Sudarshan Publication

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THE PHARMA RESEARCH

An International Journal of Pharmacy Research

IN-VITRO ANTIOXIDANT ACTIVITY OF ETHANOLIC EXTRACT OF STEPHANIA GLABRA (ROXB.) MIERS TUBERS

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ARTICLE INFO

Published on: 15-12-2016
ISSN: 0975-8216

Keywords:
Diabetes, medicinal plants, hypoglycemic activity

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ABSTRACT

In the last few years, there has been an exponential growth in the field of herbal medicine and gaining popularity both in developing and developed countries because of their natural origin and less side effects. Indians are genetically more susceptible to diabetes, for which World Health Organization predicts the number of diabetic persons in India may rise up to 74 million by 2025. Herbal drugs are the oldest known healthcares available to mankind, enlisted in naturopathic, ayurvedic, homeopathic and other medicine systems obtained from natural sources. The plant based medicinal system is very useful since a long time for treatment of diabetes. Many of the herbs are available having antidiabetic activity and shows their action by different mechanism like stimulating or regenerating the effect on β cell or extra pancreatic effect for hypoglycemic activity. This article presents a review on some reported antidiabetic medicinal plants (with their Family, botanical name, activity with route of administration and reported mechanism of action for antidiabetic action). The large number of plants described in this review (belonging to 50 families) clearly suggested the importance of herbal plants in the treatment of diabetes.

INTRODUCTION

Diabetes mellitus (DM) is a chronic incurable disease caused by inherited and/or acquired deficiency in production of insulin by the pancreas, or by the ineffectiveness of the insulin produced. Diabetes is associated with short and long term complications that can affect an individual's physical and psychological well being and quality of life. Such a deficiency results in increased glucose concentrations in the blood, which in turn damage many of the body's systems, in particular the blood vessels and nerves. The World Health Organization (WHO) estimates that 4 billion people, 80 percent of the world population, presently use herbal medicine.

Diabetes affects the major global population ***[1]*** and management of diabetes without any side effects is still a challenge to the medical system ***[2]***.

The therapeutic measurements include use of insulin and other agents like amylin analogues, alpha glycosidase inhibitors like acarbose, miglitol and voglibiose, sulphonylureas, biguanides for the treatment of hyperglycemia. These drugs also have certain adverse effects like causing hypoglycemia at higher doses, liver problems, lactic acidosis and diarrhea. Apart from currently available therapeutic options, many herbal medicines have been recommended for the treatment of diabetes. Since time immemorial, traditional plants are used throughout for a range of diabetic presentations. Herbal drugs are prescribed widely because of their effectiveness, less side effects and relatively low cost ***[3].***

There have been several reviews on the medical plants which possess potential hypoglycemic activity in Indian system of medicines. ***[4, 5]***. Therefore, investigation for beneficial use on such agents from traditional medicinal plants has become more important in different types of diabetes and reported in numerous scientific journals ***[6]***. The present review, deals with some selective medicinal plants from Indian biosphere for treating diabetes with major emphasis on the dose and possible mode of action of the herbal hypoglycemic so far reported.

Further, profiles of various plant species from Indian origin, having potent hypoglycemic activity are described in the following section.

Table I: Selected Indian medicinal plants with blood glucose lowering activity

Sr. No.	Family	Botanical Name of the plant	Activity with route of administration/dosage	Reported mechanism of action
1	Acanthaceae	*Andrographis paniculata* Nees Common name: King of Bitter.	Hypoglycemic and antihyperglycemic activity of *Andrographis paniculata* and andrographolide in normal and streptozotocin induced diabetic rats, orally ***[7,8]*** Antioxidant activity of *Andrographis paniculata* extract in diabetic rats ***[9]***	Prevents glucose absorption from gut ***[7,8]***. Has hypotriglyceridemic effect and antioxidant activity, which may be responsible for beneficial effect in the diabetic state ***[9]***
2	Alliaceae	*Allium sativum* L. Common name: garlic	Antihyperglycemic activity of ethanol, petroleum ether and ethyl acetate extract in alloxanized rabbits at a dose of 0.25 mg/kg, orally ***[10]*** Antioxidant activity of allicin, isolated from garlic ***[11]***	Has strong antioxidant activity and rapid reactivity with thiol containing proteins responsible for the hypoglycemic property ***[11]***

3	Aloaceae	*Aloe vera* (L.) Burm.f. Common name: Aloe	Hypoglycemic activity of the plant (200 and 300 mg/kg p.o.) on normal fasted rats, oral glucose-loaded rats and streptozotocin-induced diabetic rats ***[12]*** Hypoglycaemic activity of leaf pulp extracts in type I and type II diabetic rats ***[13]***Hypoglycemic effect of aloe and its bitter principle in alloxanized mice ***[14]*** Antihyperglycemic activity of dried sap in five non-insulin-dependent diabetic patients and in alloxanized Swiss albino mice ***[15]***	Maintains glucose homeostasis by controlling the carbohydrate metabolizing enzymes ***[12]*** and stimulates insulin release from pancreatic beta cells ***[14]***
4	Anacardiaceae	*Mangifera indica* L. Common name: Mango	Hypoglycemic activity of aqueous leaf extract (1 g/kg p.o.), given along with as well as 60 min before glucose administration in streptozotocin-induced diabetic rats ***[16]*** Hypoglycemic activity of Mangiferin (10 and 20 mg/kg, i.p. once daily for 28 days) in STZ induced diabetic rats and improvement in oral glucose tolerance in glucose-loaded normal rats upon chronic administration (10 and 20 mg/kg, i.p.) for 14 days ***[17]***	Possibly acts through intestinal reduction of the absorption of glucose ***[16]*** as well as pancreatic and extra-pancreatic mechanisms ***[17]***
5	Anacardiaceae	*Mangifera indica* Linn. Common name: Mango	The aqueous leaf-extract (1 g/kg) failed to exert any hypoglycemic activity in normoglycemic as well as streptozotocin-induced diabetic rats upon oral administration ***[16]***.	Reduction of intestinal absorption of glucose ***[16]***.
6	Annonaceae	*Annona squamosa* L. Common name: Sugar apple	Hypoglycemic activity of aqueous leaf extracts in streptozotocin-nicotinamide induced diabetic rats ***[18]*** Hypoglycemic and antihyperglycemic activities of ethanolic leaf-extract (350 mg/kg, orally) in normal, streptozotocin (STZ)-diabetic rats and alloxanized rabbits ***[19]***	Lowers blood glucose level ***[18]***
7	Apocynaceae	*Catharanthus roseus* (L.) G. Don Common name: Madagascar periwinkle	Hypoglycemic activity of ethanolic leaf extract in normal rats upon oral administration at graded dose. Hypoglycemic activity of the extract (500 mg/kg) in streptozotocin rats and in oral glucose tolerance test ***[20]***	Increases metabolization of glucose ***[21]*** and enhances secretion of insulin either from the beta cells of Langerhans or through extra-pancreatic mechanism ***[22]***

