Caspian Journal of Internal Medicine 2025 (Summer); 16(3): 417-423
DOI: 10.22088/cjim.16.3.417

Original Article

Effectiveness of sumac seed *(Rhus coriaria L.)* capsules prepared from an aqueous extract in diabetic patients: A double-blind clinical trial study

Hossein Asgarirad (PhD) [1]
Soleiman Mahjoub (PhD) [2,3]
Mohsen Yadollahi (PhD) [4*]
Siamak Navaee (PhD) [5]
Shervin Amirkhanloo (PhD) [6]
AliSina Shohreh (PhD) [7]

1. Department of Pharmaceutics, Faculty of Pharmacy, Mazandaran University of Medical Sciences, Sari, Iran
2. Cellular and Molecular Biology Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran
3. Department of Clinical Biochemistry, School of Medicine, Babol University of Medical Sciences, Babol, Iran
4. Department of Food Hygiene and Quality Control, Faculty of Health, Mazandaran University of Medical Sciences, Sari, Iran
5. Graduated from General Medicine, Kerman University of Medical Sciences, Kerman, Iran
6. Ph.D Student in Pharmaceutics, Student Research Committee, Faculty of Pharmacy, Mazandaran University of Medical Sciences, Sari, Iran
7. Graduated in Pathology, Shahid Beheshti University of Medical Sciences, Tehran, Iran

*** Correspondence:**
Mohsen Yadollahi, Department of Food Hygiene and Quality Control, Faculty of Health, Mazandaran University of Medical Sciences, Sari, Iran

E-mail:
mohsen.21501@yahoo.com
Tel: 09374232238

Received: 8 Jan 2024
Revised: 28 April 2024
Accepted: 12 May 2024
Published: 15 May 2025

Abstract

Background: Type 2 diabetes or non-insulin-dependent diabetes is one of the most common types of diabetes. The existing treatments for type 2 diabetes have not been able to completely cure this disease in affected cases. Sumac showed antioxidants, reducing blood sugar and serum cholesterol levels. In this study, according to the positive effects of sumac in diabetic diseases, it was tried that sumac capsules were prepared from the aqueous extract of this plant, and its effect on the factors of diabetes in patients was evaluated.

Methods: This double-blind randomized controlled clinical trial was conducted on sixty type 2diabetic volunteers. The volunteers were divided into two groups, control, and sumac supplement groups. Baseline venous blood samples were collected after overnight fasting before intervention and a second sampling was done in the 12th week. Hb1AC, FBS, TG, TC, LDL-C, and HDL-C were measured via commercial kits.

Results: FBS, HDL-C, and HbA1C measured in the sumac supplement group were significantly different ($p<0.01$) compared to the control group and baseline of the study. Moreover, there is no significant difference in levels of the sumac supplement group (CHOL, LDL-C, and TG) compared to the control group and baseline of the study ($p>0.05$).

Conclusion: Our data confirmed the anti-diabetic effect of sumac in patients. Because of sumac safety, it seems that sumac capsules can be used for the treatment of diabetic patients along with routine chemical drugs.

Keywords: Sumac, Rhus Coriaria L., Diabetes, Clinical trial.

Citation:
Asgarirad H, Mahjoub S, Yadollahi M, et al. Effectiveness of sumac seed (*Rhus coriaria L.*) capsules prepared from an aqueous extract in diabetic patients: A double-blind clinical trial study. Caspian J Intern Med 2025; 16(3): 417-423.

