Herbal Medicines in Diabetes

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ABSTRACT
The use of herbal medicines in diabetes is promising but still far from proven. The purpose of this article is to examine the effect of herbal medicines in the treatment of diabetes, focusing on potential benefits and risks.

Medline, expert interviews, books, articles and internet searches were used to identify herbal medicines with anti-diabetic properties and their diabetes-related health effects, proposed anti-diabetic effect, adverse effects, contraindications and drug interactions. Forty five herbs with known effect in the treatment of diabetes were selected for review, including: Trigonella foenum graecum L, Allium cepa L. & Allim sativum L., Silybum marianum, Mamordica charantia L., Camellia sinensis L. Morus nigra L., Gymnema sylvestre L., Ginkgo biloba L., …. Anti-diabetic health effects included increasing serum insulin, decreasing blood glucose, increasing glucose metabolism, and/or stimulating pancreatic function. Side effects were few or not reported. Many herbal medicines can be used for treatment, prevention and control of diabetes and as a component of diabetic patients’ diet. Of course some of these plants have adverse effects, contraindications, and drug interactions and also interactions between herbal medicines and synthetic drugs exist and may cause serious clinical consequences however at these researches side effects were few or not reported, but patients should inform their physician of the use of herbal products and consider the possibility of herb-drug interactions.

KEYWORDS: herbal medicine, diabetes, research

INTRODUCTION
Diabetes mellitus is one of the most important health problems in all countries, and despite great improvement in its treatment, serious complications such as retinopathy, nephropathy and lower extremity amputation are still observed (1). Diabetes is the most common endocrine disorder that affects more than 194 million people worldwide (2). If nothing is done to control this disease, the number will exceed 333 million by 2025 (6.3% of population) (2).

In diabetic patients, medical education programs for pharmacists and patients, offering medical advice about blood glucose control, beginning and adjustment of insulin doses is important (3). According to the Iranian Diabetes Society, in 1990, the prevalence of diabetes in Iran was more than 8 percent (about 3 million people) (4). High prevalence of diabetes among working segments of the society could have serious consequences especially in developing countries (5). In Isfahan in 1993, 7/54% of people 40 years-old and older suffered from diabetes (6). Insulin deficiency or reduction in diabetic patients is associated with acute and chronic metabolic complications (7). In a study conducted in 2007, fluctuations in drugs, especially in the case of insulin in pharmacies
in Isfahan, were perfectly clear (8). On the other hand, while the main and effective treatments of diabetes mellitus are insulin and hypoglycemic agents, these medications result in such undesirable side effects as hyperglycemia which could be a major safety concern (9).

One of the main factors for treatment to be successful is the correct and logical use of herbal medicines or chemical drugs (10). Although, from ancient times, medicinal plants and their derivatives were considered in the treatment of diabetes mellitus and its complications, the exact effectiveness of these drugs is not completely known (11). Appropriate diet and alternative therapies, can reduce the cost of treatment and prevent or cure many cases of type II diabetes and improve some cases of type I diabetes. Medicinal plants consumption is remarkable particularly when conventional therapies are not able to control the disease and patients need insulin (12).

Karaka and Susrota and many other medicinal plants with various oral formulations have been recommended for the treatment of diabetes (13). Of course, the use of herbal medicines instead of chemical drugs, depends on the physician’s opinion about this drugs in addition to patient beliefs (14).

Due to side effects of some chemical drugs, and the beliefs of some people to practice traditional medicine, folk medicine especially the herbal therapy used to treat diabetes and its values and positive aspects should be studied (1,15).

In this study, we have reviewed the latest medical literature on the effect of anti-diabetic medicinal plants on diabetes and we have not intended to advise the usage of the effective medical plants on diabetes directly or indirectly. There are several reviews by different authors about anti-diabetic herbal plants (16-18). In a review more than 300 plant species with hypoglycemic properties are introduced (19). Also in reviewing the literature, we found a paper entitled "Review of anti-diabetic medicinal plant used in traditional medicine" in year 2006 which was written by Dr. Falah Hosseini H et al (20).

