

Complementary and Alternative Medicine Therapies for Psoriasis

A Systematic Review

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IMPORTANCE Up to 51% of patients with psoriasis report the use of complementary and alternative medicine (CAM) in their treatment regimen, although it is unclear which CAM therapies are effective for treatment of psoriasis.

OBJECTIVE This review compiles the evidence on the efficacy of the most studied CAM modalities for treatment of patients with plaque psoriasis and discusses those therapies with the most robust available evidence.

EVIDENCE REVIEW PubMed, Embase, and ClinicalTrials.gov searches (1950-2017) were used to identify all documented CAM psoriasis interventions in the literature. The criteria were further refined to focus on those treatments identified in the first step that had the highest level of evidence for plaque psoriasis with more than 1 randomized clinical trial supporting their use. This excluded therapies lacking randomized clinical trial (RCT) data or showing consistent inefficacy.

FINDINGS Primary CAM therapy searches identified 457 articles, of which 107 articles were retrieved for closer examination. Of those articles, 54 were excluded because the CAM therapy did not have more than 1 RCT on the subject or showed consistent lack of efficacy. An additional 7 articles were found using references of the included studies, resulting in a total of 44 RCTs (17 double-blind, 13 single-blind, and 14 nonblind), 10 uncontrolled trials, 2 open-label nonrandomized controlled trials, 1 prospective controlled trial, and 3 meta-analyses. Compared with placebo, application of topical indigo naturalis, studied in 5 RCTs with 215 participants, showed significant improvements in the treatment of psoriasis. Treatment with curcumin, examined in 3 RCTs (with a total of 118 participants), 1 nonrandomized controlled study, and 1 uncontrolled study, conferred statistically and clinically significant improvements in psoriasis plaques. Fish oil treatment was evaluated in 20 studies (12 RCTs, 1 open-label nonrandomized controlled trial, and 7 uncontrolled studies); most of the RCTs showed no significant improvement in psoriasis, whereas most of the uncontrolled studies showed benefit when fish oil was used daily. Meditation and guided imagery therapies were studied in 3 single-blind RCTs (with a total of 112 patients) and showed modest efficacy in treatment of psoriasis. One meta-analysis of 13 RCTs examined the association of acupuncture with improvement in psoriasis and showed significant improvement with acupuncture compared with placebo.

CONCLUSIONS AND RELEVANCE The CAM therapies with the most robust evidence of efficacy for treatment of psoriasis are indigo naturalis, curcumin, dietary modification, fish oil, meditation, and acupuncture. This review will aid practitioners in advising patients seeking unconventional approaches for treatment of psoriasis.

JAMA Dermatol. doi:10.1001/jamadermatol.2018.2972
Published online September 5, 2018.

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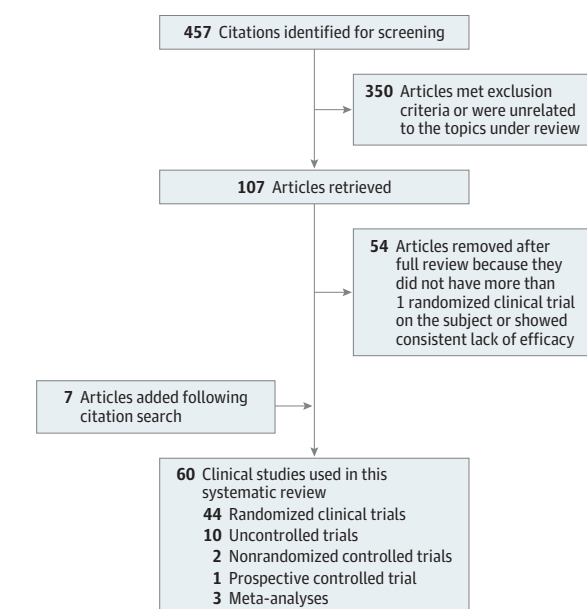
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Pсориаз vulgaris, a chronic inflammatory disorder affecting 2% of the population, is characterized by red, scaly plaques on the extensor surfaces of the skin. Evidence suggests that psoriasis is a T-cell-driven disorder resulting in keratinocyte proliferation and increased migration of immature cells toward the stratum corneum.¹ The T cells are thought to be activated by antigens or trauma in genetically predisposed individuals, leading to cytokine release and induction of the psoriatic phenotype.² Current pharmacological treatment uses topical agents (topical corticosteroids, tar-based preparations, dithranol, vitamin D analogues, salicylic acid, and topical retinoids),³ oral agents (methotrexate, acitretin, and cyclosporine), a growing repertoire of biologic agents (infliximab, adalimumab, etanercept, and ustekinumab among others), and UV phototherapy (UV-B and psoralen-UV-A).⁴ However, 52.3% of patients with psoriasis report dissatisfaction with their medical treatment because of treatment inefficacy and adverse effects.⁵ Not surprisingly, 51% of patients with psoriasis report use of complementary and alternative medicine (CAM).⁶ The National Center for Complementary and Integrative Health defines CAM therapies as health care and medical practices that are not currently considered part of conventional medicine. Complementary medicine combines these approaches with mainstream therapies, whereas alternative medicine is used in place of conventional therapies. Complementary and alternative medicine is divided into 2 main categories: mind-body interventions and natural products, including herbs, vitamins, and dietary supplements.⁷ Herein, we review the literature on the use of CAM interventions with the best evidence for treatment of plaque psoriasis from these 2 categories.

Methods

We conducted a review of the existing data using a 2-step approach. First, we identified all CAM interventions reported in the

Figure. Flowchart Illustrating the Article Inclusion Process



Key Points

Question Which complementary and alternative medicine therapies are effective in treating psoriasis?

Findings This systematic review of 57 trials and 3 meta-analyses found that indigo naturalis, curcumin, dietary modification, fish oil, meditation, and acupuncture had the most robust evidence of efficacy in the treatment of plaque psoriasis.

