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Review

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saberabaszade1370@gmail.com**Abstract**

Diabetes mellitus is a syndrome that is characterized by hyperglycemia, change in the metabolism of lipids, carbohydrates, and proteins, and in the long term, with eye, kidney, cardiovascular, and neurological complications. Plenty of plants from different regions of the world have been investigated for anti-diabetic effects. This review article was designed to report some of the most important medicinal plants with hypoglycemic properties according to reliable clinical and laboratory evidence, and also touched on the medicinal plants that are prescribed in Iranian traditional medicine, for the treatment of diabetes. The information in this review was obtained from the eligible articles retrieved using the search terms diabetes mellitus, medicinal plants, type 1 diabetes and medicinal plants, type 2 diabetes and medicinal plants, and the effect of extract and essential oil of medicinal plants affecting diabetized tissues in the human body indexed in databases such as Iran medex, Irandoc, ISI, PubMed, Scopus, SID, Magiran, Google Scholar, etc. Based on the results drawn in this review the plants, *Urtica*, *Trigonella foenum-graecum*, *Allium sativum*, *Carthamus tinctorius*, *Ferula assa-foetida*, *Bauhinia*, *Gymnema sylvestre*, *Swertia*, *Combretum*, *Sarcopoterium*, *Liriope*, *Caesalpinia bonduc*, *Coccinia grandis*, *Syzygium cumini*, *Mangifera indica*, *Momordica charantia*, *Ocimum tenuiflorum*, *Pterocarpus*, *Tinospora cordifoli*, *Salvia officinalis*, *Panax*, *Cinnamomum verum*, *Abelmoschus moschatus*, *Vachellia nilotica*, *Achyranthes*, *Fabaceae*, *Mentha*, *Asphodelaceae*, *Andrographis paniculata* L, *Artemisia herba-alba*, *Artemisia dracunculus*, *Azadirachta indica*, *Caesalpinioideae*, *Pachira aquatic*, *Gongronema latifolium*, *Nigella Sativa*, *Tinospora cordifolia* (guduchi), *Chrysanthemum morifolium*, *Zingiber zerumbet*, *Symphytum*, *Cactaceae*, *Symplocos*, *Perilla frutescens*, *Terminalia chebula* and *Aloe vera* are effective to control and treat diabetes.

The most useful medicinal herbs to treat diabetes

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1. Introduction

Diabetes mellitus is a syndrome that is characterized by hyperglycemia, change in the metabolism of lipids, carbohydrates, and proteins [1]. Diabetes mellitus is the most common chronic and metabolic disease characterized by an increase in glucose levels due to absolute or relative insulin deficiency. The disease is associated with eye, renal, cardiovascular, and neurological complications in the long term. This disease is also associated with symptoms such as polyuria, fatigue, weight loss, delayed wound healing, blurred vision, increases in urine glucose levels, etc. [2-4]. Destruction of beta-cells of the islets of Langerhans in the pancreas and consequently development of insulin-dependent diabetes is one of the impairments of the regulation of the immune system. Several environmental and genetic factors affect the immune system, leading to the attack of lymphocytes, especially lymphocytes, and pancreatitis. This inflammatory response may cause insulinitis and diabetes [5,6]. There are currently more than 150 million people with diabetes across the globe, which seems to reach 300 million by 2025 [7]. In the absence of proper treatment, cardiac, vascular, neurological, and renal damage and neuropathy may occur. Treatment includes diet, exercise, and medication [8]. Currently, the main and effective treatment for diabetes is the use of insulin and hypoglycemic drugs, but these compounds also have many adverse side effects [9]. Medicinal plants have a long history of usage and today, they are being extensively used for various diseases [10-14]. There are several reasons for increasing the use of medicinal plants. Many plants from different parts of the world have been investigated for antidiabetic effects. This review article reported some of the most important medicinal plants with hypoglycemic properties according to reliable clinical and laboratory evidence, and also touched on the medicinal plants that are prescribed, in Iranian traditional medicine, for the treatment of diabetes.

