Original Article

Cinnamon improves metabolic factors without detectable effects on adiponectin in women with polycystic ovary syndrome

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Background and Objectives: The objectives of this study were to investigate the effects of cinnamon supplementation on glycemic indices, serum lipids and adiponectin in patients with polycystic ovary syndrome (PCOS). **Methods and Study Design:** This double-blind randomized controlled clinical trial was conducted on 84 overweight or obese PCOS patients. Subjects in cinnamon (n=42) and placebo (n=42) groups were given 3 cinnamon capsules (each one contained 500 mg cinnamon) or placebo daily for 8 weeks. Fasting blood samples, anthropometric measurements and dietary intake data were collected at the baseline and at the end of the trial. Data were analyzed by independent t test, paired t test and analysis of covariance. **Results:** Cinnamon significantly decreased serum fasting blood glucose, insulin, homeostatic model assessment for insulin resistance, total cholesterol and low-density lipoprotein cholesterol and weight and increased high-density lipoprotein cholesterol compared with placebo (all $p<0.05$). Serum triglyceride and body mass index significantly decreased in the cinnamon group, in comparison with baseline values ($p=0.001$ and $p=0.002$, respectively). No significant changes were seen in serum adiponectin in either group. **Conclusions:** Short term supplementation of cinnamon had some favourable effects on metabolic risk factors of women with PCOS and may be useful in management of PCOS complications.

Key Words: polycystic ovary syndrome, cinnamon, glycemic indices, lipid profile, adiponectin

INTRODUCTION

Polycystic ovary syndrome (PCOS) is an important female endocrine and reproductive disorder.

The prevalence of PCOS is about 18 % according to Rotterdam criteria.[1] These patients demonstrate an irregular menstrual cycle, chronic anovulation and hyperandrogenism. PCOS involve metabolic alteration such as insulin resistance (IR), hyperinsulinemia, dyslipidemia and obesity in most cases.[2] IR is present in about 50-70% of these patients independent of body mass index (BMI) and is considered as the main pathogenic factor in development of metabolic manifestations.[2,3] Affected women have a greater risk for type 2 diabetes mellitus (T2DM), atherosclerosis, arterial stiffness and altered vascular endothelium.[4]

PCOS is closely linked to functional derangements in adipose tissue. Adiponectin is an adipocytokine secreted solely by adipose tissue and has been shown to have both antidiabetic and antiatherogenic properties.[5] Adiponectin is regarded as a possible link between adiposity and IR.[6] Studies have shown that circulating levels of adiponectin are low in women with PCOS.[5-8]

Insulin sensitizing agents such as metformin and thiazolidines have been prescribed to treat PCOS.[9] However, the most widely used drugs in PCOS, are often poorly tolerated because of gastrointestinal side effects.[10] Limited effects of current drug treatments for PCOS have fueled the search for alternative approaches. *Cinnamomum zeylanicum* is the dried inner bark of various trees in the Lauraceae family that is native to Sri Lanka and India but is cultivated extensively in the tropical regions of the world.[11] It is one of the most important spices used in traditional medicines because of its antidiabetic effect.[12] Cinnamaldehyde, cinnamic acid tannin and methylhydroxychalcone polymer are its main compo-

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nents.[11] Cinnamon polyphenols display insulin like properties.[13] In animal studies, aqueous cinnamon extracts have been shown to regulate IR and adipogenesis, resulting in improved lipid and glucose metabolism.[14,15] Kopp et al in an experimental study, showed that treatment with cinnamaldehyde stimulated the secretion of adiponectin and the phosphorylation of 5'adenosine monophosphate-activated protein kinase (AMPK) in 3T3-L1 adipocytes rat and therefore improved IR.[16]

Effects of different amounts of cinnamon consumption on reducing fasting blood sugar (FBS), IR and serum lipid profile has been reported in patients with T2DM,[17-20] impaired glucose tolerance,[21] nonalcoholic fatty liver diseases[22] and healthy subjects[23,24] in various intervention periods. Wang et al in a pilot study reported an improvement in IR by taking 1 g/day cinnamon extract for 8 week in patients with PCOS.[25] On the other hand, Kort and Lobo showed that supplementation with 1.5 g/day cinnamon for 6 months, did not change serum insulin and glucose parameters in women with PCOS.[10]

Although some studies have reported the effects of cinnamon on the metabolic status of several diseases,[26-29] studies in PCOS patients are few. Moreover, effects of cinnamon on serum lipids and adiponectin levels have not been investigated in these patients. Therefore, we initiated a study to evaluate the effects of cinnamon supplementation on metabolic factors including, serum insulin, homeostasis model assessment-insulin resistance (HOMA-IR), lipid profile and adiponectin in women with PCOS.

