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Title: Effect of Oral Cinnamon Extract on the Metabolic and Hormonal Status of Women with Polycystic Ovary Syndrome: A Blinded Randomized Controlled Clinical Trial

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Abstract

Background: Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in the women of reproductive age. The aim of this study was to investigate the effect of oral capsules of cinnamon extract on the metabolic profile and hormonal status of women with PCOS.

Methods: This blinded randomized clinical trial was performed on 66 women with PCOS referred to the gynecology and infertility clinics in Tehran, Iran; 2016 - 2017. Eligible women were randomly allocated into intervention (n=33) and placebo (n=33) groups. The oral capsule of three grams' cinnamon extract was taken once a day for 12 consecutive weeks by the intervention group and the placebo capsule was given in the same way to the control group. Before and 12 weeks after starting the intervention, blood tests were performed to measure fasting blood sugar, fasting insulin, triglycerides, total cholesterol, low-density lipoprotein, high-density lipoprotein, total testosterone, and sex hormone binding globulin. The student t-test, paired t-test, chi-square and ANCOVA were used to compare groups using SPSS v. 16 software. A p-value of less than 0.05 was considered significant.

Results: The results showed that consumption of cinnamon extract only leads to a significant decrease in total testosterone level compared to placebo (P=0.001), and has no significant effect on fasting blood sugar, fasting insulin, triglyceride, total cholesterol, low-density and high-density lipoprotein cholesterol, sex hormone binding globulin, and free androgen index.

Conclusion: our study revealed that cinnamon extract at a dose of 3 grams per day (3g/day) for twelve consecutive weeks could decrease total testosterone in women with PCOS, and had no significant effects on metabolic and hormonal indicators in these women. Nevertheless, it is suggested that more studies be conducted with a larger sample size and the use of various doses of cinnamon.

Keywords: Herbal medicine, Polycystic ovary syndrome (PCOS), Testosterone, Androgen, Cholesterol

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Highlights:

- Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women of reproductive age.
- Cinnamon extract significantly reduces total testosterone in women with PCOS.
- Cinnamon extract has no significant effect on sex hormone binding globulin (SHBG) and free androgen index (FAI) in women with PCOS.
- Cinnamon extract has no significant effect on metabolic indices in women with PCOS.

Plain Language Summary

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women of reproductive age. Women with PCOS experience sex hormone imbalances and metabolic complications. The present study revealed that consuming cinnamon extract at a dose of 3 grams per day for 12 consecutive weeks can reduce only the total testosterone levels in these women and has no effect on other studied hormonal and metabolic indices.

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Introduction

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age. The prevalence of PCOS, according to Rotterdam criteria, is about 6-18% (Blagojevic et al., 2017). The prevalence of this disease in various studies conducted in Iran has been reported from 7 to 19.4 percent (Farhadi-Azar et al., 2022; Ghiasi, 2019). PCOS has received a lot of attention due to its high prevalence and possible consequences such as infertility, and also metabolic and cardiovascular disorders in women. The exact cause of PCOS is not known, but today it has been proven that its occurrence is due to genetic and environmental factors (Boyle and Teede, 2012). In addition, some environmental factors such as diet, physical activity, smoking and stress can also be involved in causing this syndrome (Michalak et al., 2015). Although compensatory insulin resistance and hyperinsulinemia are not diagnostic criteria for polycystic ovary syndrome but its prevalence among women with this syndrome is 50-70% and may reach 95% in overweight women (Qin et al., 2010). PCOS is also the most common cause of infertility, such that 50-70% of women with infertility due to anovulation have this syndrome (Nasir Amiri et al., 2013). These have made PCOS a frustrating experience for women and a complex scientific challenge for researchers and physicians (Johnson, 2014).

