

# Complementary and alternative medicine treatments for common skin diseases: A systematic review and meta-analysis



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**Background:** Complementary and alternative medicine (CAM) treatments are growing in popularity as alternative treatments for common skin conditions.

**Objectives:** To perform a systematic review and meta-analysis to determine the tolerability and treatment response to CAM treatments in acne, atopic dermatitis (AD), and psoriasis.

**Methods:** PubMed/Medline and Embase databases were searched to identify eligible studies measuring the effects of CAM in acne, AD, and psoriasis. Effect size with 95% confidence interval (CI) was estimated using the random-effect model.

**Results:** The search yielded 417 articles; 40 studies met the inclusion criteria. The quantitative results of CAM treatment showed a standard mean difference (SMD) of 3.78 (95% CI [−0.01, 7.57]) and 0.58 (95% CI [−6.99, 8.15]) in the acne total lesion count, a SMD of −0.70 (95% CI [−1.19, −0.21]) in the eczema area and severity index score and a SMD of 0.94 (95% CI [−0.83, 2.71]) in the scoring of atopic dermatitis score for AD, and a SMD of 3.04 (95% CI [−0.35, 6.43]) and 5.16 (95% CI [−0.52, 10.85]) in the Psoriasis Area Severity Index score for psoriasis.

**Limitations:** Differences between the study designs, sample sizes, outcome measures, and treatment durations limit the generalizability of data.

**Conclusions:** Based on our quantitative findings we conclude that there is insufficient evidence to support the efficacy and the recommendation of CAM for acne, AD, and psoriasis. (JAAD Int 2021;2:76-93.)

**Key words:** acne vulgaris; aloe vera; atopic dermatitis; coconut oil; colloidal oatmeal; complementary alternative medicine; curcumin; eczema; green tea; honey; meta-analysis; natural ingredients; psoriasis; shea butter; sunflower seed oil; systematic review; tea tree oil; turmeric; witch hazel.

## INTRODUCTION

Use of complementary and alternative medicine (CAM) has been on the rise in the past decade with an increasing number of outpatient visits to CAM professionals.<sup>1</sup> Physicians must be made aware of the values and pitfalls of these widely used natural

skincare ingredients so they can answer relevant patient inquiries. The efficacy and safety of these popular ingredients have been studied with clinical trials, albeit not extensively. Therefore, this systematic review and meta-analysis aims to synthesize the existing data regarding the treatment efficacy of

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these ingredients in commonly diagnosed dermatologic conditions (acne, atopic dermatitis [AD], and psoriasis) in order to further counsel physicians in guiding patients on the use natural ingredients.

## METHODS

### Literature search

A literature review was performed using PubMed/Medline and Embase in January 2020 to identify published randomized clinical trials and cohort studies measuring the efficacy of CAM natural skincare ingredients in the treatment of acne, AD, and psoriasis. The following search terms were used: (aloe vera or coconut oil or honey or apple cider vinegar or tea tree oil or oatmeal or sunflower seed oil or shea butter or witch hazel or green tea or lemon or turmeric) AND (acne or psoriasis or eczema or AD) AND (clinical trial).

### Inclusion and exclusion criteria

Studies were included if they were clinical trials or cohort studies, included at least 15 human subjects, and were published in English in an indexed journal. For the quantitative analysis, a comparison of treatment against a placebo was required. We excluded studies if they were literature reviews, case series, case reports, conference abstracts, or animal studies.

### Data extraction

Two authors (V.J., P.P.) independently screened and reviewed the titles and abstracts identified in the electronic databases to establish eligibility. For records that were deemed relevant, the full-text studies were then reviewed independently by the same 2 authors (V.J., P.P.) employing the inclusion and exclusion criteria. A third independent author (C.W.) resolved any disagreements. After the inclusion of all relevant studies, data extraction was carried out.

### Methodological quality assessment

The risk-of-bias assessment was conducted using the Cochrane risk-of-bias tool<sup>2</sup> for the randomized controlled studies and the Newcastle-Ottawa quality assessment score<sup>3</sup> for the nonrandomized studies included in the systematic review, whereas Egger's test<sup>4</sup> for publication bias was used to analyze the

studies included in the meta-analysis. For the Newcastle-Ottawa quality assessment score studies, the bias was graded as low risk, some concerns, or high risk. Studies included within the systematic review mostly ranged from "low risk" to "some concerns," with one "high risk study" (Fig 1, Table I).<sup>5-13</sup> The Egger's test grouped by treatment

showed no bias for aloe vera (AV) or turmeric. Bias was present for green tea (GT); however, further analysis through the "fill and trim" publication bias technique<sup>14</sup> deemed no publication bias. Tea tree oil (TTO), sunflower seed oil (SSO), and colloidal oatmeal (CO) had too few studies for assessment of bias risk.

### Statistical analysis methods

Analyses were conducted using R software<sup>15</sup> version 4.0.2 (R Core Team, Vienna, Austria), and forest plots were produced using the dmetar package. Heterogeneity was assessed using the  $I^2$  statistic and the effect size was calculated as the standardized mean difference (SMD) using Cohen's d statistic.<sup>16</sup> Because of the significant between-study heterogeneity, the random-effect model was used for all analyses. Analyses were performed on studies measuring the same outcome variable, CAM treatment, and disease. All statistical tests and confidence intervals were two-sided, with a significance level of  $P < .05$ .

## RESULTS

Using the aforementioned search criteria, we identified 417 articles, of which, 40 in total met the inclusion criteria. Of these, 25 were included in our qualitative analysis and 15 were included in our quantitative analysis. The publication years of the eligible articles ranged from 1990 to 2019. The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow was used for the quantitative studies (Fig 2). Details regarding the included study designs, baseline characteristics, intervention, and studied variables were collected and summarized by 3 authors independently (V.J., P.P., C.W.) (Tables II and III).<sup>5-13,17-46</sup>

### Quantitative analysis

**Total lesion count reduction (TLC) in acne.** A total of 6 studies, including 280 acne patients, 188 treated with GT<sup>35-38</sup> and 92 patients

### CAPSULE SUMMARY

- Patients with common skin conditions, such as acne, atopic dermatitis, and psoriasis, report the use of complementary and alternative medicine in their treatment regimen. Yet, response to this therapy is undetermined.
- This systematic review and meta-analysis will aid practitioners worldwide in counseling patients pursuing such treatment for common skin disorders.

