Review Article

Open Access

Iranian Journal of Diabetes and Obesity (IJDO)

A Review of Clinical Trial Studies on Medicinal Plants in the Treatment of Diabetes

Bahare Fallah[1], Akram Mehrabbeik[2], Naiire Salmani[3]*

[1]Instructor of Nursing Education, Research Development Center, Research Center for Nursing and Midwifery Care, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
[2]PhD of Health Education & Promotion Diabetes Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
[3]Assistant Professor. Faculty of Nursing and Midwifery, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

Abstract

Objective: The use of medicinal plants in diabetic patients is rising, it is essential to increase knowledge about the effects of medicinal plants and subsequently perform evidence-based action, so, review studies are a helpful way for the present purpose. Current study was conducted to investigate the clinical trials of medicinal plants used in the treatment of diabetes in Iran.

Materials and Methods: Articles published online between 2010 - 2020 were googled in Magiran, SID, Scopus, and, Iran Medex with Persian keywords such as “type 2 diabetes”, “medicinal herbs”, “healing herbs” “herbs”, “medicinal plants” and “clinical trial”. The inclusion criteria for articles were conducting in the form of a clinical trial, conducting in Iran, publishing in Persian language and having at least a score of 3 based on the Jadad scale.

Results: 20 clinical trial studies were extracted. Five studies were conducted on cinnamon and two studies on cumin and the rest of the plants were examined just in one study. Although some trials showed positive effects of the medicinal plants on reducing fasting blood sugar (FBS) and glycosylated hemoglobin (HbA1c), some others demonstrated that medicinal plants had no effect on important variables in diabetes control.

Conclusion: Conclusions about the benefits of plants should be made with caution, safety and efficacy of plants in the treatment of diabetes should be investigated further. It is essential that patients take any herbal supplements under physician’s supervision and after receiving the necessary advice.

Keywords: Type 2 diabetes, Medicinal herbs, Healing herbs, Medicinal plants, Clinical trial

QR Code:

Citation: Fallah B, Mehrabbeik A, Salmani N. A Review of Clinical Trial Studies on Medicinal Plants in the Treatment of Diabetes. IJDO. 2022; 14 (2) :117-130

URL: http://ijdo.ssu.ac.ir/article-1-709-en.html

10.18502/ijdo.v14i2.9456

Article info:

Received: 18 December 2021
Accepted: 12 March 2022
Published in May 2022

Corresponding Author:

Naiire Salmani, Assistant Professor of Nursing, Department of Nursing, Meybod School of Nursing, Nursing and Midwifery Care Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
Tel: (98) 353 824 1751
Email: n.salmani@sbmu.ac.ir
Orcid ID: 0000-0002-4723-0984

Introduction

Diabetes mellitus is a disease characterized by high blood sugar as a result of insulin secretion defect or impaired insulin function or both of them (1,2). It is estimated that the number of diabetic patients will rise from 190 Million in 2000 to 360 million in 2030 (3,4). Nowadays, there are various treatments of diabetes including oral therapy, insulin therapy (5), and some methods such as pancreatic and Langerhans transplantation and even the use of cellular methods (6).

Although drug and insulin therapy are the cornerstones of diabetes treatment (7), their side effects, inability to prevent disease complications, and effectiveness over time, have encouraged researchers to explore new methods. Scientists have always tried to discover more appropriate strategies to control the disease and its complications (8,9). So, the use of complementary medicine has been considered an acceptable method and in this method, the use of medicinal plants is more popular than others (10).

Since medicinal plants are usually cheaper, easier, and more accessible than chemical-based treatments, people prefer to use them. Additionally, in many cases, these herbs have fewer side effects (11,12). The results of studies carried out in Jordan (13), Turkey (14), and Iran (15) have shown that the percentage of patients using herbal medicines is 31%, 57.6%, and 70.3%, respectively.

The prevalence of using medicinal plants is different among diabetics. Patients' beliefs, values, and attitudes toward complementary and alternative medicine, availability of medicinal plants, lack of access to health care systems, and other consumers' feedbacks are effective factors in using these plants (16). In parallel with the prevalence of using medicinal plants among diabetic patients, the incidence of complications of this kind of treatment is also noteworthy. Hence, the World Health Organization strongly emphasizes that herbal supplements can cause adverse effects, especially when combined with medical treatments (17). Various side effects, such as headache, nausea, dizziness, itchy skin, sweat, hypoglycemia (18), diarrhea and vomiting (14) have been reported in patients with diabetes mellitus. In previous studies different types of medicinal plants have been reported based on the place of study and different ethnicities and races. Cinnamon, common sage (Salvia officinalis), thyme, turmeric and ginseng are some of the most common herbs for diabetes in Turkey (14) and cinnamon, fenugreek, dill, garlic(Anethum graveolens), and ginger (Zingiber officinale) are common in Iran (15).

The increasing trend of using the various types of medicinal plants and their adverse effects, increasing the knowledge, and subsequently performing evidence-based action in medicinal plants can provide proper health care (19,20).

Referring to the local and indigenous uses of medicinal herbs in different cultures and ethnicities in Iran and the lack of information and clinical evidence on the effectiveness of herbs used in the treatment of diabetes, investigating this type of plant seems necessary to provide quality health services.

The primary purpose of the present study is to summarize the findings of clinical trials regarding the effect of medicinal plants in the treatment of diabetes in Iran.

Materials and Methods

To conduct this review, all Iranian articles published during 2010-2020 in Persian and indexed in Magiran, SID, Scopus, and IranMedex by using the Persian keywords "type 2 diabetes", "medicinal herbs", "healing herbs" "herbs", "medicinal plants" and "clinical trial", were reviewed.

The inclusion criteria for articles were conducted in the form of a clinical trial, working in Iran, publishing in the Persian language and having at least a score of 3 based on the Jadad scale. Some studies that had no access to the full text or were performed on

[DOR: 20.1001.1.20086792.2022.14.2.5.2]
[DOI: 10.18502/ijdo.v14i2.9456]

animals, were excluded. The reported outcomes included measuring the patients' blood sugar and any positive or negative effects of medicinal plants.

To evaluate the articles and investigate the possible bias in the studies, we used the Jadad scale. This criterion examines reports based on the likelihood of bias in randomization, patient follow-up, and blindness. Scale scores can range from 0 to 5 points. According to this criterion, the articles that received a score of 3 or more remained in the study, and finally extracted 20 articles. Magiran (7 articles), SID (6 articles), Scopus (4 articles), and IranMedex (3 articles) were found.

Results

In this study, 20 articles were reviewed. Medicinal plants included nettle (one study), cumin (two studies), cinnamon (five studies), saffron (one study), fenugreek (one study), colocynth (one study), strawberries (one study), turmeric (One study), Zingiber officinale (two studies), green tea and sour tea (one study), dill (one study), pumpkin (one study), thymes (one study), garlic (one study) and glycogol (one study). These articles were summarized in Table 1.