**MATERIALS AND METHODS**

We used Medline, expert interviews, books, papers and searching the internet to determine the effects of anti-diabetic medicinal plants, plants which were claimed to have association with diabetes, plants which were proposed for anti-diabetic effects as well as plants with incompatible interactions.

Forty-five plants have been selected and were reviewed (these plants had a role in treating diabetes). Such as fenugreek, garlic, onion, Mary thistle plant, bitter cucumber, green tea, mulberry plant, plant Gymnema Sylvester, Ginkgo Biloba and ....

Anti-diabetic effects of herbal medicine include: increasing serum insulin, lowering blood glucose, increasing glucose metabolism and/or stimulating the pancreas. In this study, side effects were not frequent or not reported.

**DISCUSSION**

Review on research done:

Fenugreek (Trigonella Foenum Graecum L), is one of the safest and most effective plants in treating diabetes. Fenugreek extract, like insulin, significantly reduces blood sugar levels (21). Clinical and laboratory studies also have shown that fenugreek seeds have anti-diabetic effects (22).

"Bitter melon" (Momordica Charantia) is an alternative therapy that has primarily been used for lowering blood glucose levels in patients with diabetes mellitus (23). "Bitter melon" fruit extract reduces blood glucose and is effective in treating diabetes (24).

Garlic has been reported to possess a variety of medicinal properties including hypoglycemic, hypocholesterolemic and hypolipidemic activities (25) and several studies suggest that garlic and onion (Allium Cepa L. & Allim Sativum L.) have roles in reducing blood glucose levels due to producing active nitrogen compounds (2, 26). Raw garlic possesses a beneficial potential in reversing proteinuria in addition to reducing blood sugar, cholesterol and triglyceride in....
diabetic rats. Therefore, garlic could be of great value in managing the effects and complications of diabetes in affected individuals (2).

Silybum Extract (Silybum Marianum L. Gaertn) or silymarin is also one of the plants used in the treatment of liver disorders. This herb increases the cellular sensitivity to insulin and thus reduces blood glucose (27).

In another research it was shown that prescription of herbal silymarin (Mary's thistle) for type II diabetic patients who were candidates of insulin therapy, reduces glycosylated hemoglobin, blood glucose (fasting and two hours postprandial) and serum total cholesterol and LDL levels in these patients (28).

Bitter cucumber plant fruit (Mamordica Charantia L.) have polypeptide composition similar to insulin but with less complications. This plant doesn’t need subcutaneous injection and can reduce blood glucose I patients with type 1 diabetes. Also sap of this plant that is very bitter is used for reducing blood sugar (29).

Oral administration of mountain celery (Apium Graveolens L.) for 6 weeks, in an experimental model of diabetes mellitus had no significant hypoglycemic effect, but it caused desirable and beneficial changes in blood lipid levels (30).

Green tea (leaves of Camellia Sinensis, Theaceae) is a popular beverage in East Asia, and also is used as an herbal remedy in Europe and North America (31). Green tea (Camellia Sinensis L.) can reduce blood sugar in diabetic patients. Studies show that the consumption of one and a half gram dry powder of green tea, can improve the metabolism of blood sugar in diabetic patients (32). Tea offers an attractive potential strategy to regulate postprandial hyperglycemia toward an overall dietary support for type 2 diabetes management (33).

Kampuchea tea and black tea prevent weight loss in animals that is a sign of diabetes (34). Morus Nigra, commonly known as black mulberry, is widely used in Brazilian folk medicine for the treatment of diabetes (35). Black mulberry (Morus Nigra L.) leaves also has the effect of compounds that are hypoglycemic, although their mechanism of action in reducing serum glucose is not yet properly clear (36).

Mary pea (Teucricum Vulgare) can be used to control blood sugar in diabetic patients (37). Madhunashini (Gymnema Sylvestre R. Br.) commonly known as ‘Gudmar’ in India is an important medicinal climber and is extensively used in almost all Indian System of Medicine as a remedy for diabetes (38). Clinical research shows that this plant is effective in treating patients with type I and II diabetes (39 and 40).

