

REVIEW

Chinese herbal medicine for atopic dermatitis: A systematic review

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Background: Atopic dermatitis (AD) is a chronic, itching skin disease, and conventional therapies offer inadequate symptom management. Patients with AD are increasingly turning to Chinese medicine.

Objective: We systematically evaluated the clinical evidence of the efficacy and safety of oral Chinese herbal medicine for AD.

Methods: Searches were conducted on major electronic databases using the following key words: “randomized controlled trials,” “atopic dermatitis,” “traditional Chinese medicine,” “traditional East Asian medicine,” “herbal medicine,” “Chinese herbal drugs,” “medicinal plants,” “phytotherapy,” “Kampo medicine,” and “Korean traditional medicine.” The results were screened to include English/Chinese randomized controlled trials. A metaanalysis was conducted on suitable outcome measures.

Results: Seven randomized controlled trials were included (1 comparing Chinese herbal medicine and Western medicine with Western medicine alone; 6 comparing Chinese herbal medicine with placebo). Combined Chinese herbal medicine with Western medicine was superior to Western medicine alone. Three placebo controlled trials showed significant treatment efficacy and 2 showed significantly reduced concurrent therapy with Chinese herbal medicine. No abnormalities in safety profile or severe adverse events were reported.

Limitations: A metaanalysis of all included studies could not be conducted because of study heterogeneity.

Conclusions: Chinese herbal medicine significantly improved symptom severity of AD and was reported as well tolerated. However, the poor quality of studies did not allow for valid conclusions to support its tolerability and routine use. Additional studies addressing the methodologic issues are warranted to determine the therapeutic benefit of Chinese herbal medicine for AD. (J Am Acad Dermatol 10.1016/j.jaad.2013.01.019.)

Key words: allergy; alternative and complementary medicine; atopic dermatitis; Chinese herbal medicine; eczema; systematic review.

Atopic dermatitis (AD) is a chronic, inflammatory skin disease that affects approximately 15% to 30% of children and 2% to 10% of adults.¹ It is characterized by severe itching, skin

redness and dryness, weeping, scarring, and lichenification.^{2,3} AD impacts activities of daily living and increases financial burden of patients and their carers.⁴ In the United Kingdom, the annual

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Supported by the Guangdong Provincial Academy of Chinese Medical Sciences, Guangdong Provincial Hospital of Chinese Medicine, China.

Conflicts of interest: None declared.

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Published online June 04, 2013.

0190-9622/\$36.00

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<http://dx.doi.org/10.1016/j.jaad.2013.01.019>

expenditure on AD was approximately £465 million⁵; in the United States, the national direct costs ranged from \$364 million to \$3.8 billion USD.⁶ In Australia, the annual personal financial costs ranged from \$330 to \$1255 AUD, and is said to be greater than the management costs of asthma.⁷

The exact pathophysiology of AD has not been fully elucidated, and there is currently no cure. Symptomatic management has been the focus of management,⁸ involving the long-term use of topical corticosteroids and calcineurin inhibitors. However, these treatments have been associated with adverse events^{9,10} and the development of drug tolerance.¹¹

Consequently, patients frequently seek other therapeutic options, such as Chinese herbal medicine (CHM).¹² CHM is part of traditional Chinese medicine (TCM) therapy, whereby inquiry of the condition and observation of the patient leads to the TCM diagnosis and treatment. Two previously published systematic reviews on CHM for AD were inconclusive,^{8,13} and the current state of evidence of CHM treatment of AD remains unknown.^{4,13,14} The different pathways of medication administration affect treatment actions and indications; oral and topical CHM are therefore considered different interventions.¹⁵ This systematic review aims to evaluate the published randomized controlled trials (RCTs) on the safety and efficacy of treatment of AD with orally administered CHM compared with placebo, pharmacotherapy, or no treatment.

METHODS

Protocol

This systematic review was not registered with the Cochrane Collaboration but was conducted with reference to the Cochrane Handbook.¹⁶ Electronic searches were carried out on the following databases: CINAHL, Cochrane Library, Embase, ProQuest, PubMed, ScienceDirect, Scopus, Web of Science, VIP Database for Chinese Technical Periodicals (CQVIP), and China National Knowledge Infrastructure (CNKI). All databases were searched from their inception to 2011. The search terms were a combination of Medical Subject Heading terms and their synonyms (Table 1).

