Health aspects of partially defatted flaxseed, including effects on serum lipids, oxidative measures, and ex vivo androgen and progestin activity: a controlled crossover trial¹–³


ABSTRACT

Background: Currently there is considerable interest in the potential health benefits of oil seeds, such as soy and flaxseed, especially in relation to cardiovascular disease and cancer.

Objective: We therefore evaluated health aspects of partially defatted flaxseed in relation to serum lipids, indicators of oxidative stress, and ex vivo sex hormone activities.

Design: Twenty-nine hyperlipidemic subjects (22 men and 7 postmenopausal women) completed two 3-wk treatment periods in a randomized, crossover trial. Subjects were given muffins that contributed ~20 g fiber/d from either flaxseed (~50 g partially defatted flaxseed/d) or wheat bran (control) while they consumed self-selected National Cholesterol Education Program Step II diets. Both muffins had similar macronutrient profiles. Treatment phases were separated by 2 wk.

Results: Partially defatted flaxseed reduced total cholesterol (4.6 ± 1.2%; P = 0.001), LDL cholesterol (7.6 ± 1.8%; P < 0.001), apolipoprotein B (5.4 ± 1.4%; P = 0.001), and apolipoprotein A-I (5.8 ± 1.9%; P = 0.005), but had no effect on serum lipoprotein ratios at week 3 compared with the control. There were no significant effects on serum HDL cholesterol, serum protein carbonyl content, or ex vivo androgen or progestin activity after either treatment. Unexpectedly, serum protein thiol groups were significantly lower (10.8 ± 3.6%; P = 0.007) at week 3 after the flaxseed treatment than after the control, suggesting increased oxidation.

Conclusions: These data indicate that partially defatted flaxseed is effective in lowering LDL cholesterol. No effects on lipoprotein ratios, ex vivo serum androgen or progestin activity, or protein carbonyl content were observed. The significance of increased oxidation of protein thiol groups with flaxseed consumption requires further investigation. Am J Clin Nutr 1999;69:395–402.

KEY WORDS Flaxseed, soluble fiber, lignans, vegetable protein, α-linolenic acid, serum cholesterol, hyperlipidemia, androgen, progestin, sex hormone activity, protein carbonyl content, protein thiol groups, protein thiol oxidation, cardiovascular disease, cancer, oxidative stress, antioxidants, humans, functional foods

INTRODUCTION

There is considerable interest in the potential health benefits of oil seeds, such as soy and flaxseed, especially regarding cardiovascular disease and cancer. This interest in oil seeds relates to their high content of polyunsaturated fatty acids [particularly α-linolenic acid (1–3)], vegetable protein (4–6), soluble fiber (7), and flavonoids and related compounds (8–10), which may possess cholesterol-lowering (11), antioxidant (12), and sex hormone agonistic (13, 14) and antagonistic (15, 16) activities.

There is evidence that whole flaxseed may lower serum cholesterol in both normal (17, 18) and hyperlipidemic (19) subjects. Whole flaxseed contains 41% oil by weight, of which 70% is polyunsaturated; more than half of the total fatty acid is α-linolenic acid (20). However, no studies have been carried out with partially defatted flaxseed (<10% fat by wt) to determine whether the non-lipid components, especially the viscous fiber seed coat, are responsible for the cholesterol-lowering effects. We therefore selected partially defatted flaxseed as a more concentrated source of the viscous seed coat gum to study the effects of flaxseed on serum cholesterol in the absence of high n−3 fatty acid intake. Flaxseed is also a rich source of lignans, with potential weak estrogenic and antiestrogenic activity similar to that of the isoflavones found in soy (9, 21). These plant-derived sex hormone analogues have attracted attention as possible anticancer agents, especially for breast and prostate cancers (22, 23). In addition to their estrogenic activity, if lignans block androgen or progesterone receptors, they may alter the cardiovascular disease risk profile by changing HDL-cholesterol metabolism (24). Lignans, like flavonoids (12), have antioxidant activity (25) and therefore may also be of benefit in the prevention of cardiovascular disease (12, 26, 27) and cancer (28, 29). We therefore assessed the potential health benefits of partially defatted flaxseed in hyperlipidemic...
Mean subject age was 57 years and body mass index (in kg/m²) was 24.9. Nine subjects (22 men, 7 postmenopausal women) completed both phases, but 9 subjects failed to enter the final phase because of changes in personal circumstances and general availability. Three subjects withdrew during the course of 1 of the 2 phases because of either recurrent, unrelated health problems (2 subjects in control phase) or dislike of the muffins (1 subject in flaxseed phase). Twenty-nine subjects (22 men, 7 postmenopausal women) completed both phases of the study. Most subjects had normal weights [body mass index (in kg/m²): 24.9 ± 0.5 (± SEM); range: 19.6–29.8]. Mean subject age was 57 ± 2 y (range: 41–73 y). After following an NCEP Step II diet for the minimum 2-mo run-in period, all but 9 subjects still had baseline serum lipid concentrations above the desirable range (35). Thirteen subjects had LDL-cholesterol concentrations >4.1 mmol/L, 3 had triacylglycerol concentrations >2.3 mmol/L, and 4 had both LDL-cholesterol concentrations >4.1 mmol/L and triacylglycerol concentrations >2.3 mmol/L. Two men were taking hypolipidemic agents (hydroxymethylglutaryl-CoA reductase inhibitors) and 3 were being treated with β-adrenergic blocking agents. One man and one woman were taking l-thyroxin.

