

The Effect of Ketogenic Diet with Resistance Training on Serum Adropin Level and Insulin Resistance in overweight women

Niloufar Bolourian Kashi¹

1. Master Student of Exercise Physiology, Ferdowsi University of Mashhad

Zahra Koohestani Sini^{2*}

2. Lecturer, Faculty of Medicine, Mashhad University of Medical Sciences

Mahnaz Seifi³

3. Master in Exercise Physiology, Ferdowsi University of Mashhad

Hamideh Nakhayi⁴

4. PhD Student in Exercise Physiology, Birjand University

* Corresponding author: Zahra Koohestani Sini
Email: koohestanzahra@yahoo.com

Abstract

Abstract— the aim of the present study was to evaluate the effect of eight weeks of ketogenic diet combined with resistance training on serum adropine levels and insulin resistance in overweight women. 40 women aged 30 to 40 years in Mashhad with a body mass index of more than 25 but less than 30 were purposefully selected and participated in this study voluntarily. After selecting the subjects, they were randomly divided into four groups: resistance training, ketogenic diet, resistance training + ketogenic diet and control (10 people in each group). Interventions were applied for four weeks. The results showed that only the effect of diet on weight loss, BMI, WHR, fat percentage and body fat mass was significant ($P < 0.05$) but the effect of exercise and the interactive effect of exercise and diet were not significant ($P > 0.05$). Also, the results showed that the effect of exercise and the interactive effect of exercise and diet on reducing glucose, insulin and insulin resistance were significant ($P < 0.05$) but the effect of diet was not significant ($P > 0.05$). Finally, the results showed that the effect of exercise and the interactive effect of exercise and diet on increasing adropin was significant ($P < 0.05$) but the effect of diet was not significant ($P > 0.05$). A four-week ketogenic diet will probably improve the body composition of overweight women. Meanwhile, resistance training without changing weight and body fat seems to increase adropine and improve insulin resistance.

Keywords— Adropine, Insulin resistance, Ketogenic diet, Exercise, Weight loss

I. Introduction

It has been well established that the increase in body fat is the main cause of metabolic disorders such as insulin resistance in women (1). These metabolic abnormalities, in turn, are major contributors to dangerous diseases such as hypertension, cardiovascular disease, and tow type diabetes (1). Adropine, on the other hand, is a new peptide of hepatic origin that is associated with carbohydrate metabolism as well as blood pressure. Adropine contains 76 amino acids encoded by a gene associated with energy homeostasis in the liver called Enho (2) and is expressed in several tissues including the brain, heart, kidney, liver, pancreas, skeletal muscle, and small intestine (3). Circulating levels of adropine decrease with age (4). Adropine is involved in fat and carbohydrate metabolism, metabolic diseases, central nervous system function, endothelial function, and cardiovascular disease. Information on the exact role and mechanism of action of this interesting protein is not yet complete (5). Recently, adropine has been shown to be important in the choice of skeletal muscle fuel (6). Adropine has been shown to increase pyruvate dehydrogenase activity to increase glucose oxidation (7). Therefore, it is possible that an increase in adropine with an increase in glucose metabolism leads to a decrease in blood sugar and thus a decrease in insulin resistance. This effect can prevent diabetes in the elderly and also reduce the risk of heart disease. Adropine also reduces the oxidation of muscle fatty acids in parallel by inhibiting carnitine, a key fatty acid-transporting enzyme in mitochondria (6). In addition, adropine can reduce exercise-induced vascular stiffness by increasing nitric oxide (NO) (8). However, not much research has been done on the effect of exercise on adropine, and it seems that studies on the effect of exercise on this peptide, which was discovered in 2008 and have not yet reached its discovery age of 15 years, at the beginning it has its own path. Recently, the effect of exercise on changes in adropin levels has been considered. Fujie et al. (2015) reported that 8 weeks of aerobic exercise significantly increased serum adropin levels in middle-aged and elderly adults (8). It has also been reported to increase in sedentary obese women after 16 weeks of aerobic exercise with calorie restriction. On the other hand, Sanchis-Gomar et al. (2015) did not observe a significant change in professional football players during one season (9). There is only one study on the effect of an activity session conducted by Sato et al. (2017) on diabetic rats. They reported that one session of aerobic activity increased adropin levels (10). However, there are not many findings in this regard.

