Down-regulation of partial substitution for staple food by oat noodles on blood lipid levels: A randomized, double-blind, clinical trial

Miao-Yu Liaoa,b, You-Cheng Shen c, Hui-Fang Chiu d, Siew-Moi Ten e, Yan-Ying Lu f, Yi-Chun Han e, Kamesh Venkatakrishnan e, Shun-Fa Yang a,g,*,1, Chin-Kun Wang e,*,**

a Institute of Medicine, Chung Shan Medical University, 110, Sec. 1, Jianguo North Road, Taichung City, 40201, Taiwan
b Department of Family Medicine, Taichung Hospital Ministry of Health and Welfare, Taichung, 40301, Taiwan
c School of Health Diet and Industry Management, Chung Shan Medical University, 110, Sec. 1, Jianguo North Road, Taichung City, 40201, Taiwan
d Department of Chinese Medicine, Taichung Hospital Ministry of Health and Welfare, Taichung, 40301, Taiwan
e School of Nutrition, Chung Shan Medical University, 110, Sec. 1, Jianguo North Road, Taichung City, 40201, Taiwan
f Department of Neurology, Chung Shan Medical University Hospital, 110, Sec. 1, Jianguo North Road, Taichung City, 40201, Taiwan
g Department of Medical Research, Chung Shan Medical University Hospital, 110, Sec. 1, Jianguo North Road, Taichung City, 40201, Taiwan

A B S T R A C T

This clinical trial was conducted to assess the lipid-lowering activity of oat noodles by replacing partial staple food (wheat or rice noodle) in normal and mildly hypercholesterolemic subjects. Totally 84 healthy and mild hypercholesterolemic subjects were recruited and divided into 2 groups as experimental (oat noodles) and placebo (wheat noodles) and instructed to consume 100 g of oat noodles or wheat noodles (replacing one or two meals/day) for 10 weeks and followed by 2 weeks of follow up (without noodle consumption). Various anthropometric measurements and biochemical analysis were carried out during initial (baseline), 2nd, 6th, 10th and 12th week (follow-up). Consumption of oat noodles by replacing staple food for 10 weeks significantly reduced (**p < 0.01) the levels of total cholesterol (TC; 17.46%) and low-density lipoprotein LDL-c (19.03%) in both healthy and mildly hypercholesterolemic subjects. However, the hypocholesterolemic effect is significantly higher in mildly hypercholesterolemic subjects as compared with normal subjects. A pronounced decline (*p < 0.05) in the levels of various cardiovascular diseases (CVDs)
markers including TC/HDL and LDL/HDL ratios and blood pressure (SBP; 11.09% and DBP; 7.48%) were observed in oat noodles supplemented subjects as equivalence with the placebo group. The partial replacement of staple food with oat noodle could considerably improve the health status of all subjects especially in hypercholesterolemic subjects and thus lower the risk of CVDs.

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1. Introduction

Elevated cholesterol level (hypercholesterolemia) and hypertension are the pivotal contributor (risk factor) for various cardiovascular diseases (CVDs) [1,2]. World health organization (WHO) predicted that CVDs alone would claim more than 23.3 million of lives by the year 2030 [3]. Several reports have demonstrated that hypercholesterolemia can be modifiable by altering lifestyle through balanced diet with high dietary fibers and regular exercise [4,5]. Moreover, numerous meta-analysis studies have demonstrated that consumption of cereals like oats, barley (nutraceuticals) rich in fibers could considerably lower the lipid/cholesterol levels and thus reduce the risk of CVDs [6,7]. The major contributor to the hypolipidemic activity of these cereals (oat/barley) are β-glucan, which is a viscous soluble fiber (linear polysaccharide) and aids in lipid digestion (excretion) owing to its structural and fermentable property [2,8]. Also, US Food and Drug administration (FDA) has recommended a dose of 3 g/day (β-glucan) is sufficient to elite its biological properties [9,10].

