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The Effect of Pyramid Aerobic Training and Karela Herbal Supplement on Glycemic Control in Patients with Type 2 Diabetes

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Abstract

Introduction: Exercise and the use of herbal supplements are among the therapeutic interventions in controlling type 2 diabetes. This study aimed to compare the effect of exercise and karela supplement on glycemic control and metabolic complications in patients with type 2 diabetes.

Methods: In the present quasi-experimental study, 120 patients with type 2 diabetes were selected by purposive sampling and were randomly divided into 4 groups of exercise, karela supplement, combined, and control. Exercises included 8-week pyramid aerobic training, 3 sessions per week. Karela was consumed in a dose of 50 mg/kg body weight daily in form of karela powder.

Results: There was a significant decrease in fasting blood sugar (FBS), 2-hour postprandial glucose (2hPP), insulin resistance, and glycated hemoglobin (HbA_1c) in the intervention groups compared to the control group ($P<0.001$). Further, there was no significant difference between changes in FBS in the intervention groups ($P<0.05$), but 2hPP, insulin resistance, and HbA1c were higher in the training and combined groups compared to supplement group ($P<0.001$); however, there was no difference between the two groups ($P>0.05$).

Conclusion: According to the results, it can be said that both methods of exercise and karela consumption have a positive effect on glycemic control in type 2 diabetes, but interventions and the combination of exercise and the supplement are more effective in glycemic control than karela alone.

Keywords: Type 2 diabetes, Aerobic training, Karela, Glycemic control

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Introduction

Diabetes mellitus includes a group of common metabolic disorders that share the hyperglycemic phenotype.[1] The prevalence of type 1 and type 2 diabetes is increasing worldwide, but type 2 diabetes is more rapid than type 1. The causes of this increase include lifestyle changes, the prevalence of obesity, and reduced physical activity.[2] For the prevalence of type 2 diabetes, management and treatment of this disease, especially hyperglycemic control are of special importance due to the association of micro- and macrovascular complications with blood glucose levels.[3,4]

Glucose is a vital energy source for the body. Many cells in the body such as muscles and adipose tissues are insulin sensitive and use glucose transporter type 4 (GLUT4) to get glucose into the cell. Insulin signaling at this receptor increases the regulation of these transmitters and helps them absorb glucose. In insulin resistance, cells' sensitivity to insulin is reduced, and sugar removal from the blood is disrupted by insulin-sensitive cells. Hence, to

keep blood glucose in the normal range, the body needs to produce more insulin. Over time, insulin resistance causes hyperglycemia and damages the cells in different body tissues. Unlike type 1 diabetes, where the main problem is deficiency or absence of endogenous insulin, resistance is the main problem in patients with type 2 diabetes, and pharmacological and non-pharmacological treatments are planned accordingly.[5,6]

Due to the high cost of treatment, non-pharmacological methods can play an important role in glycemic control in diabetic patients.[4] Momordica charantia (karela) is used as a nutrient and traditional herbal medicine for type 2 diabetes.[7] Karela is one of the famous vegetables in South Asia and is cultivated for food and medicine in tropical regions such as India and some parts of southern Iran, including Chabahar. It is an annual plant with a single base and is similar to a cucumber, which has warts on the surface. Karela has both medicinal and food consumption and various components of this plant such as its roots, stems, leaves, fruits, and seeds have many uses.[8] Research has demonstrated that diabetics also use this plant as an herbal medicine for glycemic control and complications of diabetes.[8,9]

Exercise training is one of the essential parts in the treatment of type 2 diabetes,[4] and a lot of research has been done in this field, and the usefulness of exercise in diabetes management, especially glycemic control has been confirmed.[1,4,10]

The climatic conditions of some regions in Iran, including parts of Zahedan are favorable for growing the karela plant as an herbal medicine in the treatment of diabetes. This study is novel since there is limited information about the effect of karela on glycemic control; furthermore, no study has not been done, specifically to compare the effect of exercise and karela consumption on glycemic control. Therefore, this study aims to compare the effect of exercise training and karela consumption on glycemic control in patients with type 2 diabetes.