1) Nettle

Nettle is a medicinal herb that has been introduced in traditional medicine as an anti-diabetic agent. Nettle is scientifically named Urtica Dioica and it is a member of the Urticaceae family. There are several natural compounds on the leaves of nettle (flavonoids, peptides, and amines), that the anti-diabetic effects of some have been proven (11).The mechanisms of mentioned compounds are stimulation of glycogenesis, blockage of potassium channels of pancreatic beta cells and involvement in absorbing glucose from the Intestinal wall (21).

Tarighat Esfanjani (2011) conducted a study on 50 people divided into two equal groups (25 nettle extract and 25 received placebo). Patients dissolved 100 mg of nettle extract or placebo in water and consumed it during the day after the main meals.

The findings indicated that consumption of nettle extract decreased the levels of glycosylated hemoglobin (HbA1c) and fasting blood sugar (FBS) in the test group compared to the placebo group (22).

2) Cumin

Cumin Cyminum (or cumin) is a flowering plant in the family Apiaceae, native to India, Iran, the Mediterranean and Egypt. This plant has antioxidant properties and is used as a stimulant, anti-flatulence, and anti-hemorrhage (23). Cuminaldehyde, gamma-terpinene, sabinene, α phellandrene, and α codeine are its internal efficient compounds. The most

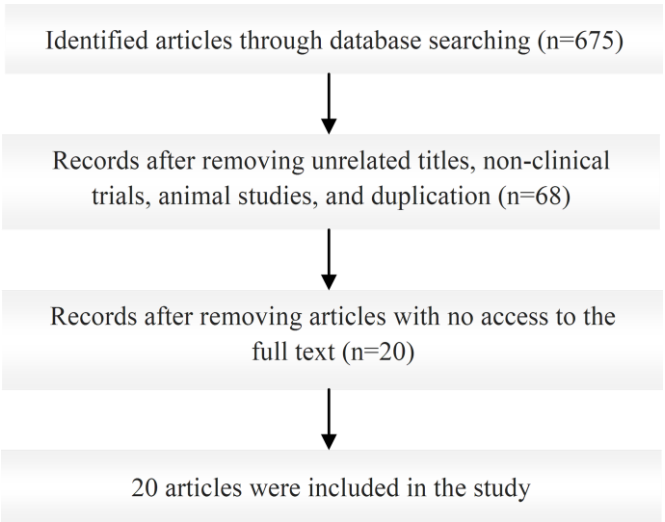

Figure 1. Flowchart of included studies for systematic review

[DOR: 20.1001.1.20086792.2022.14.2.5.2]
[DOI: 10.18502/ijdo.v14i2.9456]

important active compound in Cumin is Cuminaldehyde or 4-Isopropylbenzaldehyde. This natural organic compound inhibits the two enzymes (alpha-glucosidase and aldoserductase) in the pathway of carbohydrate metabolism and it is possible to cause anti-diabetic properties. It is likely that the improvement in insulin function by cumin is partly due to the role of cumin in maintaining pancreatic integrity, which leads to a significant increase in β cells. It also increases the susceptibility of hepatocytes to the insulin (24).

In a study, Heidarian et al. (2018) divided 165 diabetic patients into four groups randomly. 1) Recipient of cumin (3 capsules after each meal- 75 milligrams daily), 2) Resveratrol supplement (1 capsule- 200 milligrams daily), 3) Vitamin C (1 tablet- 500 milligrams daily), and 4) Placebo. Supplements and placebo with numbers one to four in similar containers by the pharmacy were given for two months. The findings showed that resveratrol and cumin reduced HbA1c, which, in turn, cumin has more effectiveness (25).

In a clinical trial conducted by Jafari et al. (2016) 99 diabetic patients were allocated into equal three groups (receiving Cuminum cyminum extract of 50 and 100 mg per day and receiving placebo (oral paraffin) randomly. Participants take their medicine before lunch and dinner. According to the results consumption of cumin improves FBS, HbA1c and insulin serum. It is noticeable that the dose of 100 mg showed more pronounced effects than the dose of 50mg on HbA1c (1)

3) Cinnamon

Cinnamon with scientific name “Cinnamomum zeylanicum “increases glucose consumption and glycogen production and also phosphorylation of insulin receptor that ultimately leads to increased insulin sensitivity (26).

Stimulation of insulin secretion and prevention of increased cellular insulin resistance has been introduced as a mechanism of cinnamon, function in some studies. Furthermore cinnamon can stimulate glucose uptake and glycogen synthesis (27,28).

Mirfeizi et al. (2014) carried out a survey of 90 people who received cinnamon (n=45) and placebo (n=45). Participants took cinnamon and placebo capsules (starch) 500mg twice a day for 90 days. Findings showed that cinnamon consumption reduced FBS, two-hour postprandial plasma glucose (2hpp), HbA1C, insulin serum, homeostatic model assessment (HOMA) and body mass index (BMI) in the case group compare to placebo (29).

In another study was done by Zahedifar et al. (2018), the biological markers in two groups were compared. Participants took 500 mg of cinnamon or placebo three times a day for 90 days. According to the results, although cinnamon consumption in the intervention group reduced HbA1c levels compared to the placebo group, it had no effect on FBS (30).

Khadem Haghigian (2010) conducted a similar study to evaluate the effect of cinnamon on glycemic control and insulin resistance in type II diabetes patients. All participants received 1.5 mg capsules (cinnamon or placebo) three times a day for 60 days. The findings showed that consuming cinnamon reduced FBS, HbA1c, and insulin resistance in patients with type 2 diabetes (31).

Hasanzade et al. (2013) performed a clinical trial study. Subjects were selected randomly in two groups (35 were in cinnamon group and 36 placebo groups). Intervention group took one gram of cinnamon in addition to the normal treatment for 60 days and another group took a placebo for a similar period. There was no difference in FBS or HbA1c between the two groups (32).

4) Saffron

Crocus satiuus L, commonly known as saffron, is a perennial stemless herb of the Iridaceae family. The most common saffron compounds are alkaloids (picrocrocin and safranal) and flavonoids (crocin and crocetin) .Since saffron contains polyphenols and

[DOR: 20.1001.1.20086792.2022.14.2.5.2]
[DOI: 10.18502/ijdo.v14i2.9456]

antioxidants, it seems to have beneficial effects on health (33).

It appears that presence of various metabolites in saffron, especially crocin and crocetin and its strong anti-oxidant effect reduces insulin resistance, stimulates glucose uptake through peripheral tissue, and inhibits the absorption of intestinal glucose, is involved mechanism in improving the function of pancreatic cells and ultimately reducing serum glucose (34-37).

Milajerdi et al. (2017) carried out a survey in which 27 people who received saffron and 27 people received placebo. Both groups took 15mg capsules twice daily for 8 weeks. The findings showed consumption of saffron reduced FBS and 2hpp (7).

5) Fenugreek

Another medicinal plant that affects diabetes is fenugreek seed (Trigonella Foenum graecum L), that has been used as lowering glucose and anti-diabetic agent in traditional medicine (38).

Because of its high antioxidant effect, fenugreek reduces lipid peroxidation. In addition, fenugreek contains saponin, steroids and alkaloids such as trigonelline and tricoumarin that all have the effects of lowering blood sugar. It is mentionable that fenugreek fibers reduce glucose uptake (39).