In order to reduce and treat the physical complications of PCOS and promote the health of women with this syndrome, many pharmacological and non-pharmacological methods have been considered and studied. Complementary therapies in these women has increased over the past 10 years (Smith et al., 2013). One of the common types of alternative drugs is herbal medicine such as saliva officinalis (Amini et al., 2020), curcumin, bebeerine (Joshi et al., 2021), and cinnamon (Baker et al., 2008). Herbal medicines have fewer side effects than conventional treatments (Nagarathna et al., 2014). Cinnamon is a low-risk medicinal plant that has been used in daily life without any side effects (Rao and Gan, 2014). The use of cinnamon as a potentially useful drug for the treatment of type 2 diabetes began almost about 20 years ago (Sangal, 2011). It has been shown during laboratory and animal studies that cinnamon stimulates insulin secretion (Broadhurst et al., 2000) and cinnamon extract increases the activity of insulin kinase receptors by increasing the activity of phosphatidylinositol 3-kinases (PI3K) in the insulin signaling pathway in the cell, resulting in improved insulin function and increased blood glucose uptake (Heibashy et al., 2013). A study showed the ability of cinnamon in reducing lipid levels in fructose-fed mice (El-Bidawy et al., 2014). The effect of these compounds is also positive in reducing triglycerides, cholesterol and low-density lipoprotein (Modaresi et al., 2009). Although, another study showed that daily intake of one gram of cinnamon for three months did not cause significant changes in fasting glucose and glycosylated hemoglobin (Blevins et al., 2007a). Despite several studies that have examined the effects of cinnamon on PCOS aspects, there is controversies in this regard. So, this study was conducted to determine the effect of oral cinnamon on metabolic profile in women with PCOS.

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Materials and Methods

Design, setting and sample

This study was a triple-blinded randomized placebo-controlled clinical trial with parallel groups and was performed on 66 women with PCOS referred to the gynecology and Infertility clinic of Firoozgar Hospital affiliated with Iran University of Medical Sciences and some selected private centers in Tehran, Iran from June 2016 to November 2017 to investigate cinnamon effects on the metabolic status of women with PCOS. Sample size was calculated based on fasting blood sugar (FBS) mean differences between cinnamon and placebo groups using the following formula. It was assumed that a total sample size of 66 subjects (33 participants in each group), would provide an 80% power with a type I error of 0.05 to detect a statistical significant difference in FBS mean between the two studied groups.

$$n = \frac{1}{1-f} \times \frac{2(z_{1-\frac{\alpha}{2}} + z_{1-\beta})^2 s^2}{(\mu_1 - \mu_2)^2}$$

$$\frac{1}{1-0.10} \times \frac{2(1.96+0.84)^2 \times (2.9)^2}{(2.2)^2} \approx 33$$

Iranian women aged 18-40 years, with definitive diagnosis of PCOS by an expert gynecologist, were included in the study according to Rotterdam criteria. The Rotterdam criteria require the presence of two of the following symptoms in the patient: a) Oligo-ovulation or anovulation; b) Hyperandrogenism clinical (such as hirsutism) or biological (including increased free androgen or free testosterone) signs; and c) Polycystic ovaries in ultrasound view (Wang and Mol, 2017). Hirsutism defined as a Ferriman-Gallwey score more than 8 (Ferriman and Gallwey, 1961). In this study all the women who have used other herbal remedies, glucose or lipid metabolism affecting drugs, vegetarians, women with body mass index under 19 or over than 35 kg/m^2, patients with metabolic disorders, and pregnant or nursery women were excluded. Finally, out of 113 participants assessed, 81 women were eligible for the trial and signed an informed consent form. Participants were randomly allocated to cinnamon (n=41) or placebo (n=40) groups by using randomization list. Randomization was performed by a person who was not involved in the research process. The main outcome measure was metabolic status including fasting blood sugar (FBS), Triglyceride (TG), low density cholesterol (LDL and LDL-C), high density cholesterol (HDL and HDL-C), total cholesterol, Sex Hormone Binding Globulin (SHBG), total testosterone (TT), Fasting Insulin (FI), and free androgen index (FAI).

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Measurements

All the subjects completed a demographic and fertility questionnaire, which included information such as age, marital status, duration of education, occupational status, economic status, age of menarche, and body mass index (BMI) using the self-report method before the intervention. Blood test results were recorded before and 12 weeks after intervention by the researcher in a data sheet based on laboratory test reports. All blood samples were collected after 12-14 hours of overnight fasting. After taking blood, the samples were placed at the room temperature for 20-30 minutes, and then were centrifuged at 2500-3500 revolutions per minute (rpm) for 10-15 minutes. Blood sera were isolated and stored at -80º C for later assessments. All the samples were analyzed in the laboratory of the research in the Laboratory of Gynecology and Infertility Clinic of Firoozgar Hospital. FBS was measured in milligrams per deciliter (mg/dl), triglyceride (mg/dl), and total cholesterol (mg/dl) levels were determined by Pars Azmoon company enzymatic kits (Tehran, Iran) and Hitachi 912 auto analyzer (Japan), and levels of LDL cholesterol (mg/dl) and HDL cholesterol (mg/dl) were determined by Pishtaz Teb company kit (Tehran, Iran) and Hitachi 912 auto analyzer (Japan). Also, the fasting insulin (milli-international units per liter or mIU/l) were measured by enzyme-linked immunosorbent assay (ELISA) method using the commercial kit (Insulin: Monobind Inc., Lake Forest, CA, USA) with an automated micro plate reader (Hyperion Inc., USA). FAI was calculated to determine androgen status of the subjects using the equation: FAI= (100× total testosterone (nanomoles per liter or nmol/l)) / sex hormone binding globulin (nmol/l). Also, BMI was calculated using the following formula: BMI (kg/m^2) = weight (kg)/ $height^2$ (m). Variables were measured twice: once before the intervention and once 12 weeks after the onset of the intervention.

