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The Effect of Combined Exercise and Propolis Supplementation on Glycemic Index in Women with Type 2 Diabetes

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ABSTRACT

Introduction: Diabetes is a metabolic disorder characterized by long-term hyperglycemia. However, nutrition and exercise can both help to lower blood sugarlevels. This study aimed to investigates the effect of eight weeks of combined exercise and propolis supplements on glycemic indicators in women with type 2 diabetes.

Method: This applied research was conducted on 60 women with type 2 diabetes, who were selected from Shiraz Medical Center and divided into four groups of 15, including 1) placebo, 2) exercise with placebo, 3) exercise with propolis, and 4) propolis. Groups 3 and 4 received propolis in the form of 500 mg capsules three times a day (morning, noon, and night) after each meal for eight weeks. Groups 2 and 3 also performed three sessions of combined training (resistance-aerobic) per week.

Combined training was resistance training with an intensity of 60-85% of a maximum repetition and aerobic training with an intensity of 50-70% of the maximum heart rate.

Results: Exercise, propolis consumption and exercise led to a significant reduction in fasting blood glucose, insulin, insulin resistance and glycosylated hemoglobin simultaneously with propolis consumption (P≤0.05). In addition, exercise with propolis consumption compared to exercise and propolis had a more significant effect on lowering fasting blood glucose, insulin, IR, and glycosylated hemoglobin (P≤0.05).

Conclusion(s): According to the results, exercise and propolis could positively affect the glycemic indicators of diabetic patients. Nevertheless, the combination of exercise and propolis had more favorable effects on improving glycemic indicators than each one alone in Non-insulin-dependent diabetes.

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Introduction

Diabetes Mellitus Type 2 (DMT2) is the most common type of chronic diabetes, which is characterized by elevated plasma glucose levels due to insulin resistance (IR) and impairment of insulin secretion or insulin receptors (1). As a result of this factor, glucose is excreted from the blood in the kidneys and then excreted in the urine. According to studies conducted from 2005 to 2011, 6.8% of the world's population without diabetes were diagnosed with diabetes. Iranian studies indicate that 7.7% of the population aged 25 to 64, or two million people have diabetes and 16.8% have impaired glucose tolerance (2). This disease is the most common cause of kidney problems, amputation without trauma and blindness (3). Chronic hyperglycemia is a symptom of diabetes, as is difficulty metabolizing carbohydrates, fats, and proteins. This disease resulted from the interaction between IR and decreased pancreatic beta-cell function caused by poor motility and stress. Diabetes is a chronic endocrine disorder with long-term hyperglycemia facing by a lack of permanent or low secretion of insulin or IR (4). Based on research conducted by the International Illegal Federation, 382 million children and adults worldwide were affected by the disease in 2003, and projections show that number will surpass 592 million by 2025 (5). Studies have shown that nutrition essential in improving and controlling diabetes.

Recently, honey and other substances associated with bees, such as propolis, have gained more attention. Pollen, enzymes, pollen, and wax are combined with propolis, a resin-like substance

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collected from buds of poplar and cone trees. Propolis is also combined with bee enzymes, pollen, and wax. "Propolis" refers to a substance used in hives where pro means defense and polis refers to a city, which is this hive here, and its general meaning is defense of the hive. Propolis is used by bees to soften and seal their hives' interior walls and cavities (6). Propolis is rarely available in pure form, and the primary active materials in propolis are flavonoids such as chrysinas potent antioxidants that bees take from plant and flower parts. In recent decades, propolis has been the subject of extensive research around the world, in which its chemical composition and biological properties have been extensively studied.

There has been some recent research into the mechanisms and functions of propolis, and its therapeutic applications have been reviewed to illustrate its importance, but limited evidence suggests it could be useful for diabetics (7). On the other hand, studies have shown that exercise helps control blood sugar (BS) in DMT2 patients (8). In addition, physical activity can increase the response of skeletal muscles to plasma insulin levels and insulin signaling and metabolism. Therefore, physical activity increases glucose transporter expression and glycogen synthesis function (9). Regular exercise improves glucose metabolism by increasing insulin. The stimulation of insulin by muscle tissue causes more than 75% of glucose to be absorbed by the body due to long-term exercise increasing glucose transporters to muscle cells, and insulin receptor bases, which prevents obesity and complications of DMT2 in winter (10). Exercise can reduce BS and glycosylated hemoglobin (HbA1C) in patients with type 2 diabetes, as well as prevent long-term complications (11). Patients with DMT2 may benefit from endurance and resistance exercise, including blood glucose control study aimed to investigate a course of combined exercise and propolis supplementation on glycemic indicators in women with DMT2 considering the therapeutic role of sports activities and consumption of propolis, as well as the small amount of research in this field.