Type 2 diabetes or non-insulin-dependent diabetes is one of the most common types of diabetes which constitutes a large part of diabetic patients (1). Unlike type 1 diabetes, in this type, the body produces insulin while suffering from type 2 diabetes; But either the amount of insulin produced by the pancreas is not enough or the body cannot use the produced insulin which leads to the non-use of glucose by the body and the entry of glucose into the cells has a problem (2). It causes the accumulation of glucose in the body which causes a significant problem in vital organs accounts for 90% of all cases (3). According to the studies, nearly 50% of children and adults have type 2 diabetes, statistics show that in 1997, there were about 125 million people with diabetes, and the World Health Organization (WHO) estimates show that this number should increase to 300 million in 2025 (4). The existing treatments for type 2 diabetes have not been able to completely cure this disease in affected cases. On the other hand, the side effects of these treatments are important for the affected person. Therefore, efforts are being made to find therapeutic agents that increase the effectiveness of the treatment and have fewer side effects (5).

Sumac (*Rhus coriaria L.*) belongs to the *Anacardiaceae* family, which is a short shrub that is considered in Iranian traditional medicine to prevent heart diseases (6). The tannins in sumac are soluble in water, which shows antioxidant effects that are effective in preventing cancer. Sumac fruit contains phenolic compounds, including phenolic acids, flavonols, and anthocyanins, which act as antioxidants, and reduce blood sugar and serum cholesterol levels (7). In the study conducted by Shidfar et al. on the effect of sumac powder on blood sugar status, apolipoprotein B and apolipoprotein A-I in type 2 diabetic patients, it was found that sumac powder has a reducing effect on blood sugar status, apoenzyme A and B levels in patients (8). In addition, various studies reported the positive effects of the sumac plant on diabetes and related factors in animal models (9-11). In this study, according to the positive effects of sumac in diabetic diseases, it was tried that sumac capsules were prepared from the aqueous extract of this plant, and its effect on the factors of diabetes in patients was evaluated.

Methods

Extraction and preparation of sumac capsules: The fruit of the sumac plant is collected in the ripening stage in the autumn season from the Balde Noor summer cottage area, and after the preparation operation including removing thorns and weeds and cleaning, the plant is placed in the shade and exposed to the sunlight for a few days to dry. For extracting, first, the sumac fruit is completely powdered with the electric grinder (Feller model EG 850) and then separated from its core with the help of a strainer. The obtained powder is soaked in a ratio of 1:10 with sterile distilled water for 24 hours and after passing the solution through a strainer, the extract is filtered by a concentrator finally, the extract is used to prepare the formulation for the production of hard capsules and other related tests in place. It is kept cool and dry (12).

To prepare the capsule, first, the ingredients of the formulation, which includes sumac extract as an active ingredient, and auxiliary ingredients such as microcrystalline cellulose (Avicel) (as a filler to determine the volume of the capsule) and colloidal silicon dioxide Aerosil (to improve the flowability of the formulation) are carefully it was weighed (13) and then mixed by a mixer for 5 minutes, and the flow test was performed using the Repose Angels method to determine the amount to ensure uniform distribution of the active ingredient. Then, the formulation mixture was prepared for the preparation of capsules in a small amount manually and also for mass production according to the flowability of the formulation by a drill capsule filling machine in the required amount and the necessary tests for the capsules produced according to the monograph pharmacopoeia was done.

Subjects: This double-blind randomized controlled clinical trial was conducted on sixty type 2 diabetic volunteers which were randomly selected from 70 volunteers with a computer-generated random number list (figure 1). Inclusion criteria include being diagnosed with type 2 diabetes (diagnosis of diabetes with fasting blood sugar (FBS) ≥ 125 or 2-hour glucose ≥ 200 or glycosylated hemoglobin ≥ 6), Glycosylated hemoglobin level of more than 7% despite treatment with glucose control drugs (metformin or glibenclamide in the last 2 months), age 20-60 years, signing the informed consent form, at least three months have passed since the onset of the disease. Exclusion criteria include smoking and alcohol consumption, pregnancy and lactating, using insulin to control blood sugar or diagnose type 1 diabetes, Glycosylated hemoglobin more than 9%, corticosteroid use, using any antioxidant supplements such as selenium, zinc and beta-carotene at least 3 months before the intervention, cardiovascular disorders, thyroid disorders, history of brain (stroke), liver, kidney problems, suffering from complications of diabetes, such as vision problems, kidney problems, diabetic ulcers, allergy to the sumac, lack of blood glucose control or need to chemical drugs intervention. The study protocol was approved by the Ethics Committee of the Mazandaran University of Medical Sciences. Written informed consent was obtained from all the participants.