*Abbreviations used:*

AD:	atopic dermatitis
AV:	aloe vera
CAM:	complementary and alternative medicine
CCO:	coconut oil
GT:	green tea
PASI:	psoriasis area and severity index
SCORAD:	scoring of atopic dermatitis
SMD:	standardized mean difference
SSO:	sunflower seed oil
TCS:	topical corticosteroid
TLC:	total lesion count
TTO:	tea tree oil

treated with TTO<sup>12,33,34</sup> were analyzed (Table III). The primary outcome evaluated was the reduction of the total lesion count (TLC) of pustules and papules. With GT use, the TLC was reduced by a SMD of 3.78 (95% CI [-0.01, 7.57]) ( $P = .05$ ) (Fig 3, A). For the improvement of TLC with TTO, the SMD was 0.58 (95% CI [-6.99, 8.15]) ( $P = .88$ ) (Fig 3, B). In both the CAM treatment groups, the TLC reduction was not statistically significant.

**Eczema area and severity index in AD.** One study that included 68 patients with AD examined the efficacy of treatment with CO<sup>15</sup> (Table III). The primary outcome measured was improvement of the

Study ID	Randomization process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall
Camplone et al., 2014	?	?	-	-	?	-
Bassett et al., 1990	+	?	+	+	?	!
Giordano et al., 2006	+	+	+	?	+	!
Lubtikulthum et al., 2019	+	?	+	+	+	!
Mazzarello et al., 2018	+	+	+	+	+	+
Hajheydari et al., 2014	+	?	+	+	+	!
Semprini et al., 2015	+	?	+	+	+	!
Danby et al., 2012	+	?	+	+	+	!
Khiljee et al., 2015	+	?	+	+	+	!
Verallo-Rowell et al., 2008	+	?	+	+	+	!
Carrion et al., 2015	+	+	+	+	?	!
Geroge et al., 1993	+	+	+	+	+	+
Klaber et al., 2000	+	?	+	?	+	!
Evangelista et al., 2014	+	+	+	+	+	+
Korting et al., 1995	+	+	+	+	+	+



**Fig 1.** Cochrane risk-of-bias summary: the authors’ judgments about the studies. Studies included within the systematic review mostly ranged from low risk to some concerns except for one high-risk study per the risk-of-bias assessment.

**Table I.** Newcastle-Ottawa risk assessment for non-randomized studies

Study	Selection	Comparability	Outcome	Final
Elsaie et al, 2009 <sup>5</sup>	...	...	...	Some concerns
Haris et al, 2012 <sup>6</sup>	...	...	...	Some concerns
Al-Waili et al, 2003 <sup>7</sup>	...	...	...	Low
Alangari et al, 2017 <sup>8</sup>	...	...	...	Low
Rawal et al, 2008 <sup>9</sup>	...	...	...	Some concerns
Diluvio et al, 2019 <sup>10</sup>	...	...	...	Some concerns
Mariano et al, 2018 <sup>11</sup>	...	...	...	Some concerns
Malhi et al, 2016 <sup>12</sup>	...	...	...	Some concerns
Lisante et al, 2017 <sup>28</sup>	...	...	...	Low

eczema area and severity index score. When compared to a barrier cream, treatment with CO proved inferior with a mean eczema area and severity index reduction of  $-0.70$  (95% CI  $[-1.19, -0.21]$ ) (Fig 4, A).

**Scoring of atopic dermatitis (SCORAD) in AD.** Two studies including 98 patients with AD examined the efficacy of treatment with sunflower seed oil (SSO)<sup>39,40</sup> (Table III). The primary outcome measured was improvement of the scoring of atopic dermatitis (SCORAD) in AD score. One study found a 1.81 improvement in SCORAD (95% CI  $[1.30, 2.32]$ ) while the other study found 100% reduction in SCORAD. Notably, the patients in the second study also experienced 100% reduction in SCORAD with the control- a moisturizing cream. The SMD in SCORAD was 0.94 (95% CI  $[-0.83, 2.71]$ ), improvement with SSO was not statistically significant ( $P = .30$ ) (Fig 4, B).

**Psoriasis Area and Severity Index (PASI) reduction.** Three studies including 175 patients with psoriasis examined the efficacy of treatment AV on the primary outcome measure of psoriasis area and severity index (PASI) score reduction<sup>41-43</sup> (Table III). SMD with AV was 3.04 (95% CI  $[-0.35, 6.43]$ ) (Fig 5, A). Three separate studies including 167 patients examined the efficacy of treatment turmeric on PASI score reduction<sup>44-46</sup> (Table III). Analysis of these studies yielded a SMD 5.16 (95% CI  $[-0.52, 10.85]$ ) (Fig 5, B).

