Extracted Oat and Barley β-Glucans Do Not Affect Cholesterol Metabolism in Young Healthy Adults

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Abstract

β-Glucans are known to exhibit hypocholesterolemic effects. Increased intestinal viscosity is thought to be crucial for cholesterol lowering. It is suggested that concentration, molecular mass, and structure, including the ratio of (1→3) to (1→4) glucan bonds in the molecule, are of importance for β-glucan functionality. This study investigated the effects of 3 different β-glucan sources, incorporated into a beverage and yogurt, on blood lipids and fecal endpoints. Fourteen participants completed this randomized, crossover, single-blinded study with four 3-wk periods: control and 3.3 g/d oat, barley, and barley mutant β-glucans of similar molecular mass. Before and after each period, fasting and postprandial blood samples were drawn and 3-d fecal samples were collected. Treatment did not affect changes in total, LDL, and HDL cholesterol compared with control; however, consumption of 3.3 g/d of oat β-glucans for 3 wk resulted in greater decreases in total (−0.29 ± 0.09 mmol/L, P < 0.01), LDL (−0.23 ± 0.07 mmol/L, P < 0.01), and HDL (−0.05 ± 0.03 mmol/L, P < 0.05) cholesterol compared with baseline. Changes in LDL in the β-glucan treatments were not related to β-glucan structure (cellotriosyl:cellotetraosyl). Decreases in fasting triacylglycerol were substantially greater after oat β-glucan treatment compared with control (P = 0.03). Fecal dry and wet weight, stool frequency, fecal pH, and energy excretion were unaffected. The results do not fully support the hypocholesterolemic effects by differently structured oat and barley β-glucans. However, substantial differences compared with baseline suggest a potential for oat β-glucan, presumably due to its higher solubility and viscosity. This underlines the importance of elusive structural β-glucan features for beneficial physiologic effects. J. Nutr. 143: 1579–1585, 2013.

Introduction

Dietary fibers have long been recognized for their positive effects on health (1). Observational studies have shown an association between dietary fiber intake and a reduced risk of the development of cardiovascular diseases (2). This is partly ascribed to their hypocholesterolemic properties, which are especially observed for soluble dietary fibers (3), because high serum cholesterol concentrations represent a major cardiovascular risk factor and cholesterol reduction is a target in the management of cardiovascular disease risk (4).

In a meta-analysis by Brown et al. (3) it was shown that oat products lower LDL cholesterol by 0.037 mmol/L (1 g soluble fiber); however, the included studies constituted a heterogeneous group of studies in terms of both study design and intervention product characteristics. Molecular mass (MM) and molecular structure of the β-glucan are assumed to be the most important determinants of physicochemical properties, which, in turn, influence their physiologic impact after consumption. Thus, differences in MM and structural characteristics constitute the most likely reason for the successful cholesterol lowering seen in some human intervention studies and the lack of effect in other studies of oat and barley β-glucans (5,6).

Both oat and barley are rich sources of soluble (1→3), (1→4)-β-D-glucan (β-glucan), a linear, nonstarch polysaccharide consisting of ~70% of 1,4-O-linked and 30% 1,3-O-linked β-D-glucopyranosyl units (7). The polymer chain is composed of

1 The study was carried out as part of the research program of the UNIK (Food, Fitness & Pharma for Health and Disease). The UNIK project is supported by the Danish Ministry of Science, Technology, and Innovation. The study was also supported by the strategic research program “BEST” at the Faculty of Science, University of Copenhagen, Denmark.


3 Supplemental Figure 1 and Supplemental Tables 1 and 2 are available from the “Online Supporting Material” link in the online posting of the article and from the same link in the online table of contents at http://jn.nutrition.org.

4 This trial is registered at www.clinicaltrial.gov as NCT 01317264.

5 To whom correspondence should be addressed. E-mail: mekr@life.ku.dk.

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85–90% cellotriosyl (DP3) and cellotetraosyl (DP4) units connected by β-D-(1→3) linkages (7). The relative proportion of DP3 and DP4 units is also referred to as the DP3:DP4 ratio (8), which differs between cereal genera as well as genotypes of the same genera and is considered a “fingerprint” of the individual β-glucans. Generally, β-glucans derived from oat have been reported to exhibit smaller DP3:DP4 ratios (1.5–2.3) than those derived from barley (1.8–3.5) (8).

