Effect of Cocoa Bran on Low-Density Lipoprotein Oxidation and Fecal Bulking

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**Background:** Legumes have reported benefits in terms of reduced risk for coronary heart disease and of colonic health. A novel legume fiber, cocoa bran, also may have favorable health effects on serum lipid levels, low-density lipoprotein (LDL) cholesterol oxidation, and fecal bulk.

**Methods:** Twenty-five healthy normolipidemic subjects (13 men and 12 women) (mean±SEM age, 37±2 years; mean±SEM body mass index [calculated as weight in kilograms divided by the square of height in meters], 24.6±0.7) ate cocoa-bran and chocolate-flavored low-fiber breakfast cereals for 2-week periods, with 2-week washout, in a double-blind crossover study. The cocoa-bran cereal provided 25.0 g/d of total dietary fiber (TDF). The low-fiber cereal (5.6 g/d TDF) was of similar appearance and energy value. Fasting blood samples were obtained at the start and end of each period, and 4-day fecal collections were made from days 11 through 14.

**Results:** High-density lipoprotein (HDL) cholesterol level was higher (7.6%±2.9%; *P* = .02) and the LDL/HDL cholesterol ratio was lower (6.7%±2.3%; *P* = .007) for cocoa-bran compared with low-fiber cereal at 2 weeks. No effect was seen on LDL cholesterol oxidation. Mean fecal output was significantly higher for cocoa-bran than for low-fiber cereal (56±14 g/d; *P* < .001) and equal to the increase seen in the same subjects with wheat fiber in a previous study.

**Conclusions:** A chocolate-flavored cocoa-bran cereal increased fecal bulk similarly to wheat bran and was associated with a reduction in the LDL/HDL cholesterol ratio. In view of the low-fat, high-fiber nature of the material, these results suggest a possible role for this novel fiber source in the diets of normal, hyperlipidemic, and constipated subjects.

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**RESULTS**

All breakfast cereals during the cocoa-bran and low-fiber control phases were reported as consumed. The diet macronutrient profiles as recorded were similar for both diets, with the exception of an increase in protein of 1% of total energy...
SUBJECTS AND METHODS

Twenty-five healthy subjects (13 men and 12 women) with a mean (±SE) age of 37 ± 2 years (range, 22-57 years) and mean body mass index (calculated as weight in kilograms divided by the square of height in meters) of 24.6 ± 0.7 were recruited from university staff and students who had taken part in previous similar studies. They were normocholes-
terolemic (low-density lipoprotein [LDL] cholesterol, <4.1 mmol/L [160 mg/dL]).14 None had evidence of diabetes or renal or hepatic disease, and none were taking agents that lowered lipid levels or medications that might influence lipid metabolism. Subjects were studied for two 2-week peri-
dods with a 2-week washout period between phases. Cocoa-
bran and low-fiber control breakfast cereal flakes were taken in random order after a double-blind crossover design. Dur-
ing the cocoa bran 2-week period, cocoa bran (total di-
etary fiber [TDF], 25.0 g/d) was consumed daily as a flaked cocoa-bran breakfast cereal. A chocolate-flavored low-
fiber control breakfast cereal (TDF, 5.6 g/d) was also taken for 2 weeks in the same manner. Because of the volume of both breakfast cereal supplements, subjects were advised to take them in 2 servings daily, ie, morning and evening. The macronutrient profiles of the breakfast cereals are given in Table 1. Diet histories were recorded for the last week of each study period, and subjects were asked to return any uneaten breakfast cereals to assess compliance.