Noodles and its related products are the staple food in many Asian countries like China, Japan, Korea and Taiwan. Noodles are made from simple ingredients like wheat, rice, starch (potatoes, tapioca) with salt and water [11]. However, these noodles lack the essential nutritional components like vitamins, minerals, and fibers [12]. To overcome this problem researchers started to incorporate/enrich the wheat flour with few cereals/food crops like oats, buckwheat, sorghum, banana, beans (unique noodle products) to enhance the nutritive value, flavor and texture [13,14]. Hence, for our study, we used the oat noodle (oat + wheat flour) rich in β-glucan, minerals, and vitamins. Since, oat contains high levels of essential amino acids, unsaturated fatty acids, vitamin B, E and magnesium, potassium, calcium [15–17]. Moreover, numerous reports have shown that dietary oat (rich in β-glucan) can lower the cholesterol level and subsequent the incidence of CVD, obesity, and diabetic mellitates [18,19].

Even though extensive studies have been carried out with oat related to the cholesterol-lowering activity, but the results are still controversial; few researchers showed no significant change in lipid profile after consumption of oats [5,20,21]. Whereas, few researchers have demonstrated the lipid/cholesterol-lowering activity of oats [2,22]. The reason for controversial results are due to the cultivator of oat (growing condition, processing procedure) and the ethnicity of the population, as well as the mode of supplementation, might influence the properties as well as the contents of β-glucan [21,23]. In addition, no clinical trials are conducted till date with oat noodles as compared with wheat noodles (placebo). Therefore, this clinical trial was conducted to examine the lipid-lowering activity of oat noodles by replacing partial staple food (wheat or rice noodle) in mildly hypercholesterolemic subjects.

2. Materials and methods

2.1. Noodles or samples

Oat noodles and wheat noodles were provided by Quaker (Standard Food Corporation, Taipei, Taiwan). The oat noodles (100 g; 366 kcal) were made from 80% of oat (with 3.12 g of β-glucan), and 20% of wheat flour (75% carbohydrate, 15% protein and 10% fat) and its full composition were listed in Table 1. Whereas placebo (wheat noodles-100 g; 190 kcal) contains 100% wheat flour, sodium, dextrose, starch with 70% carbohydrate, 18% protein and 12% fat. Both noodle samples

| Nutrients          | Unit  | Contents |
|--------------------|-------|----------|
| Energy (kcal)      |       | 410      |
| Water (g)          |       | 9.4      |
| Crude protein (g)  |       | 10.3     |
| Crude fat (g)      |       | 10.3     |
| Carbohydrate (g)   |       | 68.7     |
| Crude fiber (g)    |       | 1.7      |
| Dietary fiber (g)  |       | 12.0     |
| Ash (g)            |       | 1.3      |
| Cholesterol (mg)   |       | –        |
| Vitamin A (RE)     |       | 0.05     |
| Vitamin E (α-TE)   |       | 0.69     |
| Vitamin B1 (mg)    |       | 0.53     |
| Vitamin B2 (mg)    |       | 0.07     |
| Niacin (mg)        |       | 0.86     |
| Vitamin B6 (mg)    |       | 0.15     |
| Vitamin B12 (ug)   |       | –        |
| Vitamin C (mg)     |       | 23.5     |
| Sodium (mg)        |       | 3        |
| Potassium (mg)     |       | 290      |
| Calcium (mg)       |       | 11       |
| Magnesium (mg)     |       | 105      |
| Phosphorus (mg)    |       | 424      |
| Iron (mg)          |       | 4.4      |
| Zinc (mg)          |       | 1.9      |

Table 1 – Composition of oat (per 100 g).
were packed in a similar kind of bag (same size and shape) as it’s a double-blind study.