Sample size: Based on previous research (8), and with a significance level of 0.05 (α), a statistical power of 0.95 (β), and an effect size (d) of 1.02, we calculated that a minimum of 52 participants (26 in each group) would be needed. Anticipating potential dropouts, we aimed for a final sample size of 60 individuals (30 in each group). We performed the sample size calculation using G*Power software Version 3.1.9.2.

Blinding and allocation: All the patients, individuals involved in health and treatment systems, and the collectors of data were blind to the treatment procedure. Only, the data supervisor of the trial who did not have a function in the treatment or care procedure was not blind. Every individual was randomly given a sealed envelope containing a labeled paper indicating either group A or B. One group received the drug, while the other received the placebo.

Intervention procedure: The volunteers were divided into two groups: control and sumac supplement groups: patients in the supplement group were given a capsule containing

sumac powder extract at night before sleep for 3 months, and those in the control group received a capsule containing powder calcium dibasic phosphate (Emcompress) and Aerosil. The glucose control drugs used in the cases were continued according to the instructions without changing the dosage.

Anthropometric parameters assessment: A portable scale with a 125kg±100 g was used for weight measurement, and cases recommended to remove shoes and heavy clothes before weighing. Also, the height of cases was measured via a tip with an accuracy of 1 cm. BMI is calculated by dividing weight (kg) by height (m2).

Physical activity and dietary assessment: Physical activity assessment is performed via the Physical Activity Questionnaire (IPAQ) including diaries, recall questionnaires, and interviews. For nutritional assessment, three-day food questionnaire records were used.

Biochemical variables assessment: Baseline venous blood samples were collected after overnight fasting before intervention and a second sampling was done in the 12th week. Serums were collected after centrifugation (at 3000 RPM) of the samples for 20 min and then stored at -70 °C until analysis.

All information about sex, age, physical activity, and education was recorded. Hb1AC, FBS, TG, TC, and HDL-C were measured via commercial kits (Pars azmon, Iran). Fried Wald formula was used for calculating the concentration of LDL-C and it was measured directly in the samples with higher levels of TG (400 mg/dl) (14).

Statistical analysis: SPSS software (Version 22.0, Chicago, IL, USA) was used for all of the statistical analyses. The Kolmogorov-Smirnov test was used to determine the normality of the distribution of data. All values were reported as median (highest- lowest) value or mean ± SD. For unpaired data, the Mann–Whitney U-test and independent sample t-test were used, and the Wilcoxon test and a paired student *t*-test were used for paired data. A $p<0.05$ is considered statistically significant.