One overnight fasting blood sample was taken in the morning at the start and end of each study period, and blood pressure was measured in the left arm with the subject seated as the mean of 2 successive readings. Four-day fecal collec-
tions were obtained on days 11 through 14 during both phases of the study. Collections were made on an outpatient basis. Participants were provided with under-seat lavatory frames on which to attach plastic collection bags. After use, bags were sealed, labeled and placed on frozen carbon dioxide in a poly-
estrene container. At the end of day 4, these containers were returned to the laboratory, where samples were weighed. The fecal data from our study were also compared with wheat-
fiber data from studies performed 1 and 2 years previously with 19 of these subjects.13,16 In these earlier studies, sub-
jects had consumed standard American Association of Cereal Chemists (AACC) wheat bran, which provided the same increase in fiber intake compared with the respective low-
fiber control breakfast cereals as was achieved in the cocoa-
bran study (TDF, 20 g/d). Symptom diaries were recorded during the last week of each study period. Using a 5-point scale, subjects were asked to record their degree of flatus (0 indicates no gas; 5, severe flatulence), bloating (0 indicates no bloating; 5, severe bloating), ease of bowel movement (0 indicates easy to pass; 5, difficult to pass), stool consistency (0 indicates watery; 5, hard), and abdominal pain (0 indicates no pain; 5, severe pain). Subjects were asked to main-
tain the same diet pattern across all study periods and to main-
tain their usual level of physical activity.

The study was approved by the ethics committee of the University of Toronto, Toronto, Ontario. Informed con-
sent was obtained from each volunteer.

Nutrient values of diet records were calculated using a database derived primarily from the US Department of Ag-
riculture Handbook 8,37 with added values for fiber derived from direct analysis of foods18 and fiber values of Anderson and Bridges.19 Particle sizes of the cocoa bran and AACC wheat bran were measured by the Rho-tap method as calculated by Mongeau and Brassad.20 The mean particle sizes of the cocoa bran and AACC wheat bran were estimated to be less than 0.04 and 1.00 mm, respectively.

Serum samples stored at −70°C were analyzed in a single batch according to the Lipid Research Clinics’ protocol21 for total cholesterol, triacylglycerol, and high-density lipoprotein (HDL) cholesterol levels, after precipitation in dextran sulfate and magnesium chloride.22 Previous studies showed that the average between-run coefficients of variation (CVs) for these analyses were as follows: total cholesterol, 1.3% (range, 0.8%-3.2%); HDL cholesterol, 3.2% (range, 1.6%-5.3%); and triglycerides, 3.0% (range, 1.9%-5.0%).23 Low-
density lipoprotein cholesterol concentrations were calcu-
lated24 for all subjects except for 1 who had an elevated serum triacylglycerol concentration (>4.0 mmol/L). Serum apoli-
poprotein (apo) A-1 and B levels were measured by means of end-point nephelometry (Behring Diagnostics, Frankfurt, Germany).25 Within-run CV for apo A-1 was 3.4% (range, 3.0%-3.5%) and for apo B, 2.7% (range, 1.8%-2.9%).21

For direct assessment of LDL cholesterol oxidation, LDL particles were isolated by precipitation with buffered heparin at their isoelectric point (pH, 5.05).20 The LDL precipi-
ticate was centrifuged at 1000g and resuspended in iso-
tonic sodium chloride solution. Low-density lipoprotein cholesterol was estimated enzymatically21 on an aliquot of the isotonic sodium chloride solution resuspension using a commercial cholesterol assay kit (Sigma-Aldrich Corp, St Louis, Mo). On a further aliquot, LDL cholesterol oxida-
tion was estimated as conjugated dienes in LDL fatty ac-
ids. Lipids from the resuspended LDL cholesterol were ex-
tracted using a 2:1 ratio of chloroform-methanol, dried under nitrogen, dissolved in cyclohexane, and analyzed spectrophotometrically at 234 nm using a molar extinction coeffi-
cient of 29 300 mol−1·L·cm−1 for conjugated dienes.28 Ox-
dized LDL cholesterol was expressed as total LDL conjugated dienes (micromoles per liter of serum) and as the ratio of conjugated dienes (micromoles) per millimole of LDL cho-
lesterol.20 The coefficient of variation for this assay on 6 replicates was 2.5% for conjugated dienes. Studies using this method have demonstrated the antioxidant effect of high isoflavone protein10,20 on LDL cholesterol and con-
firmed similar conclusions reached using the lag phase as-
sessment of LDL cholesterol oxidation.30,31 The results are expressed as mean±SE. The percentage of difference between test and control treatment means was assessed by means of the t test (2-tailed) for paired data. The absolute difference was confirmed by means of analysis of co-
variance using the General Linear Model Procedure (PROC GLM/SAS version 6.12; SAS Institute, Cary, NC), with end-
of-treatment value as the dependent variable; treatment, se-
quence, and sex as main effects; and a random term reflect-
ing the individual subject variable nested within sequence × sex interaction and, where available, baseline value as a covariate.32 For the 19 subjects who had participated in previous studies of low- and high-fiber wheat-bran cere-
als,13,16 the variance in fecal weights between cocoa- and wheat-
bran diets was also compared using a similar approach. The increases in fecal weight were calculated relative to the values for the respective low-fiber diets. In addition, the absolute fecal output data on the cocoa- and wheat-bran diets and their respective low-fiber diets were compared using the Student-Newman-Keuls procedure after establishment of a signif-
ificant overall F value by means of analysis of variance.32