2.2. Subject recruitment

This single centered, double-blind, placebo-controlled, randomized, clinical trial was conducted at Chung Shan Medical University Hospital, Taichung, Taiwan from Aug 2016 to Dec 2016. This experimental protocol was approved by the institutional ethical review board of Chung Shan Medical University Hospital, Taichung, Taiwan (CS03029) and conducted according to the guidelines laid down in the Declaration of Helsinki (2008). For the current clinical trial, 104 healthy normal subjects (without any heath issue) and healthy mild hypercholesterolemic subjects (aged between 35 and 70) are recruited by flyer posted in the public places and Chung Shan Medical University Hospital. Taiwan. Initial assessment was carried out by questionnaires (medical history, work and lifestyle patterns), followed by biochemical analysis (lipid profile/liver function test/renal function test/hematological parameters) to ensure the health status of each individual as we recruited only healthy normal and mild hypercholesterolemic subjects (180–220 mg/dL) a crucial inclusion criteria. Also, the exclusion criteria are the history of CVD, treated for hypertension or hyperlipidemia, diabetic mellites, chronic renal, hepatic disorders, allergic to cereals, adherence to specific diet, lactating or pregnant women. Based on the above inclusion and exclusion criteria only 84 eligible healthy normal and mild hypercholesterol- emic subjects were enrolled into our trial.

2.3. Study design

Those enrolled 84 subjects (48 mild hypercholesterolemic subjects and 36 are normal subjects) aged between 38 and 76 were randomly divided (by computerized coding) into two groups as experimental (oat noodles: 3.12 g of β-glucan) and placebo (wheat noodles) and instructed to consume 100 g of oat noodles [(n = 42) with 25 hypercholesterolemic subjects and 17 normal subjects] or wheat noodles [(n = 42) with 23 hypercholesterolemic subjects and 19 normal subjects] by partially replacing the staple food (one or two meals every day) for 10 consecutive weeks and followed by 2 weeks of follow up period without noodle consumption to monitor the impact of oat noodles.

All the subjects are asked to avoid supplementations/oat related products or any medications throughout the intervention. Also, request to follow their usual lifestyle activities during the intervention. Anthropometric measurements (body weight, BMI, body fat by Omron body composition monitor; Kyoto, Japan), blood pressure (SBP and DBP by Omron M7 Intelli IT; Kyoto, Japan) and biochemical analysis (serum—lipid profile) were carried out during initial (baseline), 2nd, 5th, 10th and 12th week (follow-up). Written consent was signed by each subject before the intervention. At the end of the intervention, 5 subjects from each were dropped out due to personal issues and illness. Hence, only 74 subjects completed the intervention with the average consumption rate of 89.50% (placebo group) and 87.71% (Oat group). None of the subjects experience any adverse effect upon consumption with either oat (experimental) or wheat (placebo) noodles. The flow chart of the current study was illustrated in Fig. 1.

2.4. Blood sample collection

Blood samples were collected from overnight fasting subjects by venipuncture and collected in tubes and allow the blood to clot by leaving undisturbed for 15 min. Then the clotted blood samples are centrifuged at 2000 × g for 10 min at 4 °C, and the resultant supernatant (serum) was used for biochemical analysis.

2.5. Biochemical analysis

Serum lipid profile like total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-c) and low-density lipoprotein cholesterol (LDL-c) were evaluated by using commercial lipid profile kit from Roche Diagnostics (Mannheim, Germany) with the help of Shimadzu 7600 fully automated analyzer (Shimadzu Corp; Kyoto, Japan).

2.6. Statistical analysis

Values are expressed as a mean ± standard error of the mean (SEM). Data are analyzed by the Statistical Package for the Social Sciences (SPSS) version 23.0 (SPSS Inc., IBM, USA) using paired t-test to compare the difference within each group from baseline (initial). All statistical results with a p-value of less than 0.05 were considered as statistically significant.

3. Results

3.1. Anthropometric measurements

Effect of oat or wheat noodles on anthropometric measurements in healthy normal and mild hypercholesterolemic subjects is shown in Table 1. Ten weeks of supplementation with oat or wheat noodles at breakfast did not exhibit any considerable change in any of the anthropometric parameters (body weight, body fat, BMI). A similar trend was also noted in follow-up period as well.