Some previous studies have emphasized the benefits of a carbohydrate-restricted diet, and have traditionally used the relationship between insulin and carbohydrates to justify this type of diet. Glycemic index and glycemic load are other issues in diets and with the explanation that foods with high glycemic index and glycemic load are related to hyperinsulinemia and other post-meal metabolisms, it is theoretically related to body weight regulation (11). In studies that have investigated the effect of dietary carbohydrates, low-carbohydrate and ketogenic diets (carbohydrates less than 20 grams per day) have also reported positive results in terms of fat reduction and liver size (12). Studies have shown that reducing carbohydrates in the diet improves the body's metabolic syndrome and tow type diabetes even without weight loss (13). Liu et al. (2014) showed that the combination of exercise and low-carbohydrate diet has beneficial effects on body fat percentage and factors affecting insulin resistance in pre-diabetic individuals (14). Studies have shown a greater reduction in blood glucose and insulin resistance in the low-carbohydrate diet than in the low-fat diet (15).

However, no study has been performed to evaluate the effect of resistance training combined with ketogenic diet on adropine and insulin resistance. The aim of the present study was to evaluate the effect

of a four-week ketogenic diet with resistance training on serum adipone levels and insulin resistance in overweight women.

II. Methodology

This quasi-experimental study was conducted with a pre-test and post-test design with a control group. 40 women aged 30 to 40 years in Mashhad with a body mass index of more than 25 but less than 30 were purposefully selected and participated in this study voluntarily. After selecting the subjects, they were randomly divided into four groups: resistance training, ketogenic diet, resistance training + ketogenic diet and control (10 people in each group). Before starting the research, the nature, goals and risks of this study were explained to the subjects in a face-to-face meeting and written consent was obtained from them to participate in this study. Subjects attended the pre-test session 24 hours before the intervention. The interventions were then applied for four weeks. During these four weeks, the control group did not participate in any regular physical activity program and only engaged in their normal daily activities and followed their normal diet. The resistance training group participated in a resistance training program, so they followed their natural diet. The ketogenic diet group used a high-fat, low-carbohydrate, and natural protein ketogenic diet. Resistance training group + ketogenic diet, in addition to doing a resistance training program similar to the resistance training group, also followed a ketogenic diet. 48 hours after the interventions, the subjects were present in the test session again and post-test measurements were performed. In both pre-test and post-test, the body composition of the subjects including weight, body mass index, body fat percentage, body fat mass weight and lean body mass weight were measured and blood samples were collected in 12 hours of fasting. The collected samples were poured into sterile tubes containing K3EDTR. The heparinized tubes and EDTR were placed in ice and then left at room temperature for several minutes. The serum was then separated from the plasma by centrifugation for 10 minutes at 3500 RPM. All blood samples were frozen at -20°C and used during laboratory testing. The resistance training program included Barbell Bench Press, squat, Underhand Cable Pulldowns and Lying Leg Curls movements with 45 to 75% of a maximum repetition (1RM) and 8 to 12 repetitions in 2 to 4 sets, which were performed for 3 sessions per week for 4 weeks.

Table1. Resistance training program

Week	Repetition	% 1RM	Rest of between each station	Rest of between each circle	Number of circles
First	8	45	60 to 90 seconds	2 to 3 minutes	2
Second	9	55	60 to 90 seconds	2 to 3 minutes	2
Third	10	65	60 to 90 seconds	2 to 3 minutes	2
Fourth	10	75	60 to 90 seconds	2 to 3 minutes	2

Due to the fact that very precise control was not possible, diet control was based on the recommendations of the researcher but by the subjects themselves. A ketogenic diet plan should include about 75% fat, 15 to 20% protein, and 5 to 10% carbohydrates. Recommended foods for the ketogenic diet are presented in Table 2.