The primary aim of the present study was to relate structural characteristics of 3 different β-glucans, which were derived from oat and barley and were of similar MM (9), with cholesterol-lowering properties. Second, it is reported how the 3 β-glucans affected blood pressure, body weight, and plasma concentrations after 10 min of rest with an automatically inflated cuff (UA-787; A&D Co. Ltd.). Two measurements were performed, and the mean value was calculated. Thereafter, subjective appetite sensation was assessed by using a visual analog scale (VAS) and a fasting blood sample was drawn. After taking all fasting measurements, a breakfast meal, including a daily β-glucan dose, was served together with 300 mL of water (~2000 kJ; 14, 22, and 64% of energy from protein, fat, and carbohydrates, respectively). The palatability of the breakfast meal was assessed by using a VAS. During the following 240 min, appetite sensation was assessed every 30 min and blood samples were drawn after 120 and 240 min. At the end of the meal test day, a pasta Bolognese lunch meal was served and consumed ad libitum.

The participants were instructed to keep a weighed food record during the 4 days before each meal test day. Furthermore, all feces samples were collected in preweighed plastic containers during the 3 days before and the 3 last days of each treatment period. Also, 24-h urine samples were collected at the day before and at the last day of each period. At the end of each period, participants evaluated gastrointestinal tract (GIT) comfort by using a VAS. Furthermore, they were asked to guess which of the 4 intervention products they had been consuming in order to assess the successfulness of blinding.

**Participants and Methods**

**Study participants**

Sixteen young adults were recruited through advertising at university campuses in the Copenhagen area. The exclusion criteria were as follows: known chronic illnesses (e.g., diabetes, hypertension, hyperlipidemia), smoking, excessive physical activity (>10 h/wk), regular use of medication (oral contraceptives were allowed), use of dietary supplements, and food intolerances relevant to the protocol. All study participants gave written consent after having received verbal and written information about the study. The study was carried out at the Department of Nutrition, Exercise, and Sports, Faculty of Science, University of Copenhagen, Denmark, and was approved by the Municipal Ethical Committee of the Capital Region of Denmark in accordance with the Helsinki Declaration (H-4-2009-111).

**Randomization and concealment**

Participants were randomly assigned to the order of the 4 treatments by simple randomization generated by a computer. Treatment assignment was performed by one of the authors (M.K.) not involved with the study participants and treatments were assigned according to the day of enrollment. The participants were instructed not to discuss the product appearance with the study staff to prevent unblinding of the outcome assessors.

**Study design**

The study was designed as a single-blinded, randomized crossover trial examining 4 different intervention products during four 3-wk dietary intervention periods, which were separated by a washout period of at least 2 wk. The study was performed at the Department of Nutrition, Exercise, and Sports at the University of Copenhagen. During each of the 4 intervention periods, the participants consumed both a beverage and a serving of yogurt with or without added β-glucan derived from the 3 different sources. Participants did not know which study product they received. They were instructed to consume each serving of β-glucan with a meal. The study participants received freshly prepared products twice weekly. In addition to the 2 daily doses of intervention products, they consumed their habitual diet and were asked to maintain their habitual physical activity level throughout the study. Furthermore, they were instructed to abstain from oat and barley products containing intact β-glucans.

Before and after each intervention period (d 1 and 22), the participants came to the department for a meal test day after an overnight fast (>10 h) and abstention from alcohol and physical exercise for 24 h. Body weight was measured in light clothing to the nearest 0.05 kg (Tanita BWB-600) and height was assessed (only at the first visit) to the nearest 0.5 cm by using a wall-mounted stadiometer (Seca). Blood pressure measurements were performed on the right arm in a supine position after 10 min of rest with an automatically inflated cuff (UA-787; A&D Co. Ltd.). Two measurements were performed, and the mean value was calculated. Thereafter, subjective appetite sensation was assessed by using a visual analog scale (VAS) and a fasting blood sample was drawn. After taking all fasting measurements, a breakfast meal, including a daily β-glucan dose, was served together with 300 mL of water (~2000 kJ; 14, 22, and 64% of energy from protein, fat, and carbohydrates, respectively). The palatability of the breakfast meal was assessed by using a VAS. During the following 240 min, appetite sensation was assessed every 30 min and blood samples were drawn after 120 and 240 min. At the end of the meal test day, a pasta Bolognese lunch meal was served and consumed ad libitum.

