REVIEW ARTICLE

Herbal drugs and phytoconstituents useful for the management of diabetes

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Abstract

Diabetes mellitus is a chronic disorder characterized by hyperglycemia because of impaired insulin action, diminished insulin production, increased hepatic glucose production, and oxidative stress. Chronic diabetes can cause other heath complications which affect arteries, eyes, kidneys, and nerves. There are multiple therapies available to treat diabetics, but total recovery from diabetes may not possible. In addition, allopathic drugs have some adverse effects such as renal impairments, mal-absorption, flatulence, diarrhea, and abdominal bloating. The anti-diabetic medicines from plants have a similar mechanism of action as allopathic drugs and negligible side effect with low cost. Anti-diabetic effects of herbals are attributed to their ability to restore the function of pancreatic tissues by causing an increase in insulin release or inhibit intestinal absorption of glucose or increase facilitation of metabolites in insulin-dependent processes. Various plants contain polyphenols, alkaloids, glycosides, flavonoids, polysaccharides, terpenoids, and steroids. These constituents represent a source for the discovery and development of new antidiabetic agents. In many developing countries, a wide number of populations believe on traditional herbal plants to meet primary health care needs. In the present review, authors have collected information about some medicinal plants and phytoconstituents that have been studied pre-clinically against diabetics, with special emphasis on the botanical source, common name, and mechanism of actions, which may open new arena for the development of antidiabetic herbal formulations.

Key words: Antidiabetic drugs, antidiabetic phytoconstituents, antidiabetic plants, diabetics

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder manifested as the presence of higher concentrations of glucose in the blood either because of improper production of insulin from pancreas or reduced insulin production.[1] It is the 5th fastest growing disorder. The global prevalence of this disorder is estimated to increase from 4% in 1995 to 5.4% by the year 2025. It is characterized by classical symptoms such as polyuria (frequent urination), polyphagia (increased hunger), and polydipsia (increased thirst).[2] It is one of the most leading reasons to increases the risk of heart disease, kidney damage, stroke, pregnancy complications, and birth defects in children born to diabetic mothers.[3] Classification of diabetes is shown in Table 1.

DIAGNOSIS AND TREATMENT OF DIABETES

Various diagnostic tests are available to test diabetes such as measurement of blood glucose level, oral glucose tolerance test, glycated hemoglobin, fasting blood glucose test, and random blood glucose test. Currently, available therapies for diabetes include insulin injections and oral anti-diabetic medicines sulfonylureas, meglitinides (agents that increase insulin secretion), biguanides (agents that decrease glucose production), thiazolidinediones (agents that increase insulin sensitivity), and α-glucosidase inhibitors. These therapies are producing several types of unwanted side effects such as renal impairments, mal-absorption, flatulence, diarrhea, and abdominal bloating. These associated problems demand the search for newer drugs with fewer side effects. Herbal drugs have been used as traditional agents for the management of diabetes are considered one of the excellent sources for a new drug or a lead to make a new drug with

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negligible side effects.[5] As per the WHO approximately 21,000 plants are used as an antidiabetic plants, some of them have been highlighted in Table 2. Therefore, the demand for herbal medicine is increasing day to day in the developed as well as developing countries for human health because of their various remedial activities, more safety margins and lesser costs.[6,7] Medicinal plants are the major source of phytoconstituents such as polyphenols, tannins, alkaloids, terpenoids, steroids, flavonoids, and carbohydrates can preserve function of β-cells by preventing diabetes-induced reactive oxygen species formation.[8] These compounds represent a source for the development of new safe anti-diabetic compounds. Some phytoconstituents, which have antidiabetic, are displayed in Table 3.

Table 1: Classification of diabetes mellitus[4]

Type 1 diabetes: It is known as IDDM, juvenile-onset diabetes or immune-mediated diabetes. It occurs due to autoimmune damage of the pancreatic β-cells, which are insulin-producing cells
Type 2 diabetes: It is known as NIDDM or adult-onset diabetes. It is cause by insulin resistance with relative insulin deficit to a predominantly insulin secretary deficiency
Gestational diabetes: This type of diabetes occurs in pregnant women, who never had diabetes earlier, but have a high blood glucose level during pregnancy. It may lead development of type 2 diabetes mellitus between 5 to 10 years after delivery

NIDDM: Non-insulin-dependent diabetes mellitus, IDDM: Insulin-dependent diabetes mellitus

Possible mechanisms of action of herbal antidiabetic agents are:[1,9]

