Evidence of effectiveness of herbal medicinal products in the treatment of arthritis. Part 1: Osteoarthritis

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CRD summary
This review assessed the effectiveness of a range of herbal medicinal products in treating osteoarthritis and concluded that despite some evidence, no definitive conclusions on effectiveness could be drawn. Given the many treatments and outcomes considered in the review, this conclusion appears justified and is likely to be reliable.

Authors’ objectives
To assess the effectiveness of herbal medicinal products in treating osteoarthritis.

Searching
Ten electronic databases, which included three Cochrane registers, MEDLINE, EMBASE, CISCOM, AMED, CINAHL, Dissertation Abstracts and BIDS-ISI, were searched from inception to June 2007. No language restrictions were applied. Search terms were specified.

Study selection
Randomised controlled trials (RCTs) were eligible for inclusion if patients had been diagnosed for osteoarthritis according to American College of Rheumatology criteria and the study compared any form of herbal intervention with an inert or active control. To be included, it appeared that trials had to report (as primary outcomes) on either changes in clinical or self-reported measures of effectiveness, or adverse effects. If herbal therapy was used in conjunction with other treatments or non-herbal substances, they were included if the intervention was both consistent among all groups and quantifiable. Homeopathy, aromatherapy and synthetic preparations were excluded, as were papers where the herbal components of the intervention could not be identified.

Within treatments for which meta-analyses were reported, the Chinese herbal mixture SK1306X was compared to either placebo or diclofenac (doses ranged from 200 to 600mg/day), topical capsaicin was compared to placebo (preparations ranged from 0.025% weight/weight (w/w) to 0.075% w/w) and avocado-soybean unsaponifiables were compared to placebo (doses ranged from 300 to 600mg/day). Where reported, product preparations included aqueous extract, ethanolic extract, acetone extract, butanol extract and tincture; drug/extract ratios and doses varied substantially. Outcomes included changes in Western Ontario and McMaster Universities Arthritis Index (WOMAC) total and stiffness score, changes in pain according the visual analogue scale (VAS), patient global assessment and Lequesne index.

Three reviewers independently assessed whether the articles were suitable for inclusion.

Assessment of study quality
Two reviewers independently assessed trial quality with methods recommended by the Cochrane Collaboration in terms of sequence generation, allocation concealment, blinding, missing data, selective reporting and other sources of bias. Each paper was rated either as meeting, not meeting or unclear with regard to each criterion. Papers that met more criteria were judged to have a lower risk of bias.

Disagreements between assessors were resolved by consensus and arbitration.

Data extraction
Two reviewers independently extracted primary outcomes, which included changes in assessed clinical and self-reported effectiveness, and adverse reactions. Secondary outcomes included general well being and satisfaction indicators. Where studies were comparable, odds ratios (ORs) and relative risks (RRs) were calculated for dichotomous outcomes and mean differences (MDs) and 95% confidence intervals (CIs) for continuous outcomes. Only pre-
crossover results were included from crossover designs in order to be comparable with parallel designs. Disagreements between assessors were resolved by consensus and arbitration.

**Methods of synthesis**

For studies that used the same outcome measures and comparators, a meta-analysis was used to pool the effect sizes; otherwise, a narrative synthesis was used. Heterogeneity was investigated using Χ² and I² statistics and where it was identified, results were either pooled using a random-effects (rather than fixed-effect) model or were not pooled (if I² values were >80%) and described separately.

**Results of the review**

Thirty-five studies were included in the review. Studies evaluated 22 different types of herbal medicinal product, 17 of which were discussed within the paper. Twenty-six of the 35 studies used a parallel design and eight used a crossover design. The review stated that results evaluating trial quality were presented in tabulated form, but this table was missing. A written summary stated that six of the 35 studies met all criteria; other studies were variable.

**Statistically significant results based on meta-analysis of more than one trial:**

SK1306X: two trials (n=388 participants) reported a statistically significant reduction in pain using the visual analogue scale (MD -17.36, 95% CI -22.57 to -12.15) and improved physical function using the Lequesne index (MD -2.73, 95% CI -3.71 to -1.74).

Topical capsaicin: a statistically significant reduction in pain scores using the visual analogue scale was reported four weeks after intervention (MD -8.26, 95% CI -14.88 to -1.65; two studies, n=179 participants).

Avocado-soybean unsaponifiables: within two studies (n=326 participants) pain scores using visual analogue scale showed a statistically significant difference after three months favouring treatment (MD -10.79, 95% CI -14.91 to -6.66).

**Statistically significant results based on a single trial:**

Ginger extract: improvements were reported in terms of WOMAC stiffness, WOMAC total scores, pain after walking 50 feet and patient global assessment.

*Boswellia-Curcuma* mixture: improvements were reported in minutes of pain-free walking time after two and three months.

*Boswellia serrata*: improvements were reported in pain, loss of movement, and swelling.

Reumalex: improvements were reported in AIMS 2 pain scores.

Avocado-soybean unsaponifiables: improvements were reported in pain scores after six months.

Statistically significant findings favouring the following herbal medicinal products were also reported for cat's claw extract, comfrey extract and stinging nettle leaf. Full results were available in the paper.

No serious side effects were reported with any herbal intervention.

**Authors' conclusions**

Despite some evidence, no definitive conclusions on the effectiveness of herbal medicinal products could be drawn.

**CRD commentary**

This review addressed a broad question with relevant inclusion and exclusion criteria. A range of databases was searched. No language restrictions were applied. Search terms were reported. It appeared that no search for unpublished papers was conducted, which raised the possibility of publication bias. Trial validity assessment was conducted. The
review process was conducted with sufficient attempts to minimise error and bias. Only RCTs were eligible for inclusion. Other trial characteristics and results of the validity assessment were not reported in a clear and systematic way. Given the wide range of interventions considered, the choice of (primarily) a narrative approach seemed justified. Where meta-analyses were used, only two studies were pooled for each herbal medicinal product and it was not clear how the results of the heterogeneity analysis were applied.

Given the wide range of treatments and outcomes included, the conclusion appears justified and is likely to be reliable.

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

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

**Research:** The authors stated that further clinical trials were necessary before herbal medicinal products could be adopted in osteoarthritis treatment guidelines.

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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.