Two women were receiving hormone replacement therapy. Medications and dosages were held constant during the course of the study, and subjects were also asked to maintain a consistent level of physical activity. The study was approved by the Ethics Committee of the University of Toronto. Informed consent was obtained from all subjects.

**Study design**

In this randomized, crossover study the test and control phases were separated by a washout period of ≥2 wk. Subjects were blinded to the muffin type, but the flaxseed muffins were darker and had a heavier consistency. Subjects were instructed to consume an NCEP Step II diet throughout the study, including the washout period. Fasting blood samples were obtained and blood pressure and body weight were measured on day 0 and at the end of week 3 in both phases. Seven-day diet records were obtained during the last week of each phase and were analyzed to assess compliance.

**Supplements**

Muffins were baked in 2 batches and were kept frozen at −20°C; both test and control muffins were baked in each batch. They were provided to the subjects frozen and were kept frozen until required for consumption. Subjects thawed the muffins overnight in the refrigerator or heated them in a microwave oven for immediate consumption. The test and control muffins had similar macronutrient profiles (Table 1). The daily supplement consisted of 4 test or control muffins. In the test muffins, this dose provided ≈50 g partially defatted flaxseed meal. In the control muffins, wheat bran and whole-meal flour replaced flaxseed and white flour. Canola oil was added to the control muffin mix to balance the residual oil in the partially defatted flaxseed so that the total fat content of the 2 types of muffins would be equivalent. Fatty acid analysis of the muffins indicated that α-linolenic acid accounted for 31% and 8% of total fat in the test and control muffins, respectively (17, 18). Subjects were instructed by a dietician to reduce their consumption of cereals and breads to minimize any potential effect of the muffins on the dietary macronutrient profile.

**Table 1**

Muffin composition and contribution to daily diet

<table>
<thead>
<tr>
<th></th>
<th>Control muffin</th>
<th>Flaxseed muffin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily supplement (g)</td>
<td>186</td>
<td>229</td>
</tr>
<tr>
<td>Energy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(MJ)</td>
<td>1.74</td>
<td>1.75</td>
</tr>
<tr>
<td>(kcal)</td>
<td>415</td>
<td>418</td>
</tr>
<tr>
<td>Protein</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(g)</td>
<td>21.4</td>
<td>24.2</td>
</tr>
<tr>
<td>(% of energy)</td>
<td>20.6</td>
<td>23.2</td>
</tr>
<tr>
<td>Total fat</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(g)</td>
<td>11.0</td>
<td>11.3</td>
</tr>
<tr>
<td>(% of energy)</td>
<td>23.8</td>
<td>24.3</td>
</tr>
<tr>
<td>SFA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(g)</td>
<td>1.1</td>
<td>1.1</td>
</tr>
<tr>
<td>(% of energy)</td>
<td>2.5</td>
<td>2.4</td>
</tr>
<tr>
<td>MUFA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(g)</td>
<td>5.3</td>
<td>3.9</td>
</tr>
<tr>
<td>(% of energy)</td>
<td>11.6</td>
<td>8.4</td>
</tr>
<tr>
<td>PUFA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(g)</td>
<td>4.1</td>
<td>5.9</td>
</tr>
<tr>
<td>(% of energy)</td>
<td>8.8</td>
<td>12.8</td>
</tr>
<tr>
<td>Available carbohydrate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(g)</td>
<td>57.8</td>
<td>55.0</td>
</tr>
<tr>
<td>(% of energy)</td>
<td>55.7</td>
<td>52.6</td>
</tr>
<tr>
<td>Total dietary fiber</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(g)</td>
<td>17.2</td>
<td>19.4</td>
</tr>
<tr>
<td>(g/MJ)</td>
<td>9.9</td>
<td>11.1</td>
</tr>
<tr>
<td>(g/1000 kcal)</td>
<td>41.4</td>
<td>46.4</td>
</tr>
</tbody>
</table>

*SFA, saturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids.

