Soy isoflavone intake lowers serum LDL cholesterol: a meta-analysis of 8 randomized controlled trials in humans
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CRD summary
This review found that the consumption of soy protein with a high isoflavone content significantly decreases serum low-density lipoprotein cholesterol concentration compared with the same soy protein intake with a low isoflavone content, in people with normal and elevated levels of cholesterol. Given the lack of a quality assessment, poor reporting of the methods and the limited search, the reliability of the conclusions cannot be assessed.

Authors' objectives
To evaluate the effects of isoflavones (IFs) on blood low-density lipoprotein (LDL) cholesterol concentration, independently of soy protein level.

Searching
PubMed was searched from its inception to 2003; the search terms were reported. In addition, the reference lists of relevant articles were checked. It was not reported whether any language restrictions were applied.

Study selection
Study designs of evaluations included in the review
Only randomised controlled trials (RCTs) with either a crossover or parallel design were eligible for inclusion in the review.

Specific interventions included in the review
Studies that included the ingestion of soy protein for 1 to 3 months, and had comparable groups with at least two different levels of IF (high and low) for the same soy protein intake level, were eligible. All of the studies included in the review used soy protein isolate with intakes ranging from 25 to 100 g/day, with measured IF intakes ranging from 3 to 132 mg/day. The mean low IF intake was 6 mg/day and the mean high IF intake was 96 mg/day.

Participants included in the review
Studies with human participants were eligible for inclusion; no further details were provided. Half of the included studies involved postmenopausal women only. The mean ages of the participants ranged from 26.3 to 62.7 years, the mean body mass index ranged from 22.8 to 26.6 kg/m2, and the mean baseline serum LDL-cholesterol concentrations ranged from 2.32 to 4.81 mmol/L. Participants in about half of the studies were mildly or moderately hypercholesterolaemic.

Outcomes assessed in the review
Studies that provided blood cholesterol and end point LDL-cholesterol concentrations were eligible for inclusion. Half of the eligible studies reported serum LDL cholesterol concentrations and half reported values in plasma.

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.

Where studies contained treatments with different levels of IFs, data from the highest and lowest IF groups were selected for analysis and the data from the longest follow-up point were extracted. The mean and standard deviation of blood LDL cholesterol concentrations were extracted from each study. Two studies divided their participant populations into two groups based on baseline blood LDL cholesterol levels and were extracted accordingly; each study contributed two comparisons to the review. The authors stated that all results are reported in terms of serum concentrations.

**Methods of synthesis**

How were the studies combined?

Ten pair-wise comparisons from the eight included RCTs were included in the meta-analysis. The weighted mean difference in LDL cholesterol levels when comparing a high IF diet and a low IF diet was calculated, along with its 95% confidence interval (CI), using random-effects and fixed-effect models.

How were differences between studies investigated?

Subgroup analyses were performed. The studies were categorised into hypercholesterolaemic and normocholesterolaemic, using a baseline LDL cholesterol cut-off value of 4.14 mmol/L or total cholesterol greater than 6.2 mmol/L to define hypercholesterolaemia. The chi-squared statistic was also calculated, with a P-value of less than 0.1 indicating the presence of significant heterogeneity.

**Results of the review**

Eight RCTs (n=441) were included in the review.

The overall weighted mean difference suggested that the LDL cholesterol of participants consuming high IF diets decreased by 0.15 mmol/L (95% CI: 0.08, 0.23) in comparison with participants consuming the same level of soy protein but with a low IF content (P<0.0001). The fixed-effect and random-effects models gave identical results and no significant heterogeneity was identified (P=0.74). Similar decreases in LDL cholesterol levels were found in the studies with normocholesterolaemic and hypercholesterolaemic participants; no significant heterogeneity was identified in these subgroup analyses.

**Authors' conclusions**

In hypercholesterolaemic and normocholesterolaemic individuals, the consumption of soy protein with a high IF content significantly decreases serum LDL cholesterol concentration in comparison with the same soy protein intake with a low IF content.

**CRD commentary**

The review question was clear in terms of the interventions, outcomes and study designs that were eligible for inclusion in the review. A limited search was conducted to identify primary studies for inclusion, no attempt was made to locate unpublished studies, and the presence of publication bias was not addressed. It was also not reported whether any language restrictions were employed, therefore it is possible that language bias might have been present. The methods of study selection and data extraction were not reported, so it was not clear whether any attempts were made to reduce reviewer error or bias. Although only RCTs were eligible for inclusion in the review, no quality assessment of the included studies was performed. Meta-analyses were conducted but, although no significant statistical heterogeneity was identified, only limited details of the included studies were presented; this limits the ability to assess the appropriateness of the meta-analysis. Given the lack of a quality assessment, poor reporting of review methods and the limited search, the reliability of the authors' conclusions cannot be assessed.

**Implications of the review for practice and research**
Practice: The authors did not state any implications for practice.

Research: The authors stated that further studies are warranted to confirm which components of soy-related IFs play a role in lowering blood cholesterol.

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