METHODS

A total of 84 women with PCOS aged 20 to 38 years with a BMI between 25-40 kg/m^2 were recruited in this double-blind, randomized, controlled clinical trial from the gynaecology clinic, Mohheb Yas Hospital in Tehran, Iran from October 2015 to February 2016. The sample size was determined based on the information obtained from the study by kort and Lobo for IR.[10] Considering 95% confidence interval and 80% power, the sample size was computed to be 32 per group. This number was increased to 42 per group to accommodate the anticipated dropout rate.

The diagnosis of PCOS was established according to 2003 Rotterdam criteria, which require at least two of three features for diagnosis: chronic amenorrhea or oligoamenorrhea, clinical and/or biochemical features of hyperandrogenism and polycystic ovaries by ultrasonography.1 Study exclusion criteria included: thyroid disorders, hyperprolactinemia, diabetes mellitus, pregnancy and lactation, liver or kidney diseases, Cushing syndrome, cardiovascular diseases, seizure and cerebrovascular disorder, hypertension, the use of medications such as insulin sensitizers, insulin, B-blockers, cholesterol-lowering drugs and dietary supplements, smoking, current treatment of infertility, inhaled corticosteroid use, following a specific diet and consistent use of any culinary herbs and spices, regular exercise (>2 weeks) and allergy to cinnamon. The Ethical Committee of Tabriz University of Medical Science approved the study protocol and was registered on the Iranian Registry of Clinical Trials website (Clinical Trial Registration Number: IRCT201508173664N14). Written informed consent was obtained from each subject prior to the study. To match subjects based on age and BMI, at first, the subjects were stratified according to these variables and then the participants were randomly allocated into two groups using a block randomization procedure of size 2. The sequence of the procedure was generated using RAS software.[30] Subjects were asked to maintain their usual dietary intakes and physical activity throughout the study.

A general questionnaire was completed for each subject. Body weight was measured using a scale (Seca, Hamburg, Germany), without shoes and wearing light clothing. Height was measured using a mounted tape without shoes. BMI was calculated as the weight in kilogram divided by the height in meters squared. Information about daily energy and macronutrient intakes was obtained by 24-h recall method for 3 d, including 2 d during the week and 1 during the weekend. A three day average for energy and macronutrient intakes of all subjects was analyzed by Nutritionist 4 software (First Databank Inc., San Bruno, CA).

Cinnamon bark was provided from the Iranian Institute of medicinal plants, Tehran, Iran. Cinnamon barks were grinded with a plant tissue grinder. Each capsule containing approximately of 500 mg cinnamon powder was manufactured on October 2015. Subjects in the treatment group received three capsules of cinnamon and control group subjects received three placebo capsules (wheat flour) that they were required to take daily for 8 weeks. The compliance of the volunteers with the study protocol was monitored via phone interviews once per week and also by counting returned capsules every 2 weeks.

