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The effect of a swim workout program along with the use of arbutin on glucose and insulin levels in rats with hyperglycemia

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Abstract

Arbutin has antioxidant effects that cause to reduce glucose levels. There is little information about the effect of swim workout along with arbutin on glucose and insulin level. Hence, objective of the present research is to investigate the effect of a swim workout program with the use of arbutin on glucose and insulin levels in rats with hyperglycemia. Experimental study was done on 28 adult male Wistar rats and after the injection of alloxan and becoming diabetic, they were divided into four groups including control, receiving arbutin, receiving arbutin + swimming and swim workout. Swim workout protocol for was conducted for 6 weeks, 5 days a week. Data were analyzed using ANOVA and dependent t-tests. After 6 weeks, blood glucose levels had a significant decrease in groups of swim workout, receiving arbutin + swim workout (p=0.02). On the other hand, mean insulin levels were significantly reduced in swim workout group (p=0.01), and no significant difference was observed between other groups. The results of present research suggest that, a swim workout course along with the use of arbutin have their own positive effect on glucose and insulin levels in mice infected with Hyperglycemia, also aerobic workout showed more effectiveness.

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Introduction

Changes in lifestyle and dietary patterns lead to diseases such as diabetes type II and cardiac - vascular diseases. Diabetes is a metabolic disorder which is manifested with chronic hyperglycemia and impaired glucose metabolism, protein and fat. Diabetes type II can lead to many pathological changes such as neuropathy, nephropathy, immune deficiency, vascular damage (Raghow, 2012). The researchers believe that insulin resistance plays a key role in the pathophysiology of diabetes type II. Consequence of insulin resistance is to increase hepatic production and to decrease uptake by muscle and fat tissues and consequently, resulting in the inability of insulin to maintain normal glucose levels (Olefsky and Glass, 2010; Belfiore and Malaguarnera, 2011). Resistance to insulin plays a key role in the pathogenesis of diabetes (Belfiore and Malaguarnera, 2011). Therefore, investigating the effects of environmental factors on the patients with diabetes type II is very important. Use of herbal medicines is one of the useful ways to deal with this disease. Given that many herbal medicines have antioxidant properties, so they can be a good alternative to the use of modern synthetic drugs to treat diabetes. Arbutin is a hydroquinone glucoside which in high values is found in peduncle, leaves and bark of some Pyrus plants and many plants such as Rosaceae and Ericaceae (Munday, 1988). Boissieriana buhse due to the high amount of phenyl and abundance in northern Iran can be used as a rich source of Arbutin in Iran (Shahaboddin *et al.,* 2011). Arbutin-containing plants have antioxidant effects; also, can be used for urinary tract disinfectant in urinary tract infections (Blumental, 1998). Research showed that in people with diabetes, postprandial blood glucose rises, on the other hand, one of the characteristics of glycyrrhizin, arbutin is to reduce the glucose levels, and hence, the use of glycyrrhizin, arbutin can be helpful to reduce the levels of glucose and resistance to insulin in people with diabetes (Takii *et al.,* 1997).

Diabetes is associated with reduced muscle strength and metabolic control (Mlinar *et al.,* 2007). Increasing physical activity in patients with type II diabetes can enhance physical performance and blood glucose control and be effective in prevention of osteoporosis through decreasing the levels of plasma lipids, blood glucose, decreased oxidative stress and improved insulin sensitivity (Praet and van Loon, 2009). Increased insulin, glucose-induced muscle contraction make aerobic exercise as a treatment tool for the patients with diabetes (Ibanez *et al.*, 2005; Kwon *et al.,* 2010). Hitherto, no research has been reported on the effects of exercise on indicators of metabolic syndrome with in diabetic subjects. Swanston Flatt *et al.* in their study on bear grass having the highest arbutin content showed that, this plant does not decrease blood sugar in diabetic rats compared to control group (Takii *et al.,* 1997). In contrast, Takii *et al.* reported that, arbutin due to antioxidant properties, lowers blood glucose (Takii *et al.,* 1997). Considering the importance of diabetes type II and potential role of physical activity in the increase of insulin sensitivity and also the little existent researches on the effect of physical activity especially swim workout along with the use of arbutin on indicators of metabolic syndrome levels, the objective of present study is to investigate the effect of a swim workout program on the levels of glucose, insulin and index of resistance to insulin in mice with diabetes type II.

Materials and methods

This research is an experimental research which was conducted in the laboratory of Medical Sciences University of Babol. In this study, 28 male Wistar rats weighing approximately 150-250 g were used. Pets were kept at room with temperature 22-18 ° C and under 12-hour light and dark, and had access to adequate food and water. After a week, transferring to the laboratory environment and getting familiar with the new environment and with the practice of swimming for a week, and 72 hours after injection of alloxan, the subjects were randomly divided into four groups:

1- Exercising group that swam five days a week.

