**Efficacy of Persian herbal remedy and electroacupuncture on metabolic profiles and anthropometric parameters in women with polycystic ovary syndrome: A randomized controlled trial**

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**Abstract**

**Introduction:** Polycystic ovary syndrome (PCOS) is the most prevalent endocrine disorder in women of reproductive age. The aim of this study was to assess the efficacy of a Persian herbal remedy, as well as electroacupuncture and both treatment techniques on metabolic profiles and anthropometric parameters in patients with PCOS.

**Methods:** 80 overweight or obese women within the age bracket of 15-40 years with PCOS were enrolled in this clinical trial and randomly divided into 4 equal groups. All of them received metformin 1000 mg per day, in addition, the second group received 5 g of herbal medicine per day, the third group were subjected to 20 electroacupuncture sessions, and the fourth group received both therapies for 12 weeks.

**Results**: After 12 weeks of intervention, Body Fat and Body Mass Index decreased the most in group 4 and Waist to Hip Ratio decreased the most in group 3. There was also a significant decrease in fasting insulin, HOMA-IR and a significant increase in QUICKI in all intervention groups; however, there was no significant difference in these parameters in the control group (1) at the end of treatment. Total cholesterol and LDL decreased significantly in groups 3 and 4 and a significant decrease in TG, AST and ALT was observed in groups 2 and 4.

**Conclusion:** Based on the above results, it is advisable to use efficacious herbal medicines, electroacupuncture or both for better treatment of metabolic complications and overweight in patients with PCOS.

Key words: Polycystic ovary syndrome, Obesity, Insulin resistance, Phytotherapy, Electroacupuncture

**Introduction**

Polycystic ovary syndrome (PCOS) is the most prevalent endocrine metabolic disorder in women of reproductive age, which varies according to the diagnostic criteria [1-3]. The prevalence of this disease in women is between 6% and 20% worldwide. In Iran, according to Rotterdam diagnostic criteria, up to 19.5% prevalence rate has been reported[4].

The most significant challenges associated with this disease are metabolic complications and obesity [3,5]. About 60% of people with this syndrome have high Body Mass Index (BMI), and are also prone to abdominal obesity, dyslipidemia, hyperglycemia and hypertension (HTN), gestational diabetes mellitus (GDM), type 2 diabetes mellitus (T2DM) and cardiovascular diseases (CVD) [1,5-7]. It should be noted that these complications lead to increase in mortality in women with PCOS in postmenopausal years [5]. Hyperinsulinemia and insulin resistance (IR) are also important conditions that are associated with the pathophysiology of the syndrome [7], which leads to more production of androgen and disturb the process of production and development of ovarian follicles. Consequently, irregular menstruation and in some cases infertility are secondary causes of this syndrome [8].

In spite of the involvement of several organs and complications, there is still no comprehensive and standard treatment in classical medicine for this disease [9]. Therefore, considering the increase in the use of complementary therapies such as electroacupuncture and herbal medicine for menstrual and fertility challenges, it is imperative to assess the efficacy of these treatments by performing relevant clinical trials.

A review of new findings on complementary interventions in this study showed that the herbal product components based on Iranian medicine were effective in reducing BMI, decreasing blood pressure, safeguarding the digestive system and liver, significantly reducing serum leptin, LDL[[1]](#footnote-1), LDL to HDL[[2]](#footnote-2) ratio, TG[[3]](#footnote-3), glucose and insulin serum [10-12]. It was also generally efficacious in increasing menstrual blood flow and follicogenesis [12-16]. Electroacupuncture was also effective in regulating menstrual periods, decreasing BMI, decreasing Waist to Hip Ratio (WHR), decreasing visceral fat and plasma concentrations of leptin, decreasing total cholesterol, increasing insulin sensitivity, LDL and triglyceride [17-20]. Among various drugs in classical medicine, metformin also significantly influenced glucose serum, BMI and insulin resistance in overweight patients with PCOS [21, 22].

Persian’s medical approach to the treatment of multiple organ diseases emphasizes the need for attention to be paid to an individual’s dietary requirements and where necessary their medication [23]. For this reason, in this study, along with the interventions, dietary recommendations were employed in all groups [24-26].

The aim of the present study was to assess the efficacy of herbal medicine obtained from Persian medicine, the efficacy of electroacunpuncture, as well as the combination of both therapies as supplements along with metformin 1000 mg on metabolic profiles and anthropometric parameters in overweight or obese people with polycystic ovarian syndrome in comparison with the administration of metformin 1000 mg alone.

**Materials and Methods**

**1.1 Study design and sample size**

This is a randomized clinical trial aimed at evaluating the efficacy of a combination of herbal medicines derived from Persian medicine and electroacupuncture on metabolic and anthropometric indices in patients with PCOS. This study was approved by the Ethics Committee of Mashhad University of Medical Sciences in the form of a research project with code number 931324 and was registered with a registration number of IRCT2015040921671N1 in the Iranian Registry of Clinical Trials (IRCT).