Study selection criteria

RCTs with the following criteria were included: published English or Chinese RCTs; diagnosis of AD (or atopic eczema) using clinical diagnosis or validated diagnostic criteria; diagnosis of “eczema” was only accepted when referring to children/infants; placebo, no treatment or non-Chinese medicine

treatments as control interventions; non-Chinese medicine cointerventions were accepted only if it was applied to all groups; and ≥ 1 of the following outcome measures: (1) disease/symptom severity scoring and (2) quality of life. Concurrent therapies, adverse events, and safety profiles were recorded as secondary outcome measures. Studies involving other forms of TCM therapy (eg, acupuncture and topical CHM) or dermatitis (eg, neurodermatitis and contact dermatitis) were excluded.

CAPSULE SUMMARY

- Previous reviews on Chinese medicine for atopic dermatitis were inconclusive. Clinical trials examining the safety and efficacy of Chinese medicine for atopic dermatitis have since been conducted but have yet to be systematically reviewed.
- A metaanalysis revealed significant improvement in symptom severity and quality of life, but the quality of studies was poor.
- Patients can potentially reduce steroid therapy use with the help of Chinese medicine and subsequently reduce the occurrence of related side effects.

Data extraction and risk

of bias assessment

Two independent reviewers extracted the data of included studies onto the Cochrane Skin Group data extraction form and conducted a risk of bias assessment using the Cochrane Collaboration's tool for assessing risk of bias¹⁶ (Fig 1). The metaanalysis was conducted in RevMan5. For CHM and Western medicine (WM) compared with WM only, the metaanalysis was performed on overall clinical scores. For CHM compared with placebo, the metaanalysis was conducted on disease or symptom severity scores, quality of life, and reduction in concurrent treatments.

RESULTS

Description of studies

The searches yield a total of 1014 articles. After screening titles and abstracts, duplicates, non-English or Chinese articles, animal or immunologic studies, studies not involving AD or CHM, and non-RCTs were excluded. Two hundred eighty-one full articles were retrieved for further evaluation. Seven studies were included for qualitative analysis (Fig 2). One study was excluded from the metaanalysis because of insufficient data. The 6 studies in the metaanalysis included a total of 432 participants with AD.

Table I. Example for search strategy (in PubMed)

No.	Search term	Hits*
1	"Randomized controlled trial" (publication type)	315,419
2	"Randomized controlled trials as topic" (MeSH)	75,706
3	"Dermatitis, atopic" (MeSH)	12,635
4	"Medicine, Chinese traditional" (MeSH)	9495
5	"Medicine, East Asian traditional" (MeSH)	11,336
6	"Herbal medicine" (MeSH)	1,116
7	"Drugs, Chinese herbal" (MeSH)	22,232
8	"Plants, medicinal" (MeSH)	48,114
9	"Phytotherapy" (MeSH)	23,989
10	"Medicine, Kampo" (MeSH)	353
11	"Medicine, Korean traditional" (MeSH)	115
12	Terms 1 or 2	385,792
13	Terms 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11	93,361
14	Terms 3 and 12 and 13	28

MeSH, Medical Subject Heading.

*As of December 19, 2011.

Table II summarizes the studies' characteristics. Table III summarizes the diagnoses, interventions, and outcome measures. One study was a single blinded RCT comparing WM with CHM (Jian Pi Shen Shi granules) with WM alone¹⁷; 6 studies were placebo controlled, double blinded RCTs (1 used Xiao Feng San,¹⁸ 3 used the formula from the study by Sheehan et al,¹⁹⁻²¹ 1 applied a Pentaherb formula,²² and 1 used Hochu-ekki-to¹⁰). The ingredients of each formula are listed in Table IV. Only 2 RCTs included TCM diagnosis,^{10,17} and 1 measured quality of life.²²

CHM and WM combination compared to WM alone

Only one study compared a combination of CHM and WM treatment to WM alone.¹⁷

Primary outcome measure. *Disease/symptom severity scoring.* The overall clinical score was calculated by summing the severity score (0-3) of each symptom (ie, itch, erythema, papules, exudation, erosion, infiltration, lichenification, dryness). A significant difference was shown in the end score (mean difference [MD], -2.56; 95% confidence interval [CI], -3.46 to -1.66; $P < .00001$), favoring the combination treatment.