Table2. Recommended foods for ketogenic diet

Breakfast	Snack	Lunch	Snack	Dinner
tomato	Strawberry	Cream	Coconut	season's salad

egg	Cream	Lettuce and cabbage	Carrots	Meatball Tabrizi
Butter	Cucumber	Skinless chicken breast olive oil	Pistachio	Peach Butter Cheese

To measure body composition, a body composition measuring device was used by bioelectric impedance method (IN BODY 0.3, Korea). Body composition indices including fat percentage, fat mass weight and lean mass weight were recorded. It also gives us height, weight, body mass index (BMI) and waist-to-hip ratio (WHR). Adropine, insulin and glucose levels were measured and insulin resistance was calculated for each blood sample. Adropine was measured using an ELISA kit made in the USA by ELISA method and spectrophotometer. Glucose was obtained by turbidimetric colorimetric method using an elitech kit made in Italy. Insulin was obtained by ELISA method using a microcalorimetry kit from Monoband Company made in USA. Insulin resistance was calculated using glucose and insulin concentrations and HOMA-IR formula as follows: $HOMA-IR = \text{Glucose concentration} \times \text{Insulin concentration} / 22.5$

Two-way analysis of variance was used to compare the changes of variables in four research groups. A significance level of $P \leq 0.05$ was considered. All statistical calculations were performed using SPSS software version 16.

III. Results

The results of analysis of variance test to examine the changes of variables are reported in Table 3. The results showed that only the effect of diet on weight loss, BMI, WHR, fat percentage and body fat mass was significant ($P < 0.05$) but the effect of exercise and the interactive effect of exercise and diet were not significant ($P > 0.05$). Regarding lean mass, the results showed that the effect of diet ($P = 0.62$), effect of exercise ($P = 0.12$) and interactive effect of exercise and diet ($P = 0.57$) were not significant. Also, the results showed that the effect of exercise and the interactive effect of exercise and diet on reducing glucose, insulin and insulin resistance were significant ($P < 0.05$) but the effect of diet was not significant ($P > 0.05$). Finally, the results showed that the effect of exercise and the interactive effect of exercise and diet on increasing adropin was significant ($P < 0.05$) but the effect of diet was not significant ($P > 0.05$).

Table3. Results of two-way analysis of variance to examine changes in variables

Variables	group	Before	After	Factor	P
Weight (kg)	Training	64.70 ± 7.46	64.40 ± 7.32	Training Diet Training × diet	0.47 0.001 * 00.73
	Diet	64.80 ± 5.76	62.90 ± 4.74		
	Training + diet	65.40 ± 3.94	63.30 ± 3.40		
	Control	64.60 ± 4.62	64.70 ± 4.54		
BMI (kg/m ²)	Training	23.36 ± 1.70	23.25 ± 1.66	Training Diet Training × diet	0.35 0.001 * 0.69
	Diet	23.44 ± 1.45	22.76 ± 1.12		
	Training + diet	23.53 ± 1.31	22.77 ± 0.97		
	Control	23.51 ± 1.23	23.55 ± 1.24		
WHR (ratio)	Training	0.75 ± 0.03	0.75 ± 0.03	Training Diet Training × diet	0.33 0.001 * 0.22
	Diet	0.76 ± 0.05	0.73 ± 0.03		
	Training + diet	0.77 ± 0.04	0.74 ± 0.02		
	Control	0.76 ± 0.03	0.77 ± 0.03		
Fat percentage (%)	Training	24.67 ± 1.10	24.38 ± 1.30	Training Diet Training × diet	0.082 0.001 * 0.15
	Diet	25.84 ± 1.72	23.37 ± 1.58		
	Training + diet	25.97 ± 1.85	23.38 ± 1.58		
	Control	24.52 ± 1.09	25.09 ± 1.19		
Fat mass (kg)	Training	13.65 ± 1.39	13.31 ± 1.09	Training Diet Training × diet	0.12 0.001 * 0.21
	Diet	14.99 ± 1.25	12.50 ± 1.29		
	Training + diet	15.12 ± 1.61	12.51 ± 1.41		
	Control	13.32 ± 1.03	13.81 ± 1.60		
Lean mass (kg)	Training	51.04 ± 4.28	51.08 ± 7.99	Training Diet Training × diet	0.62 0.12 0.57
	Diet	49.80 ± 6.11	50.39 ± 6.14		
	Training + diet	50.27 ± 5.47	50.78 ± 4.64		
	Control	51.27 ± 6.61	50.88 ± 4.73		
Glucose (mg/dl)	Training	125.60 ± 11.68	104.80 ± 9.05	Training Diet Training × diet	0.009 * 0.31 0.013 *
	Diet	118.30 ± 8.81	104.40 ± 9.67		
	Training + diet	121.60 ± 9.64	107.10 ± 10.39		
	Control	109.70 ± 4.57	110.10 ± 8.55		
Insulin (μl/mL)	Training	16.55 ± 2.68	14.11 ± 2.41	Training Diet Training × diet	0.010 * 0.20 0.020 *
	Diet	15.39 ± 3.15	13.71 ± 2.88		
	Training + diet	16.31 ± 2.38	14.49 ± 2.51		
	Control	14.42 ± 1.63	14.76 ± 1.93		
Insulin resistance (HOMA-IR)	Training	5.10 ± 1.11	3.63 ± 0.67	Training Diet Training × diet	0.003 * 0.25 0.010 *
	Diet	4.47 ± 1.13	3.54 ± 0.89		
	Training + diet	4.88 ± 0.81	3.83 ± 0.84		
	Control	3.89 ± 0.47	3.99 ± 0.55		
Adropine (ng/ml)	Training	2.23 ± 0.28	3.66 ± 0.69	Training Diet Training × diet	0.001 * 0.11 0.007 *
	Diet	2.45 ± 0.40	3.40 ± 0.81		
	Training + diet	2.35 ± 0.31	3.50 ± 0.95		
	Control	2.44 ± 0.38	2.42 ± 0.40		