2- Control group including hyperglycemic rats which was under natural conditions.

3- Group of receiving arbutin and swim workout.

4- Group of receiving arbutin.

Arbutin injection subcutaneously with a purity of 96% in the amount of 50 mg per kg body weight with two cc of normal saline solution was daily done. In order to raise blood sugar of the rats, alloxan injection subcutaneously with 90 mg fresh weight in rats, with normal saline was conducted. To be sure, the 72-hour blood glucose of rats was measured by glucometer. Animals were kept in accordance with the guidelines of the International Institute of Public Health, and the study protocols were done considering the principles of the Declaration of Helsinki and the principles of medical ethics at the Medical Sciences University of Babol.

The exercise protocol

Before conducting the main stage of the research, and considering that, this study was implemented for the first time in the country, the researcher, designed a special pool for the rats with the order to build a fiberglass water tank with dimensions 70 × 90 × 150 cm. also the water temperature were considered by 28° C. Before conducting the training program in order to meet the water and swim stress reduction and adaption with exercise conditions, they were put in the pool for two days. After that, the diabetic rats swam in training groups of once daily (five days a week) in the swimming pool during the six weeks. Swim workout was carried out for 6 weeks, 5 days a week and once a day starting from 5 minutes a day, and 1 min was added every day to rise exercise volume. Finally, at the end of the period (6 weeks), the exercise time reached 35 minutes. After 6 weeks of training in order to phlebotomy, Mice were comatose by xylazine and ketamine (per 100 g rat 0.1 ketamine and 0.25 xylazine) injection, and blood samples were taken directly from the heart and veins axillary (armpit) of the rats by five cc. After sampling the blood and put it in a water bath at 37 ° C, samples were immediately centrifuged (3000 rpm for 10 min), and obtained serum was maintained in a freezer at -80 ° C till the experiment time. Insulin and glucose levels were measured by intensive insulin ELISA kit using a special kit (ultra-sensitive), and glucose was measured by glucose oxidase with a spectrophotometer with Pars glucose kit test. After confirming the data normal distribution using Kolmogorov-Smirnov test, raw data were analyzed using SPSS version 16 (version 16, SPSS Inc., Chicago, IL) and using one-way ANOVA and Tukey test at $P<0.05$.

Results

Weight of rats are given in Table 1. There was no significant difference in body weight between the research groups at the beginning of the study. After six weeks swim workout, the animals' weight in arbutin and swimming group was less swimming group, arbutin group and control group but was statistically insignificant.

Table 1. Weight changes of rats before and after 6 weeks swimming (ANOVA tests).

Control Mean standard deviation	Arbutin Mean standard deviation	Arbutin and swimming Mean standard deviation	Swimming Mean standard deviation	Groups Variable
210.71±17.10	206.57±16.86	212±24.03	182.14±21.60	Initial weight (gr)
365.04±15.08	362±16	346±24	348±12	Final weight (gr)

Concentrations of measured variables are presented in Table 2. Intragroup study shows that the average blood glucose levels in swim workout, arbutin and swimming group decreased significantly (P=0.02 and 0.02) while, it was decreased in arbutin group but was not significant (P=0.32), and it had insignificant increase in control group (P=0.14). On the other hand, mean of insulin levels had significant reduction in swimming group (P=0.01) but, there was no significant variations in other groups.

One-way ANOVA results showed that, after exercise period, there are significant differences between serum glucose levels between the four groups

(P<0.001) while, insulin levels have no significant difference (P=0.43). The Tukey test in investigating the intragroup differences after the program showed that, there is a significant difference between the amounts of glucose levels of the subjects of swimming and control group and swimming and arbutin group and control group and no significant difference was observed between other groups (Table 2).

Table 2. Variations of measured variables in rats before and after 6 weeks swimming (ANOVA tests).

P value among the four groups	After workout period Mean standard deviation	Before workout period Mean standard deviation	Time Group	Variables
**0.000	*94.71±13.26	169.57±11.41	Swimming	Glucose(mg/dl)
	*129.33±19.89	180.41±14.21	Arbutin and swimming	
	133.00±22.71	157.21±21.51	Arbutin	
	184.67±23.20	174.42±12.15	Control	
0.431	*0.09±0.09	0.1±0.02	Swimming	Insulin (ng/l)
	0.07±0.03	0.09±0.03	Arbutin and swimming	
	0.05±0.01	0.07±0.01	Arbutin	
	0.09±0.01	0.07±0.02	Control	

* Intragroup difference at P≤0.05 ** Intergroup difference at P≤0.05.

