Oat porridge consumption alleviates markers of inflammation and oxidative stress in hypercholesterolemic adults

doi: 10.6133/apjcn.201812/PP.0006
Published online: December 2018

Running title: Oat consumption on inflammation & oxidative stress

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ABSTRACT

Background and Objectives: Oats contain antioxidant phytochemicals that may help reduce inflammation as well as oxidative stress. In this study we aimed to investigate the effect of oat porridge consumption on inflammatory marker levels and oxidative stress in Thai adults with high blood lipid levels. **Methods and Study Design:** A randomized crossover study was conducted. Hypercholesterolemic adults were randomly assigned to a 4-week daily consumption of oat or rice porridge. After 4 weeks, they were switched to alternate intervention arms for 4 weeks. At baseline, before and after each intervention period, inflammatory markers including hsCRP, IL-6, IL-8, TNF-α, and MCP-1 and antioxidant status markers including ORAC, FRAP, and MDA of all subjects were measured. **Results:** Compared to baseline, levels of hsCRP, IL-6, IL-8, and TNF-α were significantly decreased after oat porridge consumption (mean change: -0.6±0.9 mg/L, -26.9±27.6 pg/mL, -56.3±27.6 pg/mL, and -9.7±11.6 pg/mL, $p<0.05$ for all, respectively). In addition, consumption of oat porridge also increased antioxidant capacity; ORAC and FRAP levels (mean change: 2.7±1.0 μmol of Trolox/L and 2.4±0.8 μmol of Fe^{2+}/L, $p<0.001$, respectively). However, MCP-1 and MDA levels were not affected. Consumption of rice porridge did not lead to significant changes in these measures. **Conclusions:** daily consumption of 70 grams oat porridge containing 3 grams β-glucan for 4 weeks may help reduce markers of inflammation and oxidation in hypercholesterolemic adults. Therefore, oat may be an appropriate dietary recommendation for individuals with hypercholesterolemia.

Key Words: hypercholesterolemia, inflammatory markers, oxidative stress, oat, porridge

INTRODUCTION

Elevated levels of markers of inflammation including high sensitive C-reactive protein (hsCRP), interleukin-6 (IL-6), interleukin-8 (IL-8), tumor necrosis factor-alpha (TNF-α), monocyte chemoattractant protein-1 (MCP-1), and malondialdehyde (MDA) are associated with several chronic diseases including cardiovascular disease (CVD) and diabetes mellitus.[1,2] Development of inflammation is also associated with oxidative stress,[3] an imbalance between the rate of oxidant production and degradation.4 Being in an increased state of oxidative stress can lead to metabolic disorders, physiological function loss, and eventually death.[4]

Consumption of food comprising antioxidants has been shown to reduce peroxides and other oxidative stress markers.[4] Oat (Avena sativa L.) and oat porridge have long been

recognized as a healthful and nutritious food that contains antioxidant phytochemicals. These are phenolic compounds; avenanthramide, vitamin E; tocopherols and tocotrienols, phytic acid, sterols, and flavonoids.[5]

The antioxidants in oats can potentially prevent the first stage of atherosclerosis development by limiting low-density lipoprotein (LDL) oxidation.[6] Avenanthramides (alkaloids containing phenolic groups), the most abundant class of antioxidants in oats, have been shown to exhibit antioxidant activity both in vitro and in vivo.[7-10] Moreover, they may inhibit the excretion of inflammatory cytokines such as IL-6, IL-8, and MCP-1 that are released by injured human aortic endothelial cells as well as inhibit endogenous lipid peroxidation by reducing MDA levels.[11-12] Also, avenanthramides have been reported to elevate levels of antioxidants such as serum superoxide dismutase (SOD).[13] Additionally, oats are a good source of β-glucan, a soluble fiber with approved health claims for reducing risk of heart disease in the US;[14] and reducing cholesterol levels in countries like the UK and Malaysia.

Decreases in markers of inflammation and oxidative stress could reduce risk of CVD, a major cause of disability and premature death throughout the world. Therefore, we determined the effect of oat consumption, on markers of inflammation and oxidative stress in hypercholesterolemic Thai adults.