Additionally, hydroxyisolcucine, an amino acid in fenugreek seeds, stimulates insulin secretion and increases the number of insulin receptors (40).

Rafraf et al. (2015) evaluated the effect of fenugreek seed consumption on serum metabolic factors and ICAM-1 levels in T2DM patients. Intervention group and control group received 10g of Fenugreek seed powder and 5g of starch as a placebo respectively, twice a day for 8 weeks. Findings showed the levels of FBS, HbA1c, serum insulin and HOMA -IR in the intervention group was reduced and the fenugreek seed improved glucose metabolism (38).

6) Colocynth

Citrullus colocynthis L, with common name “colocynth “is a herb of the cucurbitaceace family and is used to treat diabetes and high blood fats in traditional Iranian medicine (TIM). Chemicals identified compounds in this plant include: tannins, flavonoids, terpenes, alkaloids, pectins, and various minerals (41).

Antioxidant effect has been considered as an important pharmacological effect of this plant, which can improve lipid and glucose metabolism (42). In several studies, the effectiveness of colocynth in reducing the level of blood glucose and lipid in laboratory animals, have been proven (43, 44).

Yaqoubi et al investigated the effect of colocynth capsule on blood glucose in diabetic patients during 40 days. Intervention and control group (n=28 participants in each group) were treated with processed C. colocynthis (100 mg) and placebo capsules (100 mg) three times a day respectively. The findings showed that the consumption of colocynth reduced fasting blood sugar level after one month in intervention group compared with placebo (45).

7) Strawberry

Among the berries, strawberry (Fragaria ananassa) based on the high level of essential nutrients and useful phytochemicals, have biological effects on maintaining human health.

Anthocyanins, ellagitannins, flavonoids, and vitamin C are some of the major antioxidant compounds in strawberries (46).

Possible mechanism of the strawberry is prevention of intestinal glucose uptake, increasing the glucose transfer to inside tissues, normalizing blood sugar level and inhibiting the function of carbohydrates digestive enzymes especially alpha amylase and alpha glucosidase (47).

Amani et al. (2013) conducted a study on 18 recipients of strawberry powder and 18 recipients of placebo. Test group members consumed 2 cups of freeze-dried strawberry beverage (50 grams freeze-dried strawberry)

[DOR: 20.1001.1.20086792.2022.14.2.5.2]
[DOI: 10.18502/ijdo.v14i2.9456]

and the placebo group2 cups of placebo beverage with similar taste and color at a distance of 6 hours and at least 2 hours after their meals. Findings showed that consumption of strawberry powder reduced HbA1c level compared to the placebo group (48).

8) Turmeric

Turmeric is used as a spice in Asian countries. This plant belongs to the ginger family and it is known as Curcuma longa. Its main ingredients are yellow pigments of the group of curcuminoids, which make up 3.5% of turmeric and also include curcumin, demothoxy curcumin, and bisdemethoxycurcumin. Nowadays, curcumin, as the most important turmeric compound, has the most therapeutic effects (49).

Since curcumin prevents the formation of oxygen free radicals, it is possible that its oxidants be effective in reducing the complications of diabetes. A suggested mechanism for the role of turmeric in glucose homeostasis is activating glycolysis and preventing gluconeogenesis.

The role of curcumin in glucose homeostasis through glycolysis activation, prevention of hepatic gluconeogenesis and decreased lipids metabolism is applied and insulin sensitivity is improved by reducing insulin resistance (50).

In a study was done by Adab et al. (2013) patients received 700mg of turmeric powder or placebo 3 times a day for eight weeks (two groups of 40 subjects). According to the results, consuming turmeric powder had no effect on FBS and hemoglobin levels (49).

9) Ginger

Ginger, also known as (Zingiber officinale), is a very popular spice in the world. Ginger inhibits liver phosphorylase to prevent the decline of liver glycogen storage and it can also increase the activity of enzymes that promote glycogen synthesis. Another possible effect of ginger is inhibition the activity of glucose-6-phosphatase enzyme in liver and subsequently, reducing the catalysis of glucose 6 phosphatase to glucose and thus lowers blood glucose (51).

Aryaeian et al. (2014) evaluated the impact of ginger on glycemic status, insulin resistance, and inflammatory markers in diabetics. In this study 35 recipients of ginger powder and 35 recipients of wheat flour as a placebo (800 mg twice daily) for 12 weeks, participated.

Eventually, consumption of ginger reduces FBS, insulin resistance index and HbA1c in the intervention group compared with the placebo group (52).

Also in a similar study carried out by Talaei (2011), intervention and control groups took capsules containing ginger and microcrystalline cellulose as a placebo respectively for 8 weeks (1gram capsules 3 times daily). In intervention group, decreasing in FBS and HbA1c was shown compared with the placebo group (51).

10) Green Tea and Sour Tea

Green tea, scientifically known as "Camellia sinesis", is one of the richest sources of flavonoids (51). There are various compounds and alkaloids such as ascorbic acid, anisaldehyde, anisaldehyde, beta-carotene, beta-3-sitosterol, citric acid, cyanidin 3-rutinoside, dolphinidine, galactose, mucopolysaccharides, pectin and polysaccharides, in the petals of this plant (53, 54).

The effects of sour tea are mostly due to the presence of compounds with antioxidant features and soluble fiber, as well as compounds such as hibiscus acid and hydroxy acid that have a strong inhibitory effect of pancreatic α -amylase enzyme (55).

Ahadi et al.(2012) designed an study to comparison of the effect of green and sour tea on blood glucose participants were randomly assigned into two groups. They received 3g of green tea (group 1) or sour tea (group 2) solved in 150 cc boiled water for 6 weeks. The findings demonstrated that there was no difference between the effects of green tea and sour tea on FBS level (56).

[DOR: 20.1001.1.20086792.2022.14.2.5.2]
[DOI: 10.18502/ijdo.v14i2.9456]

11) Dill

Dill, scientifically named Anethum graveolens, is a herb of the Apiaceae family. It is the only species in the genus Anethum. In English it means sedative and in Persian it is called Shevid or Shebet (57). Fresh leaves of dill are a rich source of protein, fiber and minerals. Anethoferon, carvone and limonene are the most important components of dill seed oil, with useful and healthy effects. Myristicin, anethole and umbelliferone are the rest of dill components.

Besides other beneficial effects of dill such as anti-cancer, antihyperlipidemic, and antihypercholesterolemic effects, prevention of colic in infants, stimulation of maternal secretion, and antimicrobial effects are attributed to dill (58).

Payahoo et al. (2015), carried out a clinical trial study on 30 persons received dill powder and 30 persons received starch powder as a placebo, before main meals for 8 weeks (3.3g/day). The results confirmed that the consumption of dill powder reduced FBS (57).

12) Pumpkin

Cucurbita ficifolia (Cucurbitaceae), known as Pumpkin, reduces the levels of cholesterol serum levels and improves insulin sensitivity. The mechanism of action of pumpkin may include inhibition of beta- glycosidase and alpha-amylase on pancreas function and improvement of insulin sensitivity (59).