Ginkgo biloba plant (Ginkgo Biloba L.) plays an important role in increasing blood flow in diabetic patients (41). This plant as an herbal medication is capable of lowering glucose, fat, and lipid peroxide in diabetic patients (42).

According to researches in the field, hydro-alcoholic extract of artichoke (Cynara Scolymus L.) affects blood glucose, serum lipids and lipoproteins in diabetic rats with Alexon monohydrate. The extract can repair the damaged pancreas as well, therefore, further researches are needed to investigate artichokes effect on diabetic patients (43).

In a research for assessing hypoglycemic effects of Allium porrum L. leaves in healthy and streptozotocin-induced diabetic mice, this result was obtained: the ethanol extract of leaves of this plant had hypoglycemic effects on diabetic animals and perhaps its mechanism is increasing insulin release (44).

In a research, the efficacy of stalk extract of Rheum Ribes L. on blood lipids was determined in type II diabetic patients with hypercholesterolemia. Daily administration of 1200 mg of rhubarb plant stems extract to type II diabetic patients with high blood fat caused reduced fat and fasting blood glucose concentration with no side effects on blood biochemical factors related to liver and kidney (45).

Saponin from Tribulue Terrestris could significantly reduce the level of serum glucose (46). In a study entitled "investigation of the hypoglycemic effect of caltrop plant (Tribulus Terrestris L.) extract on diabetic rats" fruit
hydro-alcoholic extract of this plant caused a
dose-dependent decrease of blood sugar in
diabetic rats and the authors proposed longer
investigations with more focus on side effects
among the target population (47).

Use of plant cactus fruit (Opuntia Ficus -
Indica L.) by some indigenous people also
have been reported for diabetes, but in a study
about cactus fruit effect on blood glucose
levels in streptozotocin-induced diabetic rats
with, no significant effects on fasting blood
glucose levels and weight of streptozotocin-
induced diabetic rats and also in non-diabetic
rats was seen (48).

Colocynth (Citrullus Colocynthis) is
prescribed by many medicinal plants sellers
for decreasing blood sugar in diabetic patients,
but scientific valid information about the
clinical anti-diabetic effects and toxicity of
this plant does not exist. In a study,
administration of 100 mg colocynth three
times a day to patients with type II diabetes
reduced fasting blood glucose and HbA1C and
administration of this dose 2 months to the
patients didn’t cause any gastrointestinal, liver
and renal side effects. But at the conclusion of
this research, to ensure about the efficacy of
this dose of colocynth another study with
larger sample size and longer duration was
proposed (49).

Hypoglycemic effect of alcoholic extract of
olive leaf (Olea Europaea L.) in healthy adult
male rats which have become diabetic by
streptozotocin was shown; Oral administration
of alcohol extract of olive leaf caused
significant increase in serum insulin levels of
diabetic animals and this is similar to the
effect of gliben clamide (50).

Olive leaf extract inhibits high glucose-
induced neural damage and suppresses
diabetes-induced thermal hyperalgesia. The
mechanisms of these effects may be due to
reduced neuronal apoptosis (51).

Also a study on wheat bran and plantain show
that wheat bran increased serum HDL (p
<0.01) and plantain consumption increased
HDL (p <0.001) and reduced LDL (p <0.02)
(52).

Prescription of meat extracts from leaves of
Aloe (Aloe Vera L.) significantly reduced
blood glucose in both types of diabetes (Type I
and Type II); this plant is effective in
preventing diabetic complications such as
diabetic ulcers (53).

New studies show that Salacia Oblonga, a
pharmaceutical plant in medicine of ancient
India, can help to control blood glucose in type
2 diabetic patients. In ancient Indian medicine
the stem and root of this plant which grows in
India and Sri Lanka with the names Ponkoranti
and Saptrangi was used for obesity and
diabetes.

This plant besides appropriate diet, physical
activity and consumption of medications are
able to control type II diabetes (54).

