Effect of Psyllium Supplementation on Insulin Resistance and Lipid Profile in Non-diabetic Women With Polycystic Ovary Syndrome: A Randomized Placebo-Controlled Trial

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Abstract
Objectives: Polycystic ovary syndrome (PCOS) is the most common cause of infertility in women. In addition, the risk of type-2 diabetes mellitus (T2DM), hyperinsulinemia, and insulin resistance is higher among women with PCOS. Psyllium can reduce the levels of fasting blood sugar (FBS), insulin resistance, and lipid profile. Thus, the present study aimed to evaluate the effect of psyllium supplementation on insulin resistance and the lipid profile in non-diabetic women with PCOS.
Materials and Methods: In this randomized double-blind placebo-controlled trial, 54 eligible non-diabetic women with PCOS aged 18-45 were recruited from an endocrinology clinic and divided into 2 groups based on their body mass index (BMI) through stratified-block randomization. Participants in intervention and placebo groups received 5 g of psyllium or cellulose microcrystalline twice a day for 8 weeks. Fasting insulin, FBS, and insulin resistance indicators including HOMA1-IR, HOMA2-IR, along with quantitative insulin sensitivity check index (QUICKI) and the lipid profile were evaluated before and after the intervention.
Results: In the psyllium group, the FBS, fasting insulin, total cholesterol, low-density lipoprotein cholesterol (LDL-C), HOMA1-IR, and HOMA2-IR indicators decreased significantly ($P < 0.05$) after 8 weeks, but the changes were not significant in the placebo group. The mean changes in LDL-C (0.28 ± 0.58 and 0.11 ± 0.67 in intervention and placebo groups, respectively, $P = 0.036$) and QUICKI (0.01 ± 0.03 and 0.02 ± 0.06 in intervention and placebo groups, respectively, $P = 0.044$) were significant between the two groups from the baseline.
Conclusions: Psyllium supplementation decreased FBS, fasting insulin, and the lipid profile while improving insulin resistance in non-diabetic women with PCOS.
Keywords: Psyllium, Polycystic ovary syndrome, Insulin resistance, Lipid profile, Clinical trial

Introduction

Polycystic ovary syndrome (PCOS), as a common metabolic-endocrine disorder, is the main cause of infertility in women (1,2). The prevalence of PCOS was reported 18% based on the Rotterdam criteria in Australia (3). Women with POS often suffer from obesity, hyperandrogenism, and their effects such as hirsutism, acne, and alopecia (4). The pathophysiologic mechanism of PCOS is unclear, but evidence shows reduced insulin sensitivity with hyperinsulinemia among 30%-80% of these women (5). The production of androgen by the ovaries and adrenal glands increases in the presence of hyperinsulinemia (5). In addition, PCOS are associated with a high incidence of hypertension, dyslipidemia, heart disease, visceral obesity, glucose intolerance, insulin resistance, and hyperinsulinemia (6,7). The prevalence of the impaired oral glucose tolerance test in obese women with PCOS is approximately 20% (2). The risk of diabetes mellitus (T2DM) in women with PCOS is 5 to 10 times higher than healthy subjects (5). Studies indicate that 70% of women with PCOS have abnormality at least in one part of their lipid profile because of the negative effect of insulin resistance on the lipid profile (8). A study of women with PCOS showed that lifestyle changes and metformin increase insulin resistance and the number of menstrual cycles while decreasing body mass index (9). Today, the Rotterdam criteria are internationally accepted for the diagnosis of PCOS (3). The angiotensin-converting enzyme (ACE) gene has 3 polymorphisms, the deletion/deletion (DD) genotype of which causes its high activity (10). In the ovarian, there is a renin-angiotensin system but its mechanism is unknown. In addition, it is possible that the high blood pressure associated with the DD genotype from the ACE gene can play a role in the occurrence of PCOS (10).

The husk or the seed of "*Plantago ovata*" or "Psyllium"

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is considered as a bulking agent with 65%-75% total fiber (11,12). As a viscose fiber soluble in water, psyllium forms a gel traditionally used in many countries such as India for the treatment of constipation and irritable bowel syndrome (13-15). Psyllium was also used to treat conditions such as diarrhea, inflammatory bowel disease, and ulcerative colitis (16). As a fiber type, it is well-tolerated and safe for human health (17).