### Qualitative results stratified by disease

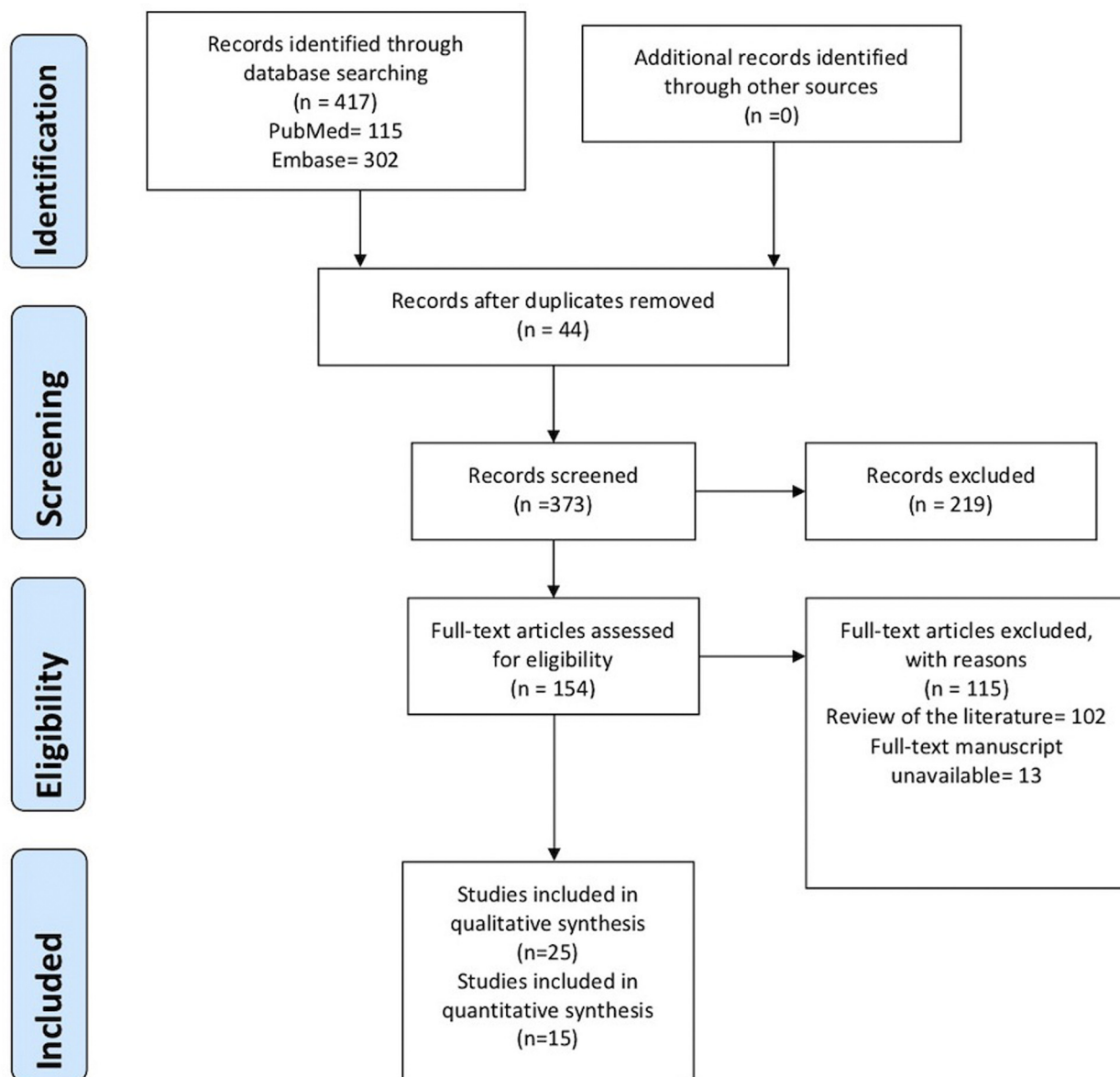
**Acne vulgaris.** Reports of efficacy and safety with coconut oil in the treatment for acne are scarce

with only one study existing in the literature. This clinical trial with virgin coconut oil treatment showed a significant reduction in inflammatory acne grading number of papules, pustules, and skin sebum.<sup>6</sup> When combined with tretinoin cream, AV gel showed statistically significant reduction of noninflammatory, inflammatory, and total acne lesions when compared with tretinoin/vehicle. Moreover, the acne severity index was decreased to a greater extent than in the control group.<sup>20</sup> A separate combination therapy study using 10% AV showed improvement in papular and scar lesions, with a statistically significant reduction in the erythema index of scars, acne severity index, and TLC.<sup>18</sup> Altogether, these studies reflect that AV may be considered as an effective adjuvant treatment in mild-to-moderate acne vulgaris.

Likewise, TTO treatment resulted in a statistically significant reduction of the mean total number of inflammatory and noninflammatory lesions.<sup>17,19</sup> Although TTO was associated with a slower onset of action compared with the control,<sup>17</sup> it was associated with fewer side effects.<sup>17,19</sup> Similarly, GT lotion treatment yielded a statistically significant reduction in the TLC and severity index.<sup>5</sup> Lastly, kanuka honey showed little improvement of the investigator's global assessment acne score, and several participants experienced worsening acne with this treatment.<sup>21</sup>

**Atopic dermatitis.** The 11 studies included in the AD qualitative analysis evaluated various outcome measures. In studies examining virgin coconut oil, 1 study examined the objective-SCORAD severity index, whereas the other looked at the mean SCORAD. For both the objective-SCORAD severity index and the SCORAD, treatment with virgin coconut oil showed statistically significant improvement.<sup>25,26</sup> Conversely, shea butter treatment did not improve the SCORAD, although xerosis and pruritus showed statistically significant improvement.<sup>29</sup> In another study, treatment with honey led to marked improvement of severity and symptoms in 80% of patients in the treatment group and allowed reduction of topical corticosteroid (TCS) use in the control group.<sup>7</sup> A separate study of honey showed statistically significant reductions in erythema, edema/papulation, and excoriation.<sup>8</sup>

Similarly, topical curcumin formulations including a microemulsion, a gel, and an ointment showed that microemulsion formulations were efficacious at healing symptoms of erythema and edema, whereas gel and ointments were more efficacious at pruritus and lichenification improvement, respectively.<sup>23</sup> Of note, all turmeric formulations resulted in statistically significant decreases in symptoms.<sup>9</sup> CO also showed statistically significant cutaneous improvement<sup>27</sup> in



**Fig 2.** The PRISMA flow diagram. *PRISMA*, Preferred reporting items for systematic reviews and meta-analyses.

areas such as epidermal thickness, skin dryness, and itching.<sup>10</sup> Whereas SSO preserved stratum corneum integrity and improved skin hydration.<sup>22</sup> Lastly, treatment with Hamamelis distillate cream proved inferior to TCS with regard to reductions in itching, erythema, and scaling.<sup>24</sup>

**Psoriasis.** A study of patients with chronic plaque psoriasis undergoing psoralen and ultraviolet A or narrow-band phototherapy ultraviolet B therapy who were pretreated with coconut oil (CCO) showed that CCO treatment failed to accelerate psoriasis clearance in comparison with non-pretreated lesions.<sup>31</sup> However, CCO scalp solution

has shown moderate statistically significant improvement in comparison with the control.<sup>32</sup> Although this study showed improvement in the treatment group, these results may be an overestimation because of the addition of other ingredients within the calcipotriol solution.<sup>32</sup>