2. Materials and methods

The information in this review was obtained from the eligible articles retrieved using the search terms *diabetesmellitus*, *medicinal plants*, *type 1 diabetes and medicinal plants*, *type 2 diabetes and medicinal plants*, and *the effect of extract and essential oil of medicinal plants affecting diabetized tissues in the human body* indexed in databases such as *Iran medex*, *IranDoc*, *ISI*, *PubMed*, *Scopus*, *SID*, *Magiran*, *Google Scholar*, etc.

3. Results

Based on the results drawn in this review the studies, *Urtica*, *Trigonella foenum-graecum*, *Allium sativum*, *Carthamus tinctorius*, *Ferula assa-foetida*, *Bauhinia*, *Gymnema sylvestre*, *Swertia*, *Combretum*, *Sarcopoterium*, *Liriope*, *Caesalpinia bonduc*, *Coccinia grandis*, *Syzygium cumini*, *Mangifera indica*, *Momordica charantia*, *Ocimum tenuiflorum*, *Pterocarpus*, *Tinospora cordifolia*, *Salvia officinalis*, *Panax*, *Cinnamomum verum*, *Abelmoschus moschatus*, *Vachellia nilotica*, *Achyranthes*, *Fabaceae*, *Mentha*, *Asphodelaceae*, *Andrographis paniculata* L, *Artemisia herba-alba*, *Artemisia dracuncululus*, *Azadirachta indica*, *Caesalpinioideae*, *Pachira aquatic*, *Gongronema latifolium*, *Nigella Sativa*, *Tinospora cordifolia (guduchi)*, *Chrysanthemum morifolium*, *Zingiber zerumbet*, *Symphytum*, *Cactaceae*, *Symplocos*, *Perilla frutescens*, *Terminalia chebula* and *Aloe vera* are effective to control and treat diabetes. The names, families, and used parts of the medicinal plants are summarized in **Tables 1, 2, 3, 4 and 5**. The mechanism of the effect of these drugs is shown in **Tables 6 and 7**.

4. Discussion

Diabetes is a condition that is characterized by high blood sugar levels. Millions of people worldwide are affected by the disease. Research on diabetes is ongoing. When a person develops

Table 1. Medicinal herbs and therapeutic information in diabetes

No.	Scientific Name	Part of plant	Family Name	Common Name	Origin of plant	Count of study	Year	Result	Ref
1	URTICA DIOICA (U. dioica)	Leaves	<i>Urticaceae</i>	stinging nettle	It is native to Europe, Asia, northern Africa	Bangladesh	In vivo 2009	Aqueous extract of U. dioica leaf improved the glycaemia levels in type 2 diabetic rats, which is mediated by the central effect on the functional status of pancreatic beta-cells.	[35]
2	Trigonella foenum graecum	Seed	<i>Fabaceae</i>	fenugreek	Indian	Iran	In vivo 2005	15 grams of powdered fenugreek prescribed to patients with type II diabetes is reduced Darqndkhvn sense.	[36]
3	Carthamus tinctorius	Flower	<i>Compositae</i>	Safflower	India, the United States and tonnes and Kazakhstan	Iran	In vivo 2016	The hydroalcoholic extract of C. tinctorius flower can be used to treat type 1 and type 2 diabetes. The phytochemical analyses of C. tinctorius flower show that it is a rich source of flavonoids, such as quercetin and kaempferol, that are the causes of antioxidant and hypoglycemic effects of these compounds.	[37]
4	Ferula assafoetida	Gum	<i>Apiaceae</i>	Asafoetida	Iran and Afghanistan	Iran	In vivo 2016	Due to the presence of antioxidant compounds, F. assafoetida gum can reduce the amount of free radicals in the cell and stimulate the synthesis and secretion of insulin in type 2 diabetes, and hyperplasia of residual pancreatic cells and reduce glucose in the blood.	[38]
5	Bauhinia forficata	Leaf	<i>Leguminosae</i>	Brazilian orchid tree	Argentina, Brazil and Peru	India	In vitro 2010	After 31 days of treatment with decoction, in the type 2 diabetic group, plasma glucose and urinary glucose levels significantly decreased.	[39]
6	Gymnema sylvestre	Leaf	<i>Asclepiadaceae</i>	cowplant,	central India and Sri Lanka	India	In vitro 2010	The G. sylvestre crude extracts and the compound isolated from it, dihydroxy gymnemic triacetate, exhibit hypoglycemic effect in rats with streptozotocin-induced diabetes mellitus in dose- and time-dependent manner.	[38]