Meaning Complementary and alternative medicine treatments are gaining popularity, and this review will serve as a comprehensive resource for practitioners treating patients with psoriasis.

treatment of psoriasis. Searches of PubMed, Embase, and ClinicalTrials.gov from 1950 to 2017 were used to identify documented cases of CAM treatments of psoriasis in the literature. The search terms *complementary and alternative medicine psoriasis*, *herbal remedies psoriasis*, *homeopathic medicines psoriasis*, *Chinese medicine psoriasis*, *massage psoriasis*, and *therapeutic touch psoriasis* were used. All relevant randomized clinical trials (RCTs) written in English were reviewed. References of included resources were examined, and sources that were not identified initially were incorporated. In the second step, we focused on the identified treatments that had the greatest level of evidence for plaque psoriasis with more than 1 RCT supporting their use. This method resulted in the exclusion of therapies lacking RCT data, including the Mediterranean diet, gluten-free diet, micronutrient supplementation, orange-peel extract, therapeutic touch, and massage therapy. Other CAM approaches were excluded based on lack of efficacy, including oral vitamin D supplementation, vitamin B₁₂ supplementation, selenium supplementation, *Aloe vera*, *Mahonia aquifolium*, and hypnosis. After a thorough review of the evidence for individual therapies with a focus on RCTs, we conducted additional focused searches using the search terms *psoriasis indigo naturalis*, *psoriasis curcumin*, *psoriasis diet*, *psoriasis fish oil*, *psoriasis meditation*, and *psoriasis acupuncture*, to ensure all relevant data, including non-RCTs, were examined and reviewed for each therapy. Forty-four RCTs, 10 uncontrolled trials, 2 controlled nonrandomized trials, 1 prospective nonrandomized controlled trial, and 3 meta-analyses⁸⁻¹⁰ were assessed in this review (Figure).

Natural Products

Topical Indigo Naturalis

Indigo naturalis (IN), derived from indigo plants such as *Baphicacanthus cusia*, has been used in traditional Chinese medicine for centuries. Along with its active component indirubin, IN has shown anti-inflammatory, antiviral, antimicrobial, antipyretic, and antitumor effects via CDK2 inhibition of the cell cycle in proliferating cancer cells.^{11,12} Oral administration can cause gastrointestinal irritation and hepatic damage when used long term. Topically, however, IN has been shown to be a safe treatment of psoriasis.

For example, in an 8-week, randomized, double-blind, placebo-controlled clinical study, patients with moderate plaque psoriasis were treated with either IN ointment (n = 16) or placebo (n = 8) (baseline Psoriasis Area Severity Index [PASI] of 10.1 for IN group vs 11.1 for controls).¹³ In that study, 56.3% of patients in the IN group showed 75% improvement in PASI scores compared with 0% of

patients in the placebo group ($P = .02$). Improvement was not sustained following termination of treatment, as shown by a worsening in PASI scores during the study follow-up period.¹³

A 12-week, randomized, observer-blind, vehicle-controlled, intra-patient comparison study also evaluated the effect of topical IN on psoriasis.¹⁴ The 42 participants had at least a 2-year history of mild to moderate psoriasis and had failed to respond to at least 2 traditional psoriasis treatments.¹⁴ The IN consisted of indigo, 1.4%, and indirubin, 0.16%, in a vehicle containing petroleum jelly, yellow wax, and olive oil. Two comparable symmetric plaques on either side of the body were selected for each patient. The one plaque was treated with IN ointment, while the other plaque was treated with the vehicle-controlled placebo ointment. The IN treatment arm showed a statistically significant decrease in the sum of scaling, erythema, and induration scores (a PASI of 18.9 at baseline decreased to 6.3 after IN treatment) vs the vehicle-controlled placebo ointment (a PASI of 18.7 at baseline decreased to 12.8 after 12 weeks).¹⁴ In addition, 74% of IN-treated plaques had a complete (100%) or near complete (75%-90%) clearance of psoriasis as assessed by 2 blinded observers, whereas the placebo group had only 3% complete or near complete clearance. No serious adverse events were reported, and no IN-treated plaques worsened during the study. Baseline severity was not a predictor of treatment response, and clinical improvement increased with length of treatment. Although IN was efficacious in treating plaque psoriasis, the long-term compliance rate may decrease owing to the dark-blue pigment of the ointment, which can stain clothing.¹⁴ These results are similar to a pilot study that had been performed in 2007.¹¹

Lin et al¹⁵ found that the active ingredient of IN, indirubin, is responsible for the antipsoriatic effects via G₀/G₁ cell cycle arrest, which decreases the hyperproliferation that characterizes psoriasis. Specifically, cell division cycle 25B (CDC25B) and epithelial growth factor receptor, which play a role in keratinocyte hyperproliferation, appear to be inhibited by both IN and indirubin.¹⁶ Lee and colleagues¹⁷⁻¹⁹ later refined the crude IN ointment to remove the blue color to improve patient compliance. However, their new proprietary ointment, Lindioil, which contains the active ingredient indirubin and is as efficacious as the crude IN ointment, is not commercially available. In the most recent publication by Lin and colleagues,²⁰ ointment with 200 µg/g of indirubin (compared with 10, 50, and 100 µg/g of indirubin) applied twice daily showed the greatest decrease in PASI scores (69.2% decrease from a baseline PASI of 10.5). The efficacy of IN treatment of nail psoriasis has also been shown in several publications.^{18,19}

In conclusion, there is reasonable evidence to recommend a trial period of IN for the treatment of psoriasis. These studies demonstrate that topical IN may inhibit keratinocyte proliferation and repair the psoriatic epidermal barrier.²⁰ Most of the studies evaluating IN, however, have a small number of participants, and the studies do not evaluate consistent dosages of indirubin, making the optimal concentration of IN difficult to discern (Table).^{2,4,9,11,13,14,17,20-27} Its blue pigment may affect compliance, and finding a reputable source for IN may prove to be a barrier for use because there are limited commercial sources for this product. Sources of IN can be found at traditional Chinese herb pharmacies as *qing dai*, but consumers should be wary of counterfeit chemical dyes.²⁸

Curcumin

Curcumin, a phytochemical found in the spice turmeric, has been used in traditional Chinese and Ayurvedic medicine for centuries. In

vitro and animal models have shown a wide range of medicinal benefits, including anticancer (curcumin inhibits signal transducer and activator of transcription 3, nuclear factor κβ, and specificity protein 1 activation²⁹), anti-inflammatory, antimicrobial, and antioxidant activity.²² After many positive anecdotal reports of successful curcumin treatment of psoriasis,³⁰⁻³² RCTs have been conducted to examine curcumin efficacy in humans.⁴ Curcumin is available in both topical and oral formulations, and both have been examined for the treatment of psoriasis. Recent data from an in vitro psoriasis model using human keratinocytes found that curcumin inhibits proliferation of keratinocytes through downregulation of the proinflammatory cytokines interleukin 17 (IL-17), IL-6, interferon γ, and tumor necrosis factor.³³

Topical Curcumin | Sarafian et al²¹ examined topical curcumin as an adjunctive therapy for patients with mild to moderate psoriasis. A hydroalcoholic turmeric extract, in which curcumin is the active ingredient, is part of their patented topical formulation. In this 9-week, randomized, intraindividual, double-blind, placebo-controlled clinical study, 34 patients applied the turmeric microemulgel to a plaque on the right side of their body and the vehicle-controlled placebo to a symmetric plaque on the left side. The primary outcome measure was PASI. The use of turmeric gel resulted in statistically significant decreases in scaling, erythema, and plaque thickness. Burning, irritation, and dryness were the most common reported adverse effects.