Blood sampling and biochemical assays

Blood samples (5mL) were collected after a 12-h overnight fasting, in the morning. The serum samples were separated from whole blood by centrifugation at 2606.8 × g for 10 min (Beckman Avanti J-25; Beckman Coulter, Brea, CA, USA). The serum samples were frozen immediately at -70 °C until assay. Serum adiponectin level was measured by enzyme-linked immunosorbent assay (ELISA) method using Mediagnost kit (Germany). The intracoefficients and intercoefficients of variation for adiponectin were 5% and 7.5%, respectively and the detection limit was 0.27 ng/mL. Serum glucose was measured using the standard enzymatic methods with commercially available Pars Azmun kit (Karaj, Iran). Serum insulin level was measured by ELISA method using Monobind kit (Monobind Inc, Lake Forest, CA, USA) and insulin resistance was determined by HOMA index with formula.[26] HOMA-IR = fasting insulin (μU/mL) × fasting glucose (mg/dL) / 405. Serum total cholesterol (TC), triacylglycerol (TG) and high-density lipoprotein cholesterol (HDL-C) were measured using the standard enzymatic methods by Pars Azmun kit (Karaj, Iran). Low-density lipoprotein cholesterol (LDL-C) concentration was determined by the Friedewald formula: LDL-C = TC − (HDL-C + TG / 5).[31] All anthropometric, dietary intakes, blood sampling and biochemical measurements were assessed again at the end of intervention period in both groups.

Statistical analyses

The collected data were analyzed using the statistical

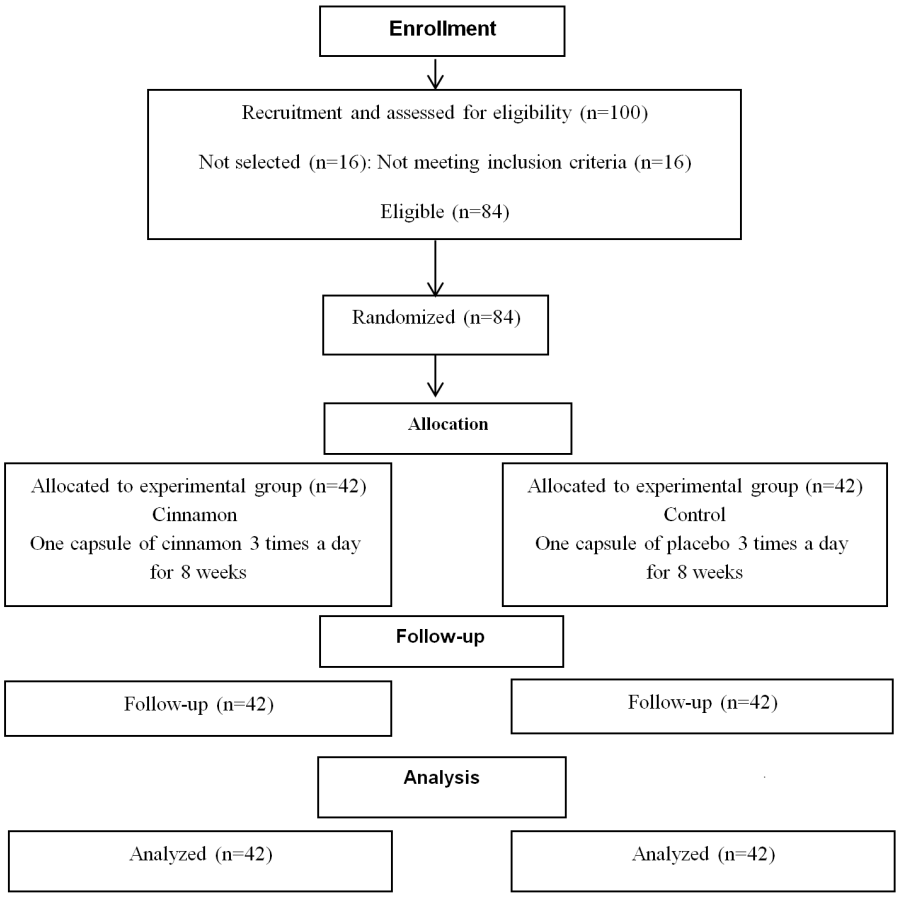

Figure 1. Participants flow diagram.

software SPSS, version 22. (SPSS Inc., Chicago, IL, USA) and the results are expressed as means ± SD. The normality of the distribution of variables was checked by Kurtosis-Skewness test. The baseline measurements and dietary intakes of subjects in two groups were compared using independent samples t test and chi-square test for quantitative and qualitative variables respectively. Analysis of covariance (ANCOVA) was used to identify any differences between the two groups after intervention, adjusting for baseline measurements and confounders (BMI and energy changes during study). The changes in anthropometric measurements, energy and nutrient intakes and blood parameters of the participants between the beginning and end of the trial were compared by paired samples t test. The percentage of changes in variables after intervention was determined with the formula: [(after values – before values) / before values] × 100. Results with $p<0.05$ were considered as statistically significant.