As shown in the above studies, there is insufficient research concerned with the simultaneous effects of aerobic and resistance training with propolis. A Synergistic placement of exercises and propolis was conducted to examine the effects of eight weeks of combined exercise with and without propolis on glycemic index and insulin resistancein women with DMT2.

Materials and Methods

This appliedstudy was conducted on 60 women with DMT2, who referred to Shiraz Medical Center and selected as a statistical sample. The inclusion criteria included being between 40 and 60 years old, lack of having a history of cardiovascular disease, having a history of diabetes longer than six months, smoking, no supplements, just food. The exclusion criteria included having regular exercise in the last six months and missing more than three sessions of exercise. Upon completion of the informed consent process, subjects were randomly divided into four groups: a placebo, exercise with placebo, exercise with propolis supplement. The present study was registered in the Ethics Committee of the Islamic Azad University of Khorasgan, Iran (with the code IR.IAU.KHUISF.REC.1400.265) and the Iranian clinical trial database (with the number IRCT20211229053561N1). Supplemental propolis capsules of 500 mg were given to subjects three times a day after each meal for eight weeks (12). Exercise groups performed three sessions per week of selected exercise. The supplement and placebo groups did not participate in any sports activities during the study period. In this research, two different types of training programs were used: an aerobic training program and a resistance training program for eight weeks (24 sessions). The aerobic exercise program includes: pedaling using a stationary bike and each session 35-50 minutes with an intensity of 50-70 % was the maximum heart rate. The training program consisted of three warm-up sections, including static and dynamic stretching exercises (5 minutes), cycling on a stationary bike (25-40 minutes), and cooling down (5 minutes), including stretching exercises. The training program in the first and second week was It was performed for 35 minutes with an intensity of 50-60% of the reserve heart rate and in the seventh and eighth week for 50 minutes with an intensity of 60-70% of the reserve heart rate. The maximum heart rate was calculated with the formula age-220 to determine the training intensity (13). The exercise program was performed in the first and second week for 35 minutes with an intensity of 50-60% of the reserve heart rate and in the seventh and eighth week for 50 minutes with an intensity of 60-70% of the reserve heart rate. The training intensity was controlled through a Polar watch heart rate monitor during the training. The resistance training program was designed similar to the study of de Valens et al. (2017). The resistance training program included upper body and lower body exercises, in a progressive manner, using 6 exercise machines, and the duration of each session was about 40-50 minutes. Warming up and cooling down at the beginning and end of each exercise were done for 5 minutes by stretching movements. To perform upper body exercises in each session, special devices for chest vertical press, back arm extension, and open front bending were used, and for lower body exercises, leg bending and thigh bending and extension devices were used. The training intensity was increased every two weeks, so that the first and second week, 60%, the third and fourth week, 70%, the fifth and sixth week, 80%, and the seventh and eighth week, 85% was a maximum repetition. Subjects were encouraged to complete 8-12 repetitions until they were able to complete the repetitions. 30 seconds rest between each set and 1 minute between devices. The range of load and repetitions was in accordance with the hypertrophy exercise set by the American College of Sports Medicine regarding resistance exercise for health in the adult population (14). A sample of 5 cc of blood was taken from subjects' arms before the pre-test and 48 hours after the last training session. After separating the serum at a temperature of two to eight, the blood was centrifuged (Behdad brand made in Iran) for ten minutes and transferred to the laboratory to measure sugar indicators. Serum HbA1C level was measured by ELISA method to measure fever and fasting blood glucose (FBG) using the Iranian Pars kit. Plasma insulin level was measured using the Diaplus kit by ELISA method made in America. Fasting insulin × (mg/dL) FBG ÷22/5 was used to calculate the IR of the formula HOMA IR= (MU/ml, (15). The Kolmogorov-Smirnov test was used to determine the normality of the data distribution, and a one-way analysis of variance was used to analyze the data using Tukey's post hoc test (P≤0.05).