CHM compared to Placebo

Five studies compared CHM with placebo. Two studies compared the formula used by Sheehan et al²¹ with a placebo of inert plant materials of similar appearance, taste, and smell, but without known benefits to AD^{20,21}; another study compared

Pentaherb with an identical-looking placebo containing corn starch and caramel²²; 1 study compared Xiao Feng San with a placebo made of caramel, lactose, and starch¹⁸; and the fifth study compared Hochu-ekki-to with placebo, with no details of placebo content.¹⁰ The authors of the Pentaherb trial²² provided raw data for analysis. The Hochu-ekki-to trial presented results in graphs only¹⁰; consequently, estimate figures from the graphs were used in analysis.

Primary outcome measures. *Disease/symptom severity scoring.* Three studies reported overall clinical scores—1 used the validated Scoring Atopic Dermatitis (SCORAD) instrument,²² another used the scoring system by the Atopic Dermatitis Severity Evaluation Committee of Japanese Dermatological Association,¹⁰ and the third study used a standardized scoring system calculating the extent and severity of dermatitis.¹⁸ The former 2 studies presented results as means and standard deviations, and the latter study presented the scores as least-square means. Only 1 trial showed significant improvement in overall clinical score by CHM compared to placebo.¹⁸ Because of the heterogeneity of instruments, metaanalysis of overall clinical scores could not be conducted.

Three studies^{18,20,21} used a standardized scoring system to calculate the extent and severity of erythema and surface damage. Erythema and surface damage scores were presented as least-squares means, percentage of median change, and geometric mean, respectively. The metaanalysis of erythema scores (standard mean difference, -0.76; 95% confidence interval [CI], -1.05 to -0.47; $P < .00001$) and surface damage scores (standard mean difference, -1.08; 95% CI, -1.59 to -0.56; $P < .0001$) favor CHM compared to placebo (Fig 3).

One trial reported pruritus score.¹⁸ A significant difference was seen in CHM treatment compared to placebo (mean difference [MD], -1.10; 95% CI, -1.59 to -0.61; $P < .0001$). In a crossover trial by Sheehan et al,²¹ out of 31 participants, 14 reported improvement in itching during CHM treatment and 1 during the placebo phase.

Cheng reported that CHM significantly improved sleep scores when compared with placebo (MD, -0.80; 95% CI, -1.12 to -0.48; $P < .00001$).¹⁸ Two other studies reported sleep improvement.^{20,21} In the former study, out of 37 participants, 19 had improved sleep during CHM treatment and 3 during placebo treatment; in the latter study, out of 31 participants, 15 experienced improved sleep with CHM and 6 with placebo.

Quality of life. One study measured quality of life.²² The metaanalysis found that CHM significantly

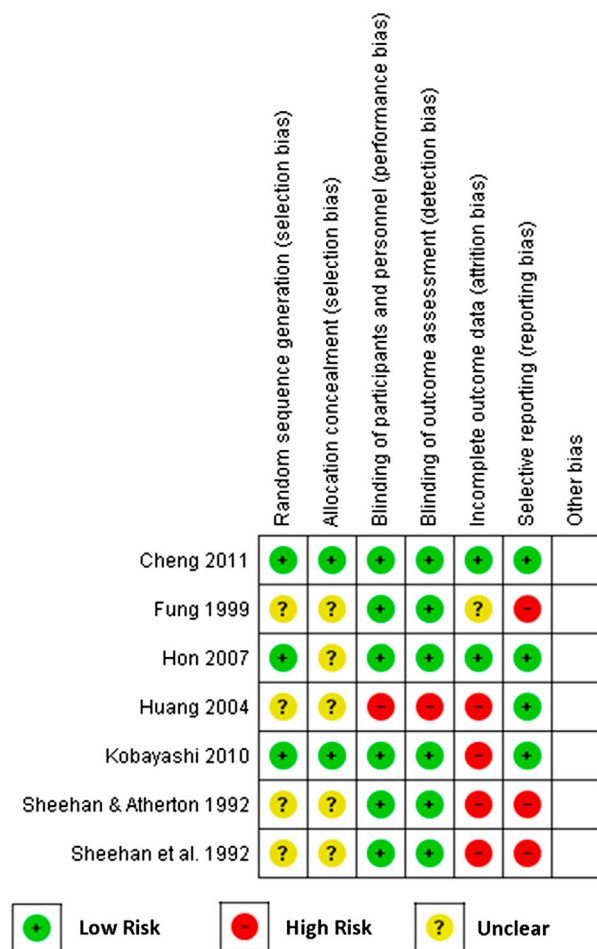


Fig 1. Summary of risk of bias assessment.

improved Children's Dermatology Life Quality Index (CDLQI) compared to placebo (MD, -2.50 ; 95% CI, -4.77 to -0.23 ; $P < .05$).