Table 2. Medicinal herbs and therapeutic information in diabetes (Table 1 continued)

No.	Scientific Name	Part of plant	Family Name	Common Name	Origin of plant	Country of study	Year	Result	Ref
7	Swertia punicea	Whole plant	Gentianaceae	Swertia	much of Eurasia and western North America	India	In vitro	The action mechanism of hypoglycemic effect of S. punicea was confirmed by the improvement of insulin resistance in the mice with diabetes.	[38]
8	Combretum Micranthum	Leaves	Combretaceae	known as kinkeliba in Benin, Senegal and known as 'geza' in Hausa	Africa	India	In vitro	The hypoglycemic activity of this plant's extract was tested by using glucose tolerance and fasting blood sugar assessment in normal rats. The aqueous extract of C. micranthum leaf was has potential antidiabetic property for both type 1 and type 2 diabetes mellitus.	[38]
9	Sarcopoterium spinosum	Root	Rosaceae	S. spinosum	southeast Mediterranean region	India	In vitro	The aqueous extract of S. spinosum root may produce antidiabetic effect on progressive hyperglycemia in genetically diabetic mice. The aqueous root extract of the plant shows insulin-like actions in targets tissues.	[38]
10	Liriope spicata	Leaves	Liliaceae	monkey grass	East Asia and china	India	In vitro	The aqueous extract of the plant caused a marked decrease of fasting blood sugar level and a significant improvement of glucose tolerance and insulin resistance in streptozotocin-induced type 2 diabetic mice, confirming its hypoglycemic effects.	[38]
11	Caesalpinia bonducella	Seeds	Caesalpinaceae	Gray Nicker	india	India	In vitro	The aqueous and 50% ethanolic extracts of C. bonducella seed showed antihyperglycemic and hypolipidemic activities in streptozotocin-diabetic rats. Both the aqueous and ethanolic extracts showed potent hypoglycemic activity in chronic type II diabetic models. the antihyperglycemic action of the seed extracts may be due to the blockage of glucose absorption.	[39]
12	Coccinia indica	Leaves and shoots	Cucurbitaceae	Gourd	Worldwide	India	In vitro	Oral administration of 500 mg/kg of C. indica leaf produced significant hypoglycemic effects in all experimental groups. The aqueous extract showed hypoglycemic effects in both normal and diabetic dogs.	[39]

Table 3. Medicinal herbs and therapeutic information in diabetes (Table 1 continued)

