# Effects of oat and wheat bread consumption on lipid profile, blood sugar, and endothelial function in hypercholesterolemic patients: A randomized controlled clinical trial

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**Original Article**

## Abstract

**BACKGROUND:** Increased lipid profile after each meal can disturb the endothelial function. The present study assessed the effects of bread supplemented with oat bran on serum lipids and endothelial dysfunction in patients with hypercholesterolemia.

**METHODS:** This clinical trial was conducted on 60 isolated hypercholesterolemic patients. The subjects were randomly allocated to either intervention (consuming at least five daily servings of oat bread with 6 g beta-glucan) or control (receiving at least five servings of wheat bread). Anthropometric indicators, fasting blood sugar and lipid profiles ere measured at baseline and after 6 weeks (in the end of the intervention). Endothelial function was assessed using flow-mediated dilation (FMD). Within the group and between group differences were investigated using paired t-test and Student's t-test, respectively.

**RESULTS:** Oat bread consumption could significantly reduce total cholesterol ($P = 0.029$). A significant increase in baseline and after ischemia brachial artery diameters at the end of the study was seen. However, it did not have a significant effect on FMD ($P = 0.825$). In the control group, none of the measured indices had changed significantly at the end of the study. Finally, only the mean change of brachial artery diameter after ischemia and baseline brachial artery diameter were significantly higher in the intervention group than in the control group ($P = 0.036$ and $P = 0.012$ respectively).

**CONCLUSION:** Oat bread with beta-glucan could successfully reduce cholesterol levels. Furthermore, in this study oat bread did not reduce FMD more than wheat bread. Since hypercholesterolemia is a proven risk factor for endothelial dysfunction, hypercholesterolemic patients can hence be advised to eat oat bread.

**Keywords:** Bread, Diet, Flow-Mediated Dilation, Hypercholesterolemia

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## Introduction

Hypercholesterolemia has been identified as a risk factor for the development of various diseases including cardiovascular diseases, diabetes, and a number of cancers.[1,2] It is also known to increase oxidative stress through decreasing access to vascular nitric oxide (NO). Such conditions will induce a potent proinflammatory state, disturb and change vascular reactivity, and finally endothelial dysfunction.[3,4]

Proper functioning of the endothelium is essential to vascular tone and regulation of blood flow in response to alterations in different organs and tissues' need for blood.[5,6] Endothelial function is affected by several mediators.[7] Hypercholesterolemia is a major risk factor for the

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incidence of endothelial dysfunction.[8,9] Great attention has been paid to the role of dietary fiber in controlling lipid and lipoprotein metabolism.[10] Fibers can reduce total cholesterol (TC) by affecting low-density lipoprotein-cholesterol (LDL-C) via different mechanisms.[11]

Potential hypocholesterolemic effects of different dietary components, for example, beta-glucan, have been recently evaluated.[12] Beta-glucan, a non-starch polysaccharide, is the fiber in barley (especially in its bran), oat, yeast, rye, and mushrooms.[13] Degroot was the first to show that a 3-week course of daily consumption of 300 g bread containing 140 g oat can reduce serum TC in men by 11%. Therefore, the Food and Drug Administration has suggested consuming 3 g/day oat to reduce serum TC.[14] Later studies have also confirmed the efficacy of beta-glucan in serum TC reduction.[15-17]

Since bran is usually separated from wheat, Iranian breads currently lack fiber, vitamins, and minerals. As this deficiency may cause different diseases, supplementing flour with beneficial compounds and hence producing proper, high-quality bread will contribute to public health. Bread is a widely used food item whose production with oat flour will allow for adding useful properties. The present study aimed to assess the effects of bread containing oat bran on serum lipid levels and endothelial dysfunction in patients with hypercholesterolemia.

## Materials and Methods

This randomized controlled clinical trial was conducted on 60 patients (age: 20-60 years old) who were receiving statins for hypercholesterolemia. The subjects were selected from hypercholesterolemic participants in out-patient clinics.[18] Considering $\alpha = 5\%$, $\beta = 0.2$, standard deviation (SD) = 6, and d = 4, the sample size was calculated as n = 30 in each group using the following formula:

$$n = \left(\frac{2(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta}) \times SD}{d}\right)^2$$

Individuals with diabetes type one or two, hypothyroidism, renal failure, anemia, cholestasis, pancreatic cancer or malignancy, and secondary dyslipidemia were not included. Patients who used antihypertensive drugs or alcohol, smoked, did vigorous regular exercise, had a history of eating disorders, or had weight changes (losing or gaining more than three kilogram weight during the 3 months prior to the study) were not included, either.