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### Interventions products

**Formulation of intervention products.** Three β-glucans, derived from oat, barley, and a barley mutant, were extracted and characterized according to Mikkelsen et al. (9). Physicochemical characteristics of the extracts are summarized in Table 1.

Fresh 2% (wt/v) β-glucan solutions were prepared from the dry β-glucan extracts by stirring for 30 min at 80°C to secure proper hydration of the dietary fibers. Subsequently, the fresh solutions were mixed into a beverage with blackcurrant syrup (Minimum, Dansk Supermarked) or a low-fat vanilla yogurt (Arla Cheasy, Arla Foods). Each preparation contained 1.65 g of β-glucan, corresponding to a daily dose of 3.3 g of β-glucan. The 4 beverage preparations had an equal total volume of 250 mL, whereas the volume of the vanilla yogurt preparation ranged from 100 to 174 mL, because different amounts of β-glucan extract were added to 100 mL of yogurt (Table 1).

**Viscosity of intervention products.** Viscosity measurements of the pure β-glucan solutions and the prepared intervention products were performed with a StressTech rheometer (Reologica Instruments AB) by using a cup (26.0 mm) and bob (25.0 mm) geometry over a shear rate range of 1–100 s⁻¹ and temperatures of 10°C and 37°C. The viscosity behavior was approximated with a consistency coefficient (related to viscosity; Pa·s) and flow behavior index n from the Power Law model as SS = c SRⁿ, where SS (Pa·s) is shear stress and SR (s⁻¹) is shear rate. True replicate measurements of the β-glucan drink and yogurt intervention products were performed. The repeatability of the β-glucan drink and yogurt intervention products was calculated. Thereafter, subjective appetite sensation was assessed by using a visual analog scale (VAS) and a fasting blood sample was drawn. After taking all fasting measurements, a breakfast meal, including a daily β-glucan dose, was served together with 300 mL of water (~2000 kJ; 14, 22, and 64% of energy from protein, fat, and carbohydrates, respectively). The palatability of the breakfast meal was assessed by using a VAS. During the following 240 min, appetite sensation was assessed every 30 min and blood samples were drawn after 120 and 240 min. At the end of the meal test day, a pasta Bolognese lunch meal was served and consumed ad libitum.

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### Table 1 Compositional and structural features of the β-glucan extracts and composition of the daily administered intervention product

<table>
<thead>
<tr>
<th>β-Glucan extract characteristics</th>
<th>Oat</th>
<th>Barley</th>
<th>Barley mutant</th>
</tr>
</thead>
<tbody>
<tr>
<td>TDF, % of DM</td>
<td>72</td>
<td>46</td>
<td>58</td>
</tr>
<tr>
<td>IDF, % of DM</td>
<td>83</td>
<td>44</td>
<td>71</td>
</tr>
<tr>
<td>Molecular mass, kDa</td>
<td>76</td>
<td>28</td>
<td>45</td>
</tr>
<tr>
<td>DP3:DP4</td>
<td>305</td>
<td>280</td>
<td>280</td>
</tr>
<tr>
<td>Dose of intervention product, g/d</td>
<td>2.3</td>
<td>3.5</td>
<td>4.7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>β-Glucan</th>
<th>Oat</th>
<th>Barley</th>
<th>Barley mutant</th>
</tr>
</thead>
<tbody>
<tr>
<td>TDF</td>
<td>3.3</td>
<td>3.3</td>
<td>3.3</td>
</tr>
<tr>
<td>IDF</td>
<td>3.8</td>
<td>3.2</td>
<td>4.0</td>
</tr>
<tr>
<td>SDF</td>
<td>0.3</td>
<td>1.4</td>
<td>1.5</td>
</tr>
<tr>
<td>Total dietary fiber</td>
<td>3.6</td>
<td>1.7</td>
<td>2.6</td>
</tr>
</tbody>
</table>

1 DM, dry matter; DP3:DP4, ratio between cellotriosyl and cellotetraosyl oligomer units in the β-glucan chain; IDF, insoluble dietary fiber; SDF, soluble dietary fiber; TDF, total dietary fiber.
products, control samples, and pure β-glucan solutions were performed in separate weeks throughout the intervention period. Intervention product stability over time, i.e., viscosity and flow behavior, was monitored over a 4-d period corresponding to the time that test persons stored the products in their refrigerators. Before the measurements, the intervention products were shaken according to the instructions given to the participants before consumption of the products.