RESULTS

All of the patients (42 patients in cinnamon group and 42 patients in placebo group) completed the study (Figure 1). Compliance was good, with more than 94% of the supplements prescribed being consumed during the study period. Participants did not report any adverse effects or symptoms with the cinnamon consumption during the study.

General and biochemical characteristics of subjects at the beginning of the study are shown in Table 1. There were no significant differences between two groups in weight, BMI and daily energy and macronutrients intakes at baseline. No significant differences were observed between two groups in serum glucose, insulin, HOMA-IR, adiponectin and lipids at baseline.

Table 2 shows anthropometric, dietary intakes and biochemical characteristics of subjects at before and after 8 week intervention. Significant difference was found in weight and BMI of subjects in cinnamon group after intervention compared to baseline values (both, $p<0.05$). Changes in weight and BMI were not significant in control group. Significant differences were seen in energy, protein and fat intakes in cinnamon groups after intervention compared to beginning of study ($p=0.02$, $p=0.04$ and $p=0.04$, respectively). Significant differences were detected in means of serum glucose, insulin and HOMA-IR in cinnamon group after intervention compared to their baseline values (all, $p<0.05$). Supplementation with cinnamon significantly decreased serum glucose, insulin and HOMA-IR in the intervention group by 10.63% (vs 1.78% increase in control group), 12.63% (vs 7.21 % increase in control group) and 20.25% (vs 9.8% increase in control group) respectively, at the end of the study in comparison to baseline values. Changes in these variables were not significant in control group. Variations in serum adiponectin were not significant in any of groups. Significant differences were found in means of all serum lipid variables in cinnamon group after intervention compared to their baseline values (all $p<0.05$). Serum TG, TC and LDL-C significantly decreased in the intervention group by 18.24 % (vs 5.42 % decrease in control group), 7.73 % (vs 2.10 % decrease in control group) and 10.24 % (vs 0.63 % decrease in control group), respectively, at the end

Table 1. Baseline characteristics in women with PCOS

Variable	Cinnamon group (n=42)	Control group (n=42)	MD (95 % CI), *p* value
Demographic data			
Age (y)	29.3 (6.14)	30.2 (6.69)	--
Anthropometric measurements			
Height (cm)	157 (6.77)	156 (6.24)	
Weight (kg)	76.6 (12.3)	77.7 (12.8)	-1.09 (-6.55 to 4.33), 0.69
BMI (kg/m^2)	30.7 (5.04)	31.6 (4.84)	-0.85 (-3.00 to 1.28), 0.42
Dietary intakes			
Energy (kcal/day)	1651 (251)	1749 (265)	-98.0 (-210 to 14.1), 0.86
Carbohydrate (g/day)	228 (44.2)	241 (50.3)	-12.5 (-33.1 to 8.00), 0.43
Protein (g/day)	54.9 (15.9)	60.5 (13.5)	-5.6 (-12.0 to 0.79), 0.30
Total fat (g/day)	60.7 (20.5)	64.8 (17.3)	-4.08 (-12.3 to 4.14), 0.32
Serum biomarkers			
Glucose (mg/dL)	94.4 (10.5)	97.8 (18.2)	-3.47 (-9.92 to 2.97), 0.36
Insulin (μIU/dL)	17.1 (7.84)	14.8 (6.29)	2.25 (-0.82 to 5.34), 0.03
HOMA-IR	3.95 (1.8)	3.57 (1.60)	0.37 (-0.36 to 1.12), 0.19
Adiponectin (ng/mL)	26.7 (15.1)	22.0 (12.0)	4.77 (-1.36 to 10.9), 0.2
TC (mg/dL)	183 (27.5)	177 (26.7)	6.61 (-5.15 to 18.4), 0.57
TG (mg/dL)	117 (59.3)	132 (56.9)	-14.0 (-39.2 to 11.2), 0.79
LDL-C (mg/dL)	118 (24.5)	109 (26.2)	9.06 (-1.95 to 20.0), 0.87
HDL-C (mg/dL)	42.3 (4.63)	41.9 (5.89)	0.34 (-1.95 to 2.64), 0.52