TC levels higher than 200 mg/dl or LDL-C levels greater than 160 mg/dl were considered as hypercholestrolemic.[3] Participants were normal in other part of their lipid profile.

Overall, 600 hypercholesterolemic participants of the third phase of Isfahan Healthy Heart Program, Iran, (IHHP) were contacted. Although 100 patients accepted to refer to the center, only 64 were found eligible after base test, medical history, and physical examinations. Moreover, four of these subjects withdrew during the course of study.

A total of 60 subjects out of 100 participants were randomly selected. They were explained about the aims, methods, benefits, and probable hazards of the study and asked to sign a consent form. Non-consenting individuals were excluded and replaced by a new randomly selected person.

Before the intervention, demographic characteristics (age, gender, and marital status) of all participants were recorded. Height, weight, pulse rate, and systolic and diastolic blood pressure (after 20-min rest, in sitting a position) were then measured. All height measurements were performed with one particular measuring tape. A Seca scale was used to measure weight for all subjects. Body mass index (BMI) was calculated as weight divided by height squared. Hip and waist circumference were also measured based on standard protocols.

After completing the questionnaires, 10 ml fasting blood samples were taken to determine serum lipid concentrations [TC, triglyceride, LDL-C, and high-density lipoprotein cholesterol (HDL-C)] and fasting blood sugar (FBS) and were measured using Autoanalyzer.

Endothelial function was assessed with flow-mediated dilation (FMD). FMD is a noninvasive technique where forearm ischemia is induced by inflating a sphygmomanometer cuff to 50-100 mmHg for 5 min. Increased blood flow after the transient ischemia increases NO levels and consequently vasodilation. In this study, a resident of cardiology used ultrasound to measure brachial artery diameter before ischemia (baseline brachial artery diameter) and immediately (< 60 s) after deflation (brachial artery diameter after ischemia). The percentage increase in vessel diameter from baseline conditions to maximum vessel diameter (FMD %) was also calculated as a measure of brachial artery endothelial dysfunction.[19]

The ultrasound system (Vivid Echo, UK) comprised 2D imaging, color Doppler, and electrocardiography. The timing of the images was synchronized with patients' echocardiograms, and all measurements were performed from the internal part of the wall to the internal part of the other wall at the end of the diastole (the peak of R wave). The process of the present study is shown in figure 1.