Preparations of the Cinnamon extract capsules and the placebo

The cinnamon was taken from herbal market in Tehran city and was approved by a pharmacognosy expert of the School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran-Iran. The appropriate dosage was selected based on recommended dosage in Iranian Traditional Medicine (ITM) and Physician's Desk Reference (PDR) for herbal medicines. According to the mentioned references, the average dose of 3 g/day was selected. In the next step, cinnamon was grounded using an electrical grinder and the resulting powder was combined with 96º ethanol as the solvent. After the solvent evaporation, the remaining extract was mixed with corn starch and turned into a powder. Three grams of that powder then were placed into each size 0 capsules manually. For the placebo, the same capsules filled with corn starch alone. Finally, the capsules were packaged and coded in the similar boxes and named A or B by a person independent of research team. All of participants, researchers, or statisticians were blinded to the groups.

After initial measurements, intervention was started. Some of the subjects in both groups withdrew during the follow up (Figure 1). Participants in cinnamon group (n=33) took the cinnamon extract capsules 3 g/day

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orally for twelve consecutive weeks, and placebo group (n=33) simultaneously and in parallel took placebo capsules orally once a day for twelve consecutive weeks. During the study period, the subjects were monitored by telephone once or twice a week and were asked to report any drug side effects, complication, or stop taking the drug. Women who did not take more than 2 capsules for any reasons, were excluded from the study (Figure 1).

Statistical analysis

Normal distribution of the data was checked by Kolmogorov-Smirnov test and graphical methods. Data was presented as mean and standard deviation for quantitative data or frequency and percent (for qualitative data) in tables. The student t-test was used for between group comparison of quantitative variables with normal distribution, while the paired t-test was used to compare them before and after the intervention in each group. The Mann Whitney U test was used for between group comparison of quantitative variables without a normal distribution. Categorical variables were compared using the chi-square test. Analysis of Covariance (ANCOVA) was used when there were significant differences between the groups before the intervention. All statistical analyses were performed using SPSS version 16 software (SPSS Inc., Chicago, IL, USA). Significance level was set at < 0.05.

Results

The mean age of the subjects was 27.4±78.9 and 26.31±4.0 in the intervention and control groups, respectively. The characteristics of the subjects are summarized in the table 1. As this table shows, random allocation has been able to balance between the two groups in term of demographic and reproductive characteristics of the participants. Therefore, there were no statistically significant difference between the groups regarding these variables.

The results of independent t-test in table 2 shows that there are no significant differences between the groups before intervention regarding FBS, TG, LDL-C, HDL-C, SHBG, TT, and FAI; but total cholesterol (P=0.015) and FI (P=0.003) were statistically lower in the placebo group than the cinnamon group. At the end of the study, the two groups did not show any significant differences in terms of FBS, TG, LDL-C, HDL-C, total cholesterol, SHBG, and FAI; but the women in cinnamon group had a significant lower TT than other group (P=0.001). Also, the results of paired t-test showed that in the placebo group, FBS, LDL-C, HDL-C, total cholesterol, TT, SHBG, and FAI had a significant increase at the end of the study ($P<0.05$); but TG, and FI did not show any statistical changes. In cinnamon group, only HDL-C showed a significant increase after the intervention compared to before (P=0.042), and the other hormones and metabolic indicators remained unchanged. It should be noted that since total cholesterol and FI were significantly lower in the placebo group compared to the cinnamon group, ANCOVA was used to compare the mentioned

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variables between the two groups at the end of the study. The results showed that there were no significant differences between two groups regarding total cholesterol and FI (table 2).

