis with *Aloe vera* extract in a hydrophilic cream: a placebo-controlled, double-blind study. Tropical Medicine and International Health 1(4):505-509.
Tang TY (2012). A nonimmunosuppressant approach on Asia psoriasis subjects: 5-year follow-up and 11-year data analysis. Dermatological Research Practice 304172.
Tang L, He S, Wang X (2018). Cryptotanshinone reduces psoriatic epidermal hyperplasia via inhibiting the activation of STAT3. Experimental Dermatology 27(3):268-275.
Tse WP, Che CT, Liu K (2006). Evaluation of the anti-proliferative properties of selected psoriasis-treating Chinese medicines on cultured HaCaT cells. Journal of Ethnopharmacology 108(1):133-141.
Tse WP, Cheng CH, Che CT (2007). Induction of apoptosis underlies the *Radix rubiae*-mediated anti-proliferative action on human epidermal keratinocytes: implications for psoriasis treatment. International Journal of Molecular Medicine 20(5):663-672.
Tucker LJ, Coates LC, Helliwell PS (2019). Assessing disease activity in psoriatic arthritis: a literature review. Rheumatology and Therapy 6(1):23-32.
Wang A, Wei J, Lu C (2019). Genistein suppresses psoriasis-related inflammation through a STAT3-NF-κB-dependent mechanism in keratinocytes. International Immunopharmacology 69(1):270-278.
Wang Y, Zhao J, Zhang L (2015). Suppressive effect of β, β-dimethylacryloyl alkannin on activated dendritic cells in an imiquimod-induced psoriasis mouse model. International Journal of Clinical and Experimental Pathology 8:6665-66673.
Wang MX, Zhao JX, Meng YJ (2018). Acetyl-11-keto-β-boswellic acid inhibits the secretion of cytokines by dendritic cells *via* the TLR7/8 pathway in an imiquimod-induced psoriasis mouse model and *in vitro.* Life Science 207(1):90-104.
Wee SS, Shin YW, Bae EA (2005). Effect of chunghyuldan in chronic oxazolone-induced mouse dermatitis. Biological Pharmacology Bulletin 28(6):1079-1082.
Weng SW, Chen BC, Wang YC (2016). Traditional Chinese medicine use among patients with psoriasis in Taiwan: A nationwide population-based study. Evidence-Based Complementary and Alternative Medicine 3164105.
Weng JR, Huang TH, Lin ZC (2019). Cutaneous delivery of [1-(4-chloro-3-nitrobenzenesulfonyl)-1H-indol-3-yl]-methanol, an indole-3-carbinol derivative, mitigates psoriasiform lesion by blocking MAPK/NF-kappaB/AP-1 activation. Biomedical Pharmacotherapy 119: 109398.
Wei JA, Han L, Lu CJ (2016). Formula PSORI-CM01 eliminates psoriasis by inhibiting the expression of keratinocyte cyclin B2. BMC Complementary and Alternative Medicine 16:255.
Wollina U, Franca K, Lotti T (2018). Adjuvant treatment of chronic plaque psoriasis in adults by a herbal combination: Open German trial and review of the literature. Dermatology Therapy e12624.
Wu J, Li H, Li M (2015). Effects of baicalin cream in two mouse models: 2,4-dinitrofluorobenzene-induced contact hypersensitivity and mouse tail test for psoriasis. International Journal of Clinical and Experimental Medicine 8(2):2128-2137.
Wu C, Jin HZ, Shu D (2015). Efficacy and safety of *Tripterygium wilfordii* hook F versus acitretin in moderate to severe psoriasis vulgaris: a randomized clinical trial. Chinese Medical Journal 128(4):443-449.
Xie XJ, Di TT, Wang Y (2018). Indirubin ameliorates imiquimod-induced psoriasis-like skin lesions in mice by inhibiting inflammatory responses mediated by IL-17A-producing γδ T cells. Molecular Immunology 101:386-395.
Xie X (2017). Paeonol ameliorates imiquimod-induced psoriasis-like skin lesions in BALB/c mice by inhibiting the maturation and activation of dendritic cells. International Journal of Molecular Medicine 39:1101-1110.
Xiong H, Xu Y, Tan G (2015). Glycyrrhizin ameliorates imiquimod-induced psoriasis-like skin lesions in BALB/c mice and inhibits TNF-α-induced ICAM-1 expression via NF-κB/MAPK in HaCaT cells. Cell Physiology and Biochemistry 35(4):1335-1346.
Xu XG, Zhang H, Bi XL (2012). Xiaoyin recipe for psoriasis induces a Th1/Th2 balance drift toward Th2 in peripheral blood mononuclear cells of experimental autoimmune thyroiditis rats. Chinese Journal of Integrative Medicine 18(2):137-145.