			The hypoglycemic activity of dichloromethane: methanol extract of leaves and twigs in streptozotocin (STZ) induced diabetic rat (500 mg/kg p.o., for 7 and 15 days) ***[21]*** Hypoglycemic and antihyperglycemic activity of leaf juice or water decoction of the plant in normal and alloxan-induced diabetic rabbits ***[22]***	
8	Asclepiadaceae	*Gymnema sylvestre R Br.* Common name: Gudmar	Blood glucose lowering activity both in vitro and in vivo ***[23-28]*** .	Lowers plasma glucose level ***[28]***
9	Asclepiadaceae	*Gymnema montanum*	Blood glucose lowering activity of alcoholic leaf extract (200 mg/kg orally) was studied in alloxan diabetic rats along with an increase in plasma insulin level ***[29]*** . The extract also produced significant antioxidant and antiperoxidative activity in alloxanized rats ***[30-32]***.	Antioxidant & anti-peroxidative ***[30-32]***
10	Brassicaceae	*Brassica juncea* (L.) Czern. Common name: Brown Mustard	Hypoglycemic activity of *Brassica juncea* diet (10%, w/w) in normal rats upon oral administration for 60 days ***[33]***	Increases the concentration of hepatic glycogen and glycogenesis and suppressed the activity of glycogen phosphorylase and gluconeogenic enzymes, lead to reduction in glycogenolysis and gluconeogenesis ***[33]***
11	Caesalpiniaceae	*Caesalpinia bonducella* (L.) Roxb. Common name: Chinese Cinnamon	Hypoglycemic and antihyperglycemic activities of the aqueous and 50% ethanolic seed extracts in normal and streptozotocin-diabetic rats ***[34]*** Antihyperglycemic activity of the seed extracts in type II diabetic Long Evans rat ***[35]*** Hypoglycemic activity of aqueous and ethanolic extracts in chronic type II diabetic model with an increase in secretion of insulin from isolated islets ***[36]***	Increases the release of insulin from pancreatic cells ***[34]***
12	Capparidaceae	*Capparis deciduas* Common name: Karir or	Hypoglycemic effect was seen in alloxanized rats when the rats were fed with 30% extracts of (C. decidua) fruit powder for 3 weeks.	Hypoglycemic, antioxidant, hypolipidaemic activity ***[37]***

		Pinju	C. decidua was also found to alter superoxide dismutase and catalase enzyme levels to reduce oxidative stress ***[37]***	
13	Celastaceae	*Salacia reticulata* Wight. Common name: Salacia	Blood glucose lowering effect of aqueous decoction in fasted animals with improved glucose tolerance in laboratory animals ***[38,39]*** Hypoglycemic activity of plant tea in type II diabetic patients in a randomised single centre double blind cross over clinical trial ***[40]***	Inhibits alpha-glucosidase activity ***[38,39]***
14	Celastaceae	*Salacia Oblonga* Wall.	Serum glucose lowering activity of aqueous methanolic extract of the roots in sucrose and maltose loaded rats and alpha-glucosidase and aldose reductase inhibitory activities of water soluble and ethyl acetate soluble fractions of the aqueous methanolic extract in same animal model ***[41]*** Antihyperglycemic, antihypoinsulinemic and antioxidant activity of petroleum ether extract of the root bark in streptozotocin diabetic rats ***[42]*** Antihyperglycemic effect of water extract in the obese Zucker rat (OZR) (genetic model of Type II diabetes) along with the effect on cardiac fibrosis upon chronic administration ***[43]***	Acts through inhibition of alpha-glucosidase activity ***[40]***
15	Chenopodiaceae	*Beta vulgaris* L. Common name: Garden beet	Hypoglycemic activity of Betavulgarosides II–IV, isolated from the root of *Beta vulgaris* L. in an oral glucose tolerance test in rats ***[44]***	Lowers blood glucose level ***[44]***
16	Compositae	*Artemisia pallens* Wall. Ex DC. Common Name: Davana	Antihyperglycemic activity of aerial parts (100 mg/kg, orally) in glucose-fed hyperglycaemic and alloxan-induced diabetic rats. Moderate hypoglycaemic effect (1000 mg/kg) in fasted normal rats ***[45]***	Inhibits glucose re-absorption or increase in peripheral glucose utilization ***[45]***

17	Convolvulaceae	*Ipomoea batatas* (L.) Lam. Common name: Sweet potato	Hypoglycemic effect of the plant against diabetic Zucker fatty rats and inhibition of the increased blood glucose level in a glucose tolerance test in rats ***[46]*** Postprandial glucose suppression effect (reduced blood glucose level by 16.5% at 30 min) of Peonidin 3-*O*-[2-*O*-(6-*O*-*E*-feruloyl-beta- d-glucopyranosyl)-6-*O*-*E*caffeoyl-beta- d-glucopyranoside]-5-*O*-beta- d-glucopyranoside, a diacylated anthocyanin, isolated from storage roots in male 8-week-old Sprague-Dawley rats upon single oral administration ***[47]***	Reduces insulin resistance ***[46]*** and possibly acts by maltase inhibition, not by sucrase or glucose transport inhibition at the intestinal membrane ***[47]***
18	Cucurbitaceae	*Citrullus colocynthis* (L.) Schrad. Common name: Bitter apple	Hypoglycemic activity of aqueous extract (300 mg/kg), glycosidic and saponin extract (50 mg/kg), orally in normal rabbits ***[48, 49]*** Blood glucose lowering activity of aqueous seed extract in normal and streptozotocin (STZ)-induced diabetic rats upon daily oral administration for 2 weeks ***[50]***	Exerts an insulinotropic effect ***[48, 49].***
19	Cucurbitaceae	*Coccinia indica* Wight & Arn. Common name: Ivy gourd	Hypoglycemic activity of alcoholic leaf extract in normoglycemic guinea pig ***[51]*** Blood glucose lowering activity of 60% ethanol leaf extract (200 mg/kg, orally) ***[52]*** Hypoglycemic activity of the leaf extract in a double blind control trial in human subjects ***[53, 54]*** Antihyperglycemic activity of dried extract (500 mg/kg p.o., for 6 weeks) in 30 diabetic patients ***[55]***	Suppresses glucose synthesis and enhances glucose oxidation by shunt pathway through activation of its principal enzyme glucose-6-phosphate dehydrogenase ***[52]*** Also has an insulin secretagogue effect ***[53, 54]***
20	Cucurbitaceae	*Momordica cymbalaria*	Blood glucose level reducing activity of fruit powder in fasted alloxan-induced diabetic rats after a treatment for 15 days ***[56]*** Blood glucose lowering effect of aqueous fruit extract in alloxan diabetic rats ***[57]*** Antihyperglycemic activity of aqueous fruit extract (0.5 g/kg dose for 6 weeks) in alloxan-induced diabetic rats upon oral administration ***[58]***	May act by increasing hepatic glycogen ***[56]***

21	Euphorbiaceae	*Phyllanthus niruri L* Common name: Bhumyamalaki	The antidiabetic potentials of methanol extract (ME) of aerial parts of *P. niruri* was evaluated in normal and alloxan diabetic rats ***[59]***	Insulin-like effect probably mediated via peripheral glucose consumption ***[60, 61]*** Also, postprandial hyperglycemia is related to postprandial hyperinsulinemia ***[62]***
22	Fabaceae	*Cajanus cajan* (L.) Millsp. Common name: Pigeon pea	Glucose tolerance enhancing activity of aqueous leaf and stem extract in oral glucose tolerance test ***[63]*** Hypoglycemic activity of cooked diet in healthy human volunteers ***[64]***	Lowers plasma glucose level ***[65]***
23	Flacourtiaceae	*Casearia esculenta* Roxb. Common name: Carilla Fruit	Blood glucose lowering activity of aqueous extract in normal and glucose loaded rats. ***[66]*** Antioxidant activity of aqueous extract in STZ diabetic rats at doses of 200 and 300 mg/kg for 45 days ***[67]***	Exhibits significant reduction in blood glucose level, a decrease in the activities of glucose-6-phosphatase and fructose-1,6-bishosphatase and an increase in the activity of liver hexokinase, resulting in potent hypoglycemic activity ***[68]***
24	Gentiaceae	*Enicostemma littorale* Blume	Antihyperglycemic activity of whole plant aqueous extract in alloxan induced diabetic rats along with reduction of glycosylated haemoglobin and glucose-6-phosphatase activity in liver ***[69]*** Insulin enhancing activity of a single dose of aqueous extract of plant (15 g dry plant equivalent extract per kg) in alloxan-induced diabetic rats ***[70]*** Reduction in glycosylated haemoglobin, liver glucose-6-phosphatase activity and significant increase in serum insulin levels of the diabetic rats by aqueous extract ***[71]***	Enhances glucose-induced insulin release from isolated rat pancreatic islets, mediated through K (+)-ATP channel-dependent pathway ***[70]***
25	Gentianaceae	*Swertia chirayita* (Roxb. Ex Fleming) H. Karst. Common name: Indian Gentian	Blood sugar lowering activity of swerchirin, (1,8-dihydroxy-3,5-dimethoxyxanthone), isolated from hexane fraction of the plant in fasted, fed, glucose loaded and tolbutamide pretreated albino rats ***[72]*** Blood sugar lowering effect of Swerchirin (50 mg/kg p.o.) in	Stimulates insulin release from islets of Langerhans by depleting aldehyde-fuchsin stained beta-granules and immunostained insulin ***[74]***