Secondary outcome measures. *Concurrent treatment.* Kobayashi et al¹⁰ measured the effects of CHM on the amount of concurrent topical treatments used by participants during the trial. At the end of the study, the total equivalent amount of topical agents used was significantly lower in the CHM group compared to the placebo group (MD, -24.50 ; 95% CI, -27.92 to -21.08 ; $P < .00001$). In the study by Hon et al,²² the amount of topical mometasone furoate used at the end of the trial was significantly lower in the CHM group ($P = .024$) compared to the placebo group.²²

Safety profile and adverse events. Out of the included studies, 1 study did not evaluate safety profile and occurrence of adverse events.¹⁷ In the other studies, no significant differences in safety profiles were reported. However, there was 1 case of transient elevation in aspartate aminotransferase that was reversed within 8 weeks of treatment cessation.¹⁸

One study reported 2 cases of mild transient gastrointestinal upset during CHM treatment.¹⁸ Three studies^{10,21,22} reported the occurrence of mild or moderate side effects, such as gastrointestinal upset, various dermatoses (including "new rash," hives, acne pustulosa, and facial herpes), and dizziness in both the treatment and control groups. One study in children required participants' parents to complete a questionnaire relating to adverse effects but did not report the occurrence of any adverse events.²⁰

DISCUSSION

Results from the metaanalysis revealed significant improvement in disease severity scores by the combination treatment of CHM and WM compared with WM alone ($P < .00001$). When compared with placebo, CHM revealed significant improvement in erythema ($P < .00001$), surface damage ($P < .0001$), pruritus ($P < .0001$), sleep scores ($P < .00001$), and quality of life ($P < .05$). CHM also significantly reduced the need for concurrent pharmacotherapy ($P < .00001$).

The overall risk of bias assessment found that the quality of studies was poor; therefore, the results from the metaanalysis have to be translated with caution. Only 1 study was judged with "low risk" in all domains for bias assessment,¹⁸ while the other studies had "unclear" or "high risk" judgments in ≥ 1 domains.^{10,17,19-22} In the study comparing CHM and WM with WM alone, despite being labeled as a "single blind" trial, there were no details on blinding. Aside from selective reporting and a lack of details regarding random sequence generation and allocation concealment, the main flaw was the lack of intention to treat (ITT) analysis, leading to incomplete outcome data. ITT analysis stresses that any exclusions from analysis would affect the comparability generated through randomization between groups.²³ In addition, dropouts may reflect a flaw of the intervention.²⁴ The 4 studies with high risk in this domain had exclusions likely related to the intervention, such as side effects, noncompliance, and the use of prescribed drugs.^{10,17,20,21} One study that excluded 2 participants at baseline because of family objections¹⁸ was considered low risk because the withdrawals were not related to the intervention.

Two previous systematic reviews evaluating CHM for AD focused on the clinical evidence of the formula used by Sheehan et al.²¹ The conflicting evidence with regard to the efficacy of the formula used by Sheehan et al²¹ was said to be related to the variance in dosage, dropout rates, or racial variability in drug responsiveness.⁸ In addition, the investigators did not provide details on the chemical properties of the herbal placebo; its similar smell and taste

