

Effect of *Rhus Coriaria L* on Glycemic Control and Insulin Resistance in Patients with Type 2 Diabetes Mellitus

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Abstract

Objective: There are association between oxidative stress and incidence of some chronic diseases, such as type 2 diabetes mellitus (T2DM). Food containing antioxidant compounds, such as some spices, are the natural ways to deal with oxidative stress. The purpose of this study was to determine the effect of sumac powder (*Rhus coriaria L*) on the glycemic profile in patients with T2DM.

Materials and Methods: In this experimental study, 60 T2DM patients were selected and randomly divided into two groups: intervention and control groups. The intervention group received 2 packs of 3 grams sumac powder once a day for 3 months in two bowls of low-fat yoghurt for lunch and dinner and the control group received two bowls of low-fat sumac-free yoghurt for lunch and dinner. Data collection was performed by a checklist at the beginning and end of the study and blood samples were collected. Data were analyzed using paired T-test and independent t-test. The significance level was considered at $P < 0.05$.

Results: In this study, the fasting serum insulin levels decreased in the intervention group. But the mean changes of variables were not statistically significant between two groups. There was also no difference in other factors between the beginning and end of the study.

Discussion: This study showed that daily intake of 6 grams sumac powder for three months had no significant effect on the glycemic profile (fasting blood sugar and 2-hours post-prandial glucose and glycosylated hemoglobin A1C) and serum insulin levels of diabetic patients.

Keywords: Sumac (*Rhus coriaria L*), Diabetes, Antioxidants, Herbal treatment

Introduction

Type 2 diabetes mellitus (T2DM) is a chronic progressive metabolic disease characterized by increase in blood glucose. DM is presented as the epidemic of the 21st century. DM is still not fully understood (1,2) and is a serious hazard for the

society(3). Characteristics of diabetes include hyperglycemia, insulin resistance, reduced number and secretion of beta cells, increased production of hepatic glucose, abnormal metabolism in adipocytes and lipids, increased appetite, obesity, systemic inflammation,

increased cytokines, disruption of endothelial cells' activities, and etc. (2).

Rapid globalization with change in life style and nutrition are the main concerns about this disease (3). In 2010, 285 million adults aged 20-79 years were affected and it is anticipated that this number will reach more than 400 million people by 2030. Between 2010 and 2030, 69% increase occurs in the number of adults with T2DM in developing countries and 20% in developed countries (4). According to the World Health Organization (WHO) reports in 2000, there were 2.2million patients with T2DM in Iran and is predicted to reach 5.6 million by 2030 (5).

Diabetes complications are numerous, involving almost all parts of the body. These complications are divided into two groups of microvascular (damage to small blood vessels) and macrovascular (damage to large blood vessel) complications. Microvascular complications include retinopathy, nephropathy, neuropathy, and diabetic foot. The macrovascular complications include cardiovascular disease, such as angina pectoris, heart attacks, strokes, congestive heart failure and peripheral artery disease. (6-8)

Varieties of herbs are used for the control and treatment of diabetes and its complications, like sumac. Sumac, with the scientific name of *Rhus coriaria* L, is related to the pistachio group with small shrubs of 1-5 meters high. The blooms are gathered like clusters at the end of main stem and convert to small and round berries. Berries are of the shaft type, the ripe berries are reddish-brown when the unripe berries are green and poisonous. In Iranian traditional medicine, sumac was used for treatment of many diseases such as diarrhea, trachoma and ear infections (9).

Sumac contains significant amounts of antioxidants such as tannins and organic acids (malic citric and tartaric acids). The taste of sumac is mainly because of the two different components; tannin and organic acids. Using sumac as a spice and natural remedy triggered

studies to assess the nutritional value of this spices.

Antioxidants, such as phenolic compounds in sumac have a protecting role against free radicals and sumac shows anti-inflammatory effects because of these antioxidants. Some studies suggest the inhibitory effects of alpha-amylase enzyme in sumac (10). Alpha-amylase enzyme is responsible for breaking down starch into simpler sugars and inhibition of this enzyme increases diabetic patients' tolerance to glucose.

Research considering the effect of sumac on glycemic and lipid profile is all conducted on animals and have proven desirable effects (11-14). As the studies on human are rare, we assessed the effect of sumac on glycemic profile in patients with T2DM.

Materials and Methods

This clinical trial was performed on 60 patients with T2DM referring to Ardakan diabetes center (Mehr clinic). Inclusion criteria were; age between 30-60 years with at least 3 years diabetes duartion, no liver, biliary or renal disease, not a professional athlete, no use of antioxidant supplements, selenium, zinc, beta-carotene, omega-3 and alcohol at least 3 months prior to the study, no insulin treatment and gave consent to participate in this study.

