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REVIEW ARTICLE

# Complementary and Alternative Medicine for Psoriasis: What the Dermatologist Needs to Know

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**Abstract** Complementary and alternative medicine (CAM) use is common among patients with psoriasis. CAM modalities include traditional Chinese medicine (TCM), herbal therapies, dietary supplements, climatotherapy, and mind/body interventions. In this review, evidence from clinical trials investigating the efficacy of CAM for psoriasis is reviewed. There is a large amount of evidence from controlled trials that have shown that the combination of TCM with traditional therapies for psoriasis is more efficacious than traditional therapies alone. Herbal therapies that have the most evidence for efficacy are *Mahonia aquifolium* and indigo naturalis, while there is a smaller amount of evidence for aloe vera, neem, and extracts of sweet whey. Dietary supplementation in patients with psoriasis demonstrates consistent evidence supporting the efficacy of fish oil supplements. Zinc supplementation has not been shown to be effective; however, some evidence is available (albeit conflicting) for vitamin D, vitamin B12, and selenium supplementation. Overwhelming evidence supports the effectiveness of Dead Sea climatotherapy. Finally, mindfulness-based stress reduction can be helpful as adjuvant treatment of psoriasis. There are potential benefits to these modalities, but also potential side issues. Concerns with CAM include, but are not limited to, contamination of TCM products with heavy metals or corticosteroids, systemic toxicity or contact dermatitis from herbal supplements, and ultraviolet light-induced carcinomas from climatotherapy. Dermatologists should be aware of these benefits and side effects to allow for informed discussions with their patients.

**Key Points**

Complementary and alternative medicine (CAM) use is common among patients with psoriasis.

A large body of randomized controlled trial data exists for the use of traditional Chinese medicine, certain herbal therapies (*Mahonia aquifolium* and indigo naturalis), climatotherapy, and fish oil.

CAM has potential side effects that dermatologists should be aware of.

## 1 Introduction

Complementary and alternative medicine (CAM) is defined by the National Center for Complementary and Integrative Health (NCCIH) as "a group of diverse medical and health care systems, practices and products that are not currently considered to be part of conventional medicine" [1]. CAM for psoriasis includes traditional Chinese medicine (TCM), herbal therapies, dietary supplements and dietary modifications, climatotherapy, and mind/body interventions. CAM use among psoriasis patients is common, with prevalence estimations varying between 42 and 69 % [2–6]. Herbal therapies seem to be the most commonly used modality [2, 3, 7]. Most often, patients use CAM as 'complementary' therapy, as opposed to 'alternative'

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therapy, i.e. rather than using CAM as monotherapy, most patients are taking CAM in combination with traditional treatment modalities in an effort to do everything possible to control their disease [3]. Other reasons patients choose CAM include a preference for 'natural' approaches to their skin disease, a perceived lower risk of side effects, and dissatisfaction with the efficacy or toxicity of traditional medicine [8]. Studies have shown that patients do not willingly offer information regarding CAM use to their physicians [3, 5, 9, 10]; therefore, the onus is on the physician to ask questions regarding CAM use. Interestingly, even though patients do not frequently offer information regarding CAM use, they are willing to discuss it if asked and, in fact, expect their dermatologists to have a basic knowledge of CAM [11].

In the US, the demographic profile of patients who use CAM for skin disease (not specifically psoriasis) tends to be White females between the ages of 26 and 50 years, who have at least a high-school diploma [1, 12]. The demographics of CAM use specifically among patients with psoriasis is not well understood and has not been investigated on a population-based level in the US.

The aims of this review are to first highlight the evidence for efficacy of CAM modalities in the treatment of psoriasis and, second, to provide the reader with clinically relevant considerations with regard to the implementation of CAM, reported drug interactions, and known side effects of CAM therapies. A PubMed search was performed using the terms 'psoriasis' and 'complementary and alternative medicine', as well as search terms for other, more specific CAM modalities such as 'fish oil' and 'traditional Chinese medicine'. Lists of references were consulted for additional articles. The discussion of efficacy was limited to randomized controlled trials (RCTs).

## 2 What is the Evidence?

This section will review the evidence of efficacy for the following CAM modalities: TCM, herbal therapies, dietary supplements, climatotherapy and mind/body interventions. When we consider the likelihood of an RCT demonstrating efficacy of a particular intervention, it becomes important to distinguish whether a CAM modality is self-administered or given under medical supervision and subject to a protocol tailored to that individual. For example, TCM, Dead Sea climatotherapy, and mind/body interventions are generally performed under medical supervision and are therefore subject to a protocol that is amended based on patient-specific characteristics. In contrast, herbal therapies and dietary supplements can be self-administered, and allow for more rigid study design as intervention can be more uniform across patients.

### 2.1 Traditional Chinese Medicine

TCM is a whole system of medicine rather than a specific treatment or ingredient. Imbalances in 'yin' and 'yang' are thought to contribute to disease states such as chronic plaque psoriasis, which is termed 'blood-heat syndrome'. TCM incorporates herbal therapies, acupuncture, exercise (such as Tai Chi), massage, dietary changes, and meditation. Although herbal medicines (HMs) are often used in TCM, the two are not one and the same as HMs are often used outside the context of TCM. Herbal therapies are the primary component of TCM and include oral herbal therapies in the form of 'granules' or 'decoctions', topical herbal creams or ointments and herbal baths.

Typically, a treatment recommendation by a TCM practitioner will include a combination of extracts from several herbs, with the particular combination being determined by patient-specific characteristics [13]. Herein lies the essential problem with evaluating and comparing clinical trials of TCM. If the treatments are designed to be tailored to each patient and contain numerous different herbs, the innate heterogeneity of studies makes it difficult to perform meta-analyses of individual trials or to interpret the results of clinical trial data for one's own clinical use. Another issue that arises when evaluating TCM clinical trials is the particular way in which some of these trials measure clinical efficacy. While some trials use Psoriasis Area and Severity Index (PASI) scores, most will use terms such as 'total effective rate' or 'remarkably effective rate', which are benchmarks that are difficult to compare with conventional PASI scores. Nevertheless, several authors have reviewed the TCM data. A summary of randomized controlled clinical trial data of TCM for psoriasis from published meta-analyses is presented in Table 1. Unless otherwise stated, the trials presented in this table were either not blinded for the investigators or the participants, or it was not stated in the trial whether blinding was performed.

A recent systematic review and small meta-analysis by Zhang et al. [14] supported the use of complementary TCM. Seventeen RCTs where included, all conducted in China, with some published in the English language and others in Chinese. The trials all investigated 'complementary' use of TCM, in the form of oral Chinese HM combinations. They therefore compared the combination of TCM with a traditional allopathic medicine versus control, which was the traditional medicine alone. To obtain the lowest amount of heterogeneity possible, the pooled meta-analysis was limited to five studies that used a 'well known' therapeutic (such as acitretin) as the control and had the outcome of efficacy listed as a >60 % improvement (reduction in PASI) in the psoriasis. The results of the pooled analysis showed a benefit in 'total effective rate' of