			healthy and streptozotocin treated (35 mg/kg i.v.) Charles Foster strain albino rats ***[73,74]***	
26	Lamiaceae	*Ocimum sanctum* L. Common name: Holy Basil	Plasma glucose lowering activity of plant extract (200 mg/kg for 30 days) in STZ induced diabetic animals revealing the effect of the extract on three important enzymes of carbohydrate metabolism, namely glucokinase, hexokinase and phosphofructokinase ***[75]*** Glucose and cortisol lowering activity of the plant in male mice ***[28]***	Acts by cortisol inhibiting potency ***[28]***
27	Leguminosae	*Acacia arabica* (Lam.) Muhl.ex Willd. Common name: Indian Gum Arabic tree	Hypoglycaemic activity of 94% seed diet in normal rats orally with no blood sugar lowering activity in alloxanized rats at the same dose level ***[76]*** Hypoglycemic effect of powdered seeds in normal rabbits (2, 3 and 4 mg/kg) administered orally ***[77]***	Acts through release of insulin from pancreatic beta cells, which accounts for the hypoglycemic activity ***[76, 77]***
28	Leguminosae	*Cassia auriculata* L. Common name: Tanner's Cassia	Antihyperglycemic and anti-hyperlipidemic activity of aqueous flower extract in streptozotocin-induced diabetic rats upon oral administration at different doses for 30 days ***[78, 79]*** Antioxidant activity of aqueous flower extract in the brain of streptozotocin diabetic rats ***[80, 81]***	Suppresses enhanced gluconeogenesis during diabetes and enhance utilization of glucose through increased glycolysis ***[78, 79]*** in addition to pronounced alpha-glucosidase inhibitory actions resulting in a significant and potent lowering of blood glycemic response ***[80, 81]***
29	Leguminosae	*Mucuna pruriens* (L.) DC. Common name: Velvet bean	Blood glucose lowering activity of powdered seeds (0.5, 1 and 2 g/kg) in normal rabbits and hypoglycemic activity of the seed (1 and 2 g/kg body weight) in alloxan-diabetic rabbits ***[82]*** Blood glucose lowering activity of plant extract (200 mg/kg) upon daily oral feeding for 40 days in STZ-diabetic mice ***[83]***	Possibly acts through stimulation of the release of insulin and/or by a direct insulin-like action due to the presence of trace elements like manganese, zinc, etc. ***[82]***
30	Leguminosae	*Glycerrhiza glabra* Linn Common name: Mulethi	The flavonoids have abdominal fat-lowering and hypoglycemic effects, possibly mediated through activation of peroxisome proliferator activated receptor-gamma (PPAR-gamma) ***[85]***	Lowers plasma glucose level ***[84]***

31	Liliaceae	*Allium sativum* Linn. Common name: Lehsun	Aqueous homogenate of garlic (10 ml/kg/day) administered orally to sucrose fed rabbits (10 g/kg/day in water for two months) significantly increased hepatic glycogen and free amino acid content, decreased fasting blood glucose, and triglyceride levels in serum in comparison to sucrose controls ***[86]*** S-allyl cystein sulfoxide (SACS), the precursor of allicin and garlic oil, stimulated in vitro insulin secretion from beta cells isolated from normal rats ***[87]***	Increased hepatic metabolism, increased insulin release from pancreatic beta cells and/or insulin sparing effect ***[88]***
32	Liliaceae	*Allium cepa* L. Common name: onion	Hypoglycemic activity of ether soluble fraction of onion (0.25 mg/kg p.o.) in normal rabbits ***[89]*** Antihyperglycemic, antioxidant and hypolipidemic activity of a diet containing 3% freeze dried onion powder upon prolonged administration in STZ diabetic rats ***[90]***	Lowers blood glucose level and has potent antioxidant activity, which may account for the hypoglycemic potential ***[90]***
33	Malvaceae	*Hibiscus rosa sinensis* L. Common name: China Rose	Hypoglycemic activity of single dose of ethanol extract of the plant in glucose-loaded rats at 120 min and blood glucose lowering effect after repeated administration for seven consecutive days at 30, 90 and 120 min after glucose loading ***[91]*** Hypoglycemic activity of alcoholic leaf extract (250 mg/kg p.o. for seven consecutive days) in glucose induced hyperglycemia model in rats ***[92]*** Blood glucose lowering activity of ethanol flower extract in streptozotocin induced diabetic rats along with a reduction in total cholesterol and serum triglycerides ***[93]***	Stimulates insulin secretion from pancreatic beta cells ***[91]*** and increases utilization of glucose, either by direct stimulation of glucose uptake or via the mediation of enhanced insulin secretion ***[92]***
34	Meliaceae	*Azadirachta indica* A.Juss. Common name: Neem	Hypoglycemic activity of hydro alcoholic plant extract in normal rats and hypoglycemic activity in glucose fed and streptozotocin induced diabetic rats ***[94, 95]*** Hypoglycemic and anti-hyperglycemic activities of leaf	Inhibits action of epinephrine on glucose metabolism, resulting in increased utilization of peripheral glucose ***[97, 95]*** and exhibits hypoglycaemic activity without altering the

			extract in normal and streptozotocin-induced diabetic rat ***[96,28]***	serum cortisol concentration ***[96,28]***
35	Menispermaceae	*Tinospora cordifolia* Common name: Guduchi	Oral administration of the root extract (T. cordifolia) for 6 weeks resulted in a significant reduction in blood and urine glucose and in lipids in serum and tissues in alloxan diabetic rats. ***[98]*** Aqueous extract at a dose of 400 mg/kg could elicit significant antihyperglycemic effect in different animal models, its effect was equivalent to only one unit/kg of insulin ***[99]*** It is reported that the daily administration of either alcoholic or aqueous extract of T. cordifolia decreases the blood glucose level and increases glucose tolerance in rodents ***[100, 101]***	Decrease blood glucose & brain lipid. ***[98]***
36	Moraceae	*Ficus bengalensis* L. Common name: Banyan tree	Blood glucose lowering activity of bark extract in streptozotocin-induced diabetic animals upon oral administration and enhancement of serum insulin levels in normoglycemic and diabetic rats ***[102]*** Blood sugar lowering activity of a dimethoxy derivative of leucocyandin 3-*O*-beta- d-galactosyl cellobioside isolated from the bark in normal and moderately diabetic rats along with an increase in serum insulin in the diabetic rats at a dosage of 250 mg/kg for a 2h period ***[103]***	Stimulates insulin secretion from beta cells of islets of langerhans ***[102]*** and inhibits insulin degradative processes ***[103]***
37	Moraceae	*Morus alba* L. Common name: White mulberry	Hypoglycemic activity of hot water extract of leaves in fasted and non-fasted streptozotocin induced diabetic mice at a dose of 200 mg/kg, i.p. ***[104]*** Degranulation effect of leaf-extract on the beta cells of islets of langerhans of rabbits upon chronic subcutaneous administration ***[105]***	Acts by increasing glucose uptake ***[104]***
38	Musaceae	*Musa sapientum* Linn. Common name: Banana	Blood glucose lowering activity of flower extract (0.15, 0.20 and 0.25 g/kg p.o. for 30 days) in experimental animals in an oral glucose tolerance test along with a	Reduce blood glucose & glycosylated Hb ***[107]***