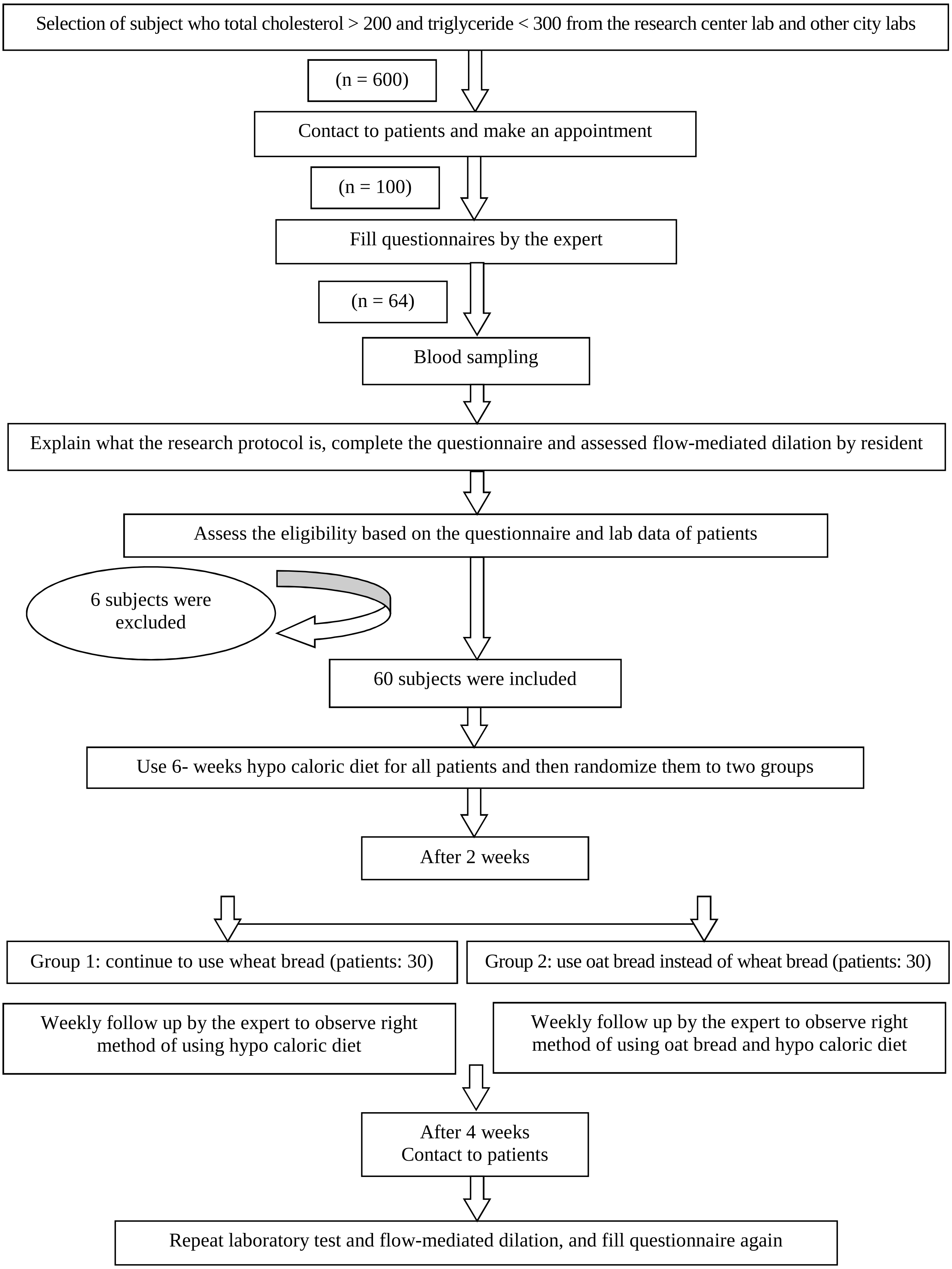


**Figure 1.** The chart of study process

The 6-week duration of our study was divided into a 2-week weight-maintenance phase followed by a 6-week weight-loss phase. In the first phase, all subjects had the same diet of usual food items in order to maintain their constant body weight by week 2. In the following phase, all subjects were provided with a hypo caloric diet in the calorie range of 1500-2000 for 4 weeks. Energy intake for each was calculated based on maintenance energy needs minus 500-700 kcal/d depending on their BMI. In the next stage, the participants were randomly allocated to two groups of 30 (intervention and control) with computerized random-number generator. In this phase, subjects were randomized to consume one of these diets: the intervention group received the hypocaloric diet containing an experimental bread rich in beta-glucan from oat bran [at least five servings (150 g/day) based on their needs, each serving of which had 6 g beta-glucan], and the control group consumed the hypocaloric diet with control bread rich in wheat fiber [at least five servings (150 g/day) based on their needs, with no beta-glucan]. In both phases, energy needs were predicted using the recommended dietary allowances for energy and the target macronutrient composition for all the subjects was 55% of energy as carbohydrate, 30% of energy as fat (with a focus on unsaturated fats), and 15% of energy as protein. Every week new batches of both experimental and control bread were prepared by a local bakery and then delivered at home to each subject once a week based on their request. For their next use of remaining breads, the participants were taught to deep freeze them at −18 °C. Their adherence to diet was checked weekly by a dietitian through a diary log in which the daily amounts of all consumed foods including bread were recorded. In addition, the participants were instructed to keep a detailed 3-day diet record every week that would be reviewed by a dietitian in the next visit during the 6 weeks protocol.

Both groups were asked to continue their routine levels of physical activity and not to consume fiber supplements, weight loss drugs, herbals medicines, or laxatives. During the 6-week course of the intervention, the participants attended weekly visits with the mentioned resident and nutritionist (who evaluated their daily intake of food items).

Individuals who were not willing or able to continue the study were excluded. At the end of the intervention, all initially measured variables were re-assessed.

Quantitative variables were presented as mean ± SD, while qualitative variables were compared in terms of frequency and relative frequency. Paired t-test was used to compare variables before and after the intervention. Between group, differences were evaluated using Student's t-test. All analyses were performed in SPSS for Windows (version 18.0, SPSS Inc., Chicago, IL, USA) and at a significance level of 0.05.