Similarly, a parallel study of plaque psoriasis patients showed a significant response to a honey mixture alone, whereas patients undergoing treatment with a TCS showed no relapse upon 75% reduction of the TCS doses,<sup>7</sup> proving the efficacy of the use of honey in psoriasis. In patients with mild-to-moderate scalp psoriasis, a prospective

**Table II.** Characteristics of the studies included in the qualitative analysis

Reference	Country	Age (years)	Sex (female/ male)	Study design	Disease	Variable studied	Treatment ingredient	Control ingredient	n total	n treatment total	n controls total
Bassett et al, 1990 <sup>17</sup>	Australia	Range: 12-35 Mean: 19.7	60/64* (before dropout)	Single-blind RCT	Acne	Total number of inflamed lesions (superficial and deep) as well as noninflamed lesions (open and closed comedones) Assessment of skin tolerance	TTO	BP	119	58	61
Mazzarello et al, 2018 <sup>18</sup>	Italy	Range: 14-34	41/19	Single-center, randomized, double-blinded, comparative study	Acne	TLC, ASI	TTO-PTAC, ERC	Vehicle gel	60	PTAC-20, ERC-20	20
Lubtikulthum et al, 2019 <sup>19</sup>	Thailand	Mean (treatment): 21.79 ± 2.238 Mean (control): 21.89 ± 2.153	47/27	Observer-blinded, noninferiority randomized controlled study	Acne	TLC, adherence, porphyrin counts, DLQI, satisfaction, side effects	TTO	BP	74	38	36
Malhi et al, 2016 <sup>12</sup>	Australia	Range: 16-39 Mean: 26	9/5	Open-label, uncontrolled phase II pilot study	Acne	TLC	TTO	None	14	14	0
Elsaie et al, 2009 <sup>5</sup>	Egypt	Range: 15-36	14/6	Open-label, prospective cohort study	Acne	TLC, SI	GT	None	20	20	0
Hajheydari et al, 2014 <sup>20</sup>	Iran	Range (treatment): 11-32 Range (Control): 14-37 Mean (treatment): 22.33 ± 4.82 Mean (control): 24.70 ± 5.56	60/0	Randomized (simple- random sampling), double-blind, prospective trial	Acne	TLC, ASI	TR/AVG	TR/vehicle	60	30	30

Continued

Table II. Cont'd

Reference	Country	Age (years)	Sex (female/ male)	Study design	Disease	Variable studied	Treatment ingredient	Control ingredient	n treatment n total	n controls total	
Haris et al, 2012 <sup>6</sup>	India	Range: 15-38	12/9	Open, single centric, non- comparative clinical trial	Acne	Acne score, papule count, pustule count and skin sebum  Subject self- assessment of satisfaction	AVCO	None	21	21	0
Al-Waili et al, 2003 <sup>7</sup>	United Arab Emirates	Range: 5-16	4/17	Patient-blinded, partially controlled study	AD	Erythema, scaling, lichenification, excoriation, indurations, oozing and itching on a 0-4 points scale	Honey, OO and beeswax mixture	TCS	21	10	11
Semprini et al, 2015 <sup>21</sup>	New Zealand	Range: 16-40* Mean: 21.2 ± 5.8*	N/A	Single-blind RCT	Acne	IGA, mean lesion count (Leeds revised acne grading system), VAS, DLQI	KH	Protex soap: triclocarban- based antibacterial soap	106	68	67
Alangari et al, 2017 <sup>8</sup>	Saudi Arabia	Mean: 33 ± 10	8/6	Proof-of-concept, open-label, split-treatment pilot study	AD	TIS Staphylococci and enterotoxin production via skin swab  Interleukin release via enzyme linked immunosorbent assay	MH	No treatment	14	14	14
Danby et al 2012 <sup>22</sup>	UK	18+ Mean Cohort 1 34 ± 4.0	14/5	Two randomized forearm- controlled mechanistic studies	AD	Stratum corneum integrity and cohesion, intercorneocyte cohesion, moisturization, skin-surface pH, and erythema	SSO	OO	19	Cohort 2 (SSO Cohort 1 +OO): 12	(OO): 7
Khiljee et al, 2015 <sup>23</sup>	Pakistan	18+	N/A	Double-blind RCT, comparative study	AD	Degree of erythema, edema, scaling, itching and lichenification	Indian penny wort, walnut and turmeric	Prepared without plant extracts for the 3 formulations of microemulsion, gel, ointment	360	270	90

Korting et al, 1995 <sup>24</sup>	Germany	Range: 18-62 Mean: 32	58/12	Double-blind, randomized, split-body, paired trial	AD	Itching, erythema and scaling (basic criteria) as well as for edema, papules, pustules, exudation, lichenification, excoriation and fissures (minor criteria) according to a 4-point scale	Hamamelis distillate	Vehicle cream or TCS	72	72	36 vehicle cream, 36 TCS
Rawal et al, 2008 <sup>9</sup>	India	Range: 12-80 Mean: 39.04	69/50	Clinical trial	AD	Change in symptom score: erythema, scaling (crusting), thickening, and itching	Curcumin-Herbavate cream	None	119	119	0
Verallo-Rowell et al, 2008 <sup>25</sup>	Philippines	Range (VCO): 29-35 Range (VOO): 21-39 Mean (VCO): 32 ± 3 Mean (VOO): 31 ± 4	25/27	Double-blind, RCT	AD	SCORAD, O-SSI	VCO	VOO	52	26	26
Evangelista et al, 2014 <sup>26</sup>	Philippines	Range (VCO): 3.84-5.55 Range (Mineral oil): 3.43-4.85 Mean (VCO): 4.69 Mean (Mineral Oil): 4.14	50/47	Double-blind RCT	AD	SCORAD, TEWL, skin capacitance	VCO	Mineral oil	117	59	58
Camplone et al, 2004 <sup>27</sup>	Italy	<14	128/134 + 1 not known	RCT	AD	Physician judgment, PT compliance with skin care products	CO	None	263	5 groups: Colloid: 55, Derm: 29 Fluid: 75 Milk: 37 Oil: 67	0
Lisante et al, 2017 <sup>28</sup>	USA	Range: 10-80; 8-67 Mean: 32.9 ± 22.7; 27.1 ± 20.6	23/6; 18/12	Two Separate single-center, single-arm clinical trial	AD	Study 1: EASI, Investigators' Global Atopic Dermatitis Assessment, VAS Study 2: EASI, Patient-reported itch severity	CO	None	30; 29	30;29	0
Diluvio et al, 2019 <sup>10</sup>	Italy	Range: 3-17 Mean: 9	18/12	Clinical trial	AD	IGA, EASI, Itch severity, IDQOL	Mix of CO, avenanthramides, SB, and oat oil	None	30	30	0