PCOS: Polycystic Ovary Syndrome; BMI: body mass index; HOMA-IR: homeostatic model assessment for insulin resistance; TC: total cholesterol, TG: triglyceride; LDL: low-density lipoprotein; HDL: high-density lipoprotein; MD: means difference.
Data are presented as mean (SD).
MD (95 % CI); *p* value is reported based on the analysis of independent sample t test.

of the study in comparison to baseline values. Serum levels of HDL-C significantly increased in intervention group by 5.49 % (vs 2.19 % decrease in control group). Changes in serum lipid profile were not significant in control group.

Changes of variables between two studies groups after intervention are shown in Table 3. Results of analysis of covariance showed statistically significant differences between the two studied groups in weight of subjects at the end of study, adjusted for energy intake and baseline value. Changes in BMI were not significant between two groups at the end of the study. Total energy and macronutrients intakes did not change significantly between two groups at the end of study.

Results of analysis of covariance showed statistically significant differences between the two studied groups in serum glucose (p=0.001), insulin (p=0.007) and HOMA-IR (p=0.001) at the end of the study, adjusted for energy intake, BMI and baseline values. Changes in serum adiponectin (p=0.289) was not significant between two groups at the end of study.

Results of analysis of covariance indicated statistically significant differences between the two studied groups in serum TC (p=0.04), LDL-C (p=0.04) and HDL-C (p=0.001) at the end of the study, adjusted for energy, BMI and baseline values. Changes in serum TG (p=0.71) was not significant.

DISCUSSION

Cinnamon has been used for its anti-diabetic, anti-hyperlipidemia and anti-obesity effects.[11] Nevertheless, findings about their effects on metabolic status in PCOS are limited.

Based on our results, supplementation with cinnamon decreased serum levels of glucose, insulin and HOMA-IR in studied patients. Our results are in agreement with findings of some previous human and animal studies.[32-34] Khan et al showed that using 1, 3 and 6 g/day cinnamon powder for 40 days improved blood glucose in patients with T2DM.[29] Mang et al demonstrated that administration of 3 g/day of cinnamon aqueous extract to T2DM patients under oral hypoglycemic medication reduced the initial FBS values, significantly.[35] Wang et al also reported reduced fasting glucose, as well as IR in women with PCOS after oral cinnamon extract (1 g/day) administration for 8 weeks.[25] An in vitro study, demonstrated that cinnamon has a potential for reducing post-prandial intestinal glucose absorption by inhibiting the activity of enzymes involved in carbohydrate metabolism (pancreatic a-amylase and a-glycosidase).[36] It stimulates glucose metabolism and glycogen synthesis,[37] inhibits gluconeogenesis by effects on key regulatory enzymes[38,39] and motives insulin release and insulin receptor activity and increases Glucose transporter type 4 (GLUT-4) receptor synthesis.[16,34] In animal studies, aqueous cinnamon extracts have been shown to increase the expression of peroxisome proliferator-activated receptors (PPARs), which are transcriptional factors involved in the regulation of IR.[40]

Our results confirmed the potential effects of cinnamon on improving glycemic indices by reducing HOMA-IR and subsequent lowered FBS in studied subjects. In contrast, a number of other studies on patients with T2DM have failed to show beneficial effects of 1.5 g/day or 1 g/day cinnamon supplementation for 6 or 12 weeks on metabolic status.[41,42] In a recent cross-sectional study, IR in subjects with impaired glucose tolerance was not related to using cinnamon in usual home food preparation.[43] In Kort and Lobo study with high dropout rate of patients with PCOS during study period (cinnamon group (n=11) and control group (n=6)) no changes were seen in insulin/glucose parameters after 6 months cinnamon supplementation.[10] Differences in metabolic status of subjects

Table 2. Anthropometric measurements, dietary intakes and biochemical parameters in women with PCOS