* Significant at the level of P≤0.05

IV. Discussion

According to the findings of the present study, four weeks of resistance training, ketogenic diet and their combination improved the body composition of overweight women, but this improvement was significant only in the two groups that followed the ketogenic diet. The difference between the two groups of ketogenic diet and exercise + ketogenic diet was not significant and in fact resistance training despite non-significant improvement could not lead to a significant improvement in body composition, which may be due to insufficient duration of intervention. The present results regarding the effect of ketogenic diet consumption on weight loss and body fat were in line with the findings of Zinn et al. (2017) (16). The calorie deficiency created by the ketogenic diet may have led to a reduction in body fat. It has been reported that after a ketogenic diet, body weight decreases through dehydration following glycogen depletion (17). Due to the low consumption of carbohydrates, insulin levels remain low during the ketogenic diet and can help break down more fats (18). Zinn et al. (2017) showed that oxidation of free fatty acids increases following consumption of ketogenic diet (16). A ketogenic diet reduces calorie intake by restricting dietary carbohydrates, but may impair athletic performance by reducing glycogen storage (19). This may be one of the reasons why physical activity does not affect weight loss and body fat. For example, although a ketogenic diet leads to positive effects on fat metabolism (20), it reduces aerobic function (21). In general, previous studies have shown a further reduction in body fat mass due to a ketogenic diet (22). Research in weight loss studies shows that ketogenic diets lead to more weight loss than carbohydrate-based diets (23). Studies show that physical activity alone has a moderate effect on weight loss, but when diet is added to physical activity, fat loss becomes more significant (24). Evidence suggests that abdominal fat accumulation is the most dangerous risk factor for metabolic syndrome and cardiovascular disease (24). Well-controlled studies show that physical activity is an appropriate therapeutic intervention to reduce abdominal fat in obese people (24). However, in the present study, resistance training could not lead to a further improvement in body composition compared to diet, which may be due to the type of training or insufficient duration of training. The data from the present study showed that four weeks of resistance training significantly reduced the percentage of fat and fat mass. These results contradict the findings of Ferreira and Carraio (25), Wolkodoff et al. (26) and Rogers and Gibson (27), but are consistent with the findings of Segal et al. (28). Intensity of exercises, age of subjects and number of weekly sessions can be the reasons for the difference in results. In Segal et al.'s study, the number of weekly sessions was one session and the subjects were middle-aged women who did not attend the sessions regularly and there was no control group (29). Also, the data from the present study showed that resistance training increased muscle mass, but this increase was not statistically significant. These results are consistent with the results of research conducted by Rogers and Gibson (27), Segal et al. (28) and Jago et al. (30) but it contradicts the results of research conducted by Weibert et al. (26) and Ferreira and Carraio (25). One of the differences is the type of exercises used. Another difference may be related to the duration of training in the study of Ferreira and Carraio (25), in which the duration of training was 12 weeks. Studies show that the training period required for a change in lean body mass should be more than three months (31), so the reason for the lack of change in lean body mass may be that the training period in this study was four weeks. Research shows that exercise activities that contribute to weight loss are diet-dependent (32), which confirms the findings.

