Special Red Clover Extract Lowers LDL Cholesterol in Men, Not Women in Clinical Trial


Isoflavones are believed to be partially responsible for the cholesterol-lowering effects of soy protein, derived from soy (Glycine max [L.] Merr., Fabaceae). Consumption of soy protein has been shown to reduce blood levels of low-density lipoprotein cholesterol (LDL-C). LDL-C contributes to the buildup of plaque in the arteries, and reducing blood levels of LDL-C decreases the risk of heart disease. However, clinical trials using purified isoflavones have shown inconsistent results. The purpose of this study was to evaluate the impact of two isoflavone-rich extracts of red clover (Trifolium pratense L., Fabaceae) leaf and stem.

This study was a randomized, double-blind, placebo-controlled, crossover trial among 80 men and women living in Australia. The average age of the participants was 58 years and all the women were postmenopausal. The participants were randomly assigned to one of two isoflavone groups. One group took 40 mg per day of a red clover extract of which the isoflavone fraction contained mainly biochanin (B) (biochanin to formononetin ratio = 3.5:1 with 4% genistein and <1% daidzein). The second group took 40 mg per day of a red clover extract, the primary isoflavone being mainly formononetin (F) (formononetin to biochanin ratio = 4.9:1 with <1% genistein and daidzein). Both extracts were provided by Novogen Ltd, North Ryde, NSW, Australia. In this crossover design, half of the participants in each group took the red clover isoflavone extract for 6 weeks and then switched to the placebo for 6 weeks, and the other half took the placebo for 6 weeks and then switched to the isoflavone for 6 weeks. There was a one-week washout period (no isoflavones or placebo given to help ensure that there was no carryover effect from the isoflavone period to the placebo period). Blood lipids (cholesterol and triacylglycerols), urinary excretion of isoflavones, and dietary intake were evaluated at the end of each 6-week period.

Men in the B group had significantly lower LDL-C levels when taking the B extract compared to placebo (P < 0.05). Men in the F group had slightly lower LDL-C levels when taking the F extract compared to placebo, but the difference was not statistically significant. There were no significant changes in LDL-C levels for women taking the B or F extracts. There were no changes in blood levels of high-density lipoprotein cholesterol (HDL-C) or triacylglycerols among men or women in the study. Urinary analysis showed that most of the biochanin was converted to genistein, most of the formononetin was converted to daidzein, and there was large variability among individuals in terms of excretion of isoflavones. These urinary results are consistent with those of previous trials.

In this study, only the biochanin-rich red clover extract lowered LDL-C and that effect was observed only in men. These results support the theory that individual isoflavones affect LDL-C differently. The mechanism of LDL-C lowering by biochanin may involve stimulation of LDL-C receptors and increased clearance of LDL-C from the blood in a manner similar to estrogen. This study is the first to report that a red clover extract could lower LDL-C and that there appears to be a gender difference in lipid responses to isoflavone supplementation. These findings require confirmation and duplication in additional clinical trials.

— Heather S. Oliff, PhD