Continued



Table II. Cont'd

Reference	Country	Age (years)	Sex (female/ male)	Study design	Disease	Variable studied	Treatment ingredient	Control ingredient	n total	n treatment total	n controls total
Giordano et al, 2006 <sup>29</sup>	France	Range: 6 months- 12 years Mean: 4 years	N/A	Multicenter RCT	AD	SCORAD, CDLQI	Shea Butter- Exomega@milk	Cleansing bar alone	76	37	39
Al-Waili et al, 2003 <sup>7</sup>	United Arab Emirates	Range: 20-60 Mean: 32	4/14	Patient-blinded, partially controlled study	Psoriasis	Redness, scaling, Thickening, and itching, on a 0-4 points scale	Honey, OO and beeswax mixture	TCS	18	8	10
Carrion et al, 2015 <sup>30</sup>	Spain	Mean: 41.3 ± 12.0	8/13	Phase IV, randomized, double-blind, placebo- controlled, pilot clinical trial	Psoriasis	BSA, severity signs total score, PGA, PASI	VLST	Curcuma extract with VLRT	21	10	11
George et al, 1993 <sup>31</sup>	UK	Range: 18-68	16/13	Single-blind, randomized controlled (half-body) study	Psoriasis	Mean psoriasis severity scores	PUVA + CO	UVB + CO	29	14	15
McKinnon and Klauer, 2000 <sup>32</sup>	UK	Mean (treatment): 45.8 ± 15.6 Mean (control): 44.7 ± 16.1	228/247	Multicenter, prospective, randomized, open-label design	Psoriasis	Extent of scalp psoriasis estimated on 6-point scale	CCO-Calcipotriol scalp solution	Coal tar-based solution	475	238	237
Mariano et al, 2018 <sup>11</sup>	Italy	Range: 18-65	N/A	Prospective multicenter open study	Psoriasis	Clinical and patients' evaluation of scalp itching, erythema, and desquamation	Honeydew Honey-Mellis Cap shampoo	None	30	30	0

AD, Atopic dermatitis; ASI, acne severity index; AVCO, activated virgin coconut oil acne gel; AVG, aloe vera gel; BP, benzoyl peroxide; BSA, body surface area affected; CCO, coconut oil; CDLQI, children's dermatology life quality index; CO, colloidal oatmeal; DLQI, dermatology life quality index; EASI, eczema area and severity index composite score; ERC, 3% erythromycin cream; GT, green tea; IDQOL, infant's dermatitis quality of life index; IGA, investigator's global assessment for acne; KH, kanuka honey; MH, manuka honey; N/A, not applicable; OO, olive oil; O-SSI, objective-SCORAD severity index; PASI, psoriasis area and severity index; PGA, physician global assessment; PT, patient; PTAC, propolis, tea tree oil, and aloe vera cream; PUVA, photochemotherapy; RCT, randomized clinical trial; SB, shea butter extract; SCORAD, severity scoring of atopic dermatitis; SH, skin hydration; SI, severity index; SSO, sunflower seed oil; TCS, topical corticosteroid; TEWL, transepidermal water loss; TIS, 3 item severity score including erythema, edema/papulation, and excoriation; TLC, total lesion count reduction; TR, tretinoin cream; TTO, tea tree oil; UK, United Kingdom; USA, United States of America; UVB, narrow-band ultraviolet B phototherapy; VAS, visual analog score; VCO, virgin coconut oil; VLRT, real visible light phototherapy; VLST, simulated visible light phototherapy; VOO, virgin olive oil.

\*Sex ratio does not represent patients who dropped out of the study.

**Table III.** Characteristics of the studies included in the quantitative analysis

Reference	Country	Age (years)	Sex (female/ male)	Study design	Disease	Variable studied	Treatment ingredient	Control ingredient	n total	n treatment total	n controls total
Enshaieh et al, 2006 <sup>33</sup>	Iran	Range: 15-25	47/13	Double-blind clinical trial	Acne	TLC	TTO	Vehicle gel	60	30	30
Kwon et al, 2014 <sup>34</sup>	South Korea	Mean: 25.9 ± 5.6	23/11*	Prospective double-blind randomized controlled split-face trial	Acne	TLC	TTO	LFCO	32	32	32
Sharquie et al, 2006 <sup>35</sup>	Iraq	Range: 14-22 Mean: 17.8 ± 3.3	35/25*	Single-blind, randomly controlled therapeutic study	Acne	TLC	GT	Control solution made of 75 mL distilled water and 25 mL ethanol	49	25	24
Sharquie et al, 2008 <sup>36</sup>	Iraq	Range: 13-27 Mean: 19.5 ± 3.5	29/11	Single-blind, randomly comparative therapeutic clinical trial	Acne	TLC	GT	Control solution made of 5% zinc sulfate	40	20	20
Yoon et al, 2013 <sup>37</sup>	South Korea	Mean: 22.1	18/17	Randomized, split-face, clinical trial	Acne	TLC	GT	Vehicle control	35	17 (used the 1% GT) <sup>†</sup> 18 (used the 5% GT)	35
Lu et al, 2016 <sup>38</sup>	Taiwan	Range: 25-45	64/0	Randomized, double-blind, placebo- controlled clinical trial	Acne	TLC	GT	Placebo (cellulose)	64	33	31
Msika et al, 2008 <sup>39</sup>	France	Range: 4-48 months Mean: 16 months	41/45	RCT, multicenter study	AD	SCORAD	SSO	TCS	86	53	33

