

Effect of eight weeks circuit resistance training with *Zataria multiflora* supplementation on plasma levels of leptin and adiponectin in postmenopausal women

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Abstract

Introduction: Aging and low physical activity results in a decrease in Adiponectin and an increase in leptin, which can cause cardiovascular diseases, obesity and diabetes. The aim of present study was to investigate the effect of 8 weeks circuit-resistance training (CRT) with *Zataria multiflora* (*Z. multiflora*) supplementation on plasma leptin and adiponectin in postmenopausal women.

Materials and methods: 48 untrained postmenopausal women took part in this study. The participants were randomly divided in 4 groups with 12 persons in each: resistance training (RTG), *Z. multiflora* (ZG), control (CG) and *Z. multiflora*- resistance training (ZRTG). Resistance training program contained 12 stations (each station 30 second with 35 percent of one maximum repetition) and continued for 8 weeks (3 sessions per week). Participants in the ZG and ZRTG consumed 500 mg of *Z. multiflora* supplementation daily before breakfast. Blood samples were collected 48 hours before first session and 48 hours after last session to measure plasma levels of leptin and Adiponectin.

Results: Significant difference between ZRTG and CG in plasma Adiponectin was observed ($P < 0.05$). However, there was no significant difference between groups in leptin ($P > 0.05$).

Conclusion: This study indicated that CRT can cause a decrease in leptin and an increase in Adiponectin. Also, when *Z. multiflora* intervention included in the training program, this effects increased.

Keywords: Circuit-resistance training, *Zataria multiflora* supplementation, Adiponectin, Leptin, Postmenopausal women

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Introduction

Menopause, stage in a women's life that happens at age of 49-52 years old, usually is accompanied with metabolic syndrome risks (1). According to previous researches, the spread of metabolic syndromes during menopause is about 55-31 percent, which is much more than any other period (2). For example, Eshtiaghi et al (2010) showed the increase of metabolic syndromes in Iranian aged women. They also cited menopause as an independent metabolic syndrome, attending with insulin resistance (3). In fact, development of abdominal obesity is as a result of metabolic syndromes as well as type 2 diabetes in menopausal women, followed by disappearing of protectoral role of estrogen, and relative increment of circulating endogens (4).

Additional abdominal fat results in inflammatory response, insulin resistance and cardiovascular risks; in fact, they are produced by specific adipose cells, named adipokines (5). Adiponectin, which is an important adipokines, derived from adipose tissue, is responsible for some key metabolic roles including, energy expenditure, fat catabolism, Free Fatty Acids (FFA) oxidation and insulin secretion. Unlike most adipokines, adiponectin concentration would be decreased in obese people, and is considered as a resistant factor in pathogenesis of heart diseases. It seems that adiponectin, through a direct influence of endothelial cells, acts as an anti-atherosclerosis element. As a result, it could be useful in lipid and glucose metabolism as well as insulin sensation. Therefore, adiponectin plasma concentration is significantly less in people with diabetes or heart diseases (6). In spite of the researches on the role of adiponectin in such chronic conditions, it should be noted that recent studies have been shown elevated levels of adiponectin would bring reverse effects to heart diseases (7). Human studies which support this interpretation, state that the increased level of adiponectin can increase

death caused by cardiovascular disease among older population (8).

It is clear that the imbalance between pro and anti-inflammatory cytokines in adipose tissue plays a main role in obesity complications (9). Leptin, is released from adipose tissue and involved in thrombotic and inflammatory pathways (10).

