Isoflavone supplements containing predominantly genistein reduce hot flash symptoms: a critical review of published studies
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CRD summary
The authors concluded that isoflavone supplements derived from soy and providing at least 15 mg genistein per day can be effective in reducing the frequency and severity of hot flushes in postmenopausal women. Inadequate reporting of review methods, study quality and results data mean that the authors’ conclusion might not be reliable.

Authors' objectives
To evaluate the efficacy of soy isoflavone extracts for the relief of hot flashes in generally healthy menopausal women, and to examine the effects of different levels of genistein.

Searching
PubMed, Chemical Abstracts and Nerac's database were searched for peer-reviewed published studies. Some search terms were reported but the search dates were not.

Study selection
Study designs of evaluations included in the review
Controlled studies were eligible for inclusion. All of the included studies were randomised controlled trials (RCTs); some were parallel-group and others were crossover RCTs.

Specific interventions included in the review
Studies that compared soy-derived semipurified isoflavone extracts used as dietary supplements with placebo or control were eligible for inclusion. The studies had to use isoflavone alone and not in combination with other herbal extracts. Studies that evaluated dietary soy sources of isoflavone or red clover isoflavone extracts were excluded. The total aglycone isoflavone dose evaluated in the included studies ranged from 30 to 114 mg/day. In the review, studies were classified as low-genistein-containing (less than 15 mg genistein per treatment; actual range: 5 to 9 mg) and high-genistein-containing (at least 15 mg genistein per treatment; actual range: 15 to 75 mg) soy isoflavone supplements. The overall, average total isoflavone treatments for the low and high genistein groups were 56.8 mg and 64.8 mg, respectively. The duration of the included studies ranged from 6 to 52 weeks, with most studies ranging from 12 to 24 weeks.

Participants included in the review
Studies of otherwise healthy women receiving treatment for hot flashes (either alone or in combination with other menopausal symptoms) in the early postmenopausal period were eligible for inclusion. Studies of women with a surgically induced menopause or cancer patients currently receiving oestrogen-like treatments were excluded. All of the included studies defined postmenopausal status as the absence of menses for at least 6 months. The mean age of the participants was 52.2 years and the mean number of hot flashes per day was reported to range from 4 to 10 (based on 8 studies).

Outcomes assessed in the review
Inclusion criteria were not specified in terms of the outcomes. The primary review outcome was the reduction in hot flash occurrence. Three studies that used a menopausal index to measure overall menopausal symptoms but did not apparently report the occurrence of hot flashes were also included.

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 state that they assessed validity.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Studies were classified as positive (p<0.05) or no treatment effect (p>0.05). To allow comparisons between studies, each evaluated isoflavone extract was expressed as milligram aglycone isoflavone equivalents. Where the exact composition and amount of isoflavone was not clear, the original authors were contacted for this information. In the absence of relevant information, the exact composition of the isoflavone was obtained either from public information or independent analysis of commercially available products. In addition, the total genistein composition of each extract was calculated.

Methods of synthesis
How were the studies combined?
The studies were stratified by the dose of genistein used and combined in a narrative.

How were differences between studies investigated?
Some differences between the studies were apparent from the tables. The distributions of total isoflavone dose were compared between the low-dose and high-dose genistein studies.

Results of the review
Eleven RCTs (n=745) were included: 9 parallel-group and 2 crossover RCTs.

The authors stated that they believed the studies to be of generally good quality, but no evidence was presented to support this statement.

All 5 high-dose genistein studies reported a statistically significant decrease in hot flashes in the isoflavone treatment group. Only 1 of the 6 low-dose genistein studies reported a statistically significant decrease in hot flashes in the isoflavone treatment group.

Authors' conclusions
The authors’ conclusion appears to be that isoflavone supplements derived from soy and providing at least 15 mg genistein per day can be effective in reducing the frequency and severity of hot flushes in postmenopausal women. The specific composition of isoflavone supplements should be considered in future studies.

CRD commentary
The review addressed a clear question that was defined in terms of the participants and intervention; inclusion criteria were broad for the study design and not specified for the outcomes. The review included studies that did not assess the primary outcome; this lack of specificity could lead to reporting error. Three databases were searched but the inclusion of only published studies raises the possibility of publication bias. In addition, since it was unclear whether any language restrictions had been applied, the potential for language bias could not be assessed. The methods used to select the studies and extract the data were not described, so it is not known whether any efforts were made to reduce reviewer errors and bias. Study validity was not assessed, therefore the results from these studies and any synthesis might not be reliable. Given that results data were not reported, it is not possible to verify the reported statistical significance of results from individual studies.

Three of the four authors are employees of Archer Daniels Midlands Company, a manufacturer of soy.
Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that future evaluations of isoflavone supplements should fully describe the source, report the composition of the supplements in a standardised manner, and take account of the apparent minimum genistein content (10 to 15 mg) needed for the effect found in this review. Further research is required to evaluate the effects of isoflavones containing at least 15 mg genistein on nonvasomotor menopausal symptoms.

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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.