**Table 1** Randomized clinical trials comparing traditional Chinese medicine with conventional anti-psoriatic pharmacotherapy (trials were identified from four published meta-analyses [14–16, 22])

| Study, location; duration, follow-up | Trial design (sample size, *n*) | TCM ingredients, dosage, administration | APP (conventional anti-psoriatic therapy) dosage, administration | Outcome measures: results | AEs |
|---|---|---|---|---|---|
| Trials with oral CHM as primary intervention | | | | | |
| Liu et al. [78], Huangshi, China; 4 weeks, NS | Oral CHM + topical APP (42) vs. topical APP (42) | Commercial Binghuang Ointment, qd (night) for 4 weeks | Tazarotene 0.05 % gel, 2× day, for 4 weeks | Reduction in PASI: T > C ($p < 0.05$) | Slight itching and burning (T: 3, C: 5) |
| Zhang [79], China; 4 weeks, no follow-up | Oral CHM + acitretin (56) vs. acitretin alone (56) | CHM decoction (Qing Ying Tang), tid, no individual modification | Oral acitretin capsules: 10 mg tid | TER based on lesions reduction 75 %: T > C for TER; ES for 75 % lesion reduction: RR 1.64 (CI 1.23–2.19) | NS |
| Zheng [80], China; 8 weeks, no follow-up | Oral CHM + acitretin (60) vs. acitretin alone (60) | CHM decoction (Xiao Yin Ke Bi Tang), bid, no individual modification | Oral acitretin capsules: started at 20 mg/day, then increased to 30–40 mg/day, then decreased to 10–20 mg/day | TER based on PASI 60; PASI score: T > C for TER and PASI score; ES for PASI 60: RR 2.00 (CI 1.21–3.32); ES for PASI score: MD −2.45 (CI −3.60 to −1.30) | Mild in both groups: GI reactions in both groups; leukocyte decrease in C group only; no SAE |
| Luo [81], China; 6 weeks, no follow-up | Oral CHM + acitretin + co-interventions (74) vs. acitretin + co-interventions[b] (100) | CHM decoction (no formula name), bid, no individual modification | Oral acitretin capsules: 0.5 mg/kg per day; IV complex glycyrrhizin, 30 ml qd; topical calcipotriol, bid | TER based on PASI 60: T > C for TER; ES for PASI 60: RR 1.71 (CI 1.30–2.24) | Mild in C group only, caused by pharmacotherapies; no SAE |
| Wang et al. [82], Changchun, China; 6 weeks, NS | Oral CHM + topical and systemic APP (22) vs. topical and systemic APP (20) | Herbal bath as 3000 ml bath for 20–30 min 1× day for weeks 1–2, then 1 × 2 days for weeks 3–4, then 2× week for weeks 5–6 | Salicylic acid cream 2× day, methotrexate, oral 5–15 mg/week | Overall clinical efficacy[a]: T > C ($\chi^2 = 8.24$, $p < 0.05$) | Hair loss (T: 1), slightly increased ALT (T: 1 = 50 U/L; C: 1 = 55 U/L), stomach discomfort (T: 1, C: 2) |
| Wu [83], China; 12 weeks, no follow-up | Oral CHM + acitretin + co-interventions[b] (79) vs. acitretin + co-interventions[b] (79) | CHM decoction (Yin Xie Kang), qd, individual modification according to symptoms | Oral acitretin capsules: 0.5 mg/kg/day; boric acid ointment, bid | TER based on PASI 60; PASI score; liver and kidney function: T > C for TER and PASI score; ES for PASI 60: RR 1.32 (CI 1.11–1.57); ES for PASI score: MD −4.03 (CI −4.97 to −3.09) | Mild in both groups, dry and scaly skin, due to pharmacotherapy, T<C; no SAE |
| Yang et al. [84], Xiangfan, China; 4 weeks, 6 months | Oral CHM + topical APP (82) vs. topical APP (47) | Herbal bath decocted in water adequate for a body bath. Frequency of use not specified | Halcinolone acetonide cream 2× day, thymosin IV solution 40 mg/day | Overall clinical efficacy[a]: T > C ($\chi^2 = 4.649$, $p < 0.05$) Follow-up relapse: T: 1 (3.55 %), C: 2 (18.2 %) | No obvious issues |

**Table 1** continued

| Study, location; duration, follow-up | Trial design (sample size, *n*) | TCM ingredients, dosage, administration | APP (conventional anti-psoriatic therapy) dosage, administration | Outcome measures: results | AEs |
|---|---|---|---|---|---|
| Yang et al. [85], Luzhou, China; 4 weeks, NS | Oral CHM + topical and systemic APP (58) vs. topical and systemic APP (46) | Herbal steam with additions of various herbs according to individual syndromes<br>Applied using specific device, 20 min/day for 5 days, 2 days' break, for 4 weeks | Hydrocortisone butyrate cream 2 × day, urea cream 29 days, acitretin capsules, oral 30–40 mg 1× day | Overall clinical efficacy[a]: T > C ($\chi^2$ = 9. 91, $p < 0.01$) | (T/C): dry mouth, dry lips and chapped lips (44/46), dry eyes (28/38), dry skin on body (22/34), epistaxis (4/6), body itching (13/19), desquamation (11/25), increased ALT (2/8), hyperlipidemia (1/1) |
| Feng et al. [86], Beijing, China; 3 weeks, NS | Oral CHM + topical APP (32) vs. topical APP (33) | Herbal bath, various herbs totaling 20 g in 2000 ml water, 20 min, 19 days, for 3 weeks | Kangminzhiyang cream (triamcinolone acetonide) 2× day, ammonium glycyrrhizinate IV solution 150 mg/day | Reduction in lesion area: T > C ($\chi^2$ = 5.54, $p$ = 0.019); clearance time: T < C ($\chi^2$ = 4.32, $p$ = 0.001); lesion score: itching T < C ($\chi^2$ 2.72, $p$ = 0.008), scaling T<C ($\chi^2$ = 2.84, $p$ = 0.006), erythema and induration (not significant) | Slight dizziness and palpitation (T: 2) |
| Mao and Mao [87], China; 8 weeks, 3 months | Oral CHM + acitretin + co-interventions[b] (31) vs. acitretin + co-interventions[b] (31) | CHM decoction (no name), bid, individual modification according to psoriasis vulgaris stage | Oral acitretin capsules, 10 mg bid; oral 'Diyin' tablets, five tablets bid | TER based on PASI 60; recurrence rate; liver and kidney function: T > C for TER; ES for PASI 60: RR 1.09 (CI 0.81–1.46) | Mild skin dryness, pruritus, T/C: (1/3); no SAE |
| Han et al. [88], Huangshi, China; 4 weeks, NS | Oral CHM + topical APP (43) vs. topical APP (32) | Commercial Binghuangfule ointment qd | Clobetasol cream qd | PASI T ≈ C ($\chi^2$ = 0.327, $p < 0.05$); overall clinical efficacy[a]:<br>T ≈ C ($\chi^2$ = 0.040, $p > 0.05$); follow-up relapse: T: 5 (26.32 %), C: 8 (47.06 %) | Skin pigmentation (C: 1), hypopigmentation and skin atrophy (C: 2), Malassezia folliculitis (C: 3), skin pigmentation (T: 2) |
| Tang [89]; Hangzhou, China; 10 times (over 10–20 days), NS | Oral CHM + topical APP (36) vs. topical APP (36) | Herbal bath of various herbs, each 60 g of raw herbs. In warm bath, 1:40,000, 30 min qd or bid, total 10× as a course | Dexamethasone ointment, salicylic acid ointment, and triamcinolone acetonide acetate ointment, slow injection of procaine 4–6 mg/kg plus vitamin C 300 mg in 300 ml saline once a day for 10–15 days as a course, warm water bath qd or 1 × 2 days (only for the control group) | Overall clinical efficacy[a]: T > C ($\chi^2$ = 5.796, $p < 0.05$) | NS |