- Adrenomimeticism, pancreatic β-cell potassium channel blocking, cyclic adenosine monophosphate stimulation
- Decrease in insulin resistance
- Diminish lipid peroxidation

Table 2: List of some medicinal plants having antidiabetic property

Botanical source	Common name	Part used	Activity	References
Abroma augusta Family: Sterculiaceae	Devil's cotton	Stem bark and leaf	Antidiabetic	[10]
Abrus precatorius L. Family: *Fabaceae*	Kundumani or wild liquorice	Leaves	Antidiabetic	[11]
Abutilum indicum Family: Malvaceae	Thuthi	Stem bark	Antidiabetic	[10]
Acacia arabica Family: *Leguminosae*	Babul	Bark	Hypoglycemic	[12]
Aconitum palmatum Family: Ranunculaceae	Aconite, monkshood	Root	Antidiabetic	[10]
Aegle marmelos Family: Rutaceae	Bael, holy fruit tree	Fruit	Antidiabetic	[13]
Albizia odoratissima Family: Mimosaceae	Black siris	Bark	Antidiabetic	[14]
Allium cepa L. Family: Alliaceae	Onion	Bulb	Antihyperglycemic	[11]
Allium sativum Family: Liliaceae	Garlic	Bulb	Hypoglycemic, antidiabetic	[15]
Aloe barbadensis Family: Liliaceae	Aloe vera	Leaves	Hypoglycemic, antidiabetic	[11]
Annona squamosal Family: Annonaceae	Sugar apple and sharifa	Leaf	Hypoglycemic	[16]
Asparagus racemosusa Family: Liliaceae	Satavari	Shoots	Antidiabetic	[10]
Axonopus compressus Family: Poaceae	Savannah	Leaves	Antidiabetic	[17]
Azadirachta indica Family: Meliaceae	Neem	Leaves, seeds	Antihyperglycemic	[18]
Barleria cristata Family: Acanthaceae	Philippine violet	Seeds	Hypoglycemic	[5]

(*Contd*...)

Table 2: (*Continued*)

Botanical source	Common name	Part used	Activity	References
Berberis aristata Family: Berberidaceae	Indian berberry	Root bark	Antidiabetic	[10]
Berberis vulgaris Family: Berberidaceae	European berberry	Root	Hypoglycemic	[19]
Boenninghausenia albiflora Family: Rutaceae	White Himalayan rue	Whole plant	Antidiabetic	[10]
Bougainvillea glabra Family: Nyctaginaceae	Paper flower	Leaves	Antidiabetic	[20]
Brassssica juncea Family: Cruciferae	Mustard, sarsu	Seeds	Antihyperglycemic	[21]
Bryonia alba Family: Cucurbitaceae	White bryony	Roots	Antidiabetic	[22]
Beta vulgaris Family: Amaranthaceae	Sugar beet	Leaves	Hypoglycemic	[23]
Caesalpinia digyna Family: Fabaceae	Vakerimool	Root	Antidiabetic	[24]
Cajanus cajan Family: Fabaceae	Pigeon pea	Leaves	Antidiabetic	[25]
Campylandra aurantiaca Family: Liliaceae	Nakima	Flower	Antidiabetic	[10]
Cannabis sativa Family: Cannabaceae	Hemp, bhang	Leaves	Antidiabetic	[10]
Cassia auriculata Family: Caesalpiniacae	Avartaki	Leaves	Antihyperglycemic	[26]
Catharanthus roseus Family: Apocynaceae	Vinca periwinkle, sadabahar	Leaves	Hypoglycemic	[27]
Ceibapentandra Family: Bombacaceae	Silk cotton tree	Roots, bark	Antidiabetic, hypoglycemic	[28]
Centaurium erythrea Family: Gentianaceae	European centaury	Leaves	Antidiabetic	[29]
Chaenomeles sinensis Family: Rosaceae	Chinese quince	Fruit	Antidiabetic	[30]
Cinnamomum tamala Family: Lauraceae	Tejpat or bayberry	Leaves	Hypoglycemic	[31]
Cissampelo pareira Family: Menispermaceae	Velvet leaf	Root bark	Antidiabetic	[10]
Citrullus colocynthis Family: Cucurbitaceae	Bitter apple	Fruit	Antidiabetic	[32]
Coccinea grandis Family: Cucurbitaceae	Ivy guard or kunderi	Whole plant	Hypoglycemic	[33]
Costus speciosus Family: Costaceae	Crepe ginger	Rhizome	Antidiabetic	[10]
Cocos nucifera Family: Arecaceae	Coconut	Leaves	Antihyperglycemic	[34]
Dillenia indica Family: Dilleniaceae	Elephant apple	Leaves	Antidiabetic	[35]
Embelia ribes Family: Myrsinaceae	False black pepper, vidanga	Berries	Antidiabetic	[36]
Enicostemma littorale Family: Gentianaceae	Indian gentian	Whole plant	Antidiabetic	[37]

(*Contd*...)