On the other hand, the present results showed that exercise alone and in combination with ketogenic diet led to a significant increase in adipone and a significant decrease in insulin resistance, but the combination of both had no significant effect on these changes. It seems that resistance training without affecting body weight and body fat leads to favorable effects on insulin and adipone resistance. The

ketogenic diet reduces blood glucose and insulin resistance due to its higher levels of fat, protein and lower carbohydrates (33). Exercise also changes the substrate from free fatty acids (the dominant fuel at rest) to glucose and glycogen (34). Absorption of blood glucose by skeletal muscle during exercise independent of the insulin signaling pathway reduces blood glucose in tow type diabetics (35). It seems that the combination of exercise and ketogenic diet by activating two separate pathways, including reducing glucose uptake and increasing glucose intake, have the greatest impact on lowering blood sugar in tow type diabetics. The present results were in line with the findings of Fuji et al. (2015) on the increase of adropine due to training. The exact mechanism by which adropine changes during acute physical activity or increases fat metabolism is not yet fully understood, but it is possible that adropine regulates energy homeostasis through mechanisms that suppress lipogenesis (8). It seems that the mechanism of increasing adropin in fasting state and after physical activity is due to depletion of glycogen and ATP sources in the liver and also the role of adropin in reducing food intake (8). Reducing food intake by increasing adropin can lead to improved fat metabolism and insulin resistance. Kumar et al. (2008) reported that adropine enhances the stimulatory secretion of insulin by blood glucose, the mechanism of action of which is also facilitated by the entry of calcium through calcium channels independent of protein kinase and phospholipase in mouse beta cells (8). Increased adropine appears to have played a role in lowering blood glucose and insulin resistance following four weeks of resistance training. Other mechanisms of glucose lowering and insulin resistance in the present study include increased postsynaptic insulin messages (36), increased mRNA and protein of glucose transporter (36), increased glycogen and hexokinase synthesis (37), decreased release, and increase in depletion of free fatty acids (38) and an increase in muscle glucose transport and changes in muscle structure (39). These findings are consistent with other findings (39, 40). However, increasing adropin and suppressing lipogenesis is probably one of the mechanisms reducing insulin resistance.

V. Conclusion

It is concluded that a four-week ketogenic diet improves the body composition of overweight women. Adding resistance training to this diet can not significantly increase the effectiveness of the diet in this regard. The duration of the exercise may not have been enough to lose weight and body fat. On the other hand, the results showed that resistance training with and without ketogenic diet for four weeks leads to a significant increase in adropine and a significant decrease in insulin resistance in these women, but ketogenic diet alone has no significant effect in this regard. It seems that resistance training without changing weight and body fat leads to an increase in adropine and improved insulin resistance.

REFERENCES

1. S. H. Sudhaa, B. Rupali, R. Vishal, "tandon, Annil Mahajan. Postmenopausal obesity" *Journal of Medical Education and Research*, 2008; 10 PP: 6-105.
2. K. G. Kumar, J. L. Trevaskis, D. D. Lam, G. M. Sutton, R. A. Koza, V. N. Chouljenko, et al., "stephens JM, Butler AA. Identification of adropin as a secreted factor linking dietary macronutrient intake with energy homeostasis and lipid metabolism" *Cell Metab*, 2008; 8, PP: 468–481.

