Phyto-anti-inflammatory: a systematic review of randomized, placebo-controlled, double-blind trials

Ernst E, Chrubasik S

Authors' objectives
To summarise the evidence from double-blind placebo-controlled randomised trials testing the usefulness of herbal drugs for rheumatic diseases.

Searching
MEDLINE, EMBASE, CISCOM and the Cochrane Library were searched from inception to October 1997. Additional material was located by searching the authors' own files, and reviews and books on phytotherapy and herbalism, and by contacting manufacturers of herbal remedies and experts in the field. Bibliographies of retrieved studies and reviews were also searched for further relevant trials. No language restrictions were reported.

Study selection
Study designs of evaluations included in the review
Randomised placebo-controlled double-blind trials.

Specific interventions included in the review
Orally administered herbal remedies (evening primrose oil, eicosapentaenoic acid, blackcurrant seed oil, borage seed oil, Harpagophytum extract, willow bark extract, feverfew extract, phytodolor, ayurvedic herbal mixture, complex herbal mixture) as an analgesic or anti-inflammatory treatment for rheumatic conditions versus placebo. Trials of non-characterised herbal remedies (where the extract or mixture used was not defined in chemical terms), trials of semisynthetic plant-based drugs, studies of herbal treatment against another active drug, and studies using routes other than oral administration were excluded.

Participants included in the review
People with rheumatic conditions (chronic rheumatoid arthritis, acute lower-back pain, osteoarthritis, spinal osteoarthritis, mixed rheumatic diseases, chronic epicondylitis). No details of the participants' age or sex are given.

Outcomes assessed in the review
All clinical outcomes reported by the studies. Trials that did not include clinical end points were excluded.

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

Assessment of study quality
Validity was assessed using the scoring system of Jadad et al. (see Other Publications of Related Interest no.1). All studies were read in full by both authors, and any discrepancies were settled through discussion.

Data extraction
The data were extracted independently in a standardised predefined fashion by both authors. Any discrepancies were settled through discussion. Data were extracted into the following categories: study details, sample size, illness or disease condition, treatment, main outcome variables and main results.

Methods of synthesis
How were the studies combined?
A narrative synthesis was undertaken with studies grouped by intervention.

How were differences between studies investigated?
Differences between the studies were discussed in the narrative.

Results of the review

Nineteen randomised controlled trials (n=1,194) were included.

The Jadad scores ranged from 3 to 5.

Evening primrose oil: one 12-month study (n=49) showed concomitant non-steroidal anti-inflammatory drugs (NSAIDs) could be reduced significantly in both experimental groups (540 mg gamma-linolenic acid/day or 240 mg eicosapentaenoic acid plus 450 mg gamma-linolenic acid/day), compared to placebo after 12 months, although clinical symptoms remained essentially unchanged in all groups.

Blackcurrant seed oil: one 24-week study (n=34) showed objective signs of a reduction in disease activity on active medication, but the overall clinical response was no better than placebo. No adverse effects were noted but many patients withdrew because they disliked taking 15 capsules of blackcurrant seed oil per day.

Borage seed oil: two 6-month trials (n=93) were included. One showed clinically-relevant and statistically-significant improvements in measured signs and symptoms compared to placebo, whilst the other found no significant differences in relation to physicians' and patients' assessments, but did find significant reductions in subjective and objective signs and symptoms of disease activity. The first trial reported that borage seed oil was well tolerated and adverse effects were 'negligible'.

Harpagophytum procumbens: four studies (n=454) were included. One study in people with acute lower-back pain found no statistically-significant difference between groups for the main outcome measure of using less analgesics, but secondary end points favoured the active medication and at the end of the trial period there were more pain-free patients in the active group (p=0.008). Another trial in people with acute lower-back pain also found significantly more pain-free patients in the active treatment group (p=0.027), with subgroup analyses suggesting that the effect was confined to patients with more severe radiating pain accompanied by neurologic deficits. Possible adverse events included mild and infrequent gastrointestinal symptoms.

A trial in people with osteoarthritis found a statistically-significant decrease in the severity of pain in the active group, with improvements more frequent in moderate than severe cases. Another trial in people with osteoarthritis found a significant drop in pain intensity and a significant increase in spinal and coxofemoral mobility in the treated group. No adverse effects were observed.

Willow bark extract: one study (n=78) in people with osteoarthritis found a statistically-significant analgesic effect in the active, compared with placebo group, using the WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) pain index. A pilot study reported similar results.

Feverfew: one study (n=41) in female patients with rheumatoid arthritis showed a significant difference between active and placebo groups in terms of grip strength, but not in joint stiffness, pain or articular index.

Phytodolor (herbal mixture): six studies (n=300) were included. One trial in people with at least one rheumatological diagnosis found a substantial and statistically-significant reduction in conventional drug dose was achieved in the active group, while maintaining the same clinical status as in the control group. In another study in people with rheumatic pain, there was a significant reduction in pain in the active groups compared with the placebo group. There was no significant difference in outcome between different doses of the active treatment. One trial in people with rheumatic pain found both phytodolor and piroxicam (a NSAID) reduced pain significantly compared with placebo. Another trial versus diclofenac (another NSAID) and placebo in people with epicondylitis produced a similar result, and reported that treatment with the herbal medicine was not associated with adverse effects. A trial in people with osteoarthritis showed a significant improvement in grip strength in the active group compared with the placebo group.
The sixth trial showed that patients with rheumatic pain needed significantly less rescue medication when treated with phytodolor than when treated with placebo.

Ayurvedic herbal mixture (Withania somnifera, Boswellia serrata, Curcuma longa): one trial (n=42) in people with osteoarthritis found the herbal mixture to be superior to placebo in terms of pain severity and disability score, but did not improve morning stiffness.

Herbal mixture (white willow bark extract, black cohosh, sarsaparilla, guaiacum resin, poplar bark): one trial (n=82) found disability score to be significantly better in the active group than in the placebo group. There was no significant difference between groups in analgesic consumption.

**Authors’ conclusions**
The authors’ systematic review suggests that several herbal remedies have potential in alleviating the pain of rheumatic diseases. This area is still grossly under-researched and firm conclusions are, therefore, not possible. The authors hope that the present boom in medical herbalism in the United States will contribute to generating the research that is so badly needed to fill the obvious gaps in present knowledge.

**CRD commentary**
The research question was clear, and the inclusion criteria were clearly stated and were relevant to the question. The search strategy was comprehensive and unpublished data has been sought. The validity assessment was undertaken using a validated scale and the results were reported, although not incorporated into the synthesis. A narrative synthesis was appropriate given the diversity in interventions and outcome measures, but more could have been done to present the results clearly, e.g. subheadings and summaries of the numbers of studies included. Details of the studies were reported, but the results for treated and untreated groups were not reported separately. There was no real pooling of evidence from multiple studies relating to a single herbal remedy.

The authors’ conclusions follow from the results but, unlike the results, do not address the efficacy of any individual remedy.

**Implications of the review for practice and research**
Practice: The authors state that for mild-to-moderate chronic pain, phyto-anti-inflammatory drugs could be tried with, or even as a replacement for NSAIDS, with a view to minimising NSAID use and adverse effects.

Research: The authors state that research is badly needed to fill the obvious gaps in present knowledge.

**Bibliographic details**

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10680191

**Other publications of related interest**

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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.