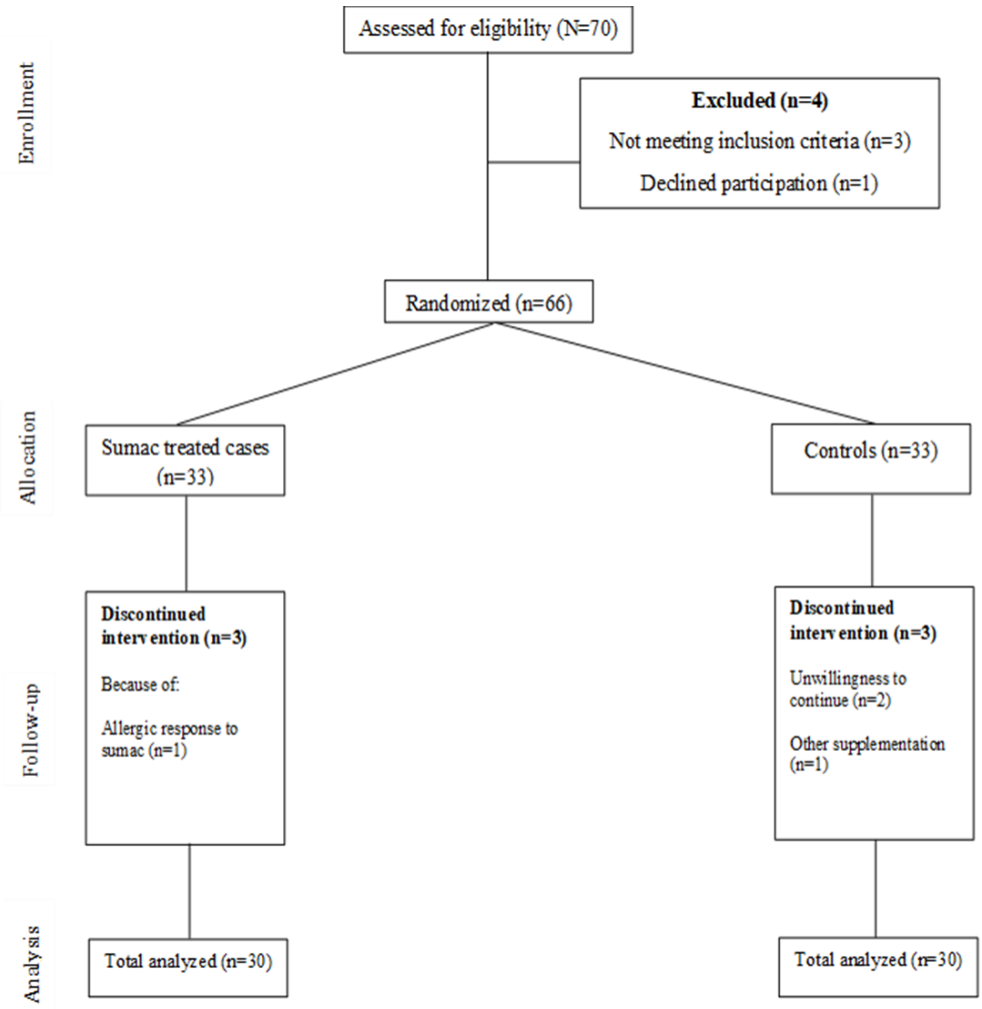

Figure 1. Flow diagram of study

Results

In this study, a total of 60 participants aged 20-50 years were randomly assigned into two groups (sumac treatment group, and control group). There were no statistically significant differences in demographic variables between the groups of study at baseline (table1). The rising popularity of herbal medicines can be attributed to the belief that they possess lower toxicities. However, it is important to acknowledge that herbal medicines may lead to undesired effects, including allergic or toxic reactions (15), nevertheless, this study found no evidence of such toxic reactions. As shown in tables 2, 3, 4, 5, 6, and 7 the biochemical indices (FBS, HDL-C, and HbA1C) measured in the sumac supplement group were significantly different ($p<0.01$) compared to the control group and baseline of the study, while no significant change was observed in the control group. Moreover, there is no significant difference in levels of the sumac supplement group (CHOL, TG, and LDL-C) compared to the control group and baseline of the study ($p>0.05$).

Table 1. Baseline characteristics of the study subjects

Variable/ groups	Case group (n=30)	Control group (n=30)	P-value
Age (years)	36.7±5.7	35.00±4.9	≥0.05
Physical activity **Low** **Moderate** **High**	 20 (66%) 10 (34%) 0	 21 (70%) 9 (30%) 0	 ≥0.05
BMI	27.1±1.02	26.5±2.00	≥0.05

Table 2. Comparison of median LDL-C in control and intervention groups

Variable	Group	Before	After	#P-value
LDL-C Med (IQR)	Intervention	85 (62, 100)	80 (48, 95)	0.263
	Control	78 (60, 85)	73 (51, 95)	0.322
	*P-value	0.286	0.582	