3. C. M. Wong, Y. Wang, J. T. Lee, Z. Huang, D. Wu, A. Xu, K. S. Lam, "adropin is a brain membrane-bound protein regulating physical activity via the NB-3/ Notch signaling pathway in mice" *J Biol Chem*, 2014; 289, PP: 25976–25986.
4. A. A. Butler, C. S. Tam, K. L. Stanhope, B. M. Wolfe, M. R. Ali, M. O’Keeffe, et al., "low circulating adropin concentrations with obesity and aging correlate with risk factors for metabolic disease and increase after gastric bypass surgery in humans" *J Clin Endocrinol Metab*, 2012; 97, PP: 3783–3791.
5. N. Marczuk, E. Cecerska-Heryć, A. Jesionowska, B. Dołęgowska, "adropin - physiological and pathophysiological role" *Postepy Hig Med Dosw (Online)*, 2016; 26 (70), PP: 981-988.
6. S. Gao, R. P. McMillan, J. Jacas, Q. Zhu, X. Li, G. K. Kumar, et al., "regulation of substrate oxidation preferences in muscle by the peptide hormone adropin" *Diabetes*, 2014; 63 (10), PP: 3242-3452.
7. R. W. Braith, D. T. Beck, "resistance exercise: training adaptations and developing a safe exercise prescription" *Heart Fail Rev*, 2008; 13, PP: 69-79.
8. S. Fujie, N. Hasegawa, K. Sato, S. Fujita, K. Sanada, T. Hamaoka, M. Iemitsu, "aerobic exercise training-induced changes in serum adropin level are associated with reduced arterial stiffness in middle-aged and older adults" *Am J Physiol Heart Circ Physiol*, 2015; 15. 309(10), PP: 1642-7.
9. F. Sanchis-Gomar, R. Alis, E. Rampinini, A. Bosio, D. Ferioli, A. La Torre, et al., "adropin and apelin fluctuations throughout a season in professional soccer players: Are they related with performance?" *Peptides*, 2015; 70, PP: 32-6.
10. K. Sato, T. Nishijima, T. Yokokawa, S. Fujita, "acute bout of exercise induced prolonged muscle glucose transporter-4 translocation and delayed counter-regulatory hormone response in type 1 diabetes" *PloS One*, 2017; 12, PP: e0178505.
11. M. Rizzo, G. B. Rinni, E. Carmina, "androgen excess and cardiovascular risk. *Minerva Endocrinol*, 2007; 32, PP: 67-71.
12. D. Tendler, S. Lin, W. Yancy, J. Mavropoulos, P. Sylvestre, D. Rockey, et al., "the effect of a low-carbohydrate, ketogenic diet on nonalcoholic fatty liver disease: a pilot study" *Dig Dis Sci*, 2007; PP: 52: 589-93.
13. R. M. Krauss, P. J. Blanche, R. S. Rawlings, H. S. Fernstrom, P. T. Williams, "separate effects of reduced carbohydrate intake and weight loss on atherogenic dyslipidemia" *The American journal of clinical nutrition*, 2006; 83(5), PP: 1025-31.
14. W. Y. Liu, X. M. Du, J. Q. Sun, J. Ge, R. W. Wang, R. Wang, et al., "effect of aerobic exercise and low carbohydrate diet on pre-diabetic non-alcoholic fatty liver disease in postmenopausal women and middle aged men—the role of gut microbiota composition: study protocol for the AELC randomized controlled trial" *BMC public health*, 2014; 14(1), PP: 1.
15. M. R. Ruth, A. M. Port, M. Shah, A. C. Bourland, N. W. Istfan, K. P. Nelson, et al., "consuming a hypocaloric high fat low carbohydrate diet for 12weeks lowers C reactive protein, and raises serum adiponectin and high density lipoproteincholesterol in obese subjects" *Metabolism*, 2013; 62(12), PP: 1779-87.
16. C. Zinn, W. Wood, M. Williden, S. Chatterton, E. Maunder, "ketogenic diet benefits body composition and well-being but not performance in a pilot case study of New Zealand endurance athletes" *Journal of the International Society of Sports Nutrition*, 2017; 14, PP: 22.
17. K. Dipla, M. Makri, A. Zafeiridis, D. Soulas, S. Tsalouhidou, V. Mougios, S. Kellis, "an isoenergetic high-protein, moderate-fat diet does not compromise strength and fatigue during resistance exercise in women" *Br J Nutr*, 2008; 100(2), PP: 283–6.
18. J. S. Volek, T. D. Noakes, S. D. Phinney, "rethinking fat as a performance fuel" *Eur J Sport Sci*, 2015; 15(1): 13–20.
19. S. D. Phinney, "ketogenic diets and physical performance" *Nutr Metab*, 2004; 1(1), PP: 2.
20. A. Zajac, S. Poprzecki, A. Maszczyk, M. Czuba, M. Michalczyk, G. Zydek, "the effects of a ketogenic diet on exercise metabolism and physical performance in off-road cyclists" *Nutrients*, 2014; 6(7), PP: 2493–508.
21. L. Burke, B. Kiens, "fat adaptations" for athletic performance: the nail in the coffin?" *J Appl Physiol*, 2006; 100, PP: 7–8.
22. P. T. Jabekk, I. A. Moe, H. D. Meen, S. E. Tomten, A. T. Hostmark, "resistance training in overweight women on a ketogenic diet conserved lean body mass while reducing body fat" *Nutrition & metabolism*, 2010; 7, PP: 17.
23. J. S. Volek, D. J. Freidenreich, C. Saenz, L. J. Kunces, B. C. Creighton, J. M. Bartley, et al., "metabolic characteristics of keto-adapted ultra-endurance runners" *Metabolism*, 2016; 65(3), PP: 100-110.
24. K. Shaw, H. Gennat, P. O’Rourke, C. Del Mar, "exercise for overweight or besity. *Cochrane database of systematic reviews*" (Online), 2006; 4, PP: CD003817.
25. C. Ferreira, A. Carraihó, "effects of three months of pilates-based exercise in women on body composition" *Medicine and Science in Sports and Exercise*, 2009; 41(5), PP: 16-7.