Bayat et al. (2016) studied the effect of pumpkin consumption alone or with probiotic yogurt on blood sugar levels in patients with type 2 diabetes. Subjects were divided into four groups: 1) pumpkin consumption (100g), 2) probiotic yogurt consumption (150 g), 3) pumpkin and probiotic yogurt (100g and 150g, respectively), and 4) control group. Pumpkin and yogurt probiotics were consumed at lunch for 8 weeks. Based on the results of the study, consumption of pumpkin and probiotic yogurt separately and simultaneously reduced FBS and HbA1c (60).

13) Thymus kotschyanus

Thymus kotschyanus is an herb of Lamiaceae family. It is one of the medicinal plants with therapeutic properties and very few side effects (61). The main known compounds of this plant include carvacrol, thymol, gamma-terpinen, paracetamol, borneol, linalool and geraniol. The therapeutic benefits of this plant are related to carvacrol and thymol. These phenolic monoterpenes have a wide range of bacterial and fungicidal and antioxidant activities (62-64).

Taleb et al. (2017) evaluated the effect of Thymus kotschyanus aqueous extract on glycemic control in type 2 diabetes. Patients were randomly divided into two groups. The first group received the usual drugs and the second group received Thymus kotschyanus aqueous extract (20 grams daily along with routine therapy). After three months, the findings indicated that Thymus kotschyanus aqueous extract in combination with the usual anti-diabetic drugs, led to a decrease in the level of HbA1c, FBS and increased the level of HOMA-beta index as an indicator of beta cell function in T2DM patients. However there was no changes in fasting insulin level and HOMA-IR index, which is the indicator of insulin resistance level (65).

14) Garlic

Garlic belongs to the Liliaceae family. The medicinal properties of garlic have been considered for many years. Garlic contains a variety of compounds such as amino acids, vitamins, and minerals. Some sulfur-containing compounds, such as allicin, ajoene, S-allyl cysteine, and diallyl sulfide are responsible for garlic therapeutic features. In many studies, various types of garlic sulfur compounds were investigated and contradictory results were obtained (66).

In a survey conducted by Khademian et al. (2015) intervention group took garlic tablets (400 mg/day) and control group took the placebo (Microcrystalline Cellulose), before the main meals for three months. The results revealed that garlic decreased FBS, HbA1c

[DOR: 20.1001.1.20086792.2022.14.2.5.2]
[DOI: 10.18502/ijdo.v14i2.9456]

and it was helpful in control the complications and treatment of diabetes (67).

15) Glycogol tablet (a combination of sage, fenugreek and ginseng)

Among medicinal plants, the positive effect of sage, fenugreek, and ginseng in reducing blood sugar has been proven in human and animal studies (68).

Salvia officinalis is an herb that is used to treat constipation, infections, cholera, colds, fever, liver disorders, epilepsy,cancer, muscle strengthening, and nerve relaxation. As other therapeutic effects of Salvia officinalis, bile secretion and stimulating digestion are considerable. This plant has aromatic compounds (69) that, diterpene, triterpenoids, tannins, flavonoids, resins, saponins and phenols are the most important of them. Other major constituents of Salvia officinalis are carnosic acid, rosmarinic acid, resmanol, carnosol, salvinol and salvanic acid (70).

Many of these compounds have antioxidant effectswhile lowering blood sugar, inhibiting free radicals and, reducing the effects of high sugar and fat. Most of the effects of sage leaves on human health have been attributed to the high antioxidant properties of this plant (68).

Ginseng is another herb that has been used as a medicine in Eastern countries since 4,000 years ago. Its root extract is one of the most widely used herbal products in the United States (71).

The physiological effects of ginseng are related to its ginsenosides. Conforming to the cell and animal culture, ginseng extract and some ginsenosides, have positive effects on glucose metabolism and insulin function. Ginseng-derived ginsenoside increases glucose sensitivity. Most research with human subjects have demonstrated a reduction in blood sugar levels in glucose tolerance tests (72).

Behradmanesh et al. (2012), in a double-blind clinical trial investigated the effect of glycogol on blood glucose level. For this purpose, 80 diabetic patients were randomly allocated into two groups. The intervention and control group took glycogol and placebo tablets, respectively three times a day for three months. HbA1c, lipid profile, FBS, and 2hpp were measured at the baseline and every 2 weeks, for three months. In the intervention group, compared to the control group, 2hpp blood sugar was significantly decreased, but there were no significant changes in HbA1c and FBS between the two groups (73).

Table 1. Characteristics of studies included in the systematic review

Authors (year)	Type of study	Type of medicinal plant	Study design	Results
Esfanjani et al (2011)	One-blinded randomized clinical trials (RCTs)	Nettle	25 people (case) and 25 people (control) 100 mg/ kg hydroalcoholic extract of nettle or placebo dissolved in a glass of water three times daily after the main meals.	The level of HbA1c and FBS after eight weeks in the intervention group compared to the control group showed a significant decrease. However, there was no significant change in fasting insulin and insulin resistance index.
Jafari Kargar et al.(2017)	Double-blinded clinical trials	Green cumin	99 patients were randomly assigned to 3 groups (recipient of 100 g and 50 mg of alcoholic extract of cumin and recipient of placebo (oral paraffin)	Average fasting blood sugar, insulin serum levels and investigation of the hemostatic model of insulin resistance in two complementary groups, were significantly reduced and short-term administration of 50 or 100 mg alcoholic supplementation of green cumin in type 2 diabetics could improve insulin sensitivity. It should be noted that the dose of 100 mg created more significant effects than 50 mg, especially on HbA1c.
Heydarian et al. (2018)	Double-blinded randomized clinical trials (RCTs)	Green cumin, resveratrol supplement, vitamin C.	165 diabetic patients were randomly divided into 4 groups who received green cumin (75 mg/day), resveratrol supplementation (200 mg/day), vitamin C (500 mg/day) and the control group (placebo)	Resveratrol and cumin reduced HbA1c, but green cumin improved blood sugar in diabetic patients

Continued

[DOR: 20.1001.1.20086792.2022.14.2.5.2]
[DOI: 10.18502/ijdo.v14i2.9456]