**Table 1** continued

| Study, location; duration, follow-up | Trial design (sample size, *n*) | TCM ingredients, dosage, administration | APP (conventional anti-psoriatic therapy) dosage, administration | Outcome measures: results | AEs |
|---|---|---|---|---|---|
| Wang et al. [90], China; 24.7 days average, 1 year | Oral CHM + topical APP (675) vs. topical APP (200) | Yin Xie Ling ointment, 0.3 mm thickness, qd | Dichlorodiethyl sulphide (1:10,000 in petroleum jelly), 0.3 mm thickness, qd | Overall clinical efficacy[a]: T > C (90.7 > 84 %, $p < 0.05$); mean inpatient time to lesion clearance: T < C (24.7 < 32.5 days); follow-up relapse: T < C (13 < 76 %) | 'Allergic response rate' T\C (1.93/5 %) |
| Trials with topical CHM as primary intervention | | | | | |
| Yang et al. [91], Qingdao, China; 8 weeks, NS | Topical CHM + oral APP (96) vs. topical APP + oral APP (86) | Liubaibaibi cataplasm: apply enough cataplasm to cover the lesions for 6 h, bid | En Fu cream (clobestasol): bid<br>Co-intervention: folic acid (10 mg): oral, tid; vitamin E (0.2 g): oral, tid | Clinical efficacy based on reduction of PASI score: T > C ($\chi^2 = 5.0$, $p < 0.05$) | No SAE, mild itching and burning (T = 4, C = 5) |
| Xu J [92], Beijing, China; 8 weeks, 3 months | T1: topical HM + oral HM (30) vs. T2: topical HM + oral HM (30) vs. C: topical placebo + oral HM (30) | T1: Conventional Qinbai Ruangao (ointment)<br>T2: Fine Qinbai Ruangao (ointment) | C: white vaseline ointment. Clean the affected skin, then apply the ointment, bid<br>Co-intervention: Liangxue Huoxue Tang (decoction) in 400 ml decoction, oral, bid | Clinical efficacy: T1/T2 > C ($p < 0.05$), T1 ≈ T2 ($p > 0.05$); reduction of modified PASI scores: T1/T2 > C ($p < 0.05$), lesion area rating: T1 ≈ T2 ≈ C; single-symptom scores (erythema, scaling, infiltration, and itching): all T1/T2 < C ($p < 0.05$); single symptom time to improvement: all T1/T2 < C ($p < 0.05$) | Slight erythema and irritation (T1 = 2, T2 = 1, C = 1) |
| Zhou et al. [93], Beijing, China; 4 weeks, NS | Topical CHM + oral CHM (51) vs. topical placebo + oral CHM (49) | New Pulian Ointment | Placebo ointment: mainly contained Jian qu (Massa Fermentata Medicinalis bid<br>Co-intervention: conventional clearing heat and cooling blood decoction qd | RER: T > C ($\chi^2 = 13.0998$, $p = 0.0003$); TER: T > C ($\chi^2 = 12.7298$, $p = 0.0004$); PASI scores: T < C ($p < 0.05$); score of erythema, infiltration, and lesion area: all T < C ($p < 0.01$); score of scaling: T ≈ C ($p > 0.05$); score of itching: T < C ($\chi^2 = 8.1145$, $p = 0.0044$) | AEs: none |

**Table 1** continued

| Study, location; duration, follow-up | Trial design (sample size, *n*) | TCM ingredients, dosage, administration | APP (conventional anti-psoriatic therapy) dosage, administration | Outcome measures: results | AEs |
|---|---|---|---|---|---|
| Zhu et al. [94], Sichuan, China; 2 weeks, NS | Topical CHM (41) vs. topical APP (44) | Xiaoxuanling formula bid | Tretinoin cream (0.025 % Diwei cream: vitamin A acid cream) bid | Clinical efficacy based on PASI: T ≈ C ($\chi^2 = 2.125$, $p = 0.05$) | T: slight tingling sensation (7), C: slight burning (6) |
| Song et al. [95], Beijing, China; 4 weeks, 0.5 years | T: topical CHM + oral CHM (60) vs. C1: topical APP + oral CHM (29) vs. C2: topical placebo + oral CHM (29) | CEBO bid | C1 (WM): Daivonex ointment (calcipotriol) bid; C2 (placebo): vehicle of CEBO bid | Modified PASI scores: T < C2 ($p < 0.01$), C1 < C2 ($p < 0.01$), T < C1 ($p < 0.01$)<br>Clinical efficacy: T > C2 ($p < 0.01$), C1 > C2 ($p < 0.01$), T ≈ C1 ($p > 0.05$)<br>Single symptom scores: T < C2 ($p < 0.01$), C1 < C2 ($p < 0.01$)<br>Time to symptom improvement: (1) itching: T < C1/C2 ($p < 0.01$); (2) erythema, scaling, and induration: T/C1 < C2 ($p < 0.01$); (3) lesion area: T ≈ C1 ≈ C2 | T: slight erythema and irritation (2), C1: erythema and lesion enlarged (2), C2: none |
| Gao et al. [96], Qingdao, China; 8 weeks, NS | Topical CHM + oral APP (192) vs. topical APP + oral APP (184) | Liubai Baibi cream | En Fu cream (clobestasol) bid<br>Co-interventions[b]: folic acid (10 mg): oral, tid; Vitamin E (0.2 g): oral, tid | Clinical efficacy based on reduction of PASI score: T > C ($\chi^2 = 36.15$, $p < 0.01$) | No SAE, mild itching, and burning (T = 7, C = 9) |
| Lu and Miao, 2004 [97], Shenyang, China; 18 days, NS | Topical CHM (31) vs. topical APP (22) | Queyin tincture in water with 75 % alcohol, 1000 ml, for 2 weeks, then filter and set aside<br>Lesion on the limbs/chest–back used as target area (7.5–30 $cm^2$) bid | Piyanning tincture (compound fluocinonide tincture): lesion on the limbs/chest–back used as target area (7.5–30 $cm^2$) bid | Clinical efficacy based on reduction of symptom score: T > C ($p < 0.05$) | NS |

**Table 1** continued

| Study, location; duration, follow-up | Trial design (sample size, *n*) | TCM ingredients, dosage, administration | APP (conventional anti-psoriatic therapy) dosage, administration | Outcome measures: results | AEs |
|---|---|---|---|---|---|
| Wang et al. [98], Changsha, China; 8 weeks, 1 year | Topical CHM (112) vs. topical APP (56) | 1# Herbal bath formula (for blood-heat syndrome)<br>2# Herbal bath formula (for blood-deficiency syndrome) 30 g<br>1#/2#: In 180–200 L water boiled for 20 min, then filter into warm liquid for bath, 20 mins, bid | 0.1 % Anthralin ointment bid (in the morning and at night) | Global PASI: T < C ($p < 0.001$)<br>Clinical efficacy: T > C ($\chi^2 = 6.25$, $p < 0.05$)<br>Relapse comparison: T < C ($\chi^2 = 5.50$, $p < 0.05$) | NS |
| Trials with bath CHM as primary intervention | | | | | |
| Shi et al. [99], Beijing, China; 56 days, NS | CHM bath plus phototherapy (170) vs. phototherapy alone (168) | CHM bath: 20 min, qod: NB-UVB: consistent with control intervention | NB-UVB (310–315 nm): 0.2–0.4 J/cm$^2$ as initial dosage, increased by 0.1 J/cm$^2$ each time, qod | TER based on PASI 60: TER T: 84.7 %; C: 70.2 % ($p < 0.01$) | Mild redness, pruritus (T: 11/170; C: 29/168); skin pigmentation in all (resolved without medical assistance within 3 months); no SAE |
| Wang et al. [100], Kaifeng, China; 28 days, NS | CHM bath plus phototherapy (50) vs. phototherapy (50); co-interventions used also | CHM bath: 30 min, qod; NB-UVB: consistent with control intervention; urea emollient after NB-UVB, qd | NB-UVB (310–315 nm): 0.3–0.5 J/cm$^2$ as initial dosage, increased by 10–20 % each time, qod; urea emollient after NB-UVB, qd | TER based on PASI 60: TER T: 86.0 %; C: 72.0 % ($p < 0.05$) | Mild skin dryness, burning pain after NB-UVB (T: 4/50; C: 5/50); no SAE |
| Wu et al. [101], Chengdu, China; 40 days, NS | CHM bath plus phototherapy (75) vs. phototherapy (65); co-interventions used also | Halometasone emollient for 1-week pre-trial treatment: qd; CHM bath: 15–20 min, qod; NB-UVB: consistent with control intervention; urea emollient, qd | Halometasone emollient: consistent with treatment intervention; NB-UVB (310–315 nm): 0.5–0.6 J/cm$^2$ as initial dosage, increased by 0.1 J/cm$^2$ each time, qod; urea emollient, qd | TER based on PASI 60; PASI score: TER T: 78.67 %; C: 56.92 %, ($\chi^2 = 10.54$, $p < 0.01$); PASI score T: 9.24 ± 2.17; C: 5.46 ± 1.86 | Slight light skin dryness, burning pain after NB-UVB (T: 2/75; C: 3/65); no SAE |
| Lin et al. [102], Hefei, China; 49 days, NS | CHM bath plus phototherapy (95) vs. phototherapy (90); co-interventions used also | CHM bath: 20–30 min, three times a week; NB-UVB: consistent with control intervention; Bing Huang Fu Le ointment after NB-UVB, qd | NB-UVB (311 nm): 0.3–0.5 J/cm$^2$ as initial dosage, increased by 0.1 J/cm$^2$ each time, 110 s, three times a week; Bing Huang Fu Le ointment after NB-UVB, qd | TER based on PASI 60; PASI score: TER: T: 96.7 %; C: 70 %, ($\chi^2 = 17.69$, $p < 0.01$); PASI score T: 11.15 ± 8.11; C: 14.74 ± 9.05 | Redness (T: 9/95; C: 22/90; $\chi^2 = 4.44$, $p < 0.05$); pruritus (T: 11/95; C: 26/90; $\chi^2 = 4.94$, $p < 0.05$); skin dryness (T: 15/95; C: 17/90; $p > 0.05$); no SAE |