Yan Y, Liu W, Andres P (2015). Exploratory clinical trial to evaluate the efficacy of a topical traditional Chinese herbal medicine in psoriasis vulgaris. Evidence-Based Complementary and Alternative Medicine 719641
Yan Y, Furumura M, Gouya T (2015). Shikonin promotes skin cell proliferation and inhibits nuclear factor-κB translocation via proteasome inhibition *in vitro.* Chinese Medical Journal 128916):2228-2233.
Yang Z, Zeng B, Tang X (2016). MicroRNA-146a and miR-99a are potential biomarkers for disease activity and clinical efficacy assessment in psoriasis patients treated with traditional Chinese medicine. Journal of Ethnopharmacology 94:727-732.
Yang R, Zhou Q, Wen C (2013). Mustard seed (Sinapis Alba Linn) attenuates imiquimod-induced psoriasiform inflammation of BALB/c

mice. Journal of Dermatology 40(2):543-552.
Yang XG, Jiang BW, Jing QQ (2019). Nitidine chloride induces S phase cell cycle arrest and mitochondria-dependent apoptosis in HaCaT cells and ameliorates skin lesions in psoriasis-like mouse models. European Journal of Pharmacology 863:172680.
Yang BY, Cheng YG, Liu Y (2019). *Datura metel* L. ameliorates imiquimod-induced psoriasis-like dermatitis and inhibits inflammatory cytokines production through TLR7/8-MyD88-NF-κB-NLRP3 inflammasome pathway. Molecules 24(11):2157-2162.
Ye H, Wang Y, Jenson AB, Yan J (2016). Identification of inflammatory factor TNFα inhibitor from medicinal herbs. Experimental Molecular Pathology 100(2):307-311.
Yehuda H, Khatib S, Sussan I (2009). Potential skin antiinflammatory effects of 4-methylthiobutylisothiocyanate (MTBI) isolated from rocket (*Eruca sativa*) seeds. Biofactors 35(30):295-305.
Yu J, Xiao Z, Zhao R (2017). Paeoniflorin suppressed IL-22 *via* p38 MAPK pathway and exerts anti-psoriatic effect. Life Science 180:17-22.
Yu C, Fan X, Li Z (2017). Efficacy and safety of total glucosides of paeony combined with acitretin in the treatment of moderate-to-severe plaque psoriasis: a double-blind, randomised, placebo-controlled trial. European Journal of Dermatology 27(1):150-154.
Zhang Y, Ma X (2010). Triptolide inhibits IL-12/IL-23 expression in APCs via CCAAT/enhancer-binding protein alpha. Journal of Immunology 184(7):3866-3877.
Zhang WJ, Song ZB, Bao YL (2016). Periplogenin induces necroptotic cell death through oxidative stress in HaCaT cells and ameliorates skin lesions in the TPA- and IMQ-induced psoriasis-like mouse models. Biochemical Pharmacology 105:66-79.
Zhang J, Hu X, Wang P (2018). Investigation on species authenticity for herbal products of *Celastrus Orbiculatus* and *Tripterygum wilfordii* from markets using ITS2 barcoding. Molecules 23(4):967-275.
Zhang Y, Xia Q, Li Y (2019). CD44 assists the topical anti-psoriatic efficacy of curcumin-loaded hyaluronan-modified ethosomes: a new strategy for clustering drug in inflammatory skin. Theranostics 9(1):48-64.
Zhang LX, Bai YP, Song PH (2009). Effect of Chinese herbal medicine combined with acitretin capsule in treating psoriasis of blood-heat syndrome type. Chinese Journal of Integrative Medicine 15(1):141-144.
Zhao J, Di T, Wang Y (2016a). Paeoniflorin inhibits imiquimod-induced psoriasis in mice by regulating Th17 cell response and cytokine secretion. European Journal of Pharmacology 772(1):131-143.
Zhao J, Di T, Wang Y (2016b). Multi-glycoside of *Tripterygium wilfordii* Hook. f. ameliorates imiquimod-induced skin lesions through a STAT3-dependent mechanism involving the inhibition of Th17-mediated inflammatory responses. International Journal of Molecular Medicine 38(3): 747-757.
Zhou LL, Lin ZX, Fung KP (2011). Celastrol-induced apoptosis in human HaCaT keratinocytes involves the inhibition of NF-kappaB activity. European Journal of Pharmacology 670(2-3):399-408.
Zhou J, Gao Y, Yi X (2015). Ginsenoside Rh2 suppresses neovascularization in xenograft psoriasis model. Cell Physiology and Biochemistry 36(3):980-987.
Zhou N, Bai YP, Man XHl (2019). Effect of new Pulian Ointment in treating psoriasis of blood-heat syndrome: A randomized controlled trial. Chinese Journal of Integrative Medicine 15(6):409-414.