Authors (year)	Type of study	Type of medicinal plant	Study design	Results
Zahmatkesh et al (2011)	Double-blinded clinical trials	Cinnamon	Diabetic patients (n=61) took 500 mg of cinnamon or placebo, 2 capsules each 12 hours.	Cinnamon at a dose of 2 gr/day had no significant effect on lowering blood glucose level.
Zahedifar et al (2017)	randomized clinical trial	Cinnamon	68 cinnamon recipients and 68 placebo recipients took 500 mg capsules containing cinnamon or placebo three times daily after breakfast, lunch, and dinner for 90 days	The level of HbA1c showed a significant statistical difference in Cinnamon consumers compared to the control group. But, FBS level in the case group after 31 days of taking 1.5 grams of cinnamon did not have a significant statistical difference with the placebo group.
Khadem Haghighiyan (2010)	randomized clinical trial	Cinnamon	30 people received cinnamon and 30 received placebo. All subjects took 1.5 grams of cinnamon or placebo capsules three times a day after main meals for 60 days.	Based on the results, cinnamon consumption was effective in controlling FBS, HbA1c, and reducing insulin resistance in patients with type 2 diabetes.
Hassanzadeh et al(2012)	Clinical trial	Cinnamon	35 persons received cinnamon and 36 persons received placebo. Along with the usual daily treatment, the intervention group took 1g of cinnamon for 60 days and placebo group took the same period of placebo (microcrystalline cellulose).	In this study, the level of HbA1c was not reduced in diabetic patients
Milajerdi et al (2016)	Triple blinded randomized clinical trials (RCTs)	Saffron	48 obese women with type 2 diabetes were randomly divided into four equal groups (saffron + exercise, exercise + placebo, saffron and placebo). Saffron + exercise and placebo+ exercise groups performed the aerobic exercise with 60 to 75% intensity (three sessions per week, for 8 weeks). 400 mg of saffron powder (or wheat flour as a placebo) was used for two months.	There was a significant difference between saffron + exercise with placebo, exercise + placebo with placebo and saffron with placebo group.
Maryam Raf Raf et al (2015)	Triple-blind randomized controlled clinical trial	Fenugreek	88 diabetic patients participated in this study. Intervention group (n = 44) received 10 g of fenugreek seed powder and the control group (n = 44) received 5 g of starch twice a day for 8 weeks	FBS, HbA1c, insulin serum, and IR-HOMA levels decreased after intervention in the fenugreek seeds recipients, and the fenugreek seed improved glucose metabolism.
Yaqoubi et al (2014)	Randomized controlled clinical trial	Citrullus colocynthis	Intervention and control groups (n=28 in each group) received 100 mg capsule of colocynth processed with vinegar and placebo (capsules in the same shape and color as breadcrumbs), three times a day, respectively.	The findings showed that the consumption of colocynth reduced FBS level after one month in intervention group compared to the placebo group. No gastrointestinal, hepatic, or renal complications were observed in this study.
Amani et al (2013)	Double-blinded randomized clinical trials (RCTs)	Strawberry	Thirty-six patients (23 women and 13 men) in the experimental group received 2 cups of freeze-dried strawberry beverage (50 grams freeze-dried strawberry) and the placebo group 2 cups of placebo beverage with similar taste and color at least 2 hours after their meals	The mean decrease in glycosylated hemoglobin levels in the intervention group was significantly higher than in the control group.
Adab et al (2013)	Double-blinded randomized clinical trials (RCTs)	Turmeric	Eighty patients were divided into equal two groups. Patients received 700mg oral capsules containing of Turmeric powder or placebo three times a day for eight weeks	Turmeric powder did not have a significant effect on the glycemic status.
Ariyaeian et al(2012)	Double-blinded randomized clinical trials (RCTs)	Ginger	35 recipients of ginger powder and 35 recipients of wheat flour as a placebo (800 mg twice daily) for 12 weeks	Consumption of ginger significantly reduced the levels of FBS, insulin serum, HbA1c and insulin resistance index in the ginger group compared with the control group.

Continued

[DOR: 20.1001.1.20086792.2022.14.2.5.2]

[DOI: 10.18502/ijdo.v14i2.9456]

Authors (year)	Type of study	Type of medicinal plant	Study design	Results
Talaei et al (2011)	Double-blinded randomized clinical trials (RCTs)	Ginger	The intervention (n=42) and the control groups (n=42) took capsules containing ginger and microcrystalline cellulose as a placebo respectively for 8 weeks (1gram capsules 3 times daily).	Ginger powder reduced FBS and HbA1c in patients with diabetes.
Ahadi et al (2012)	randomized clinical trials (RCTs)	Green and Sour tea	100 diabetic patients were randomly assigned into two groups. Both groups drank 150 cc of green tea and sour tea 2 hours after each meal, three times a day for 4 weeks, each time.	There was no difference between the effects of green tea and sour tea on FBS level.
Payahoo et al(2015)	Double-blinded clinical trials (RCTs)	Dill	30 persons received dill powder and 30 persons received starch powder as a placebo (in form of 3.3g oral capsules), before main meals for 8 weeks.	Dill has a beneficial effect on fasting insulin concentrations.
Bayat et al(2016)	Parallel randomized clinical trial	Pumpkin and probiotics yogurt	Eighty patients were randomly divided into four groups 1) pumpkin consumption (100g), 2) probiotic yogurt consumption (150 g), 3) pumpkin and probiotic yogurt (100g and 150g, respectively) and 4) control group. Pumpkin and yogurt probiotics were consumed at lunch for 8 weeks.	consumption of pumpkin and probiotic yogurt separately and simultaneously reduced FBS and HbA1c.
Taleb et al (2017)	Clinical trial	Thymus kotschyanus	Patients were randomly divided into two groups (each group n=32). 1) receiving usual drugs and 2) receiving Thymus. K aqueous extracts 20 gr/day with conventional therapy. After 3 months, HbA1c, lipid profile, FBS) and 2hpp glucose were measured in both groups	Thymus kotschyanus improved the indicators for blood glucose control by significantly reducing HbA1c and FBS levels, and increasing beta-HOMA levels as a beta cell function index. However, there is no change in fasting insulin levels and the IR-HOMA index, which is an indicator of insulin resistance.
Khademian Ravandi et al (2015)	Double-blinded clinical trials (RCTs)	Garlic	The intervention group (n=25) took garlic tablets (400 mg/day) and the control group (n=25) took placebo (Microcrystalline Cellulose), before the main meals for 3 months.	The results showed that garlic reduced FBS, HbA1c and it was helpful in controlling the complications and treatment of diabetes.
Heydarian et al (2017)	Double-blinded clinical trials (RCTs)	Cumin and resveratrol supplement	165 diabetic patients were randomly divided to 4 groups: green cumin (75 mg/day), resveratrol supplement (200 mg /day), vitamin C (500 mg /day) and placebo	Resveratrol and cumin demonstrated a decrease in HbA1c level, but green cumin had better efficiency in improving glucose indicators in diabetic patients
Behradmanesh et al (2012)	Double-blinded randomized clinical trials (RCTs)	Salvia officinalis (Glycogol pill)	Subjects were randomly assigned into two groups. The intervention and control group took glycogol and placebo tablets, respectively, three times daily within three months.	In Glycogol group, compared to the controls, 2hpp blood sugar was significantly decreased. But there were no significant changes in HbA1c and FBS between the two groups.

Conclusions

Identified plants including nettle, cumin, cinnamon, saffron, fenugreek, Citrullus colocynthis, strawberry, turmeric, ginger, green tea, sour tea, dill, pumpkin, garlic, and Salvia officinalis. Among all the studies, the impact of cinnamon was investigated in five articles, cumin in two articles, and the rest of the medicinal plants were just in one study. In some research, the results indicated the positive effects of the plants on FBS and HbA1c, and in others, the consumption of medicinal plants had no beneficial effects on important variables in diabetes control. Therefore, it seems that in order to trust in using plants as complementary therapies

[DOR: 20.1001.1.20086792.2022.14.2.5.2]
[DOI: 10.18502/ijdo.v14i2.9456]

alongside conventional medical treatments in diabetic patients, more clinical evidence is needed to support the effect of plants on controlling blood sugar. As regards the methodological limitations of the studies (small sample size, short-time tests, and lack of control group or placebo), based on the available evidence, conclusions about the benefits of medicinal plants should be made cautiously. It is notable that the safety and efficacy of herbs in diabetes treatment should be investigated further and it is necessary for patients to take any herb under the supervision of their doctors and after receiving the necessary advice.

