Horse-chestnut seed extract for chronic venous insufficiency: a criteria-based systematic review

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Authors' objectives
To assess the evidence for or against horse-chestnut seed extract (HCSE) as a symptomatic treatment of chronic venous insufficiency (CVI).

Searching
MEDLINE, EMBASE, BIOSIS Previews, CISCOM, and the Cochrane Library were searched for relevant studies (all from the date they started until December 1996). The search terms were "horse chestnut," "Aesculus hippocastanum," "escin," and "Rosskastanie" (German for "horse chestnut"). In addition all manufacturers of HCSE preparations were asked to contribute published and unpublished materials and the authors’ own extensive files were scanned. Bibliographies of all studies retrieved were searched for further trials. There were no restrictions on the language of publication.

Study selection
Study designs of evaluations included in the review
Double-blind, randomised controlled trials (RCTs) of oral HCSE. Eight of the included studies were placebo controlled and five compared HCSE with another medication. Nine used a parallel group design and 5 used a cross-over design. Duration of the studies ranged from 4 weeks to 20 weeks.

Specific interventions included in the review
Oral horse-chestnut seed extract (HCSE) versus placebo or another medication (not stated). Participants in the included studies took one to two capsules a day.

Participants included in the review
People with chronic venous insufficiency. Most included studies used the classification system by Widmer and Stahelin (see Other Publications of Related interest no.1) for categorising patients and defining inclusion criteria (stage I: ankle oedema without tropic changes; stage II: oedema, hyper-pigmented or depigmented areas, indurations; stage III: open or healed leg ulcer).

Outcomes assessed in the review
Leg volume, capillary filtration coefficient, CVI-related symptoms, leg circumference at ankle and calf, and adverse effects.

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
A scoring system was used to measure the likelihood of bias which was adapted from Jadad et al (see Other Publications of Related Interest no.2). Items included randomisation and method of allocation concealment, double blinding and method of double blinding, description of withdrawals and drop-outs. Articles scoring below 3 (out of a maximum of 5 points) on the quality scale were excluded. The methodological quality of each trial was independently assessed by the 2 reviewers. Disagreements were resolved by discussion.

Data extraction
Data were collected on trial design, outcomes, compliance and treatment period. Identifiers were removed from all
publications before assessment. Data were extracted in a standardised, predefined manner. Trial outcomes of each trial were independently assessed by the 2 reviewers.

**Methods of synthesis**
How were the studies combined?
Narrative summary, as meta-analysis was deemed inappropriate due to the variations in devices used for assessment and insufficient reporting of data.

How were differences between studies investigated?
Studies were grouped by comparison group (placebo or another medication).

**Results of the review**
Thirteen RCTs with a total of 1083 participants.

The quality scores ranged from 3-5 points.

The superiority of HCSE was suggested by all placebo-controlled studies. The use of HCSE was associated with a decrease of the lower-leg volume and a reduction in leg circumference at the calf and ankle. Symptoms such as leg pain, pruritus, and a feeling of fatigue and tenseness were reduced. Five comparative trials against the reference medication indicated that HCSE and O-(beta-hydroxyethyl)-rutosides were equally effective. One trial suggested a therapeutic equivalence of HCSE and compression therapy.

Adverse effects.

Eight studies reported on adverse drug reactions, which included gastrointestinal tract symptoms, nausea, headache and pruritus. The frequency of adverse reactions ranged from 0.9% to 3.0%. In three studies the frequency of adverse events was not significantly different from that of placebo.

**Authors' conclusions**
These data imply that HCSE is superior to placebo and as effective as reference medications in alleviating the objective signs and subjective symptoms of CVI. Thus, HCSE represents a treatment option for CVI that is worth considering.

**CRD commentary**
This is a well-written and well-conducted systematic review. The study question was clear, and inclusion criteria are provided. The literature search was extensive and an attempt was made to locate unpublished studies. The authors do discuss the possibility, however, that some trials may have been missed, particularly those with negative results. Assessment of the validity of the studies was undertaken, and data were independently extracted by two reviewers. A meta-analysis was not undertaken and this was appropriate. The conclusions of the author appear to follow on from the results of the review.

**Implications of the review for practice and research**
The authors state that more rigorous RCTs are required to verify the usefulness of the treatment, especially for long-term use and as an adjunct to compression therapy.

**Bibliographic details**
Original Paper URL
http://archderm.ama-assn.org

Other publications of related interest

This additional published commentary may also be of interest. Melchart D. Horse-chestnut seed extract for chronic venous insufficiency: a systematic review. FACT 1999;4:128-9.

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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.