**Dietary intake assessment**
All recorded foods and energy-containing beverages were entered into the Dankost 3000 dietary assessment software (Dankost 3000, version 2.5; Danish Catering Center) and the mean total intake of energy, fat, carbohydrates, protein, alcohol, and total dietary fiber was calculated for each 4-d diet registration period.

**Analytical procedures**

**Blood samples.** Fasting concentrations of serum total and LDL cholesterol and both fasting and postprandial plasma TGs were assessed by using colorimetric test kits (Roche TG; Roche Diagnostics GmbH); intraassay variations were 0.6% and 0.9%, respectively. Serum HDL cholesterol was measured by using homogeneous enzymatic colorimetric test kits (Roche HDL-C plus 2nd generation; Roche Diagnostics GmbH); intraassay variations were 1.8%. All analyses were performed on a COBAS MIRA Plus (Roche Diagnostic Systems).

Samples for analysis in this project used the biobank core-facility CUBE (www.cube.ku.dk) as a repository.

**Fecal endpoints.** All fecal samples were weighed, and the mean wet weight of the 3-d collection period was calculated. One fecal sample from each participant in each 3-d collection period was mixed with demineralized water (1:1) and homogenized for measurement of pH (PH-208; Lutron Electronic Enterprise). All fecal samples were freeze-dried, weighed, and homogenized. For each participant, all samples for each 3-d collection period were pooled. Fecal energy was measured by bomb calorimetry (Ika-calorimeter system C4000; Heitersheim).

**Sample size**
The number of study participants was based on a power calculation of 2 previous intervention studies on the effect of dietary fibers on fasting total cholesterol concentrations conducted in our laboratory (10,11). Here, the change in total cholesterol differed from control by −0.3 and −0.5 mmol/L, with standardized differences of 0.39 and 0.48 mmol/L, respectively. A total of 14 study participants needed to complete the 2 periods corresponding to the time that test persons stored the products in their refrigerators. Before the measurements, the intervention products were shaken according to the instructions given to the participants before consumption of the products.

**Calculations and statistical analysis**
The AUC for TGs was calculated by using the trapezoidal method. Energy digestibility was calculated as mean daily energy excreted based on the Dankost 3000 dietary assessment software (Dankost 3000, version 2.5; Danish Catering Center) and the mean total intake of energy, fat, carbohydrates, protein, alcohol, and total dietary fiber was calculated for each 4-d diet registration period.

**Intervention product characteristics.** At 10°C, control beverage and yogurt products exhibited viscosity and flow behavior stability over time and replicate measurements: beverage c = 1 mPa s, n = 1 (Supplemental Fig. 1). For all samples, a 60–70% decrease in viscosity after a temperature increase from 10°C to 37°C was observed, which agrees well with our previous study on the temperature dependence of β-glucan viscosity (12). Oat and barley β-glucan blackcurrant beverages showed viscosity and flow behavior stability over time. The β-glucan beverages differed in viscosity at 10°C in the following order: oat (c = 180 mPa s) > barley (c = 80 mPa s) > barley mutant (c = 30 mPa s); all preparations showed Newtonian flow behavior (n = 0.95–1). Yogurts also showed viscosity and flow behavior stability over time. Mixing of hydrated β-glucans into ready-made yogurt additionally prevented yogurt phase separation. Both barley β-glucan yogurts showed similar viscosities around 1000 mPa s, whereas the oat β-glucan yogurt had a higher viscosity (c = 3400 mPa s). The yogurts displayed shear thinning behavior (n = 0.5–0.7). Compared with the control products, the addition of β-glucan solution to the beverage increased the product's viscosity, whereas the addition to yogurt decreased the product's viscosity.