Variable	Measurement period	Cinnamon group (n=42)	Control group (n=42)
Anthropometric measurements			
Weight (kg)	Baseline	76.6 (12. 3)	77.7 (12.6)
	After Intervention	76.1 (12.2)	77.7 (12.9)
	MD (95% CI), *p* value	-0.45 (-0.67 to -0.23), 0.00	0.02 (-0.23 to 0.28), 0.85
BMI (kg/m^2)	Baseline	30.7 (5.04)	31.6 (4.84)
	After Intervention	30.6 (4.99)	31.6 (4.87)
	MD (95% CI), *p* value	0.13 (-0.22 to -0.03), 0.002	-0.00 (-0.12 to 0.10), 0.89
Dietary intakes			
Energy (kcal/day)	Baseline	1651 (251)	1749 (265)
	After Intervention	1602 (265)	1696 (264)
	MD (95% CI), *p* value	-48.8 (-89.6 to 8.13), 0.02	-53.0 (-112 to 6.08), 0.07
Carbohydrate (g/day)	Baseline	228 (44.2)	241 (50.3)
	After Intervention	226 (40.0)	251 (48.3)
	MD (95% CI), *p* value	-2.54 (-18.9 to 13.8), 0.75	9.96 (-2.97 to 22.9), 0.12
Protein (g/day)	Baseline	54.9 (15.9)	60.5 (13.5)
	After Intervention	59.2 (12.6)	61.8 (15.8)
	MD (95% CI), *p* value	4.32 (0.2 to 8.43), 0.04	0.95 (-3.86 to 5.78), 0.69
Total fat (g/day)	Baseline	60.7 (20.5)	64.8 (17.29)
	After Intervention	54.2 (17.2)	52.5 (14.6)
	MD (95% CI), *p* value	-6.44 (-12.7 to -0.19), 0.04	-12.2 (-17.6 to -6.73), 0.00
Serum biomarkers			
Glucose (mg/dL)	Baseline	94.4 (10.5)	97.8 (18.2)
	After Intervention	84.3 (10.9)	99.6 (19.8)
	MD (95% CI), *p* value	-10.0 (-13.1 to -6.9), 0.00	1.73 (-0.67 to 4.14), 0.15
Insulin (μIU/dL)	Baseline	17.1 (7.84)	14.8 (6.29)
	After Intervention	14.9 (6.69)	15.9 (7.11)
	MD (95% CI), *p* value	-2.16 (-3.89 to -0.43), 0.01	1.06 (-0.57 to 2.71), 0.19
HOMA-IR	Baseline	3.95 (1.8)	3.57 (1.6)
	After Intervention	3.15 (1.59)	3.92 (1.80)
	MD (95% CI), *p* value	-0.79 (-1.22 to -0.37), 0.00	0.35 (-0.06 to 0.76), 0.09
Adiponectin (ng/mL)	Baseline	26.7 (15.1)	21.1 (12)
	After Intervention	27.4 (16)	21.2 (12.4)
	MD (95% CI), *p* value	0.61 (-1.53 to 2.77), 0.56	-0.72 (-2.67 to 1.22), 0.45
TC (mg/dL)	Baseline	183.9 (27.5)	177 (26.7)
	After Intervention	169.2 (24.5)	173 (28.8)
	MD (95% CI), *p* value	-14.7 (-22.0 to -7.28), 0.001	-3.17 (-10.9 to 3.43), 0.3
TG (mg/dL)	Baseline	117 (59.3)	131 (56.9)
	After Intervention	96.1 (51.4)	124 (55.6)
	MD (95% CI), *p* value	-21.6 (-30.7 to -12.6), 0.001	-7.14 (-20.8 to 6.53), 0.29
LDL-C (mg/dL)	Baseline	118 (24.5)	108 (26.2)
	After Intervention	105 (21.8)	108 (29.6)
	MD (95% CI), *p* value	-12.07 (-19.2 to -4.98), 0.001	-0.69 (-8.11 to 6.72), 0.85
HDL-C (mg/dL)	Baseline	42.3 (4.63)	41.9 (5.89)
	After Intervention	44.6 (4.85)	41.0 (5.99)
	MD (95% CI), *p* value	2.32 (1.49 to 3.14), 0.0001	-0.92 (-1.92 to 0.06), 0.06

PCOS: Polycystic Ovary Syndrome; BMI: body mass index; HOMA-IR: homeostatic model assessment for insulin resistance; TC: total cholesterol, TG: triglyceride; LDL: low-density lipoprotein; HDL: high-density lipoprotein; MD: means difference.
Data are presented as mean (SD).
MD (95 % CI); *p* value is reported based on the analysis of independent sample t test.

might be involved in various results in glycemic parameters.