No.	Scientific Name	Part of plant	Family Name	Common Name	Origin of plant	Countr Of study	Year	Result	Ref
13	<i>Syzygium cumini</i>	Seeds	Myrtaceae	Jambolan	Indian Subcontinent and Southeast Asia	India	In vitro 2007	The extract of jamun pulp showed hypoglycemic activity in streptozotocin-diabetic mice within 30 min of administration while the seed of the same fruit needed 24 h. These extracts also inhibited insulinase activity in the liver and kidney.	[39]
14	<i>Mangifera indica</i>	Leaves	Anacardiaceae	mango	in Bangladesh, India and Pakistan	India	In vitro 2007	The results indicated that aqueous extract of <i>M. indica</i> has hypoglycemic activity. This may be due to a reduction in the intestinal glucose absorption.	[39]
15	<i>Momordica charantia</i>	Fruit pulp, seed, leaves and whole plant	Cucurbitaceae	bitter melon	grown in Asia, Africa, and the Caribbean	India	In vitro 2007	Ethanol extracts of <i>M. charantia</i> (200 mg/kg) showed an antihyperglycemic and hypoglycemic effect in normal and streptozotocin-diabetic rats. This may be because of inhibition of glucose-6-phosphatase and fructose-1, 6-biphosphatase in the liver and stimulation of hepatic glucose-6-phosphate dehydrogenase activities.	[39]
16	<i>Salvia nemorosa</i>	Aerial part	Lamiaceae	s. nemorosa	Central Europe and Western Asia	Iran	In vitro 1387	These aerial parts of the plant that contain megastigmane glycoside and salvionoside cause a significant increase in insulin levels in diabetic rats compared to healthy rats, and is also responsible for intense insulin activity.	[40]
17	<i>Ginseng</i>	Roots, stalk, leaves, and berries	Araliaceae	Asian ginseng	North America and in eastern Asia	China	In vitro 2011	<i>Ginseng</i> significantly decreased insulin resistance and fasting blood glucose (FBG) in T2DM patients. among 30 cases of T2DM treated with Renshen tangtai, an injection contained <i>Ginseng</i> polypeptide and polysaccharides; 86.7% of the patients showed appreciable effect on diabetic symptoms.	[41]
18	<i>Momordica charantia</i>	Fruit	Cucurbitaceae	bitter melon	Asia	China	In vitro 2011	Bitter melon lowered fasting and postprandial serum glucose levels in T2DM patients. Bitter melon exerted an antihyperglycemic Effect by inhibition of protein tyrosine phosphatase 1B (PTP1B), activation of AMPK, increase of glucose transporter type 4 (GLUT4) expression, promotion of the recovery of beta cells And insulin-mimicking action.	[41]

Table 4. Medicinal herbs and therapeutic information in diabetes (Table 1 continued)

No.	Scientific Name	Part of plant	Famil. Name	Common Name	Origin of plant	Count of study	year	Result	Ref
19	Trigonella foenum-graecum	Leaves	Fabaceae	Fenugreek	Near East and Indian	China	In vivo 2011	Combined therapy of total saponins of Fenugreek with sulfonylureas hypoglycemic drug lowered the blood glucose level and ameliorated clinical symptoms in 46 cases of T2DM compared with 23 cases of controls.	[41]
20	Allium sativum	Bulb	Amaryllidaceae	Garlic	central Asia, Africa, and Europe	China	In vivo 2011	Garlic had antihyperglycemic and antihyper-lipidemic Effect in T2DM patients. In the 4-week double-blinded placebo-controlled study in 60 T2DM patients, Garlic lowered FBG. Garlic improved glycemic control through increased insulin secretion and enhanced insulin sensitivity	[41]
21	Cinnamon	Whole Plant	Lauraceae	Cinnamomum verum	Asia and Africa	China	In vivo 2011	cinnamon in the diet of patients with T2DM would reduce risk factors associated with diabetes and cardiovascular diseases. Cinnamon lowered hemoglobin A1c (HbA1C) by 0.83% compared with usual care alone lowering HbA1C by 0.37% in patients with T2DM in a randomized, controlled trial.	[41]
22	Dendrobium chrysotoxum	aerial parts	orchidaceae	Golden-bow Dendrobium	native to Southeast Asia,	China	In vivo and in vitro 2014	DC alleviated the increased I and phosphorylated p65, I κ B, and I κ B kinase (IKK) in diabetic rats. Therefore, DC can alleviate DR by inhibiting retinal inflammation and preventing the decrease of tight junction proteins, such as occludin and claudin-1.	[42]
23	Zingiber zerumbet	root	Zingiberaceae	Bitter ginger	Asia and india	Taiwan	In vitro 2015	Zingiber zerumbet rhizome ethanol extracts (ZZRext) After three months of diabetes, the weight gain in STZ-diabetic rats was significantly less when compared with normal rats, and the blood glucose levels were significantly higher. The reduction in body weight was not obvious in STZ-diabetic rats receiving ZZRext during the experimental period.	[43]
24	Kaempferia parviflora	root	Zingiberaceae	(KP) or Krachaidum belongs or Thai ginsengs	in Thailand	Thailand	In vitro 2017	KP (Kaempferia parviflora) treatment demonstrated a significant recovery of sexual behaviour and serum testosterone levels in diabetic rats.	[44]