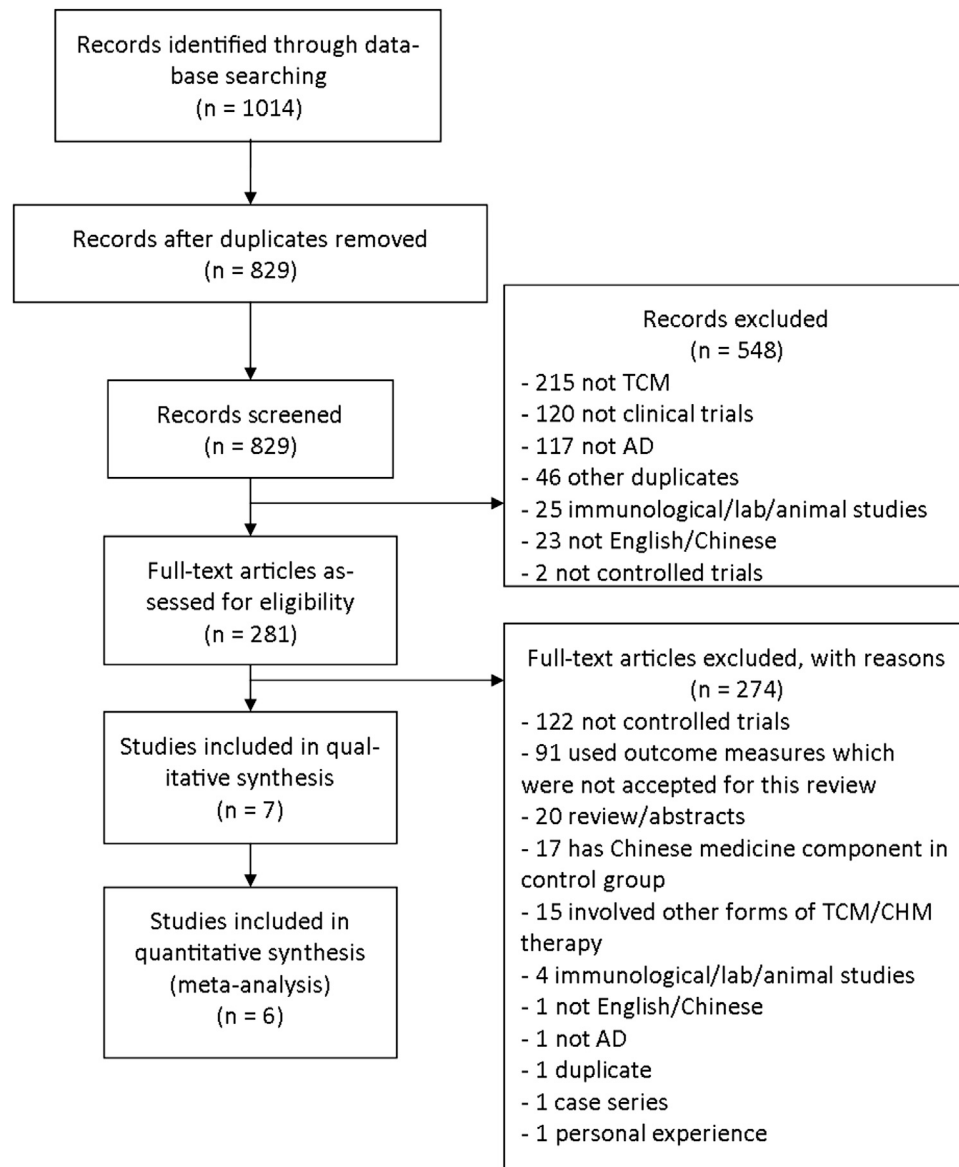


Fig 2. Study selection process. *CHM*, Chinese herbal medicine; *TCM*, traditional Chinese medicine.

to the active treatment indicates a possibility of containing similar chemical properties and, subsequently, similar or other pharmacologic actions.

From the metaanalysis of the placebo controlled trials, 3 studies favored CHM compared to placebo, 2 of which were studies by Sheehan and Atherton²⁰ and Sheehan et al.²¹ The third trial used a CHM formula commonly used for atopic dermatitis, Xiao Feng San. However, participants were given CHM granules with daily doses that were significantly higher than the recommended dose.²⁵ Also, the placebo of caramel, lactose, and starch may pose a risk to lactose intolerant individuals. In addition, according to TCM theory, sweet foods such as caramel could aggravate skin conditions.²⁶

In contrast, 2 trials found no significant difference in clinical scores. The lack of efficacy in the study by Hon et al²² may be related to an inadequate dose of CHM.²⁷ Although the capsule dose calculation was not stated, the Pentaherb formulation consisted of 9 g of raw herbs for patients 5 to 21 years of age.²² Despite the lack of efficacy, the Pentaherb group saw significant improvement in CDLQI, decrease in days of corticosteroid use and amount of mometasone furoate. However, it was unclear if the “days of corticosteroid use” comprised of corticosteroids other than mometasone furoate, including those of higher potencies. Kobayashi et al’s study¹⁰ only included patients with *Ki-kyo* (Qi deficiency) constitution, which did not address the condition as per