Table 2: (*Continued*)

Botanical source	Common name	Part used	Activity	References
Eucalyptus globulus Family: Myrtaceae	Blue gum tree	Leave	Antidiabetic	[38]
Ficus bengalenesis Family: Moraceae	Banyan tree or Bur	Bark	Hypoglycemic	[39]
Ficus racemosa Family: Moraceae	Gular	Fruit	Antidiabetic	[10]
Girardiana heterophylla Family: Urticaceae	Stinging nettle	Root	Antidiabetic	[10]
Gynocardia odorata Family: Flacourtiaceae	Chaulmurga seeds	Fruit	Antidiabetic	[10]
Gymnema sylvestre Family: Asclepiadaceae	Gurmar	Leaves	Hypoglycemic, antidiabetic	[18]
Ipomoea batatus Family: Convolvulaceae	Sweet potato	Leaves	Antidiabetic	[40]
Hybanthus enneaspermus Family: Violaceae	Spade flower	Whole plant	Antidiabetic	[41]
Hibiscus rosasinesis Family: Malvaceae	Shoe flower	Leaves	Antidiabetic	[42]
Jatropha curcas Family: Euphorbiaceae	Barbados nut	Leaves	Antidiabetic	[43]
Lantana aculeate Family: Verbenaceae	Red sage	Leaves	Antihyperglycemic	[44]
Lippa nodiflora Family: Verbenaceae	Hairy fogfruit	Whole plant	Antidiabetic, hypoglycemic	[45]
Litsea cubeba Family: Lauraceae	May chang	Fruit	Antidiabetic	[10]
Ocimum sanctum Family: Lamiaceae	Holy basil, tulsi	Leaves	Antidiabetic, hypoglycemic	[11]
Ophiopogon japonicas Family: Asparagaceae	Mondo grass	Root	Hypoglycemic	[46]
Oroxylum indicum Family: Bignoniaceae	Indian trumpet flower	Stem bark	Antidiabetic	[10]
Paederia foetida Family: Rubiaceae	Chinese fever vine	Leaves	Antidiabetic	[10]
Panax pseudo ginseng Family: Araliaceae	Himalayan ginseng, Nepal ginseng	Rhizome	Antidiabetic	[10]
Picrorhiza kurrooa Family: Scrophulariaceae	Kutki	Rhizome	Antidiabetic	[10]
Psidium guajava Family: Myrtaceae	Guava, amrud	Fruit	Antihyperglycemic	[47]
Potentilla fulgens Family: Rosaceae	Cinquefoils	Root	Antidiabetic	[10]
Prosopis glandulosa Family: Fabaceae	Honey mesquite	Whole plant	Antidiabetic	[48]
Pterocarpus marsupium Family: Fabaceae	Vijayasar or Indian Malabar	Wood	Hypoglycemic	[49]
Punica granatum Family: Punicaceae	Pomegranate, anar	Flower	Antidiabetic	[50]
Quercus lanata Family: Fagaceae	Woolly leaved oak	Stem bark	Antidiabetic	[10]

(*Contd*...)

Table 2: (*Continued*)