Table 5. Medicinal herbs and therapeutic information in diabetes (Table 1 continued)

No.	Scientific Name	Part of plant	Family Name	Common Name	Origin of plant	Country of study	Year	Result	Ref
25	<i>Opuntia megacantha</i>	leaves	Cactaceae	culinary	South Africa and South America	Zimbabwe	1999	Administration of the leaf extract was also associated with an invitro increased GFR in STZ-diabetic rats. although the rate was unaltered in non-diabetic rats.	[45]
26	<i>Symplococina</i>	Seed and leaves	Symplocaceae		endemic to Mexico	India	2014	Invitro But SCE (hydroethanol Extract of <i>Symplocos cochinchinensis</i>) Administration resulted in a lower plasma level of urea and creatinine in treated groups compared to the diabetic control group This Shows protective property of SCE Against renal damage.	[46]
27	<i>perilla</i>	Leaves	Lamiaceae	"perilla"	America and Asia and Europe	Japan	In vivo	The flavonoid luteolin from perilla luteolin treatment prevented the development of diabetic nephropathy by significantly lowering BUN and creatinine in diabetic animals. This could be explained that there was increased clearance of blood urea and creatinine by the kidney or that there was decreased protein degradation. Moreover, luteolin also prevented the increase in 24-h urea protein in diabetic rats.	[47]
28	<i>Allium sativum</i>	Seed	Amaryllidaceae	Garlic	China and common seasoning worldwide.	Iran	2016	Invitro Garlic extract has the opposite effect on the renal function markers and histopathology of diabetic rats. Since hyperglycaemia causes the diabetic complications, compounds that have hypoglycaemic effects can be effective in reducing of diabetic complications such as renal dysfunction.	[48]
29	<i>Terminalia chebula</i>	Seeds	Combretaceae	chebulic myrobalan	South Asia from India and Nepal east to southwest China	Canada	2006	Invitro T. chebula is more effectively inhibited the incidence of diabetic nephropathy. Diabetic nephropathy is mainly associated with excess urinary albumin excretion, abnormal renal function as represented by an abnormality in serum creatinine.	[49]
30	<i>Aloe vera . Burm</i>	leaf	Asphodelaceae	Aloe vera	around the world	Turkey	2003	Invitro the function and structure of kidney may be affected by changes in the levels of insulin Diabetic kidney exhibits characteristic changes leadin to renal insufficiency or complete kidney failure. The major alteration was observed especially in the proximal tubules of the kidney tissue in the diabetic animals. The rupturing of the brush border, shows that the structural integrity of the membrane was disrupted.	[50]