**Table 1** continued

| Study, location; duration, follow-up | Trial design (sample size, *n*) | TCM ingredients, dosage, administration | APP (conventional anti-psoriatic therapy) dosage, administration | Outcome measures: results | AEs |
|---|---|---|---|---|---|
| Wu et al. [103], Guangzhou, China; 90 days, NS | CHM bath plus phototherapy (40) vs. phototherapy alone (39) | CHM bath: 15–20 min, qod; NB-UVB: consistent with control intervention | NB-UVB (311–315 nm): 0.3–0.5 J/cm$^2$ as initial dosage, increased by 0.1 J/cm$^2$ each time, qod | TER based on PASI 60; PASI score: TER T: 75.00 %; C: 51.28 %,($\chi^2 = 4.78$, $p = 0.029$); PASI score: T: 4.21 ± 1.22; C: 6.45 ± 2.27 | Skin dryness, pruritus (T: 5/40; C: 5/39); skin pigmentation in all; no SAE |
| Gu et al. [104], Urumqi, China; 28 days, 6 months | CHM bath plus phototherapy (89) vs. phototherapy (96); co-interventions used also | CHM bath: 30 min, qod; NB-UVB: consistent with control intervention; Pu Lian ointment, bid | NB-UVB (311 nm): 0.3 J/cm$^2$ as initial dosage, increased by 0.1 J/cm$^2$ each time, qod; Pu Lian ointment, bid | TER based on PASI 60; relapse rate during follow-up: TER T: 94.38 %; C: 84.38 %, ($\chi^2 = 4.8$, $p < 0.05$); relapse rate during follow-up: T: 10.81 %; C: 30.30 % ($p < 0.05$) | Mild redness, pruritus, and skin dryness (T: 10/89; C: 23/96; $\chi^2 = 5.10$, $p < 0.05$); skin pigmentation in all (resolved without medical assistance within 2 months); no SAE |
| Cui et al. [105], Beijing and Anshan, China; 56 days, NS | CHM bath plus phototherapy (62) vs. phototherapy alone (57) | CHM bath: 20 min, qod; NB-UVB: consistent with control intervention | NB-UVB: 50 % of MED as initial dosage, increased by 0.1 J/cm$^2$ each time, maximum dosage 2.5 J/cm$^2$, twice a week | TER based on PASI 60; PASI score TER: T: 96.77 %; C: 71.93 %, ($\chi^2 = 27.755$, $p < 0.01$); PASI score: T: 4.16 ± 7.40; C: 11.40 ± 11.64; NB-UVB average dosage: T: 9.95 ± 4.76 J/cm$^2$; C: 12.77 ± 5.05 J/cm$^2$ ($p < 0.01$) | Adverse events (redness, pruritus) rate: T: 4.84 % (3/62); C: 31.58 % (18/57) ($\chi^2 = 119$, $p < 0.01$); no SAE |
| Liu et al. [106], Shijiazhuang, China; 40 days, NS | CHM bath plus phototherapy (40) vs. phototherapy alone (40) | CHM bath: 30 min, qod; NB-UVB: consistent with control intervention | NB-UVB (311–313 nm): 0.08 or 0.1 J/cm$^2$ as initial dosage, increased by 0.01–0.03 J/cm$^2$ each time, qod | TER based on PASI 60 (T: 95.0 %, C: 82.5 %, $p < 0.01$) | NS |

*AEs* adverse events, *APP* anti-psoriatic pharmacotherapy (i.e. traditional psoriasis therapy), *bid* twice daily, *C* control group, *CEBO* Compound E-Bei ointment, $\chi^2$ Chi-squared statistic, *CHM* Chinese herbal medicine, *CI* confidence interval, *ES* effect size, *GI* gastrointestinal, *HM* herbal medicines, *MD* mean difference, *NS* not stated, *PASI* Psoriasis Area and Severity Index, *qd* daily, *qod* every other day, *RER* remarkably effective rate, *SAEs* serious adverse events, *T* treatment group, *TCM* traditional Chinese medicine, *TER* total effective rate, *tid* three times daily, *WM* Western medicine (analogous to APP)

[a] Clinical efficacy scores: based on PASI using the following formula: (PASI pre-care − PASI post-care)/PASI pre-care × 100 %

[b] Co-interventions are medications administered to both treatment and control groups

using TCM in combination with acitretin versus acitretin alone [relative risk (RR) 1.5; 95 % CI 1.33–1.7]. There was a moderate amount of heterogeneity in the pooled analysis ($I^2 = 56$ %), and none of the studies were blinded, which increases the risk for bias in these results. The most commonly used herbs in these studies were *Rehmannia glutinosa* root (Chinese foxglove), *Salvia miltiorrhiza* root (red sage), and *Lithospermum erythrohizon* root (purple gromwell); however, in the 17 studies that were initially identified, a total of 70 different herbs were used in the trials. Of the five studies included in the meta-analysis, one study did not report on adverse events and the other four reported only mild adverse events. Only two studies monitored liver and kidney function.

Another recent systemic review and meta-analysis by Yu et al. [15] investigated the 'add-on' or complementary effect of Chinese HM baths to phototherapy. The concept is similar to bath–psoralen combined with Ultraviolet A (PUVA) in that the ingredients in the bath are thought to make the phototherapy more effective. Only RCTs were included in the analysis. Most studies employed narrowband ultraviolet (UV) B, one study used a combination of UVA and UVB, one study used only UVA, and no studies used PUVA. Thirteen trials were included in the review but only eight were suitable for the meta-analysis. The most commonly used herbs for the baths were *Salvia miltiorrhiza* root (red sage), *Dictamnus dasycarpus* bark (Dittany bark), *Sophora flavescens* root (bitter ginseng), and *Kochia scoparia* fruit (Broom Cyprus). The baths were taken 20–30 min prior to phototherapy. It is important to note that concomitant therapies were used in both arms of five studies. These included various TCM ointments, a urea-based emollient, and glycyrrhizin (liquorice root) tablets. The results of a pooled analysis showed that the bath therapy combined with phototherapy was slightly more effective than phototherapy alone in terms of PASI 60 (RR 1.25; 95 % CI 1.18–1.32). The amount of heterogeneity in studies was relatively low ($I^2 = 23$ %), and mild adverse events were reported in ten studies. The authors stated that the methodological quality of the studies was low. The most frequently used herbs in the bath therapy have been shown to have a variety of anti-inflammatory, antipruritic and anti-proliferative effects [15].