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intake for the cocoa-bran diet (Table 2). No difference in body weight was seen between treatments (Table 3).

Serum lipid data are presented in Table 3. For the cocoa-bran diet, no change in serum lipid levels was seen across the dietary period. However, in the low-fiber control diet, the HDL cholesterol level fell and the LDL/HDL cholesterol ratio rose. Compared with the low-fiber control diet at 2 weeks, the cocoa-bran diet resulted in a significantly higher HDL cholesterol concentration (7.6%±2.9%; P=.02), lower total/HDL (6.7%±1.9%; P=.002) and LDL/HDL cholesterol ratios, and a reduced apo B/A-I ratio (4.3%±2.1%; P=.06) that approached significance. The significance level of the treatment effect for HDL cholesterol level, total/HDL and LDL/HDL cholesterol ratios, and apo B/A-I ratio was confirmed by the General Linear Model procedure (P=.04, P=.006, P=.02, and P=.06, respectively).

No significant changes were seen across either diet or between treatments in oxidized LDL cholesterol or the ratio of conjugated dienes to cholesterol in the LDL fraction (Table 3).

Significantly lower systolic and diastolic blood pressures were seen at the end of the low-fiber control diet compared with the cocoa-bran diet (3.7%±1.5% [P=.02] vs 3.9%±1.4% [P=.01]) (Table 3). Only the rise in diastolic blood pressure for the cocoa-bran diet was significant (4.3%±1.8%; P=.02).

The mean fecal output for the cocoa-bran diet was 191±16 g/d and, for the low-fiber control diet, 135±10 g/d (Table 4). The difference between treatments was significant (56%±14%; P=.001) and represented a 2.9-g increase in fecal weight per gram of additional fiber from the cocoa-bran cereal supplement. Nineteen subjects had taken part in previous studies of wheat bran at a similar level of fiber intake.15,16 The increases in fecal weight during the cocoa- and wheat-bran diets relative to their respective low-fiber control diets were comparable at 66±15 and 83±12 g/d, respectively (P=.43), or a 3.4- and 4.2-g increase in fecal weight per gram of additional fiber from the respective cereal supplement. The mean absolute fecal weights resulting from cocoa- and wheat-bran cereals were also not significantly different (198±19 vs 224±15 g/d; P=.21) (Figure). In these 19 subjects, the