			reduction in glycosylated haemoglobin and an increase in total haemoglobin as well as significant antioxidant activity at the same dose levels were investigated and reported ***[106, 107]***	
39	Myrtaceae	*Eugenia jambolana* Lam. Common name: Indian black berry	Hypoglycemic activity of pulp extract of the fruits in normal as well as STZ diabetic rats upon oral administration ***[102]*** Hypoglycemic effect of aqueous, alcoholic extracts and lyophilized powder (200 mg/kg per day) of the plant in hyperglycemic animals ***[108]*** Hypoglycemic activity of ethanolic seed extract in alloxan-induced diabetic rabbits along with hypolipidemic effect ***[109]*** Hypoglycemic activity of ethanolic whole seeds, kernel (100 mg/kg of body weight) and seed coat extracts in streptozotocin-induced diabetic rats ***[110]***	May be mediated through an insulin release mechanism ***[102]*** or due to alteration in hepatic and skeletal muscle glycogen content and hepatic glucokinase, hexokinase, glucose-6-phosphate and phosphofructokinase levels in diabetic mice ***[108]***. It also enhances serum insulin activity ***[109]*** and exhibits normoglycemia and better glucose tolerance ***[110]***
40	Myrtaceae	*Eucalyptus globules* Labill Common name: Eucalyptus	Aqueous extract of eucalyptus (0.5 g/l) enhanced 2-deoxy-glucose transport by 50%, glucose oxidation by 60% and incorporation of glucose into glycogen by 90% in mouse abdominal muscle. The insulin-releasing effect is responsible for antihyperglycemic activity ***[111]***	Increase insulin secretion from clonal pancreatic beta line (BRIN-BD 11) ***[111]***
41	Nyctaginaceae	*Boerhavia diffusa* L. Common name: Tar vine	Hypoglycemic and anti-hyperglycemic activity of aqueous leaf extract (200 mg/kg p.o., daily for 4 weeks) in normal and alloxan induced diabetic rats ***[112, 113]***	Increases plasma insulin levels and improves glucose tolerance, produced significant antioxidant activity ***[112, 113]***
42	Nymphaeaceae	*Nelumbo nucifera aertn* Common name: Sacred lotus	Oral administration of the ethanolic extract of rhizomes markedly reduces the blood sugar level of normal, glucose-fed hyperglycemic and streptozotocin-induced diabetic rats. The extract also found to improve glucose tolerance and potentiated the action of exogenously injected insulin in normal rats ***[114, 115]***	Reduce blood sugar level ***[114]***

43	Oxalidaceae	*Biophytum sensitivum* (L.) DC. Common name: Life Plant	Hypoglycemic activity of the plant leaf extract in alloxan diabetic male rabbits ***[116]*** Hypoglycemic activity of the plant on glucose homeostasis in rabbits ***[117]***	Stimulates pancreatic beta cells to release insulin ***[116]***
44	Palmacea	*Areca catechu* Common name: Supari, Betelnut	Subcutaneous administration of alkaloid fraction of Areca catechu (0.05 0.5 mg/kg) in alloxanized rabbits (140 mg/kg) showed significant hypoglycemic effect lasting for 4 6 h ***[118]***.	Decreases blood sugar level ***[118]***
45	Punicaceae	*Punica granatum* L. Common name: Pomegranate	Blood glucose lowering activity of a 50% (v/v) ethanolic flower extract in glucose fed and alloxanized hyperglycemic rats ***[119]*** Plasma glucose lowering activity of methanolic extract of the flowering part in non-fasted Zucker diabetic fatty rats ***[120]***	Inhibits intestinal alpha-glucosidase activity, leading to anti-hyperglycemic property ***[120]***
46	Rutaceae	*Aegle marmelos* (L.) Correa ex Roxb. Common name: Holy Fruit Tree	Antihyperglycemic activity of the leaves in glucose induced hyperglycemic rat at an oral dose equivalent to 250 mg/kg ***[121]*** Antihyperglycemic activity of aqueous fruit extract (250 mg/kg, twice daily for 1 month) in streptozotocin induced female albino Wistar diabetic rats ***[122]*** Hypoglycaemic activity of water extract of fruits in streptozotocin-induced diabetic Wistar rats (125 and 250 mg/kg) twice a day for 4 weeks, orally ***[123]***	Increases utilization of glucose; either by direct stimulation of glucose uptake or via the mediation of enhanced insulin secretion ***[121]***and also decreases the elevated glucose and glycosylated hemoglobin levels ***[122]***
47	Rutaceae	*Murraya koenigii* (L.) Spreng. Common name: curry-leaf tree	Fasting as well as post-prandial blood sugar lowering effect of leaf-powder in Type II diabetic patients upon administration for a period of 1 month ***[124]*** Blood sugar lowering effect of the leaves in normal rats when administered as a diet (10%, v/v) for 60 days ***[125]***	Increases glycogenesis and decreases glycogenolysis and gluconeogenesis ***[125]***
48	Scrophulariaceae	*Scoparia dulcis* L. Common name: Sweet Broomweed	Hypoglycemic activity of aqueous leaf extract (0.15, 0.30 and 0.45 g/kg body weight for 45 days p.o.) in experimental diabetic rats along with a reduction in glycosylated haemoglobin and an increase in total haemoglobin ***[126]***	Suppresses glucose influx into the polyol pathway leading to increased activities of antioxidant enzymes and plasma insulin and decreases activity of sorbitol dehydrogenase ***[128]*** Also

			Plasma insulin and plasma antioxidants enhancing activity of aqueous extract for 6 weeks at a dose of 200 mg/kg p.o. in diabetic rats ***[127]*** The insulin secretagogue activity of the plant extracts in isolated mice pancreatic islets at a dose of 10 mg/ml ***[129]*** In vitro insulin secretagogue activity of the extract of this plant in rat insulinoma cell lines (RINm5F cells) treated with streptozotocin ***[130]***	potentiates insulin release from pancreatic islets ***[129]***
49	Sterculiaceae	*Helicteres isora* L. Common name: Screw tree	Plasma glucose lowering activity of ethanolic root extract (300 mg/kg, after 9 days of administration) in insulin resistant and diabetic C57BL/KsJdb/db mice associated with a reduction in plasma triglyceride level ***[131]*** Antihyperglycemic activity of butanol root extracts (250 mg/kg) in glucose loaded rats ***[132]***	Acts through insulin-sensitizing activity ***[131]***
50	Theaceae	*Camellia sinensis* Kuntze. Common name: Green tea	Antihyperglycemic activity of hot water extract of green tea in streptozotocin (STZ)-diabetic rats ***[133, 134]***	Epigallocatechin gallate, present in tea increases insulin activity and prevent oxidative damages, responsible for the hypoglycemic activity ***[133, 134]***

Antidiabetic Plants in Clinical trials:

Cecropia obtusifolia and *Marrubium vulgare* produced beneficial effects on carbohydrate and lipid metabolisms when it was administered as an adjunct on patients with type 2 diabetes and reduced the blood glucose levels ***[135]***. *Asteracantha longifolia* was reported to improve glucose tolerance in healthy human subjects and diabetic patients. Significant reduction in glycaemia was observed when *Panax quinquefolius* was taken 40 min before glucose load in non-diabetic subjects and the same result was seen in diabetic subjects. *Gymnema Sylvestre* treated patients showed a significant reduction in blood glucose, glycosylated haemoglobin and glycosylated plasma proteins. Intake of *Opuntia streptacantha* by the type II group was followed by a significant reduction in serum glucose and insulin concentration than basal values at 180 min. In 10 human subjects, when treated with a preparation of the whole plant, *Phyllanthus amarus* for ten days, the blood glucose level was reduced. The treatment with *Withania somnifera* produced a decrease in blood glucose levels that was comparable with effects of an oral hypoglycaemic drug ***[136]***.