Sample size was computed based on the test of the difference in mean of LH levels considering the variance and the mean values from similar articles (Johansson (2013) study) with 95% confidence and was equal to 15 for each group[[4]](#footnote-4). However, to increase the accuracy of the study, each group members were increased to 20 [27]. For this purpose, 80 samples were selected from clients with this syndrome in women's clinics, Iranian medicine and Chinese medicine clinic at Imam Reza Hospital, Mashhad University of Medical Sciences, Iran from October 2015 to December 2016.

**1.2 Diagnostic and inclusion criteria**

All women who had polycystic ovary syndrome within the age bracket of 15 to 40 years and who had BMI equal to or greater than 25 were enrolled in the study. Diagnostic criteria for this disease were selected according to the 2006 AE-PCOS[[5]](#footnote-5), which includes the following:

1) Hyperandrogenism (clinical or paraclinical)

2) Ovarian dysfunction (oligo-anovulation or polycystic ovary in sonography)

3) Other disorders, which may lead to an increase in androgens or related disorders should be rejected [5, 7, 28]. Clinical hyperandrogenism was considered to be the presence of acne and/or hirsutism and having a score more than 8 in the modified Ferriman Gallwey (mF-G) scoring technique. Paraclinical hyperandrogenism was also diagnosed based on values ​​higher than normal testosterone and/or androstenedione. Menstrual periods occurring at intervals greater than 42 days or less than 6 times in a year were considered as oligomenorrhea and absence of menstrual period or menstrual period occurring less than two times during 6 consecutive months were considered as amenorrhea. Presence of at least 12 follicles with diameters of 2 to 9 mm and/or ovarian volume greater than 10 cm3 is a positive criterion for diagnosis in sonography [5, 7, 29].

**1.3 Exclusion criteria**

(1) Hyperprolactinemia (2) Use of hormonal, anti-diabetes, antihypertensive and anticoagulant drugs three months before the start of the study (3) Presence of mass in sonography (4) Suspected androgen producing tumor (5) Thyroid dysfunctions (6) Suspected insulin resistance syndromes (7) Uncontrolled blood pressure greater than 160/100 mmHg (8) Smoking (9) Hemorrhagic disorders (10) Pregnancy

**1.4 Technical information**

The ingredients of the tested herbal medicine include *Foeniculum vulgare*: 38425 (FUMH), *Urtica dioica*: 45491 (FUMH), *Dacus carota*: 41633 (FUMH) and *Trifolium pratense*: 40926 (FUMH) and *Curcuma longa* (FUMH\_E1007) prepared at the Mashhad medicinal herbs market. Herbarium code was obtained from the Faculty of Agriculture of Mashhad University of Medical Sciences. Microbiology tests were carried out on several samples of the above-mentioned herbal medicine to determine the presence of aerobic mesophilic bacteria, salmonella, E. coli and other possible pathogens according to the standards of 11804, 9933 and 1810 in the Testa laboratory three times. The drug was tested for microbial contamination according to the WHO standard for herbal medicines and was approved. The essential oil obtained was dried over anhydrous sodium sulphate, and then analyzed employing GC and GC-MS technique. The GC analysis was performed using a Varian CP-3800 GC equipped with a FID detector, fused-silica column (CP-Sil 8CB, 50 m × 0.25 mm, film thickness, 0.12 m). The GC-MS analyses were performed using an Agilent 5975 apparatus with a HP-5ms column (30 m x 0.25 mm i.d., 0.25 µm film thickness) interfaced with a quadruple mass detector and a computer equipped with Wiley 7n.l library

In addition, trans-anethol was identified as the most important compound present in the extracted essence after undergoing standardization procedure at the Faculty of Pharmacy, Mashhad University of Medical Sciences, Iran. The drug was registered by the Patent and Intellectual Property Organization in Iran with approval number: 139650140003004422 and was scientifically approved by the Research and Technology Unit of Mashhad University of Medical Sciences.

In the electroacupuncture, Huan-Qiu (single use steel needles, length: 30-50 mm, diameter: 0.30mm) were employed, and in all groups, 500 mg metformin hydrochloride enteric-coated tablets manufactured by Aria Pharmaceutical Company with approval number: 9609356 were used.