Heng et al² conducted a nonrandomized trial in which 10 male participants were assigned to 4 subgroups: normal skin without psoriasis, untreated psoriasis, moderate to severe psoriasis treated with calcipotriol, and moderate to severe psoriasis treated with curcumin (an alcohol-based gel preparation containing curcumin, 1%). The level of phosphorylase kinase and the percentage of the stratum corneum parakeratosis in each biopsy sample were compared for each group; higher levels of phosphorylase kinase and higher percentages of parakeratosis correlated with greater severity of psoriasis. Phosphorylase kinase levels were highest in the untreated participants, slightly lower in the calcipotriol treatment group, lower still in the curcumin treatment group, and lowest in normal skin ($P < .001$). Severity of parakeratosis, measured as the percentage of stratum corneum involvement, followed the same pattern ($P < .001$). In the curcumin group, 5 of 10 participants had a 90% resolution of psoriasis, and the remaining 5 participants showed 50% to 85% improvement. Similarly, in the calcipotriol group, all participants experienced 50% to 80% improvement; however, the treatment effect took 4 to 18 months to appreciate compared with 2 to 8 weeks in the curcumin group. Thus, topical curcumin, 1%, in an alcohol-based vehicle showed a superior outcome compared with topical calcipotriol in the treatment of moderate to severe psoriasis. However, it is not clear whether the evaluators were blinded to treatment assignment, and the method used to grade severity was not specified.

Oral Curcumin | A 16-week, randomized, double-blind, placebo-controlled clinical study examined the efficacy of oral curcumin for 63 patients with mild to moderate psoriasis.²² The efficacy of a lecithin-based delivery system of curcumin with increased bioavailability (2 g/d of Meriva; Indena, Milan, Italy) was compared with placebo, and topical methylprednisolone aceponate, 0.1%, ointment applied daily was continued in both groups. By week 12, 92% of patients in the cur-

Table. Summary of CAM Therapy for Psoriasis^a

Type of Therapy, Source	CAM and Dose tested	Study Region	Publication Year	Study Length and Design	Patients, No.	Baseline Severity Level	Comparison Treatment	Study Results
Indigo naturalis								
Cheng et al ¹³	Topical indigo naturalis	Taiwan	2017	8 wk; randomized, double-blind, placebo-controlled	24	Mean PASI scores: indigo naturalis group, 10.1; placebo group, 11.1	Vehicle ointment is a mixture of blue dye powder (54.8% indigo carmine-aluminum lake [Blue No. 2], 45.2% Allura Red AC [Red 40 aluminum lake] powders), Vaseline, microcrystalline wax, and olive oil.	Indigo naturalis ointment composed of a 1:10 mixture of indigo naturalis powder and a vehicle; concentration levels of 2.83% indigo and 0.24% indirubin; decreased PASI scores to 2.64 vs 8.3 for placebo ($P = .01$); 56.3% of the topical indigo naturalis group had 75% improvement in PASI scores, whereas 0% of placebo group had 75% improvement
Lin et al ¹¹	Topical indigo naturalis	Taiwan	2007	8 wk; randomized, observer-blind, placebo-controlled	14	Sum of scaling, erythema, and induration scores was 10.0 for both groups	Vehicle ointment containing Vaseline (25%), yellow wax (30%), and olive oil (45%)	Indigo naturalis (20% indigo naturalis powder and 80% vehicle) decreased the sum of scaling, erythema, and induration scores to 3 after 8 wk of treatment ($P < .05$); vehicle ointment decreased scores to 7.5 (not significant).
Lin et al ¹⁴	Topical indigo naturalis	Taiwan	2008	12 wk; randomized, intrapatient comparison, observer-blind, vehicle-controlled	42	Mean PASI scores: indigo naturalis group, 18.9; control group, 18.7	Vehicle ointment	Indigo naturalis (1.4% indigo and 0.16% indirubin) decreased PASI score to 6.3, an 81% improvement ($P < .001$); control, PASI score 12.8, a 26% improvement ($P < .001$)
Lin et al ¹⁷	Refined topical indigo naturalis (Lindiol)	Taiwan	2012	8 wk; observer-blind, intrapatient RCT	35	Mean PASI score, 11.5	Crude indigo naturalis with blue pigment	PASI for refined indigo naturalis (indirubin concentration, 0.105 mg/g), 9.1; PASI for crude indigo naturalis (indirubin concentration, 0.138 mg/g), 8.8 ($P = .14$, no significant difference); refined indigo naturalis is as effective as the crude form
Lin et al ²⁰	Refined topical indigo naturalis (Lindiol), 10, 50, 100, and 200 µg/g	Taiwan	2017	8 wk; randomized, multicenter, double-blind, dosage-controlled, phase 2a trial	100	Mean PASI score each group: 10 µg/g, 12.6; 50 µg/g, 11.3; 100 µg/g, 11.4; 200 µg/g, 10.5	NA	Indirubin (active ingredient in indigo naturalis) dose of 200 µg/g had greatest efficacy in clearing plaques compared with 10, 50, or 100 µg/g applied twice daily, resulting in a 69.2% decrease in PASI scores ($P = .04$).
Curcumin								
Sarafian et al ²¹	Topical microemulgel curcumin (containing hydroalcoholic turmeric extract)	Iran	2015	9 wk; randomized, prospective, intraindividual, right-left, double-blind, placebo-controlled	34	Mean PASI scores: curcumin/right-sided lesions, 3.6; control/left-sided lesions, 3.7	Vehicle ointment	Curcumin decreased redness from 1.3 to 0.2, thickness from 1.1 to 0.3, scale from 1.5 to 0.1, and area (all $P < .05$). Control decreased redness from 1.4 to 1, thickness from 1.2 to 1.1, and scale from 1.5 to 0.7 (none were statistically significant); area involved did not decrease.
Heng et al ²	Topical curcumin (alcoholic gel containing 1% curcumin)	United States	2000	18 mo; nonrandomized, prospective, placebo-controlled (blinding not specified)	40	Moderate to severe (psoriasis severity scale not specified)	Untreated psoriasis; calcipotriol; normal skin	Decreased pH activity, Ki67 expression, severity of parakeratosis, and density of CD8 ⁺ T cells in psoriatic plaques ($P < .001$); these variables were highest in active untreated psoriasis, lower in calcipotriol-treated group, even lower in curcumin-treated group and lowest in normal skin.
Antiga et al ²²	Oral curcumin (Meriva), 2 g daily plus topical steroid	Italy	2015	16 wk; randomized, double-blind, placebo-controlled	63	Median PASI scores: oral curcumin plus topical steroids arm, 5.6; placebo plus topical steroids arm, 4.7	Placebo plus topical steroid	PASI scores decreased at 16 wk: oral curcumin plus topical steroid, 1.4 ($P < .05$); 92% of participants achieved 50% improvement in PASI score; placebo plus topical steroids, 2.5 ($P < .05$); 54% of participants achieved 50% improvement in PASI score