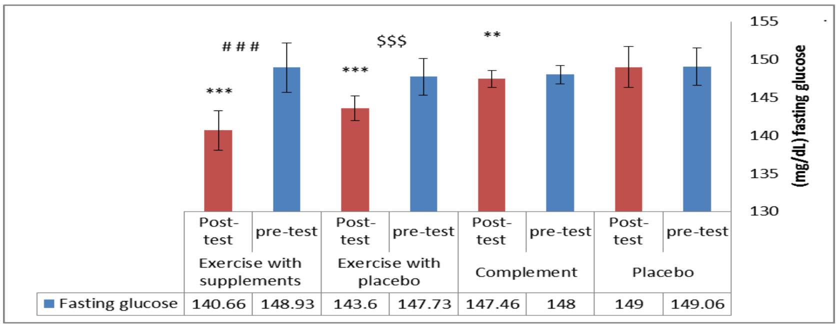
Table 1. Demographic characteristics of the subjects in the four groups of research (mean ± standard deviation)

Practice with Supplement	Placebo with Exercise	Complement	Placebo	Measurement Time	Subject Specifications
54.07±2.86	51.67±4.67	52.53±5.90	53.67±5.01	pre-test	Age (years)
164.20±2.56	164.93±1.83	164.66±2.76	165.40±1.91	pre-test	Height (cm)
75.53±2.56	76.11±2.92	75.80±2.42	74.87±1.80	pre-test	Weight (kg)
72.67±2.64	74.33±2.84	75.40±2.53	74.80±1.74	Post-test	
28.04±1.56	27.94±1.21	27.99±1.63	27.37±0.76	pre-test	Body mass index (kg / m2)
26.98±1.62	27.33±1.20	27.84±1.66	27.34±0.72	Post-test	

Results

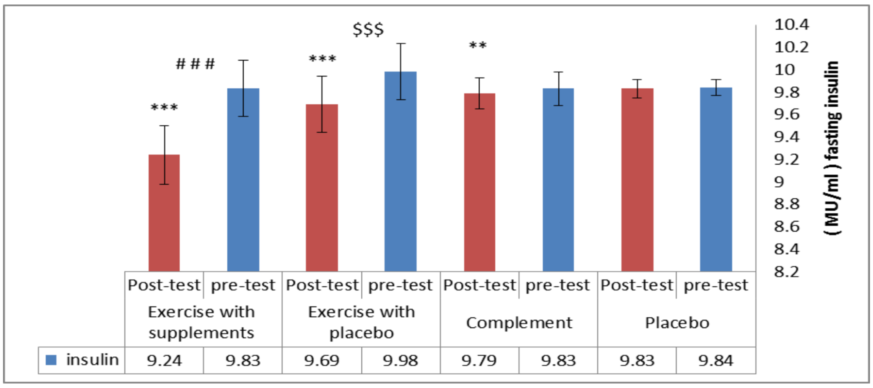
Table 1 shows the demographic characteristics of the subjects the levels of FBG, insulin, IR, and Hb A1C for the four research groups are shown in Figures 1 to 4, respectively. There was IR (P=0.001 and F=80.02) and Hb A1C (P= 0.001 and F=41.90) among the research groups according to the analysis of one-way variance (SiD) in changes in FBG (P=0.001 and F=72.08), insulin (P=0.001 and F=36.44)Tukey's post-hoc test showed that FBG levels in the exercise group with propolis were significantly lower than the exercise with placebo, propolis, and placebo groups (P=0.001 The exercise group with placebo was significantly lower than in propolis and placebo groups (P=0.001). However, there was no SiD in FBG changes between propolis and placebo groups (P= 0.83) (Figure 1) as well as insulin levels (Figure 2). IR (Figure 3) and Hb A1C (Figure 4) in the exercise group with propolis were significantly lower than in the exercise with placebo, propolis, and placebo groups (P= 0.001). In addition, the exercise in the placebo group was significantly lower than in the placebo and propolis groups (P=0.001). The results of the paired-sample t-test showed that the FBG, insulin, IR, and Hb A1C in the post-test were significantly reduced compared to the pre-test (P=0.001) in training with placebo and propolis groups FBG (P=0.001), insulin (P=0.001), IR (P=0.001), and Hb A1C (P=0.001) in the post-test were significantly reduced compared to the pre-test in the exercise with the placebo group. In the propolis group, the FBG (P=0.006), insulin (P=0.003), and IR (P=0.001) reduced compared to the pre-test in the post-test significantly.

However, no significant difference in Hb A1C level (P=0.21) was observed in the post-test compared to the pre-test. Furthermore, in the placebo group FBG (P=0.33), Hb A1C (P=0.58), IR (P=0.17), and insulin (P=0.23) did not change in the post-test compared to the pre-test.