As table 3 shows, there was no significant difference between the two groups in term of all hormonal and metabolic indices changes, except TT changes. That is, an increase in TT in the placebo group at the end of the study was statistically greater than the cinnamon group (P=0.001).

Discussion

Nowadays, the prevalence of PCOS is getting increased and it is becoming a common cause of endocrine and metabolic disorders in women. Nevertheless, the PCOS management and treatment approaches remain a challenge (Joshi et al., 2021). Although the mechanisms underlying the effects of herbal extracts on PCOS are needed further investigations (Arentz et al., 2014). Recently, medicinal plants and herbal compounds have attracted much attention in the management of PCOS due to their lower side effects and appropriate metabolic and hormonal effects in women with PCOS (Joshi et al., 2021). Our study results indicated that taking oral capsules of cinnamon extract at a dose 3 g /day for twelve consecutive weeks only has favorable effect on decreasing TT in PCOS women and had no beneficial effects on other studied parameters including FBS, TG, total cholesterol, LDL-C, HDL-C, FI, SHBG, and FAI. The results of different studies in this field, have not been the same. For example, in line with our study, Dou et al. (2018) have demonstrated the favorable effects of cinnamon on the hormonal status of the PCOS mouse model (Dou et al., 2018). Blevins et al. (2007) found that cinnamon taken at a dose of 1 g/day for 3 months has no significant effect on fasting glucose, lipid, or insulin levels in subjects with non-insulin-dependent type 2 diabetes (Blevins et al., 2007b). Contrary to our results, the findings of other studies confirmed that cinnamon complementation can significantly reduce FBS, insulin or insulin resistance and raises insulin sensitivity in women with PCOS (Heydarpour et al., 2020; Wahyuningtyas and Sa'adi, 2021). Differences in the metabolic status of subjects may be involved in different results of various outcomes related to glycemic parameters (Borzoei et al., 2018). While our study results did not show any effect of cinnamon on metabolic indices, other studies confirm the positive effects of cinnamon on lipid profile in women with PCOS (Borzoei et al., 2018; Maleki et al., 2021). Since the results concerning the potential effects of cinnamon on metabolic and hormonal profiles are inconsistent, further studies are needed to explore the precise mechanisms of clinical, metabolic, and hormonal changes following cinnamon supplementation, as well as the appropriate dosage in PCOS (Maleki et al., 2021). It is difficult to explain how cinnamon extract could induce its beneficial effects on TT or other hormonal and metabolic indices at the molecular level in women with PCOS. This maybe because peroxisome proliferator-activated receptor gamma/alpha (PPAR-gamma/alpha), as well as lipid hemostasis target genes such as lipoprotein lipase (LPL) and CD36

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expression may be induced by cinnamon. In addition, cinnamon with activating AMP-activated protein kinase (AMPK) can suppresses acetyl CoA-carboxylase, thereby increasing beta-oxidation and decreasing fatty acids biosynthesis (Maleki et al., 2021). Also, some researchers have suggested that since insulin resistance is the major cause of androgen excess in PCOS women, cinnamon can regulate androgen production by controlling insulin resistance. In fact, cinnamon can downregulate androgen production in PCOS women by reducing advanced glycation end products (AGEs) (Garg and Merhi, 2016; Talaei et al. 2017). In other words, in women with PCOS, hyperinsulinemia can cause ovarian hyperandrogenemia, and it seems that cinnamon can modify the androgen excess status in PCOS women by improving insulin sensitivity (Maleki et al., 2021). This effect is achieved through the insulin receptor autophosphorylation simulation and protein tyrosine phosphatase inhibition by cinnamon. Insulin exerts its effects on androgen production through IGF-1 receptors located on the ovarian theca and stroma cells. Insulin-like growth factor 1 (IGF-1), along with Insulin-like growth factor binding protein-1 (IGFBP-1) affect the maturation of follicles through paracrine and/or autocrine mechanisms. In this context, cinnamon acts as an amplifier of insulin-receptor function and can also regulate the signaling pathways of insulin and IGF-1 (DOU, 2018; Talaei et al. 2017). Nonetheless, in our study, the effect of cinnamon on FI and FBS was not observed. Talaei et al. (2017), who also reported that 3 grams of cinnamon per day for eight weeks had no beneficial effect on glycemic indices such as fasting plasma glucose, suggested that relative shortening of the intervention period may have contributed to these results. On the other hand, it seems that the conflicting results of the effects of cinnamon on metabolic or hormonal status may be relevant to different research communities. For instance, the study by Blevins et al. (2007), which showed the beneficial effects of cinnamon on glycemic markers, has been done on individuals with type 2 diabetes; while the present study on non-diabetic women, does not approved these results. Generally, the heterogeneity of studies reports on the cinnamon's effect on metabolic or hormonal status can be justified by differences in related factors such as duration, dosage, and pharmaceutical form of cinnamon use, ethnicity, sample size, and BMI of study population. So, it is still early to suggest evidence-based cinnamon supplementation and for knowing cinnamon's mechanism of action and its effects on human body, large-scale and well-designed clinical trials are needed (Blevins et al., 2007).

