THE EFFECT OF WALNUT OIL CONSUMPTION ON BLOOD SUGAR CONTROL IN PATIENTS WITH TYPE TWO DIABETES

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Introduction: Various epidemiological studies have shown the relationship between increased risk of atherosclerosis and cardiovascular diseases (CAD) on the one hand and poor control of blood sugar and lipid profile on the other hand. Furthermore, it has been shown that substitution of saturated fatty acids with polyunsaturated fatty acids (PUFAs) and α linolenic acid (ALA) would improve glucose homeostasis.

Material and methods: One hundred diabetic patients were assigned to the experiment and control groups randomly. For the experiment group, walnut oil (15 g/day for three months) was added to the diet, while the control group did not undergo any interventions. Before initiation of the experiment and after the end of the experiment, the systolic and diastolic blood pressure (SBP and DBP) levels of the patients were measured and recorded. Also, weight and height of the patients were recorded, and a blood sample was taken for measurement of fasting blood sugar (FBS) and HbA1c and using paired t-test and t-test for analysis.

Results: The results demonstrated that HbA1c and FBS levels decreased significantly in the experiment group (p = 0.032 and p = 0.029, respectively). However, the two groups were not significantly different in terms of SBP (p = 0.103), DBP (p = 0.687), body weight (p = 0.202), and BMI (p = 0.416).

Conclusions: Consumption of walnut oil (15 g/day for three months) improved blood glucose homeostasis in type 2 diabetic patients. Because no changes in the bodyweight and blood pressure of the patients were seen, it could be used in hypertensive or obese patients.

Key words: type 2 diabetes, FBS, glycosylated haemoglobin.

Introduction
Prevalence of type 2 diabetes mellitus (DM) is increasing globally and in the USA. The health and economic burden of the disease is very large and will increase in future. It is estimated that in western countries, the prevalence of DM will increase by 40-45%, and the number of patients will grow from 51 million cases in 1995 to 72 million in 2025 [1].

Diabetes is one of the major causes of blindness and kidney transplantation. The disease increases the risk of cardiovascular diseases (CAD), especially in women (by 2-5 fold) [2, 3]. Researchers believe that the disease prevalence has rapid growth in India, China, Central and South America, Africa, and the Middle East [4].

Hyperglycaemia caused by impaired insulin secretion or insulin resistance or both are known as the characteristics of type 2 DM [5].

A higher share of fats and proteins of plant origin in the diet is associated with reduced risk of CAD and DM [6]. Studies have demonstrated that increased intake of mono- and polyunsaturated fatty acids (MUFAs and PUFAs) and lower intake of saturated and trans-fatty acids are associated with lower risk of type 2 DM [7]. Furthermore, replacement of carbohydrates with MUFAs and PUFAs in the daily diet is known as a therapeutic strategy in DM [8]. In this regard, MUFA intake in the daily diet of diabetic patients restores HDL levels and improves blood sugar control [9].

Among foods that contain a desirable fatty acid composition, nuts have received attention because of the epidemiological relationship found between their regular intake and a protective role against CAD [10, 11]. Accordingly, in prospective studies, reduced risk for CAD development and the mortality caused by CAD has been reported with increased consumption of the nuts [12, 13]. The risk of progression of type 2 DM is reduced by consuming nuts such as walnuts. In this regard, because of the lower mortality caused by CAD and cancers in the Mediterranean population, the Mediterranean diet is considered favourable [14]. A diet rich in walnuts has a positive effect on the endothelial function and endothelium-dependent vasodilation in type 2 DM. This consequently reduces the overall risk of CAD [15].
According to the reports of the US Department of Agriculture (USDA), 100 g of walnut contains 15.2 g of protein, 65 g of fat, and 6.7 g of fibre. Moreover, it contains higher amounts of PUFAs (47%) when compared with other nuts, of which 38% is n6 PUFAs (linoleic acid) and 9% is n3 PUFAs (α-linolenic acid – ALA) [16].

Considering the high prevalence of diabetes and the complications caused by the disease, diet modification by adding oils such as walnut oil containing PUFAs and ALA would improve glucose homeostasis and prevent cardiovascular complications of diabetes.