Exclusion criteria included: consuming less than 80% of sumac sachets, change in the type and dose of medication, unwillingness to continue the study, use of any supplemental antioxidant or insulin therapy, becoming pregnant during the study.

The participants were randomly divided into two groups using random computer codes. According to the previous studies, the supplemental dose varied from 1 to 3 gram in a day. Thus, the dose of 6 g was considered in this study. The intervention group received 2 sachets of 3 g sumac powder twice a day in 100 g of low-fat yoghurt before lunch and dinner and the control group received 100 g of low-fat sumac-free yoghurt for lunch and dinner. The duration of study was considered 3 months, during which 180 sachets were

needed for each participant. Half of the sachets were delivered in the first session. The correct consumption was controlled by telephone calls during this period. After the end of the first half of the study, participants were invited to get the share of the second half of the sumac powder. The number of packets not taken in the first half were counted and those who did not act in accordance with the protocol were excluded. The second half of the share was given to each person and participants were invited again at the end of the study and the number of unused packages was counted. Participants were asked not to change their diet, physical activity and life style during the study.

The general information questionnaire was completed at the beginning of the interview. The anthropometric assessment of weight was performed using a digital scale, Seca (Germany) with accuracy of 100 g with minimal clothing and without shoes. Height was measured with a stadiometer with accuracy of 0.5 cm while 4 parts of the body were attached to the wall and without shoes. The questionnaire of 24 hours dietary recall (two week-day and one weekend) was completed to estimate the intake of energy, macro- and micro-nutrients, as well as International Physical Activity (IPAQ) questionnaire for the assessment of physical activity at the beginning and end of the study. Biochemical tests included fasting glucose and insulin, glycosylated hemoglobin (HbA1C), and 2-hours post prandial glucose. The required blood sample was 10 ml, collected after 10 to 12 hours of fasting. Fasting insulin was measured by ELISA method using monobind kit and other measurements were performed by enzymatic method and classic alpha auto-analyzer device (Iran).

The procedure was performed by one laboratory to eliminate any measurement error. Insulin resistance (HOMA-IR) was calculated using the following equation (16):

$$\text{Insulin resistance} = \{ \text{fasting blood sugar (mmol/lit)} \times \text{fasting serum insulin (u/ml}\mu\} / 22.5$$

The following equation was also used to calculate the beta-cell function (17):

$$\text{Beta-cell function} = (\text{fasting insulin} \times 20) / (\text{fasting glucose} - 3.5)$$

All analyses were performed using SPSS statistical software (version 16, SPSS). Normality of variables was assessed by Kolmogorov–Smirnov test. For the variables with non-normal distribution, logarithmic conversion was used. The differences were assessed by the Student's T-test. Differences between groups were compared with independent samples T-test. Differences within groups (before and after intervention) were compared with paired samples T-test. We also calculated the mean of differences (before and after intervention) in serum glycemic profile. The data are presented as mean \pm standard deviation (SD). Differences were compared for statistical significance at the level $P < 0.05$.

Participation in the project was fully voluntarily and written consent was obtained from participants after full explanation by the researcher. The study was approved by Ethics Committee of the Shahid Sadoughi University of Medical Sciences and the IRCT code was IRCT2014050410826N9.

Results

The current study was performed with the full participation of 58 patients with T2DM. The mean and SD of height, age, weight and BMI of participants in both groups are shown in Table 1. Statistical analysis showed that anthropometric measurements of individuals were not statistically significant different.

Table 2 demonstrates the average intake of energy, carbohydrates, fat, protein, vitamins C, and E before and after the intervention in two groups of receiving sumac and the control one. Paired T-test showed that the intake of energy and nutrients did not differ before and after the intervention in both groups. No significant differences were also observed between the two groups in terms of these variables.