On a study it was shown that long-term and
oral administration of plant Walcott (Allium
Ursinum L) in an experimental model of
diabetes mellitus, was effective in reducing the
contractile response of the vascular system and
prevention of the development of hypertension
in diabetic rats (55).

Fig leaf reduces blood glucose in diabetic rats
(56). The laboratory and the animal studies
show that cinnamon raises the glucose
metabolism about twenty times. Diabetic
patients can help themselves by adding a little
cinnamon to their food. Cinnamon helps to
recognize fat cells and respond to insulin.
Bioactive compounds may increase the effects
of insulin (57).

Borage plant can stimulate insulin secretion
and be effective in the treatment of diabetic
patients (58).

Sage (Salvia Officinalis) reduces blood sugar.
Of course, you must be careful in taking it too,
because taking high doses of it can cause
significant hypoglycemia and even death (59).

Ginseng plant is used for treatment and
prevention of diabetes (60).

Plant crap (Securigera Securidaca) is one of
the plants of traditional medicine with
attributed lowering blood sugar effect. Hydro-
alcoholic extract of Securigera Securidaca
seeds can reduce blood glucose levels in the
rats and probably with more researches this
plant will probably be introduced as a drug to treat diabetes (61).
The effect of Allium Ampeloprasum consumption on serum level of glucose, triglyceride, and total cholesterol of diabetic rats was identified. Oral administration of Allium Ampeloprasum for one month caused significant reduction in the level of glucose, cholesterol and triglyceride in experimental models of diabetes mellitus induced by streptozotocin in rats (62).
In a research entitled "effect of nutrients containing bean and chicory on blood glucose of diabetic rats" results showed that the diet containing chicory, reduced blood glucose concentration. Chicory diet for reducing blood sugar in diabetic animals is more effective than beans diet and chicory and also has a direct relation with consumption percentage of chicory. This diet is probably effective in the treatment of type I diabetes mellitus in humans (63).
Study on the effect of coriander, pomegranate and walnut leaves on serum biochemical parameters of diabetic rats showed that consumption of pomegranate significantly reduced cholesterol, triglyceride and enzyme activity of serum AST and ALT (P<0/05), but the most effective ones in reducing glucose, cholesterol, triglyceride, and enzyme activity of ALP, AST, ALT were walnut tree leaves (64).
In a study on diabetic rats, glucose, cholesterol, triglyceride, creatinine, ALT, AST and ALP, were compared with healthy rats that used celery, carrot and apple tart. All of them showed significantly reduced blood sugar, but overall, the most effective one in reducing glucose, creatinine and serum AST and ALT enzyme activity, was celery (65).
Dietary fibers such as psyllium can reduce blood sugar (66).
Salt grass plant (Atriplex Halimus L.) is effective in the treatment of type II diabetic patients (67).
Black Gylh (Vaccinium Arctostaphylos L.) which grows in the forests of northern Iran has anti-diabetic effects. The plant's active ingredient is Myrtylyn anthocyanosides and has effects similar to insulin, but weaker (68).
Saffron is used in folk medicine for treatment of diabetes (69).
In another study entitled "protective effect of saffron extract and crocin on reactive oxygen species-mediated high glucose-induced toxicity in PC12 cells" showed that crocin in saffron can affect diabetes but this combination has not been tested on people with diabetes by now, however, preliminary results show saffron has a positive effect on diabetes (70).
Finally (Securigera Secuidaca L) seed , that is known as bitter lentils in grocery stores, is commonly used for reducing blood sugar in diabetic patients in Iranian traditional medicine, but so far no scientific clinical study have been reported for evaluation of its therapeutic effects or toxicity in diabetic patients (71).

CONCLUSION
Many herbs can help to treat, prevent and control diabetes, but some of them have side effects or interactions.
On the other hand, there are interactions between herbal and synthetic drugs that can lead to adverse clinical results, although in most researches little or no side effects were reported, nonetheless the patient and the physician should take care when using medicinal plants.

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