Table II. Characteristics of the included studies

Author (year)	Age group	Study design	No. of participants	Dropout	Run-in/treatment/ follow-up/washout period
Cheng et al (2010)	Not specified	Double blind RCT—computer generated randomization list by an independent statistician	TCM, 47; placebo, 24	2 (dropped out at baseline, not included in ITT)	Run-in, not mentioned; treatment, 8 wks; follow-up, 4 wks
Fung et al (1999)	7-50 years of age	Double blind, crossover RCT	TCM, 40; placebo, 40	3 (ITT analysis not mentioned)	Run-in, not mentioned; treatment, 8 wks; follow-up, not mentioned; washout, 4 wks
Hon et al (2007)	5-21 years of age	Double blind RCT—computer generated randomization code	TCM, 42; placebo, 43	ITT analysis to include all participants	Run-in, 2 wks; treatment, 12 wks; follow-up, 4 wks
Huang et al (2004)	3-11 years of age	Single blind RCT—simple randomization method (ratio 1:1)	TCM plus WM, 49; WM, 49	6 (ITT analysis used to analyze overall treatment effect)	Run-in, not mentioned; treatment, 4 wks; follow-up, 3 months
Kobayashi et al (2010)	20-40 years of age	Double blind RCT—block randomization	TCM, 43; placebo, 48	7 (excluded from analysis)	Run-in, not mentioned; treatment, 24 wks; follow-up, not mentioned
Sheehan and Atherton (1992)	“Children” (age group not specified)	Double blind, crossover RCT	TCM, 47; placebo, 47	10 (excluded from analysis)	Run-in, 4 wks; treatment, 8 wks; follow-up, not mentioned; washout, 4 wks
Sheehan et al (1992)	16-65 years of age	Double blind, crossover RCT	TCM, 40; placebo, 40	9 (excluded from analysis)	Run-in, not mentioned; treatment, 8 wks; follow-up, not mentioned; washout, 4 wks

ITT, Intention to treat; RCT, randomized controlled trial; TCM, traditional Chinese medicine; WM, Western medicine.

TCM theory and may have reduced the treatment efficacy. Nevertheless, there was a significant decrease in the total equivalent amount of topical agents in the CHM group when compared to the placebo group.¹⁰ These 2 studies indicate that CHM may function as an adjunct treatment for AD.

The CHM in 4 of the studies underwent quality check for potential contaminants (including steroids),^{18,20-22} while the Hochu-ekki-to was manufactured by a Good Manufacturing Practice—certified company.¹⁰ Three of the 5 studies that had adverse events reported nonsignificant differences between

both groups.^{10,20,21} However, the Pentaherb group in the study by Hon et al²² had significantly more general practitioner visits without further explanation, making it difficult to determine whether these visits were related to Pentaherb. There was 1 case of transient elevation of aspartate amino transferase that was reversed within 8 weeks of treatment cessation.¹⁸ Elevated aspartate amino transferase levels can have multiple causes, including alcohol abuse, medications, such as antihistamines or nonsteroidal antiinflammatory drugs, and certain herbs.²⁸ However, the herbal ingredients of the respective

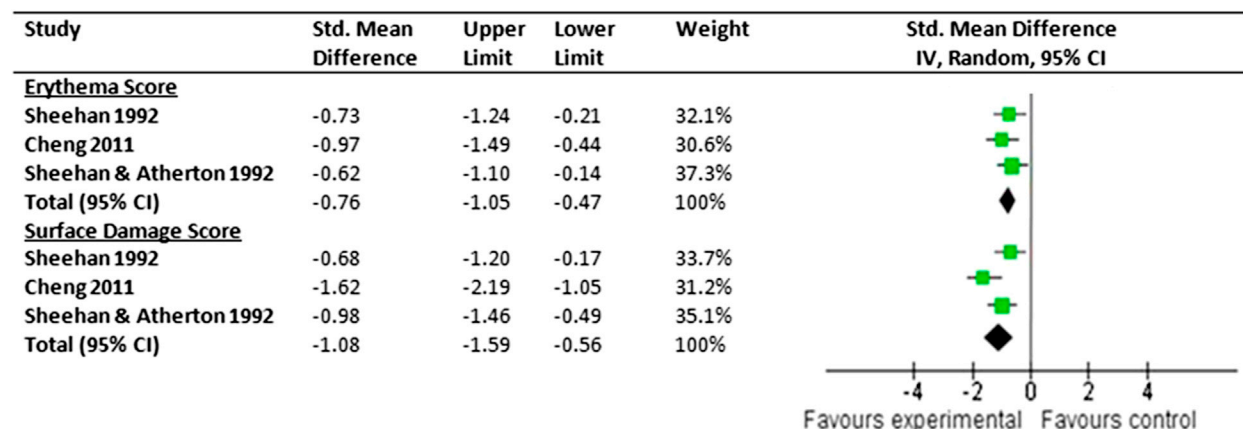
Table III. Diagnosis, interventions, and outcome measures of included studies