Botanical source	Common name	Part used	Activity	References
Tinospora cordifolia Family: Menispermaceae	Guduchi, giloy	Root	Antidiabetic	[11]
Trigonella foenum-graecum Family: Fabaceae	Fenugreek	Seed	Hypoglycemic, antidiabetic	[11]
Saraca asoca Family: Caesalpiniaceae	Ashoka tree	Flower	Antidiabetic	[10]
Solanum torvum Family: Solanaceae	Devil's fig	Fruit	Antihyperglycemic	[51]
Sonneratia alba Family: Lythraceae	Mangrove apple	Leave	Antidiabetic	[52]
Stephania glabra Family: Menispermaceae	Thaya nuya	Root	Antidiabetic	[10]
Solanum xanthocarpum Family: Solanaceae	Kantkari	Leaves	Antihyperglycemic	[53]
Semecarpus anacardium Family: Anacardiaceae	Bhilawa, bhallataka	Nut	Antidiabetic	[54]
Symplocos cochinchinensis Family: Symplocaceae	Kambli-vetti	Leaves	Antidiabetic	[55]
Syzygium cuminii Family: Myrtaceae	Jamun, jambul	Seeds	Antidiabetic	[18]
Vitex negundo Family: Lamiaceae	Chinese chastetree	Leaves	Antihyperglycemic	[56]
Vitis vinifera Family: Vitaceae	Woody vine	Leaves	Antidiabetic	[57]
Wattakaka volubilis Family: Asclepiadaceae	Perun-kurinjan	Leaves	Antidiabetic	[11]
Withania somnifera Family: Solanaceae	Winter cherry, ashwagandha	Root, leaf	Hypoglycemic	[58]
Zea mays Family: *Gramineae*	Maize, makkai	Corn silk	Hyperglycemic and antihyperglycemic	[59]
Zingiber officinale Family: Zingiberaceae	Ginger, adrak	Rhizomes	Hypoglycemic	[60]

Table 3: Plants derived antidiabetic phytoconstituents[61]

Alkaloids: Berberine, Catharanthin, Calystegine B_2, Cryptolepine, Jambosine, Javaberine A, Javaberine A, Lepidine, Lupanine, Mahanimbine, Piperumbellactam A and Tecomine

Glycosides: Pseudoprototinosaponin AIII and Prototinosaponin AIII, Vitexin, Isovitexin, Myrciacitrins I, Myrciacitrins II, Myrciaphenones A, Myrciaphenones B and Neomyrtillin

Flavonoids: Kaempferitrin, Hesperidin, Naringin, Genistein, Kaempferol, Quercetin, Rutin, Mangiferin, Shamimin, Marsupsin, Pterostilbene, and Leucodelphinidin

Terpenoids and steroids: Andrographolide, Bassic acid, Charantin, Colosolic acid, Christinin A, Maslinic acid, Elatosides E, Forskolin, Ginsenosides, and Gymnemic acid IV

Polysaccharides: Aconitans A-D, Atractans A, Galactomannan gum, Ganoderans A and B

Others: Allicin, Bellidifolin, Bakuchiol, Curcuminoids, Ferulic acid, Ginseng polypeptides, Ellagitannins, 4-hydroxyisoleucine, Paeoniflorin, and 8-debenzoylpaeoniflorin

- Improvement in digestion and reduction in blood sugar
- Increasing glucose utilization
- Increasing glyoxalase 1 activity in liver
- Increasing the creatine kinase levels in tissues
- Increasing the number and size of cells in islets of Langerhans
- Inhibition glycogen-metabolizing enzymes
- Inhibition in renal glucose reabsorption
- Inhibition of alpha-amylase
- Inhibition of insulin degradation processes
- Inhibition of β-galactocidase and α-glucocidase
- Oxygen radical scavengers
- Providing essential elements such as calcium, copper, magnesium, manganese, and zinc for the β-cells
- Reduction absorption of glucose from gastrointestinal tract
- Reduction of lactic dehydrogenase
- Reduction of γ-glutamyl transpeptidase
- Repairing pancreatic β-cells
- Stimulation of glycogenesis and hepatic glycolysis
- Stimulation of insulin secretion from β-cells of islets.

Marketed Formulations

Herbal medicines have received considerable preference because of their safe and potential therapeutic effects. There are some herbal formulations available in the market, which have been studied clinically and proved their positive effect on human beings. Some herbal formulations are displayed in Table 4.

CONCLUSION

Medicinal plants considered potent candidates for new drug discovery. Furthermore, these medicinal plants provide a rich mine for bioactive constituents that are free from side effects and have powerful pharmacological actions. Diabetes mellitus is the one of the most leading disorders, which

Table 4: Some herbal preparation for the management of diabetes[18,62]

