Topical and oral CAM in acne: a review of the empirical evidence and a consideration of its context
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CRD summary
This review examined topical and oral complementary and alternative treatments for acne. The authors concluded that the evidence base was limited; this reflects the poor quality of most of the included studies. The review methodology was poorly reported and the reliability of the review's conclusions is therefore unclear.

Authors' objectives
To examine the efficacy of different methods of complementary and alternative medicine (CAM) in the treatment of acne.

Searching
MEDLINE, EMBASE, AMED, DARE and the Cochrane Library were searched using the reported search terms. The dates of the search were not reported. The reference lists of identified articles were checked. Only studies reported in English were eligible.

Study selection
Study designs of evaluations included in the review
Inclusion criteria were not explicitly reported, although the authors did state that no studies were excluded on methodological grounds. Randomised controlled trials (RCTs), clinical controlled trials and before-and-after studies were included in the review.

Specific interventions included in the review
Studies of topical and oral CAM interventions were eligible for inclusion. Other CAM therapies, such as acupuncture, skin pricking, cupping and blood letting, were excluded from the review. The interventions included in the review were tea tree oil, Nigerian Toto oil and soap, Ocimum gratissimum oil, Ocimum basilicum leaves, Aloe vera, linoleic acid, gluconolactone, glycolic acid, ayurvedic herbal formulations, gugulipid, mask containing several Chinese ingredients, compound oldenlandsis mixture, Chinese-Japanese Kampo formulations, Japanese shark liver and gallbladder extract (isolutrol and benzoyl peroxide), pyroxidine and vitamin A. The comparators included placebo and active interventions.

Participants included in the review
Studies of participants with acne were eligible for inclusion. Limited details on the severity of the participants' acne and participant demographics were provided.

Outcomes assessed in the review
Inclusion criteria were not stated. Most of the studies included in the review reported efficacy as improvements in inflammatory and non-inflammatory lesions; others reported ‘response to treatment’ or incidental symptoms.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not explicitly state the criteria on which validity was assessed. However, from the details provided in the table of included studies and the text, the criteria appeared to have included randomisation, blinding, use of a power calculation, use of a placebo control group, and rigour of the outcome assessment. It was unclear how the validity assessment was performed.
Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the extraction. Efficacy results and methodological details were extracted.

Methods of synthesis
How were the studies combined?
The studies were grouped by the intervention evaluated and combined in a narrative.

How were differences between studies investigated?
Differences in intervention and methodological rigour of the studies were discussed in the narrative synthesis.

Results of the review
Twenty-three studies with more than 1,634 participants were included in the review.

There were methodological flaws in the majority of the included studies.

Tea tree oil.
One RCT compared tea tree oil water-based gel with 5% benzoyl peroxide lotion. The tea tree oil was significantly less effective than benzoyl peroxide in reducing inflammatory lesions, although it produced an improvement over baseline.

Nigerian Toto ointment and soap.
One RCT compared Toto ointment and soap with sulphur ointment. It reported that participants showed good response to Toto ointment or soap, or to both.

Ocimum gratissimum oil and Ocimum basilicum leaves; Aloe vera. Three studies examined products containing Ocimum gratissimum oil or Ocimum basilicum. One reported that three of 16 Ocimum gratissimum oil products produced a significantly greater reduction in lesion count than a comparison treatment of 10% benzoyl peroxide. A second study found that Ocimum gratissimum oil combined with 50% and 100% Aloe vera was superior to placebo. A methodologically poor study found that topical application of Ocimum basilicum leaves were as effective as oral tetracycline combined with topical sulphur.

Linoleic acid.
A double-blind, placebo-controlled, crossover RCT found that linoleic acid reduced follicular size in patients with comedonal acne. However, this was not a study of efficacy on clinical acne. A second study of uncertain design claimed a 75% reduction in inflammatory acne lesions with linoleic acid, but no supporting data were presented.