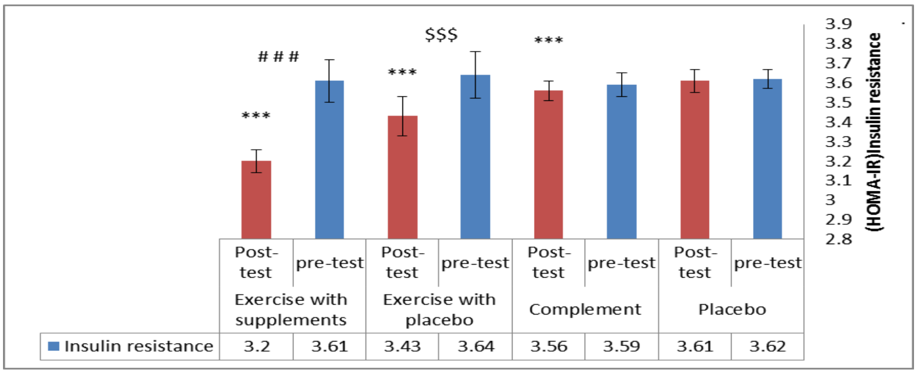
*** P = 0.001 Significant decrease compared to pre-test
** P = 0.006 Significant decrease compared to pre-test
P=0/001 Significant decrease compared to exercise groups with placebo and propolis and placebo
$$$ P= 0/001 Significant decrease compared to placebo and propolis groups

Figure 1. FBG levels in pre-test and post-test in four research groups



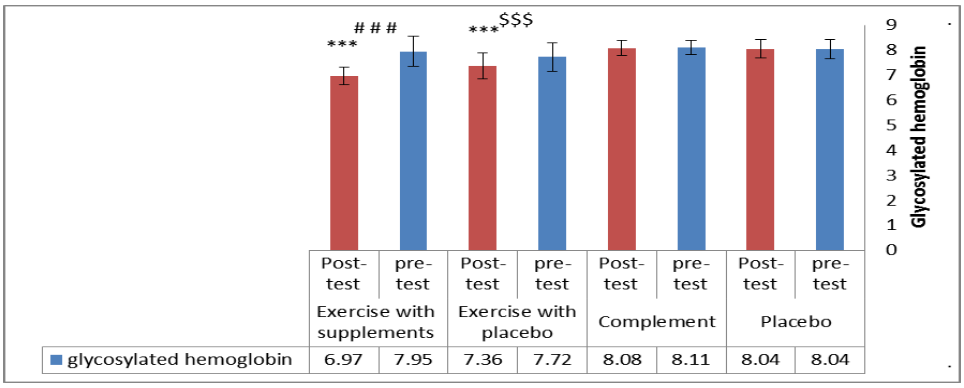
*** P = 0.001 and ** P = 0.003 Significant decrease compared to pre-test
P=0.001 Significant decrease compared to exercise groups with placebo, propolis and placebo
$$$ P= 0.001 Significant decrease compared to placebo and propolis groups

Figure 2. Insulin levels in pre-test and post-test in four research groups



*** P = 0.001 Significant decrease compared to pre-test
P=0.001 Significant decrease compared to exercise groups with placebo, propolis and placebo
$$$ P=0.001 Significant decrease compared to placebo and propolis groups

Figure 3. IR levels in pre-test and post-test in four research groups



*** P = 0.001 Significant decrease compared to pre-test
P= 0.001 Significant decrease compared to exercise groups with placebo, propolis and placebo
$$$ P= 0.001 Significant decrease compared to placebo and propolis groups