Materials and Methods

In the present quasi-experimental study, 120 patients with type 2 diabetes were selected by purposive sampling and randomly divided into 4 groups of 30 (each group includes 15 women and 15 men) which were exercise, karela, exercises with karela consumption (combined), and control groups.

$$n = \frac{S_1^2 + S_2^2}{\left(\mu_{2-\mu_1}\right)^2} \int(\alpha, \beta)$$

Inclusion criteria included having type 2 diabetes, being in the age range of 30-50 years, fasting blood sugar (FBS) below 250 mg/dL, no insulin injection, use of common diabetes medications, (e.g., metformin and glibenclamide), no smoking, no acute cardiovascular disease, no respiratory diseases and musculoskeletal problems, the sedentary standard of living (no regular exercise training for the past 6 months), and maximal oxygen consumption (VO_2max) less than 40 mL/kg/min. Exclusion criteria included the consecutive absence of more than 2 training sessions or 3 non-consecutive training sessions, regular exercise in the control group, changes in the patient's medication schedule, and any injuries or illnesses that resulted in the subject's inability to continue the study.

Exercise training intervention in the present study consisted of 8 weeks, 3 sessions per week, and each exercise training session included 45-60 minutes of pyramid aerobic training under the supervision of an exercise physiologist. Warm-up training included 5-10 minutes of walking and jogging, then static and dynamic stretching exercises were performed for 5 minutes. At the end of the main exercise training, cooling down was performed, which included walking and stretching exercises.[11] The main exercise training program consisted of aerobic exercises performed by the increasing pyramid system method in 3 training intervals with 3 intensities (Table 1).

The volume of each training interval was started from the light intensity in the first interval based on the intensity of training, the ability of the subjects, and the increase in each interval. The intensity of training was

Table 1. The Aerobic Training Program

Week	Weekly Frequency	Warm-up (min)	Main training		Cooling Down (min)
			Time (min:s)	Intensity (HRR)	
1	3	10-15	7:30-5:00-2:30	35-50-65%	5-10
2	3	10-15	10:00-6:40-3:20	35-50-65%	5-10
3	3	10-15	10:00-6:40-3:20	40-55-70%	5-10
4	3	10-15	12:30-8:20-4:10	40-55-70%	5-10
5	3	10-15	12:30-8:20-4:10	45-60-75%	5-10
6	3	10-15	15:00-10:00-5:00	45-60-75%	5-10
7	3	10-15	15:00-10:00-5:00	50-65-80%	5-10
8	3	10-15	17:30-11:40-5:50	50-65-80%	5-10

Note. HRR: Heart rate reserve; min: Minute; s: Second.

calculated according to the reserve heart rate (HR) of each person and using the following Karvonen formula.[11]

HRmax = 220 – age

Target Heart Rate = [(max HR – resting HR) × %Intensity] + resting HR

In the present study, karela powder was used as an herbal supplement. To make karela powder, fresh karela fruit was first bought and washed. After slicing, it was placed in a dryer and then powdered using a grinder. Karela's consumption in the karela groups and training with karela were 2 servings a day after breakfast and after dinner, 50 mg of karela powder per each kg of body weight.[12]

Blood samples were taken in pre-test and post-test (48 hours after the last intervention session) at 8-9 in the morning after overnight fasting. Glycated hemoglobin (HbA_1c) was measured by a biosystem kit and enzymatic colorimetric method. Blood glucose measurement was obtained using a Pars Azmoon kit made in Iran with sensitivity of 1 mg/dL by enzymatic method, insulin was obtained with a Monobind kit made in the USA with sensitivity of 0.75 µm/mL, and insulin resistance was obtained through the evaluation of homeostasis model and the following formula:

Homeostatic model assessment for insulin resistance (HOMA-IR) = fasting insulin (microU/L) × fasting glucose (nmol/L)/22.5

Subjects' height was measured standing without shoes, and their weights were measured with the least possible clothing and Seka scales. Further, weight (kg)/height^2 (meter) was used to measure body mass index, and the Rockport test was used to measure patients' VO_2max.[1,4]

In this study, Kolmogorov-Smirnov statistical test was used to check the normality of data distribution, and Levene's test was used to check the variance homogeneity. Paired samples t-test and covariance were utilized to test the hypotheses. Moreover, SPSS software version 26 was used for statistical analysis, and the significance level was considered $P < 0.05$.

Results

Table 2 indicates demographic characteristics, including age, weight, and history of disease in subjects by research groups.

The results of the paired samples t-test analysis (Table 3) indicated a significant decrease in FBS, 2-hour

Table 2. Demographic Characteristics

Variables	Exercise	Karela	Combined	Control	*P*
Age (y)	38.70 ± 6.94	41.06 ± 7.34	38.21 ± 5.24	40.45 ± 7.52	0.526
Weight (kg)	75.12 ± 7.92	75.48 ± 6.15	74.31 ± 7.36	74.27 ± 7.70	0.680
Body mass index (kg/m^2)	29.10 ± 1.77	29.63 ± 1.42	28.74 ± 1.93	28.09 ± 1.67	0.074
Disease duration (y)	2.23 ± 1.92	3.02 ± 1.36	3.13 ± 1.61	2.81 ± 2.04	0.327
VO_2max (mL/kg/min)	36.66 ± 1.41	35.85 ± 1.58	37.09 ± 1.86	36.30 ± 1.47	0.439

Note. VO_2max: Maximal oxygen consumption.