Evidence demonstrates that psyllium can bind to the bile acids in the digestive tract after consumption and inhibit the reabsorption of bile acids in the ileum (18). Therefore, psyllium can reduce cholesterol absorption and be effective in the treatment of mild to moderate hypercholesterolemia (18).

Further, psyllium can correct the insulin and blood glucose levels in people with T2DM (19). However, there are inconsistencies about high-fiber diets lowering blood sugar levels (20).

It is hypothesized that psyllium can reduce the blood glucose levels and lipid profiles while improving insulin resistance with its viscosity properties, gel formation, and changes in motility and absorption in the gastrointestinal tract (14).

Considering the effect of glucose-lowering drugs in insulin resistance in diabetic patients, the present study included non-diabetic women with PCOS to evaluate the effect of psyllium on the glycemic and lipid profile in non-diabetic patients with PCOS. Although several studies in this area have focused on patients with T2DM, no study has evaluated this effect in patients with PCOS. It is likely that hyperinsulinemia is responsible for most PCO symptoms (21). Therefore, this study aimed to evaluate the effect of supplementation with the viscose fiber of psyllium on blood glucose and insulin levels, as well as lipid profiles and insulin resistance in non-diabetic women with PCOS.

Materials and Methods
Study Design
This randomized, double-blind, parallel-group, placebo-controlled trial was conducted on non-diabetic women with PCOS. The possible side effects of taking psyllium were explained to the patients, including stomach pain, diarrhea, constipation, nausea, and headache (22). However, psyllium is a laxative agent with good safety, which has been used for many years (23). After explaining the study conditions, participants gave written informed consent. Moreover, they were assured of the confidentiality of the information and were allowed to discontinue the study at any time. Accordingly, 54 women with PCOS aged 18-45 were recruited from patients who referred to the Endocrine Clinic of Urmia Imam Khomeini University Hospital during September 2016 - January 2017.

Study Population
The inclusion criteria were the Rotterdam criteria (7) and not-diabetic individuals with a fasting blood sugar (FBS) of less than 6.99 mmol/L (126 mg/dL). The diagnosis of PCOS according to the Rotterdam criteria was conducted by an endocrinologist using a blood androgen test and ultrasound ovarian exam. Anyone with 2 of the three characteristics of the Rotterdam criteria (i.e., Oligo or anovulation-clinical and/or the biochemical signs of hyperandrogenism, and polycystic ovaries having 12 or more follicles in size from 2 to 9 mm in diameter) was considered a PCO patient (7). The exclusion criteria involved subjects who received glucose-lowering agents except for metformin, anti-lipids, corticosteroids, antidepressants, lithium, warfarin, carbamazepine, and digoxin. Additionally, subjects with a history of heart, liver, or gastrointestinal diseases, thyroid disorders, type-1 and type-2 diabetes, gastrectomy, congenital adrenal hyperplasia, Cushing's syndrome, hyperprolactinemia, and adrenal tumor secretion were excluded from the study. Based on the mean ± standard deviation (SD) of 1-hour insulin in a previous study (24) with type I error (α) 5% and a power of 90%, along with a 20% drop out, the sample size was calculated 27 subjects in each group by the following formula.

$$n= (Z_{1-\alpha/2} + Z_{1-\beta})^2(S_1^2 + S_2^2) / (\mu_1 - \mu_2)^2$$

Intervention
The participants were divided into intervention and placebo groups using the stratified-block randomization method based on their body mass index (BMI) levels (BMI <18.49, 18.5<BMI<24.99, and 25 <BMI). The participants received 5 g psyllium (intervention group) or microcrystalline cellulose (placebo group) twice a day for 8 weeks. In addition, they were asked to solve the content of each psyllium or placebo sachets in 250 mL of water and then consume it 30 minutes before breakfast and dinner twice a day. The dietary intake was evaluated using 3-day food records at weeks 1 and 7. The sachets of psyllium and placebo were delivered biweekly and the patient's compliance was assessed by checking the number of envelopes returned on each visit.

The body composition measures including height, weight, BMI, fat mass (FM), fat-free mass (FFM), skeletal muscle mass (SMM), and waist to hip ratio (WHR) were measured using a bioelectrical impedance analysis device (BIA) before and after the intervention (InBody 770-BIA).