Formulation name	Ingredients
Adcaps	Haldi, Jambuphal, Amla, Mamajov, Neem, Karela, Vijaysar, Tejba, Gulvel Sudha, Guggl, Trivang Nag Suvarnamakshik bhasm, Shilajeet, Ashok and Madhunasni
Bitter gourd powder	*Momordica charantia*
BZR-34	*Bereris aristata, Ptercarpus marsupium, Gymnema sylvestre, Rubia cordifolia, Trigonella feounum, Berberis aristata,* and *Tinopora cordifolia*
Asanand	Arjuna, Ganasar, Karanja, Kanth, Lodhra, Palash and Shirish
Diasulin	*Cassia auriculata, Coccinia indica, Momordica charantia, Syzygium cumini, Emblica officinalis, Trigonella foenum graecum, Curcuma longa, Gymnema sylvestre, Tinospora cordifolia,* and *Scoparia dulcis*
Diabecon	*Balsamodendron mukul, Pterocarpus marsupium, Casearia esculenta, Gymnema sylvestre, Glycyrrhiza glabra, Tinospora cordifolia, Swertia chirata, Tribulus terrestris, Phyllanthus, Amarus, Gmelina arborea, Berberis aristata, Aloe vera, Eugenia jambolana, Asparagus racemosus, Boerhaavia diffusa, Sphaeranthus indicus, Gossypium herbaceum, Shilajeet,* powders of *Momordica charantia, Piper nigrum, Ocimum sanctum, Abutilon indicum, Curcuma longa, Rumex maritimus,* and *Trikatu*
Dabur-Madhu Rakshak	*Phyllanthus emblica, Cinnamomum tamala, Pterocarpus marsupium, Gymnema sylvestre, Eugenia jambolana, Piper nigrum, Azadiracheta indiaca, Trigonella foenum-graecum, Terminalia belerica, Momordica charantia, Terminalia chebula,* Bhavana Dravyas and Shudh Shilajit
Diabecure	*Berberis vulgaris, Erytherea centaurium, Juglans regia,* millefolium and taraxacum
Epinsulin	*Pterocarpus marsupium*
Giloysatva	Giloysatva
Gokshuradi guggul	Gokshuradi guggul
Hyponidd	*Momordica charantia, Curcuma longa, Cassia auriculata, Emblica officinalis, Eugenia jambolana, Enicostemma littorale, Gymnema sylvestre, Pterocarpus marsupium, Tinospora cordifolia, Melia azadirachta, Swertia chirata,* Yashad Bhasma and Shilajit
Indrajav churana	Indrajav churana
Karneem	Karela, Kulki, Neem, Sounth, Shudha guggul and Tulsi
Madhumehari Granules	*Gymnema sylvestre*, *Syzygium cumini, Tinospora cordifolia, Momordica charantia, Acacla catechu, Curcuma longa, Emblica officinalis, Pterocarpus marsupium, Cinnamomum tamala,* Asphaltum, *Ficus glomerata, Picrorhiza kurroa, Plumbago zeylanica, Trigonella foenum graecum, Azadirachta indica* and *Aegle marmelos*
Mamajov	Mamajov powder
Ojamin	*Aegle marmelos, Trigonella foenum graecum, Carum carvi, Emblica offcinails, Terminalia chebula, Terminalia belarica, Swertia chirata, Tinospora cordifolia, Eugenia jambolana, Picrorhiza kurroa, Gymnema sylvestre, Salacia chinensis* Linn., *Curcuma longa* and *Melia azadirachta*
Panvli	Amla, Gudmar, Gul vel, Haldi, Kanth, Karvas, Panvelley and Yashti,
Shilajeet	Shudha shilajeet
Syndrex	*Berberis vulgaris, Erytherea centaurium, Juglans regia,* millefolium and taraxacum
Triphala guggul	Triphala guggul
Trivang bhasma	Trivang bhasma
Zpter	*Tinospora cordifolia, Gymnema sylvestre,* Amalaki, Bibhitaki, Chtrak, Dalchini, Haridra, Haritaki, Jasad Bhasma, and Vijayasara

may increase the risk of secondary complications affecting the eyes, kidneys, nerves, heart, and arteries. It is metabolic diseases manifested as the presence of high concentration of glucose in the blood because of improper release of insulin from pancreas or inactivity of cells to the insulin. Multiple of therapies are available for the treatment of diabetics. However, allopathic drugs are producing several unwanted side effects. It has been reported that antidiabetic herbal medicines have a similar mechanism of action as allopathic drugs but negligible side effect with low cost. These plants have polyphenols, alkaloids, glycosides, polysaccharides, terpenoids, steroids, and flavonoids. These constituents are helpful in the treatment of many diseases including diabetics. In this review, we have made humble attempt to emphasize some medicinal plants, which are having antidiabetic or hypoglycemic or antihyperglycemic property. However, very few plants have been studied clinically. It is worthwhile isolate phytoconstituents from these reported antidiabetic plants may deserve further evaluation in clinical studies.

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