MATERIALS AND METHODS

Subjects

Hypercholesterolemic men and women aged between 30 and 60 years who had; total cholesterols levels 221-300 mg/dL and LDL 130-190 mg/dL, a body mass index (BMI) of 23.0-30.0 kg/m^2 and agreed to retain steady weight throughout the study were recruited. Those who were pregnant or in lactation period; or had been diagnosed with cardiovascular, hepatic, renal and diabetic diseases; had baseline triglycerides > 300 mg/dl, were unable to consume oat or rice; had been taking food supplements or drugs to control any chronic diseases; and had lost a significant amount of weight in the previous 3 months were excluded from the study. Total number of study subjects recruited was 24. The study procedure was approved by the Ethics Committee for Human Research, Faculty of Public Health, Mahidol University (MUPH 2012-026).

Dietary intervention

This randomized-controlled crossover study contained two periods of dietary intervention, 4 weeks each (Figure 1). The subjects were randomly divided into two groups of equal size. They were asked to maintain their routine lifestyle including dietary intake and physical activity throughout the study. Subjects were instructed to avoid oat or β-glucan and antioxidant supplements one week before the initial intervention period.

The oat porridge experimental meal, was made with instant oat flake made with 100% whole grain oat and the rice porridge control meal, was made with instant white rice flake. Seventy grams of instant oat flakes provided 290 kcal, 6.79 g of fat, 6.65 g of total dietary fiber, and 3.36 g of β-glucan while 70 g of instant white rice flakes provided 270 kcal, 1.12 g of fat, 0.42 g of total dietary fiber, but no β-glucan (Table 1).

Each group was asked to consume 2 regular meals along with the provided oat-based or rice-based meal for breakfast daily. During the first 4-week intervention period, 70 g of instant oat flakes were given to treatment group A and 70 g of instant white rice flakes were given to treatment group B. The subjects were asked to prepare their breakfast, oat porridge or rice porridge, by mixing the provided ingredient with 160 ml of hot water and then set aside for 1-2 minutes before consuming. The dietary intervention was switched after the first 4 week period was completed – treatment group A switched to rice porridge and group B to oat porridge.

Dietary assessment

To perform dietary assessment, the subjects were assigned to record the type and amount of food and beverage they consumed for 3 days; 2 weekdays and 1 weekend day, before and at the end of each intervention period. Portion size of food was estimated using standard household measures i.e. tablespoon, teaspoon, and cup. The recorded data was then analyzed by the computer analysis program; INMUCAL-Nutrients program.

Anthropometric assessment

A bioelectrical impedance analyzer; BIA (model HBF-356, Omron) was used to determine individual body weight and body composition; body fat percentage and visceral fat. Every Monday, the subjects body weight was recorded. Body composition waist circumference at umbilicus level was assessed before starting and at the end of each intervention period. To define level of obesity, body mass index (BMI) was calculated using individual weight in kilograms and height in meters.

Biochemical analysis

Blood was obtained from all subjects before and after each of the intervention periods. Before collecting blood, subjects were asked to fast for 12 hours overnight. Blood samples were stored in lithium-heparin tubes prior to assessing levels of inflammatory markers and oxidative stress.

The measurement of high sensitivity C-reactive protein (hsCRP) concentrations were performed through latex immunoturbidimetry method.[15] Tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), interleukin-8 (IL-8), and monocyte chemoattractant protein-1 (MCP-1) were determined by enzyme-linked immunosorbent assay (ELISA) technique.[16] Oxygen radical absorbance capacity (ORAC) and ferric reducing ability of plasma (FRAP) were evaluated according to Fernández-Pachón MS. et al.[17] Analysis of Malondialdehyde (MDA) was performed by thiobarbituric acid reactive substances assay.[18]

Statistical analysis

Levels of inflammatory markers and antioxidant capacity at baseline and after each of the interventions oat porridge consumption and rice porridge consumption were statistically compared using paired t-tests. The comparison between the levels after consumption of oat porridge and rice porridge was also analyzed using paired t-tests. To determine the differences in changes between each treatment, a One-way repeated-measures analysis of variance (ANOVA) was conducted. p-value <0.05 was statistically significant.

RESULTS

Twenty-four subjects completed this study. There were no significant differences in nutrients and energy intake, and anthropometry; body weight, body fat percentage, visceral fat, waist circumference and body mass index between baseline, oat consumption and rice consumption period.[19]

Levels of inflammatory markers and antioxidant capacity at baseline, and after each intervention with oat porridge and rice porridge, are shown in Table 2. After consuming oat porridge, levels of inflammatory markers including hsCRP, IL-6, IL-8, and TNF-α were significantly decreased (p<0.05) compared to the levels at baseline and after rice porridge consumption. However, no significant difference was observed in the levels of monocyte chemoattractant protein-1 (MCP-1). Significant difference was observed in antioxidant capacity parameters: oxygen radical absorbance capacity (ORAC) and ferric reducing ability of plasma (FRAP). ORAC and FRAP levels were also significantly increased after oat

porridge consumption (p<0.01). However, malondialdehyde (MDA) levels were remarkably elevated after consuming rice porridge (p<0.05).