Blood Sampling
FBS, insulin levels, and lipid profiles were measured before and after the intervention. FBS, triglyceride, and total cholesterol levels were estimated using the Pars Azmoon kit (Iran). Further, high-density lipoprotein (HDL) and low-density lipoprotein cholesterol (LDL) were determined using the Paadco kit (Spain), followed by measuring the insulin levels using the Monobind kit (USA) following the ELISA method. All the experiments were performed in the laboratory of Urmia Imam

Khomeini University Hospital. The blood samples (6 mL) were taken from each subject between 7 and 9 AM and stored in the refrigerator and then centrifuged after a maximum of 30 minutes. Furthermore, the homeostatic model assessment for insulin resistance (HOMA-IR) and quantitative insulin sensitivity check index (QUICKI) were used to evaluate insulin resistance (25). HOMA-IR and QUICKI were computed using the following formulas (25).

HOMA1-IR = [Fasting plasma glucose (FPG) (mmol/L) * Fasting plasma insulin (FPI) (mU/L)]/22.5
QUICKI = 1/ [log (FPI) _log (FPG)]

The HOMA2-IR index was calculated by the HOMA2 calculator, version 2.2.3 (Available at http://www.dtu.ox.ac.uk). HOMA2-IR is a non-linear computer model solution that shows insulin sensitivity and function of β-cells (25).

Statistical Analysis

All the values were reported as mean ± SD. Statistical analyses were performed using the IBM SPSS software, version 20.0 (IBM Corporation, Armonk, NY) and $P < 0.05$ was considered statistically significant. The normality of data was tested using the Kolmogorov-Smirnov test. Moreover, the baseline data and the mean changes were compared between intervention and placebo groups using the independent t test or Mann-Whitney U test for the normal and non-normal variables, respectively. The within-group comparison was analyzed using the paired t test or Wilcoxon test. Additionally, Little's chi-square statistic for testing whether values were missing completely at random (MCAR) is printed as a footnote

to the expectation-maximization matrices. Given that Little's MCAR test was not significant at the 0.05 level, the per-protocol method was used for analysis (chi-square = 273.609, $df = 337$, and $P = 0.995$).

Results

Of 54 eligible participants, 88.9% completed the study (24 in each group) although 2, 1, 1, and 2 subjects were excluded from the study due to pregnancy, unavailability, the lack of taking the entire supplements, and unwillingness to cooperate, respectively (Figure 1). At the end of the study, the subjects were asked about the possible side-effects of supplementation although no significant side-effects were reported concerning the consumption of psyllium and microcrystalline cellulose.

A dietary assessment was made for controlling the intake of energy, carbohydrate, protein, fat, and fiber in order to avoid the impact of potential diet changes on the results of the intervention. The dietary evaluation demonstrated no significant changes within the 2 groups in terms of food intake (Table 1). In addition, the results showed no significant changes from the baseline between the two groups in terms of body composition (Table 2). Figure 2 illustrates the error bar chart of FBS, fasting insulin, lipid profile, and insulin resistance indicators between intervention and placebo groups before and after the intervention.

Baseline Characteristics

Table 3 summarizes the baseline characteristics of the participants in intervention and placebo groups. The patients' age average was 27.70 ± 5.55 and 27.33 ± 5.79 in intervention and placebo groups, respectively. Therefore, the average age was not significantly different between the
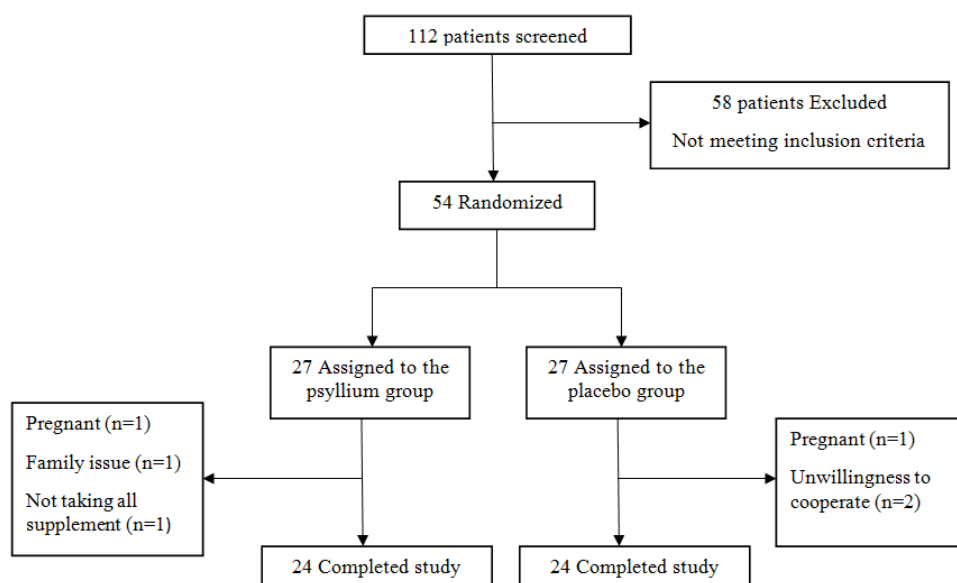

Figure 1. The Study Flow Diagram.