Author (year)	WM/TCM diagnosis	Severity	Treatment interventions	Control interventions	Outcome measures
Cheng et al (2010)	AD: Hanifin and Rajka diagnostic criteria	Extensive AD (>20% BSA involved)	Xiao Feng San granules (3-7 years of age, 3 g tid; 8-12 years of age, 6 g tid; >13 years of age, 9 g tid)	Placebo	Total clinical lesion; erythema score; surface damage score; pruritus score; sleep score
Fung et al (1999)	AD: Hanifin and Rajka diagnostic criteria	Moderate to severe AD	Sheehan's formula (decoction): 7-13 years of age, 2 large plus 2 small sachets of herbs per day; >14 years of age, 3 large plus 3 small sachets	Placebo	Clinical scores for erythema, surface damage, lichenification, and scaling
Hon et al (2007)	AD: Hanifin and Rajka diagnostic criteria	Moderate to severe AD (objective SCORAD >15)	Pentaherb capsule 3 capsules bid	Placebo	SCORAD; CDLQI; allergic rhinitis symptoms; concurrent treatment
Huang et al (2004)	AD: UK diagnostic criteria/ SP deficiency	Moderate AD	Jian Pi Shen Shi granules (3-5 years of age, 5 g tid; 6-11 years of age, 10 g tid plus cyproheptadine tablets 0.25 mg/kg/day tid; triamcinolone urea cream)	Cyproheptadine tablets 0.25 mg/kg/day tid; triamcinolone urea cream	Rajka and Langeland scoring; overall treatment effect; total immunoglobulin E; rate of recurrence 3 months posttrial
Kobayashi et al (2010)	AD: diagnostic criteria according to the Japanese Dermatological Association for AD/Kikyo condition (Qi deficiency)		Hochu-ekki-to granules 3.25 g bid	Placebo	Skin severity score; dose of topical steroids/tacrolimus used; prominent efficacy rate; aggravated rate
Sheehan and Atherton (1992)	AD: diagnostic criteria not stated	Extensive nonexudative AD, not confined to flexural sites	Sheehan's formula (decoction): 1-7 years of age, 2 large plus 2 small sachets of herbs per day; 8-13 years of age, 3 large plus 3 small sachets; >14 years of age, 4 large plus 4 small sachets (100 mL decoction/day)	Placebo	Erythema score; surface damage score; preference in treatment; improvement in ability to sleep
Sheehan et al (1992)	AD: Hanifin and Rajka diagnostic criteria	Extensive AD (>20% BSA involved)	Sheehan's formula (decoction): 4 large plus 4 small sachets (200 mL decoction/day)	Placebo	Erythema score; surface damage score; improvement in itching, sleep and asthma; preference of treatment

AD, Atopic dermatitis; *bid*, twice daily; BSA, body surface area; CDLQI, Children's Dermatology Life Quality Index; SCORAD, Scoring Atopic Dermatitis; SD, spleen deficiency; *tid*, three times daily.

Table IV. Herbal ingredients used in Chinese herbal medicine formulas of included studies