**1.5 Data collection**

Height and weight of the patients were measured without shoes early in the morning. Weight, body mass index and anthropometric measurements of the body were recorded by the Gaia 359 (Body Composition Analyzer System) at the beginning and end of the treatment. Hip circumference (HC) was measured at the level of the major trochanters through the pubic symphysis, and waist circumference (WC) was measured midway between the lateral lower rib margin and the iliac crest to the nearest ±0.1 cm employing a scale. To prevent errors, all measurements were done by the same person. Venous blood samples were taken twice after a 12-hour fasting period (from 08:00 AM to 09:00 AM) during the study (at the beginning and 12 weeks later). The metabolic parameters evaluated included FPG[[6]](#footnote-6), AST[[7]](#footnote-7), ALT[[8]](#footnote-8)(Pars Azmoon Company, Tehran, Iran), total cholesterol, TG (Man Lab, Tehran, Iran), LDL-C and HDL-C (PISHTAZTEB, Tehran, Iran). They were measured enzymatically using commercial kits in Special Medical Laboratories (Imam Reza Hospital, Mashhad University of Medical Sciences, and Mashhad, Iran). Fasting serum insulin was measured by Insulin IRMA kit purchased from IZOTOP company, H-1121 Budapest, Hungary). We also computed HOMA-IR[[9]](#footnote-9), HOMA-β[[10]](#footnote-10) and QUICKI[[11]](#footnote-11) to evaluate insulin sensitivity and insulin secretion [30-32].

HOMA-IR was computed as fasting insulin (μU/mL) × fasting glucose (mg/dl) / 405.

HOMA-β was calculated as fasting insulin (μU/ml) × 360/ (fasting glucose (mg/dl) − 63).

QUICKI was calculated as 1 / [log (fasting insulin (μU/mL)) + log (fasting glucose (mg/dl)].

Then, in the clinical stage, the patient’s history was obtained in order to enter the demographic information and signs and symptoms associated with the disease. At the end of the treatment, an overview of the process was done to assess the complications associated with the patient's treatment.

**1.6 Interventions**

The patients were randomly assigned into four groups (20 individuals each). Before randomization, using menstrual dysfunction (amenorrhea, oligomenorrhea) and body mass index (25 ≤ BMI < 30, 30 ≤ BMI < 35, 35 ≤ BMI), matching was done in four groups. random numbers table was used for random allocation. The research assistant assigned participants to interventions. She was blind to interventions and assigned numbers.

Then, the informed consent form was given to the patients after the treatment method was explained and a decision-making capacity had been created for the patients.

Each of the 4 groups received 2 pills of metformin 500 mg daily; in addition, the second group was given granulated herbal medicine in sachet (5 grams) daily, the third group was subjected to 20 sessions of electroacupuncture (2 sessions a week in the first and second month and one session in the third month) and the fourth group received a combination of both treatments in a 12-week period.

Acupuncture points identified by Liangmen (ST21), Tianshu (ST-25), Shuidao (ST 28), Guilai (ST 29), Zhangmen (liver13) and Abd Zigong on both sides of the body were selected. Acupucture points identified by Zhongwan (REN-12), Qihai (REN-6), Guanyuan (REN-4) and Yinlingquan (SP9), Sanyinjiao (SP-6), Fenglong (ST-40) on both lower legs were also selected [33].

All needles were inserted to a depth of 15 to 35 mm after sterilization and were rotated by hand after inserting to induce the de qi sensation[[12]](#footnote-12). To stimulate the ST28, ST25 and liver 13 points, the electrodes (KWD-808 Pulse acupuncture & moxibustion treatment device) were connected to the needles, they were employed at a frequency of 2 Hz; the degree of stimulation intensity was such that it induced muscle contraction of the site without any pain or discomfort. The needles that were not attached to the electrode were rotated manually every 10 minutes to induce the de qi sensation. The needles were left for 30 minutes. Patients were educated on the need to slow down on their eating habit as much as possible and eliminate foods with low nutritional value, as well as avoid excessive consumption of food prior to participation in the study. Recommended foods for all patients were similar in terms of nutritional requirement. In addition, the different types of food were extracted from Persian medical reference books according to dietary recommendations. Patients were visited once a week to ascertain compliance with dietary recommendations, as well as examine the possible side effects of the treatment. Also, during the three months of treatment, the patients did not use any other medication or supplement in addition to the treatment they received.

**Statistical methods**

Data obtained from clinical and paraclinical observations were analyzed by SPSS software, version 11. Chi-square test and one-way ANOVA test were employed to compare the qualitative and quantitative variables in the four groups, respectively. Initially, the normal distribution of the quantitative variables was evaluated using one sample Kolmogorov test. For comparison of quantitative variables before and after the study within each group, paired t-test was employed. In the absence of normal distribution, Wilcoxon non-parametric test was used. To compare the variations among the four groups, it was made one-way ANOVA or Kreskas-Wallis test. In all calculations, P value of <0.05 was considered statistically signiﬁcant in all analytical tests.