Considering the potential role of PUFAs in the prevention of DM and lipid profile improvement, some studies have been carried out on walnut. However, there are no studies on the control of blood sugar in DM patients using a diet containing walnut. Thus, the current study was carried out to evaluate the effect of walnut oil on blood sugar control in type 2 DM patients.

**Material and methods**

This controlled clinical trial (without placebo medication) was performed on type 2 DM patients referred to the Shiraz Healthy Heart Home, affiliated with the Shiraz Cardiovascular Research Centre. The project was approved by the Ethics Committee of Shiraz University of Medical Sciences in advance by the number CT.P.92.5670. The study was registered in the Iranian Registry of Clinical Trials (IRCT) with the code IRCT2014022216682N1.

The sample size for the experiment group was determined to be 45 patients with regard to 5% level of significance, power level of 95%, and the results obtained from similar studies. Moreover, 45 patients were considered as the control group. The research methodology was firstly explained to the participants, and then all the participants signed a written consent form. Moreover, they were assured of the confidentiality of their data and their right to withdraw from the study if they were not willing to continue. The study was carried out on 100 male and female type 2 DM patients, who were regularly monitored in the Shiraz Healthy Heart Home for at least two years. The inclusion criteria were having type 2 DM according to the definition of the American Diabetes Association (ADA), taking a maximum of two oral hypoglycaemic agents, having diabetes diagnosis for at least two years, being in the age range of 20-80 years, and lacking other chronic metabolic diseases. These patients had received nutritional education about a low-fat diabetic diet and were familiar with appropriate administration of hypoglycaemic medications. The participants did not have chronic metabolic disorders, including liver, kidney, and thyroid diseases. All the patients received oral hypoglycaemic agents and did not have a history of receiving insulin. They took a maximum of two oral hypoglycaemic agents, and during the previous three months their medications had been kept unchanged and they had eaten a low-fat diet. The patients were randomly assigned to the experiment and control groups. Before initiation of the experiment, the systolic and diastolic blood pressure (SBP and DBP) levels of the patients were measured by a standard sphygmomanometer (ALPK2, Japan) and recorded. Blood pressure was measured when the patient had at least 10 min rest and did not drink coffee or tea, had or smoked in the past 30 minutes. Also, the weight and height of the patients were measured by a digital measure (Sahand, Iran). A blood sample was taken for measurement of fasting blood sugar (FBS) and HbA1c, and the values were determined using enzymatic assay kits (Pars Azmoon, Iran). The control group did not receive any intervention. The experiment group received walnut oil (15 g/day for three months). Before initiation of the experiment, the walnut oil used (prepared according to the cold-press method) was analysed in the Faculty of Pharmacy, Shiraz University of Medical Sciences.

According to the results obtained, the oil contained 72.5% PUFAs (64% linoleic acid, 8.5% ALA), 13.1% MUFA (oleic acid), 13.1% palmitic acid, and 1.3% stearic acid. All the participants were examined by a physician and a nutritionist at the beginning of the study and then on a monthly basis. Moreover, the patients had weekly follow-up telephone calls. Nutritional recommendations, evaluation of adherence to the food and medication regimen, and check for maintaining unchanged diet, medications, and physical activity were done for all the patients. At the end of a three-month period, blood sampling was performed to measure the FBS and HbA1c levels. Moreover, weight, SBP, and DBP were measured and recorded. The patients in the control group did not undergo any intervention. The data obtained were analysed using SPSS version 16. Normal distribution of the data was measured using the Kolmogorov-Smirnov test. Comparison of pre- and post-test means of the variables was carried out using paired t-test, and the mean comparison between the groups was performed by the t-test; p values < 0.05 were considered statistically significant.

**Results**

In the study, 100 diabetic patients were evaluated – 50 in the experiment group and 50 in the control group. Among the participants in the experiment group, two patients had GI intolerance of the oil and three of them did not cooperate in following the diet and medication regimen, so they were excluded from the study (24 women and 21 men).

In the control group, one was excluded because of lack of cooperation in the diet control and four were
The patients were re-evaluated for the variables evaluated at the beginning of the study. According to the analysis, the two groups were not significantly different with regard to the weight, BMI, SBP, and DBP. A statistically significant decrease was observed in the FBS level of the experiment group. Such finding was not observed for the control group, and the FBS level remained relatively unchanged. Comparing the two groups after the experiment indicated that the FBS level decreased significantly in the experiment group ($p < 0.05$).