Leptin is an OB gene production, a hormone and a 16 kDa protein. It plays a role in weight control by preventing food absorption and increasing energy expenditure. The amount of leptin in white adipose tissue is much more than brown adipose tissue (11). Leptin levels in obese people is high, and this could be due to its receptors perturbation or resistance. The increased levels of leptin may be linked to endothelial tissue perturbation, smooth muscle proliferation, platelets accumulation and oxidative stress in endothelial cells. Therefore, its increased levels particularly in childhood could predict heart disease in adulthood. Recently, leptin has been introduced as a hormonal risk factor in cardiovascular diseases (12). Nowadays, it is well known that there is a considerable correlation between leptin and insulin, and their role in obesity. This is because of the relevancy of both to body weight or better to say; body fat (13). In polak et al (2006) study (14), who surveyed the effect of 12 weeks chronic exercise on pro and anti-inflammatory adipokines, the levels of leptin and adiponectin decreased and increased respectively, and the levels of TNF- α , IL-6 and leptin decreased, with 53, 3 and 32 % respectively. Pilo and Han (2014) studied the effect of Electro-acupuncture on both adiponectin and leptin levels and measured their levels in white adipose tissue in obese rats. Their results showed a significant decrease and increase in leptin and adiponectin respectively. However, the leptin levels remained almost stable in white adipose tissue (15). In another study resistant exercise was introduced as a therapeutic plan by American College of Sports Medicine

(ACSM) (16, 17), in a way that, muscular hypertrophy due to resistant training was alongside with a decrement in inflammatory markers (18). For example, it has been shown that 12 weeks resistant training lead to improvements of metabolically factors (TC, TG), muscular hypertrophy, insulin sensation and inflammatory markers in obese women (18). Also study has shown that Implementing nutritional intervention during exercise trainings would be more advantageous related to health than exercise alone (19).

Z. multiflora only grows in Iran, Pakistan and Afghanistan (20) and is used as tea, curies and herbal medicine. Sodden type of the plant is useful for Asthma treatment. It is also a practical stomach disinfectants, diuretic drug and anti-inflammatory element (21). The most important compounds of *Z. multiflora* are carvacrol, thymol and Gama trippin, which are anti-inflammatory factors (20, 22). Many researchers have shown that *Z. multiflora* compounds are able to inhibit inflammatory reactions and act as anti-oxidant, anti-spasm and pain (22). In a case study, it was an effective treatment in first dysmenorrhea (23). Recently, in animal subjects, both carvacrol and thymol have decreased the levels of some pro inflammatory cytokines including IL-1b, IL-6 and TNF- α (24). For instance, *Z. multiflora* can increase adiponectin, and this could be because of increased levels of PPAR Gama (20). There has not been any studies on the interaction of *Z. multiflora* and resistant training on some important metabolically factors. Therefore, the aim of this study was to investigate the interaction effect of *Z. multiflora* and resistant training on leptin and adiponectin plasma levels in menopause women.

Methods

Study design: Following collecting baseline testing data, participants were matched based on their weight, height, and body mass index (BMI), and randomly

divided into four equal groups by a person independent of the trial with group allocation provided in sequentially numbered opaque sealed envelopes. The four groups were as follow: 1) control group (CG) who received 8 weeks of usual care 2) resistance training group (RTG) who received an eight week of supervised CRT program 3) *Z. multiflora* group (ZG) who received daily supplementation with a *Z. multiflora* supplement for 8 weeks and 4) *Z. multiflora* and resistance training group (ZRTG) who received both the 8-week CRT program and daily *Z. multiflora* supplementation.

Participants: Women were eligible for inclusion if they were at least six months post-menopause (as confirmed by a gynecologist), had no addiction to drugs or alcohol, had no recent exercise history (at least 6 months), no history of renal, hepatic, cardiovascular disease, diabetes, and/or any physical injury or problem preventing participation in an exercise program. They were advised that no new exercise should be commenced and not to use non-prescription medications and supplements during the trial. Before participating in the study, all procedures were explained to volunteers and after complete awareness of the study's terms and completion of a medical questionnaire, written informed consents were obtained.