3.2. Lipid profile

Table 3 presented the effect of oat or wheat noodles on serum lipid profile in healthy normal and mild hypercholesterolemic subjects. A notable reduction (**p < 0.01) in the levels of total cholesterol TC (17.46%) and LDL-c (19.03%) were noted in oat group on 10th week as compared with initial (0 week). However, no substantial changes were noted in TG or HDL-c levels. However, preventing of supplementation with oat noodle (follow up), the levels of TC and LDL-c were considerably increased.

Since both normal and hypercholesterolemic subjects are recruited for this study, we separated the normal and
Fig. 1 – Portrait the schematic representation of current trial.

Table 2 – Effect of oat noodles or placebo on anthropometric measurements in healthy normal and mild hypercholesterolemic subjects.

| Parameters | Placebo group (n = 37) | Experimental group (n = 37) |
|------------|------------------------|-----------------------------|
|            | Initial | 10th week | Follow-Up | Initial | 10th week | Follow-Up |
| BW (Kg)    | 58.24 ± 2.83 | 58.11 ± 2.07 | 58.17 ± 2.91 | 58.66 ± 2.09 | 58.36 ± 2.17 | 58.36 ± 2.17 |
| BMI (Kg/m²) | 23.66 ± 0.69 | 23.63 ± 0.77 | 23.65 ± 1.23 | 23.38 ± 0.62 | 23.53 ± 0.61 | 23.53 ± 0.61 |
| BF (%)     | 28.63 ± 1.55 | 28.24 ± 1.66 | 28.40 ± 2.22 | 29.73 ± 2.02 | 28.59 ± 1.18 | 28.59 ± 1.18 |

Values are expressed as mean ± SEM. BW: Body weight, BMI: Body mass index, BF: Body fat.

Table 3 – Effect of oat noodles or placebo on serum lipid profile in healthy normal and mild hypercholesterolemic subjects.

| Periods | Experimental group (n = 37) | Placebo group (n = 37) |
|---------|-----------------------------|------------------------|
|         | Initial | 2nd week | 6th week | 10th weeks | Follow-up |
| TC (mg/dL) | 192.32 ± 7.64 | 179.95 ± 5.53* | 172.00 ± 6.68* | 158.74 ± 7.11** | 181.76 ± 5.42 |
| HDL-C (mg/dL) | 53.15 ± 2.14 | 51.18 ± 2.12 | 50.24 ± 1.82 | 48.41 ± 1.75 | 51.84 ± 1.77 |
| LDL-C (mg/dL) | 129.97 ± 5.98 | 117.97 ± 5.14* | 116.69 ± 5.69* | 105.23 ± 5.99** | 124.00 ± 5.05 |
| TG (mg/dL) | 112.26 ± 10.95 | 109.44 ± 8.47 | 112.24 ± 8.26 | 105.12 ± 8.95 | 117.78 ± 9.00 |

Values are expressed as mean ± SEM. *p < 0.05; **p < 0.01 was considered significantly different as compared with initial for each parameter in each group. TC: Total Cholesterol, HDL-c: High density lipoprotein cholesterol, LDL-c: Low density lipoprotein cholesterol, TG: Triglyceride or Triacylglycerol.
hypercholesterolemic subjects (data) in each group and explored the impact of oats or wheat noodles (Fig. 2). We found an interesting outcome, that intake of oats by hypercholesterolemic subjects showed a significant reduction (**p < 0.001) in levels of TC and LDL-c levels as compared to the initial period. Whereas in normal subjects consumed oat noodles also significantly lowered (*p < 0.05) the levels of TC and LDL-c levels as compared to the initial period. Nevertheless, an oat administrated group in hypercholesterolemic subjects showed superior lipid-lowering activity than in normal subjects.

### 3.3. CVDs marker ratios

Table 4 represented the effect of oat noodles on CVDs marker ratios in healthy normal and mild hypercholesterolemic subjects. A significant decrease (**p < 0.001) in the levels of various CVDs ratio markers like TC/HDL-c (3.61–3.37) and LDL-c/HDL-c (2.44–2.17) are noted in the oat intook group. While placebo (wheat noodle) consumed, group, did not show any significant difference as compared with baseline.