**Results**
Of the 16 enrolled participants (10 women and 6 men), 13 persons completed all 4 treatment periods (7 women and 6 men). One person dropped out due to dislike of the intervention products and 1 person dropped out for personal reasons not related to the study. Finally, 1 female participant dropped out before the fourth period due to pregnancy. Data from the 3 periods completed by this participant were included in the statistical analysis. Participants were enrolled in January and February 2010, and the last participant finished in October 2010. All 14 participants were young, healthy adults with BMI, blood cholesterol concentration, and blood pressure within the normal range (Table 2). During 1 period, 1 participant was provided a dry β-glucan powder for 10 d due to travel activities. No other deviations from the protocol were reported; thus, compliance to the intervention was high. On the basis of the participants’ guesses as to which intervention product they were allocated in each period, the blinding was not entirely successful. When given the control products, all participants answered correctly, whereas they were not able to distinguish between the 3 β-glucan sources (data not shown).

**TABLE 2** Baseline characteristics of study participants

<table>
<thead>
<tr>
<th></th>
<th>All (n = 14)</th>
<th>Women (n = 8)</th>
<th>Men (n = 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>22.9 ± 2.1</td>
<td>23.6 ± 1.3</td>
<td>22 ± 2.6</td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>70.3 ± 12.7</td>
<td>61.7 ± 5.3</td>
<td>84.2 ± 10.1</td>
</tr>
<tr>
<td>Height, m</td>
<td>1.75 ± 0.12</td>
<td>1.67 ± 0.07</td>
<td>1.86 ± 0.09</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>22.8 ± 2.3</td>
<td>22.2 ± 2.4</td>
<td>23.5 ± 2.2</td>
</tr>
<tr>
<td>Plasma total cholesterol, mmol/L</td>
<td>4.46 ± 0.26</td>
<td>4.75 ± 0.4</td>
<td>4.06 ± 0.24</td>
</tr>
<tr>
<td>Plasma LDL cholesterol, mmol/L</td>
<td>2.37 ± 0.20</td>
<td>2.53 ± 0.28</td>
<td>2.17 ± 0.29</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>120 ± 14</td>
<td>111 ± 9</td>
<td>131 ± 12</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg</td>
<td>74 ± 8</td>
<td>71 ± 6</td>
<td>78 ± 9</td>
</tr>
</tbody>
</table>

1 Values are means ± SEMs. BP, blood pressure.
Dietary intake. There was no overall effect of treatment on changes in energy and dietary fiber intake or on changes in percentage of energy from protein (P > 0.15) (Supplemental Table 1). However, treatment affected changes in percentage of energy from carbohydrates (P = 0.04) and a tendency was observed for percentage of energy from fat (P = 0.08), where post hoc pairwise comparisons revealed that decreases in percentage of energy in carbohydrate intake in the oat treatment differed from the increase in the barley treatment (P < 0.01) and the decrease in percentage of energy from fat during oat β-glucan consumption tended to differ from control (P = 0.08). Total dietary fiber intake was not increased with any of the treatments compared with baseline despite the dietary fiber supplementation, but tended to decrease with oat β-glucan consumption compared with baseline (P = 0.09).

Blood lipids. Changes in fasting total, LDL-, and HDL-cholesterol concentrations did not differ between treatments (P > 0.15) (Table 3). However, consumption of 3.3 g of oat β-glucans for 3 wk resulted in reductions in total (−0.29 ± 0.09 mmol/L, P < 0.01), LDL (−0.23 ± 0.07 mmol/L, P < 0.01), and HDL (−0.05 ± 0.03 mmol/L, P < 0.05) cholesterol compared with baseline (Table 3), whereas this was not the case for either of the 2 barley β-glucans. No association between the β-glucan structural feature (DP3:DP4 ratio) and changes in LDL cholesterol after β-glucan treatment was found (R² = 0.04, P = 0.92). A weak inverse association between habitual dietary fiber intake and LDL cholesterol lowering after oat treatment was found (R² = 0.41, P = 0.02) (data not shown).