2 groups ($P > 0.05$). Moreover, the mean of all the studied variables was not significantly different between the two groups at the baseline ($P > 0.05$).

Glucose Profile

Table 1 presents the mean comparison for the 2 groups. In the intervention group, the fasting insulin (115.86 ± 93.35 pmol/L at week 0 and 78.77 ± 37.80 pmol/L at week 8, $P = 0.030$), FBS (4.58 ± 0.41 mmol/L at week 0 and 4.20 ± 0.42 mmol/L at week 8, $P < 0.001$) and the insulin resistance indicators including HOMA1-IR (3.49 ± 2.88 at week 0 and 2.19 ± 1.23 at week 8) and HOMA2-IR (2.13 ± 1.60 at week 0 and 1.40 ± 0.69 at week 8) decreased significantly. However, the HOMA2-IS% increased significantly from 80.07 ± 63.00 at week 0 to 95.38 ± 61.07 at week 8 but their changes were not statistically significant in the placebo group.

The changes from the baseline between the 2 groups are shown in Table 2. The mean changes of QUICKI demonstrated a significant difference between the 2 groups (0.01 ± 0.03 and 0.02 ± 0.06 in intervention and placebo groups, $P = 0.044$). In the placebo group, the changes of any variables were not significant. Although the reduction

of fasting insulin (37.09 ± 78.69 pmol/L), HOMA1-IR (1.29 ± 2.36), HOMA2-IR (0.72 ± 1.32), and HOMA2-β% (12.45 ± 88.72) was higher in the intervention group compared to the placebo group, these differences were not significant.

Lipid Profiles

At the end of the study, total cholesterol and LDL-C significantly decreased in the intervention group ($P < 0.05$), but their changes were not significant in the placebo group. For the intervention group, the mean total cholesterol and LDL-C changed from 5.13 ± 0.10 mmol/L (baseline) to 4.65 ± 1.08 mmol/L (endpoint) and from 2.55 ± 0.69 mmol/L (baseline) to 2.26 ± 0.74 mmol/L (endpoint), respectively (Table 1). Finally, the mean changes of LDL-C (0.28 ± 0.58 mmol/L and 0.11 ± 0.67 mmol/L in intervention and placebo groups, respectively) showed a significant difference between the two groups ($P = 0.036$), the related data are provided in Table 2.

Discussion

Many studies evaluated the effect of soluble fibers on the glycemic response in individuals. Considering that