(continued)

Table. Summary of CAM Therapy for Psoriasis^a (continued)

Type of Therapy, Source	CAM and Dose Tested	Study Region	Publication Year	Study Length and Design	Patients, No.	Baseline Severity Level	Comparison Treatment	Study Results
Carrion-Gutierrez et al ²³	Oral curcumin, 100 mg, 6 times daily plus real visible light phototherapy	Spain	2015	8 wk; phase 4, randomized, double-blind, placebo-controlled, single-center, pilot clinical trial	21	Moderate to severe based on the Physician Global Assessment score with a total surface area >30 cm ²	Oral curcumin plus simulated visible light phototherapy	81% of patients in the real phototherapy group showed a response to treatment vs 30% of patients in the simulation group ($P < .05$). Oral curcumin was a successful photosensitizer in combination with UV-A and visible light phototherapy.
Kurd et al ⁴	Oral curcumin, 4.5 g daily	United States	2008	16 wk; phase 2, single-arm, single-dose, noncontrolled, open-label clinical trial	12 (8 completed study, 4 did not)	Mean PASI scores: completed, 13.7; did not complete, 14.6	NA	Decreased PASI from baseline to 12 wk in participants completing the trial: 5.4 ($P = .04$)
Meditation and guided imagery								
Kabat-Zinn et al ²⁴	Meditation plus phototherapy for up to 13.5 min, 3 times/wk	United States	1998	13 wk; randomized, observer-blind, placebo-controlled trial	37	Moderate to severe as defined by >15% body area involvement	Phototherapy alone	Meditation plus phototherapy group was 3.8 times more likely to reach clearing point and reached clearing point 4 times faster than placebo group ($P = .03$)
Gaston et al ²⁵	Meditation and imagery 60 min/wk training session plus 30 min/d individual practice	Canada	1991	12 wk; randomized, observer-blind, placebo-controlled	24	Psoriasis rating treatment groups, 12.5; control group, 11.3; study-specific numerical grading system	No therapy group	Post treatment scores: meditation, 8.9; meditation plus imagery, 9.3; control, 11.5 ($P < .01$)
Zachariae et al ²⁶	Psychotherapy plus stress management, guided imagery, and relaxation	Denmark	1996	12 wk; randomized, observer-blind, placebo-controlled	51	Baseline mean PASI scores: treatment group, 7.4; control group, 8.1	No therapy group	Statistically significant decrease in PASI score in the treatment group from baseline ($P < .05$); no significant decrease in scores in control group
Acupuncture								
Yeh et al ⁹	Acupoint stimulation for 2–18 wk	Taiwan	2017	Meta-analysis of 13 RCTs (1 double-blind, 1 observer-blind, 11 unblinded)	13 studies, 1060 patients	NA	Various	Statistically significant difference between acupoint and nonacupoint stimulation (odds ratio, 2.57; 95% CI, 1.81–3.65)

Abbreviations: CAM, complementary and alternative medicine; PASI, Psoriasis Area Severity Index; PhK, phospholase kinase; NA, not applicable; RCT, randomized clinical trial.

^a Quality of evidence rating based on standard JAMA Dermatology specific guidelines was 1 for all studies except Kurd et al,⁴ which was rated 2. For weight reduction and fish oil, see Ford et al.²⁷

cumin plus topical steroid treatment group achieved a 50% improvement in PASI vs 54% in the placebo plus topical steroid treatment group ($P < .05$; baseline PASI scores were 5.6 and 4.7 for treatment and placebo groups, respectively). Furthermore, 48% of the curcumin plus topical steroid treatment group achieved 75% improvement vs 12% of participants in the placebo plus topical steroid treatment group. Finally, 12% of the curcumin plus topical steroid treatment group had 100% improvement vs 4% of participants in the placebo plus topical steroid treatment group. Interleukin 17 levels remained similar for both groups at week 12; however, IL-22 levels were significantly decreased in the curcumin plus topical steroid treatment group compared with the placebo plus topical steroid treatment group ($P < .001$). Oral curcumin in a phospholipid delivery system that enhances its bioavailability, when given with topical steroids, may be a safe and effective adjunctive treatment of psoriasis.

Carrion-Gutierrez et al²³ performed a 2-month randomized, double-blind, placebo-controlled clinical study of 21 participants with moderate to severe psoriasis to determine oral curcumin safety and efficacy as a photosensitizer when used with phototherapy. The placebo group received simulated visible light therapy with oral curcumin. In the placebo group, 30% of patients were classified as responders to therapy vs 81% in the visible light phototherapy group ($P = .05$). Curcumin was safe and effective when combined with either UV-A phototherapy or visible light phototherapy, with 80% in both groups achieving a 90% decrease in PASI scores by the final visit. There was no significant difference in the time course of clinical improvement between UV-A and visible light phototherapy.