### Table 1. Daily Contribution and Composition of Cereals as Analyzed*

<table>
<thead>
<tr>
<th>Cereal</th>
<th>Low-Fiber†</th>
<th>Cocoa-Bran†</th>
<th>Low-Fiber, % of Energy</th>
<th>Cocoa-Bran, % of Energy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily supplement</td>
<td>159</td>
<td>183</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Energy, MJ (kcal)</td>
<td>2.50 (598)</td>
<td>2.50 (598)</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Protein</td>
<td>7.0</td>
<td>14.0</td>
<td>4.7</td>
<td>9.4</td>
</tr>
<tr>
<td>Fat</td>
<td>2.4</td>
<td>2.6</td>
<td>3.6</td>
<td>3.9</td>
</tr>
<tr>
<td>SFA</td>
<td>1.7</td>
<td>1.1</td>
<td>2.6</td>
<td>1.7</td>
</tr>
<tr>
<td>MUFA</td>
<td>0.2</td>
<td>0.7</td>
<td>0.2</td>
<td>1.1</td>
</tr>
<tr>
<td>PUFA</td>
<td>0.5</td>
<td>0.5</td>
<td>0.7</td>
<td>0.8</td>
</tr>
<tr>
<td>Available carbohydrate</td>
<td>137.0</td>
<td>130.0</td>
<td>91.6</td>
<td>87.0</td>
</tr>
<tr>
<td>Total dietary fiber</td>
<td>5.6</td>
<td>25.0</td>
<td>2.24 (9.4)‡</td>
<td>10.00 (41.82)‡</td>
</tr>
</tbody>
</table>

* SFA indicates saturated fatty acids; MUFA, monosaturated fatty acids; and PUFA, polysaturated fatty acids.
† All data are given as grams per day unless otherwise indicated.
‡ Data are given as grams per megajoule (grams per 1000 kcal).

### Table 2. Calculated Dietary Intakes for Week 2 of Treatment Periods*

<table>
<thead>
<tr>
<th>Cereal</th>
<th>Low-Fiber</th>
<th>Cocoa-Bran</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy, MJ/d (kcal/d)</td>
<td>8.45 ± 0.27 (2020 ± 64)</td>
<td>9.05 ± 0.38 (2164 ± 90)</td>
<td>.09 (.09)</td>
</tr>
<tr>
<td>Total protein, g/d (%)</td>
<td>71 ± 4 (14 ± 1)</td>
<td>82 ± 5 (15 ± 1)</td>
<td>.02 (.03)</td>
</tr>
<tr>
<td>Available carbohydrate, g/d (%)</td>
<td>314 ± 9 (62 ± 1)</td>
<td>335 ± 14 (62 ± 1)</td>
<td>.10 (.93)</td>
</tr>
<tr>
<td>Total dietary fiber, g/d</td>
<td>17 ± 1</td>
<td>39 ± 1</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>g/MJ (g/1000 kcal)</td>
<td>2.1 ± 0.2 (8.7 ± 0.4)</td>
<td>4.3 ± 0.3 (18.6 ± 0.6)</td>
<td>&lt;.001 (&lt;.001)</td>
</tr>
<tr>
<td>Soluble fiber, g/d</td>
<td>4 ± 0</td>
<td>9 ± 0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>g/MJ (g/1000 kcal)</td>
<td>0.51 ± 0.03 (2.2 ± 0.1)</td>
<td>1.05 ± 0.04 (4.5 ± 0.2)</td>
<td>&lt;.001 (&lt;.001)</td>
</tr>
<tr>
<td>Total fat, g/d (%)</td>
<td>48 ± 2 (21 ± 1)</td>
<td>50 ± 3 (21 ± 1)</td>
<td>.19 (.94)</td>
</tr>
<tr>
<td>SFA, g/d (%)</td>
<td>17 ± 1 (8 ± 0)</td>
<td>18 ± 1 (8 ± 0)</td>
<td>.18 (.86)</td>
</tr>
<tr>
<td>MUFA, g/d (%)</td>
<td>17 ± 1 (7 ± 0)</td>
<td>18 ± 1 (7 ± 0)</td>
<td>.12 (.47)</td>
</tr>
<tr>
<td>PUFA, g/d (%)</td>
<td>10 ± 1 (4 ± 0)</td>
<td>10 ± 1 (4 ± 0)</td>
<td>.49 (.98)</td>
</tr>
<tr>
<td>Dietary cholesterol, mg/d</td>
<td>183 ± 14</td>
<td>200 ± 13</td>
<td>.79</td>
</tr>
<tr>
<td>g/MJ (mg/1000 kcal)</td>
<td>22 ± 2 (91 ± 7)</td>
<td>22 ± 1 (95 ± 6)</td>
<td>.11 (.11)</td>
</tr>
<tr>
<td>Alcohol, g/d (%)</td>
<td>7 ± 2 (2 ± 1)</td>
<td>6 ± 2 (2 ± 1)</td>
<td>.31 (.42)</td>
</tr>
</tbody>
</table>