### 3.4. Blood pressure

The effect of oat or wheat noodles on blood pressure in healthy normal and mild hypercholesterolemic subjects are indicated in Table 4. The levels of both SBP (11.09%) and DBP (7.48%) were considerably lowered (**p < 0.01) upon replacing (breakfast) with oat noodle for 10 consecutive weeks. No marked difference was noted in the follow-up period, and this indicates the hypotensive activity of oats. In all the

### Table 4 – Effect of oat noodles or placebo on ratios and blood pressure in healthy normal and mild hypercholesterolemic subjects.

| Periods               | Initial  | 2nd weeks | 6th weeks | 10th weeks | Follow-up |
|-----------------------|----------|-----------|-----------|------------|-----------|
| **Experimental group (n = 37)** |          |           |           |            |           |
| TC/HDL-C              | 3.61 ± 0.15 | 3.47 ± 0.13 | 3.48 ± 0.14 | 3.27 ± 0.13* | 3.50 ± 0.14 |
| LDL-C/HDL-C           | 2.44 ± 0.13 | 2.30 ± 0.13* | 2.32 ± 0.12 | 2.17 ± 0.13* | 2.39 ± 0.13 |
| SBP (mmHg)            | 126.23 ± 3.81 | 118.23 ± 3.28** | 117.64 ± 3.02** | 112.38 ± 4.12** | 121.20 ± 4.04 |
| DBP (mmHg)            | 78.91 ± 1.89 | 76.09 ± 2.25 | 73.69 ± 1.84* | 73.00 ± 2.31* | 75.33 ± 2.39 |
| **Placebo group (n = 37)** |          |           |           |            |           |
| TC/HDL-C              | 3.39 ± 0.15 | 3.40 ± 0.13 | 3.50 ± 0.14 | 3.51 ± 0.15 | 3.46 ± 0.14 |
| LDL-C/HDL-C           | 2.34 ± 0.15 | 2.24 ± 0.12 | 2.38 ± 0.12 | 2.34 ± 0.13 | 2.238 ± 0.12 |
| SBP (mmHg)            | 116.95 ± 2.42 | 120.00 ± 2.45 | 120.43 ± 2.93 | 119.50 ± 3.03 | 118.80 ± 3.29 |
| DBP (mmHg)            | 77.73 ± 2.07 | 74.05 ± 2.13 | 73.75 ± 2.04 | 73.33 ± 1.76 | 73.86 ± 1.99 |

Values are expressed as mean ± SEM. *p < 0.05; **p < 0.01 was considered significantly different as compared with initial for each parameter in each group. SBP: Systolic blood pressure, DBP: Diastolic blood pressure.
above-mentioned parameters, no significant changes were observed in the placebo group.

4. Discussion

Daily consumption of oat noodles for 10 weeks by substituting with other staple food (wheat or rice noodle, rice) would significantly decrease the lipid profile as well as blood pressure in both normal and mild hypercholesterolemic subjects. However, the reduction in mild hypercholesterolemia is superior to normal subjects. The outcome of this study clearly showcased that the presence of increased dietary fiber (β-glucan) after consumption of oat noodle might contribute to the hypolipidemic or hypocholesterolemic activity. Intake of oat or wheat noodles for 10 weeks did not show any significant change in the anthropometric parameters (body weight, body fat, BMI). The reason behind the insignificant data is probably due to the enrollment of only healthy and mild hypercholesterolemic subjects. This result was consistency with the finding of Romero and his colleagues, who also inferred that consumption of cookies enriched with oat bran did not exhibit a significant change in BMI, body fat or weight in normal and mild hypercholesterolemic men from Mexico [24].