Table 3. Comparison of Changes in Measured Variables in Research Groups

Variables	Groups	Pre-test	Post-test	P^a	P^b
FBS (mg/dL)	Exercise	183.03 ± 10.34	168.19 ± 8.17	0.012	0.008
	Karela	187.54 ± 11.51	170.32 ± 10.34	0.031	
	Combined	178.41 ± 8.94	153.32 ± 9.23	0.007	
	Control	172.64 ± 12.43	174.61 ± 12.83	0.154	
2hpp (mg/dL)	Exercise	254.24 ± 18.42	221.36 ± 16.81	0.008	0.004
	Karela	283.67 ± 20.48	267.80 ± 18.25	0.011	
	Combined	265.58 ± 19.36	234.08 ± 17.14	0.001	
	Control	261.59 ± 21.12	268.39 ± 22.16	0.236	
HOMA-IR	Exercise	5.41 ± 1.27	4.36 ± 1.13	0.014	0.015
	Karela	5.78 ± 1.32	5.39 ± 1.34	0.048	
	Combined	5.67 ± 1.42	4.41 ± 1.26	0.009	
	Control	5.52 ± 1.36	5.74 ± 1.34	0.536	
HbA1c%	Exercise	7.63 ± 1.28	6.44 ± 16.81	0.001	0.001
	Karela	7.12 ± 1.46	6.93 ± 1.32	0.040	
	Combined	7.48 ± 1.54	6.23 ± 1.28	0.001	
	Control	7.52 ± 1.31	7.61 ± 1.29	0.532	

Note. FBS: Fasting blood sugar; 2hPP: 2-hr postprandial glucose; HOMA-IR: Homeostatic model assessment for insulin resistance; HbA1c: Glycated hemoglobin.
[a] Significant level of change within the group ($P < 0.05$); [b] Significant level of change between the group ($P < 0.05$).

postprandial glucose (2hPP), HOMA-IR, and HbA_1c in the intervention groups compared to the pre-test stage ($P<0.05$). Covariance test results also showed a significant difference in the FBS, 2hPP, HOMA-IR, and HbA_1c in the research groups ($P<0.05$). Bonferroni post hoc test also revealed that FBS, 2hPP, HOMA-IR, and HbA_1c changes in the intervention groups were significant compared to the control group ($P<0.001$). Moreover, no significant difference was observed in FBS changes in the intervention groups ($P<0.05$); however, changes in 2hPP, HOMA-IR, and HbA_1c were higher in the training and combination groups than those in the karela group ($P<0.001$), but there was no difference between the two groups ($P>0.05$).

Discussion

The present study is the first study to investigate the simultaneous effect of pyramid aerobic training and karela supplementation on glycemic control in patients with type 2 diabetes. The results of the study revealed that 8 weeks of pyramid aerobic training significantly reduced the levels of FBS, 2hPP, HOMA-IR, and HbA_1c.