#: Wilcoxon Signed Ranks Test *: Mann-Whitney Test

Table 3 .Comparison of median HDL-C in control and intervention groups

Variable	Group	Before	After	#P-value
HDL-C Med (IQR)	Intervention	46 (45, 48)	50 (48, 54)	<.001
	Control	46 (45, 48)	50 (46, 51)	٠.008
	*P-value	٠.797	٠.211	

#: Wilcoxon Signed Ranks Test *: Mann-Whitney Test

Table 4. Comparison of mean CHOL in control and intervention groups

Variable	Group	Before	After	#P-value
CHOL Mean±SD	Intervention	180.43±57.73	157.48±48.63	٠.244
	Control	169.83±50.31	168.17±51.44	٠.795
	*P-value	٠.510	٠.473	

#: Paired sample T-Test *: Independent Sample T-Test

Table 5. Comparison of mean TG in control and intervention groups

Variable	Group	Before	After	#P-value
TG Mean±SD	Intervention	159.65±67.59	134.43±53.13	٠.197
	Control	152.22±113.97	143.87±68.27	٠.586
	*P-value	٠.789	٠.604	

#: Paired sample T-Test *: Independent Sample T-Test

Table 6. Comparison of mean HbA1C in control and intervention groups

Variable	Group	Before	After	#P-value
HbA1C Mean±SD	Intervention	7.74 plus. 74 plus4 plus±1.47	6.47±1.16	٠.007
	Control	7.81±1.40	8.91±1.49	<٠.001
	*P-value	٠.878	<٠.001	

Table 7. Comparison of median FBS in control and intervention groups

Variable	Group	Before	After	#P-value
FBS Med (IQR)	Intervention	147 (122, 167)	100 (92, 121)	٠.002
	Control	117 (109, 186)	200 (140, 236)	<٠.001
	*P-value	٠.435	<٠.001	

#: Wilcoxon Signed Ranks Test *: Mann-Whitney Test

Discussion

The global prevalence of *H. pylori* infection has been *Rhus coriaria L.* (Sumac), widely used as a spice, is renowned not only for its culinary appeal but also for its medicinal properties, attributed to its antioxidant and insulin-like activities. Reduced bioavailability of nitric oxide (NO) can lead to endothelial damage, characterized by an increase in inflammatory cytokines, heightened platelet aggregation, and thrombus formation (16) .Therefore, sumac's potential to lower superoxide levels, alleviate inflammation, and reduce oxidation could play a crucial role in preventing cardiovascular disease (CVD) and atherosclerosis (17).

Previously, many clinical trials reported the potential anti-diabetic effect of sumac but the results on glycemic parameters were inconclusive. In this study, our results showed that sumac decreased the levels of (FBS, HDL-C, and HbA1C) without a significant effect on (CHOL, TG, and LDL). In the study by Mohit et al., results showed that sumac powder supplementation has no significant effects on the levels of FBS, homeostatic model assessment for insulin resistance (HOMA-IR), and insulin (18). However, along with our findings, a few animal studies also showed that treatment with sumac extract could significantly reduce the blood glucose level in diabetic rats (17, 19). Moreover, the positive effects of sumac were confirmed by Chakraborty et al. who introduced sumac as a potent antioxidant with protective effects against oxidative DNA damage and improvement of insulin production that led to thus maintained glucose homeostasis (20). In addition to the helpful effects of sumac on diabetic indices, more recent supporting effects of sumac on the early wound healing on diabetic rate were reported by two studies (9, 21).