Subjects and methods

Subjects were men and postmenopausal women with hyperlipidemia [LDL cholesterol >4.1 mmol/L (160 mg/dL) or triacylglycerol >2.3 mmol/L (200 mg/dL)] (35) who had no clinical or biochemical evidence of diabetes, liver disease, or renal disease. After recruitment, subjects were instructed to follow a National Cholesterol Education Program (NCEP) Step II diet (35). They received biweekly dietary counseling on the NCEP Step II diet for a run-in period of ≥2 mo to stabilize their baseline serum lipid concentrations.

Thirty-seven subjects participated during the run-in period, and 36 remained for random assignment to the test (flaxseed) and control (wheat bran) phases. Four subjects completed only 1 of the 2 phases and failed to enter the final phase because of changes in personal circumstances and general availability. Three subjects withdrew during the course of 1 of the 2 phases because of either recurrent, unrelated health problems (2 subjects in control phase) or dislike of the muffins (1 subject in flaxseed phase). Twenty-nine subjects (22 men, 7 postmenopausal women) completed both phases of the study. Most subjects had normal weights [body mass index (in kg/m²): 24.9 ± 0.5 (± SEM); range: 19.6–29.8]. Mean subject age was 57 ± 2 y (range: 41–73 y). After following an NCEP Step II diet for the minimum 2-mo run-in period, all but 9 subjects still had baseline serum lipid concentrations above...
Serum concentrations of apolipoproteins A-I and B were measured with a Behring BN100 nephelometer (Behring Werke AG, Marburg, Germany) in samples that had been stored at \(-70^\circ\text{C}\) (38). Jenkins et al (37) reported previously that the average within-run CVs were 3.4% for apolipoprotein A-I (range: 3.0–3.5%) and 2.7% for apolipoprotein B (range: 1.8–2.9%). Serum lipoprotein(a) concentrations were measured with a commercial enzyme-linked immunosorbent assay (Mogra Lp(a) Kit; Strategic Diagnostics, Newark, DE).

Serum protein thiol groups were measured spectrophotometrically by using 5,5'-dithio-bis(nitroso-benzene acid) (DTNB) (39). Serum samples were diluted with 0.25 mol tris-EDTA buffer/L, pH 8.2, and were incubated with 100 μmol DTNB/L (final concentration) and methanol for 15 min at room temperature. Samples were centrifuged (3000 \(\times\) g for 5 min at room temperature) and the absorbance of the supernate was measured at 412 nm. Thiols were calculated by using the molar extinction coefficient of 13.6. Serum protein carbonyl groups were measured spectrophotometrically with the 2,4-dinitrophenylhydrazine (DNPH) binding assay (40). Serum samples were incubated with 5 mmol DNPH/L (final concentration) for 1 h at room temperature, were precipitated with ethanol:ethyl acetate (1:1, by vol) and was redissolved in 6 mol guanidine/L, pH 2.3. Absorbance of the solution was measured at 366 nm against a blank, and protein carbonyl groups were calculated by using the molar extinction coefficient of 22.0. CVs of replicates were 1.6 \(\pm\) 1.0% and 9.8 \(\pm\) 1.1% for protein thiols and carbonyls, respectively.

We recently developed a tissue culture system suitable for assessing agonistic and antagonistic activity of steroid hormones ex vivo (33, 34). In this system, breast cancer cell lines (BT-474 or T-47D) that are positive for steroid hormone receptors are stimulated with the agonist of interest, and prostate-specific antigen protein is measured after 8 d in the tissue culture supernate with a highly sensitive immunofluorometric assay (41). Androgens and progestins, but not estrogens, up-regulate this gene. To study antagonistic activity, the cell line is first treated with the antagonist and then stimulated with a progestin (norgestrel) or an androgen (dihydrotestosterone). By comparing experiments with and without the antagonist, the androgen- and progestin-blocking activity can be calculated as a percentage. The experimental procedures are described in detail elsewhere (33, 34). We showed that agonistic and antagonistic activity can be assessed in serum samples after a 3-fold dilution in culture media (42).