Previous research has demonstrated the role of aerobic training in glycemic control, [1,4,11] which is consistent with the results of the present study. Physical activity has a beneficial effect on reducing insulin resistance in people with type 2 diabetes, and exercise training reduces insulin resistance.[1,13,14] It is stated that the accumulation of free fatty acids in muscle cells disrupts the transport of GLUT4 to the cell surface. By increasing the oxidation of fatty acids, aerobic activity prevents their accumulation in muscle cells.[13] Among the factors that reduce blood sugar is the increase of capillary density, the increase of the insulin receptors sensitivity, the change in phospholipid composition of the sarcolemma, and the increase in the activity of oxidative enzymes and in glycogen synthase.[11,15,16] Other positive mechanisms regulating glucose metabolism include increasing insulin function and insulin signaling.[13,16] Skeletal muscle fibers consume blood glucose to supply carbohydrates as an energy source during physical activity. The absorption process involves complex molecular signaling processes that differ from the molecular mechanism activated by insulin. Exercise-stimulated glucose uptake is maintained in insulin-resistant muscles, and the emphasis on exercise is a treatment option for patients with metabolic diseases such as type 2 diabetes.[17] Regarding the effect of exercise on glucose uptake, it was found that acute exercise stimulates glucose uptake by upregulating exercise on GLUT4 levels in skeletal muscle membranes. This effect is independent of insulin, and glucose uptake continues for several hours after the end of the exercise. Second, exercise increases insulin sensitivity in skeletal muscle. This effect lasts for several hours after the end of exercise and is insulin-dependent.[1,16,18] Moreover, exercise training increases glucose uptake by up to 50% through simultaneous stimulation of three main stages: delivery, membrane transfer, and intracellular charging through metabolic processes (i.e., glycolysis and oxidation of glucose). The results of the existing research suggest that no signal transmission path alone can be effective. Regulating each of these key steps is due to the redundancy of the signaling pathways used to increase glucose uptake to ensure the maintenance of muscle energy during physical activity.[17] Regarding the chronic effect of exercise on glycemic control, it can be said that exercise improves glycaemia by increasing cell sensitivity via insulin-dependent molecular pathways that enhance insulin signaling (PI3-kinase/ACC and MAPKs), and insulin-independent pathways (AMP-kinase/Akt/mTOR) lead to glycemic control.[18,19] By improving insulin resistance, glucose metabolism improves and causes a reduction in hyperglycemia in response to carbohydrate intake, which was observed in the present study as a decrease in blood glucose 2 hours after consuming 75 grams of carbohydrates. HbA_1c also decreased due to the effectiveness of exercise on reducing insulin resistance and improving euglycemia during the day for 8 weeks, indicating the positive role of pyramid aerobic training on glycemic control in patients with type 2 diabetes.

The results of karela supplementation on glycemic-related variables showed similar results, and a significant decrease was observed in FBS, 2hPP, HOMA-IR, and HbA_1c. In a study on streptozotocin-induced diabetic male Wistar rats, Moqbel et al observed that 5% and 10% doses of the standard karela fruit diet included in the rats' diets for 12 weeks can have effective anti-diabetic effects on diabetic animals.[20] In another study, Salam et al noted that taking 20 mg karela tablets by patients with type 2 diabetes reduces blood sugar after 1 to 8 weeks, and there are no side effects; furthermore, the treatment course should last at least 4 weeks.[9] Akhtar also reported that consuming 50 mg/kg body weight of karela powder in 2 servings per day causes glycemic control in the form of FBS, 1hPP, and 2hPP in diabetic patients.[12] This finding is consistent with the results of the present study.

By comparing the intervention methods on glycemic control, the results suggested that although most changes in FBS reduction are observed in the combined, karela, and exercise groups, no significant difference is observed between the intervention groups. The study on other glycemic indicators such as 2hPP as an indicator of insulin function, HOMA-IR, and HbA_1c indicated that the changes in these glycemic-related variables in the exercise and combination groups are greater than those in the supplement group. Although the results of the present study indicated the effectiveness of karela supplement on glycemic control in diabetic patients, due to the significant differences in the groups that had exercise training, the importance of exercise as a mainstay of treatment on glycemic control in patients with type 2 diabetes can be confirmed.

Although the present research evaluated the clinical variables of glycemic control, it was not possible to

sample and study the molecular mechanisms of insulin signaling due to the invasiveness of the biopsy, which is one of the limitations of the present study.

Conclusion

The results of the present study showed that both pyramid aerobic training intervention and karela supplementation with a dose of 50 mg/kg karela powder per each kg body weight have a positive role in glycemic control in patients with type 2 diabetes. However, it seems that using two methods in combination is more effective in controlling blood sugar. Furthermore, according to the results, it can be said that the effectiveness of aerobic training on glycemic control is more prominent than that of exercise training and karela supplementation. Therefore, it is suggested that these patients devote part of their treatment program to exercise training and also take advantage of karela's complementary benefits in managing their illness.

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Authors' Contribution

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Competing Interests

The authors have no conflict of interests to declare

Ethical Approval

All stages of the research were performed according to the Ethics Committee of Zabol University of Medical Sciences (code: IR.ZBMU.REC.1398.177).