Acknowledgments

Hereby, the authors of this research appreciate all the contributors in this research and dear personnel of Yazd Diabetes Center .

Funding

This research is funded by Shahid Sadoughi University.

Conflict of Interest

The authors declare no conflict of interest, financial or otherwise.

References

1. Jafari S, Mehdizadeh A, Ghavamzadeh S. The effect of two different doses of cuminum cyminum extract on serum glycemic indices and inflammatory factors in patients with diabetes type II: a randomized double-blind controlled clinical trial. Journal of Ardabil University of Medical Sciences. 2016;16(2):200-10.(in Persian)
2. Fallah Tafti B, Vaezi AA, Moshtagh Z, Shamsi F. The assessment of barriers to the self-care behaviors in type 2 diabetic patients of Yazd province in 2014. Tolooebehdasht. 2016;15(3):115-29.(in Persian)
3. Esmaillzadeh A, Zakizadeh E, Faghihimani E, Gohari M, Jazayeri S. The effect of purslane seeds on glycemic status and lipid profiles of persons with type 2 diabetes: A randomized controlled cross-over clinical trial. Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences. 2015;20(1):47.
4. Fallah B, Moshtagh Eshgh Z. The effects of basic conditioning factors on self-care behaviors of patients with type 2 diabetes referred to Yazd Research Center, 2014.Journal of Shahid Sadoughi University of Medical Sciences. 2018;25(10):770-9.(in Persian)
5. Abdul-Ghani MA, Williams K, Kanat M, Altuntas Y, DeFronzo RA. Insulin vs GLP-1 analogues in poorly controlled type 2 diabetic subjects on oral therapy: a meta-analysis. Journal of endocrinological investigation. 2013;36(3):168-73.
6. Farhadnejad H, Asghari G, Mirmiran P, Azizi F. Association of Dietary Approach to Stop Hypertension (DASH) diet with 3-year changes in body mass index and risk of obesity in adolescents: Tehran Lipid and Glucose Study. Iranian Journal of Endocrinology and Metabolism. 2017;18(5):325-33.(in Persian)
7. Zamani-nour N, Ahmadi A, Tahbaz F. Postprandial glucose and insulin responses to onion ingestion with breakfast in patients with type 2 diabetes. Journal of Shahrekord Uuniversity of Medical Sciences. 2012;13. 2012, 13(6): 19-26.(in Persian)
8. Dashtban R, Mansouri A. A Comparative Study on the Effect of Garlic and Cumin on Glycosylated Hemoglobin in Patients with Type II Diabetes. Journal of Diabetes Nursing. 2017 10;5(3):186-79.(in Persian)
9. Milajerdi A, Jazayeri S, Bitarafan V, Hashemzadeh N, Shirzadi E, Derakhshan Z, et al. The effect of saffron (Crocus sativus L.) hydro-alcoholic extract on liver and renal functions in type 2 diabetic patients: A double-blinded randomized and placebo control trial. Journal of Nutrition & Intermediary Metabolism. 2017;9:6-11.
10. Ogbera AO, Dada O, Adeleye F, Jewo PI. Complementary and alternative medicine use in diabetes mellitus. West African journal of medicine. 2010;29(3).
11. Ghalavand A, Motamedi P, Delaramnasab M, Khodadoust M, Mahmoodkhani Koosskaki R. Cardiometabolic effects of urtica dioica in type II diabetes. Journal of Diabetes Nursing. 2017;5(1):59-69.(in Persian)
12. Al-Aboudi A, Afifi FU. Plants used for the treatment of diabetes in Jordan: A review of scientific evidence. Pharmaceutical biology. 2011;49(3):221-39.
13. Otoom SA, Al-Safi SA, Kerem ZK, Alkofahi A. The use of medicinal herbs by diabetic Jordanian patients. Journal of herbal pharmacotherapy. 2006;6(2):31-41.
14. Karaman E, Erkin O, Senman S, Yildirim Y. The use of herbal supplements by individuals with

[DOR: 20.1001.1.20086792.2022.14.2.5.2]
[DOI: 10.18502/ijdo.v14i2.9456]