Clinical studies have shown that every 1% reduction in total cholesterol is directly correlated with a 2% reduction in CVD risk [25]. Serum lipid profile (TC < TG, HDL-c, and LDL-c) were determined to explore the hypocholesterolemic activity of oat noodles. The levels of TC and LDL-c were markedly abolished after supplementation with oat noodles. Nevertheless, no changes were observed in TG or HDL-c levels. Our results were in agreement with the outcomes of Bell and his co-workers as well as Brown et al. [26,27]. Available data portrayed that only modest significant changes in lipid levels were noted in oat groups as it had both normal and hypercholesterolemic subjects. Hence, the oat and placebo group were further divided into hypercholesterolemic and normocholesterolemic groups to explore the in-depth hypocholesterolemic or hypolipidemic effect of oat noodles.

The results in oat groups with hypercholesterolemic patients showed relatively better hypocholesterolemic activity (lowering TC and LDL-c) than normocholesterolemic subjects. Treatment with oat bran (6 g of β-glucan) in bread for 8 weeks could significantly reduce the total cholesterol and LDL-c in mildly hypercholesterolemic subjects [28]. Likewise, Zhang and his colleagues, supplemented 100 g of oat (3.6 g of soluble fiber) and found a significant reduction in the levels of total cholesterol and LDL-c in urban Chinese adults with hypercholesterolemia [22].

The above hypolipidemic activity of oat noodles might be due to the presence of β-glucan, which is reported to inhibit the lipid absorption can enhance fecal cholesterol and bile acid excretion [7,29]. Also, it upregulates the expression of LDL-R in hepatic tissue and thereby uptake more amount of TC and LDL-c [30]. In addition, β-glucan are reported to suppress the insulin secretion and thus halt the endogenous cholesterol synthesis [31,32]. Furthermore, the protein and lipid contents in oat might also be responsible for the cholesterol-lowering activity. Guo and his coworkers, also hinted that protein and lipid present in the oat could contribute to the hypocholesterolemic activity [15].

The lipemic or CVDs markers such as LDL/HDL and TC/HDL ratios are used to estimate the cardiovascular risk [33,34]. Similar impression as that of lipid profile was noted in the levels of various CVDs ratio markers like TC/HDL-c, and LDL-c/HDL-c in the oat consumed subjects. Behall and his coworkers, also reported that intake of barley (rich in β-glucan) could significantly reduce the levels of LDL/HDL and TC/HDL ratios in mildly hypercholesterolemic men and women [35]. The above data indicates the hypocholesterolemic activity of oats noodle in both healthy normal and mild hypercholesterolemic subjects.

The effect of hypercholesterolemia on hypertension is based on several mechanisms mainly oxidative stress, endothelial dysfunction, vascular inflammation and altered renin-angiotensin-aldosterone system [36,37]. Since mild hypercholesterolemic subjects are recruited for this study, we would like to assess the blood pressure (SBP/DBP) after the consumption of oat or wheat noodles. A considerable decline in the levels of SBP and DBP were noted upon supplementation with oat noodle for 10 consecutive weeks. The reduction in BP is might be due to the anti-inflammatory, antioxidant and hypolipidemic activity of oats [38,39]. Likewise, Keenan and his coworker, reported that intake of oat could lower the systolic and diastolic blood pressure [40]. A meta-analysis of randomized clinical trials conducted by Khan et al. with soluble fiber (β glucan) on blood pressure also concluded that supplementation of various types of soluble fiber could considerably lowered SBP and DBP and thereby reduce the CVD risk [41]. The major limitation of this study is the limited number of subjects, as well as the inclusion of only healthy normal and mild hypercholesterolemic subjects and hence no significant changes, were observed in few parameters (anthropometric). Moreover, lack of data related to Apo proteins, Ox-LDLc and the activities of lipid metabolizing enzymes.

5. Conclusion

To conclude, consumption of oat noodle by partially replacing staple food (breakfast) for 10 weeks could significantly decrease the lipid profile as well as blood pressure in both normal and mild hypercholesterolemic subjects and thus considerably improve the health status of all subjects especially in hypercholesterolemic subjects and thereby lower the risk of CVDs. Further studies are required to explore the molecular weight of β glucan present in the oat noodles, and its molecular mechanism underlying the hypolipidemic or hypocholesterolemic activity need to be evaluated.

Conflict of interest

No conflict of interest to declare.
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