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FILE: ▪ Flaxseed (*Linum usitatissimum*)
▪ Cardiovascular Disease
▪ Cholesterol

HC 060683-365

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RE: Flaxseed Intake Provides Mixed Lipoprotein Results in Hypercholesterolemia

Bloedon LT, Balikai S, Chittams J, et al. Flaxseed and cardiovascular risk factors: results from a double blind, randomized, controlled clinical trial. *J Am Coll Nutr*. Feb 2008;27(1):65-74.

Flaxseed (*Linum usitatissimum*) is a good source of phytochemicals that benefit cardiovascular health, including the omega-3 fatty acid alpha-linolenic acid (ALA), soluble fiber, and dietary lignans. According to the authors, "flaxseed has the potential to be an attractive functional food for cardiovascular risk reduction." This randomized, controlled clinical trial is designed to examine the effect of 40 g of ground flaxseed delivered in baked products on low-density lipoprotein (LDL) cholesterol and other markers of cardiovascular disease (CVD) risk in subjects with high cholesterol.

The study, conducted at the University of Pennsylvania (Philadelphia, Pennsylvania), included 31 men and 31 post-menopausal women with high cholesterol levels recruited from the Philadelphia, Pennsylvania area between January 2003 and December 2004. Ground whole yellow omega flaxseed provided by the Flax Section of the North Dakota Oilseed Council (Bismarck, North Dakota) was used as the treatment, and ground durum wheat bran was used as the control. Flaxseed (20 g) or wheat bran (20 g) were added to 3 breads or muffins that were similar in appearance, taste, and texture. For a 4-week run-in period, the subjects followed a low-fat low-cholesterol diet after first meeting with a registered dietician. If the subjects were compliant with the diet, then they were randomized (flaxseed n=30, wheat bran n=32) to receive 2 baked products daily for 10 weeks. The percent change from baseline in LDL cholesterol was the primary endpoint.

After 10 weeks, the subjects who received flaxseed had significantly higher plasma levels of ALA ($P<0.001$) and docosapentaenoic acid (DPA) ($P=0.004$), as well as lower levels of arachidonic acid ($P=0.01$) compared to the wheat group. After 5 weeks, serum levels of total cholesterol (TC), LDL cholesterol, and apolipoprotein B (Apo B) were significantly lower

in the flaxseed group, when compared to the wheat group (P<0.001 for all). At 10 weeks, LDL cholesterol was not significantly different between the groups in the ITT analysis, but it was significantly lower in the adherence analysis (P=0.05). The lack of a significant reduction in LDL cholesterol at 10 weeks may be due to a lack of adherence or to body adaptation, according to the authors. More research is needed to determine the mechanism of action for an adaptation effect. There was also no significant difference in TC or Apo B between the groups at 10 weeks. There were significant gender effects on changes in high-density lipoprotein (HDL) cholesterol. At 5 weeks and 10 weeks, flaxseed significantly reduced HDL "good" cholesterol in men, but not women, when compared to the wheat group (P<0.05 for both). Changes in HDL cholesterol were negatively correlated to serum ALA levels at 5 weeks (r=-0.42, P=0.05), and 10 weeks (r=-0.50, P=0.02), which suggests that ALA levels may be involved in this effect. More research is needed to determine a mechanism of action.

There were no significant changes in body weight, glucose, or insulin levels in the flaxseed group after 10 weeks of treatment. There was a significant improvement in insulin sensitivity as measured by the homeostasis model assessments of insulin resistance (HOMA-IR) and the quantitative insulin sensitivity check index (QUICKI) in the flaxseed group compared to the wheat group at 10 weeks (P=0.03 and P=0.05, respectively). Among the most adherent patients and adjusting for body mass index (BMI) strengthened the effect (logHOMA-IR: P=0.02, QUICKI: P=0.03). The results also showed that treatment with flaxseed did not increase oxidative stress, and no change was noted in inflammatory markers. There were a total of 40 adverse events, including 20 in each treatment group. One serious adverse event, bowel obstruction, was judged as "possibly related" to flaxseed treatment. The most common adverse side effects were diarrhea, flatulence, and headache. Flaxseed treatment resulted in reductions in the levels of liver transaminases aspartate aminotransferase (AST) (P=0.01) and alanine aminotransferase (ALT) (P=0.008) compared to the wheat group.

This trial is the largest on flaxseed to include men, and the second largest to date overall. In this study, flaxseed failed to maintain lower LDL cholesterol levels but was associated with improvements in insulin sensitivity, which may reduce the risk of developing type 2 diabetes. However, a significant reduction of HDL in men warrants further assessment. Flaxseed was also associated with reductions in non-elevated liver transaminases. No pro-oxidant effects due to flaxseed treatment were observed. Clinical trial with durations of 6-12 months enrolling a sample size of over 100 subjects "are needed to fully assess the potential of this functional food as a component of a healthy cardioprotective diet."

—Marissa Oppel, MS

The American Botanical Council has chosen not to reprint the original article.