## Results

The mean age of participants was 51.12 ± 9.31 years. Females (n = 39) constituted 65% of the study population. In the beginning of the study, the mean TC and LDL-C levels were 229.48 ± 23.33 and 131.88 ± 24.31 mg/dl, respectively. The mean FMD of all participants was 5.25 ± 2.54% in the beginning of the study and 5.35 ± 2.79% at the end.

Data normality was confirmed with Kolmogorov–Smirnov test and histograms.

The two groups were identical in terms of age, gender, and marital status. They were not significantly different in baseline anthropometric indices, systolic and diastolic blood pressure, heart rate, FBS, and blood lipids. Although there was no significant difference in baseline brachial artery diameter and brachial artery diameter after ischemia between the two groups, FMD was significantly higher in oat bread consumers than in wheat bread users.

At the end of the study oat bread consumption could significantly reduce BMI and TC. It also caused a significant increase in baseline and after ischemia brachial artery diameters. However, it did not have a significant effect on FMD. In the control group (wheat bread consumers), on the other hand, only hip circumference decreased significantly at the end of the study. Compare the final measurements of various indices between the two groups. The mean difference between baseline brachial artery diameter and brachial artery diameter after ischemia was significantly higher in the intervention group than in the control group. Although, this was the only significant difference between the two groups, at the end of the intervention course, FMD had decreased in the intervention group, but increased in the control group ($P > 0.05$) (Table 1).

## Discussion

Our findings suggested the efficacy of a 6-week course of oat bread consumption in increasing baseline and after ischemia brachial artery diameters in hypercholesterolemic patients. Significant reductions in TC and BMI were also observed in oat bread consumers. However, this type of bread failed to change FMD. No such changes were seen in wheat bread consumers.

**Table 1.** The mean of anthropometrics variables in two groups before and after breads consumption

| Variable | Bread | Before | After | P |
|---|---|---|---|---|
| BMI ($kg/m^2$) | Oat | 28.94 ± 3.52 | 28.68 ± 3.55 | 0.531 |
| | Wheat | 28.99 ± 4.92 | 28.81 ± 4.85 | |
| Hip circumference (cm) | Oat | 105.33 ± 6.44 | 104.90 ± 6.39 | 0.631 |
| | Wheat | 106.68 ± 10.32 | 105.98 ± 10.28 | |
| Waist circumference (cm) | Oat | 93.42 ± 9.97 | 93.23 ± 9.53 | 0.762 |
| | Wheat | 97.60 ± 11.67 | 97.49 ± 11.96 | |
| Systolic blood pressure (mmHg) | Oat | 114.83 ± 10.95 | 112.50 ± 12.16 | 0.434 |
| | Wheat | 115.17 ± 14.65 | 114.83 ± 13.55 | |
| Diastolic blood pressure (mmHg) | Oat | 77.00 ± 9.15 | 76.33 ± 8.90 | 0.739 |
| | Wheat | 76.33 ± 10.74 | 75.33 ± 9.37 | |
| Heart rate (beat/min) | Oat | 71.37 ± 6.30 | 71.70 ± 7.07 | 0.535 |
| | Wheat | 72.70 ± 5.93 | 73.40 ± 6.43 | |
| LDL (mg/dl) | Oat | 137.40 ± 24.48 | 135.57 ± 30.59 | 0.755 |
| | Wheat | 126.37 ± 23.45 | 128.90 ± 23.82 | |
| HDL (mg/dl) | Oat | 52.17 ± 11.92 | 51.20 ± 10.38 | 0.306 |
| | Wheat | 50.10 ± 11.67 | 52.30 ± 14.90 | |
| Triglyceride (mg/dl) | Oat | 179.67 ± 63.14 | 177.40 ± 63.49 | 0.628 |
| | Wheat | 172.93 ± 59.40 | 165.83 ± 74.56 | |
| TC (mg/dl) | Oat | 234.90 ± 27.05 | 227.57 ± 30.88 | 0.748 |
| | Wheat | 224.07 ± 17.76 | 219.27 ± 33.86 | |
| FBS (mg/dl) | Oat | 87.97 ± 8.39 | 91.10 ± 11.17 | 0.070 |
| | Wheat | 92.30 ± 9.58 | 89.93 ± 6.71 | |
| Baseline brachial artery diameter (mm) | Oat | 3.48 ± 0.68 | 3.55 ± 0.67 | 0.050 |
| | Wheat | 3.67 ± 0.54 | 3.66 ± 0.55 | |
| Brachial artery diameter after ischemia (mm) | Oat | 4.15 ± 0.65 | 4.25 ± 0.66 | 0.014 |
| | Wheat | 4.22 ± 0.54 | 4.24 ± 0.55 | |
| FMD change (%) | Oat | 5.99 ± 2.85 | 5.91 ± 2.73 | 0.867 |
| | Wheat | 4.54 ± 1.99 | 4.77 ± 2.77 | |