This was true for the HbA1c level, so that a statistically significant decrease was observed in the experiment group, while the value did not change significantly in the control group. Comparison of the two groups after the intervention indicated that the HbA1c level significantly decreased in the experiment group ($p < 0.05$).

The values related to the variables before and after the experiment were compared using the $t$-test. The results are shown in Table 2.

Considering the data provided in Table 2 and Table 3, and comparison of the values obtained for each parameter before and after the experiment in each group, it can be observed that none of the variables changed significantly in the control group.

However, this is not the case with the experiment group; weight, BMI, SBP, and DBP did not change significantly when compared with the values obtained before the experiment, while FBS ($p < 0.05$) and HbA1c ($p < 0.05$) decreased significantly after the intervention.

### Table 1. Comparison of distribution of the variables studied for the experiment and control groups before the experiment

<table>
<thead>
<tr>
<th>Variable</th>
<th>Experiment group</th>
<th>Control group</th>
<th>$p$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>55.5 ±10.75</td>
<td>54 ±11.37</td>
<td>0.507</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>75.9 ±8.56</td>
<td>73.81 ±8.15</td>
<td>0.212</td>
</tr>
<tr>
<td>BMI (m²/kg)</td>
<td>27.60 ±2.47</td>
<td>27.21 ±2.27</td>
<td>0.453</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>137.75 ±14.5</td>
<td>132.57 ±17.01</td>
<td>0.124</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>81.62 ±7.65</td>
<td>81.13 ±7.01</td>
<td>0.753</td>
</tr>
<tr>
<td>FBS (mg/dl)</td>
<td>158.37 ±48.1</td>
<td>153.88 ±54.76</td>
<td>0.681</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>7.003 ±1.08</td>
<td>6.97 ±1.208</td>
<td>0.894</td>
</tr>
</tbody>
</table>

BMI – body mass index, SBP – systolic blood pressure, DBP – diastolic blood pressure, FBS – fasting blood sugar; ± indicates standard deviation

### Table 2. Comparison of the mean values of the variables before and after the experiment for the experiment group using $t$-test

<table>
<thead>
<tr>
<th>Variables</th>
<th>Before intervention</th>
<th>After intervention</th>
<th>$p$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (kg)</td>
<td>75.90 ±8.56</td>
<td>75.75 ±8.25</td>
<td>0.225</td>
</tr>
<tr>
<td>BMI (m²/kg)</td>
<td>27.60 ±2.47</td>
<td>27.55 ±2.34</td>
<td>0.233</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>137.75 ±14.5</td>
<td>137.51 ±12.27</td>
<td>0.688</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>81.62 ±7.65</td>
<td>81.42 ±7.21</td>
<td>0.692</td>
</tr>
<tr>
<td>FBS (mg/dl)</td>
<td>158.37 ±48.1</td>
<td>137.91 ±23.24</td>
<td>0.005</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>7.00 ±1.08</td>
<td>6.37 ±1.29</td>
<td>0.001</td>
</tr>
</tbody>
</table>

BMI – body mass index, SBP – systolic blood pressure, DBP – diastolic blood pressure, FBS – fasting blood sugar; ± indicates standard deviation

### Table 3. Comparison of the mean values of the variables before and after the experiment for the control group using $t$-test

<table>
<thead>
<tr>
<th>Variables</th>
<th>Before intervention</th>
<th>After intervention</th>
<th>$p$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (kg)</td>
<td>73.81 ±7.15</td>
<td>73.65 ±7.22</td>
<td>0.504</td>
</tr>
<tr>
<td>BMI (m²/kg)</td>
<td>27.21 ±2.27</td>
<td>27.15 ±2.30</td>
<td>0.500</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>132.57 ±17.01</td>
<td>132.42 ±16.70</td>
<td>0.707</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>81.73 ±7.01</td>
<td>80.84 ±6.83</td>
<td>0.605</td>
</tr>
<tr>
<td>FBS (mg/dl)</td>
<td>153.88 ±54.76</td>
<td>153.93 ±42.06</td>
<td>0.995</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>6.97 ±1.21</td>
<td>6.98 ±1.33</td>
<td>0.941</td>
</tr>
</tbody>
</table>

BMI – body mass index, SBP – systolic blood pressure, DBP – diastolic blood pressure, FBS – fasting blood sugar; ± indicates standard deviation

### Discussion

The prevalence of DM is increasing around the world, and the health and economic burden caused by the disease is very large and is set to increase in the future [1]. Several epidemiological studies have confirmed the relationship between increased risk of atherosclerosis and CAD on the one hand and poor control of blood sugar and lipid profile, on the other hand. The studies performed on the role of diet in blood sugar control in DM patients emphasise the replacement of conventional oils with the oils containing PUFAs.