Kurd et al⁴ conducted a 16-week, noncontrolled, phase 2, open-label trial of oral nonmodified curcumin, 4.5 g/d, for patients with moderate to severe psoriasis. Of the 12 participants enrolled, 8 completed the trial. Only 2 participants responded to the curcumin, with improvement rates of 83% and 85% in these individuals; thus, the trial was terminated at the 16-week visit. Adverse effects included mild gastrointestinal upset and hot flashes. The low response rate could be due to the low bioavailability of oral curcumin (40%-90% of oral doses are excreted in stool) or the ineffectiveness of treatment of moderate to severe psoriasis.

In conclusion, based on the available literature (Table), there is little evidence to support the use of topical curcumin for adults with plaque psoriasis. Because the evidence is limited regarding the effectiveness of oral nonmodified curcumin supplementation for psoriasis, a recommendation cannot be made at this time. On the basis of preliminary high-quality evidence, a trial period of oral curcumin in a phospholipid-based delivery system can be recommended as an effective adjunctive treatment of psoriasis.

Curcumin, while promising for the treatment of psoriasis, has significant limitations. It has low oral bioavailability, and, topically, it has poor absorption and its distinct yellow pigment is undesirable. However, there has been progress in overcoming these limitations, including formulations with increased oral bioavailability, long-lasting subcutaneous injection, intraperitoneal injection, intravenous administration, nasal administration, and nanoparticle and gel-based topical preparations that enhance topical absorption.³⁴ These novel delivery systems for curcumin show promise as potential future treatments of psoriasis.

Both topical and oral curcumin formulations are widely available via the internet and from health food or supplement stores.

However, there is no oversight of such products by the US Food and Drug Administration; topical products containing curcumin are often confounded by the use of other ingredients in combination, and formulations, prices, and efficacy vary widely.

Dietary Modification

A recent systematic review by Ford et al²⁷ reviewed the evidence for dietary interventions for patients with psoriasis. We summarize herein the recommendations discussed in that publication that have RCTs supporting their efficacy.

Weight reduction via a hypocaloric diet, in which calories expended outnumber calories consumed, is strongly recommended as an adjunct to traditional treatments for patients with psoriasis who are overweight or obese (body mass index ≥ 25 [calculated as weight in kilograms divided by height in meters squared]) and has been endorsed by the National Psoriasis Foundation's medical board. Based on high-quality evidence and consistent benefits reported by RCTs and meta-analyses, a hypocaloric diet has been shown to significantly improve psoriasis severity, dermatologic quality of life, and weight loss.^{10,27}

Oral fish oil supplements are the most common CAM used by dermatology patients;³⁵ however, these supplements are not recommended at this time for the treatment of chronic plaque psoriasis because fish oil was not shown to be effective at several examined doses and durations (which varied markedly from 216 mg/d to 14 g/d for eicosapentaenoic acid [EPA], from 80 mg/d to 9 g/d for docosahexaenoic acid [DHA], and from 14 days to 9 months). It should be noted that there are conflicting results from fish oil studies.^{8,27} Two double-blind RCTs (one of which evaluated EPA, 1.8 g, and DHA, 1.2 g, consumed daily for 12 weeks,³⁶ and the other evaluated EPA, 3.6 g, and DHA, 2.4 g, consumed daily for 15 weeks³⁷) found evidence supporting the use of oral fish oil. One open-label RCT³⁸ and 1 open-label nonrandomized controlled trial³⁹ also showed statistically significant benefit. Seven other RCTs⁴⁰⁻⁴⁶ found lack of efficacy for daily EPA (216 mg to 5.4 g) or DHA (132 mg to 3.6 g) treatment. The remainder of the data supporting efficacy of oral fish oil treatment were based on uncontrolled trials, of which 6⁴⁷⁻⁵² of the 7 studies⁴⁷⁻⁵³ found significant benefit of oral fish oil. There are also 2 double-blind RCTs^{54,55} evaluating the efficacy of intravenous ω -3 compared with ω -6 fatty acids. Treatment with intravenous ω -3 fatty acids at doses of 50 to 100 mL were found to be more efficacious than intravenous ω -6 at similar doses. Because evidence is limited regarding the effectiveness of intravenous fish oil supplementation for treatment of psoriasis in adults, a recommendation for intravenous ω -3 fatty acids cannot be made at this time.

Mind-Body Therapies

Meditation and Guided Imagery

The role of stress as a trigger in psoriasis has been long recognized.⁵⁶ This has led some researchers to speculate that reduction in stress via meditation, psychotherapy, and relaxation techniques using guided imagery, biofeedback, and hypnosis may reduce the physical and emotional manifestations of the disease.⁵⁶

Kabat-Zinn et al²⁴ examined the effect of meditation on psoriasis by randomly assigning 37 patients to receive UV-B or psoralen-UV-A phototherapy with or without listening to a meditation recording during the phototherapy sessions. Outcome was assessed through direct inspection by nurses as well as through photograph

assessments conducted by physicians blinded to the treatment groups. The results suggested a therapeutic benefit of meditation during phototherapy compared with phototherapy alone. The skin of the patients who listened to the recording cleared 4 times faster than the skin of the patients who did not listen to the recording ($P = .03$), and those in the meditation group were 3.8 times more likely to clear.²⁴ Offering similar meditation recordings to patients during phototherapy would be a simple and inexpensive way to implement a CAM therapy for patients with psoriasis. For example, such meditation tapes are available for purchase online for \$10.⁵⁷

A 12-week randomized, observer-blind, placebo-controlled clinical study examined the effect of meditation on patients with scalp psoriasis.²⁵ Twenty-four participants were assigned to 4 groups: 5 participants were in the meditation group, 4 participants were in the meditation and imagery group, 5 participants were on the waiting list, and 4 participants received no treatment. Eighteen participants completed the study. Two patients in each treatment group (meditation and meditation with imagery) showed improvement in psoriasis as assessed by a dermatologist blinded to the subgroup status. A study-specific numerical grading system was used to assess the severity of thickness, erythema, silvery plaques, and the surface area of involvement. There was a positive correlation between psychological distress and psoriasis severity ($P < .01$). These preliminary findings suggest that meditation may lessen the severity of psoriasis in some patients.

An observer-blind controlled study of 51 patients assessed the effects of guided imagery and meditation, in addition to cognitive-behavioral stress management, on psoriasis severity.²⁶ Patients in the treatment group received 7 individual psychotherapy sessions over the course of 12 weeks, whereas the control group did not receive psychotherapy. All participants were assessed for PASI, and there was a small but statistically significant improvement in the psychotherapy group compared with the control group.