Table 1. Mean Comparison of the 2 Groups Before and After the Intervention

	Baseline		Week 8		P^a	P^b
	Psyllium Group	Placebo Group	Psyllium Group	Placebo Group		
Weight (kg)	69.81 ± 12.05[1]	67.09 ± 12.10	69.52 ± 12.17	66.46 ± 12.28	0.629*	0.087*
BMI (kg/m²)	27.37 ± 5.13	26.88 ± 5.25	27.11 ± 5.14	26.02 ± 4.77	0.415*	0.065*
FM (kg)	28.72 ± 8.01	26.97 ± 9.09	28.17 ± 8.05	26.17 ± 8.95	0.165*	0.039*
FFM (kg)	41.09 ± 4.82	40.13 ± 4.68	41.34 ± 5.04	40.28 ± 5.10	0.433*	0.589*
WHR	0.94 ± 0.05	0.92 ± 0.05	0.93 ± 0.05	0.91 ± 0.05	0.257*	0.825**
SMM (kg)	22.35 ± 2.96	21.80 ± 2.90	22.84 ± 3.53	21.94 ± 3.06	0.230*	0.447*
Dietary Energy (kcal)	2200.04 ± 274.9	2112.38 ± 325.39	2198.79 ± 277.6	2110.33 ± 338	0.971*	0.921*
Dietary Carbohydrate (g)	292.35 ± 57.25	281.09 ± 60.11	290.34 ± 60.30	285.39 ± 51.94	0.826*	0.631*
Dietary Protein (g)	86.42 ± 24.92	95.32 ± 35.72	90.55 ± 25.65	93.04 ± 32.94	0.230**	0.689*
Dietary Fat (gr)	76.51 ± 21.99	70.52 ± 23.57	76.57 ± 19.2	69.19 ± 22.77	0.987*	0.622*
Dietary Fiber (g)	14.47 ± 3.80	13.81 ± 3.92	14.73 ± 3.75	14.01 ± 4.24	0.284*	0.433*
FBS (mmol/L)	4.58 ± 0.41	4.52 ± 0.51	4.20 ± 0.42	4.33 ± 0.51	0.001*<	0.086*
Fasting Insulin (pmol/L)	115.86 ± 93.35	79.06 ± 85.17	78.77 ± 37.80	69.74 ± 36.51	0.030*	0.732**
Total cholesterol (mmol/L)	5.13 ± 0.10	5.29 ± 1.13	4.65 ± 1.08	5.05 ± 0.71	0.020*	0.298*
Triglycerides (mmol/L)	1.72 ± 0.83	1.59 ± 0.67	1.82 ± 0.86	1.61 ± 0.80	0.709**	0.846*
LDL-cholesterol (mmol/L)	2.55 ± 0.69	2.47 ± 0.63	2.26 ± 0.74	2.58 ± 0.66	0.026*	0.436*
HDL-cholesterol (mmol/L)	1.35 ± 0.36	1.41 ± 0.32	1.40 ± 0.24	1.36 ± 0.28	0.347*	0.192*
HOMA1-IR	3.49 ± 2.88	2.35 ± 2.59	2.19 ± 1.23	1.92 ± 1.02	0.022**	1.000**
HOMA2-IR	2.13 ± 1.60	1.64 ± 1.48	1.40 ± 0.69	1.35 ± 0.63	0.024**	0.654**
HOMA2-IS%	80.07 ± 63.00	103.96 ± 66.60	95.38 ± 61.07	97.09 ± 59.01	0.045**	0.823**
HOMA2-β%	180.53 ± 94.21	155.7 ± 90.19	168.08 ± 61.68	169.82 ± 75.82	0.508*	0.398*
QUICKI	0.34 ± 0.04	0.37 ± 0.07	0.35 ± 0.03	0.35 ± 0.03	0.105*	0.175*

Note. FM: fat mass; FFM: fat free mass; WHR: Waist-hip ratio; SMM: skeletal muscle mass; FBS: fasting blood sugar; LDL: low density lipoprotein; HDL: high density lipoprotein; HOMA1-IR: homeostatic model assessment of insulin resistance; HOMA2-IR: Updated HOMA nonlinear computer model of insulin resistance; HOMA2-IS%: HOMA2 of insulin sensitivity; HOMA2-β%: HOMA2 of percentage β cell function; QUICKI: Quantitative insulin sensitivity check index. The values are presented as mean (standard deviation).
[a] *P* values of within group comparison in the intervention group; [b] *P* values of within group comparison in the placebo group.
* Paired *t* test; ** Wilcoxon test.

Table 2. Comparison Mean changes From the Baseline Between Psyllium and Placebo Groups

	Psyllium	Placebo	P value
Weight (kg)	0.29± 2.96[a]	0.64±1.74	0.628[b]
BMI (kg/m2)	0.26±1.52	0.86±2.16	0.274[b]
FM (kg)	0.54±1.85	0.79±1.77	0.635[b]
FFM (kg)	0.24 ± 1.50	0.15±1.38	0.827[b]
WHR	0.005±0.02	0.002± 0.02	0.600[b]
SMM (kg)	0.48 ± 1.92	0.13±0.84	0.418[b]
FBS (mmol/L)	0.39 ± 0.36	0.19±0.52	0.141[b]
Fasting Insulin (pmol/L)	37.09±78.69	9.31± 65.00	0.189[b]
Total cholesterol (mmol/L)	0.47 ± 0.93	0.24±1.08	0.428[b]
Triglycerides (mmol/L)	0.95± 0.53	0.02±0.56	0.663[b]
LDL-cholesterol (mmol/L)	0.28±0.58	0.11± 0.67	0.036[b]
HDL-cholesterol (mmol/L)	0.05±0.26	0.06±0.20	0.121[b]
HOMA1-IR	1.29±2.36	0.42±2.04	0.087[c]
HOMA2-IR	0.72 ±1.32	0.29 ±1.17	0.201[c]
HOMA2-IS%	15.30 ± 58.80	6.87±59.99	0.197[c]
HOMA2-β%	12.45 ± 88.72	14.11±73.04	0.295[b]
QUICKI	0.01±0.03	0.02 ± 0.06	0.044[b]