The findings of this study should be considered in light of certain limitations. An important limitation was that the women included in our study with any PCOS phenotypes. While, the PCOS phenotypes may experience different degrees of insulin resistance (Amini et al, 2020), and so the effects of cinnamon on these phenotypes maybe different. The other limitation was our participants BMI. We studied cinnamon effects on hormonal and metabolic markers of women with PCOS, regardless to their BMI. Therefore, we strongly recommend that more extensive research should be done to determine the effect of cinnamon in women with PCOS according to the weight of women.

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Conclusion

In conclusion, we found that the use of oral capsules of cinnamon extract, which is equivalent to 3 grams of cinnamon for 12 consecutive weeks, causes a statistically significant reduction in total testosterone and has no effect on changes in SHBG, FAI, and metabolic and glycemic parameters in women with PCOS. To better understand the molecular pathways and evaluate effects of cinnamon in these women, more detailed studies with larger sample sizes are still needed. Besides, it seems future studies should focus on the effects of cinnamon in PCOS women based on their phenotypes.

Ethical Considerations

Complying with ethical guidelines

The research protocol was approved by the Ethical Committee of Iran University of Medical Sciences (Code: IR.IUMS.REC.1395.9311373027). Also the trial protocol was registered in the Iranian Registry of Clinical Trials (IRCT) with code: IRCT2016021326161N2, Date: 31/5/2016; and performed in accordance with the ethical standards of the Declaration of Helsinki (2013 version) and its later amendments or comparable standards of ethics. All participants were initially informed completely about study goals and methods and then signed an informed written consent form.

Authors contribution: Leila Amini: Supervised all stages of study and provided article draft; Sanam Hadipoor: Participated in designing, sampling, and writing the project; Bahareh Afshar: Participated in writing the project; Afsaneh Ghasemi: Participated in designing and sampling the project; and Hamid Haghani: Performed statistical analysis.

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Conflict of interests: The authors declare that they have no conflicts of interest.

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Table 1. Characteristics of the subjects

Variables	Groups	Cinnamon N (%)	Placebo N (%)	Test Result
Age (Year)	<25	8 (24.2)	14(42.4)	t=1.571 df=64 p=0.121
	25-29	11 (33.4)	12 (36.4)	
	>30	14 (42.4)	7 (21.2)	
Marital status	Single	25 (75.8)	18 (54.5)	χ^2 =3.27 df=1 p=0.071
	Married	8 (24.2)	15 (45.5)	
Duration of education (Year)	≤12	5 (15.2)	4 (12.1)	χ^2 =0.129 df=1 p=0.72
	>12	28 (84.8)	29 (87.9)	
Being employed	No	5 (15.2)	11 (33.3)	χ^2 =2.97 df=1 p=0.085
	Yes	28 (84.8)	22 (66.7)	
Economic status	Relatively desirable	31 (93/9)	29 (87.9)	χ^2 =0.733 df=1 p=0.392
	Optimal	2 (6.1)	4 (12.1)	
Menarche age (Year)	11-12	6 (18.2)	9 (27.2)	t=0.541 df=64 p=0.59
	13-14	17 (51.5)	15 (45.5)	
	15-17	10 (30.3)	9 (27.3)	
BMI (kg/m^2)	19-24.9	16 (48.5)	13 (39.4)	t=1.293 df=64 p =0.201
	25-29.9	10 (30.3)	20 (60.6)	
	30-34.9	7 (21.2)	0 (00.0)	

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Table 1. Comparison of metabolic indices before and after the intervention within and between the groups