In present study, cinnamon supplementation decreased serum TC and LDL-C and increased HDL-C. These findings are in line with some other studies.[14,19,22,29] In khan et al study on T2DM subjects, cinnamon prevented hypercholesterolemia and hypertriglyceridemia and lowered plasma free fatty acids and TG.[29] However, Blevins et al and Wickenberg et al did not find favorable changes in serum lipids of patients with impaired glucose tolerance after taking 1 g/day and 12 g/day cinnamon for 12 weeks.[42,44] It was proposed that cinnamaldehyde inhibit fatty acid synthesis and may stimulate lipolysis via activation of AMPK.[45] AMPK is involved in the maintenance of lipid and cholesterol homeostasis. It stimulates the β-oxidation of fatty acids in mitochondria for lipid utilization. AMPK prevents the activity of acetyl-CoA carboxylase through phosphorylation.[16] Patil et al indicated that increased activity of lecithin cholesterol acyl transferase by cinnamaldehyde, may also contribute to the regulation of blood lipids including elevated HDL-C.[46] Cinnamon promotes the expression of PPARγ/α and their target genes in 3T3-L1 adipocyte. Activation of PPARα up-regulates genes involved in hepatic lipid, lipoprotein metabolism and fatty acid oxidation in skeletal muscle.[14] It was also demonstrated that IR leads to the overproduction of very low density lipoproteins and reduces lipoprotein lipase activity, thereby resulting in dyslipidemia.[47] In our study, cinnamon administration by lowering of HOMA-IR might be contributed to improved serum lipid profile

Table 3. All variables in women with PCOS at the end of study

Variable	Cinnamon group (n=42)	Control group (n=42)	MD (95 % CI), *p* value
Anthropometric measurements			
Weight (kg)	76.1 (12.1)	77.7 (12.9)	-0.47 (-0.81 to 0.13), 0.00†
BMI (kg/m^2)	30.6 (4.99)	31.6 (4.87)	-0.12 (-0.27 to 0.01), 0.08†
Dietary intakes			
Energy (kcal/day)	1602 (265)	1696 (264)	4.23 (-66.5 to 74.1), 0.9‡
Carbohydrate (g/day)	226 (40.0)	251 (48.3)	-12.5 (-33.0 to 8.05), 0.23‡
Protein (g/day)	59.2 (12.6)	61.5 (15.8)	3.36 (-2.88 to 9.6), 0.28‡
Total fat (g/day)	54.2 (17.2)	52.5 (14.6)	5.80 (-2.41 to 14.0), 0.16‡
Serum biomarkers			
Glucose (mg/dL)	84.3 (10.1)	99.6 (19.8)	-11.8 (-15.7 to -7.89), 0.00§
Insulin (μIU/dL)	14.9 (6.69)	15.9 (7.11)	-3.34 (-5.75 to -0.93), 0.00§
HOMA-IR	3.15 (1.59)	3.92 (1.80)	-1.17 (-1.76 to -0.58), 0.00§
Adiponectin (ng/mL)	27.4 (16.0)	21.2 (12.4)	1.56 (-1.35 to 4.49), 0.28§
TC (mg/dL)	169 (24.5)	173 (28.8)	-10.6 (-21.0 to -0.18),0.046§
TG (mg/dL)	96.1 (51.4)	124 (55.6)	-15.2 (-31.7 to 1.23),0.069§
LDL-C (mg/dL)	105 (21.8)	108 (29.6)	-10.9 (-21.3 to -0.49), 0.04§
HDL-C (mg/dL)	44.6 (4.85)	41.0 (5.99)	3.21 (1.89 to 4.52), 0.000§

PCOS: Polycystic Ovary Syndrome; BMI: body mass index; HOMA-IR: homeostatic model assessment for insulin resistance; TC: total cholesterol, TG: triglyceride; LDL: low-density lipoprotein; HDL: high-density lipoprotein; MD: means difference.
†MD (95 % CI); *p* value is reported based on the analysis of covariance, adjusted for energy intake and baseline values.
‡MD (95 % CI); *p* value is reported based on the analysis of independent sample t test.
§MD (95 % CI); *p* value is reported based on the analysis of covariance, adjusted for energy intake, BMI and baseline values.

in intervened group.