Deng et al. [16] reviewed topical HMs combined with traditional pharmacotherapy for the treatment of psoriasis in the context of a systematic review and meta-analysis. The authors investigated whether topical HMs had any additional effect exceeding that provided by anti-psoriatic pharmacotherapy (APP) alone. Eight studies were included in the review, all of which were conducted in China. Four studies investigated herbal baths, three studies used ointments, and one study investigated herbal steam as the treatment arm. Although a wide variety of HMs were used, some of the most commonly found herbal products in these studies were *Sophora flavescens* root (bitter ginseng), *Cnidium monnieri* seed (Monnier's snowparsley), *Dictamnus dasycarpus* bark (Dittany bark), Borneol, *Scutellaria baicalensis* (Chinese skullcap) root, *Rheum palmatum* (Turkish rhubarb) root, *Rehmannia glutinosa* (Chinese foxglove) root, *Salvia miltiorrhiza* (red sage) root, *Carthamus tinctorius* (safflower) flower, and sulfur. For the pooled analysis of efficacy, the studies were divided into two groups. Group one included studies in which the investigational group used topical HMs combined with topical APP versus the control group which used only topical APP. The topical APP products included potent topical corticosteroids or topical retinoids. Only cases with an efficacy rate $\geq$50 % were included. The pooled data showed a higher efficacy rate for the treatment group (HM plus APP) versus the control group (RR 1.18; 95 % CI 1.05–1.34); however, heterogeneity was high ($I^2 = 63$ %). Group two included two studies that compared topical HM combined with topical and systemic APP versus the control group which used only topical APP and systemic APP. A 60 % reduction in PASI score was considered the threshold for data pooling. Again, the pooled data showed higher efficacy compared with the control group (RR 1.67; 95 % CI 1.21–2.30). The heterogeneity in these two studies was zero, and the incidence of most adverse effects was lower in the treatment groups than in the control groups.

Regarding acupuncture, which could be considered a part of TCM, efficacy of classic acupuncture for psoriasis has not been demonstrated in RCTs [17].

However, a trial investigating 'point injection with magnetic blood' versus placebo did show a statistically significant benefit. This trial included 128 patients. The 'cure rate' in the treatment group was 72.7 versus 32.2 % in the control group ($p < 0.001$) and the 'efficacious rate' was 95.5 % in the treatment group versus 77.4 % in the control group ($p < 0.001$) [18].

### 2.2 Herbal Therapies

A recent systematic review and meta-analysis by Deng et al. [19] looked at the evidence for plant extracts in the topical management of psoriasis. The study included 12 trials; however, only six studies were included in the meta-analysis. The herbs studied were *Mahonia aquifolium* (Oregon grape extract), aloe vera, Indigo naturalis, Kukui nut oil, and Camptotheca acuminate nut. Indirubin, the active ingredient in indigo, has anti-proliferative and anti-inflammatory effects, as does *Mahonia aquifolium* [19]. Aloe vera has been shown to have anti-psoriatic activity comparable to tazarotene in a mouse model [20]. The pooled data for clinical efficacy (defined by PASI 50) was in favor of the plant extracts over the control groups (RR 3.37; 95 % CI 1.36–8.33). For five of the studies included

in the meta-analysis, the control group was a placebo vehicle, and in one study of topical aloe vera the control was 0.1 % triamcinolone. Heterogeneity was high in the studies included in the meta-analysis (78 %). The authors concluded that there is 'limited support' for *Mahonia aquifolium*, Indigo naturalis, and aloe vera; however, because of the methodological weaknesses in the studies, 'strong conclusions cannot be made'. Since the publication of this review, another RCT by Lin et al. [21] compared indigo extract oil with olive oil for nail psoriasis in 31 patients for 12 weeks. Nail Psoriasis Severity Index (NAPSI) scores showed a greater reduction in the treatment group compared with the control group (49.8 vs. 22.9 %) when one hand was used as the comparison. When single nails were compared with each other, the results were also in favor of the indigo oil (59.3 % reduction in NAPSI for the treatment group vs. 16.3 % reduction for the control group).

Another systematic review and meta-analysis by Deng et al. [22] investigated the use of topical HM for the treatment of psoriasis. Nine studies were included in the review, some of which were trials of TCM. Some studies compared topical HM with placebo, while other studies compared it with both topical and systemic APP. The pooled data was divided into four groups. Group 1 was topical HM versus topical placebo with oral HM as a co-intervention. This means both groups received oral HM. Group 2 was topical HM versus topical APP; group 3 was topical HM versus topical APP with oral HM co-intervention; and group 4 was topical HM versus topical APP, with both groups receiving systemic APP. Within group 3, the authors found no statistically significant difference between topical HM and topical APP, concluding that the topical HM E-Bei ointment was not inferior to calcipotriol. In all other groups, there was a statistically significant benefit in efficacy (defined as 50 % improvement or better) in favor of the topical HM group (group 1: RR 1.19, 95 % CI 1.04–1.37; group 2: RR 1.32, 95 % CI 1.10–1.58; group 4: RR 1.36, 95 % CI 1.23–1.50). No serious adverse events were reported. The most commonly used herbs were *Sophora flavescens* (bitter ginseng) and *Lithospermum erythrorhizon* root (purple gromwell).

May et al. [23] conducted a review of oral HMs for psoriasis, which included 12 studies in the analysis: four case studies and eight controlled trials. Four studies comparing plant extracts plus marine oils were all RCTs. Three studies investigated 'Efamol marine', which is a combination of evening primrose oil, fish oil, and vitamin E, and the results showed no difference compared with the control group. Another study using a product called 'HESA-A', a combination of herbal and marine ingredients, showed a benefit compared with placebo. The exact ingredients in HESA-A were not listed in the study. Eight studies (seven of which used Chinese HM) investigated multi-ingredient systemic herbal formulations. Four of these studies were case-series and four were controlled trials. Of the four controlled trials investigating multi-ingredient systemic herbal formulations, two showed a benefit compared with the control group, and two studies showed no difference.

In an RCT of 50 patients, Pandey et al. [24] investigated an extract of the neem tree (an evergreen tree found mostly in India) for the treatment of psoriasis. The active ingredient in neem is nimbidin, which has hypoglycemic and antitumor effects, and it is more potent than acetylsalicylic acid at reducing prostaglandin synthesis. All subjects applied 5 % crude coal tar and 3 % salicylic acid in an ointment base. The treatment group received once capsule of neem extract three times daily and the control group received a control capsule. All subjects were exposed to natural sunlight and had a morning bath. At week 12, the treatment group showed statistically significantly lower PASI scores compared with the control group (4.74 vs. 9.47; $p < 0.001$).

An oral extract of sweet whey has been shown to improve psoriasis when compared with the control group, based on the Physician's Global Assessment (PGA) and PASI scores ($p < 0.05$ for both PGA and PASI comparisons) [25].

## 2.3 Dietary Supplements

### *2.3.1 Fish Oil (Omega-3 Fatty Acid)*

Omega-3 fatty acids are unsaturated fatty acids present in fish, plants, eggs and, to a lesser extent, grass-fed animals. Fish, particularly cold-water fish such as herrings and sardines, are the best source. The specific active molecules in the oil of these fish are eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). The omega-3 fatty acid present in plant sources (flaxseed, walnuts, leafy green vegetables, soybean, hemp) is known as alpha lipoic acid (ALA). The body converts ALA into EPA and DHA. These molecules compete with arachidonic acid (AA) as substrates for cyclooxygenase and lipoxygenase, which thereby reduces downstream pro-inflammatory molecules in psoriatic plaques. Omega-3 fatty acids also contain 'resolvins', molecules that have potent anti-inflammatory and immunomodulating properties [26]. A recent study showed that fish oil and Omega-3 supplements were overwhelmingly the most commonly used CAM supplements among patients presenting to a dermatology clinic (not specifically used for psoriasis) [12].

