

Issue 102

In a nutshell

There is interesting epidemiological, laboratory and some clinical evidence that phytoestrogens can be beneficial in preventing heart disease, for example through improvements to lipid profile and arterial compliance.

However, the evidence is not definitive at this point and further clinical trials are needed .

Phytoestrogens and heart disease

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NUTRITION RESEARCH REVIEW

Study one: Dietary soy and cardiovascular status

The effects of dietary soy on the cardiovascular system are complex, according to results from a recent Australian study.

Subjects: 213 healthy subjects aged between 50 and 75 years old (108 men and 105 postmenopausal women).

Method: Randomized, controlled, double-blind trial in which subjects were given either soy protein isolate (40 g soy protein, 118 mg isoflavones) or casein for 3 months.

Results: The soy treated group had a mildly greater fall in both diastolic and systolic blood pressure than the casein group (systolic 7.5 vs 3.6 mm Hg, diastolic 4.3 vs 1.9 mm Hg both $p < 0.05$).

There was a significantly greater improvement in overall lipid profile in the soy compared with casein group., although no significant difference between groups was observed in relation to the individual components HDL and LDL cholesterol levels.

There were no benefits seen in relation to peripheral arterial resistance and endothelial function.

Reference: Teede HJ et al. Dietary soy has both beneficial and potentially adverse cardiovascular effects: a placebo-controlled study in men and postmenopausal women. *J Clin Endocrinol Metab* 2001;86:3053-60

Study two: Soybean tablet and cardiovascular outcome

There was no benefit on lipoprotein profile or endothelial function from a soy tablet supplement, according to another Australian study.

Subjects: 20 healthy post-menopausal women.

Method: Randomized, placebo-controlled, double-blind crossover trial. Active treatment involved subjects taking a soybean tablet containing 80 mg/day of isoflavone for 8 weeks (with 8 week washout period).

Results: There were no significant effects of soy supplementation on blood pressure, peripheral vasodilation, endothelial function or lipoprotein levels.

Reference: Simons LA et al. Phytoestrogens do not influence lipoprotein levels or endothelial function in healthy, postmenopausal women. *Am J Cardiol* 2000;85:1297-301

Study three: Red clover isoflavones

Yet another recently reported Australian study found and impact of supplementation on lipid profile and bone metabolism.

Subjects: 46 post-menopausal women.

Method: Cross-over randomised, controlled study in which a red clover isoflavone preparation was given to the subjects (28.5 mg, 57 mg, or 85.5 mg of phytoestrogens/day for 6 months). The active treatment was given using a double-blind protocol after single-blind placebo and wash-out phases.

Results: The HDL cholesterol rose by 15-28% whilst the serum apolipoprotein B fell by 11-17% for the different doses used (all changes significant at $p < 0.05$, but there was no dose-response effect found). Bone mineral density rose by approximately 4% with the two higher doses ($p < 0.03$ for each of the two doses).

Reference: Clifton-Bligh PB et al. The effect of isoflavones extracted from red clover (Rimostil) on lipid and bone metabolism. *Menopause* 2001;8:259-65

Study four: post-menopausal women

There was a significant fall in LDL cholesterol (6.5% fall $p < 0.02$) and LDL:HDL ratio (8.5% fall $p < 0.02$) from high isoflavone soy supplementation in a randomised crossover trial of 18 postmenopausal women with normal or mildly elevated cholesterol levels.

The women were given isolated soy protein with control, low and high levels of isoflavone for 3x 3 month periods.

However, there was no clear dose-response relationship.

Reference: Wangen KE et al. Soy isoflavones improve plasma lipids in normocholesterolemic and mildly hypercholesterolemic postmenopausal women. *Am J Clin Nutr* 2001;73:225-31

Comments

We last reviewed research on phytoestrogens and cardiovascular disease in mid-1998. At that time, we found quite a bit of interesting epidemiological and laboratory evidence and a few clinical trials to suggest that these foods and compounds may have useful applications in preventing heart disease. This effect was mediated through favourable changes to lipid profile and a possible improvement in arterial compliance.

We pointed out that the overall trend from the different studies was not clearcut. Also that it was not clear whether the benefits that were seen were due specifically to phytoestrogens, or some other element of the soy extract from which the phytoestrogens were usually obtained.

Since 1998, quite a few new clinical studies have been reported. Epidemiological and laboratory data also continue to appear (e.g. see ¹). It is clearly a subject that attracts research interest.

But in our view, the overall picture on clinical benefit remains the same - interesting but not definitive. The earlier benefits on arterial compliance have not been consistently reproduced. The red clover study reported here is useful in that it shows a benefit that is obviously not related to soy. On the other hand, another study reported last year ² found falls in total and LDL cholesterol of similar degree when hypercholesterolaemic subjects were given soy protein with and without high isoflavone levels. They concluded that the effect probably was related to soy.

What is clearly needed now are some larger clinical trials, preferably including studies comparing placebo with low and high isoflavone, whether from soy products or otherwise. Later this year we will review some clinical trials on phytoestrogens and menopausal symptoms.

References:

1. Goodman-Gruen D, Kritz-Silverstein D. Usual dietary isoflavone intake is associated with cardiovascular disease risk factors in postmenopausal women. *J Nutr* 2001;131:1202-6
2. Mackey R et al. The effects of soy protein in women and men with elevated plasma lipids. *Biofactors* 2000;12:251-7

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