Also *Allium cepa, Clerodendron phlomoides, Cinnamomum tamala, Trigonella foenum-*

graecum, Coccinia indica, Enicostemma littorale, Ficus bengalensis, Momordica charantia, Pterocarpus marsupium, Cyamopsis tetragonolobus, Cephalandra indica, Casearia esculenta, Cannabis indica, and Syzygium cumini when subjected to clinical trials, showed promising hypoglycaemic effects ***[137, 138]***.

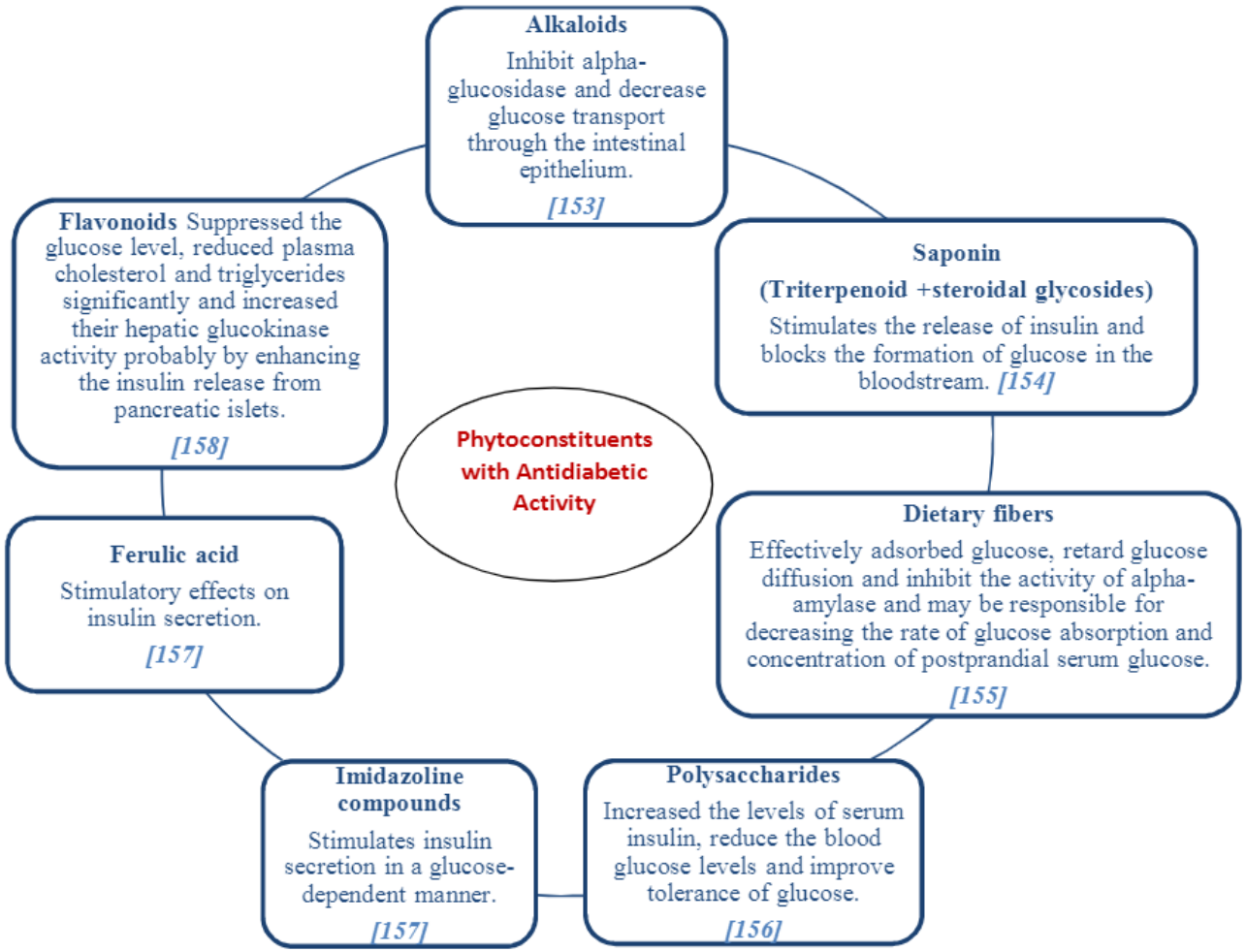
In randomized double-blind placebo and controlled trial *Aegle marmelos* was reported to decrease Post prandial blood glucose, increases oral hypoglycemic drugs actions in type II Diabetes patients ***[139-141]***. Clinical usefulness of *Salacia reticulate* consumption (2 g/day for 3 months) in the management of diabetes has been also observed in patients ***[142]*** with decrease in fasting blood glucose and HbA1c levels in type II patients ***[143]***. In controlled trial of *Nigella sativa* for type II Diabetes decreases in fasting blood glucose, lipids, blood pressure was observed ***[144, 145]*** whereas pre- & post-treatment decreases in fasting blood glucose and increases insulin secretion along with enhancement of oral hypoglycemic drugs actions ***[146, 147]***.

A significant decrease in diabetic symptoms (polydypsia, polyphagia and tiredness) has been seen in patients consuming (2 g/day/for 3 months) leaf powder of *Ocimum sanctum* ***[148]***. Hypoglycemic and hypolipidemic effects were confirmed ***[149]*** in a randomized placebo-controlled, single blind trial performed on type II diabetes patients. Beneficial effects of *Silybum marianum* and its flavonolignans (silymarin) on reducing fasting blood glucose, HbA1c, total cholesterol, LDL, TG, serum glutamic oxalacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT) in T2D patients (30 cases) receiving conventional therapy was observed ***[150-152].***

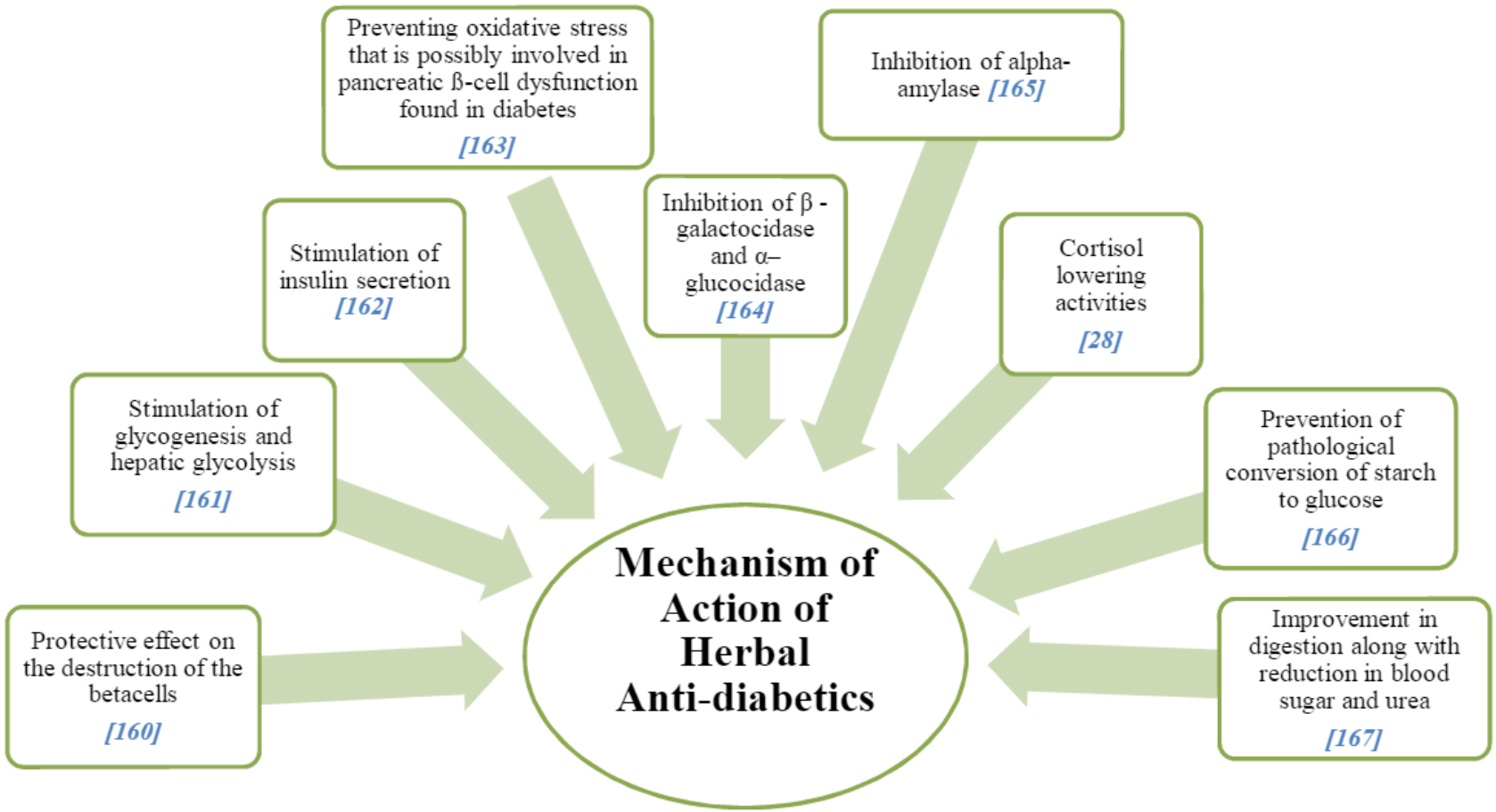
Phytoconstituents with Antidiabetic Activity