Millsop et al. [27] recently reviewed the evidence for fish oil supplementation in patients with psoriasis. These authors identified a total of 15 trials and determined that, overall, there was a 'moderate evidence of benefit' for the

use of fish oil supplementation. Twelve of the 15 trials showed a benefit (six trials were controlled, six were uncontrolled), and three trials (two controlled, one uncontrolled) showed no benefit. Most of the trials that showed a positive benefit used fish oil either intravenously or as an oral supplement in combination with standard therapies such as phototherapy or retinoids. The dosages of fish oil used in the studies were highly variable; however, in the positive trials that used oral fish oil supplements, the average dose of EPA was 4 g daily, and the average dose of DHA was 2.6 g. In general, the range of improvement with fish oil supplements seen in clinical trials was a 40–75 % reduction in PASI scores. However, oral fish oil supplements taken as monotherapy needs to be taken for long periods of time—within the range of 6 weeks to 6 months—to see an improvement in psoriasis [27].

An alternative study investigated the effects of fatty fish consumption on psoriasis. The control arm consumed white fish, which is much lower in omega-3 fatty acids. This study found that just eating six ounces of fatty fish daily could improve psoriasis when compared with white fish consumption [28].

#### 2.3.2 Turmeric

Although basic science evidence exists that curcuminoids (the active components in turmeric) could be active against psoriasis [29], no RCTs have been conducted and a small pilot study using 4 g of curcuminoid extracts in patients with psoriasis was not encouraging. However, the pilot study did show that curcuminoid use had no serious adverse effects [30].

#### 2.3.3 Ginger

Evidence from a large RCT showed that ginger supplementation (0.5–1 g daily) can significantly reduce chemotherapy-induced nausea [31]. Although the ginger is not specifically treating psoriasis, ginger extract could be considered for the management of drug-induced nausea in patients with psoriasis who are receiving methotrexate.

#### 2.3.4 Vitamins

Psoriasis has been reported to be associated with vitamin D deficiency. Millsop et al. [27] reviewed seven prospective trials of oral vitamin D3 supplementation in psoriasis patients. In the only RCT performed to date, no statistical significance was seen between groups in a trial of 41 subjects. The group receiving 1 μg of 1-hydroxyvitamin D3 showed a slight improvement in 45 % of subjects versus 38 % in the placebo group, but this difference did not reach statistical significance. In six other open-label uncontrolled studies, various forms of vitamin D3 have been shown to decrease psoriasis severity from baseline.

Psoriasis has been reported to be associated with vitamin B12 deficiency, and at least one retrospective study has shown lower B12 levels in patients with psoriasis compared with control subjects [32, 33]. However, the results of intramuscular vitamin B12 injections are conflicting. One RCT showed no difference between the treatment group, which received 1000 μg vitamin B12 intramuscularly 5 days per week for 3 weeks, and the placebo group [34]. Although, another open-label trial showed a 32 % complete clearance rate and a 29 % PASI 75 in subjects receiving intramuscular vitamin B12 1000 $\mu g/cm^3$ for 10 consecutive days followed by a maintenance dose [35]. A third RCT studied the use of topical vitamin B12, in a cream containing avocado oil; however, no difference was seen between the treatment group and the control group [36].

Among psoriasis patients taking lithium, an RCT showed that inositol 6 g/day showed a statistically significant (albeit modest) improvement compared with placebo [27].

Oral zinc supplementation has not shown any efficacy in psoriasis [17].

Decreased serum selenium levels have been shown to be associated with increased psoriasis severity [37]. Kharaeva et al. [38] performed a double-blinded, placebo-controlled study in hospitalized patients with either erythrodermic psoriasis or psoriatic arthritis. These patients were treated with an oral combination of coenzyme Q-10 (50 mg/day), vitamin E (50 mg/day), and selenium (48 μg/day). This study showed a statistically significant improvement in PASI compared with placebo. In contrast to this positive study, three other studies with oral selenium supplementation had negative results [27].

### 2.4 Climatotherapy

The classic form of climatotherapy with regard to psoriasis treatment involves spending several weeks at the Dead Sea in Israel, bathing in the sea and lying in sun. This form of CAM is difficult to replicate in RCTs; however, there has been a plethora of studies showing that artificial climatotherapy (bathing in a bathtub with Dead Sea minerals prior to phototherapy treatment) is effective for clearing and inducing remission of psoriasis [39–45]. The clinical evidence for efficacy is not only vast but also consistent. The in vivo reversal of pathologic molecular and cellular markers induced by Dead Sea climatotherapy has been previously described [46].

A recent study by Harari et al. [47] showed that Dead Sea climatotherapy may be even more effective for early-onset psoriasis (onset under 40 years of age). The efficacy

of Dead Sea climatotherapy is likely explained by a combination of the anti-inflammatory effects of stress reduction, the keratolytic and anti-proliferative effects of Dead Sea minerals, and the unique UV characteristics that exist at that particular latitude. Specifically, UVA and longer wavelength therapeutic UVB rays exist at the Dead Sea, and shorter erythrogenic UVB rays are typically filtered. Versions of climatotherapy or balneotherapy (bathing in hot springs) exist in the Canary Islands, the Black Sea, the Blue Lagoon in Iceland, and the Kangal Hot Springs in Turkey, although this is not a complete list as hot springs with claimed benefits for psoriasis exist in many other countries. The Kangal Hot Springs offer a very specific type of balneotherapy, termed 'ichthyotherapy,' where tiny predatory fish present in the springs feed on psoriatic scales. In Croatia, naphtalotherapy, the practice of bathing in naphtalan (a black-green, tar-like substance), is used in the treatment of psoriasis. In contrast to Dead Sea climatotherapy, evidence from RCTs for most of these other locations is lacking [17].

Contraindications of climatotherapy include, but are not limited to, photo-aggravated dermatoses such as lupus erythematosus, porphyrias, disseminated superficial actinic porokeratosis, lichen planus actinicus, epidermolysis bullosa, solar urticaria, polymorphous light eruption, and hydroa vacciniforme, as well as a history of skin cancers [48].

### 2.5 Mind/Body Interventions

The psychological effects of a diagnosis of psoriasis has been studied extensively and the mechanisms by which stress alters the immune system have been well described. In addition to quality-of-life deficits, patients have higher rates of depression, anxiety, and suicide [49]. Unfortunately, little evidence has been obtained from RCTs investigating psychological interventions for psoriasis; however, several observational studies have shown benefit.

Gaston et al. [50] performed a small RCT of 24 subjects using meditation as adjunctive treatment for scalp psoriasis. The two treatment groups showed lower severity scores compared with the two control groups, but this was not statistically significant.

Tausk and Whitmore [51] evaluated the effects of hypnosis in an RCT of 11 subjects. The results showed that highly hypnotizable subjects showed greater improvements in their psoriasis than those who were only moderately hypnotizable. The authors of this pilot study stated that hypnosis may be a helpful treatment modality in patients who are highly hypnotizable.

Kabat-Zinn et al. [52] performed an RCT which showed that using mindfulness-based stress reduction tapes during phototherapy was associated with a more rapid improvement in psoriasis within the intervention group.

Zachariae et al. [53] performed an RCT in 51 subjects using cognitive behavioral stress management as the intervention. The results showed slight but clinically significant improvements in the treatment group in terms of 'total sign score' and Doppler blood flow to psoriatic plaques. No differences in PASI scores were seen.

Keinan et al. [54] treated 32 subjects in an RCT that compared biofeedback and relaxation techniques with relaxation only, including a third group who received no treatment. No significant differences were found between the groups.