For changes in TGs, an overall effect of treatment was found when including all observations (P = 0.05), and post hoc pairwise comparisons showed that the change after oat β-glucan −0.15 mmol/L (95% CI: −0.47, 0.17 mmol/L) differed from the change observed with control (−0.02 mmol/L, 95% CI: −0.13, 0.09 mmol/L) (P = 0.03) (Table 3). Neither of the barley β-glucans differed from the control treatment. Despite fasting, 2 individuals had strikingly high fasting and postprandial TG concentrations on 1 meal test day, which occurred either before or after oat β-glucan treatment. Therefore, the effect on TGs was repeated excluding these observations. No effect was observed when these 2 outlying observations were removed (P = 0.30), although the median change with oat treatment remained unchanged (−0.15 mmol/L; 95% CI: −0.30, 0.00 mmol/L). Furthermore, the effect of treatment on acute postprandial TGs was compared by testing the effect of treatment on d 1 and d 22 separately. After adjustment for period, sex, baseline TG, and habitual fiber intake, differences in AUC were not affected by treatment on d 1 or 22, whether or not outlying observations were included.

Fecal endpoints. Changes in total fecal output, fecal dry matter content, stool frequency, fecal pH, energy excretion, and energy digestibility did not differ between treatments in the oat, barley, and barley mutant treatments compared with control (P > 0.40) (Supplemental Table 2).

Discussion

Our results do not fully support the hypothesis that 3 wk of daily intake of 3.3 g of structurally different β-glucans of similar MM, extracted from an oat, barley, and barley mutant breed, affects concentrations of total, LDL, and HDL cholesterol, because changes from baseline in the different β-glucan treatments did not differ from the change observed with control treatment. A reduction in total, LDL, and HDL cholesterol compared with baseline concentrations in the oat β-glucan treatment group does, however, suggest a hypcholesterolemic potential of the oat β-glucan. We propose that structural differences between the β-glucans, mainly different DP3:DP4 ratios affecting solubility, explain why changes from baseline were observed for the oat β-glucan.

The ability of β-glucans to lower plasma cholesterol is commonly ascribed to their ability to form highly viscous solutions (13). It is thought that an increased viscosity of the upper GIT content upon β-glucan consumption may entrap or encapsulate mixed bile acid micelles leading to a greater bile acid excretion (14,15). As a consequence, the feedback inhibition of the key enzyme of bile acid synthesis, cholesterol 7α-hydroxylase, is reduced and thus the de novo synthesis of bile acids is increased, with plasma cholesterol as substrate (16).

Viscosity measurements of the β-glucan beverages, at a concentration of 0.7%, showed a greater apparent viscosity for the oat β-glucan at both 10° and 37°C than for both the barley and the barley mutant β-glucan, which most likely reflects a higher solubility of the oat β-glucan. The viscous properties of β-glucans are determined by their MM, concentration, and molecular structure, where the latter determines the solubility (13). The MM of the extracted β-glucans in our study ranged from 250 to 300 kDa (9), which is medium compared with other extracted β-glucans (17) but low in comparison to the average MM of 2000 to 3000 kDa reported for native cereal β-glucans (18). However, it has previously been shown in a large intervention study that 3 g of high-MM (2100 kDa) and medium-MM (530 kDa) oat β-glucans lowered LDL cholesterol similarly, but that the efficacy was reduced by 50% when MM was reduced to 210 kDa (19). In the current study, the MMs of the 3 β-glucans were similar; thus, the observed viscosity differences cannot be attributed to differences in MM.

Another influencing factor on viscosity is the solubility of the β-glucan molecules, because only solubilized β-glucan polymers are able to entangle and form highly viscous solutions (13). Although cereal β-glucans are classified as soluble dietary fibers, they are only partly soluble in water. The extent to which they are soluble is closely related to their molecular structure (8). Substantial block structural differences were found for barley mutant, mother barley, and oat β-glucans with DP3:DP4 ratios of 4.7 > 3.5 > 2.3, respectively, implying a greater relative amount of DP3 oligomers in the barley β-glucans relative to the oat β-glucan. The higher number of DP3 units of the barley β-glucans may result in lower solubility, because DP3 units are likely to be organized in longer, repetitive DP3 sequences, which are prone to aggregate and form insoluble species (8,20). Therefore, the amount of insoluble β-glucan may determine viscosity and, in turn, physiologic effects. Because the same solubilization procedure was applied for all 3 dry extracts, it is likely that a greater proportion of the oat β-glucan than of the 2 barley β-glucans was solubilized, which is also indicated by the dietary fiber assay. This may likely account for the cholesterol reductions compared with baseline observed for the oat β-glucan treatment but not for the 2 barley β-glucan treatments.