26. N. Wolkodoff, S. Peterson, J. Miller, "the fitness effects of a combined aerobic and pilates program an eight-week study using the stamina aero pilates Pro XP555" [Online]. 2008.
27. K. Rogers, A. L. Gibson, "effects of an 8-week mat pilates training program on body composition, flexibility, and muscular endurance" *Med Sci Sport Exercise*, 2006; 38, PP: 279-80.
28. N. A. Segal, J. Hein, J. R. Basford, "the effects of Pilates training on flexibility and body composition: an Observational Study" *Arch Phys Med Rehabil Vol*, 2004; 85, PP: 1977-1981.
29. R. T. Weibert, "textbook of therapeutics, drugs and dis eases management" 7th ed. Philadelphia: Lippincott Company, 2000; PP: 345-51.
30. R. Jago, M. L. Jonker, M. Missaghian, T. Baranowski, "effect of 4 weeks of Pilates on the body composition of young girls" *Prev Med*, 2006; 42(3), PP: 177-80.
31. E. T. Howley, B. D. Franks, "health fitness instructor's handbook" 3rd ed. London, UK: Human Kinetics Pub; 1997.
32. M. J. Mayo, J. R. Grantham, G. Balasekaran, "exercise-induced weight loss preferentially reduces abdominal fat" *Med Sci Sports Exerc*, 2003; 35(2), PP: 207-13.
33. S. K. Arora, S. I. McFarlane, "The case for low carbohydrate diets in diabetes management" *Nutrition & metabolism*, 2005; 2(1), PP: 16.
34. M. L. Goodwin, "blood glucose regulation during prolonged, submaximal, continuous exercise: a guide for clinicians" *Journal of diabetes science and technology*, 2010; 4(3), PP: 694-705.
35. V. Taddibi, M. Rahimi, "comparing the effect of two protocols concurrent training (strength-aerobic) on fasting blood glucose, glycosylated hemoglobin" *highsensitivity C - reactive protein and insulin resistance in women with type 2 diabetes*, *Eexercise physiology*, 2017; 2(2), PP: 95-100.
36. F. Dela, T. Ploug, A. Handberg, L. N. Petersen, J. J. Larsen, K. J. Mikines, et al., "physical training increases muscle GLUT4 protein and mRNA in patients with NIDDM" *Diabetes*, 1994; 43, PP: 862-5.
37. P. Ebeling, R. Bourey, L. Koranyi, J. A. Tuominen, L. C. Groop, J. Henriksson, et al., "mechanism of enhanced insulin sensitivity in athletes. Increased blood flow, muscle glucose transport protein (GLUT-4) concentration, and glycogen synthase activity" *J Clin Invest*, 1993; 92, PP: 1623- 31.
38. J. L. Ivy, "role of exercise training in the prevention and treatment of insulin resistance and non-insulindependent diabetes mellitus" *Sports Med*, 1997; 24, PP: 321- 36.
39. A. Andersson, A. Sjodin, R. Olsson, B. Vessby, "effects of physical exercise on phospholipid fatty acid composition in skeletal muscle" *Am J Physiol*, 1998; 274, PP: 432-8.
40. A. D. Kriketos, S. K. Gan, A. M. Poynten, S. M. Furler, D. J. Chisholm, L. V. Campbell, "exercise increases adiponectin levels and insulin sensitivity in humans" *Diabetes Care*, 2004; 27, PP: 629-30.