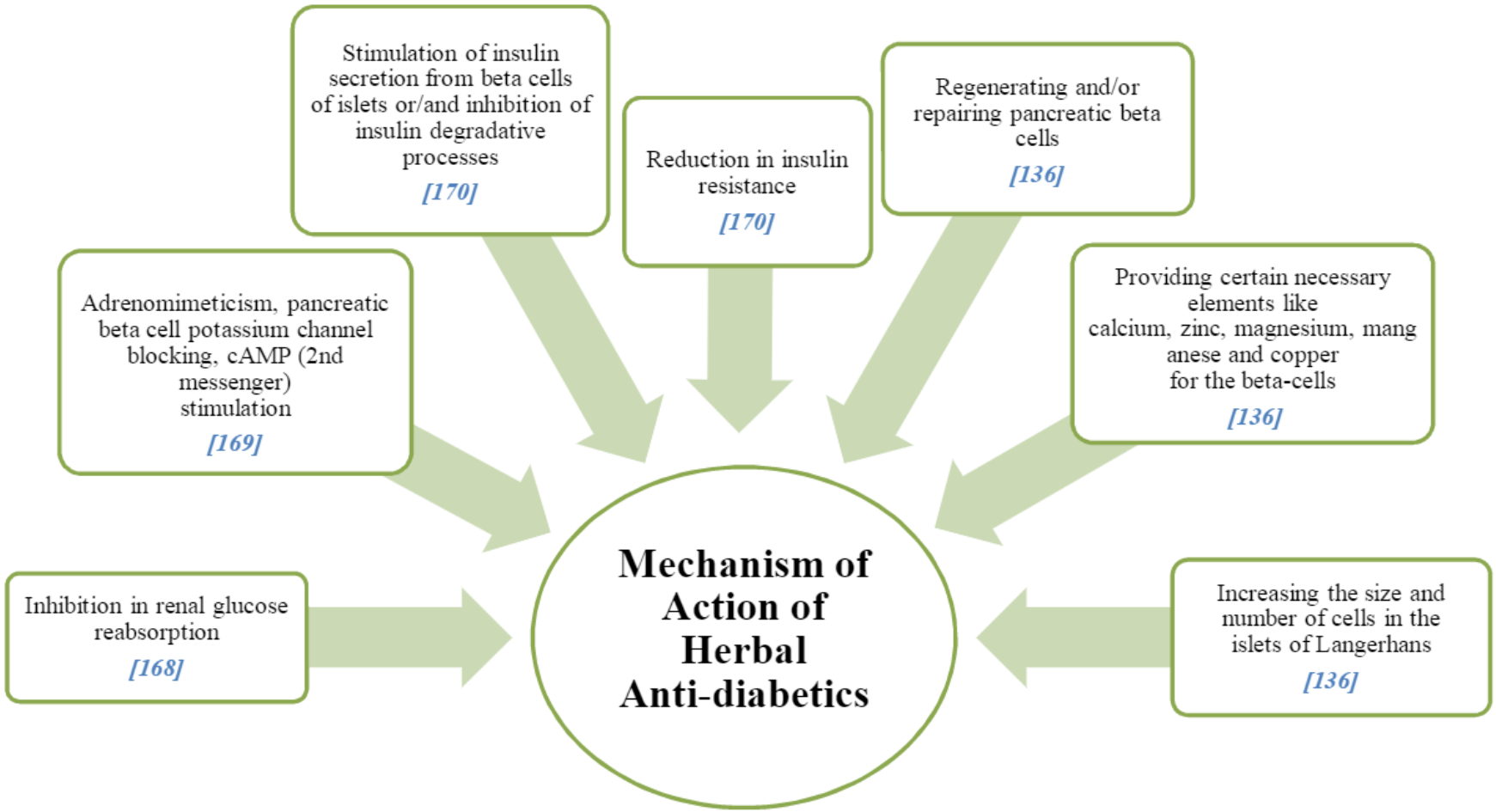
Several active principles originate from edible plants and their addition in the diet would undoubtedly be of some value because of their hypoglycemic potential. Many phytomolecules including carbohydrates, amino acids, glycolipids, dietary fibres, polysaccharides, flavonoids, alkaloids, glycosides, saponins, peptidoglycans, and others obtained from different plant sources have been reported as potent hypoglycemic and antihyperglycemic agent. This is an attempt to well organize the phytoconstituents with specific mode of action to reduce plasma glucose level. With relevance from the earlier reports on their potential efficacy against diabetes, it is concluded that the botanicals have a major role to play in the management of diabetes, which needs future investigation for necessary development of drugs and nutraceuticals from natural riches.