## 3 Clinical Considerations

In the US, herbal supplements are sold and regulated as dietary supplements that do not require proof of efficacy. In terms of safety, the FDA considers dietary supplements safe until proven otherwise through information from postmarketing reports of side effects [55]. This is in contrast to countries such as Germany, in which a regulatory body known as Commission E has reviewed the safety and clinical efficacy of herbal supplements [56]. In the UK, the Traditional Herbal Medicine Registration Scheme provides evidence-based information on herbal supplements, including drug interactions. Additionally, HMs in the UK require marketing authorization, which details the quality, safety, and efficacy of the product [57]. It is imperative that physicians, especially in countries where these supplements are not regulated like drugs, know some basic information about drug interactions and the side effects of herbal supplements. At a minimum, physicians should be able to quickly find good-quality information regarding this subject. Several online resources, applications and text books are available that are helpful references (see "Boxed text"). Table 2 provides side effect and drug interaction information for the commonly used CAM supplements in psoriasis. This is not an exhaustive list and patients should consult with their doctors before beginning any new herbal supplement. Several general guidelines are helpful when discussing herbal therapy with patients. The highest degree of caution needs to exist when a patient is considering taking a herbal medication and is also taking a prescription medication with a narrow therapeutic index. These medications include anti-coagulants, anti-diabetic drugs, antineoplastics, digoxin, and immunosuppressants [57]. In the US, Dietary supplements are required to be made under conditions of Good Manufacturing Practices (GMP), i.e. they are produced in a quality manner, without contaminants or impurities. GMP also assumes that the supplement actually contains the ingredients that are listed on the label. However, there is no required testing to confirm that dietary supplements actually adhere to GMP

**Table 2** Herbals/dietary supplements demonstrating the largest evidence of efficacy from RCTs [14, 15, 107–112]

| Common name | Latin name (Chinese name if applicable) | Reported side effects | Known drug interactions | Active compounds; mechanism of action |
|---|---|---|---|---|
| Aloe | *Aloe vera* | Dermatitis with topical use, hypokalemia, nephritis, and seizure with oral use | Anti-arrthymics, diuretics, digoxin | Anthraquinone, salicylic acid |
| Bitter ginseng | *Sophora flavescens* root (Ku shen) | Hepatotoxic in rat models, estrogenic effects | Any hepatotoxic medication, taxol, ampicillin/gentamicin | Alkaloids (matrine and oxymatrine), flavonoids (trifolirhizin); anti-inflammatory |
| Broom Cyprus | *Kochia scoparia* fruit (Di fu zi) | No topical side effects, weight loss, hyperbilirubinemia, photosensitization, and polyuria in animal model (Rankins), increased liver enzymes in steer, listed in the FDA's Poisonous Plant Database | None | Triterpenoid glycosides, saponins, alkaloids; anti-inflammatory |
| Chinese foxglove | *Rehmannia glutinosa* (Sheng Di) | Bloating, nausea, loose stool, hypoglycemia, anti-implantation effect in female mice, anti-platelet activity in vitro, listed in the FDA's Poisonous Plant Database | Anti-diabetes medications, contraindicated in pregnancy and chronic liver disease | Catalpol; anti-inflammatory |
| Chinese skullcap, Baikal skullcap | *Scutellaria baicalensis* root (huang qin) | May increase statin levels with oral use | Statins | Baicalein, baicalin; anti-inflammatory |
| Dittany bark | *Dictamnus dasycarpus* bark (Bai xian pi) | Acute hepatitis with oral decoctions | Methotrexate or any hepatotoxic medication | Alkaloids, triterpenoids, sesquiterpenoids; anti-histamine, anti-inflammatory |
| Female ginseng | *Angelica sinensis* root (Dong quai) | Increased INR and prothrombin, widespread bruising, anorexia, gynecomastia, photodermatitis | Anti-coagulants, oral contraceptives | Psoralens, coumarins |
| Fish oil | Not applicable | Fishy aftertaste, loose stool, nausea, hypervitaminosis A and D, increased LDL and increased bleeding time with oral use | Anti-coagulants, anti-platelets | Omega-3 fatty acids |
| Indigo | Indigo naturalis (Qing Dai) | Gastroenteritis, hematuria, increased liver function tests and leukopenia with oral use | None | Indirubin |
| Monnier's snowparsley | *Cnidium monnieri* seed (she chuang zi) | None known, however listed in the FDA's Poisonous Plant Database | None known | Coumarins; anti-oxidant, anti-inflammatory, anti-proliferative to keratinocytes |
| Oregon grape | *Mahonia aquifolium* | Pruritus with topical use, coagulant and neurotoxic with oral use | Anti-coagulants, anti-platelets | Berberine |
| Purple gromwell | *Lithospermum erythrorhizon* root (Zi Cao) | Hypoglycemia, hepatotoxicity, carcinogenic with oral use | None known | Shikonin; anti-proliferative, tissue-repair, anti-angiogenesis |
| Red sage | *Salvia miltiorrhiza* root (Dan shen) | GI reactions, headache with oral use; increased risk for bleeding (increased INR) | Warfarin | Matrine, oxymatrine, flavonoids; anti-inflammatory, anti-oxidant, anti-proliferative |
| Sarsaparilla | *Smilax glabra* root (Tu Fu Ling) | Gastroenteritis, nephritis | Digoxin, bismuth subsalicylate | Beta-sitosterol |

**Table 2** continued

| Common name | Latin name (Chinese name if applicable) | Reported side effects | Known drug interactions | Active compounds; mechanism of action |
|---|---|---|---|---|
| Turkish rhubarb | *Rheum palmatum* root (da huang) | Oxalic acid crystals, uterine stimulation and mild GI side effects with oral use, acute renal failure with long-term oral use | Digoxin, anti-arrhythmics, contraindicated in pregnancy, contraindicated in patients with renal stones | Anthraquinones, flavonoids, tannins; anti-inflammatory |
| Veitch's peony | *Paeonia veitchii* root (Chi Shao) | Nausea, increased bleeding time and uterine contractions with oral use, contact dermatitis with topical use | Anti-coagulants; contraindicated in pregnancy, reduces effectiveness of phenytoin | Paeonol, paeonoside, paeoniflorin; anti-inflammatory, anti-oxidant (CAM and the aging population) |

*CAM* complementary and alternative medicine, *GI* gastrointestinal, *INR* international normalized ratio, *LDL* low-density lipoprotein, *RCTs* randomized controlled trials

conditions. Considering that herbal supplements in the US do not require testing for potency or purity, patients should at least seek out supplements that are 'third-party tested' for purity (this is usually stated on the label). Another option is finding supplements that are verified by the US Pharmacopeia (USP), an independent organization that tests supplements for strength, quality, and purity. It is important to state that no patient should start therapy with an oral CAM modality before discussion with their primary physician and any physician who is actively treating the patient (i.e. the oncologist should be informed about new CAM use if the patient is undergoing chemotherapy).

### 3.1 Traditional Chinese Medicine

In general, there is a large body of evidence that supports the use of TCM in the form of oral and topical HMs for psoriasis treatment. Several RCTs using TCM have demonstrated increased treatment response rates and efficacy when compared with control groups; however, there are several caveats to this discussion. Most of these trials were not blinded, which introduces the possibility of bias in the reported results. Additionally, there is a substantial amount of heterogeneity in clinical trials of TCM, which might be unavoidable given the nature of TCM. By design, TCM treatment is supposed to be tailored to the individual's type of psoriasis within TCM (i.e. blood-heat syndrome vs. Qi and blood stasis), and the particular herbs are commonly modified according to how that patient is progressing with therapy. This degree of custom therapy is very difficult to study in the context of a randomized controlled, double-blinded trial. The authors of the meta-analyses should be commended for attempting to summarize a body of literature that is so inherently heterogeneous; however, the authors fairly consistently admit to the 'methodological weaknesses' of the individual studies included in these meta-analyses. Finally, TCM treatments are generally a combination of multiple different herbal compounds, therefore it is impossible to determine which compound leads to the clinical effect.