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Table III. Cont'd

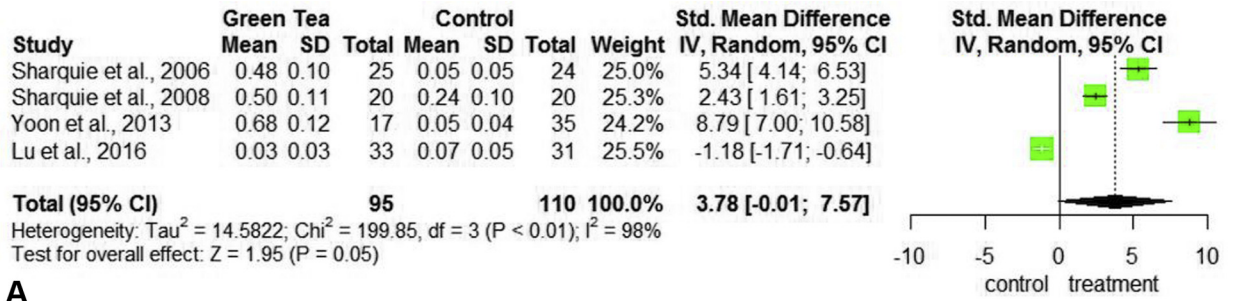
Reference	Country	Age (years)	Sex (female/ male)	Study design	Disease	Variable studied	Treatment ingredient	Control ingredient	n total	n treatment total	n controls total
Dwiyana et al, 2019 <sup>40</sup>	Indonesia	Range: 7-12	13/7	Randomized, double-blind trial	AD	SCORAD	SSO	Common moisturizer lotion	20	9	11
Lisante et al, 2017 <sup>13</sup>	USA	Mean: 8.1 ± 3.96	49/41*	Randomized, double-blind, two-arm trial	AD	EASI	CO	Prescription barrier cream	68	31	37
Syed et al, 1996 <sup>41</sup>	USA	Range: 18-50 Mean: 25.6	24/36	Double-blind, placebo- controlled study	Psoriasis	PASI	AV	Vehicle gel containing castor and mineral oil	60	30	30
Paulsen et al, 2005 <sup>42</sup>	Denmark	Range: 23-77 Median: 44	14/26	Single-center, double-blind, placebo- controlled, rand-omized, intraindividual right/left comparison	Psoriasis	PASI	AV	Vehicle gel	40	40	40
Choonhakarn et al, 2010 <sup>43</sup>	Thailand	Range (treatment): 27-65; Mean: 43.4 ± 11.2 Range (control): 23-71; Mean: 44.2 ± 13.0	39/36	Randomized, comparative, double-blind study	Psoriasis	PASI, DLQI	AV	TA	75	37	38

Sarafian et al, 2013 <sup>44</sup>	Iran	Range: 18-60 Mean: 31.7	14/20	Randomized, prospective intraindividual, right-left comparative, placebo-controlled, double-blind pilot study	Psoriasis	PASI	Turmeric	Vehicle gel	34	34	34
Shathirapathiy et al, 2015 <sup>45</sup>	India	Range: 20-60 Mean (treatment): 40.81 ± 13.39 Mean (control): 32.33 ± 8.70	20/40	Parallel-group RCT	Psoriasis	PASI	Turmeric	Naturopathy interventions including massage, yoga, hydro, diet therapy	60	30	30
Bahraini et al, 2018 <sup>46</sup>	USA	Range (treatment): 27-35 Range (control): 29-50	21/9	Randomized, double-blind, placebo-controlled prospective clinical trial	Scalp Psoriasis	PASI	Turmeric	Placebo tonic	73	15	15

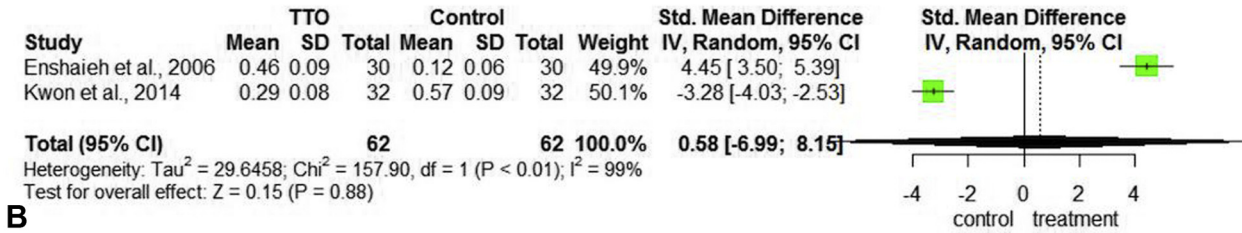
AD, Atopic dermatitis; AV, aloe vera; CO, colloidal oatmeal; EASI, eczema area and severity index; GT, green tea; LFCO, lactobacillus-fermented *C. obtusa*; PASI, psoriasis area and severity index; RCT, randomized controlled trial; SCORAD, severity scoring of atopic dermatitis; SSO, sunflower seed oil; TA, triamcinolone acetonide; TCS, topical corticosteroid; TLC, total lesion count reduction; TTO, tea tree oil; USA, United States of America.

\*Indicates that the sex ratio is not representative of patients who dropped out of the study.

†Only the 1% GT group was analyzed as the treatment group in the quantitative analysis.

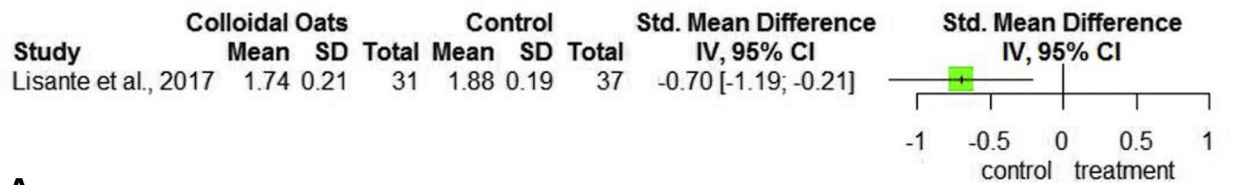


**A**

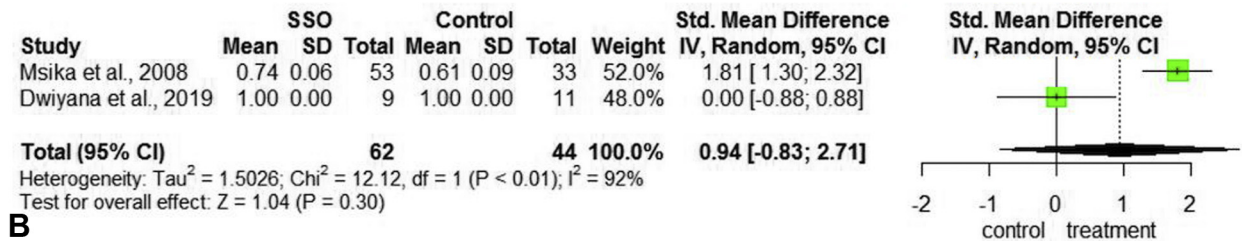


**B**

**Fig 3.** Forest plots assessing treatments for total lesion count reduction in acne. **A**, Plot for green tea versus control. **B**, Plot for TTO versus control. *CI*, Confidence interval; *SD*, standard deviation; *Std*, standardized; *TTO*, tea tree oil.