Discussion and conclusion

The most important findings of this research include the effects of swimming and arbutin complementary on blood glucose control in rats with hyperglycemia. Preliminary results of the study showed that, glucose and insulin levels were significantly reduced in swimming group, exercise and arbutin group also showed a significant decrease in glucose levels while, the rest of the groups did not show a significant change. Preliminary results of the study confirmed the results of previous studies on the relationship between physical activity and reduced glucose levels (Balducci *et al.,* 2012; Shahla Kan *et al.,* 1995; Massi-Benedtti *et al.,* 1996; Stewart, 2004).

Lee *et al.* reported reduced glucose levels after 4 weeks of swim workout, 5 days a week in rats with diabetes type II (Lee *et al.,* 2012). Kim *et al.* found that, after 4 weeks of swim workout insulin levels decreased, but no significant change was observed in glucose levels in rats with diabetes type II. Considering the conducted researches, the role of exercise in diabetes type II as increaser of sensitivity of cells to insulin, is well known while, there are little studies on the effect of physical activity in various intensities and the effect of swimming on diabetes type II, and there are also discrepancies among the studies (Lee *et al.,* 2012; Kim *et al,* 2011). One of the effective factors on the study variables levels is the exercise duration, its severity and time and also, the exercise type. The results of Lee *et al.* suggest that, swimming for four weeks, five days a week and an hour per session, decreases significantly glucose level while, in Kim *et al.* study, it seems that, exercise duration and severity are very important. Researches showed that swimming exercise improves insulin sensitivity just like aerobic exercises. Because, muscle contraction increases glucose uptake. Swim training includes activities in all muscle groups of the body consisting of active muscle contraction (Lee *et al.,* 2012). Muscle contraction improves glucose levels and insulin sensitivity through increasing muscle GLUT4 levels, receiving insulin, protein kinase B and glycogen synthase after exercise (Feng *et al.,* 2011). Skeletal muscle glucose transport is conducted via glucose transporter proteins, and GLUT4 is the most important isoform in skeletal muscle which is affected by contraction and insulin (Kraus *et al.,* 2002). By doing exercise, GLUT4 content increases in trained muscles which cause to improve the act of insulin on glucose metabolism. When insulin levels decrease, the basal insulin levels and glucose-stimulated insulin levels decreases and consequently, these events lead

to a reduction in resistance to insulin in tissues (Lee *et al.,* 2012; Kim *et al,* 2011, Kraus *et al.,* 2002).

Another important finding in this research is the effect of arbutin along with swimming on the blood glucose levels in the rats with hyperglycemia. Findings of this research approved the results of previous studies on the relationship of arbutin with glucose levels reduction (Takii *et al.,* 1997). Takii *et al.* showed that, arbutin decreases blood glucose levels due to its antioxidant property (Takii *et al.,* 1997). Despite this case, some studies also have shown no effect on blood glucose levels by arbutin Supplement. Swanston Flatt *et al.* conducted a research on bear grass which has the highest amount of arbutin among the plants, and they suggested that, extract of this plant does not cause to decrease blood sugar in diabetic rats compared with control group (Munday, 1988). Since there is no clear mechanism of the effect of exercise, especially swimming workout along with arbutin, proper explanation of the conflicting results of researches is not possible. However, studies show that, arbutin decreases the blood glucose lonely due to antioxidant property; hence, it can be used as a contributing factor to control diabetes (Blumental, 1998). Therapeutic targets in diabetes mainly include reduction of resistance to insulin and insulin secretion stimulated by improving nutrition, exercise and medication. Free radicals are generated in the patients with diabetes by glucose oxidation, non-enzymatic glycation of proteins and consequently oxidative damage of proteins. Oxidative stress which is an imbalance between the production of oxygen free radicals and antioxidant defense capacity of the body, strongly is associated with diabetes and its complications, so that, it has been shown that, during both types 1 and 2 of diabetes, oxidative stress was increased in blood, and treatment by antioxidant drugs such as arbutin led to reduce diabetes complications (Takii *et al.,* 1997).

According to the results of this research, after six weeks swimming, a significant reduction was observed in insulin levels along with significant reduction in serum glucose concentration. Also it was observed that, arbutin with swim workout led to lower glucose levels in diabetes type II in rats. Considering the significant reduction of glucose in this research it can be said that, complications of diabetes continued to improve in the rats with diabetes type II. Hence, swim workout and arbutin supplement can be used as effective factors in improvement of insulin sensitivity in patients with diabetes, after further researches.

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