In conclusion, the evidence for meditation and guided imagery is based on a small number of studies with limited numbers of participants (Table); nonetheless, early research suggests that this mind-body modality may be a beneficial adjunctive treatment as part of a holistic management approach to psoriasis.

Acupuncture

Acupuncture is a component of traditional Chinese medicine that uses various techniques to stimulate acupoints and modulate physiological reactions.⁹ A meta-analysis on acupuncture and psoriasis that included 13 RCTs analyzed a total of 590 patients who received acupoint stimulation with different acupuncture-related techniques and 461 controls with no acupoint stimulation.⁹ The pairwise meta-analysis study of RCTs concluded that the therapeutic effect of acupoint stimulation is superior to nonacupoint stimulation in treating psoriasis. The acupoint stimulation should be performed for a minimum of 6 weeks to achieve therapeutic effect. However, the included RCTs differed with respect to the specific acupoints used, the number of acupoints stimulated, and the duration of acupoint sessions, and adequate blinding was achieved only in 2 studies, making it challenging to compare these studies.

In conclusion, acupuncture appears to be beneficial for the treatment of psoriasis. However, the lack of adequate blinding is a limitation in most of the studies (Table), and owing to the variability of the RCT data, it is difficult to determine the most advantageous acupuncture technique for psoriasis.

Conclusion

There have been many CAM treatments investigated for psoriasis. There is some evidence of the efficacy for these therapies in psoriasis; however, these studies must be interpreted cautiously given their small sample sizes, variability in the quality of the study design, and differences in primary outcomes measured. Because many patients are increasingly interested in CAM treatments, the present review will help the clinician advise patients who are either uninterested in the conventional approach or who would like to incorporate one of these therapies as a complement to their current medical treatment plan. Although further larger, well-designed, controlled studies are needed to continue testing therapeutic efficacy and safety, we found that indigo naturalis, curcumin, dietary approaches, fish oil, meditation, and acupuncture had the most evidence supporting their use for the treatment of psoriasis.

ARTICLE INFORMATION

Accepted for Publication: July 10, 2018.

Published Online: September 5, 2018.
doi:10.1001/jamadermatol.2018.2972

Author Contributions: Ms Gamret and Dr Fertig had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: All authors.

Acquisition, analysis, or interpretation of data: Gamret, Price, Fertig, Nichols.

Drafting of the manuscript: Gamret, Price, Fertig, Lev-Tov.

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Statistical analysis: Gamret.

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Supervision: Gamret, Price, Lev-Tov, Nichols.

Conflict of Interest Disclosures: None reported.

Additional Contributions: John E. Lewis, PhD, Department of Psychiatry and Behavioral Sciences, University of Miami Miller School of Medicine, Miami, Florida, provided input on the figure but was not financially compensated for his contribution.

REFERENCES

1. Menter A, Korman NJ, Elmets CA, et al; American Academy of Dermatology Work Group. Guidelines of care for the management of psoriasis and psoriatic arthritis: section 6. guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. *J Am Acad Dermatol*. 2011;65(1):137-174. doi:10.1016/j.jaad.2010.11.055
2. Heng MCY, Song MK, Harker J, Heng MK. Drug-induced suppression of phosphorylase kinase activity correlates with resolution of psoriasis as assessed by clinical, histological and immunohistochemical parameters. *Br J Dermatol*. 2000;143(5):937-949. doi:10.1046/j.1365-2133.2000.03767.x
3. Mason AR, Mason J, Cork M, Dooley G, Edwards G. Topical treatments for chronic plaque psoriasis. In: Mason AR, ed. *Cochrane Database of Systematic Reviews*. Chichester, UK: John Wiley & Sons, Ltd; 2009. doi:10.1002/14651858.CD005028.pub2.
4. Kurd SK, Smith N, VanVoorhees A, et al. Oral curcumin in the treatment of moderate to severe psoriasis vulgaris: a prospective clinical trial. *J Am Acad Dermatol*. 2008;58(4):625-631. doi:10.1016/j.jaad.2007.12.035
5. Armstrong AW, Robertson AD, Wu J, Schupp C, Lebwohl MG. Undertreatment, treatment trends, and treatment dissatisfaction among patients with psoriasis and psoriatic arthritis in the United States: findings from the National Psoriasis Foundation surveys, 2003-2011. *JAMA Dermatol*. 2013;149(10):1180-1185. doi:10.1001/jamadermatol.2013.5264
6. Newman DJ, Cragg GM. Natural products as sources of new drugs over the last 25 years. *J Nat Prod*. 2007;70(3):461-477. doi:10.1021/np068054v
7. U.S. National Library of Medicine. Collection Development Manual: complementary and