Note. BMI: Body mass index; SD: Standard deviation; FM: Fat mass; FFM: Fat free mass; WHR: Waist-hip ratio; SMM: Skeletal muscle mass; FBS: Fasting blood sugar; LDL: Low density lipoprotein; HDL: High density lipoprotein; HOMA1-IR: Homeostatic model assessment of insulin resistance; HOMA2-IR: Updated HOMA nonlinear computer model of insulin resistance; HOMA2-IS%: HOMA2 of insulin sensitivity; HOMA2-β%; HOMA2 of percentage β cell function; QUICKI: Quantitative insulin sensitivity check index.
[a] The values are presented as mean (standard deviation); [b] Analyzed by an independent *t* test between the two groups; [c] Analyzed by the Mann-Whitney U test between the two groups.

Table 3. Comparison the Baseline Characteristics of Participants Between Two Groups

	Psyllium	Placebo	P Value
Subjects (n)	27	27	
Age (y)	27.70 ± 5.55a	27.33 ± 5.79	0.811[b]
Height (cm)	160.69 ±4.45	158.95 ± 5.89	0.226[b]
Weight (kg)	69.35 ± 11.53	68.19 ± 13.16	0.732[b]
BMI (kg/m²)	27.01 ± 4.96	27.03 ± 5.42	0.990[b]
FM (kg)	28.21 ± 7.73	27.50 ± 9.44	0.761[b]
FFM (kg)	41.13 ± 4.58	40.69 ± 5.15	0.741[b]
WHR	0.93 ± 0.05	0.92 ± 0.06	0.375[b]
SMM (kg)	22.38 ± 2.81	22.14 ± 3.19	0.763[b]
FBS (mmol/L)	4.57 ± 0.40	4.56 ± 0.53	0.958[b]
Fasting Insulin (pmol/L)	107.67 ± 90.96	76.46 ± 81.18	0.189[b]
Total cholesterol (mmol/L)	5.11 ± 0.96	5.28 ± 1.06	0.537[b]
Triglycerides (mmol/L)	1.69 ± 0.79	1.61 ± 0.66	0.694[b]
LDL-cholesterol (mmol/L)	2.54 ± 0.67	2.49 ± 0.60	0.765[b]
HDL-cholesterol (mmol/L)	1.36 ± 0.34	1.39 ± 0.32	0.727[b]
HOMA1-IR	3.23 ± 2.81	2.28 ± 2.47	0.099[c]
HOMA2-IR	1.97 ± 1.56	1.56 ± 1.41	0.241[c]
HOMA2-IS%	86.29 ± 61.98	106.86 ± 65.23	0.245[c]
HOMA2-B%	171.83 ± 92.22	148.06 ± 86.85	0.360[b]
QUICKI	0.34 ± 0.04	0.37 ± 0.07	0.056[b]

Note. BMI: Body mass index; SD: Standard deviation; FM: Fat mass; FFM: Fat free mass; WHR: Waist-hip ratio; SMM: Skeletal muscle mass; FBS: Fasting blood sugar; LDL: Low density lipoprotein; HDL: High density lipoprotein; HOMA1-IR: Homeostatic model assessment of insulin resistance; HOMA2-IR: Updated HOMA nonlinear computer model of insulin resistance; HOMA2-IS%: HOMA2 of insulin sensitivity; HOMA2-β%; HOMA2 of percentage β cell function; QUICKI: Quantitative insulin sensitivity check index.
[a] The values are presented as mean (standard deviation); [b] Analyzed by an independent *t* test between the two groups; [c] Analyzed by the Mann-Whitney U test between the two groups.