Sumac exerts its anti-oxidant effects via aggregate activities of anti-oxidant enzymes including glutathione S-transferase (GST) and the two isozymes (GST-α and GST-π) (22). HbA1c is an indicator which is a good indicator of diabetes control and treatment prognosis. According to our results, 3 nightly month treatment with sumac powder capsules can decrease HbA1c significantly which was in line with the study by Shidfar et al. that reported a major reduction in FBS and HbA1c after usage of 3 g of sumac powder daily for 3 months (8). In the study by Anwer et al., sumac decreased blood glucose levels, suppressed hyperinsulinemia and developed glucose tolerance in NIDDM rats (11). In the molecular view, sumac may regulate some metabolism signaling pathways including SIRT1, PI3K/Akt, and AMPK signaling pathways and so

increase insulin activity, glucose utilization, and lower insulin resistance (23). Differences in study outcomes may arise from variations in intervention durations, dosages of sumac supplements, study designs (such as double-blind or cross-over studies), and sample sizes.

Additionally, ethnicities, as well as the specific inclusion and exclusion criteria employed in each randomized controlled trial (RCT), could also contribute to these variations. Our study has some limitations including that we did not consider differences in lifestyle such as sleep, smoking, etc. which may contribute to glycemic control. In addition, only one dose of sumac has been used. It would have been better to use different doses and compare between groups to determine the most efficient dose of sumac in controlling diabetes indices. Sumac exhibits antioxidant, antifungal, and antibacterial properties, as well as anticancer, anti-inflammatory, neuroprotective, analgesic, cardioprotective, and antidiabetic effects. These properties suggest that sumac could be potentially beneficial in treating various diseases (24). Our data confirmed the anti-diabetic effect of sumac in patients. Because of sumac safety, it seems that sumac capsules can be used for the treatment of diabetic patients along with routine chemical drugs.

Acknowledgments

We thank the staff of Mazandaran University of Medical Sciences Research Center.

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Ethics approval: The research protocol received approval from the ethical committee of Mazandaran University of Medical Sciences (ID: R.MAZUMS:REC.1398.3470). Additionally, the clinical trial was registered with the Iranian Registry of Clinical Trials (IRCT) under the identifier IRCT20240126060811N1.

Conflict of interests: The authors declare that they have no conflict of interest.

Authors' contribution: All authors participated in the planning and execution of the study, the analysis of findings, and the drafting of the manuscript.

Data availability: The corresponding author's data supporting this study's findings are available upon reasonable request.

Consent for publication: Not applicable.

References

1. Mukhtar Y, Galalain A, Yunusa U. A modern overview on diabetes mellitus: a chronic endocrine disorder. Eur J Biol 2020; 5: 1-14.
2. Eizirik DL, Pasquali L, Cnop M. Pancreatic β-cells in type 1 and type 2 diabetes mellitus: different pathways to failure. Nat Rev Endocrinol 2020; 16: 349-62.
3. Malone JI, Hansen BC. Does obesity cause type 2 diabetes mellitus (T2DM)? or is it the opposite? Pediatr Diabetes 2019; 20: 5-9.
4. Pittas AG, Kawahara T, Jorde R, et al. Vitamin D and risk for type 2 diabetes in people with prediabetes: A systematic review and meta-analysis of individual participant data from 3 randomized clinical trials. Ann Intern Med 2023; 176: 355-63.
5. Perreault L, Skyler JS, Rosenstock J. Novel therapies with precision mechanisms for type 2 diabetes mellitus. Nat Rev Endocrinol 2021; 17: 364-77.
6. Alsamri H, Athamneh K, Pintus G, Eid AH, Iratni R. Pharmacological and antioxidant activities of Rhus coriaria L.(Sumac). Antioxidants (Basel) 2021; 10: 73.
7. Tohma H, Altay A, Köksal E, Gören AC, Gülçin İ. Measurement of anticancer, antidiabetic and anticholinergic properties of sumac (Rhus coriaria): analysis of its phenolic compounds by LC–MS/MS. J Food Meas Charact 2019; 13: 1607-19.
8. Shidfar F, Rahideh ST, Rajab A, et al. The effect of sumac (Rhus coriaria L.) powder on serum glycemic status, ApoB, ApoA-I and total antioxidant capacity in type 2 diabetic patients. Iran J Pharm Res 2014; 13: 1249-55.
9. Doğan A, Çelik İ. Healing effects of sumac (Rhus coriaria) in streptozotocin-induced diabetic rats. Pharm Biol 2016; 54: 2092-102.
10. Salimi Z, Eskandary A, Headari R, et al. Antioxidant effect of aqueous extract of sumac (Rhus coriaria L.) in the alloxan-induced diabetic rats. Indian J Physiol Pharmacol 2015; 59: 87-93.
11. Anwer T, Sharma M, Khan G, et al. Rhus coriaria ameliorates insulin resistance in non-insulin-dependent diabetes mellitus (NIDDM) rats. Acta Pol Pharm 2013; 70: 861-7.
12. Salimi Z, Heidari R, Nejati V, Eskandary A, Ghasemi Z. Effect of Sumac (Rhus coriaria L.) extract on lipid peroxidation and diabetic nephropathy in diabetic rats. J Birjand Univ Med Sci 2011; 18: 275-84.
13. Patel R, Podczeck F. Investigation of the effect of type and source of microcrystalline cellulose on capsule filling. Int J Pharm 1996; 128: 123-7.