Seven-day diet records, which were compiled by the subjects during week 3 of each phase, were analyzed for macronutrients and total dietary fiber by using a database in which most foods were derived from US Department of Agriculture data (43). These data were supplemented with our own analyses of foods such as flaxmeal and other muffin components; we used methods of the Association of Official Analytical Chemists for macronutrients (44) and total dietary fiber (45). Fatty acids were measured in Folch extracts of foods by gas chromatography (17, 18).

### Statistical analyses

Results are expressed as means \(\pm\) SEMs. The significance of percentage differences between and within treatments was assessed with Student’s \(t\) test for paired data (two-tailed). The treatment effect was assessed with the PROC GLM procedure in SAS (version 6.12; SAS Institute, Inc, Cary, NC), with treatment, sex, and their interaction as categorical (class) variables; subject as a random variable nested within sex; and the baseline value as a covariate (46).

A total of 29 subjects were studied in both the test and control phases. Of the 29 subjects, 4 (2 men, 2 women) were studied twice, once when receiving the first batch of test and control muffins and 93.5 \(\pm\) 1.5% of the control muffins. The mean intakes of macronutrients during the flaxseed muffin phase \((\approx 19\%\) of energy from protein, 55% from available carbohydrate, 24%

### RESULTS

The subjects reported consuming 92.5 \(\pm\) 1.8% of the flaxseed muffins and 93.5 \(\pm\) 1.5% of the control muffins. The mean intakes of macronutrients during the flaxseed muffin phase \((\approx 19\%\) of energy from protein, 55% from available carbohydrate, 24%
from fat, and 2% from alcohol) were not significantly different from intakes during the control muffin phase (Table 2). During the flaxseed phase, mean intakes of energy (8.15 MJ/d), total dietary fiber (43 g/d), and dietary cholesterol (133 mg/d) were also not significantly different from intakes during the control phase. There was no significant change in body weight during either phase and no significant difference in body weight between phases at weeks 0 or 3 (Table 3).

Baseline (week 0) serum lipid and lipoprotein concentrations did not differ significantly between the flaxseed and control phases (Table 3). From baseline to week 3 of the flaxseed muffin phase, there were significant reductions in total cholesterol (5.5 – 1.2%), LDL cholesterol (9.7 ± 1.8%), and apolipoprotein B (5.9 ± 1.5%), but a significant increase in triacylglycerol (10.2 ± 4.8%). No significant changes in blood lipids occurred between baseline and week 3 of the control phase. When serum lipoprotein and apolipoprotein concentrations at the end of the flaxseed phase were compared with those at the end of the control phase, the following were significantly lower with the flaxseed treatment: total cholesterol (4.6 ± 1.2%), LDL cholesterol (7.6 ± 1.8%), apolipoprotein B (5.4 ± 1.4%), and apolipoprotein A-I (5.8 ± 1.9%) (Figure 1). There were no significant differences in blood pressure between the control and flaxseed treatments at week 3. There were also no significant differences in treatment effects between men and women.

In the 20 subjects for whom data were available, serum protein thiol content did not change significantly during either treatment (Figure 2). However, thiol concentrations were significantly lower at the end of the flaxseed phase than at the end of the control phase (10.8 ± 3.6%). Protein carbonyl content (n = 15) did not differ significantly either across or between treatments (Figure 2).

We observed no significant differences in ex vivo androgen and progesterin agonistic and antagonistic activities of serum between the control and flaxseed phases at either week 0 or week 3 (data not shown). Androgen antagonistic activity decreased during the control phase by 7.5 ± 3.2% (P = 0.038).

**DISCUSSION**

Dietary supplementation with partially defatted flaxseed reduced serum concentrations of total cholesterol, LDL cholesterol, and apolipoprotein B compared with the control treatment. Although the decrease in HDL cholesterol was not significant, apolipoprotein A-I concentrations were reduced significantly during flaxseed supplementation. Ratios of LDL to HDL cholesterol and of apolipoprotein B to apolipoprotein A-I were not affected by flaxseed supplementation. Despite the lack of reduction in lipoprotein ratios, the changes we observed with partially defatted flaxseed supplementation have been described as beneficial for cardiovascular health (7). Partially defatted flaxseed had no effect on ex vivo androgenic or progesterogenic activity. However, flaxseed supplementation reduced protein thiol groups compared with the control, possibly indicating increased oxidative activity. The decrease in protein thiol groups, which indicates increased oxidative stress, would currently be seen as an undesirable effect. Increased oxidative stress may damage proteins, cellular membranes, and genetic material (28). On the other hand, generation of oxygen radicals appears to be involved in the initiation of apoptosis (47) and the natural defense against transformed or foreign cells (48, 49).
TABLE 3