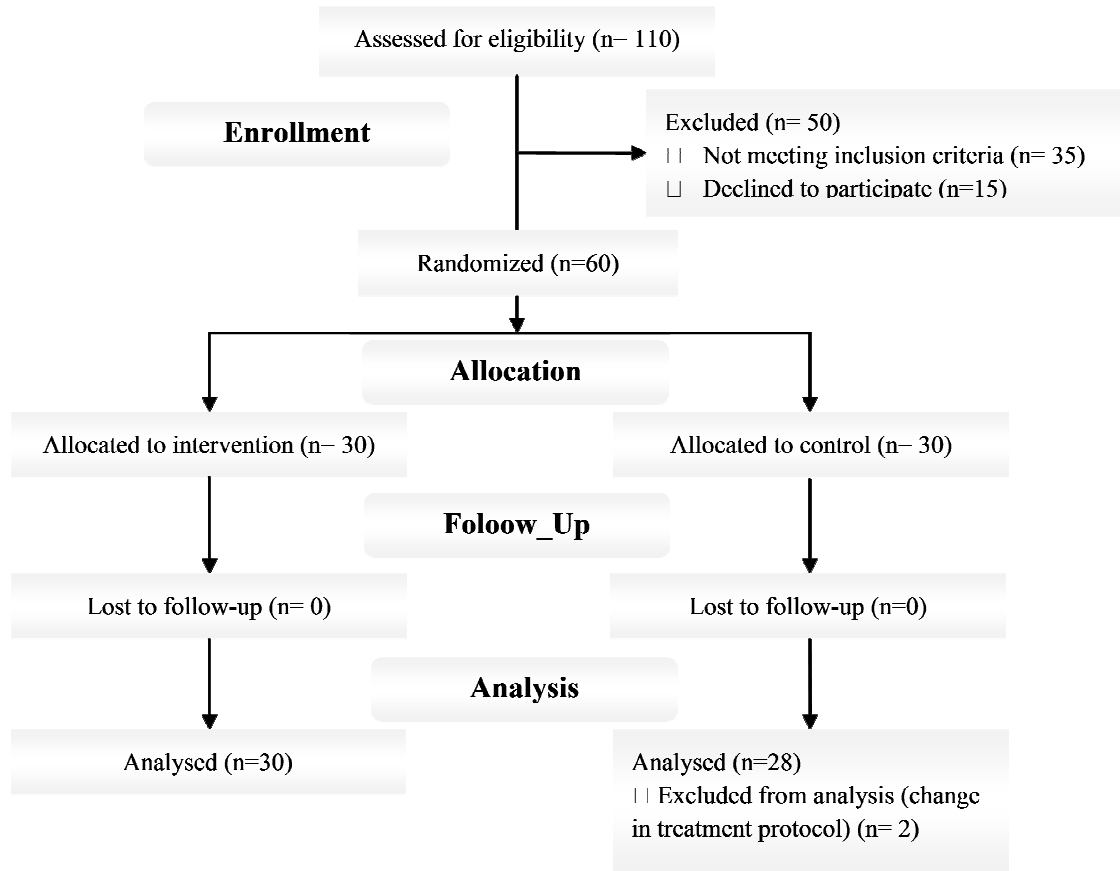


Figure 1. CONSORT flow diagram of the study

Table 3 illustrates no significant difference in the state of physical activity at the beginning and end of the study.

As it can be seen in Table 4, fasting serum insulin has reduced at the end of the study compared to before the intervention. But the mean change of variables showed no significant difference in studied groups. Also, insulin resistance reduced in the group receiving sumac ($P=0.007$). There were no difference between the beginning and end of the study regarding other factors.

Discussion

The results of this study indicated that consuming 6 grams sumac powder in diabetic patients had no effect on glycemic profile and only the serum fasting insulin and insulin resistance were reduced in intervention group,

which did not have a significant difference in mean of changes between the two groups.

Salimi et al. studied the effect of aqueous extract of sumac in alloxan-induced diabetic rats and showed significant reduction in blood glucose (18). Giancarlo and colleagues demonstrated that the alcoholic extract of sumac reduces blood glucose by inhibiting alpha-amylase enzyme due to the presence of flavonoids in sumac (10). Regarding the hypoglycemic activity of quercetin, the hypoglycemic effect of sumac extract can be related to its flavonoid component (quercetin) (19).

In another study, Shaikh and her colleagues evaluated the effect of food additives (sumac, black pepper, and cinnamon with concentrations of 0.1, 0.2, and 1.0 milligrams per deciliter) on the glycation reaction of albumin protein in-vitro and prevention of

Table 1. The mean and SD of height, age, weight and BMI of diabetic patients in intervention and control groups at baseline

Variable	Intervention (n = 30)	Control (n = 28)	P-value*
Height (cm)	165.10±8.58	161.54±9.35	0.8
Age (years)	52.30±7.05	51.61±7.07	0.9
Weight (kg)	78.90±12.19	74.43±9.93	0.7
BMI (kg/m ²)	29.10±5.30	28.65±4.15	0.9

*Independent sample T- test

Table 2. The mean and SD of energy, macronutrients, vitamins C and E in the intervention and control groups before and after the intervention

Variable	Study groups	Before	After	P-value*
Energy (Kcal)	Intervention(n=30)	2373.83±923.51	2528.30±632.08	0.3
	Control(n=28)	2277.14±831.20	2752.21±1.41	
P-value**		0.6	0.4	0.06
Carbohydrate (g)	Intervention (n=30)	406.91±197.32	390.33±108.72	0.6
	Control (n=28)	393.39±156.92	374.28±126.08	
P-value**		0.7	0.6	0.2
Fat (g)	Intervention (n=30)	54.31±30.50	52.64±18.98	0.7
	Control (n=28)	45.95±18.39	50.36±22.54	
P-value**		0.2	0.6	0.3
Protein (g)	Intervention (n=30)	82.56±34.26	79.11±23.52	0.3
	Control (n=28)	83.90±33.42	86.73±30.29	
P-value**		0.8	0.2	0.5
Vitamin C(mg)	Intervention (n=30)	96.06±72.85	92.61±54.49	0.5
	Control (n=28)	83.47±56.27	75.69±47.46	
P-value**		0.4	0.2	0.2
Vitamin E(mg)†	Intervention (n=30)	10.17±6.51	11.02±5.85	0.2
	Control (n=28)	8.42±4.71	9.50±3.80	
P-value**		0.1	0.3	0.3