Results of the present study showed no significant differences in daily energy and macronutrients intakes between two groups at baseline and after intervention. However, significant decrease was observed in body weight of subjects by cinnamon supplementation. This finding is comparable with some animal studies such as alloxan induced obese diabetic Sprague Dawley rats and high fat diet-fed mice.[48,49] The suggested underling mechanisms are delayed gastric emptying,[50] activating transient receptor potential-ankyrin receptor 1, which enhances energy expenditure and stimulating interscapular brown adipose tissue, preventing adipocyte differentiation and adipogenesis via down-regulating of PPARγ and up- regulating of AMPK pathways.[51] The AMPK acts as an intra-cellular energy sensor and hence improves IR in insulin-sensitive tissues like adipose tissue .According to our findings, weight loss in studied subjects was not sufficient to decrease BMI compared to placebo. In prediabetic overweight people, cinnamon extract supplementation (500 mg/day) for 12 weeks led to a small but statistically significant decrease in fat mass.[27] Vafa et al showed that consuming cinnamon (3 g/day) for 8 weeks decreased body weight, BMI and fat body mass of subjects with T2DM, compared to baseline.[52] It is possible that higher doses of cinnamon or longer period of intervention may be required to obtain substantial effect on BMI as overall obesity value.

Adiponectin is one of the most important adipokines in insulin-sensitive tissues like skeletal muscle and liver which improves IR and lipid metabolism.[17] Evidence on effects of cinnamon on adiponectin secretion is limited. Kopp et al in an experimental study, reported that trans-cinnamic acid (tCA) through activation of AMPK, increased secretion of adiponectin gene in differentiated 3T3-L1adipocyte.[16] In another study, Kim and Choung showed an up-regulated mRNA expression of PPARγ in adipose tissue after treatment with cinnamaldehyde. The transcription factor PPARγ is known as a stimulator of adiponectin expression.[53]

Conversely, in the study by Roffey et al treatment of the adipocytes with cinnamon water extract inhibited adiponectin secretion to levels that were no measurable.[54] Our study is the first one to report the effects of cinnamon supplementation on serum adiponectin in women with PCOS and results showed that, cinnamon supplementation did not affect serum adiponectin. It should be note that means of baseline values of serum adiponectin in all of our studied subjects were in normal range (3.2-38 ng/mL)[5,55] and changes of BMI were not significant between two groups after intervention. So, no substantial alteration in this adipokine would be expected. As a result, it seems that detected favourable effects on serum glucose and lipid parameters in our study were not mediated via adiponectin. Possible type 2 error in interpreting of obtained results about serum adiponectin might be also considered. Other studies are warranted regarding the effects of cinnamon on adiponectin concentrations in this disease.

The strengths of the present study were the double blind placebo-controlled design with no drop-outs. However, our study had some limitations including its short study duration of 8 week and the use of a fixed dose of cinnamon. This study also included subjects with BMI ≥25 kg/m^2. Therefore, the results of our study may not be applicable to underweight or normal weight PCOS patients and also to other doses of cinnamon or different intervention period durations. Studies are warranted to evaluate the effects of cinnamon on androgen status in this patient, too.

Conclusion

The present trial showed that short term cinnamon supplementation improved serum glycemic indices and lipid profile of women with PCOS, without detectable effects on adiponectin. Cinnamon may be useful in management of PCOS metabolic risk factors.

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AUTHOR DISCLOSURES

The authors declare no conflict of interest. We thank the Research Vice-Chancellor of Tabriz University of Medical Sciences, Tabriz, Iran for the financial support.

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