Body weight, blood lipid concentrations, and blood pressure at weeks 0 and 3 of control and flaxseed treatment periods

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Flaxseed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Week 0</td>
<td>Week 3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>72.0 ± 2.1</td>
<td>72.0 ± 2.0</td>
</tr>
<tr>
<td>Total C (mmol/L)</td>
<td>6.55 ± 0.18</td>
<td>6.38 ± 0.17</td>
</tr>
<tr>
<td>HDL-C (mmol/L)</td>
<td>1.21 ± 0.06</td>
<td>1.22 ± 0.06</td>
</tr>
<tr>
<td>LDL-C (mmol/L)</td>
<td>4.39 ± 0.15</td>
<td>4.26 ± 0.12</td>
</tr>
<tr>
<td>Triacylglycerol (mmol/L)</td>
<td>2.14 ± 0.16</td>
<td>2.06 ± 0.16</td>
</tr>
<tr>
<td>Apo A-I (g/L)</td>
<td>1.61 ± 0.05</td>
<td>1.62 ± 0.05</td>
</tr>
<tr>
<td>Apo B (g/L)</td>
<td>1.66 ± 0.05</td>
<td>1.63 ± 0.05</td>
</tr>
<tr>
<td>Total CHDL-C</td>
<td>5.65 ± 0.21</td>
<td>5.44 ± 0.21</td>
</tr>
<tr>
<td>LDL-CHDL-C</td>
<td>3.68 ± 0.16</td>
<td>3.54 ± 0.16</td>
</tr>
<tr>
<td>Apo B:apo A-I</td>
<td>1.05 ± 0.04</td>
<td>1.02 ± 0.03</td>
</tr>
<tr>
<td>Lipoprotein(a) (mg/L)</td>
<td>20.9 ± 4.1</td>
<td>23.4 ± 4.3</td>
</tr>
<tr>
<td>Blood pressure (mm Hg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>129 ± 3</td>
<td>125 ± 3</td>
</tr>
<tr>
<td>Diastolic</td>
<td>81 ± 2</td>
<td>80 ± 1</td>
</tr>
</tbody>
</table>

Week 0 Week 3 Percentage change2 P
1.2 0.014 1.6 0.001 0.0 0.2 0.2 0.070 1.9 0.3 2 0.001 2.1 0.2 2 0.007 0.2 0.2 0.2 0.8 0.2 0.2 0.2 0.3 0.2 0.2 0.2 0.8 0.2 0.2 0.2 0.8 0.2 0.2 0.2

1% ± SEM; n = 29 except for LDL-C and LDL-CHDL-C (n = 26), lipoprotein(a) (n = 27), and blood pressure (n = 28); C, cholesterol; Apo, apolipoprotein.

This situation may be analogous to the double-edged sword effect seen with long-chain n–3 fatty acids in marine oil. These fatty acids are more susceptible to oxidation, may increase hepatic glucose output, and may raise LDL-cholesterol concentrations (50, 51); on the other hand, they reduce VLDL-triacylglycerol concentrations and decrease platelet aggregation (52, 53). In previous studies in which full-fat flaxseed was consumed, no significant reduction was seen in thiobarbituric acid–reactive substances (TBARS), as indicators of increased lipid oxidative stress, despite high concentrations and decrease platelet aggregation (52, 53). In previous studies in which 5–10 g viscous soluble fibers, including arabinose, xylose, and galactose (55). This polysaccharide gum makes up >8% of full-fat flaxseed (55–57). The 50 g partially defatted flaxseed consumed daily in the present study provided >5–6 g flaxseed gum. The reduction in LDL cholesterol in our study was between 77% and 8%, similar to reductions measured in other studies in which 5–10 g viscous soluble fibers, including guar, pectin, psyllium, and β-glucan, were consumed in foods or given as supplements (37, 58–62). As with lipid changes observed with other viscous fiber sources, the reduction in serum cholesterol that we observed was probably related to greater fecal losses of bile acid (62, 63) and increased primary bile acid synthesis (64, 65). Partially defatted flaxseed had no effect on the ratios of LDL to HDL cholesterol or of apolipoprotein B to apolipoprotein A-I.