P-value * for comparison within group (paired sample T-test)

P-value** for comparison between groups (student T-test)

diabetes complications and concluded that these food additives can significantly reduce glycation reaction of albumin protein at all amounts ($P<0.05$). Among these additives, sumac was more effective than cinnamon and pepper. Sumac in the concentration of 1 mg/dl (80.8%), pepper (79.7%), and cinnamon (78%) inhibited the glycation of albumin (20).

Mohammadi and colleagues conducted a study on rats to identify the anti-diabetic functions of alcohol extract of sumac and observed significant reduction in postprandial glucose in intervention group compared to control (13).

One of the reasons that we have perceived no effect of sumac in this study can be contributed to the fact that the sumac berries were used instead of its extract. Perhaps if the sumac extract was used, like other studies, significant effects could be seen due to the higher concentration of the active ingredient. However, sumac was used in this form so that dietary recommendations could have been prescribed in case of positive results. On the

other hand, the mean duration of diabetes was 7.8 years in our study. So, it might have been effective on new cases of diabetic patients. Moreover, the different species of sumac may also have different effects. As Iranians use sumac habitually, higher amounts may be needed to see the treatment effects from this herb.

It should be noted that few studies have considered the anti-diabetic effects of sumac and most of them were on animal models. It may not be quite valid to extend the animals' results to humans due to physiologic, biologic, psychological, genetic, anatomic and ecological differences between humans and other animals. Another argument is the duration of diabetes. The intervention is prescribed shortly after acquiring the disease in animals, although the disease duration of humans is usually a few years.

Our study had some limitations. First, we were unable to use placebo, as 6 g sumac could not be included in capsules and thus, we used low-

Table 3. The state of physical activity of those receiving sumac and the control group before and after the study

Study groups	Physical activity	Before Frequency (%)	After Frequency (%)	P-value*
Intervention (n=30)	Light (%)	13 (43.3)	12 (40)	0.8
	Moderate (%)	17 (56.7)	18 (60)	
Control(n=28)	Light (%)	13 (46.4)	12 (42.8)	0.8
	Moderate (%)	15 (53.6)	16 (57.2)	

* Chi-square

Table 4. The mean and SD of Profile sugar in the sumac and control groups before and after the intervention

Variable	Study groups	Before	After	P-value*
FBS(mg/dl)†	Intervention (n=30)	177.70±58.31	172.20±71.17	0.4
	Control (n=28)	183.89±57.69	188.29±49.45	0.3
P-value**		0.6	0.1	
2hpp (mg/dl)	Intervention (n=30)	322.73±110.98	307.80±99.77	0.3
	Control (n=28)	310.86±108.78	316.79±110.08	0.6
P-value**		0.6	0.7	
Glycosylated hemoglobin A1c (%)	Intervention (n=30)	8.38±1.71	8.13±1.59	0.1
	Control (n=28)	8.27±1.87	8.36±1.91	0.6
P-value**		0.8	0.6	
Fasting serum insulin levels (µIU/ml) †	Intervention (n=30)	3.10±1.37	2.28±0.65	0.005
	Control (n=28)	3.39±2.10	2.69±1.74	0.07
P-value**		0.8	0.4	
Insulin resistance †	Intervention (n=30)	1.35±0.74	0.95±0.41	0.007
	Control (n=28)	1.42±0.85	1.25±0.94	0.1
P-value**		0.6	0.1	
Beta-cell function (%)†	Intervention (n=30)	13.14±8.94	11.82±13.63	0.2
	Control (n=28)	15.80±17.45	9.25±7.21	0.06
P-value**		0.8	0.3	

† Due to the lack of normal, the logarithm of the variable is used.

P-value * for comparison within groups (paired sample T-test)

P-value ** for comparison between groups (student T-test)

P<0.05

fat yoghurt in both groups and those receiving sumac free low fat yoghurt were considered as the control group. Second, the mean of affected time for diabetes in the participants was high and it may decrease the effect of natural remedies on the complex disease. Further studies should be focused on prediabetes to show more profound effects.

Conclusions

This study showed that daily intake of sumac powder can affect fasting serum insulin levels, but have no significant impact on blood sugar,

2-hours postparandial glucose, and glycosylated hemoglobin (Hb A1C).

We suggest that further studies be conducted on the use of sumac in different age groups to obtain more information

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