**Results**

In this study, at first, 80 people were included according to the inclusion criteria, out which 1 due to family reasons, 2 due to pregnancy and 1 due to migration did not complete the trial. Finally, 19 people in group 1, 21 in group 2, 18 in group 3 and 20 in group 4 completed the trial (Fig. 1). More than 90% of the patients took metformin tablets regularly and about 30% reported digestive problems such as bloating or nausea due to the use of this pill. Groups 2 and 4 did not report any specific adverse effects associated with use of herbal medication packaged in sachet.

The mean age of 78 female participants was 27.65 ± 6.70, out of which 21 (26.9%) were single and 57 (73.1%) were married. The age distribution of patients in the four groups was normal. (p-value = 0.065).

All anthropometric and laboratory parameters other than HDL, AST and ALT produced a normal distribution curve in all four groups. Comparison of the four groups showed that anthropometric parameters and mean age were not signiﬁcantly different before the intervention (Table 1, 2).

In this trial, after 12 weeks of intervention, the anthropometric variables including BMI, BF and WHR in each of the four groups reduced significantly when compared with the initial values. However, the highest reduction in BMI and BF levels were observed in group 4 and the highest difference in WHR was observed in group 3. (Table 3)

In addition, fasting insulin and HOMA-IR decreased significantly in all intervention groups (groups 2, 3 and 4); the highest insulin reduction was observed in group 3 and the highest reduction in HOMA-IR was observed in groups 2 and 3, respectively. However, in group 1, there was no significant difference in these parameters. There was also a significant decrease in HOMA-β in groups 2 and 3, while in group 1 (control) and 4 (combined therapy), no significant change was observed. Significant increase in QUICKI was observed in all three groups of intervention with the highest increase observed in group 3 (acupuncture), but in group 1 (control), no significant change was observed. (Table 2 & 3)

Total cholesterol and LDL in both groups 3 and 4 showed a significant decrease at the end of treatment compared to the beginning of treatment. The highest difference in total cholesterol was observed in group 4 and the highest reduction in LDL was observed in group 3; although differences in group 4 was also noticeable, but no significant decrease was observed in group 1 (control) and group 2. Significant decrease in TG, AST and ALT were observed in groups 2 and 4, and the highest difference was observed in group 4 while no significant changes were observed in groups 1 and 3. HDL was lower in all groups at the end of treatment, but this change was not significant in any of the groups. The LDL-HDL ratio increased slightly in groups 1 and 2 at the end of treatment, but the increase was not significant. In groups 3 and 4, this ratio decreased significantly. (Table 2 & 3)

In comparison with the control group (group 1), within-group changes showed a significant reduction in BMI in group 4 (p =0.012), HOMA-IR in group 3 (p = 0.045), SGOT in group 2 (p = 0.034) and group 4 (p = 0.006) and SGPT in group 3 (p = 0.050) and group 4 (p = 010). also it showed a significant reduction in WHR in group 3 (P = 0.050), a slight reduction in group 4 (P = 0.059) and a slight reduction in serum insulin in group 3 (P = 0.060). But they did not show a significant difference in the other anthropometric and laboratory variables. (Table 2 & 3)

**Discussion**

This study was conducted to evaluate the efficacy of traditional Persian medicine and electroacupuncture as complementary therapies on metabolic profiles, anthropometric parameters and insulin metabolism in women with polycystic ovary syndrome. The most significant findings from this study and its comparison with other studies are as follows:

1. **Anthropometric Parameters**

In relation to the above study and its efficacy on BMI and BF, they reduced significantly in each of the four groups when compared with the initial values, but statistical analysis showed that there was no significant difference among three groups (1, 2 and 3). This can be attributed to the positive effect of a healthy and uniform diet in all groups. However, the same finding indicated that group 4 had a significant and distinct statistical and clinical difference compared to other groups. As a result, combination of herbal therapy and electroacupuncture can be used to achieve a better result in reducing BMI and BF. Overweight and obesity are seen in about 60% of people with this syndrome and increase its complications [1, 5, 7]. Then, it is imperative to have more efficacious treatment options for overweight patients.

In this study, the highest decrease in WHR was observed in group 3 and 4, which indicates the beneficial effect of electroacupuncture in the reduction of abdominal fat. Patients with PCOS are prone to abdominal obesity, and an increase in WHR is associated with increased risk of cardiovascular diseases and diabetes [1, 7]. The waist circumference is related to the amount of subcutaneous fat and, as mentioned in numerous papers, the most important functions of body electroacupuncture are lipolytic activity and its effect in increasing the metabolism of lipids [20, 34]. In addition, the mechanism of the effect of phytoestrogens (like our herbal remedy) on metabolic syndrome was addressed in five main dimensions, which two of them were increasing basic metabolism and energy consumption and increasing fat burn [40].