Comparison of mean and percent changes of inflammatory markers and antioxidant capacity from baseline through the end of each intervention are shown in Table 3. Mean and percent changes in IL-6, IL-8, TNF-α, ORAC, FRAP, and MDA levels after oat porridge consumption versus rice porridge consumption were significantly different (p<0.05). Moreover, there was a significant difference found in mean change of hsCRP levels. However, both mean change and percent change of MCP-1 level after consuming oat porridge did not differ from the levels after consuming rice porridge (p=0.61).

DISCUSSION

Cardiovascular disease (CVD) was ranked as one of the most common chronic diseases in Thailand. Inflammation and oxidation of lipoprotein have been found to be a notable risk factor for CVD.[20] Studies have revealed possible correlations between whole grain consumption such as oat and cardiovascular disease.[21-22] Accordingly, this randomized controlled crossover study investigated the effect of oat porridge, that contains anti-inflammatory properties and antioxidant bioactive compounds, on levels of inflammatory markers and antioxidant capacity among 24 hypercholesterolemic Thai adults.

Subjects maintained well-controlled eating patterns and exercise habits throughout the study period, and hence, their body weight, body mass index and body fat percentage remained constant through the study period. Triglyceride and HDL-cholesterol levels of subjects at baseline, and during the oat intervention period were not significantly different. In contrast, mean and percent changes in LDL-cholesterol and total cholesterol decreased significantly after oat consumption (p<0.05) by 10% and 5% respectively but did not change after rice porridge consumption.[19]

Results from this study indicate that IL-6, IL-8, and TNF-α measures significantly dropped after consuming oat porridge for 4 weeks by 16%, 20%, and 17%, respectively (p<0.001). This impact could be due to the potential function of avenanthramide, the most abundant antioxidant compound found in oats. Previous studies suggest an athero-protective effect of avenanthramide on anti-inflammation and anti-oxidation.[14,23] Chen et al (2005) reported that flavonoids may block the expression of vascular endothelial cell adhesion molecules and cytokines via inhibition of nuclear factor kappa B (NF-kB) signaling in keratinocytes, thus reducing the expression of several pro-inflammatory proteins.[23,24] Our findings were also consistent with the cell studies of avenanthramide. The researchers reported that after

avenanthramide was added to the assay, levels of IL-6, IL-8, and MCP-1 were decreased.11 In addition to avenanthramide, beta-glucan (β-glucan), the dietary fiber found in oats is linked with reduction in inflammation and lipid peroxidation as well.[25] Also, Bedirli et al. revealed that β-glucan completely blocked the elevation of plasma IL-6 and TNF-α.[26] Hence, β-glucan contained in oat may have partially affected inflammatory markers levels and antioxidant capacity in this study.

Inflammatory markers including hsCRP, IL-6 and TNF- α were associated with a an increase in total cholesterol, and LDL cholesterol and lower HDL.[27] Also, oxidative stress particularly oxidized LDL was positively correlated with total cholesterol, LDL cholesterol and triglyceride levels.[28] However, the mechanism is not entirely clear. Further studies are needed to assess this correlation. Capacity of antioxidant evaluated by oxygen radical absorbance capacity (ORAC) and ferric reducing ability of plasma (FRAP) were significantly developed after oat consumption by 14% and 22%, respectively (p<0.001 for all). Consistently, malondialdehyde (MDA), an oxidative stress marker, was remarkably decreased by 5% (p=0.008) from the level at baseline. Belobrajdic et.al conducted the study to assess the impact of wheat bran and barley on markers of oxidative stress and inflammation in lean and obese Zucker rats. In comparison to the control diet, wheat bran and barley-based diets increased antioxidant capacity of serum lipid-soluble antioxidants. However, the elevation in serum antioxidant capacity determined by ORAC in wheat bran and barley-fed obese rats did not reduce the amount of oxidized lipids in plasma measured by MDA, or increase glutathione peroxidase activity.[29] The antioxidants in oats have the potential to limit LDL oxidation and prevent the important first stage in the development of atherosclerosis. Avenanthramides, the alkaloids containing phenolic groups, are most abundant in oats and are concentrated in the outer layers of the kernel, and are known to exhibit antioxidant activity[30] *in vitro*[31] and *in vivo*.[32]