The importance of solubility was also highlighted by others. In a study by Beer et al. (5), 9 g/d of an oat gum β-glucan incorporated into a milk-based instant whip did not affect total cholesterol concentrations despite a relatively high MM of 1000 kDa. In contrast, Braaten et al. (21) effectively lowered serum cholesterol with a smaller dose of 5.6 g of an oat gum β-glucan of similar MM (1200 kDa) given as a beverage. Apparently, the
TABLE 3  Body weight, systolic and diastolic BP, and plasma concentrations of total, LDL, and HDL cholesterol and TGs before and after a 3-wk intervention with control or 3.3 g of oat, barley, or barley mutant β-glucan and changes from baseline to wk 31

<table>
<thead>
<tr>
<th></th>
<th>BP</th>
<th>Cholesterol</th>
<th>AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Systolic</td>
<td>Diastolic</td>
<td>Body weight</td>
</tr>
<tr>
<td></td>
<td>mm Hg</td>
<td>mmol/L</td>
<td>kg</td>
</tr>
<tr>
<td>P-treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>0.90</td>
<td>0.84</td>
<td>0.31</td>
</tr>
<tr>
<td>Baseline</td>
<td>118 ± 4</td>
<td>73 ± 2</td>
<td>70.1 ± 3.4</td>
</tr>
<tr>
<td>Wk 3</td>
<td>117 ± 3</td>
<td>70 ± 1</td>
<td>70.2 ± 3.4</td>
</tr>
<tr>
<td>Δ</td>
<td>-1.2 ± 1.6</td>
<td>-2.4 ± 14</td>
<td>0.13 ± 0.20</td>
</tr>
<tr>
<td>Oat</td>
<td>119 ± 3</td>
<td>73 ± 1</td>
<td>71.1 ± 3.5</td>
</tr>
<tr>
<td>Wk 3</td>
<td>120 ± 4</td>
<td>71 ± 2</td>
<td>71.0 ± 3.6</td>
</tr>
<tr>
<td>Δ</td>
<td>0.8 ± 3.5</td>
<td>-2.0 ± 16 1</td>
<td>0.14 ± 0.17</td>
</tr>
<tr>
<td>Barley</td>
<td>117 ± 3</td>
<td>72 ± 2</td>
<td>70.1 ± 3.5</td>
</tr>
<tr>
<td>Wk 3</td>
<td>116 ± 3</td>
<td>69 ± 2</td>
<td>70.1 ± 3.5</td>
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<tr>
<td>Δ</td>
<td>-1.5 ± 1.4</td>
<td>-2.2 ± 13 2</td>
<td>-0.05 ± 0.24</td>
</tr>
<tr>
<td>Barley mutant</td>
<td>115 ± 3</td>
<td>70 ± 1</td>
<td>70.5 ± 3.5</td>
</tr>
<tr>
<td>Wk 3</td>
<td>115 ± 3</td>
<td>69 ± 2</td>
<td>70.1 ± 3.4</td>
</tr>
<tr>
<td>Δ</td>
<td>0.0 ± 1.5</td>
<td>-1.0 ± 12 3</td>
<td>-0.34 ± 0.21</td>
</tr>
</tbody>
</table>

1 Values are means ± SEMs or medians (95% CIs); n = 14 or n = 13 (oat). P values refer to comparison of changes from baseline to wk 3 in control and β-glucan treatment. Absolute value after 3 wk was different from baseline: * P < 0.01, ** P < 0.05. BP, blood pressure.

2 Presented without 2 potential outliers; n = 11 (oat).

3 Change within group differs from change in control, P < 0.05.
main difference between the 2 studies was the solubility of the applied β-glucans, which was reported as high in the study by Braaten et al. (21) and poor in the study by Beer et al. (5). Furthermore, low solubility was likely the reason why daily administration of 10 g of barley β-glucan in the form of a concentrated powder that was incorporated into various food products such as bread, waffles, and cookies exhibited poor cholesterol-lowering properties in a study by Keogh et al. (6). The pure β-glucan powder was described as largely insoluble in cold water, and apparently there was no solubilization procedure applied before incorporating it into food products.