References

1. Tahan P, Ghalavand A, Heydarzadi S, Maleki E, Delaramnasab M. Effects of aerobic interval training on iron stores and glycemic control in men with type 2 diabetes. Razi J Med Sci. 2020;27(8):105-114. [Persian].
2. Lovic D, Piperidou A, Zografou I, Grassos H, Pittaras A, Manolis A. The growing epidemic of diabetes mellitus. Curr Vasc Pharmacol. 2020;18(2):104-109. doi:10.2174/1570161117666190405165911
3. Chiu H, Tsai HJ, Huang JC, et al. Associations between triglyceride-glucose index and micro- and macro-angiopathies in type 2 diabetes mellitus. Nutrients. 2020;12(2):328. doi:10.3390/nu12020328
4. Ghalavand A, Motamedi P, Delaramnasab M, Khodadoust M. The effect of interval training and nettle supplement on glycemic control and blood pressure in men with type 2 diabetes. Int J Basic Sci Med.2(1):33-40. doi:10.15171/ijbsm.2017.08
5. Abel ED, Peroni O, Kim JK, et al. Adipose-selective targeting of the GLUT4 gene impairs insulin action in muscle and liver. Nature. 2001;409(6821):729-733. doi:10.1038/35055575
6. Chadt A, Al-Hasani H. Glucose transporters in adipose tissue, liver, and skeletal muscle in metabolic health and disease. Pflugers Arch. 2020;472(9):1273-1298. doi:10.1007/s00424-020-02417-x
7. Peter EL, Deyno S, Mtewa A, et al. Safety and efficacy of *Momordica charantia* Linnaeus in pre-diabetes and type 2 diabetes mellitus patients: a systematic review and meta-analysis protocol. Syst Rev. 2018;7(1):192. doi:10.1186/s13643-018-0847-x
8. Pahlavani N, Roudi F, Zakerian M, et al. Possible molecular mechanisms of glucose-lowering activities of *Momordica charantia* (karela) in diabetes. J Cell Biochem. 2019;120(7):10921-10929. doi:10.1002/jcb.28483
9. Salam MA, El-Gengaihi SE, Zikry EN. Preliminary clinical trials of karela, *Momordica charantia*, on non-insulin-dependent diabetes mellitus patients. Egypt Pharm J. 2015;14(1):69-74. doi:10.4103/1687-4315.154728
10. Zanuso S, Jimenez A, Pugliese G, Corigliano G, Balducci S. Exercise for the management of type 2 diabetes: a review of the evidence. Acta Diabetol. 2010;47(1):15-22. doi:10.1007/s00592-009-0126-3
11. Ghalavand A, Delaramnasab M, Afshounpour M, Zare A. Effects of continuous aerobic exercise and circuit resistance training on fasting blood glucose control and plasma lipid profile in male patients with type II diabetes mellitus. J Diabetes Nurs. 2016;4(1):8-19. [Persian].
12. Akhtar MS. Trial of *Momordica charantia* Linn (karela) powder in patients with maturity-onset diabetes. J Pak Med Assoc. 1982;32(4):106-107.
13. Flores-Opazo M, McGee SL, Hargreaves M. Exercise and GLUT4. Exerc Sport Sci Rev. 2020;48(3):110-118. doi:10.1249/jes.0000000000000224
14. Flores-Opazo M, Boland E, Garnham A, Murphy RM, McGee SL, Hargreaves M. Exercise and GLUT4 in human subcutaneous adipose tissue. Physiol Rep. 2018;6(22):e13918. doi:10.14814/phy2.13918
15. Amanat S, Ghahri S, Dianatinasab A, Fararouei M, Dianatinasab M. Exercise and type 2 diabetes. Adv Exp Med Biol. 2020;1228:91-105. doi:10.1007/978-981-15-1792-1_6
16. Heiston EM, Eichner NZ, Gilbertson NM, Malin SK. Exercise improves adiposopathy, insulin sensitivity and metabolic syndrome severity independent of intensity. Exp Physiol. 2020;105(4):632-640. doi:10.1113/ep088158
17. Sylow L, Kleinert M, Richter EA, Jensen TE. Exercise-stimulated glucose uptake - regulation and implications for glycaemic control. Nat Rev Endocrinol. 2017;13(3):133-148. doi:10.1038/nrendo.2016.162
18. Jensen J, O'Rahilly S. AMPK is required for exercise to enhance insulin sensitivity in skeletal muscles. Mol Metab. 2017;6(4):315-316. doi:10.1016/j.molmet.2017.01.012
19. Tangseefa P, Martin SK, Fitter S, Baldock PA, Proud CG, Zannettino ACW. Osteocalcin-dependent regulation of glucose metabolism and fertility: skeletal implications for the development of insulin resistance. J Cell Physiol. 2018;233(5):3769-3783. doi:10.1002/jcp.26163
20. Moqbel MS, Al-Hizab FA, Barakat SM. Clinicopathological study on the effects of *Momordica charantia* on streptozotocin-induced diabetic Wistar rats. Open J Vet Med. 2017;7(5):49-62. doi:10.4236/ojvm.2017.75006