In the current study, the effect of consumption of walnut oil (which contains high levels of PUFAs [72.5%] and ALA [8.5%]) on blood sugar control in type 2 DM patients was investigated. According to the results obtained, consumption of walnut oil for three months (15 g daily) could significantly reduce the FBS and HbA1c levels. However, no obvious changes were observed in the weight, BMI, and blood pressure levels. This is in agreement with the results of some previous studies.

In human and animal physiological studies, it has been demonstrated that the oils containing PUFAs could exert their antidiabetic effect by reducing the resistance and enhancement of sensitivity to insulin via the mechanism of overexpression of glucose trans-
porter GLUT4 and insulin receptors on the adipocyte membrane while also reducing the inflammatory effect on the adipose tissue by decreasing the inflammatory markers in this tissue [17].

In the study performed by Moloney et al. in 2007, on mice receiving a cis 9, trans 11-conjugated linoleic acid (CLA)-enriched diet for six weeks, it was demonstrated that this CLA isomer can reduce insulin resistance and decrease FBS and serum insulin levels by increasing the adipose tissue plasma membrane GLUT4. Moreover, this type of CLA can reduce inflammation in the adipose tissue via a 50% decrease in the TNF- level. Therefore, it was suggested that this CLA isomer attenuates insulin resistance by having anti-inflammatory effects in the adipose tissue [17].

Previous studies have shown that diabetes is potentially associated with increased oxidative stress [18]. Furthermore, oxidative stress could be associated with activation of stress-sensitive signalling pathways or insulin resistance [19]. Thus, based on the idea that oxidative stress can act as an activator in the initiation and progression of DM, antioxidants have been suggested as a part of DM treatment [20].

Moreover, it has been shown that the high level of antioxidants in nuts could be a protective mechanism against oxidative injury [21]. It has been reported that walnut has a higher antioxidant capacity when compared with other nuts [22]. These antioxidants are possibly of the phenolic compounds [23] including hydrolysed tannins, tocopherol [24], and melatonin, all of which have a high antioxidant capacity [25].

In the study by Ansar et al. performed in Shiraz in 2011, the effect of daily consumption of α-lipoic acid, as an antioxidant, for two months was compared with a placebo in type 2 DM patients. It was observed that in the group receiving α-lipoic acid, the FBS and insulin resistance homeostasis model assessment (IR-HOMA) decreased significantly but body weight remained unchanged. In this regard, it was concluded that α-lipoic acid could be employed as an antioxidant in the treatment and improvement of glucose homeostasis in diabetic patients [26].

In the current study, the FBS level significantly decreased in the group receiving walnut oil (p < 0.05), while no significant change was observed in weight, SBP, and DBP. Lack of change in blood pressure was also reported by Jenkins et al. [9].

In the study conducted by Rahimi et al. it was reported that diabetic rats receiving walnut oil had a statistically significant decrease in the HbA1c level, similar to receiving glibenclamide. Thus, it was suggested that walnut oil can have an anti-diabetic effect [27].

In a study performed by Tapsell et al., the effects of walnut oil on PUFA's were evaluated on the metabolic parameters of the DM patients. They reported that dietary fat change in DM patients (increase in the PUFA/saturated fatty acid ratio) could effectively decrease the FBS, HbA1c, and serum insulin levels during the six months of intervention [28].

In general, the results obtained indicate that a change in the dietary oil composition consumed by type 2 DM patients, and shifting from oils containing saturated fatty acids to oils containing PUFAs and ALA, such walnut oil (15 g/day for three months) led to statistically significant decreases in the FBS and HbA1c levels. This eventually improved blood glucose homeostasis without changing the weight or blood pressure.

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References