The effect of plant sterols or stanols on lipid parameters in patients with type 2 diabetes: a meta-analysis

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CRD summary
The review evaluated the effectiveness of the prophylactic use of plant sterols or stanols in patients with type 2 diabetes. It found that foods fortified with plant sterols/stanols significantly reduced both plasma cholesterol and low-density lipoprotein cholesterol. Given limitations in the reporting of the review process, and the limited evidence available, the reliability of the authors’ conclusions is unclear.

Authors’ objectives
To evaluate the effectiveness of the prophylactic use of plant sterols or stanols on plasma lipids in patients with type 2 diabetes.

Searching
MEDLINE, EMBASE, CINAHL, Web of Science, the Cochrane Library and the Natural Medicines Comprehensive Database were searched from inception to May 2008. Search terms were reported. Bibliographies of each retrieved article were handsearched.

Study selection
Randomised controlled trials (RCTs), including both parallel and cross-over trials, evaluating the use of plant sterols or stanols in diabetic patients, were eligible for inclusion. Included trials had to report efficacy data enabling the calculation of change from baseline in specific lipid endpoints. The four eligible primary lipid endpoint outcomes were total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, or triglycerides.

The interventions in the included trial were sterol/stanol-fortified granola bars or sterol/stanol-fortified margarines, with dosages ranging from 1.6g/day to 3g/day. Some of the interventions in the included trials had concurrent dietary modifications. Details of the placebos used and the individual plant sterols/stanols used were provided. Mean follow-up in the included trials ranged from three to 21 weeks; there was a four week washout period in the majority of the included cross-over trials. Details of the baseline levels of all four plasma lipids were provided for the intervention and control group patients in all the included trials, but no data was provided on the age or sex of the patients.

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, but certain relevant criteria were considered: duration of follow-up; study design; details of the intervention and placebo; concurrent dietary modification; and blinding.

Data extraction
Two reviewers independently extracted weighted mean differences (WMDs) and 95% confidence intervals (CI). Disagreements were resolved through discussion or by a third reviewer.

Methods of synthesis
Weighted mean differences were pooled using a random-effects model (DerSimonian and Laird). Between trial heterogeneity was determined using $I^2$ tests. Publication bias was assessed using the Egger weighted regression test and visually using funnel plots.

Results of the review
Five relevant RCTs (n=148 patients) were identified, involving seven different groups. All of the RCTs were double blind and four were cross-over studies. The interventions included sterol/stanol-fortified margarines in four RCTs and sterol/stanol-fortified granola bars in the remaining RCT. Two RCTs used rapeseed (canola) oil margarine as the
placebo without the sitostanol ester present in the intervention margarine.

Fortification with plant sterols/stanols significantly reduced plasma cholesterol (WMD -10.27mg/dL, 95% CI -17.56 to -2.98) and plasma low-density lipoprotein cholesterol (WMD -12.21mg/dL, 95% CI -17.91 to -6.52), with no significant effect on plasma triglycerides and a non-significant trend towards increasing plasma high-density lipoprotein cholesterol level. There was little statistical heterogeneity for the analyses ($I^2<23\%$). Egger’s test showed significant publication bias for the analysis for high-density lipoprotein cholesterol ($p=0.01$).

**Authors' conclusions**
In patients with type 2 diabetes, plant sterols/stanols significantly improved cholesterol and low-density lipoprotein cholesterol, with a trend towards improved high-density lipoprotein cholesterol,

**CRD commentary**
The review addressed a well-defined question in terms of participants, interventions, study design and relevant outcomes. Relevant databases were searched and it appeared that unpublished studies were considered. It was not specified whether the search included trials published in languages other than English. Publication bias was assessed. No formal assessment of study validity was reported, which made it difficult to assess the reliability of the included data. Although data extraction was carried out with efforts to reduce error and bias, it was not clear whether this process applied to other aspects of the review process. Some relevant trial details were reported, but there were no details were given of the age or sex of patients, verification of the status relevant to diabetes of the patients, sample sizes of individual trials, or loss to follow-up. Statistical heterogeneity was assessed and there was evidence for heterogeneity with one outcome. The statistical method used for the meta-analysis of the RCTs seemed appropriate. A sensitivity analysis was not carried out. In view of some potential limitations arising from the reporting of the review process, uncertainties about the quality of included trials and the small number of patients in the included trials, the extent to which the authors’ conclusions are reliable is unclear.

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

**Research:** The authors identified a need for long-term studies of plant sterols/stanols to evaluate their impact on terminal clinical outcomes.

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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.