Avenanthramide extracted from oat has also been seen to prevent the first stage in the development of atherosclerosis and inhibit inflammatory cytokines produced by human aortic endothelial cells.[33] This indicates that the reduction of oxidized lipids in plasma might be due to the unique function of avenanthramides, which is only found in oat. Additionally, the results after rice porridge consumption confirm the potential beneficial effect of oat for anti-inflammation and anti-oxidation. Compared to the levels at baseline, there no significant differences were found in any of the studied markers, except MDA. Also, these observed levels after rice porridge consumption were higher than the levels observed after oat

consumption. These results were consistent with previous studies which reported that whole grain oat has 2 to 3 times more antioxidant components compared to rice.[7,34]

A limitation of this study is that it was only conducted in hypercholesterolemic adults. More studies in other subjects for e.g. obese or hyperglycemic subjects, would be beneficial to ensure the effect of oat on inflammation and oxidative stress. However, this study had a reasonable number of participants in a crossover design. The advantage of crossover design is that it helped reduce confounding covariates as each subject served as her/his own control. Hence, the number of subjects was also statistically efficient and fewer subjects were required versus a non-crossover design.

Conclusions

Daily consumption of oat porridge containing 3g of beta-glucan for 4 weeks was shown to decrease inflammatory marker levels including hsCRP, IL-8, IL-6, and TNF-α level; and increase antioxidant, ORAC and FRAP levels; while consumption of rice porridge did not lead to significant changes in these measures. These findings suggest that oat porridge consumption has the potential to improve inflammation and oxidative stress, the risk factors for cardiovascular disease, in hypercholesterolemic Thais. Oat consumption, therefore, may be an appropriate dietary recommendation for individuals with hypercholesterolemia.

CONFLICT OF INTEREST AND FUNDING DISCLOSURE

The authors declare no conflict of interest. This research was supported by PepsiCo Thailand. The study was partially supported for publication by the China Medical Board (CMB), Faculty of Public Health, Mahidol University, Bangkok, Thailand. The views expressed in this manuscript are those of the authors and do not necessarily reflect the position or policy of PepsiCo Inc.

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Table 1. Nutrients and energy of instant oat flake and rice flake

Nutrients	Oat flake (70 g)	Rice flake (70 g)
Energy (kcal)	289.80	269.50
Total dietary fiber (g)	6.65	0.42
Total fat (g)	6.79	1.12
Saturated fat (g)	1.18	0.43
Monounsaturated fat (g)	2.61	0.25
Polyunsaturated fat (g)	2.07	0.27
Protein	8.55	5.25
Carbohydrate (g)	48.86	59.57
Calcium; Ca (mg)	32.27	4.28
Iron; Fe (mg)	2.52	0.57
Potassium; K (mg)	234.14	63.15
Sodium; Na (mg)	4.20	57.79
Vitamin E; alpha tocopherol (mg)	0.22	8.21
β-glucan (g)	3.36	-

Table 2. Comparison of inflammatory markers and antioxidant capacity of the subjects at baseline and after oat porridge and rice porridge consumption for 4 weeks[†]

Markers	Baseline (n=24)	Oat porridge consumption (n=24)	Rice porridge consumption (n=24)	*p*-value
hsCRP, mg/L	2.7±2.1[a]	2.2±1.7[b]	2.9±2.9[a]	<0.05
IL-6, pg/mL	149.7±57.9[a]	122.71±44.5[b]	144.7±54.0[a]	<0.01
IL-8, pg/mL	285.7±78.7[a]	229.46±64.9[b]	278.9±76.7[a]	<0.01
TNF-α, pg/mL	49.5±26.4[a]	39.83±15.9[b]	47.4±24.1[a]	<0.01
MCP-1, pg/mL	191.2±19.9[a]	188.38±24.7[a]	189.6±20.6[a]	0.61
ORAC, µmol of Trolox/L	20.1±5.0[a]	22.8±5.3[b]	19.9±4.6[a]	<0.01
FRAP, µmol of Fe^{2+}/L	11.47±1.4[a]	13.90±1.4[b]	11.42±1.3[a]	<0.01
MDA, nmol/L	959.8±432.2[a]	875.1±287.9[a]	1096.9±422.5[b]	<0.05

[†]Different superscripts denote significant differences between groups at 95% confidence interval (CI).