Sheehan's formula	Jian Pi Shen Shi granules	Pentaherb	Hochu-ekki-to	Xiao Feng San
<i>Glycyrrhiza uralensis</i> (Gan Cao)	<i>Wolfiporia extensa</i> (Fu Ling)	<i>Herba menthae</i> (Bo He)	<i>Glycyrrhizae radix</i> (Gan Cao)	<i>Glycyrrhiza uralensis</i> (Gan Cao)
<i>Ledebouriella seseloides</i> (Fang Feng)	<i>Codonopsis pilosula</i> (Dang Shen)	<i>Flos lonicerae</i> (Jin Yin Hua)	<i>Ginseng radix</i> (Ren Shen)	<i>Saposhnikovia divaricate</i> (Fang Feng)
<i>Schizonepeta tenuifolia</i> (Jing Jie)	<i>Atractylodes rhizoma</i> (Bai Zhu)	<i>Cortex phellodendri</i> (Huang Bai)	<i>Atractylodes rhizoma</i> (Bai Zhu)	<i>Schizonepeta tenuifolia</i> (Jing Jie)
<i>Lophatherum gracile</i> (Dan Zhu Ye)	<i>Aurantii nobilis pericarpium</i> (Chen Pi)	<i>Rhizoma atractylodis</i> (Cang Zhu)	<i>Aurantii nobilis pericarpium</i> (Chen Pi)	<i>Atractylodes lancea</i> (Cang Zhu)
<i>Paeonia lactiflora</i> (Bai Shao)	<i>Semen coicis</i> (Yi Yi Ren)	<i>Cortex moutan</i> (Mu Dan Pi)	<i>Angelicae radix</i> (Dang Gui)	<i>Angelica sinensis</i> (Dang Gui)
<i>Rehmannia glutinosa</i> (Sheng Di Huang)			<i>Bupleuri radix</i> (Chai Hu)	<i>Rehmannia glutinosa</i> (Sheng Di Huang)
<i>Anebia clematidis</i> (Chuan Mu Tong)			<i>Zizyphi fructus</i> (Da Zao)	<i>Clematis armandii</i> (Chuan Mu Tong)
<i>Dictamnus dasycarpus</i> (Bai Xian Pi)			<i>Astragali radix</i> (Huang Qi)	<i>Cryptotympana pustulata</i> (Chan Tui)
<i>Tribulus terrestris</i> (Ji Li)			<i>Zingiberis rhizome</i> (Gan Jiang)	<i>Linum usitatissimum</i> (Hu Ma Ren)
<i>Potentilla chinensis</i> (Wei Ling Cai)			<i>Cimicifugae rhizome</i> (Sheng Ma)	<i>Anemarrhena asphodeloides</i> (Zhi Mu)
				<i>Gypsum fibrosum</i> (Shi Gao)
				<i>Sophora flavescens</i> (Ku Shen)
				<i>Articum lappa</i> (Niu Bang Zi)

**Fig 3.** Metaanalysis of Chinese herbal medicine compared to placebo studies. CHM, Chinese herbal medicine; CI, confidence interval.

study were not for such effects. No additional details were provided to evaluate the possible relation between the elevation and the trial intervention.

This review showed no significant safety concerns regarding CHM treatment for AD. However, in these studies, CHM was only administered for 4 to 24 weeks under controlled conditions.

The included studies applied different methods of medication delivery: 1 study used capsules,²² 3 used

granules,^{10,17,18} and 3 used decoctions.¹⁹⁻²¹ Decoctions are the most common form of CHM, while granules and capsules are modern forms aimed to be more convenient and palatable.²⁹ It remains unclear if the different methods of CHM delivery influence their treatment effects.^{29,30} However, studies with significantly better outcomes used higher treatment doses, regardless of the method of delivery.

According to TCM, AD is caused by a congenitally weak constitution, resulting in a predisposition toward atopic diseases and susceptibility towards external or internal pathogenic factors, such as wind, dampness, and heat.³¹ Its recurrent and chronic nature can injure Yin and blood and generate dryness.³¹ However, other dermatologic conditions, such as psoriasis, can share the same TCM diagnosis. Among the included studies, only 2 applied TCM syndrome differentiation, while the others used a standardized CHM formula. Nevertheless, each formula was able to reduce AD symptom severity, improve quality of life, and/or reduce the need for topical corticosteroids. This implies that there are clinical benefits of CHM treatment of AD, and that better treatment efficacy may be seen with TCM syndrome differentiation.

There is debate regarding the effects of geographic factors on the active compounds of herbs. However, no details or concerns in this regard were mentioned in any of the studies. Although the herbal ingredients of these formulas exhibit pharmacologic and Chinese medicine actions relevant to the treatment of AD, the pharmacokinetics and pharmacodynamics of formulas may differ from that of individual herbs.³² In addition, in vitro data may not reflect treatment effects in humans.³² The absence of in vitro and in vivo pharmacologic data of a CHM formula deters the full understanding of the drug mechanism of an herbal formula. In order to provide strong evidence of the efficacy and safety of CHM treatment for AD, aside from rigorous RCTs, further laboratory studies on the pharmacokinetics and pharmacodynamics of each formula should be carried out.

There are insufficient data to show that CHM treatment in combination with WM is more effective than WM treatment alone. The meta-analysis showed significant improvement in symptom severity by CHM compared to placebo. CHM was reported as well-tolerated in all the studies and there were no reports of severe adverse events. However, the poor quality and heterogeneity of studies do not allow for valid conclusions. More rigorous RCTs and research on pharmacologic studies of CHM formulas are needed for stronger evidence regarding the efficacy and safety of CHM treatment for AD outside of clinical trial settings.

We would like to thank Iris Wenyu Zhou, PhD, for her assistance in data searching and evaluation.

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