A similar lack of change in lipoprotein ratios was reported for other diets high in soluble fiber, despite significant reductions in LDL cholesterol (58). Unchanged lipoprotein ratios have also been reported after other dietary manipulations recommended for reducing LDL cholesterol (35), including reductions in saturated fat and dietary cholesterol and increases in polyunsaturated fatty acid intake (66).

If the decreases in serum LDL cholesterol were due to flaxseed gum, it appears that this component is more hypcholesterolemic per gram than most other viscous fibers. However, the supplement also provided 24.2 g vegetable protein/d from flaxseed. Soy proteins in amounts of 30–50 g/d have been shown to lower serum cholesterol (4–6, 67) and it has been suggested that the amino acid composition of the protein may be responsible for this effect (5, 6).

Attention has focused on the ability of soy isoflavonoids and flaxseed lignans to block sex hormone receptors in the prevention of hormone-dependent cancers. It has been proposed that the low incidences of breast cancer in Japan and China relate to the large amount of soy consumed (8, 9). Studies have shown that soy isoflavonoids block estrogen activity in vitro (8, 9, 15, 16). Inhibition of tumor growth in the breast, prostate, skin, and liver has been observed in animal models (68–70), suggesting that soy may have other endocrine and nonendocrine effects. Similar data are now emerging for flaxseed (71, 72). Until now, studies have focused on estrogen activity. This study is the first attempt of which we are aware to assess androgen and progester activities ex vivo by analyzing serum from subjects who consumed flaxseed.

No agonistic or antagonistic effects that might have suggested a beneficial effect of flaxseed in prostate cancer prevention were observed. Furthermore, reduced androgen activity might have increased HDL-cholesterol concentrations (24), but this was not observed. It is possible that the lack of effect was because the lignans were primarily in the conjugated glucuronide form in urine, and this form has little such activity (10).

The phenolic lignans may also have antioxidant activity. Certain dietary antioxidants appear to offer protection from cardiovascular disease (12, 26, 27), possibly by reducing LDL-cholesterol oxidation and therefore atherogenicity. Antioxidants may also reduce cancer risk (29) by reducing oxidative damage to DNA and thereby preserving the genome (28, 73). Because we previously found no major effect of whole flaxseed on markers of lipid peroxidation, including serum TBARS and urinary malondialdehyde excretion (17, 18), we measured oxidation of plasma proteins as an indicator of longer-term oxidant activity. Serum protein thiol groups were selected because they have been.
shown to be particularly sensitive indexes of oxidation (31, 32, 74, 75). The flaxseed supplement reduced serum protein thiol groups, indicating increased oxidation. If confirmed, this would be interpreted as an undesirable effect. However, some prooxidant activity may be beneficial in cancer prevention and tumor cell destruction (76). T lymphocytes destroy foreign cells and pathogens by mechanisms including free radical generation (77). The generation of intracellular oxygen radicals also appears to play a role in the induction of apoptosis (47). Malignant tissue has diminished peroxidizability (78–81), and antioxidants appear to accumulate in malignant cells. Whether the effect of flaxseed on serum protein thiol groups has any bearing on these activities remains to be determined.

In conclusion, these data confirm that supplementing the diet with partially defatted flaxseed results in reductions in serum LDL-cholesterol concentrations similar to those observed with full-fat flaxseed (17–19). The flaxseed gum is likely the major active ingredient in flaxseed responsible for the lipid-lowering action, but the isolated gum requires testing, as do the vegetable protein and phenolic lignan components. Androgen antagonistic action, but the isolated gum requires testing, as do the vegetable protein and phenolic lignan components. Whether the effect of flaxseed on serum protein thiol groups has any bearing on these activities remains to be determined.

In conclusion, these data confirm that supplementing the diet with partially defatted flaxseed results in reductions in serum LDL-cholesterol concentrations similar to those observed with full-fat flaxseed (17–19). The flaxseed gum is likely the major active ingredient in flaxseed responsible for the lipid-lowering action, but the isolated gum requires testing, as do the vegetable protein and phenolic lignan components. Androgen antagonistic action, but the isolated gum requires testing, as do the vegetable protein and phenolic lignan components. Whether the effect of flaxseed on serum protein thiol groups has any bearing on these activities remains to be determined.

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REFERENCES

HEALTH ASPECTS OF FLAXSEED 401