Metabolic Indices	**Groups**	**Before M±SD**	**After M±SD**	**Paired t-test**	Standard Error (CI)
Fasting blood sugar (mg/dl)	Cinnamon	104.15±13.48	106.81±14.59	t=0.951 df=31 p = 0.349	0.12 (-0.36,0.60)
	Placebo	103.21±8.82	105.33±9.06	t=2.246 df=32 p = 0.032	
	Independent t-test	t=0.074 df=64 p = 0.941	t=0.493 df=63 p = 0.624		
Triglyceride (mg/dl)	Cinnamon	116.48±51.1	121.84±49.79	t=0.905 df=32 p =0.372	0.05 (-0.43,0.53)
	Placebo	116.9±44.11	19.42±44.31	t=0.753 df=32 p = 0.457	
	Independent t-test	t=0.036 df=64 p = 0.971	t=0.209 df=64 p = 0.835		
LDL cholesterol (mg/dl)	Cinnamon	98.72±28.12	103.54±29.66	t=1.467 df=32 p = 0.152	0.36 (-0.13,0.85)
	Placebo	88.27±24.42	93.63±24.44	t=2.163 df=32 p = 0.038	
	Independent t-test	t=1.612 df=64 p =0.112	t=1.481 df=64 p = 0.067		
HDL cholesterol (mg/dl)	Cinnamon	47.15±10.28	49.78±11.24	t=2.124 df=32 p = 0.042	-0.46 (-0.94,0.04)
	Placebo	48.39±8/17	55.69±14.33	t=2.851 df=32 p = 0.008	
	Independent t-test	t=0.543 df=64 p = 0.589	t=1.863 df=64 p = 0.067		
Total cholesterol (mg/dl)	Cinnamon	180.30±34.01	184.81±37.86	t=0.937 df=32 p = 0.356	0.46 (-0.03,0.94)
	Placebo	161.93±25/29	169.72±26.87	t=2.629 df=32 p =0.013	
	ANCOVA	t=2.489 df=64 p = 0.015	F=0.003 p =0.96		
Sex Hormone Binding Globulin (nmol/l)	Cinnamon	53.86±41.73	66.97±55.35	t=1.559 df=30 p = 0.130	0.03 (-0.45,0.52)
	Placebo	49.70±35.94	65.40±37.52	t=3.396 df=32 p = 0.002	
	Independent t-test	t=0.413 df=63 p = 0.681	t=0.087 df=63 p = 0.931		
Total Testosterone (ng/dl)	Cinnamon	0.39±0.21	0.39±0.20	t=0.134 df=28 p = 0.894	-2.67 (-3.30,-1.98)
	Placebo	0.37±0.14	0.60±0.24	t=5.841 df=32 p < 0.001	
	Independent t-test	t=0.229 df=64 p = 0.819	**t=3.563 df=60 p =0.001**		
Fasting Insulin (mIU/ml)	Cinnamon	15.51±13.25	12.88±8.57	t=1.305 df=28 p = 0.203	0.77 (0.26,1.26)
	Placebo	8.37±2.02	8.10±2.08	t=0.94 df=31 p = 0.354	
	ANCOVA	t=3.119 df=62 p = 0.003	F=2.194 p = 0.144		
Free Androgen Index	Cinnamon	0.96±0.62	1.20±1.08	t=-1.45 df=26 p = 0.159	-0.08 (-0.59,0.43)
	Placebo	0.96±0.40	1.28±0.98	t=-2.26 df=32 p = 0.03	
	Mann-Whitney U	t=-0.44 df=63 p = 0.965	Z=-0.75 p =0.452		

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Table 2: Comparison of mean and standard deviation changes between the groups in terms of hormonal and metabolic indices before and after the study

group Changes in Metabolic and hormonal indices	Placebo M ± SD	Cinnamon M ± SD	Independent t-test
Fasting blood sugar (mg/dl)	2.12±5.42	2.56±15.79	t=0.184 df=63 p =0.855
Triglyceride (mg/dl)	2.51±19.19	5.36±34.05	t=0.419 df=64 p = 0.677
LDL cholesterol (mg/dl)	5.36±14.24	4.81±18/86	t=0.133 df=64 p =0.895
HDL cholesterol (mg/dl)	7.30±14.71	2.63±7.13	t=1.639 df=64 p = 0.106
Total cholesterol (mg/dl)	7.78±17.01	4.51±27.68	t=0.578 df=64 p = 0.565
Sex Hormone Binding Globulin (nmol/l)	27.61±16.32	46.81±13.11	t=0.337 df=62 p = 0.737
Total Testosterone (ng/dl)	0.22±0.22	0.01±0.25	t=3.635 df=60 p = 0.001
Fasting Insulin (mIU/ml)	-0.26±1.59	-2.62±10.85	t=1.219 df=59 p = 0.228
Free Androgen Index	0.32±0.82	0.23±0.83	Z=0.439 df=59 p = 0.661