Gluconolactone and glycolic acid.
A double-blind, placebo-controlled trial found that topical gluconolactone was significantly more effective than placebo in the reduction of both inflammatory and non-inflammatory acne lesions. Its efficacy was comparable to 5% benzoyl peroxide for non-inflammatory lesions, but was significantly lower for inflammatory lesions. It was less irritating to the skin than benzoyl peroxide. An RCT found that 70% glycolic acid was as effective as Jessner’s solution and was better tolerated. An RCT that compared 15% topical glycolic acid combined with azelaic acid with topical tretinoin found a significantly greater reduction in inflammatory lesions after 12 weeks, but no difference in comedones. Two uncontrolled studies reported improvement of acne with self-administered glycolic acid peels, but statistical support for this was not provided.

Ayurvedic herbal formulations.
Three RCTs assessed ayurvedic herbal formulations. One double-blind trial found that topical and oral ayurvedic herbal formulations were effective treatments and suggested that combined treatment was superior to oral treatment alone. A
second trial found one of four Ayurvedic oral therapies to be significantly superior to placebo. The final trial found that two Ayurvedic preparations were superior to a third.

Gugulipid.

A small unblinded RCT compared oral gugulipid with oral tetracycline and found it to be equally effective.

Mask containing several Chinese ingredients.

A poor-quality uncontrolled study reported that a regimen involving a salve and a mask containing several Chinese drugs produced improvement or cure in 83.2% of participants.

Compound oldenlandis mixture.

An incompletely reported study found an oral compound oldenlandis mixture to be superior to pills containing Chinese Angelica and Flavescent Sophora.

Chinese-Japanese Kampo formulations.

One controlled trial compared oral administration of one of three Kampo formulations (Seijo-bofu-to, Jumi-haidoku-to, and Toki-shakuyuka-san) to one of two antibiotics. The Kampo formulations were reported to be as effective as the antibiotics and to be superior in the treatment of incidental symptoms, the clinical significance of which was not clear.

Japanese shark liver and gallbladder extract (isolotrol).

A double-blind RCT comparing isolotrol with benzoyl peroxide was performed, but only before-and after results for each intervention were reported. Isolotrol significantly reduced inflammatory but not non-inflammatory lesions in mild to moderate acne.

Pyroxidine.

An uncontrolled study of oral pyroxidine for premenstrual acne flares found that 72% of participants felt the intervention attenuated symptoms, 19% that it did not, and 9% were unsure. This was a self-assessed retrospective outcome measure.

Vitamin A.

Two poor-quality before-and-after studies examined vitamin A. One of these used 50,000 IU twice daily and found the majority of patients' symptoms were unchanged; the other used 300,000 IU daily and reported that the majority of patients showed a good or excellent response.

Authors' conclusions
Complementary therapies in acne should be viewed in a wider context than that of the very limited empiric evidence base which exists for their use.

CRD commentary
The review question was very broad and inclusion criteria were not explicitly defined. The search was fairly extensive, but was limited to studies reported in English. This, together with the fact that the authors did not explicitly report making any attempts to identify unpublished studies, may mean that some relevant studies were not included in the review. No details of the methods used in the review process were provided. In particular, the authors did not report using methods to minimise reviewer bias and error in the study selection, validity assessment and data extraction processes. The criteria used to assess validity could only be inferred from the data presented in the tables of included studies and in the narrative synthesis.
Limited information on patient demographics and disease severity was presented. Given the very considerable heterogeneity of the interventions examined, the decision to adopt a narrative synthesis was highly appropriate. As a result of the issues discussed above, it is unclear how reliable the results of the review are, although the majority of the included studies were of limited quality and the authors’ conclusions reflected this.

**Implications of the review for practice and research**

Practice: The authors did not state any implications for practice.

Research: The authors stated that rigorously conducted trials should be undertaken to examine the efficacy and adverse event profiles of currently used CAM therapies for acne.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.