* Data are given as mean ± SE (n = 25). SFA indicates saturated fatty acids; MUFA, monosaturated fatty acids; and PUFA, polysaturated fatty acids.
mean increase in fecal output for cocoa bran represented 79% of the wheat-bran effect. Compared with the low-fiber control diet, the cocoa-bran diet increased flatus ($P = .03$) and frequency of bowel movements ($P = .002$) (Table 4). There were no significant differences reported for indexes of ease of bowel movement, stool consistency, abdominal distension, or abdominal pain.

**COMMENT**

The cocoa-bran diet appeared to prevent the fall in HDL cholesterol levels seen with the control phase and resulted in a significantly lower LDL/HDL cholesterol ratio at 2 weeks for the test vs the control breakfast cereal. In addition, the results demonstrate that cocoa bran has a fecal bulking effect similar to that of coarse wheat bran. This was achieved despite the fine particle size to which the cocoa bran had been milled. However, the chocolate-flavored control and the cocoa-fiber cereals did not alter the concentration of oxidized LDL cholesterol, assessed as conjugated dienes in the LDL fraction, although it is possible that longer studies would be required to detect a modest effect.

The effect on serum lipid levels was unexpected. Viscous legume fibers, such as the galactomannans of guar and locust bean, have long been known to reduce serum total and LDL cholesterol levels. In general, however, viscous fiber sources have been associated with no

<table>
<thead>
<tr>
<th>Table 3. Body Weight, Serum, and Blood Pressure Data*</th>
</tr>
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<tbody>
<tr>
<td><strong>Low-Fiber Cereals</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Body weight, kg</td>
</tr>
<tr>
<td>Cholesterol level, mmol/L</td>
</tr>
<tr>
<td>Total</td>
</tr>
<tr>
<td>LDL§</td>
</tr>
<tr>
<td>HDL</td>
</tr>
<tr>
<td>Triacylglycerol, mmol/L</td>
</tr>
<tr>
<td>Apolipoproteins, g/L</td>
</tr>
<tr>
<td>Apo A-I</td>
</tr>
<tr>
<td>Apo B</td>
</tr>
<tr>
<td>Ratios</td>
</tr>
<tr>
<td>Total/HDL cholesterol</td>
</tr>
<tr>
<td>LDL/HDL cholesterol§</td>
</tr>
<tr>
<td>Apo A-I/ Apo B</td>
</tr>
<tr>
<td>Oxidized LDL level‡</td>
</tr>
<tr>
<td>Conjugated dienes, pmol/L</td>
</tr>
<tr>
<td>Conjugated dienes/LDL cholesterol§</td>
</tr>
<tr>
<td>Blood pressure, mm Hg</td>
</tr>
<tr>
<td>Systolic</td>
</tr>
<tr>
<td>Diastolic</td>
</tr>
<tr>
<td>*Data are given as mean ± SE (n = 25). LDL indicates low-density lipoprotein; HDL, high-density lipoprotein; apo, apolipoprotein.†End-treatment difference (%) is given as (test−control) × 100/control.‡To convert cholesterol to milligrams per deciliter, divide by 0.0259.$Levels of LDL cholesterol could not be calculated for 1 subject at all 4 points due to high triglyceride concentrations (&gt;4.00 mmol/L) (n = 24).</td>
</tr>
</tbody>
</table>
change in LDL/HDL cholesterol ratio, even if no significant reduction in HDL cholesterol level was recorded.57-59 Many dietary maneuvers aimed at reducing cholesterol concentrations, such as high-carbohydrate diets and increased intake of polyunsaturated fat, tend to lower LDL and HDL cholesterol levels and therefore do not improve the LDL/HDL cholesterol ratio.60 More recently, monounsaturated fats and soy protein have attracted attention, specifically because they appear to improve the LDL/HDL cholesterol ratio by reducing LDL while preserving HDL cholesterol concentrations.61-64 The effect seen herein of an apparent increase in HDL cholesterol level with cocoa bran and a corresponding reduction in the LDL/HDL cholesterol ratio is therefore unusual. This pattern of blood lipid level change has not been reported previously for legume fiber65 or whole legumes.66 No explanation can be offered yet. There was no apparent change in the total fat level or the nature of the fatty acids between the test and control diets. The small increase in protein intake resulting from the cocoa protein associated with the cocoa bran seems an unlikely candidate. However, if these results are confirmed in larger studies of longer duration, the effects of cocoa-bran protein and associated substances (flavonoids, lignans, etc) will have to be explored. It is also possible that the relatively high-carbohydrate diets eaten by our subjects may have tended to lower HDL cholesterol and raise triglyceride concentrations, and that the presence of the fiber and associated substances in the cocoa-bran cereal may have minimized this effect. Fecal sterol measurements might have helped define the effect of fiber, but these measurements were not made.