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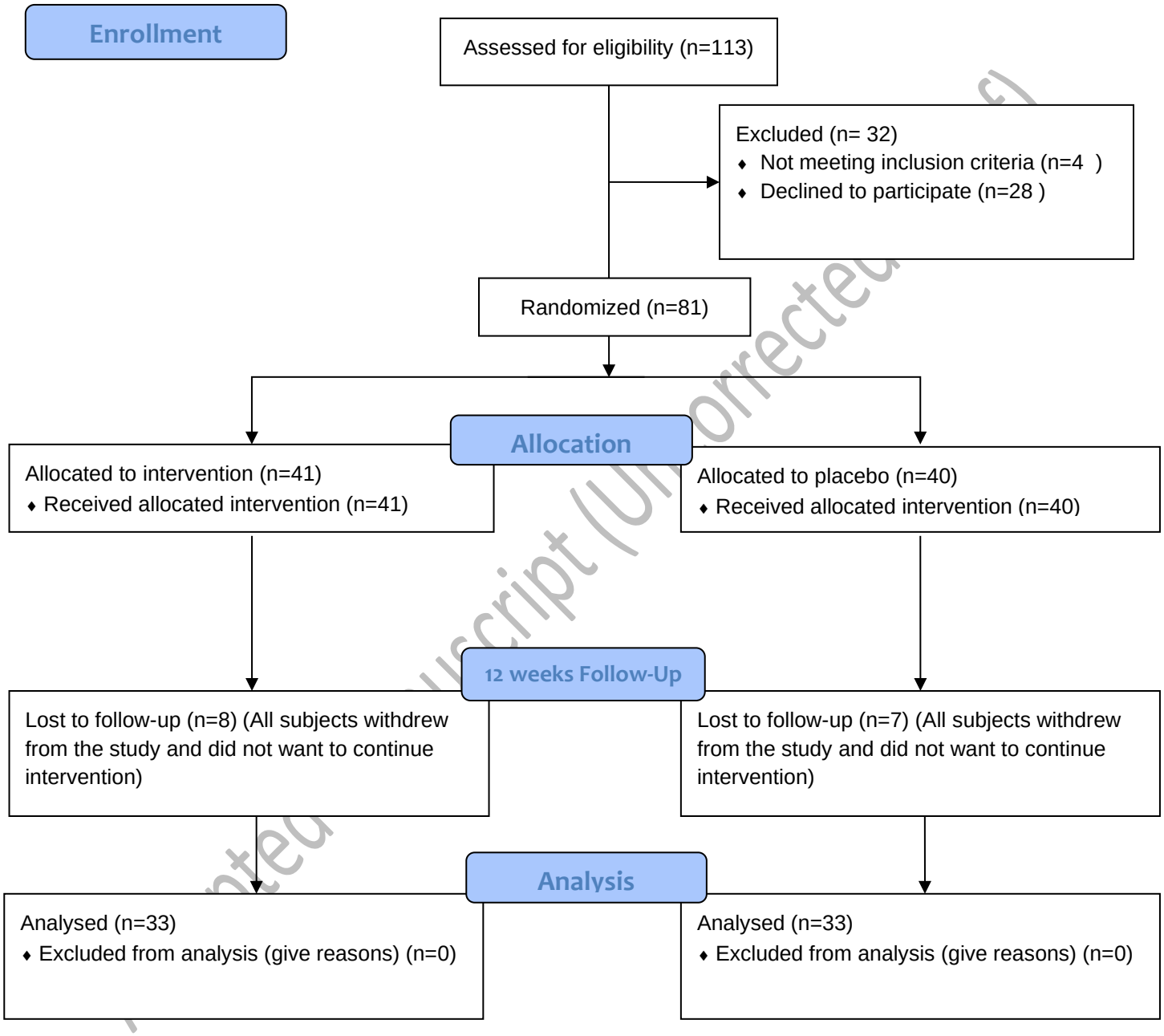

Figure 1: CONSORT Flow Diagram of the study process

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