B. **Metabolic and lipid profiles**

One of the most important findings of this study was a significant reduction in fasting insulin and HOMA-IR and a significant increase in QUICKI in all three intervention groups, also a significant decrease in HOMA-β in groups 2 and 3, and no significant changes in these parameters in group 1 (control). In other words, the effect of this herbal drug and electroacupuncture was highly significant in reducing insulin resistance and increasing its secretion in overweight patients with PCOS. FBS only decreased significantly in group 3, which may be due to normal mean blood glucose (96) at the beginning of the study.

Insulin resistance is one of the main pathophysiological causes of polycystic ovary syndrome, which itself leads to overweight and many other complications associated with the disease, such as interruption of ovulation and increased male hormones and clinical manifestations [35-38]. Consequently, considering the above results, the use of the studied herbal remedy or electroacupuncture had a positive impact on one of the most important parameters associated with PCOS and is therefore recommended in the management and treatment of insulin-related and non-blood glucose related factors; although, the combination of these two treatments does not increase the efficacy of the treatment on insulin-associated and glucose-related metabolic parameters.

As indicated in the results, the highest changes in cholesterol were observed in group 4, which shows a positive effect of the combination of herbal medicine and electroacupuncture in reducing it. In addition, reduction in TG, AST and ALT was significant in the group 2 and highly significant in the group 4, But there was no significant change in these factors in the control group and in the group 3. Regarding the prevalence of metabolic syndrome, hyperlipidemia, fatty liver and liver disorders in PCOS patients (1), prevention and control of hyperlipidemia, as well as the adoption of preventive measures against cardiovascular diseases, are among the most important guidelines in managing patients with PCOS. The above changes also indicate the positive effect of the above-mentioned herbal medicine in reducing TG and improving liver function, but electroacupuncture can also increase this effect with positive interaction with herbal medicine.

In a clinical trial by Hu. L et al., in 2014, administration of 1500 mg of metformin for twelve weeks to 40 patients with PCOS resulted in a significant decrease in the index of insulin resistance and body mass index in overweight people [22]. In another study by Esfahanian F et al., in 2013, it was observed that the markers of insulin resistance (IR) in the low-calorie group was significantly decreased in the group receiving metformin following twelve weeks of metformin administration in one group and a low-calorie diet in another group of 40 overweight or obese PCOS patients [21]. Meanwhile, in our study, metformin 1000 mg which was administered to group 1(control) per day did not have a significant effect on the reduction of markers of insulin resistance (IR). However, with an increase in the dose, more gastrointestinal complications were observed in our patients.

In a study conducted by Nizar M. Mhaidat et al., on rats in 2015, it was noted that F.vulgare was effective in preventing an increase in blood glucose, and also reduced the increased cholesterol, ALT, AST, urea and creatinine in diabetic rats. Studies have shown that triterpenoids and phenolic compounds in Foeniculumvulgare stimulate insulin secretion, and also have antioxidant properties that catalyze the removal of free radicals and prevention of the destruction of liver cells and insulin secreting cells in the pancreas [39].

In a review study published by jungbauer A et al., in 2014, the mechanism of the effect of phytoestrogens on metabolic syndrome was addressed in five main dimensions, of which the most important were increased insulin sensitivity. In this study, the extract of red clover, licorice and soybeans was identified as an effective ingredient in the treatment of polycystic ovary syndrome [40]. Another study by Kianbakht et al., on the effect of Urtica dioica leaf extract on 46 patients with type 2 diabetes, it was observed that there was a significant reduction in fasting glucose levels, but no significant effect was reported on SGOT and SGPT [11]. In another clinical trial study performed by P Chedraui et al., on 60 postmenopausal women over 40 years with oral administration of 80 mg of red clover for three months, it was found that this extract significantly reduced the levels of TG, LDLC and lipoprotein A in women with a BMI greater than 25 [41]. In another study by KB Soni et al., on 10 healthy volunteers who were given 500 mg of curcumin daily for seven days, it was found there was 33% decrease in LDL oxidation, 11% reduction in total cholesterol and 29% increase in the concentration of HDL [42]. However, in contrast to the study of Kianbakht, we administered 2 grams of granulated herbal medicine sachet containing Foeniculumvulgare seed, Dacuscarota seed as phytoestrogen, as well as 500 mg Urticadioica seeds, 200 mg of red Clover seeds and 300 mg of Curcuma *longa* in our study; a significant reduction in SGOT and SGPT as well as increase in sensitivity to insulin were observed, which may be due to the effects of other components or their synergistic effects. However, it is worth noting that although the drug resulted in a decrease in LDL and total cholesterol as reported in the above studies, this decrease was not statistically significant in group 2 (herbal medicine intervention). However, in this study, there was also a significant decrease in TG, which was directly linked to the use of herbal medicine.