A further surprise was the significant rise in blood pressure seen with cocoa fiber. Beverages such as coffee and tea are recognized to contain methylxanthines (caffeine, theophylline, and theobromine),67,68 which may raise blood pressure,69,70 and the same may be true for cocoa. The effect was not large, with no change for the low-fiber control diet and mean rises of 1.4 and 2.9 mm Hg in systolic and diastolic blood pressure, respectively, for the cocoa-bran diet. To detect as significant the same treatment difference we observed in systolic blood pressure at the 5% level 80% of the time (a = .05; B = .80), a sample size of at least 40 subjects would be required, assuming also the same standard deviation. Therefore, in many studies of this nature, blood pressure changes may not be detected because of the large numbers of subjects involved.

An increase in fecal bulk seen with the cocoa-bran diet was not unexpected in view of the insoluble fiber content of the bran (44% insoluble fiber). What was unexpected was the magnitude of the increase, especially in view of the fine mean particle size of the bran. The cocoa bran had been milled to a very fine homogeneous powder (mean particle size, <40 µm). When the particle size of wheat bran has been reduced to less than 500 to 700 µm, a significant reduction in fecal bulking activity has been reported.72 Agencies concerned with health have therefore advised that coarse-particle bran be used, especially where a laxative effect is required.72

Previous reports have indicated that chocolate may have antioxidant properties.11,12 Our interest was whether the antioxidant activity was associated with the chocolate flavor. Flavonoids in tea, fruit, and vegetables have attracted attention as antioxidants, and their consumption has been associated with a reduction in risk of cardiovascular disease.73,74 Legumes in the form of soy and their associated isoflavones are also recognized as antioxidants75 and have been shown to reduce LDL cholesterol oxidation.10 Of direct relevance to our study, consumption of isoflavone-rich soy protein reduced conjugated dienes in circulating LDL cholesterol.76,77 The lack of effect with the chocolate-flavored cocoa-fiber and low-fiber cereals suggests that the antioxidant activity is not associated with the flavor but may be more related to the protein, as in soy, or possibly the lipid fractions of cocoa.

**CONCLUSIONS**

A chocolate-flavored low-fat, high-fiber source, cocoa bran, has a beneficial effect on laxation and a potentially interesting action in maintaining HDL cholesterol levels compared with low-fiber chocolate-flavored cereal flakes used as a control. The effect on blood pressure, although small, requires confirmation and explanation of mechanism. Overall, cocoa bran warrants further study in view of its potential health benefits.

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