- alternative medicine. <https://www.nlm.nih.gov/tsd/acquisitions/cdm/subjects24.html>. Published 2003. Accessed October 23, 2017.
8. Millsop JW, Bhatia BK, Debbaneh M, Koo J, Liao W. Diet and psoriasis, part III: role of nutritional supplements. *J Am Acad Dermatol*. 2014;71(3):561-569. doi:10.1016/j.jaad.2014.03.016
 9. Yeh M-L, Ko S-H, Wang M-H, Chi C-C, Chung Y-C. Acupuncture-related techniques for psoriasis: a systematic review with pairwise and network meta-analyses of randomized controlled trials. *J Altern Complement Med*. 2017;23(12):930-940. doi:10.1089/acm.2016.0158
 10. Upala S, Sanguankeo A. Effect of lifestyle weight loss intervention on disease severity in patients with psoriasis: a systematic review and meta-analysis. *Int J Obes (Lond)*. 2015;39(8):1197-1202. doi:10.1038/sj.ijo.2015.64
 11. Lin Y-K, Wong W-R, Chang Y-C, et al. The efficacy and safety of topically applied indigo naturalis ointment in patients with plaque-type psoriasis. *Dermatology*. 2007;214(2):155-161. doi:10.1159/000098576
 12. Moon MJ, Lee SK, Lee J-W, et al. Synthesis and structure-activity relationships of novel indirubin derivatives as potent anti-proliferative agents with CDK2 inhibitory activities. *Bioorg Med Chem*. 2006;14(1):237-246. doi:10.1016/j.bmc.2005.08.008
 13. Cheng H-M, Wu Y-C, Wang Q, et al. Clinical efficacy and IL-17 targeting mechanism of Indigo naturalis as a topical agent in moderate psoriasis. *BMC Complement Altern Med*. 2017;17(1):439. doi:10.1186/s12906-017-1947-1
 14. Lin Y-K, Chang C-J, Chang Y-C, Wong W-R, Chang S-C, Pang J-HS. Clinical assessment of patients with recalcitrant psoriasis in a randomized, observer-blind, vehicle-controlled trial using indigo naturalis. *Arch Dermatol*. 2008;144(11):1457-1464. doi:10.1001/archderm.144.11.1457
 15. Lin Y-K, Leu Y-L, Yang S-H, Chen H-W, Wang C-T, Pang J-HS. Anti-psoriatic effects of indigo naturalis on the proliferation and differentiation of keratinocytes with indirubin as the active component. *J Dermatol Sci*. 2009;54(3):168-174. doi:10.1016/j.jdermsci.2009.02.007
 16. Hsieh W-L, Lin Y-K, Tsai C-N, Wang T-M, Chen T-Y, Pang J-HS. Indirubin, an acting component of indigo naturalis, inhibits EGFR activation and EGF-induced CDC25B gene expression in epidermal keratinocytes. *J Dermatol Sci*. 2012;67(2):140-146. doi:10.1016/j.jdermsci.2012.05.008
 17. Lin Y-K, See L-C, Huang Y-H, et al. Comparison of refined and crude indigo naturalis ointment in treating psoriasis: randomized, observer-blind, controlled, inpatient trial. *Arch Dermatol*. 2012;148(3):397-400. doi:10.1001/archdermatol.2011.1091
 18. Lin Y-K, Chang Y-C, Hui RC-Y, et al. A Chinese herb, indigo naturalis, extracted in oil (Lindioil) used topically to treat psoriatic nails: a randomized clinical trial. *JAMA Dermatol*. 2015;151(6):672-674. doi:10.1001/jamadermatol.2014.5460
 19. Lin Y-K, See L-C, Huang Y-H, et al. Efficacy and safety of Indigo naturalis extract in oil (Lindioil) in treating nail psoriasis: a randomized, observer-blind, vehicle-controlled trial. *Phytomedicine*. 2014;21(7):1015-1020. doi:10.1016/j.phymed.2014.02.013
 20. Lin YK, See LC, Huang YH, Chi CC, Hui RCY. Comparison of indirubin concentrations in indigo naturalis ointment for psoriasis treatment: a randomized, double-blind, dosage-controlled trial. *Br J Dermatol*. 2018;178(1):124-131. doi:10.1111/bjd.15894
 21. Sarafian G, Afshar M, Mansouri P, Asgarpanah J, Raoufinejad K, Rajabi M. Topical turmeric microemulgel in the management of plaque psoriasis: a clinical evaluation. *Iran J Pharm Res*. 2015;14(3):865-876.
 22. Antiga E, Bonciolini V, Volpi W, Del Bianco E, Caproni M. Oral curcumin (Meriva) is effective as an adjuvant treatment and is able to reduce IL-22 serum levels in patients with psoriasis vulgaris. *Biomed Res Int*. 2015;2015:283634. doi:10.1155/2015/283634
 23. Carrion-Gutierrez M, Ramirez-Bosca A, Navarro-Lopez V, et al. Effects of Curcuma extract and visible light on adults with plaque psoriasis. *Eur J Dermatol*. 2015;25(3):240-246. doi:10.1684/ejd.2015.2584
 24. Kabat-Zinn J, Wheeler E, Light T, et al. Influence of a mindfulness meditation-based stress reduction intervention on rates of skin clearing in patients with moderate to severe psoriasis undergoing phototherapy (UVB) and photochemotherapy (PUVA). *Psychosom Med*. 1998;60(5):625-632. doi:10.1097/00006842-199809000-00020
 25. Gaston L, Crombez JC, Lassonde M, Bernier-Buzzanga J, Hodgins S. Psychological stress and psoriasis: experimental and prospective correlational studies. *Acta Derm Venereol Suppl (Stockh)*. 1991;156:37-43.
 26. Zachariae R, Øster H, Bjerring P, Kragballe K. Effects of psychologic intervention on psoriasis: a preliminary report. *J Am Acad Dermatol*. 1996;34(6):1008-1015. doi:10.1016/S0190-9622(96)90280-7
 27. Ford AR, Siegel M, Bagel J, et al. Dietary recommendations for adults with psoriasis or psoriatic arthritis from the medical board of the National Psoriasis Foundation: a systematic review [published online June 20, 2018]. *JAMA Dermatol*. doi:10.1001/jamadermatol.2018.1412
 28. Boggs MDW. Indigo naturalis extract effective for psoriatic nails. *Healthy Living Magazine*. <http://www.healthylivingmagazine.us/Articles/8290/>. Published 2015. Accessed June 20, 2018.
 29. Vallianou NG, Evangelopoulos A, Schizas N, Kazakis C. Potential anticancer properties and mechanisms of action of curcumin. *Anticancer Res*. 2015;35(2):645-651. <http://www.ncbi.nlm.nih.gov/pubmed/25667441>. Accessed October 19, 2017.
 30. National Psoriasis Foundation. Natural therapies for psoriatic disease. <https://www.psoriasis.org/advance/natural-therapies>. Published 2016. Accessed September 20, 2017.
 31. The People's Pharmacy. Turmeric eases suffering from psoriasis. <https://www.peoplespharmacy.com/2011/10/13/turmeric-eases-suffering-from-psoriasis/>. Published 2011. Accessed September 20, 2017.
 32. Psoriasis Self Management. Benefits of turmeric for psoriasis. <http://www.psoriasisselfmanagement.com/natural-herbs-supplements/benefits-of-turmeric-for-psoriasis/>. Published 2014. Accessed September 20, 2017.
 33. Varma SR, Sivaprakasam TO, Mishra A, Prabhu S, M R, P R. Imiquimod-induced psoriasis-like inflammation in differentiated human keratinocytes: its evaluation using curcumin. *Eur J Pharmacol*. 2017;813:33-41. doi:10.1016/j.ejphar.2017.07.040
 34. Prasad S, Tyagi AK, Aggarwal BB. Recent developments in delivery, bioavailability, absorption and metabolism of curcumin: the golden pigment from golden spice. *Cancer Res Treat*. 2014;46(1):2-18. doi:10.4143/crt.2014.46.1.2
 35. Landis ET, Davis SA, Feldman SR, Taylor S. Complementary and alternative medicine use in dermatology in the United States. *J Altern Complement Med*. 2014;20(5):392-398. doi:10.1089/acm.2013.0327
 36. Bittiner SB, Tucker WF, Cartwright I, Bleehen SS. A double-blind, randomised, placebo-controlled trial of fish oil in psoriasis. *Lancet*. 1988;1(8582):378-380. doi:10.1016/S0140-6736(88)91181-6
 37. Gupta AK, Ellis CN, Tellner DC, Anderson TF, Voorhees JJ. Double-blind, placebo-controlled study to evaluate the efficacy of fish oil and low-dose UVB in the treatment of psoriasis. *Br J Dermatol*. 1989;120(6):801-807. doi:10.1111/j.1365-2133.1989.tb01378.x
 38. Danno K, Sugie N. Combination therapy with low-dose etretinate and eicosapentaenoic acid for psoriasis vulgaris. *J Dermatol*. 1998;25(11):703-705. doi:10.1111/j.1346-8138.1998.tb02487.x
 39. Balbás GM, Regaña MS, Millet PU. Study on the use of omega-3 fatty acids as a therapeutic supplement in treatment of psoriasis. *Clin Cosmet Investig Dermatol*. 2011;4:73-77. doi:10.2147/CCID.S17220
 40. Kristensen S, Schmidt EB, Schlemmer A, Rasmussen C, Johansen MB, Christensen JH. Beneficial effect of n-3 polyunsaturated fatty acids on inflammation and analgesic use in psoriatic arthritis: a randomized, double blind, placebo-controlled trial. *Scand J Rheumatol*. 2018;47(1):27-36. doi:10.1080/03009742.2017.1287304
 41. Søyland E, Funk J, Rajka G, et al. Effect of dietary supplementation with very-long-chain n-3 fatty acids in patients with psoriasis. *N Engl J Med*. 1993;328(25):1812-1816. doi:10.1056/NEJM199306243282504
 42. Strong AMM, Hamill E. The effect of combined fish oil and evening primrose oil (Efamol Marine) on the remission phase of psoriasis: a 7-month double-blind randomized placebo-controlled trial. *J Dermatolog Treat*. 1993;4(1):33-36. doi:10.3109/09546639309088234
 43. Gupta AK, Ellis CN, Goldfarb MT, Hamilton TA, Voorhees JJ. The role of fish oil in psoriasis. A randomized, double-blind, placebo-controlled study to evaluate the effect of fish oil and topical corticosteroid therapy in psoriasis. *Int J Dermatol*. 1990;29(8):591-595. doi:10.1111/j.1365-4362.1990.tb03477.x
 44. Madland TM, Björckjaer T, Brunborg LA, Frøyland L, Berstad A, Brun JG. Subjective improvement in patients with psoriatic arthritis after short-term oral treatment with seal oil. A pilot study with double blind comparison to soy oil. *J Rheumatol*. 2006;33(2):307-310.
 45. Veale DJ, Torley HI, Richards IM, et al. A double-blind placebo controlled trial of Efamol Marine on skin and joint symptoms of psoriatic arthritis. *Br J Rheumatol*. 1994;33(10):954-958. doi:10.1093/rheumatology/33.10.954