In another review article by Stener-Victorin et al., on the effects of electroacupuncture on PCOS patients, this treatment was shown to stimulate weight loss and increase insulin sensitivity [17]. In a study by Zheng et al., in 2013, on 86 PCOS patients, it was observed that electroacupuncture had more effect on BMI and WHR compared to the administration of 1500 mg metformin daily, which had fewer side effects [18]. In a study by Tugrul et al., on 55 obese and overweight women, it was found that electroacupuncture in some parts of the body and ear for 20 consecutive days had a significant effect on weight loss, total cholesterol, LDL and TG in patients with PCOS [20]. In another study, conducted by Abdi et al., on 196 overweight individuals, after 6 weeks of body electroacupuncture, there was a significant reduction in anthropometric and lipid profile in both the authentic and sham groups [35]. Our study also confirmed the significant effect of electroacupuncture on the reduction of anthropometric and lipid profile. It is important to note that in this study, there was a significant decrease in the ratio of LDL to HDL in groups 3 and 4, but in the control group and group 2, no decrease was observed. Based on these findings, electroacupuncture is recommended in patients with hyperlipidemia or who are susceptible to hyperlipidemia.

One of the most valuable points in this study is the investigation of the effect of the above herbal medicine and the efficacy of combination of this drug with electroacupuncture on anthropometric and metabolic variables in patients with PCOS for the first time. Moreover, none of the patients reported a specific complication regarding the use of herbal medicine or electroacupuncture during the course of treatment.

There were also some limitations in this study, which could be considered in subsequent studies. For example, we didn't use any placebo or sham acupuncture, because we had four groups in this study and Increasing the number of groups was not possible. In addition, the duration of the intervention was limited to twelve weeks, so, further follow-up and at least six months' period of treatment may lead to further changes. As observed in the clinic cases, there may also be more significant changes in individuals with longer visitation and similar interventions. Also, it seems that other factors such as HbA1c, VLDL-C, etc. which were not investigated in this study because of limited costs should be examined.

**Conclusions**

In conclusion, the proposed herbal drug, body electroacupuncture, as well as the combination of these two therapies, along with proper diet and metformin have significantly been effective in reducing weight, abdominal fat and insulin resistance. Also, the above-mentioned herbal drug and its combination with body electroacupuncture had a significant effect in reducing TG and liver enzymes. There were also significant changes in lipid profiles with electroacupuncture as well as its incorporation into herbal remedies.

Consequently, it seems that considering the results of the current study and its consonance with the findings of previous studies, it is advisable to use complementary medicine including the above drug, electroacupuncture, or both in the treatment of PCOS patients. However, further studies are needed to obtain more accurate results.

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**Conflict of interest**

None.

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**References:**

[1] Echiburu B CN, Maliqueo M, Perez-Bravo Francisco, Guevara AL, Hernadez P, et al. Metabolic profile in women with polycystic ovary syndrome across adult life. Metabolism-Clinical and Experimental 2016; 65(5): 776-82.

[2] Diamanti - Kandarakis E, Kouli CR, Bergiele AT, FILANDRA FA, TSIANATELI TC, SPINA GG, et al. A survay of the polycystic ovary syndrome in the Greek island of Lesbos: hormonal and metabolic profile. J Clin Endocrinol Metab 1999; 84(11): 4006-11.

[3] Daan NMP, Louwers YV, Koster MPH, Eijkemans MJC, Rijke YBD, Lentjes EWG, et al. Cardiovascular and metabolic profiles amongst different polycystic ovary syndrome phenotypes: who is really at risk?. Fertility and sterility 2014; 102(5): 1444-51.

[4] Sayehmiri F, Kiani F, sayehmiri K, Ahmadi M, Shohani M. Prevalence Of Polycystic Ovary Syndrome In Iranian Women: A Systematic Review and Meta-analysis. The Iranian Journal of Obstetrics, Gynecology and infertility 2014; 17(115): 11-21.

[5] Jamilian M, Razavi M, Fakhrie Kashan Z, Ghandi Y, Bagherian T, Asemi Z, et al. Metabolic response to selenium supplementation in women with polycystic ovary syndrome: a randomized, double-blind, placebo-controlled trial. Clinical endocrinology 2015; 82(6): 885-91.

[6] Lansdown A, Rees D. The sympathetic nervous system in polycystic ovary syndrome: a novel therapeutic target?, Clinical endocrinology 2012; 77(6): 791-801.

[7] Marc A, Fritz LS. Clinical Gynecologic Endocrinology and Infertility. Eighth ed, Philladelphia, Lippincott Williams & Wilkins; 2011: 501-31, 83, 93.

[8] Gupta JK, Qureshi SS, Shah K, Upmanyu N. PREVALENCE AND RISK FACTOR OF POLYCYSTIC OVARIAN SYNDROM. Asian Journal of Pharmaceutical and Clinical Research 2016; 9(2) 23-5.