Phytoconstituents with Antidiabetic Activity

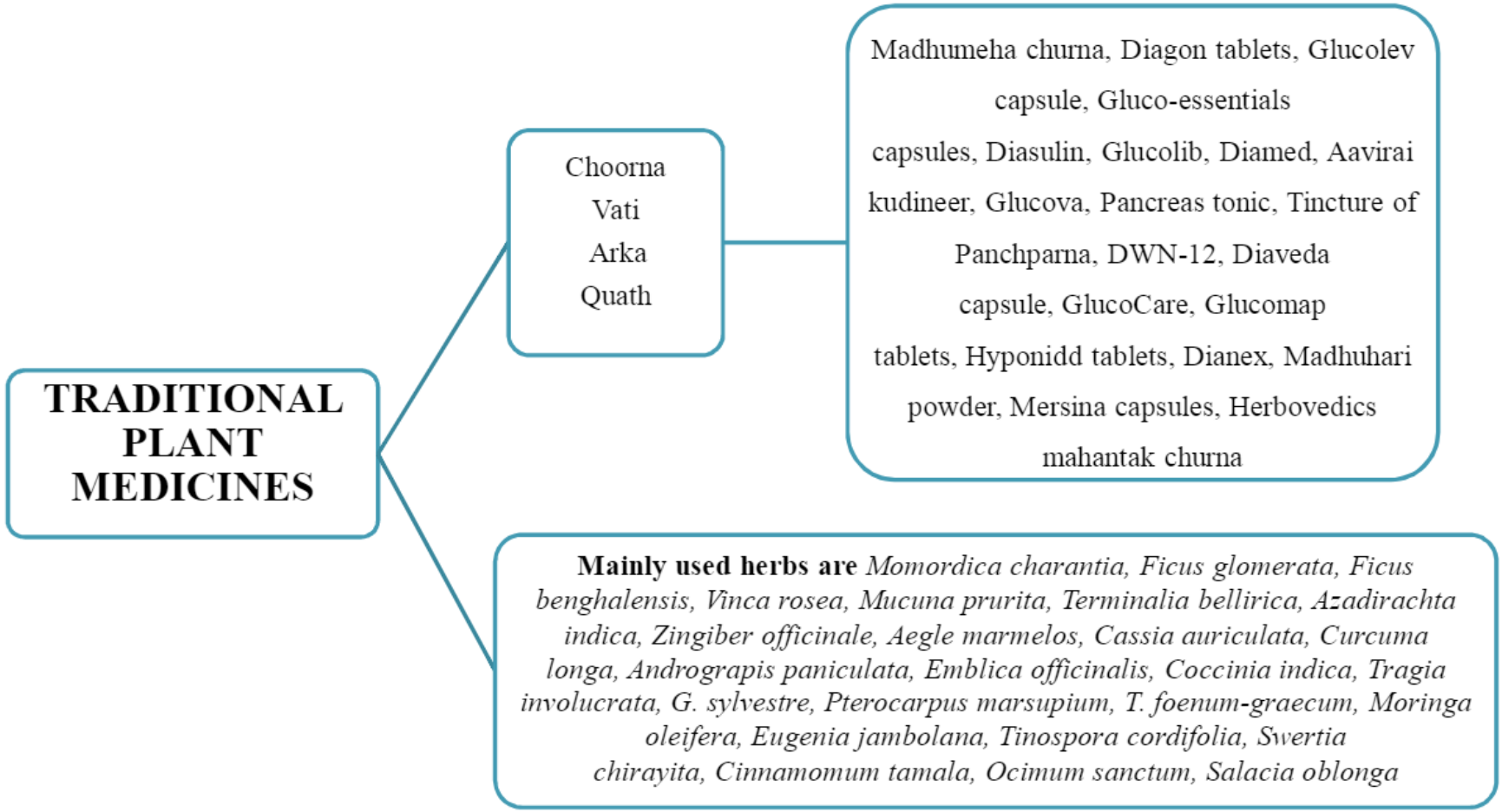


Mechanism of Action




Stimulation of insulin secretion from beta cells of islets or/and inhibition of insulin degradative processes
[170]
Reduction in insulin resistance
[170]
Regenerating and/or repairing pancreatic beta cells
[136]
Adrenomimeticism, pancreatic beta cell potassium channel blocking, cAMP (2nd messenger) stimulation
[169]
Providing certain necessary elements like calcium, zinc, magnesium, manganese and copper for the beta-cells
[136]
Mechanism of Action of Herbal Anti-diabetics
Inhibition in renal glucose reabsorption
[168]
Increasing the size and number of cells in the islets of Langerhans
[136]

Marketed Products



Conclusion:

Diabetes is a metabolic disorder of carbohydrate, fat and protein attributed to mounting resistance to its action or diminished production of insulin. Scientific validations by researchers who have carried out preliminary investigations are considered for the above-mentioned plants for their possible hypoglycemic and antihyperglycemic actions. Herbal treatments for diabetes have been followed all over the World successfully in patients with insulin-dependent and non-insulin-dependent diabetes mellitus, diabetic retinopathy, diabetic peripheral neuropathy etc. From the reports on their potential effectiveness against diabetes, it is assumed that the botanicals have a major role to play in the management of diabetes. However, there are numerous other plants which need further scientific exploration for necessary development of drugs and nutraceuticals from natural resources. Many plants, screened for their antidiabetic effect, have yielded some interesting leads as mentioned above, but have not undergone any scientific assessment as some have the potential to cause serious toxic effects and major drug-to-drug interaction. Till date no plant-based drug has reached such an advanced stage of investigation or development to bring a safer and more effective compound with all the desired parameters of a drug to replace the currently-available oral synthetic drugs. Taking all these information into account, continuing research is required and necessary to elucidate the antidiabetic effects of medicinal plants.

REFERENCES:

1. Chakrabarti, R., Vikramadithyan, R.K., Mullangi, R., Sharma, V.M., Jagadheshan, H., Rao, Y.N., Sairam, P., Rajagopalan, R., 2002. Hypoglycemic and hypolipidemic activity of *Helicteres isora* in animal models. Journal of Ethnopharmacology 81, 343–349.

2. Kameswara Rao, B., Kesavulu, M.M., Apparao, C., 2003a. Evaluation of hypoglycemic effect of *Momordica cymbalaria* fruit in alloxan-diabetic rats. Fitoterapia 74, 7–13.

3. Venkatesh, S., Reddy, G.D., Reddy, B.M., Ramesh, M., Appa Rao, A.V.N., 2003. Antihyperglycemic activity of *Caralluma attenuata*. Fitoterapia 74, 274–279.

4. Ivorra, M.D., Payaa, M., Villarb, A., 1989. A review of natural products and plants as potential hypoglycemic drugs. Journal of Ethnopharmacology 27, 243–275.

5. Rahman, A.U., Zaman, K., 1989. Medicinal plants with hypoglycemic activity. Journal of Ethnopharmacology 26, 1–55.

6. Suba, V., Murugesan, T., Arunachalam, G., Mandal, S.C., Saha, B.P., 2004a. Anti-diabetic potential of *Barleria lupulina* extract in rats. Phytomedicine 11, 202–205.

7. Borhanuddin, M., Shamsuzzoha, M., Hussain, A.H., 1994. Hypoglycaemic effects of *Andrographis paniculata* Nees on non-diabetic rabbits. Bangladesh Medical Research Council Bulletin 20, 24–26.

8. Yu, B.C., Hung, C.R., Chen, W.C., Cheng, J.T., 2003. Antihyperglycemic effect of andrographolide in streptozotocin-induced diabetic rats. Planta Medica 69, 1075–1079.

9. Zhang, X.F., Tan, B.K., 2000a. Anti-diabetic property of ethanolic extract of *Andrographis paniculata* in streptozotocin-diabetic rats. Acta Pharmacologica Sinica 21, 1157–1164.

10. Jain, R.C., Vyas, C.R., 1975. Garlic in alloxan-induced diabetic rabbits. American Journal of Clinical Nutrition 28, 684–685.

11. Rabinkov, A., Miron, T., Konstantinovski, L., Wilchek, M., Mirelman, D., Weiner, L., 1998. The mode of action of allicin: trapping of radicals and interaction with thiol containing proteins. Biochimica et Biophysica Acta 1379, 233–244.

12. Rajasekaran, S., Sivagnanam, K., Ravi, K., Subramanian, S., 2004. Hypoglycemic effect of *Aloe vera* gel on streptozotocin-induced diabetes in

experimental rats. Journal of Medicinal Food 7, 61–66.

13. Okyar, A., Can, A., Akev, N., Baktir, G., Sutlupinar, N., 2001. Effect of *Aloe vera* leaves on blood glucose level in type I and type II diabetic rat models. Phytotherapy Research 15, 157–161.

14. Ajabnoor, M.A., 1990. Effect of aloes on blood glucose levels in normal and alloxan diabetic mice. Journal of Ethnopharmacology 28, 215–220.

15. Ghannam, N., Kingston, M., Al-Meshaal, I.A., Tariq, M., Parman, N.S., Woodhouse, N., 1986. The hypoglycemic activity of aloes: preliminary clinical and experimental observations. Hormone Research 24, 288–294.