previous studies focused on the effect of psyllium on diabetic patients and that patients with polycystic ovary may also have some degrees of insulin resistance (5), the present study measured the effect of psyllium as a soluble fiber on polycystic ovarian patients. To the best of our knowledge, the current study is the first one to investigate the effect of psyllium supplementation on insulin resistance and lipid profile in patients with PCOS. It was hypothesized that psyllium can reduce the absorption of sugar from the digestive tract and thus might reduce blood sugar and insulin levels and contribute to the improvement of insulin resistance. Our findings showed that supplementation with 5 g of psyllium twice a day for 8 weeks decreased FBS and fasting insulin in women with PCOS. Amankwaah et al investigated the effect of different amounts of fiber and protein on serum glucose and insulin concentrations and found that although the increase in fiber consumption has no therapeutic effect on reducing postprandial insulin response, it can reduce this response in overweight healthy people (26). In the present study, the consumption of psyllium fiber was associated with a decrease in the fasting insulin level and insulin resistance.

Similarly, Thompson et al conducted a meta-analysis study and evaluated randomized clinical trials that examined the effect of the soluble fiber on anthropometric and metabolic results (i.e., glucose and insulin levels and HOMA-IR) in overweight and obese adults. They reported that supplementation with soluble fiber improves anthropometric and metabolic results (27). This is in line with the results of our study in which improvement was expected in glucose and insulin levels in patients with PCOS. Abutair et al also showed that the consumption of 10.5 g of psyllium daily for 8 weeks in T2DM patients significantly improved FBS and insulin levels and the insulin resistance indicators (28). Further, Frati Munari et al demonstrated that a combination of 15 g psyllium with a meal (90 g white bread) may reduce the glycemic index of food and may improve the glycemic response after meals in T2DM patients (29). In their clinical trial, Ziai et al represented that taking 5.1 g of psyllium twice a day for 8 weeks decreased FBS and insulin levels while significantly increasing high-density lipoprotein in T2DM patients (20).
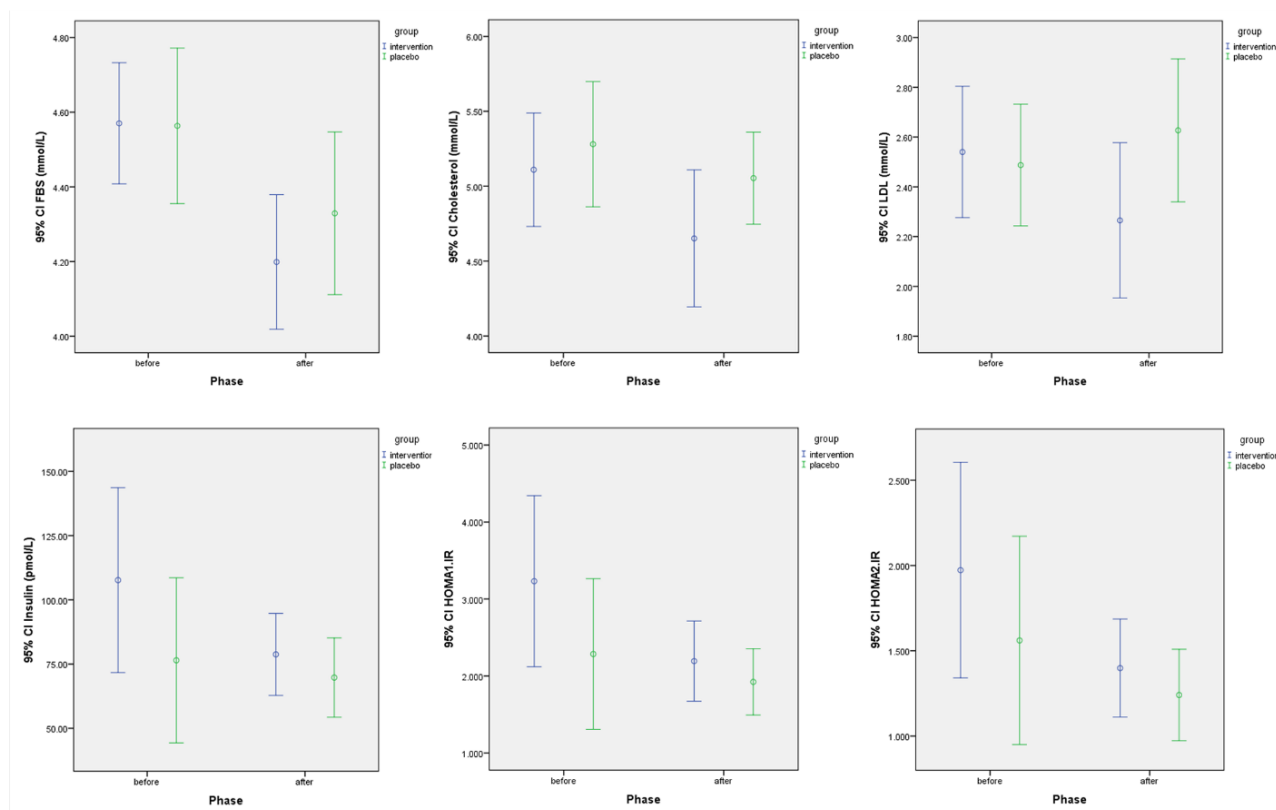
In another study by Karhunen et al, it was found that