Table 3. Comparison of mean and percent change in inflammatory markers and antioxidant capacity between the subjects after oat porridge consumption and after rice porridge consumption from baseline values

Markers		Oat porridge consumption (n=24)	Rice porridge consumption (n=24)	*p*-value
hsCRP, mg/L	Mean change	-0.6±0.9	0.2±1.5	0.031
	Percent change	-16.9±32.3	18.5±115.5	0.076
IL-6, pg/mL	Mean change	-26.9±27.6	-4.9±12.8	<0.001
	Percent change	-15.9±13.9	-1.7±12.3	<0.001
IL-8, pg/mL	Mean change	-56.3±27.6	-6.8±28.2	<0.001
	Percent change	-19.7±8.0	-2.2±8.3	<0.001
TNF-α, pg/mL	Mean change	-9.7±11.6	-2.1±5.0	<0.001
	Percent change	-17.2±8.3	-3.3±10.4	<0.001
MCP-1, pg/mL	Mean change	-2.8±9.7	-1.6±11.1	0.612
	Percent change	-1.7±5.3	-0.7±5.9	0.480
ORAC, µmol of Trolox/L	Mean change	2.7±1.0	-0.2±1.6	<0.001
	Percent change	13.8±5.8	-0.3±7.9	<0.001
FRAP, µmol of Fe^{2+}/L	Mean change	2.4±0.8	-0.1±0.5	<0.001
	Percent change	21.8±8.0	-0.2±4.6	<0.001
MDA, nmol/L	Mean change	-84.8±267.2	137.0±390.6	0.021
	Percent change	-4.8±21.4	25.3±50.7	0.008

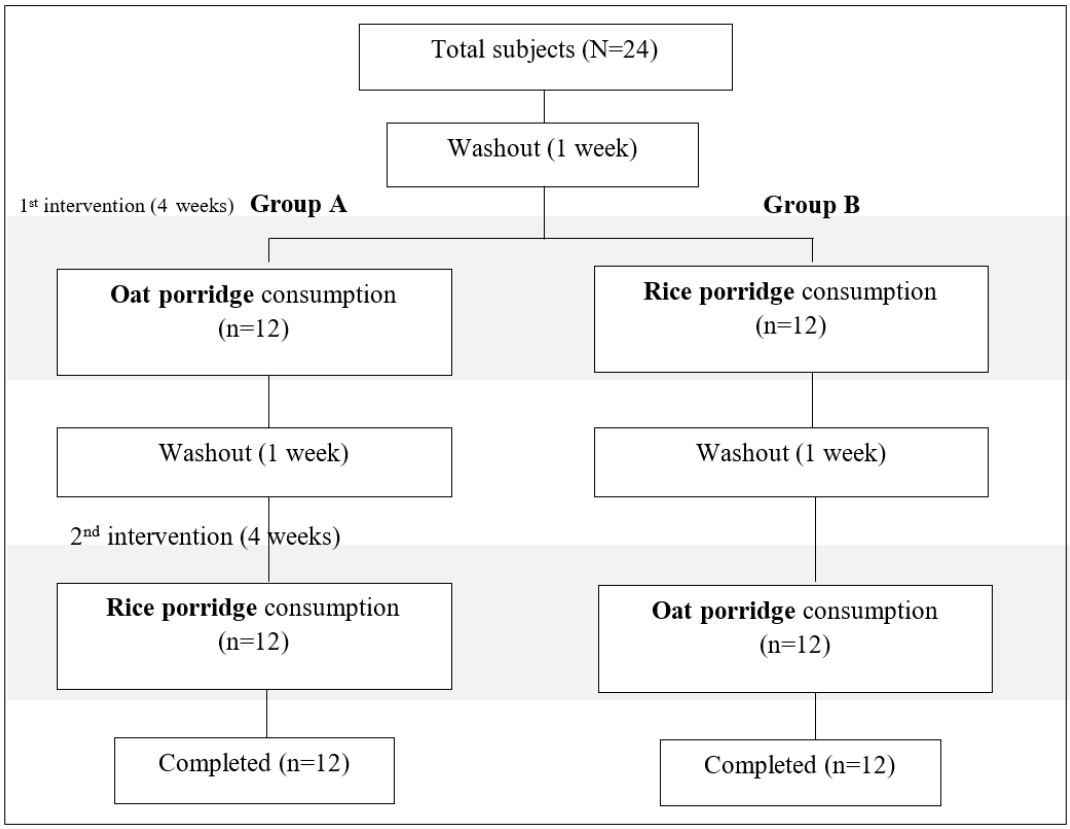

Figure 1. Dietary intervention