14. Maroufi NF, Farzaneh K, Alibabrdel M, et al. Taq1B polymorphism of cholesteryl ester transfer protein (CETP) and its effects on the serum lipid levels in metabolic syndrome patients. Biochem. Genet 2016; 54: 894-902.
15. Kazemi M, Eshraghi A, Yegdaneh A, Ghannadi A. "Clinical pharmacognosy"- A new interesting era of pharmacy in the third millennium. Daru 2012; 20: 18.
16. Eshraghi A, Talasaz AH, Salamzadeh J, et al. Evaluating the effect of intracoronary N-acetylcysteine on platelet activation markers after primary percutaneous coronary intervention in patients with ST-elevation myocardial infarction. Am J Ther 2016; 23: e44-51.
17. Candan F, Sökmen A. Effects of Rhus coriaria L.(Anacardiaceae) on lipid peroxidation and free radical scavenging activity. Phytother Res 2004; 18: 84-6.
18. Mohit M, Nouri M, Samadi M, et al. The effect of sumac (Rhus coriaria L.) supplementation on glycemic indices: A systematic review and meta-analysis of controlled clinical trials. Complement Ther Med 2021; 61: 102766.
19. Azali K. Effects of 10-weeks aerobic training with Rhus coriaria. L supplementation on TAC, insulin resistance and anthropometric indices in women with type 2 diabetes. Complement Ther Med 2017; 7: 1805-15.
20. Chakraborty A, Ferk F, Simić T, et al. DNA-protective effects of sumach (Rhus coriaria L.), a common spice: results of human and animal studies. Mutat Res 2009; 661: 10-7.
21. Alsarayreh AZ, Oran SA, Shakhanbeh JM. Effect of Rhus coriaria L. methanolic fruit extract on wound healing in diabetic and non-diabetic rats. J Cosmet Dermatol 2022; 21: 3567-77.
22. Khalilpour S, Behnammanesh G, Majid AM, Tamayol A, Majid AS. Assessment of neuroprotective properties of Rhus coriaria L. ethanol extract in an in vitro model of retinal degeneration. J Herb Med 2017; 10: 45-52.
23. Mirmiran P, Bahadoran Z, Azizi F. Functional foods-based diet as a novel dietary approach for management of type 2 diabetes and its complications: A review. World J Diabetes 2014; 50: 267-81.
24. Ataar AM, Eshraghi A, Asgari S, Naderi G, Badiee A. Antioxidant effect of Ziziphus vulgaris, Portulaca oleracea, Berberis integerima and gundelia tournefortti on lipid peroxidation, Hb glycosylation and red blood cell hemolysis. J Med Plants 2011; 10: 80-8.