Training protocol: Participants were familiarized with the environment and CRT exercise movements for one week and then 1 repetition maximum (1RM) for each of the given exercises was determined. The 1RM for each exercise movement was calculated using Brzezinski equation (25). Training sessions were delivered using CRT format with alternation between upper-body and lower-body movements as well as multi-joint movements at the beginning of the movements (26). The exercises included: 1. Squat, 2. Chest press, 3. Leg press, 4. Standing Military Press, 5. Knee extension, 6. Seated cable rowing, 7. Knee Curl, 8. Biceps curl, 9. standing calf raise, 10. Triceps press, 11. Back extension,

and 12. Abdominal crunch. Participants in the RTG and ZRTG groups performed movements at 35% of 1RM for 8 weeks (3 sessions per week). Each exercise session included a 5 min warm-up and then followed by the 12 prescribed exercises, with duration of approximately 30 seconds at each exercise station. The number of repetitions at each station was recorded for the participants. In each session, two sets (turns) of 12 exercises were carried out such that between each set, there was a 3 minutes active rest (27-30).

Blood sampling and adipokines measurements: For blood sampling, the following requirements were asked of the participants: 1) No use of drugs and/or supplement during the study, 2) No change in diet at least two days before the test, 3) No exercise other than the prescribed exercise of the study at least 72 hrs before the test, 4) No drinks or foods such as coffee, dark tea, bananas, cereal and heavy or greasy foods at least 24 hrs before the test. After a 12 hrs overnight fast, blood samples were taken from an antecubital vein with participants in a sitting position. Portions of each blood sample were placed into EDTA (plasma) and sterile (serum) tubes. All samples were centrifuged at 3000 rpm for 10 min. After centrifugation, blood samples were stored at -70°C until analysis. On the day of analysis, the levels of adiponectin and leptin were measured using commercially available assay kits: 1) plasma adiponectin (Cat. No. RD191023100, sandwich ELISA kit, Biovendor, Heidelberg, Germany); 2) plasma leptin (Cat. No. RD191001100, sandwich ELISA kit, Biovendor, Heidelberg, Germany).

Statistical analysis

Normality of the data was tested with the Kolmogorov–Smirnov test. Two way

ANOVA test with repeated measurements was used to evaluate changes within and between groups (4 groups X 2 times). Bonferroni post hoc analysis and independent t-test were used to measure within subject and between subject significant changes, respectively. Statistical significance level was set at $P < 0.05$. SPSS version 20.0 was employed to analyze the data.

Results

Statistical analysis of the plasma adiponectin levels among groups showed significant differences ($P < 0.001$). Post hoc test results showed significant differences between ZRTG and CG ($P = 0.022$). Intra-group analysis showed that value of adiponectin significantly increased in the pre-test to post-test in ZG ($P = 0.003$), RTG ($P = 0.006$) and ZRTG ($P < 0.001$) (Figure 1). Statistical analysis of the plasma leptin levels among groups did not show significant difference ($P = 0.07$). Intra-group analysis showed that value of leptin significantly decreased in the pre-test to post-test in ZG ($P = 0.011$), RTG ($P = 0.003$) and ZRTG ($P < 0.001$) (Figure 2).

Discussion

Our results showed that 8 weeks circular resistant training with 35 % 1RM lead to significant drop in leptin concentration, decreasing 5.09 percent. It is believed that leptin has an important role in energy balance (31). For example, it has been shown that after cardio exercise in diabetic people (32) or healthy people (33) leptin is decreased, specifically whenever there is a limitation in energy sources (34). On the other hand, some other researches have shown that chronic physical exercise does not change leptin levels in elderly (35) or young (36).