**A**



**B**

**Fig 4.** Forest plots assessing the treatments for EASI and SCORAD reduction in atopic dermatitis. **A**, Plot for colloidal oatmeal versus control measuring EASI improvement. **B**, Plot for SSO versus control measuring SCORAD improvement. *CI*, Confidence interval; *EASI*, eczema area and severity index; *Oats*, oatmeal; *SCORAD*, scoring of atopic dermatitis; *SD*, standard deviation; *SSO*, sunflower seed oil; *Std*, standardized.

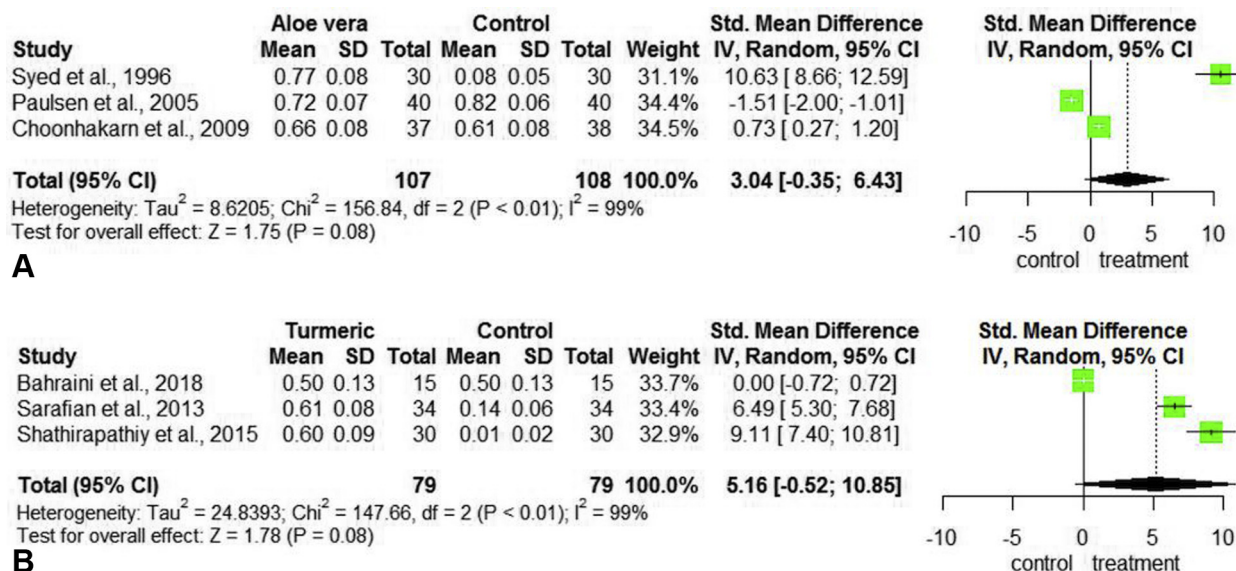
multicenter study examining treatment with honeydew honey added to a shampoo mixture showed improvement of clinical and patient-reported parameters.<sup>11</sup> This study concluded that a honeydew honey shampoo mixture is a proven alternative to medicated shampoos for mild-to-moderate scalp psoriasis.<sup>11</sup>

Lastly, a double-blind, placebo-controlled randomized clinical trial of participants with moderate-to-severe psoriasis that explored the safety and

efficacy of oral curcumin when used concomitantly with phototherapy established that curcumin was well tolerated and demonstrated a positive response as an adjunct to phototherapy, as 80% of subjects in both groups achieved a 90% decrease in PASI scores by the study conclusion.<sup>30</sup>

**DISCUSSION**

Several CAM treatments have been described for the treatment of acne, AD, and psoriasis in patients of



**Fig 5.** Forest plots assessing the treatments for PASI reduction in psoriasis. **A.** Plot for aloe vera versus control. **B.** Plot for turmeric versus control. *CI*, Confidence interval; *PASI*, psoriasis area and severity index; *SD*, standard deviation; *Std*, standardized.

all ages (Table IV).<sup>7,23,37,47-87</sup> Our meta-analysis consisted of 15 studies with a total of 280 acne patients, 174 AD patients, and 342 psoriasis patients for a combined total of 840 patients. Our systematic review analyzed data from 25 total studies; 16 were randomized clinical trials and 9 were nonrandomized studies for a combined 2249 patients (Table II). Although some information was reported in retrospective case series and case reports, we limited the data extraction to controlled clinical trials with at least 15 patients in order to review high quality studies.

Only data from the qualitative reviews showed a reduction in the primary outcome measures with CAM treatments. Within the quantitative data, there was no statistically significant difference in improvement between the CAM treatments and placebo groups in all 3 diseases examined (Figs 3, A to 5, B). Within the qualitative data, kanuka honey showed minimal improvement of the Investigator's Global Assessment acne score and exacerbated symptoms in others.<sup>21</sup> Shea butter proved ineffective in improving SCORAD,<sup>29</sup> and CCO failed to accelerate psoriasis clearance in patients with chronic plaque psoriasis undergoing psoralen and ultraviolet A or ultraviolet B therapy.<sup>31</sup> All other CAMS did show moderate to significant improvement in patients.