diabetes mellitus. JPMA. The Journal of the Pakistan Medical Association. 2018;68(4):587-94.
15. Shahandokht N, Nojomi M, Moradilakeh M. The Common Herb In Self Herbal Medication In Diabetic Patients Refer To Diabetes Medical Health Center. Iranian Journal of Diabetes and Metabolism. 2014;13(5):413-24.(in Persian)
16. Rutebemberwa E, Lubega M, Katureebe SK, Oundo A, Kiweewa F, Mukanga D. Use of traditional medicine for the treatment of diabetes in Eastern Uganda: a qualitative exploration of reasons for choice. BMC international health and human rights. 2013;13(1):1-7.
17. Karaman E, Senman S, Yildirim Y, Erkin O. KAP Study. Journal Of Pakistan Medical Association. 2018;68(4).
18. Kesavadev J. Efficacy and safety concerns regarding Complementary and Alternative Medicine use among diabetes patients. JPMA. The Journal of the Pakistan Medical Association. 2017;67(2):316-9.
19. Mekuria AB, Belachew SA, Tegegn HG, Ali DS, Netere AK, Lemlemu E, et al. Prevalence and correlates of herbal medicine use among type 2 diabetic patients in Teaching Hospital in Ethiopia: a cross-sectional study. BMC complementary and alternative medicine. 2018;18(1):1-8.
20. Hosseini SE, Tavakoli F, Karami M. Medicinal plants in the treatment of diabetes mellitus. Clinical Excellence. 2014 Sep 10;2(2):64-89.(in Persian)
21. Aliasgarzadeh A, Mobasseri M, Bahrami A, Zargami N, Tabrizi A. Effect of extract of Urtica dioica on insulin and C-peptide secretion from rats (RIN5F) pancreatic beta cells. African journal of pharmacy and pharmacology. 2012;6(29):2176-9.
22. Tarighat EA, Namazi N, Bahrami A, Ehteshami M. Effect of hydroalcoholic extract of nettle (Urtica dioica) on glycemic index and insulin resistance index in type 2 diabetic patients. Iranian journal of endocrinology and metabolism. 2012; 13(6):561-8.(in Persian)
23. Thippeswamy NB, Naidu KA. Antioxidant potency of cumin varieties-cumin, black cumin and bitter cumin-on antioxidant systems. European food research and technology. 2005;220(5):472-6.
24. Parthasarathy VA, Chempakam B, Zachariah TJ. Chemistry of spices: Cabi; 2008.
25. Froghi M, Ghatreh SK, Heidarian E, Nikokar M, Fazeli S. Study effects of resveratrol, cuminumcyminum, essence and vitamin C on blood sugar, lipid, insulin resistance and advanced glycatedend product (AGEs) in type2 diabetic patients. 2018;20(4):169-76.(in Persian)
26. Jarvill-Taylor KJ, Anderson RA, Graves DJ. A hydroxychalcone derived from cinnamon functions as a mimetic for insulin in 3T3-L1 adipocytes. Journal of the American College of Nutrition. 2001;20(4):327-36.
27. Zahmatkesh M, Fallah Huseini H, Hajiaghaee R, Heidari M, Mehrafarin A, Tavakoli-Far B. The effects of Cinnamomum zeylanicum J. Presl on blood glucose level in patients with type 2 diabetes, a double-blind clinical trial. Journal of Medicinal Plants. 2012 10;11(41):258-63.(in Persian)
28. Baker WL, Gutierrez-Williams G, White CM, Kluger J, Coleman CI. Effect of cinnamon on glucose control and lipid parameters. Diabetes care. 2008;31(1):41-3.
29. Mirfeizi M, Mehdizadeh Tourzani Z, Mirfeizi SZ, Asghari Jafarabadi M, Rezvani H, Shoghi M. Effects of cinnamon on controlling blood glucose and lipids in patients with type II diabetes mellitus: A double blind, randomized clinical trial. medical journal of mashhad university of medical sciences. 2014;57(3):533-41.
30. Zahedifar A, Khodashenas M, Bijari B, Zahedifar F. Effects of cinnamon on fasting blood sugar and hemoglobin A1C in patients with type II diabetes mellitus: A randomized clinical trial. Journal of Mazandaran University of Medical Sciences. 2018;27(156):80-8.(in Persian)
31. Khadem Hh, Farsad Na, Pourghassem Gb, Ali Aa, Nemati A. Effect Of Cinnamon On Glycemic Control And Insulin Resistance In Type Ii Diabetes Patients: A Randomized Clinical Trial. Journal of Ardabil University of Medical Sciences. 2010;10(4):295-302.(in Persian)
32. Hasanzade F, Tolyat M M, Emami A, Barakchi A, Emamimoghaadam Z. Effect of cinnamon on HbA1c in type 2 diabetes patients. Complementary Medicine Journal of faculty of Nursing & Midwifery. 2013;2(4):303-11.(in Persian)
33. Hosseinzadeh H. Saffron: a herbal medicine of third millennium. Jundishapur journal of natural pharmaceutical products. 2014;9(1): 1-2.
34. Samarghandian S, Azimi-Nezhad M, Farkhondeh T. Crocin attenuate Tumor Necrosis Factor-alpha (TNF-α) and interleukin-6 (IL-6) in streptozotocin-induced diabetic rat aorta. Cytokine. 2016;88:20-8.
35. Razavi BM, Hosseinzadeh H. Saffron as an antidote or a protective agent against natural or chemical toxicities. DARU Journal of Pharmaceutical Sciences. 2015;23(1):1-9.
36. Grace A, Chan E, Giallauria F, Graham PL, Smart NA. Clinical outcomes and glycaemic responses to different aerobic exercise training intensities in type II diabetes: a systematic review and meta-analysis. Cardiovascular diabetology. 2017;16(1):1-0.
37. Feinman RD, Pogozelski WK, Astrup A, Bernstein RK, Fine EJ, Westman EC, et al. Dietary carbohydrate restriction as the first approach in diabetes management: critical review and evidence base. Nutrition. 2015;31(1):1-3.
38. Rafraf M, Malekiyan M, Asghari-Jafarabadi M, Asgarzadeh AA, Pourmoradian S. Effect of Fenugreek Deeds on Serum Metabolic Factors and

[DOR: 20.1001.1.20086792.2022.14.2.5.2]
[DOI: 10.18502/ijdo.v14i2.9456]

ICAM-1 (Intercellular adhesion molecule-1) levels in type 2 Diabetic Patients. Journal of Zanjan University of Medical Sciences and Health Services. 2015;23(96):11-21.(in Persian)
39. Bera TK, Ali KM, Jana K, Ghosh A, Ghosh D. Protective effect of aqueous extract of seed of Psoralea corylifolia (Somraji) and seed of Trigonella foenum-graecum L.(Methi) in streptozotocin-induced diabetic rat: A comparative evaluation. Pharmacognosy research. 2013;5(4):277.
40. Hamden K, Mnafgui K, Amri Z, Aloulou A, Elfeki A. Inhibition of key digestive enzymes related to diabetes and hyperlipidemia and protection of liver-kidney functions by trigonelline in diabetic rats. Scientia pharmaceutica. 2013;81(1):233-46.
41. Yoshikawa M, Morikawa T, Kobayashi H, Nakamura A, Matsuhira K, Nakamura S, et al. Bioactive saponins and glycosides. XXVII. Structures of new cucurbitane-type triterpene glycosides and antiallergic constituents from Citrullus colocynthis. Chemical and Pharmaceutical Bulletin. 2007;55(3):428-34.
42. Benariba N, Djaziri R, Bellakhdar W, Belkacem N, Kadiata M, Malaisse WJ, et al. Phytochemical screening and free radical scavenging activity of Citrullus colocynthis seeds extracts. Asian Pacific journal of tropical biomedicine. 2013;3(1):35-40.
43. Zareei MA, Fallahhossini F, Sharifabady R, Nourouzzadeh A, Imani H, Ghoshouni H. The effect of Citrullus colocynthis extract on preventing/reducing streptozotocin-induced diabetes in rat. Kowsar Medical Journal. 2007;12(1):13-20.(in Persian)
44. Rahimi R, Amin G, Ardekani MR. A review on Citrullus colocynthis Schrad.: from traditional Iranian medicine to modern phytotherapy. The journal of alternative and complementary medicine. 2012;18(6):551-4.
45. Yaghoobi MA, Miri-Moghaddam E, Navidian A, Nikbakht R, Mehrafarin A, Fallah Huseini H. Safety and Efficacy of Processed Citrullus colocynthis L. Fruit in Treatment of Hyperlipidemic Type II Diabetic Patients: A Randomized, Placebo-controlled Clinical Trial. Journal of Medicinal Plants. 2014;13(52):81-8.
46. Orak HH, Aktas T, Yagar H, Isbilir SS, Ekinci N, Sahin FH. Effects of hot air and freeze drying methods on antioxidant activity, colour and some nutritional characteristics of strawberry tree (Arbutus unedo L) fruit. Food Science and Technology International. 2012;18(4):391-402.
47. Manzano S, Williamson G. Polyphenols and phenolic acids from strawberry and apple decrease glucose uptake and transport by human intestinal Caco-2 cells. Molecular nutrition & food research. 2010;54(12):1773-80.
48. Amani R, Moazzen S, Shahbazian H, Ahmadi Ankali K, Homayouni Rad A, Jalali M. Effects of freeze-dried strawberries on lipid profile and glycated hemoglobin in subjects with type 2 diabetes: a double blind randomized control trial. Iranian Journal of Nutrition Sciences & Food Technology. 2013;8(3):189-200.(in Persian)
49. Adab Z, Eghtesadi SH, Vafa MR, Heydari I, Shojaei A, Haqqani H, Khorraminia N. Effect of turmeric on body measurement indices, glycemic condition, and lipid profile in hyperlipidemic patients with type 2 diabetes. Iranian Journal of Nutrition Sciences & Food Technology. 2013;8(3):217-27. (in Persian)
50. Alappat L, Awad AB. Curcumin and obesity: evidence and mechanisms. Nutrition reviews. 2010;68(12):729-38.
51. Talaei B, MOZAFARI KH, Jalali B, Mahammadi SM, Najarzadeh A, Fallahzadeh H. The effect of ginger on blood glucose, lipid and lipoproteins in patients with type 2 diabetes: a double-blind randomized clinical controlled trial.Journal of Shahid Sadoughi University of Medical Sciences. 2012;20(3):383-95.(in Persian)
52. Aryaeian N, Arablou T, Sharifi F, Hosseini A, Valizadeh M. Effect of ginger consumption on glycemic status, insulin resistance, and inflammatory markers in patients with type 2 diabetes mellitus. Iranian Journal of Nutrition Sciences & Food Technology. 2014;9(1):1-0.(in Persian)
53. Kim MJ, Yoo KH, Park HS, Chung SM, Jin CJ, Lee Y, et al. Plasma adiponectin and insulin resistance in Korean type 2 diabetes mellitus. Yonsei medical journal. 2005;46(1):42-50.
54. Bhathena SJ, Velasquez MT. Beneficial role of dietary phytoestrogens in obesity and diabetes. The American journal of clinical nutrition. 2002;76(6):1191-201.
55. Sáyago-Ayerdi SG, Arranz S, Serrano J, Goñi I. Dietary fiber content and associated antioxidant compounds in roselle flower (Hibiscus sabdariffa L.) beverage. J. of Agricultural and Food Chemistry. 2007;55(19):7886-90.
56. Mozaffari–Khosravi H, Afkhami Ardekani M, Jalali-Khanabadi BA, Fallahzadeh H. Comparison of the Effect of Green and Sour Tea on Blood Glucose and Lipids Profile in Patients with Type 2 Diabetes Mellitus. Tolooebehdasht. 2013;11(3):113-24.(in Persian)
57. Payahoo LA, Khaje-Bishak Y, Mobasseri MA, Ostadrahimi AL, Asghari-Jafarabadi M. The effects of Anethum graveolens L supplementation on the insulin resistance and inflammatory biomarkers in patients with type 2 diabetes. Journal of Isfahan Medical School. 2015;32(320):2473-83.(in Persian)
58. Kaur GJ, Arora DS. Bioactive potential of Anethum graveolens, Foeniculum vulgare and

