Symptomatic efficacy of avocado-soybean unsaponifiables (ASU) in osteoarthritis (OA) patients: a meta-analysis of randomized controlled trials

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CRD summary
This generally well-conducted review investigated the efficacy of avocado-soybean unsaponifiables (ASU) in the treatment of osteoarthritis (OA), compared with a double-blinded placebo. The authors concluded that ASU therapy for OA reduces pain and increases the number of patients responding to treatment. The authors’ conclusions reflected the evidence presented but should be interpreted with a degree of caution, given the small study sizes, the small to moderate effect sizes identified, and that all included studies were industry-funded.

Authors’ objectives
To assess the efficacy of avocado-soybean unsaponifiables (ASU) in the treatment of osteoarthritis (OA).

Searching
The following databases were searched without language restriction from inception to January/February 2007: MEDLINE, EMBASE, CINAHL, BIOSIS Previews, Web of Science, SciFinder, Scopus and the Cochrane Library. The search terms were reported. The references of retrieved articles were screened. The conference proceedings of societies including OsteoArthritis Research Society International, European League Against Rheumatism and the American College of Rheumatology were also searched for the previous two years.

Study selection
Randomised controlled trials (RCTs) that compared ASUs to a double-blinded placebo in patients with clinical or radiographic evidence of OA were eligible for inclusion. Studies that included patients with non-OA joint pain, rheumatoid arthritis (RA) and pain due to surgery or injury were excluded. Also excluded were studies with mixed groups including both OA and RA patients if the subgroup data for OA were unavailable. The primary review outcome measure was pain reduction. Additional outcomes were measures in rheumatology (OMER) ACT-III relevant outcomes, the Lequesne index and numbers of patients responding to treatment.

Included trials had a mean duration of 6 months (ranging from 3 to 12 months). The mean age of participants was 64.1, 64% were female, 41.4% had hip OA and 58.6% had knee OA.

Two reviewers assessed and cross-checked studies for inclusion. The authors did not state whether assessment was independent. It appeared that disagreements were resolved by discussion.

Assessment of study quality
The quality of studies was assessed using the Jadad scale, a 5-point scale evaluating randomisation, blinding, withdrawal, and allocation concealment.

Two reviewers performed the validity assessment. The authors did not state whether assessment was independent or how disagreements were resolved.

Data extraction
Data on the point estimates (mean pain, mean body mass index, mean Kellgren-Lawrence (KL) score, mean Lequesne index score, and the number of responders in each group) were extracted in standard forms. Intention-to-treat data were extracted where possible.

Two reviewers independently extracted the data from studies, with any disagreements resolved by discussion.
Methods of synthesis
The studies were combined in meta-analyses using a random-effects model. Standardised mean differences (SMDs) for continuous outcomes, with 95% confidence intervals (CIs), were calculated. The magnitude of effect size (ES) was assessed using the SMDs. Pooled odds ratios (ORs) for dichotomous data, with 95% CIs, were also estimated. The number needed to treat (NNT) with 95% CIs was calculated based on the combined OR. It was unclear whether the studies were weighted in meta-analyses. Statistical heterogeneity was investigated using $\chi^2$ & $I^2$ statistics and meta-regressions.

Results of the review
Four RCTs (n= 664) were included in meta-analyses. All studies were generally judged as high quality, with a weighted-average Jadad score of 4.5.

When the studies were pooled, ASU was significantly associated with a reduction in pain (ES 0.39, 95% CI: 0.01, 0.76, p=0.04; four RCTs), a reduction in the Lequesne Index (ES 0.45, 95% CI: 0.21, 0.70, p=0.0003; four RCTs), an increase in the number of patients responding to treatment (OR 2.19, 95% CI: 1.24, 3.86, p=0.007; NNT 6, 95% CI: 4, 21; four RCTs). Based on the evaluation of the effect size, the effect was clinically small to moderate for outcomes of pain and the Lequesne index.

Subgroup analyses showed that at 6 months there was a significant difference between knee OA patients who experienced a large pain reduction effect (ES 0.99, 95% CI: 0.54, 1.44; four RCTs) and hip OA patients who did not (ES -0.44, 95% CI: -1.05, 0.17; four RCTs).

Statistically significant heterogeneity was observed in the outcomes of pain ($p<0.001$, $I^2= 83.5\%$), the Lequesne Index ($p=0.05$, $I^2= 61\%$) and the number of responders to treatment ($p=0.02$, $I^2= 68.9\%$).

Authors’ conclusions
ASU therapy for OA was associated with a reduction in pain and the Lequesne Index, and an increase in the number of patients responding to treatment.

CRD commentary
The inclusion criteria of the review were clear. Several relevant databases were searched. Efforts were made to find published and unpublished studies without language restriction, thereby minimising the potential for both publication and language biases. Steps were taken to minimise bias by having more than one reviewer undertake the study selection, validity assessment and data extraction, but it was unclear whether assessment was independent in some processes. Adequate details of the primary studies were provided. Relevant criteria were used to examine the study quality. Appropriate statistical methods were used to pool the results, but it was unclear whether the studies were weighted in meta-analyses. Statistical heterogeneity was explored as well as assessed and, although significant heterogeneity was found in the outcomes, the studies generally showed the same direction of treatment effect. This review was generally well conducted in most respects and the authors’ conclusions reflect the evidence presented. However, a degree of caution might be required in interpreting these conclusions, given the small study sizes in the review, the small to moderate effect sizes identified, and that all included studies were industry-funded.

Implications of the review for practice and research
Practice: The authors stated that OA patients can be recommended to give ASU therapy for 3 months. The health professional should be aware that there could be a better chance of treatment success in patients with knee OA than those with hip OA.

Research: The authors did not state any implications for research.

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