In addition to MM and solubility, β-glucan concentration also strongly influences the viscosity of a solution (22). Thus, β-glucan intake needs to be sufficient to increase intestinal β-glucan concentration and hence viscosity of the GIT content. In the present study, a daily dose of 3.3 g of β-glucan with a MM ≤210 kDa had a 50% lower effectiveness in lowering LDL cholesterol than β-glucans with a MM ≥530 kDa. The authors suggested that higher doses of soluble β-glucan might compensate for a low MM, although a substantially greater concentration is needed for compensation, because this relation is not linear. In addition, it can be speculated whether the β-glucan content of a single load rather than the daily dose as such is pivotal. In the present study, the daily dose was spread over 2 servings, which may have resulted in intestinal β-glucan concentrations that were too low considering the low MM. A minimum daily dose of 3 g of β-glucan is suggested by the European Food Safety Authority to obtain a beneficial effect on blood cholesterol with oat and barley β-glucans (23). However, the European Food Safety Authority opinion only refers to “non-processed or minimally processed” oat and barley products (23), which naturally contain β-glucans of high MM (24). Our results support that not only dose but also physicochemical properties, including MM, molecular structure, and solubility, should be considered.

In addition to a higher bile acid excretion due to an increased intestinal viscosity, it has also been suggested that β-glucans may directly bind to bile acids, leading to excess fecal bile acid excretion (25). However, the present study does not allow conclusions in regard to the structural composition of the β-glucans and their potential bile acid-binding capacity.

Normally, dietary fibers are more recognized for their cholesterol-reducing properties than for lowering of fasting TGs. This study, however, showed that oat β-glucan resulted in a greater decrease in fasting TGs compared with control. This appears to be in agreement with our previous finding that oat bran consumption lowered TGs by as much as 21% (10) and with other studies that have shown that oat bran can reduce postprandial plasma TG responses (26,27). It is likely that a decreased postprandial lipemia, if occurring repeatedly over a 3- to 4-wk period, may reduce fasting TGs. However, in the present study, we did not observe a diminished postprandial TG response, which is likely due to a too small fat load of the standardized breakfast test meal (10 g of fat).

During the course of the study, participants maintained their habitual diet. Dietary food records revealed that the mean dietary fiber intake was high, meeting the Nordic nutrition recommendations of 25–30 g/d (28). Moreover, some individuals consumed quite large amounts of rye bread, which is another source of soluble dietary fibers (29). As also indicated by an inverse relation between habitual dietary fiber intake and changes in LDL cholesterol, the supplementation of the diet with 3.3 g of extracted β-glucan may possibly be more relevant in a population with a generally low habitual dietary fiber intake. Moreover, baseline LDL-cholesterol concentrations in the present study may have been too low to observe cholesterol-lowering effects. This is in agreement with other studies in which a lack of hypocholesterolemic effects of β-glucan was observed in persons exhibiting low initial cholesterol concentrations (5,30). Most studies that reported reductions in cholesterol concentrations were conducted in hypercholesterolemic individuals (21,31,32). Therefore, it can be speculated that a similar β-glucan intervention might show more pronounced cholesterol-lowering effects if added to the diet of moderately hypercholesterolemic individuals who consume a typical Western diet that is low in dietary fiber. Finally, it should be noted that only 13, as opposed to 14, of the enrolled 16 participants completed the oat β-glucan treatment; thus, the study was not sufficiently powered for the difference between treatments to become substantial.

The current study does not provide strong support for the hypocholesterolemic effects of extracted oat, barley, and barley mutant β-glucans with major structural differences in comparison to a control treatment. However, the higher solubility and viscosity of the oat β-glucan suggest a certain hypocholesterolemic potential, which is indicated by the reductions in total and LDL cholesterol compared with baseline. Mildly hypercholesterolemic individuals, consuming a diet low in dietary fiber, might benefit by adding oat β-glucan to their diet. Further studies are required to investigate the hypocholesterolemic potential of structurally different barley and oat β-glucans in more susceptible groups of volunteers.

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Literature Cited


23. European Food Safety Authority. Scientific opinion on the substantiation of health claims related to β-glucans and maintenance of normal blood cholesterol concentrations (ID 754, 755, 801, 1465, 2934) and maintenance or achievement of a normal body weight (ID 820, 823) pursuant to article 13 (1) of regulation (EC) no 1924/2006. EFSA J. 2009;7:1254–72.