Figure 2. Error Bar Chart for FBS, Fasting Insulin, Lipid Profiles and Insulin Resistance Indicators Between Intervention and Placebo Groups Before and After the Intervention

Note. FBS: Fasting blood sugar. The *P*-values of the comparison of the mean changes from baseline between psyllium and placebo groups: *P*-value[FBS] =0.141, *P*-value[Cholesterol] =0.428, *P*-value[LDL] =0.036, *P*-value[Insulin] =0.186, *P*-value[HOMA1-IR] =0.087, and *P*-value[HOMA2-IR] =0.201.

a meal, high in dietary fiber (23 g of psyllium) decreased postprandial glucose and insulin responses (30). Furthermore, Anderson et al noted that the consumption of 5.1 g psyllium twice daily in 8 weeks significantly decreased total cholesterol and LDL-C (31). However, the results of another study evaluating the effect of 5.3 g of psyllium three times a day for two months in T2DM patients showed a significant reduction in triglyceride levels (32). Likewise, in the present study, the levels of total cholesterol and LDL-C reduced significantly in the intervention group.

Given that many women with PCOS have insulin resistance, a study was conducted to compare changes in insulin sensitivity and the clinical outcomes of similar weight loss after consuming a diet with a low glycemic index compared with normal diets in overweight and obese women with PCOS. The subjects were controlled for 12 months or as long as a 7% reduction was observed in the body weight. The results of the study showed that the subjects who consumed a low glycemic index diet significantly improved in impaired oral glucose tolerance test and the regularity of their menstrual cycles (24). Nybacka et al conducted a study on women with PCOS in order to investigate the effect of lifestyle interventions such as increasing fiber intake, reducing trans-fatty acids, and

exercise on metabolic biomarkers. In agreement with the results obtained in our study, Nybacka et al also found that increasing fiber intake may help prevent the development of metabolic disorders in women with PCOS (33).

In our study, the HOMA1-IR, HOMA2-IR, and HOMA2-IS% before and after the intervention in the intervention group and the mean changes of QUICKI from the baseline between the two groups showed significant improvements.

The results of previous research showed that lifestyle changes such as alterations in a diet (low-calorie diets), exercise, and behavioral management techniques in PCO women significantly improved the hirsutism, weight, WHR, and fasting insulin level (34).

In our study, supplementation with 5 g of psyllium twice a day did not affect weight and body composition significantly although FM significantly reduced in the placebo group. In a clinical trial conducted on overweight and obese subjects taking 12 g of psyllium for 12 weeks, no significant changes were observed in weight, BMI, body fat, and WHR (35). However, an animal study by Kang et al showed that psyllium is associated with a reduction in weight and body fat in mice with high-fat diets (36).

One limitation of this study was the lack of androgen level measurement for determining the effectiveness of

psyllium and the reduction of insulin resistance. Similar meal plans designed for all subjects could help further harmonize the distribution of macronutrients and fiber resources among individuals. Thus, further clinical trials with a longer duration are needed to evaluate the effect of psyllium on clinical symptoms resulted from insulin resistance in PCO subjects.

Conclusions

In summary, supplementation with 5 g psyllium twice a day for 8 weeks is useful in non-diabetic women with PCOS and can reduce insulin resistance while improving insulin sensitivity. Finally, the results revealed that psyllium causes a significant decrease in the FBS, fasting insulin, LDL-C, total cholesterol, and insulin resistance indicators.

Conflict of Interests

Authors declare that they have no conflict of interests.

Ethical Issues

The study was approved by the Ethics Committee of Urmia University of Medical Sciences under the code of umsu.rec.1395.223 and registered at Iranian Registry of Clinical Trials (identifier: IRCT2016091929508N4).

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