[9] RohaniM, Badiee AvalSh, Taghipour A, Amirian M, Hamedi Sh, Tavakkoli M, et al. Diagnostic Models in Polycystic Ovarian Syndrome Based on Traditional Iranian Medicine and Western Medicine. The Iranian Journal Of Obstetrics, Gynecology and Infertility 2017; 20(11): 35-45.

[10] Ahangarpour A, Amirzargar A, Oroojen AA, Bakhtiarizade H, Nikraftar O. Antidiabetic Effect of Hydroalcholic Urtica dioica Leaf Extract in Male Rats with Fructose-Induced Insulin Resistance. Iran J Med Sci 2012; 37(3): 181–6.

[11] Kianbakht S, Khalighi-Sigaroodi F, Dabaghian FH. Improved glycemic control in patients with advanced type 2 diabetes mellitus taking Urtica dioica leaf extract: a randomized double-blind placebo-controlled clinical trial, Clinical laboratory 2013; 59(10): 1071-6.

[12] Rahimi R, Ardekani MRS. Medicinal properties of Foeniculum vulgare Mill. in traditional Iranian medicine and modern phytotherapy, Chinese journal of integrative medicine 2013; 19(1): 73-9.

[13] Khazaei M, Montaseri A, Khazaei MR, Khanahmadi M. Study of Foeniculum vulgare effect on folliculogenesis in female mice, Int J Fertil Steril 2011; 5(3): 122-7.

[14] Karampoor P, Azarnia M, Mirabolghasemi G, Alizadeh F. The effect of hydroalcoholic extract of fennel (foeniculum vulgare) seed on serum levels of sexual hormones in female wistar rats with polycystic ovarian syndrome (PCOS), Arak Medical University Journal 2014; 17(86): 70-78.

[15] Sadeghpour N KA, Najafpour A, Dolatkhah H, Montaseri A. Study of Foeniculum vulgare (Fennel) Seed Extract Effects on Serum Level of Estrogen, Progesterone and Prolactin in Mouse Crescent, Journal of Medical and Biological Sciences 2015; 2(1): 23-7.

[16] Ibn Al-Nafis. Al-Shamil fi al-Tibb. Tehran, Iran University of Medical Sciences; 2007: 86, 117.

[17] Stener-Victorin E, Jedel E, Manneras L. Acupuncture in polycystic ovary syndrome: current experimental and clinical evidence, Journal of neuroendocrinology 2008; 20(3) 290-8.

[18] Zheng YH, Wang XH, Lai MH, Yao H, Liu H, Ma HX. Effectiveness of abdominal acupuncture for patients with obesity-type polycystic ovary syndrome: a randomized controlled trial, Journal of alternative and complementary medicine (New York, NY) 2013; 19(9): 740-5.

[19] Tuǧrul Cabıoǧlu M, Ergene N. Electroacupuncture therapy for weight loss reduces serum total cholesterol, triglycerides, and LDL cholesterol levels in obese women, The American journal of Chinese medicine 2005; 33(4): 525-33.

[20] Manneras L, Jonsdottir IH, Holmang A, Lonn M, Stener-Victorin E. Low-frequency electro-acupuncture and physical exercise improve metabolic disturbances and modulate gene expression in adipose tissue in rats with dihydrotestosterone-induced polycystic ovary syndrome, Endocrinology 2008; 149(7): 3559-68.

[21] Esfahanian F, Zamani MM, Heshmat R, Moini nia F. Effect of metformin compared with hypocaloric diet on serum C-reactive protein level and insulin resistance in obese and overweight women with polycystic ovary syndrome, The journal of obstetrics and gynaecology research 2013; 39(4): 806-13.

[22] Hu L, Shen H, Wu QF, Tian L, Hu MH. Treatment of polycystic ovarian syndrome with insulin resistance by insulin-sensitizer, Clinical and experimental obstetrics & gynecology 2014; 41(3): 288-92.

[23] Aghili M. Kholasato-hekmat. Qom, Esmaeilian Publication; 2011: 278, 333, 516-8.

[24] Nazem Jahan MA. Eksir - e - Azam. Tehran, Institute for Islamic and Complementary Medicine; 2009: 102, 704, 753.

[25] Ibn Sina H. Al-Qanun fi al-tibb (printed Beirut). Beirut, Dar Ihya al-Turath al-Arabi; 2005: 121-2, 396, 407.

[26] Jorjani E. Zakhire Kharazmshahi. Qom, Ehya - e - Teb - e – Tabiei; 2013: 201, 377, 911-8.

[27] Johansson J, Redman L, Veldhuis PP, Sazonova A, Labrie F, Holm G, et al. Acupuncture for ovulation induction in polycystic ovary syndrome: a randomized controlled trial. American journal of physiology Endocrinology and metabolism 2013; 304(9) E934-43.

[28] Novak E, Berek JS. Berek & Novak's gynecology. fifteenth edition, Lippincott Williams & Wilkins; 2007.