Trachyspermum ammi belonging to the family Umbelliferae-Current status. Journal of Medicinal Plants Research. 2010;4(2):087-94.
59. Kazemi S, Asgari S, Moshtaghian SJ, Rafieian M, Mahzooni P. Preventive effect of pumpkin (Cucurbita Pepo L.) on diabetic index and histopathology of pancreas in alloxan-induced diabetes in rats. Journal of Isfahan Medical School. 2011;28(117):1108-17.(in Persian)
60. Bayat A, Azizi-Soleiman F, Heidari-Beni M, Feizi A, Iraj B, Ghiasvand R,et al. Effect of Cucurbita ficifolia and probiotic yogurt consumption on blood glucose, lipid profile, and inflammatory marker in type 2 diabetes. International Journal of Preventive Medicine. 2016;7.
61. Raja RR. Medicinally potential plants of Labiatae (Lamiaceae) family: an overview. Research journal of medicinal plant. 2012;6(3):203-13.
62. Patel DK, Prasad SK, Kumar R, Hemalatha S. An overview on antidiabetic medicinal plants having insulin mimetic property. Asian Pacific journal of tropical biomedicine. 2012;2(4):320-30.
63. Zarei A, Vaezi G, Malekirad AA, Abdollahi M. Effects of ethanol extract of Salvia hydrangea on hepatic and renal functions of streptozotocin-induced diabetic rats. Avicenna journal of phytomedicine. 2015;5(2):138-147.
64. Aqababa H, Chobineh MA, Zarei A, Changizi Ashtiyani S. The effect of ethanol extract of aerial parts of Salvia hydrangea L. on plasma biochemical factors in male rats with hypercholesterolemia. Qom University of Medical Sciences Journal. 2016;10(4):78-85.(in Persian)
65. Taleb AM, Qannadi F, Changizi-Ashtiyani S, Zarei A, Rezvanfar MR, Akbari A, et al. The effect of aqueous extract thymus kotschyanus boiss. Et hohen on glycemic control and dyslipidemia associated with type II diabetes: A randomized controlled trial. Iranian Journal of Endocrinology and Metabolism. 2017;19(4):234-43.(in Persian)
66. Shahdadi H, Mansouri A, Dashtban R. A Comparative Study On The Effect Of Garlic And Cumin On Blood Pressure In Patients With Type 2 Diabetes: A Clinical Double-Blind Trial. Nursing And Midwifery Journal. 2017;15(8):605-11.(in Persian)
67. Khademian-Ravandi R, Mozaffari-Khosravi H, Esteghamati A, Meysami A. The effect of garlic tablet on blood glucose, and lipid profile in type 2 diabetic patients: a double-blind randomized placebo controlled trial. Journal of Shahid Sadoughi University of Medical Sciences. 2015;23(7):621-30.(in Persian)
68. Sajjadi F, Baghbanian P, Asgari S, Naderi G, Alikhasi H, Mohammadi Fard N. The effect of hydroalcoholic extract of Salvia officinal on diabetic patients. International Journal Of Research In Medical Sciences. 2003;4(7):318-24.
69. Schnitzler P, Nolkemper S, Stintzing FC, Reichling J. Comparative in vitro study on the anti-herpetic effect of phytochemically characterized aqueous and ethanolic extracts of Salvia officinalis grown at two different locations. Phytomedicine. 2008;15(1-2):62-70.
70. Jedinák A, Muč ková M, Košťálová D, Maliar T, Mašterová I. Antiprotease and antimetastatic activity of ursolic acid isolated from Salvia officinalis. Zeitschrift für Naturforschung C. 2006;61(11-12):777-82.
71. Christensen LP. Ginsenosides: chemistry, biosynthesis, analysis, and potential health effects. Advances in food and nutrition research. 2008;55:1-99.
72. Sievenpiper JL, Sung MK, Di Buono M, Seung-Lee K, Nam KY, Arnason JT, et al. Korean red ginseng rootlets decrease acute postprandial glycemia: results from sequential preparation-and dose-finding studies. Journal of the American College of Nutrition. 2006;25(2):100-7.
73. Behradmanesh M, Ahmadi M, Rafieian-Kopaei M. Effect of glycogol on blood glucose level of patients with type II diabetes. Iranian Journal of Endocrinology and Metabolism. 2012;14(2):163-8.(in Persian)

[DOR: 20.1001.1.20086792.2022.14.2.5.2]
[DOI: 10.18502/ijdo.v14i2.9456]