Studies elsewhere have described varying degrees of successful treatment of acne,<sup>88</sup> AD,<sup>89</sup> and psoriasis.<sup>90</sup> For acne, a meta-analysis found that essential oils, some including TTO, had equal or

non-inferior efficacy compared with standard treatment.<sup>88</sup> The effectiveness of these CAMs was attributed to an antibacterial and anti-inflammatory effect.<sup>88</sup> A separate meta-analysis and systematic review determined that CAM modalities used alone or in combination with usual care may relieve AD symptoms such as pruritus and swelling anywhere from 50% to 95%, while also reducing relapse of AD.<sup>89</sup> Our qualitative analysis agrees with these findings; however, our quantitative analysis does not. Although the CAM therapies we examined have the potential to be used safely in conjunction with standard medication regimens, our quantitative analysis deemed the CAM treatments were not superior to placebos.

Although our analysis provides important information, limitations to our study include important differences between the study design, small sample size, different outcome measures, vehicle, concentration, and treatment duration which limit the generalizability of the data for a single ingredient. Additionally, some preparations of herbal extracts consisted of combinations of different active ingredients and may have introduced over- or under-estimation of treatment efficacy depending on the preparation or vehicle used.

## CONCLUSION

In summary, the results from our quantitative analysis failed to demonstrate that the examined CAM natural treatments were superior to placebo treatments. Based on these findings, we conclude

**Table IV.** Background information on natural ingredients studied

Ingredient	Coconut oil <sup>17-51</sup>	Aloe vera <sup>52-55</sup>	Honey <sup>7,56,57</sup>	Turmeric <sup>23,48-62</sup>	Colloidal oatmeal <sup>53,64</sup>	Sunflower seed <sup>51,65-71</sup>	Shea butter <sup>72-75</sup>	Witch hazel <sup>76-78</sup>	Tea tree oil <sup>79-83</sup>	Green tea <sup>37,84-87</sup>
Background	VCO is an unrefined grade of coconut oil that is harvested prior to contamination with chemical processing by-products. High levels of lauric and myristic acid within VCO are known to have antibacterial and anti-inflammatory properties. VCO also reduces TEWL, therefore improving barrier function in patients with AD. VCO's reputation as a moisturizing agent, wide availability, and low evidence of allergenicity make it an attractive alternative therapy for dermatologic diseases.	AV or <i>Aloe barbadensis</i> Mill., derived from the Liliaceae family, has been used extensively in traditional Ayurvedic medicine and other cultures. Herbal extracts or formulations of AV gel are known for their anti-inflammatory, anti-pruritic, antibacterial, and healing properties. These studies prompted researchers to test the clinical efficacy of AV as a novel treatment option for both psoriasis and acne vulgaris.	Honey is a historically used CAM, most widely known for its antibacterial and anti-inflammatory therapeutic properties in addition to its ability to promote wound healing and stimulate tissue regeneration while minimizing scar size.	Curcumin, derived from the <i>Curcuma longa</i> Linn plant, is a polyphenol found in turmeric, known for its strong antioxidant, anti-inflammatory, antiangiogenic, and antiproliferative properties. Various studies, including randomized control trials (RCTs), have shown that curcumin may be used medically to treat an array of dermatologic conditions.	Colloidal oatmeal ( <i>Avena sativa</i> ) has served for centuries as a topical treatment for an array of skin barrier conditions, including dry skin, rashes, burns, and AD. Colloidal oatmeal extracts have been associated with induction of gene expression, including epidermal differentiation, and genes related to skin barriers such as the zonulae occludens (tight junctions) and with downregulation of pro-inflammatory mediators in keratinocytes demonstrating the benefit of its clinical use.	SSO ( <i>Helianthus annuus</i> ) has been extensively investigated in the treatment of xerosis and AD. SSO is defined consistent with the ratios of its fatty acid components: oleic acid, palmitic acid, stearic acid, and linolenic acid are also contained in SSO. Linoleic acid in SSO is a necessary fatty acid for the maintenance of normal epidermal barrier function and helps with dermatitis resolution in infants with deficiencies.	Shea butter is extracted from the <i>Vitellaria paradoxa</i> tree and is composed of triglycerides with oleic, stearic, linoleic, and palmitic fatty acids, in addition to the anti-inflammatory and antioxidant unsaponifiable agents including: tripterene, tocopherol, phenols, and sterols. Furthermore, shea butter has been shown to be as effective as a ceramide-precursor in patients with AD.	Witch Hazel, derived from the plant <i>Hamamelis virginiana</i> , has high levels of tannins and shows antioxidant, anti-inflammatory, antimicrobial, and anti-tumoral activity. Therefore, its role in the treatment of AD and other scalp disorders has been a recent point of interest among researchers and patients who commonly use witch hazel for various dermatologic conditions.	TTO, also known as melaleuca oil, is an essential oil derived from the Australian plant <i>Melaleuca alternifolia</i> . It has broad spectrum antimicrobial activity and anti-inflammatory properties especially in acne. TTO is widely available in OTC products and marketed as a treatment for acne so studies evaluating its efficacy are important to answer patient queries.	Green tea extract, derived from the tea plant, <i>Camellia sinensis</i> and their polyphenolic catechins have natural healing, photoprotective, antioxidant, and anti-inflammatory properties. The major polyphenolic catechin present is (-)-EGCG, which has been found to inhibit two-stage carcinogenesis and UVB induced photocarcinogenesis. The topical application of green tea has had limitations because of stability and epidermal penetration challenges but has been shown to be an effective treatment for mild-to-moderate acne.

AD, Atopic dermatitis; AV, aloe vera; CAM, complementary and alternative medicine; EGCG, epigallocatechin-3-gallate; OTC, over the counter; SSO, sunflower seed oil; TEWL, transepidermal water loss; TTO, tea tree oil; UVB, ultraviolet B; VCO, virgin coconut oil.

that there is insufficient evidence to support the efficacy and the recommendation of CAM for acne, AD, and psoriasis. Conversely, our systematic review found supporting evidence for the following ingredients: TTO, GT, and adjuvant use of AV for mild-to-moderate acne vulgaris; CO, honey, SSO, AV, CCO, and turmeric for AD; and honey, AV, CCO, and turmeric for psoriasis. Given our discordant data, future studies corroborating the efficacy and safety of CAM treatments in common skin conditions are warranted.

#### Conflicts of interest

None disclosed.

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