16. Aderibigbe, A.O., Emudianughe, T.S., Lawal, B.A., 1999. Antihyperglycaemic effect of *Mangifera indica* in rat. Phytotherapy Research 13, 504–507.

17. Muruganandan, S., Srinivasan, K., Gupta, S., Gupta, P.K., Lal, J., 2005. Effect of mangiferin on hyperglycemia and atherogenicity in streptozotocin diabetic rats. Journal of Ethnopharmacology 97, 497–501.

18. Shirwaikar, A., Rajendran, K., Dinesh Kumar, C., Bodla, R., 2004. Hypoglycemic activity of aqueous leaf extracts of *Annona squamosa* in streptozotocin-nicotinamide type 2 diabetic rats. Journal of Ethnopharmacology 91, 171–175.

19. Gupta, R.K., Kesari, A.N., Murthy, P.S., Chandra, R., Tandon, V., Watal, G., 2005. Hypoglycemic and hypoglycemic effect of ethanolic extract of leaves of *Annona squamosa* L. in experimental animals. Journal of Ethnopharmacology 99, 75–81.

20. Chattopadhyay, R.R., Sarkar, S.K., Ganguly, S., Banerjee, R.N., Basu, T.K., 1991. Hypoglycemic and antihyperglycemic effect of leaves of *Vinca rosea* Linn. Indian Journal of Physiology and Pharmacology 35, 145–151.

21. Singh, S.N., Vats, P., Suri, S., Shyam, R., Kumria, M.M., Ranganathan, S., Sridharan, K., 2001. Effect of an hypoglycemic extract of *Catharanthus roseus* on enzymic activities in streptozotocin induced diabetic rats. Journal of Ethnopharmacology 76, 269–277.

22. Nammi, S., Boini, M.K., Lodagala, S.D., Behara, R.B., 2003. The juice of fresh leaves of *Catharanthus roseus* Linn. reduces blood glucose in normal and alloxan diabetic rabbits. BMC Complementary and Alternative Medicine 3, 4.

23. Yoshikawa, M., Murakami, T., Matsuda, H., 1997a. Medicinal foodstuffs. X. Structures of new triterpene glycosides, gymnemosides-c, -d, -e, and -f, from the leaves of *Gymnema sylvestre* R. Br. : influence of gymnema glycosides on glucose uptake in rat small intestinal fragments. Chemical and Pharmaceutical Bulletin (Tokyo) 45, 2034–2038.

24. Yoshikawa, M., Murakami, T., Kadoya, M., Li, Y., Murakami, N., Yamahara, J., Matsuda, H., 1997b. Medicinal foodstuffs. IX. The inhibitors of glucose absorption from the leaves of *Gymnema sylvestre* R. BR. (Asclepiadaceae): structures of gymnemosides a and b. Chemical and Pharmaceutical Bulletin (Tokyo) 45, 1671–1676.

25. Chattopadhyay, R.R., 1998. Possible mechanism of antihyperglycemic effect of *Gymnema sylvestre* leaf extract, part I. General Pharmacology 31, 495–496.

26. Chattopadhyay, R.R., 1999. A comparative evaluation of some blood sugar lowering agents of plant origin. Journal of Ethnopharmacology 67, 367–372.

27. Sugihara, Y., Nojima, H., Matsuda, H., Murakami, T., Yoshikawa, M., Kimura, I., 2000. Antihyperglycemic effects of gymnemic acid IV, a compound derived from *Gymnema sylvestre* leaves in streptozotocindiabetic mice. Journal of

Asian Natural Product Research 2, 321–327.

28. Gholap, S., Kar, A., 2004. Hypoglycaemic effects of some plant extracts are possibly mediated through inhibition in corticosteroid concentration. Pharmazie 59, 876–878.

29. Ananthan, R., Latha, M., Pari, L., Ramkumar, K.M., Baskar, C.G., Bai, V.N., 2003a. Effect of *Gymnema montanum* on blood glucose, plasma insulin, and carbohydrate metabolic enzymes in alloxan-induced diabetic rats. Journal of Medicinal Food 6, 43–49.

30. Ananthan, R., Baskar, C., NarmathaBai, V., Pari, L., Latha, M., Ramkumar, K.M., 2003b. Hypoglycemic effect of *Gymnema montanum* leaves: effect on lipid peroxidation induced oxidative stress in experimental diabetes. Pharmacological Research 48, 551–556.

31. Ananthan, R., Latha, M., Ramkumar, K.M., Pari, L., Baskar, C., Narmatha Bai, V., 2004. Modulatory effects of *Gymnema montanum* leaf extract on alloxan-induced oxidative stress in Wistar rats. Nutrition 20, 280–285.

32. Ramkumar, K.M., Latha, M., Venkateswaran, S., Pari, L., Ananthan, R., Bai, V.N., 2004. Modulatory effect of *Gymnema montanum* leaf extract on brain antioxidant status and lipid peroxidation in diabetic rats. Journal of Medicinal Food 7, 366–371.

33. Khan, B.A., Abraham, A., Leelamma, S., 1995. Hypoglycemic action of *Murraya koeingii* (curry leaf) and *Brassica juncea* (mustard): mechanism of action. Indian Journal of Biochemistry and Biophysics 32, 106–108.

34. Sharma, S.R., Dwivedi, S.K., Swarup, D., 1997. Hypoglycemic, antihyperglycemic and hypolipidemic activities of *Caesalpinia bonducella* seeds in rats. Journal of Ethnopharmacology 58, 39–44.

35. Chakrabarti, S., Biswas, T.K., Rokeya, B., Ali, L., Mosihuzzaman, M., Nahar, N., Khan, A.K., Mukherjee, B., 2003. Advanced studies on the hypoglycemic effect of *Caesalpinia bonducella* F. in type 1 and 2 diabetes in Long Evans rats. Journal of Ethnopharmacology 84, 41–46.

36. Chakrabarti, S., Biswas, T.K., Seal, T., Rokeya, B., Ali, L., Azad Khan, A.K., Nahar, N., Mosihuzzaman, M., Mukherjee, B., 2005. Hypoglycemic activity of *Caesalpinia bonducella* F. in chronic type 2 diabetic model in Long-Evans rats and evaluation of insulin secretagogue property of its fractions on isolated islets. Journal of Ethnopharmacology 97, 117–122.

37. Yadav, P., Sarkar, S., and Bhatnagar, D.: Lipid peroxidation and antioxidant enzymes in erythrocytes and tissues in aged diabetic rats 1997; Indian J. Exp. Biol., 35, 389–392.

38. Karunanayake, E.H., Welihinda, J., Sirimanne, S.R., Sinnadorai, G., 1984. Oral hypoglycemic activity of some medicinal plants of Sri Lanka, Journal of Ethnopharmacology 11, 223–231.

39. Yoshikawa, M., Murakami, T., Yashiro, K., Matsuda, H., 1998. Kotalanol, a potent alpha-glucosidase inhibitor with thiosugar sulfonium sulfate structure, from hypoglycemic Ayurvedic medicine *Salacia reticulata*. Chemical and Pharmaceutical Bulletin (Tokyo) 46, 1339–1340.

40. Jayawardena, M.H., de Alwis, N.M., Hettigoda, V., Fernando, D.J., 2005. A double blind randomised placebo controlled cross over study of a herbal preparation containing *Salacia reticulata* in the treatment of type 2 diabetes. Journal of Ethnopharmacology 97, 215–218.

41. Matsuda, H., Murakami, T., Yashiro, K., Yamahara, J., Yoshikawa, M., 1999. Hypoglycemic principles of natural medicines. IV. Aldose reductase and alpha-glucosidase inhibitors from the roots of Salacia oblonga Wall. (Celastraceae): structure of a new friedelane-type triterpene, kotalagenin 16-acetate. Chemical and