Table 6. Antidiabetic mechanism activity of medicinal herbs

Scientific Name	Mechanism	Ref.
URTICA DIOICA (U. dioica)	The aqueous UD extract plays an important role by improving the morphology and / or function of beta cells. Preventing damage to beta-cell cells, repair damaged beta cells, rebuilding new cells, and stimulating insulin secretion in functional cells is one of the mechanisms of action of the extract of this plant	[35]
Trigonella foenum graecum	The therapeutic effect of fenugreek seed on diabetes is at least partly due to the direct stimuli of an amino acid called hydroxysolecaine-4 on insulin secretion from beta cells. Following cell damage, the activity of Ca ATPase and Na / K ATPase pumps decreases the consumption of fenugreek seeds by reducing the free radicals, eliminating these disorders.	[36]
Carthamus tinctorius	The rich source of flavonoids, such as quercetin and camphorol, is linked to its antioxidant and hypoglycemic activity.	[36]
Ferula assa-foetida	Due to the presence of antioxidant compounds, gum can reduce the amount of intracellular free radicals and stimulate the synthesis and secretion of insulin or hyperplasia of the remaining beta cells in the pancreas. Anthoczone gum may reduce blood glucose by stimulating the synthesis and secretion of insulin and hyperplasia of the remaining beta pancreatic cells.	[37]
Bauhinia forficata	It is rich in polyphenolic antioxidant compounds, flavonoids, which reduce blood glucose by increasing insulin secretion and inducing glucose transfer through insulin-dependent pathways.	[37]
Gymnema sylvestre	Gymnemic acid molecules have a receptor on the surface of the outer layers of the intestine that prevents the absorption of sugar molecules by the intestine, which leads to a decrease in blood sugar levels.	[38]
Swertia punicea	The mechanism of action of the Swertia Punicea Glucose Reducing Effect by Improving Insulin Resistance, which increases the absorption and secretion of insulin.	[38]
Combretum Micranthum	Stimulates the synthesis and secretion of insulin or hyperplasia of the remaining beta cells in the pancreas.	[38]
Sarcopoterium spinosum	The blue extract of the root of the Sarcopoterium spinosum plant exhibits activity similar to insulin.	[38]
Liriope spicata	Increases insulin secretion and absorption, and improves glucose tolerance in the body.	[50]
Caesalpinia bonducella	Increases insulin secretion from pancreatic islets. The anti-hyperglycaemic effect of the plant's extracts may be due to blockage of glucose uptake	[39]
Coccinia indica	These extracts lowered the lipoprotein lipase (LPL) enzyme activity and reconstituted glucose 6-phosphatase and lactate dehydrogenase, which increased in diabetic patients without treatment	[39]
Syzygium cumini	The cAMP content increases langerhans, which is associated with increased insulin production. This role plays a role in converting perinsulin to insulin with increased activity of catepsin. It increases the activity of insulin and inhibits the activity of Na / K ATPase from the patient's erythrocytes.	[39]
Mangifera indica	This may be due to decreased intestinal absorption of glucose.	[39]

diabetes, insulin deficiency or the body's inability to consume it causes the sugar to remain in the blood instead of reaching the cells and producing energy. This excess amount of sugar in the blood causes the blood sugar level to exceed normal level.

Before the discovery of insulin and hypoglycemic drugs, diabetic patients were treated with medicinal plants and traditional treatments. So far, the positive effects of over 1200 herbal drugs in reducing blood glucose levels or the complications due to hyperglycemia have been established. Each plant may have its own effective component to reduce hyperglycemia. However, these plants have been shown to possess antioxidant activities [15–20]. Oxidative stress is involved in development of diabetes and a lot of other diseases [19–24]. Therefore, these plants, at least in part, impose their anti-diabetic activities through this mechanism. Because oxidative stress is the cause of a wide variety of other disease and these plants have antioxidant activity, hence, they may have beneficial effects on other diseases, too [25–29]. It is noteworthy that these plants due to their antioxidant activities and other mechanisms are able to reduce the toxic effects of toxic agents or other drugs [30]. However, they themselves may have toxic effects and might be used with caution [31]. More importantly a lot of other plans have antioxidant capacity [32–34].

5. Conclusions

Hence, these plants may also have anti-diabetic activities and/or can reduce diabetes complications.

6. Open Access

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7. List of abbreviations

Diabetes: Diabetes mellitus

8. Competing interests

The authors declare no conflict of interest.

9. Authors' contributions

All authors searched, studies, reviewed and contributed to the design of the research. All authors reviewed, commented and approved the final draft.

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