46. Bjørneboe A, Smith AK, Bjørneboe GE, Thune PO, Dreven CA. Effect of dietary supplementation with n-3 fatty acids on clinical manifestations of psoriasis. *Br J Dermatol*. 1988;118(1):77-83. doi:10.1111/j.1365-2133.1988.tb01753.x
47. Lassus A, Dahlgren AL, Halpern MJ, Santalahti J, Happonen HP. Effects of dietary supplementation with polyunsaturated ethyl ester lipids (Angiosan) in patients with psoriasis and psoriatic arthritis. *J Int Med Res*. 1990;18(1):68-73. doi:10.1177/030006059001800109
48. Kragballe K, Fogh K. A low-fat diet supplemented with dietary fish oil (Max-EPA) results in improvement of psoriasis and in formation of leukotriene B5. *Acta Derm Venereol*. 1989;69(1):23-28.
49. Kragballe K. Dietary supplementation with a combination of n-3 and n-6 fatty acids (super gamma-oil marine) improves psoriasis. *Acta Derm Venereol*. 1989;69(3):265-268.
50. Ziboh VA, Cohen KA, Ellis CN, et al. Effects of dietary supplementation of fish oil on neutrophil and epidermal fatty acids. Modulation of clinical course of psoriatic subjects. *Arch Dermatol*. 1986;122(11):1277-1282. doi:10.1001/archderm.1986.01660230069013
51. Maurice PD, Allen BR, Barkley AS, Cockbill SR, Stammers J, Bather PC. The effects of dietary supplementation with fish oil in patients with psoriasis. *Br J Dermatol*. 1987;117(5):599-606. doi:10.1111/j.1365-2133.1987.tb07492.x
52. Kojima T, Terano T, Tanabe E, Okamoto S, Tamura Y, Yoshida S. Effect of highly purified eicosapentaenoic acid on psoriasis. *J Am Acad Dermatol*. 1989;21(1):150-151. doi:10.1016/S0190-9622(89)80363-9
53. Kettler AH, Baughn RE, Orengo IF, Black H, Wolf JE Jr. The effect of dietary fish oil supplementation on psoriasis. Improvement in a patient with pustular psoriasis. *J Am Acad Dermatol*. 1988;18(6):1267-1273. doi:10.1016/S0190-9622(88)70133-4
54. Mayser P, Mrowietz U, Arenberger P, et al. Omega-3 fatty acid-based lipid infusion in patients with chronic plaque psoriasis: results of a double-blind, randomized, placebo-controlled, multicenter trial. *J Am Acad Dermatol*. 1998;38(4):539-547. doi:10.1016/S0190-9622(98)70114-8
55. Grimmering F, Mayser P, Papavassilis C, et al. A double-blind, randomized, placebo-controlled trial of n-3 fatty acid based lipid infusion in acute, extended guttate psoriasis. Rapid improvement of clinical manifestations and changes in neutrophil leukotriene profile. *Clin Investig*. 1993;71(8):634-643. doi:10.1007/BF00184491
56. Farber EM, Nall L. Psoriasis: a stress-related disease. *Cutis*. 1993;51(5):322-326.
57. Sounds True. Mindfulness meditation for people with psoriasis. https://www.soundstrue.com/store/mindfulness-meditation-for-people-with-psoriasis.html?__SID=U. Accessed June 21, 2018.