In regard to the side effects of TCM, some case reports have described the adulteration of TCM medicines with lead, arsenic, and mercury [58]. In some instances, topical TCM preparations have even been shown to contain quite potent topical corticosteroids [59, 60]. Systemic toxicity from lead, mercury, and arsenic absorption from topical use of TCM medicines has been reported, and one case of arsenic ingestion in a TCM medicine has lead to a squamous cell carcinoma [61]. A herbal TCM ointment containing arsenic led to toxic epidermal necrolysis, and ultimately death, in a 24-year-old man [62]. Some Chinese oral HMs have been shown to contain prednisone, indomethacin, diazepam, and other medicines [63].

Furthermore, cases of agranulocytosis from a product known as 'Chuifong Toukuwan' have been reported [63], and there have also been cases of acute hepatitis from TCM herbal decoctions, raising concern for patients with any underlying liver dysfunction or those taking medications that are hepatically metabolized. TCM should be administered with caution in this patient population [16]. Recent reports show that as much as 28 % of samples of TCM have pesticide contaminants [64]. Considering these risks, the use of TCM as bath therapy or topical therapy seems to carry much less risk than oral decoctions. Based on this data, TCM exists as its own system of medicine, with multiple drug interactions and side effects to consider. This requires the practitioner to tailor a regimen for each individual patient, and it is not advisable for patients to self-treat without the guidance of a physician.

### 3.2 Herbal Therapies

The largest degree of evidence of efficacy of herbal therapies (outside the context of TCM) seems to be for *Mahonia aquifolium*, Indigo nauralis and, to a lesser degree, aloe vera. These herbal therapies are most often used as topical treatment for psoriasis. Topical creams and gels that contain these ingredients can be found at most health-food stores. Side effects of aloe vera, indigo naturalis, and *Mahonia aquifolium* are listed in Table 2. Several case reports of contact dermatitis from herbal therapies have been published, as well as further case reports concerning cutaneous reactions such as Stevens–Johnson syndrome, bullous lichen planus, and Sweet's syndrome [65]. Herbal supplements that contain furocoumarins could potentially create phototoxicity. Hematologic, nephrotoxic, cardiotoxic, and hepatotoxic reactions have also been reported from the use of herbal supplements [66].

### 3.3 Dietary Supplements and Dietary Modifications

Patients with psoriasis should be counseled to maintain a healthy body weight and avoid excessive alcohol intake [67–69]. If the patient is not allergic to fish, there is evidence that eating more fatty fish (must be 6 oz/day) or taking a fish oil supplement can be helpful for psoriasis. Best evidence for fish oil supplementation is for intravenous fish oil or oral supplements in combination with traditional therapies (such as oral retinoids or phototherapy). The average dose of fish oil supplements in clinical trials that showed a benefit of oral fish oil supplementation was 4 g of EPA and 2.6 g of DHA. Support for fish oil supplementation in patients with psoriasis becomes more compelling among those at increased risk for myocardial infarction (MI) and all-cause cardiac mortality [70]. There is insufficient evidence to suggest that fish oil supplementation decreases the risk of coronary artery disease or MI, but there is evidence to suggest that if a patient has already had a MI, 1 g of fish oil per day decreases mortality due to fatal post-MI arrhythmias [71]. Common side effects of fish oil include dyspepsia and a fishy odor upon eructation, which can be minimized by refrigerating the product. In doses higher than 4 g, fish oil has antiplatelet effects and could potentially increase the risk of bleeding, especially if the patient is already taking other anti-coagulants. Lipid profiles should be monitored periodically while taking a fish oil supplement since omega-3 supplements can increase the low-density lipoprotein (LDL). Prescription omega-3-acid ethyl ester supplements are available that are currently approved for the treatment of hypertriglyceridemia. A recent report showed that fish oil supplementation can decrease the risk of hypertriglyceridemia in patients taking isotretinoin, which could potentially be helpful in patients taking acitretin for psoriasis [72]. The American Heart Association (AHA) recommends that patients with severe hypertriglyceridemia take between 2–4 g of fish oil daily (EPA and DHA) [71]. Recent third-party testing [73] of commercially available fish oil supplements was performed in which the supplements were tested for mercury, EPA, and DHA content. Total omega-3 content ranged from −60.0 to +62.5 % compared with the stated claims on the label. The fish oil supplement Nature Made® Fish Oil ranked number one in overall label accuracy.

It is reasonable to check vitamin D levels in patients with psoriasis and, if deficient, supplement them for the purposes of bone health; however, there is conflicting evidence that vitamin D supplementation is helpful for treating psoriasis. In adults, the recommended dietary allowance of vitamin D is 600 IU, with the upper level intake at 4000 IU [74]. Evidence has also associated psoriasis with low levels of selenium and vitamin B12, which can be monitored and supplemented if low.

Patients with psoriasis should be screened for a family history of celiac disease and a personal history of symptoms of gluten intolerance (headaches, abdominal bloating or pain, flatulence, constipation or diarrhea, pale stools, weight loss, unexplained iron deficiency anemia). Relevant patients should have celiac antibodies checked, most notably the anti-gliadin antibody. If a patient has positive celiac antibodies, a gluten-free diet could improve their psoriasis [75].

Evidence from a large RCT supported the use of ginger supplementation to decrease chemotherapy induced nausea. This may be helpful for patients undergoing treatment with methotrexate. A dose of ginger capsules between 0.5 and 1 g was the most helpful with nausea.

### 3.4 Climatotherapy

Controlled trials have provided evidence that Dead Sea climatotherapy can both improve psoriasis and induce lasting remissions; however, RCTs for other locations of climatotherapy have provided little evidence. In general, any extra UV exposure increases the risk for both melanoma and non-melanoma skin cancers; therefore, the benefits should be carefully weighed against the risks for each patient. Clearly, Dead Sea climatotherapy is not feasible for most patients; however, there is evidence to indicate that synchronous balneophototherapy is more effective than phototherapy alone [76]. This involves bathing in a Dead Sea salt solution followed by traditional phototherapy (narrow-band UVB specifically). This is something that patients could easily do at home prior to their phototherapy appointments, or immediately preceding their phototherapy treatment at facilities that have bathtubs in their psoriasis centers.

### 3.5 Mind/Body Interventions

There is conflicting evidence for interventions involving medication or stress reduction techniques for the treatment of psoriasis; however, very little risk is involved in these types of interventions. One important point to consider is financial expenditure on such therapies. With insufficient evidence of efficacy to justify the cost of a certain intervention, even mind/body interventions could be considered economic exploitation of the patient [77]. A wide variety of free online resources are available for meditation practices, relaxation techniques, and mindfulness training that any patient with psoriasis could do from home.

## 4 Conclusions

The use of CAM for the treatment of psoriasis is common, and physicians should feel comfortable discussing the efficacy and potential side effects of common CAM modalities. The evidence is greatest for fish oil, climatotherapy, and the herbs *Mahonia aquifolium* and indigo naturalis. A large amount of RCT data is available for TCM; however, due to the lack of blinding in most of the studies, it is likely that the results were subject to bias. Furthermore, concerns regarding the contamination of TCM products make it difficult to recommend this modality for psoriasis patients with possible underlying medical comorbidities. Physicians should continue to have open and honest conversations with their psoriasis patients regarding the use of CAM. Most patients realize the benefit of traditional medicine but are eager to consider all treatment options. While a complete understanding of CAM treatment modalities is still underway, its use in psoriasis has shown some benefit, and should be considered among appropriate patient populations.

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**Helpful Resources for Information Regarding Complementary and Alternative Medicine Modalities, Side Effects, and Drug Interactions**

About Herbs (Memorial Sloan Kettering's application for iPad, iPhone, iPod Touch or other mobile devices)
Naturalstandard.com
Naturaldatabase.com and associated application NaturalData
Lexi.com and associated application Lexicomp
MicroMedex.com
nccih.nih.gov
Physician's Desk Reference (PDR) for Herbal Medicines, 4th edition

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