BMI: Body mass index; LDL: Low-density lipoprotein; HDL: High-density lipoprotein; TC: Total cholesterol; FBS: Fasting blood sugar; FMD: Flow-mediated dilation

Several studies have confirmed the benefits of beta-glucan in reducing serum cholesterol. A double-blind, multicenter study on 345 individuals in Canada compared the effects of diets including wheat fiber and four different doses and molecular weights of beta-glucan during a 4-week course. It found that the breakfast having beta-glucans with moderate or high molecular weight could significantly reduce LDL-C.[15] In a clinical trial on 43 male and female hypercholesterolemic patients, Biorklund et al. reported that 5 weeks of drinking soup with 4 g beta-glucagon significantly reduced LDL-C and TC levels.[16] Another clinical trial on 152 female and male patients with high LDL-C levels revealed that the oat (with 3 g beta-glucan) consumers had significantly lower LDL-C and TC levels compared to corn consumers.[17] Similarly, the present research indicated significant cholesterol reductions in patients who used bread containing beta-glucan. Although reduced cholesterol was also observed among wheat bread consumers, this difference was not significant. Since changes in cholesterol levels at the end of the study were not significantly different between the two groups, the reductions seen in both groups could have been partly caused by the hypocaloric diet.

Despite significant reductions in cholesterol levels, FMD did not significantly change in oat bread consumers. As hypercholesterolemia has been suggested to result in endothelial dysfunction, various clinical trials have sought for pharmaceutical and non-pharmaceutical methods to treat this disease. A great deal of research about the effects of medicines on serum lipids and endothelial function has clarified the benefits of cholesterol-lowering drugs on endothelial function.[20-22] Non-pharmaceutical methods have also identified the considerable effects of cholesterol-lowering food items.[23,24] In general, brachial artery has a larger diameter in hypercholesterolemic subjects than in normal individuals. In addition, endothelial dysfunction decreases FMD to levels lower than normal in these patients.[25] The results of the current study regarding baseline brachial artery diameter and brachial artery diameter after ischemia were similar to those reported by previous studies on hypercholesterolemic individuals.[23-25]

Other studies have suggested improved endothelial function following the treatment of hypercholesterolemia.[20-25] In the present study, however, FMD in oat bread consumers had no significant change despite the reduction in cholesterol and increment of baseline brachial artery diameter and brachial artery diameter after ischemia. The reason might have been an increase in both baseline brachial artery diameter and brachial artery diameter after ischemia or the short period and low dose of oat consumption in the studied population. Nevertheless, the majority of studies in this field have been similar to ours in terms of duration and dose of beta-glucan administration. On the other hand, since our participants were selected from hypercholesterolemic patients in the third phase of IHHP (in 2007), the subjects had already been suffering from hypercholesterolemia for 5 years. Due to such long duration of the disease, the desirable response could have required longer course of treatment or greater dose.

Furthermore, the presence of other risk factors (e.g., BMI > 28 kg/m$^2$, mean waist circumference > 90 cm) should not be ignored. Knowing that obesity and overweight are effective in the development of endothelial dysfunction, unimproved FMD can be justified by the failure to reduce weight to normal (changes in BMI were too little in oat bread consumers). While we did not assess the number of risk factors such as smoking and immobility, future studies are recommended to assess subjects without other risk factors.

Oat bread consumption could significantly reduce cholesterol levels. Therefore, adding oat flour to bread can be beneficial to treat high cholesterol in hypercholesterolemic patients.

## Conclusion

Overall, oat bread could successfully reduce cholesterol levels. However, changes in cholesterol levels were not significantly different between the two groups. Furthermore, in spite of increased baseline brachial artery diameter and brachial artery diameter after ischemia among oat bread consumers, FMD showed no significant change. Since hypercholesterolemia is a proven risk factor for endothelial dysfunction, its long-term treatment may affect FMD. Hypercholesterolemic patients should hence be advised to eat oat bread. Further studies with a longer course of treatment and higher dose of beta-glucan are suggested to assess subjects with a shorter history of the disease.

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## Conflict of Interests

Authors have no conflict of interests.

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