Figure 4. Hb A1C levels in pre-test and post-test in four research groups

Discussion

The results had a SiD on the consumption of propolis supplements for eight weeks to reduce FBG, insulin, IR, and Hb A1C levels in diabetic women. Clinical studies have reported the effects of propolis hypoglycemia Consistent with the results of the present study, Samadi et al. (2018) reported that 12 weeks of using 900 mg of propolis supplement improved FBG in diabetic patients (16). BS levels are regulated with supplementation by network pharmacology and Zardine bio antioxidants, which suppress free radical production (17). Bioflavonoids are highly reactive, and their interactions with free radicals trap them, whereas hydroxyl bioflavonoids are oxidized by radicals and then turned into low-reactive and more stable radicals (18). BS can be controlled by peripheral tissues that stimulate glucose uptake by using propolis, and preventing them from entering the bloodstream and reducing glucose uptake into the gut (19). In addition, propolis treatment can control BS by stimulating glucose uptake by peripheral tissues, deterring its release into the bloodstream, or decreasing intestinal glucose (20). According to studies, propolis reduced plasma insulin with its antioxidant properties, and IR. Ropolis in mice also reduced plasma insulin and IR in Hong et al. (2015). This result was also shown in Kitamura's research. The intervention also improved insulin function in the Zamami (2014). Experimental and clinical research may be affected by propolis supplementation, extracts and phenolic compounds, such as phenyl ester of caffeic acid in propolis.This research reduces IR, combats oxidative stress, creates inflammatory factors, decreases the level of adiponectin and transfer of glucose to the tissues, digestive enzymes of carbohydrates, especially alpha-amylase and alpha-glycosidase (23). The authors of Elisa et al. (2015) significantly reduced TNF* levels, followed by a significant reduction in IR and a decrease in FBG.Studies have shown thatpropolis enhances glucose transport via GLUT4 by reducing IR (24). Enhancing propolisleads to alpha-amylase, which can delay the hydrolysis of polysaccharides and reduce glucose uptake (25). According to a study by Zhou et al. (2016), reports of propolis use reduced Hb A1C (26). In this study, the glossy hemoglobin group in propolis-treated control mice was reduced by 8.4% compared to the control. In addition, Cain Clark et al. (2018) examined the use of propolis on the glycemic index in patients and stated that propolis improved FBG and Hb A1C levels, but no changes were observed in insulin levels and IR (27). Afsharpour et al. (2020) found that three servings of 500 mg of propolis per day reduced FBG, plasma insulin, Hb A1C and IR in patients at eight weeks (28). Despite similar studies, some studies do not show positive results. For example, 230 mg propolis supplement for 60 days did not affect FBG or acidic antioxidant status, which only prevented the increase of blood uric acid and reduced glomerular filtration (29). Moreover, Samadi et al (2017) observed no SiD in serum insulin level and IR between propolis and placebo after 12 weeks. Elisa et al.

(2015) reduced TNF* levels significantly, followed by significant declines in IR and FBG levels. (16). Different doses of propolis may explain the differences studies. Hyperglycemia, which causes oxidative stress in diabetic patients, is a major cause of the imbalance between antioxidants and oxidative agents (30). Reactive oxygen species (ROS) are produced as a result of increased glucose oxidation ROS are produced as a result of increased glucose oxidation Oxidative stress and IR are worsened by increased ROS, which causes lipid oxidation, particularly in the cell membrane (31). Moreover, the research findings showed that eight weeks of combined exercise significantly reduced FBG, insulin, IR, and Hb A1C in women with DMT2. Regarding the effect of combined exercise on the level of glycemic index and IR, the results of the study were consistent with the results of the study of Enteshary et al. (32) and Esmaili et al.(33), and Mirzandeh et al. (34) showing a significant decrease in IR index after combined training reported with DMT2The use of combined exercise in different order did not cause significant changes in Hb A1C, IR and functional factors. Different research results can probably be attributed to differences in training intensity and duration as well as differences in age and gender of the research samples. As a basis for explaining the mechanisms involved, chronic hyperglycemia may impair beta-cell function and worsen IR under diabetic conditions. Physical activity without insulin and two to three hours after eating with insulin cause muscles to consume large amounts of glucose. The repeated contractions of muscles during exercise have an insulin-like effect, releasing large amounts of glucose into the cells to expend energy. These frequent contractions enhance the number of insulin-dependent glucose transportersin the long run and enhance the membrane's permeability to glucose. Furthermore, muscle fibers have a low glycogen concentration for a long period, and muscle cells rebuild their glycogen reserves after exercise, and the blood glucose concentration decreases for several hours. Both aerobic and resistance training enhance the frequency of GLUT-4 and glucose uptake even in DMT2 (35). Aerobic and resistance training is the most effective type of exercise in controlling glucose and insulin activity. The combined exercise was proposed as the most effective for regulating blood glucose and plasma insulin activity (36). Exercise increases plasma insulin sensitivity by increasing mRNA and glucose transporter proteins, reducing release, and enhancing the clearance of acids. Free fat, insulin receptor signaling, glycogen synthesis, hexokinase, and glucose release from the blood to the muscle due to increased capillaries, as well as the uptake of glucose change the composition of the muscle (37).

The results showed that simultaneous use of propolis supplement and combined exercise reduced glycemic index and IR in patients with DMT2 compared to exercise and consumption of propolis alone. Therefore, the simultaneous interaction of this supplement and exercise is more effective in reducing IR, and combination exercise with propolis has interactive effects in improving glycemic index in DMT2 patients.

Conclusion

According to the results, exercise and propolis alone could affect IR and **glycemic indicators** in diabetic patients due to the results of this study However, combined exercise (aerobic-resistance) with propolis supplement ratioalone had more favorable effects on improving the glycemic index of DMT2 patients. However, more studies are needed to examine the mechanisms affecting them in more depth.

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