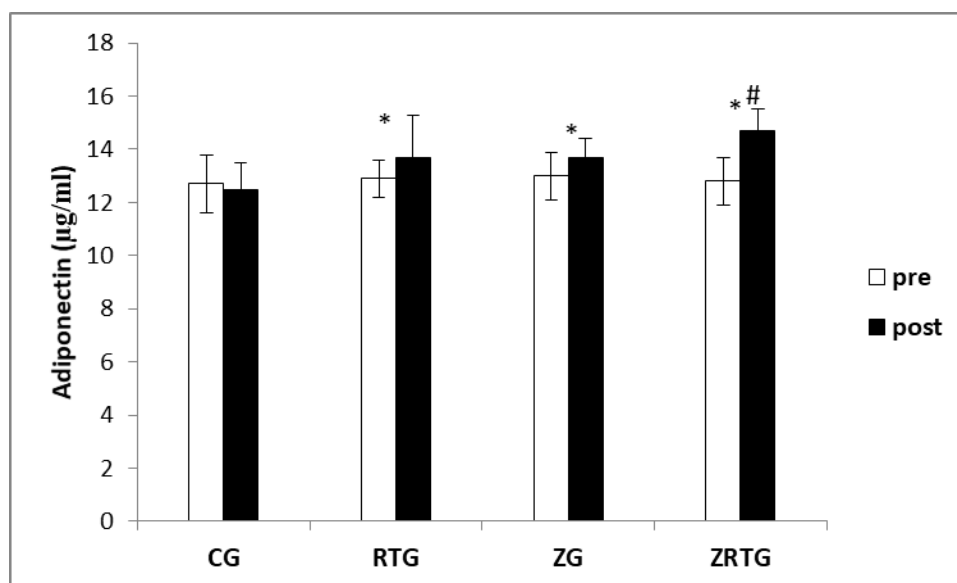


Figure 1. Plasma adiponectin levels in study groups. Control group (CG), resistance training group (RTG), *Z. multiflora* group (ZG) and *Z. multiflora* and resistance training group (ZRTG).

*As significant difference between before and after exercise in groups ($P < 0.05$).

As significant difference between ZRTG % and CG.

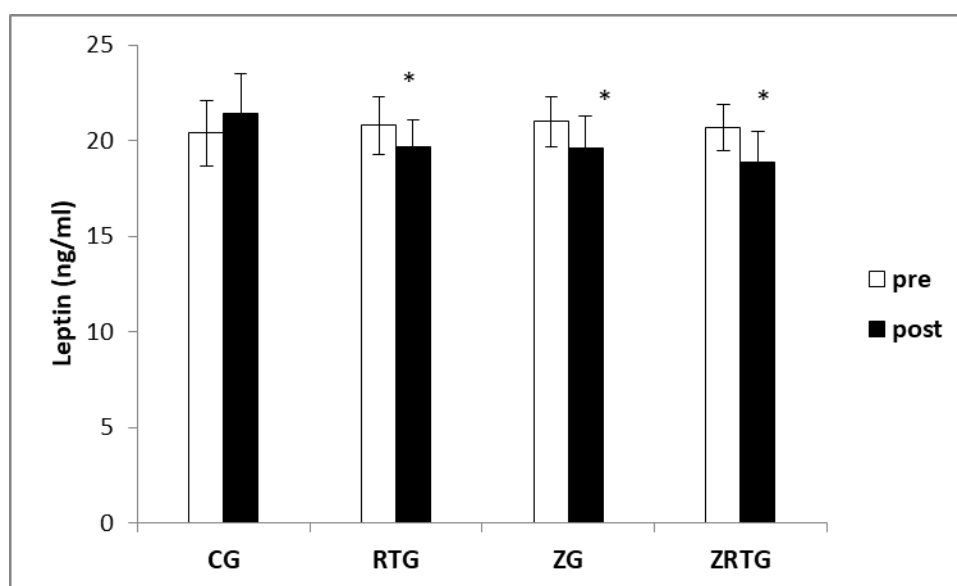


Figure 2. Plasma leptin levels in study groups. Control group (CG), resistance training group (RTG), *Z. multiflora* group (ZG) and *Z. multiflora* and resistance training group (ZRTG).

*As significant difference between before and after exercise in groups ($P < 0.05$).