[29] Kuek S, Wang WJ, Gui SQ. Efficacy of Chinese patent medicine Tian Gui Capsule in patients with polycystic ovary syndrome: a randomized controlled trial. Zhong xi yi jie he xue bao = Journal of Chinese integrative medicine 2011; 9(9): 965-72.

[30] Kawaguchi T, Yoshida T, Harada M, Hisamoto T, Nagao Y, Ide T, et al. Hepatitis C virus down-regulates insulin receptor substrates 1 and 2 through up-regulation of suppressor of cytokine signaling 3. The American journal of pathology 2014; 165(5): 1499-508.

[31] Tehrani FR, Rashidi H, Khomami MB, Tohidi M, Azizi F. The prevalence of metabolic disorders in various phenotypes of polycystic ovary syndrome: a community based study in Southwest of Iran. Reproductive biology and endocrinology 2014; 12(1): 89.

[32] Katz A, Nambi SS, Mather K, Baron AD, Follmann DA, Sullivan G, et al. Quantitative Insulin Sensitivity Check Index: A Simple, Accurate Method for Assessing Insulin Sensitivity In Humans. The Journal of Clinical Endocrinology & Metabolism 2000; 85(7): 2402-10.

[33] Lyttleton J. Treatment of Infertility with Chinese Medicine. CHURCHILL LIVINGSTONE ELSEVIER; 2013: 200-233.

[34] Abdi H, Baixiao Z, Darbandi M, Ghayour-Mobarhan M, Tavallaie Sh, Rahsepar AA, et al. The effects of body acupuncture on obesity: Anthropometric parameters, lipid proﬁle, and Inﬂammatory and Immunologic markers. The Scientiﬁc World Journal 2012; 20(12): 1-11.

[35] Bargiota A, Diamanti-Kandarakis E.The effects of old, new and emerging medicines on metabolic aberrations in PCOS. Therapeutic Advances in Endocrinology and Metabolism 2012; 3[1]: 24-7.

[36] Franasiak J, Young SL, Williams CD, Pastore LM. Longitudinal anti-mullerian hormone in women with polycystic ovary syndrome: an acupuncture randomized clinical trial, Evidence-based complementary and alternative medicine. eCAM 2012; 973712.

[37] Cussons AJ, Watts GF, Mori TA, Stuckey BG. Omega-3 fatty acid supplementation decreases liver fat content in polycystic ovary syndrome: a randomized controlled trial employing proton magnetic resonance spectroscopy, The Journal of clinical endocrinology and metabolism 2009; 94(10): 3842-8.

[38] Feng Y, Johansson J, Shao R, Manneras-Holm L, Billig H, Stener-Victorin E. Electrical and manual acupuncture stimulation affect oestrous cyclicity and neuroendocrine function in an 5alpha-dihydrotestosterone-induced rat polycystic ovary syndrome model. Experimental physiology 2012; 97(5): 651-62.

[39] Mhaidat NM, Abu-zaiton AS, Alzoubi KH, Alzoubi W, Alazab RS. Antihyperglycemic properties of Foeniculum vulgare extract in streptozocin-induced diabetes in rats. Int J Pharmacol 2015; 11(1): 72-5.

[40] Jungbauer A, Medjakovic S. Phytoestrogens and the metabolic syndrome. The Journal of steroid biochemistry and molecular biology 2014; 139(10):277-89.

[41] Chedraui P, San Miguel G, Hidalgo L, Morocho N, Ross S. Effect of Trifolium pratense-derived isoflavones on the lipid profile of postmenopausal women with increased body mass index, Gynecological Endocrinology 2008; 24(11): 620-4.

[42] Soni K, Kuttan R. Effect of oral curcumin administration on serum peroxides and cholesterol levels in human volunteers. Indian journal of physiology and pharmacology 1992; 36(2): 273-5.

1. low-density lipoprotein cholesterol [↑](#footnote-ref-1)
2. high-density lipoprotein cholesterol [↑](#footnote-ref-2)
3. triglycerides [↑](#footnote-ref-3)
4. [↑](#footnote-ref-4)
5. Androgen Excess Polycystic Ovarian Syndrome Society [↑](#footnote-ref-5)
6. Fasting plasma glucose [↑](#footnote-ref-6)
7. Aspartate aminotransferase [↑](#footnote-ref-7)
8. Alanine aminotransferase [↑](#footnote-ref-8)
9. Homeostatic model assessment of insulin resistance [↑](#footnote-ref-9)
10. Homeostatic model assessment of beta cell function [↑](#footnote-ref-10)
11. Quantitative insulin sensitivity check index [↑](#footnote-ref-11)
12. A feeling of heaviness or numbness in the area surrounding the locus of insertion [↑](#footnote-ref-12)