Fatouros et al. (2005) showed that resistance training with different intensities caused a significant decrease in leptin after exercise training ranging from 3 to 19 percent (31). Therefore, conflicting results about leptin and exercise training could be due to the quality and quantity of exercise or some other factors such as physical fitness and energy status (31). Short-term exercise training would have mild effects on leptin changes (32), with the exception

of energy imbalance status (33). Studies have shown that leptin decrement is restricted after exercise in untrained people. Resistance training is considered as an intervention to reduce some chronic conditions related to aging such as muscular atrophy, power and bone health (31). Although there are few studies on the effect of resistance training on leptin changes, it is reported that acute resistance exercise could postpone any dropping

leptin off (34). The reason could be that acute high intensity resistant exercise lead to leptin decrement probably refer to high glucose absorption by some other tissues in lactic situation, energy consumption, glycogen depletion, which in turn may inhibits glycolysis (34). There is another mechanism which can explain leptin decrement as a result of exercise. Losing body weight or body fat assumed as a perturbation in energy balance, and aging which is usually accompanied with felling physical activity, energy expenditure and finally increment of body fat source (35). Exercise trainings could rise resting energy expenditure (REE) up, and this would lead to diminish body fat and leptin decrement. It is to be noted that catecholamines may play a role (31). Fatorous et al (2005) reported different kinds of resistant exercise and its effect of BMI, skinfold fat, energy expenditure, REE, and decrease in leptin. In their study leptin was totally dependent to intensity of training (31). However, adipose tissue can release adipokines including IL-6, TNF- α and leptin (19), and the macrophages in adipose tissue are the source of pro-inflammatory cytokines in obesity (33). For example, additional fat consumption and elevated cytokines gene expression, call macrophages into adipose tissue in overweight and obesity condition (22). So, exercise training mediates fat cells, improve theirs hormonal releases and their macrophages component (33), which can help to normalize adipokines level as well as insulin resistant (19). More oxygen consumption and more energy expenditure in high intensity training compared to moderate one perturb energy balance and decrease more leptin (31). Repeated muscle contraction would send signals to CNS and mediate energy demand (36). It has been reported that CRT brings more adaptations compared to traditional method (37). Therefore, CRT has an effective way to reduce leptin than other model. However, this matter requires further analysis. Our results showed that CRT resulted in 6/24 increment in adiponectin level. There

are completely conflict results about exercise and adiponectin, so that, sometimes it remains unchanged, increases or decreases even after long-term endurance exercise (38). Rising of adiponectin after resistant exercise can be due to diminishing some enzymes, related to gluconeogenesis, G6P and pyruvate carboxykinase, and fortify insulin actions (39). It can also increase insulin sensitivity through fat oxidation (40). Some interventions, which lead to weight loss, can increase adiponectin levels (40). It is reported that weight loss plans by both nutritional and exercise elements increase adiponectin (38). So, changes in body composition might be necessary for adipokines elevation (41). To confirm this, recently, it has been reported that long-term calorie restriction can increase adiponectin levels (42). In addition to CRT, 8 weeks *Z. multiflora* supplement increased and decreased adiponectin and leptin, with 5.54 % and 6.78 % respectively. More importantly, the equivalent figure for the interaction of both CRT and *Z. multiflora* was 10.8 % and 8.6 % in the same order. As mentioned before phenol components of *Z. multiflora* are a great source of anti-oxidant and anti-inflammation ingredients, and could diminish LDL as well as ROS markers (43, 44). Jokim et al (2008) showed the effects of COX enzymes and ROS in terms of cancer progression. They stated that *Z. multiflora* with its compounds inhibit the enzyme activities, therefore, decrease oxidative stress (45). COX can increase Aromatase enzyme by prostaglandin E2 production, and it can promote the androgen to estrogen. On the other hand, *Z. multiflora* complements with Aromatase containment can inhibit oxidative stress and inflammation (46). So with regard to interaction effect of CRT and *Z. multiflora* on leptin and adiponectin changes in our study, it seems *Z. multiflora* could be considered as a good option to decrease inflammation and oxidative stress in some chronic conditions such as aging and heart diseases. *Z. multiflora*

supplementation effect on leptin and adiponectin changes might be due to presence of components such as Glucuronic acid and phenolic compounds.

Conclusion

In conclusion the interaction of CRT and *Zataria multiflora* could be a more effective and practical model to mediate changes in leptin and adiponectin levels in menopause women, rather than CRT alone. As a result, this interaction could be a possible solution

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