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Role of Herbal Medicines in the Treatment of Diabetes Mellitus: An Updated Review

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ABSTRACT

Diabetes is a serious public health problem because 70% of the patients have uncontrolled diabetes which leads to complications early. Poor monitoring is the main reason because many of the patients are not monitoring at all. So this is the main challenge to know about controlling parameters for this disease. But the best news is that major strides are operative in diabetes prohibition, diagnosis, and care. For the treatment of type 1 diabetes patients require administration of insulin 3-4 times in a day during their lives and the blood sugar level of patients should be observed routinely to prevent obstacles such as retinopathy and cardiovascular disease risks. Well-monitored glycemic control is required for the management of type 2 diabetes. As it may results in the loss of glycemic regulation, the need to regulation the continuing degradation of β-cell function is necessary. Insulin and conventional drugs are effective, but the associated glucoregulatory and metabolic dysfunctions can not be repaired. Over the years, herbal medicine has been used to cure various illnesses, such as diabetes. In addition to their mainstream therapies, herbal medicines with antidiabetic properties are used by many diabetic patients, which can present both an advantage and a possible risk for successful control of their disease. The review provides detailed report of diabetes, its diagnosis and role of herbal medicines in its treatment.

Keywords
Diabetes Mellitus, Diagnosis, Drugs, Herbs, Applications

Introduction

Diabetes mellitus (DM) is a chronic condition characterized by insulin synthesis lack and its intervention, or together. This results to chronic hyperglycemia with disruptions in most of the human body's metabolic processes [1]. Untreated cases display vascular damage and severe tissue which leads to severe complications such as neuropathy, retinopathy, cardiovascular complications and ulcerations [2-4]. Polyuria, polydipsia, weight loss, polyphagia, cardiac arrhythmia, tachycardia and hypotension are signs and symptoms of hyperglycemia [5-7].
Diabetes mellitus is categorized into 3 types: Type 1, Type 2 and third one is gestational diabetes mellitus.

Type 1 Diabetes mellitus is referred to as insulin-dependent DM due to non-functioning of the β-cell of the pancreatic islets of langerhans.
Type 2 Diabetes mellitus is referred to insulin independent DM in which transient loss of β cell mass arises that is attributed to hereditary predisposition which often occurs in obese people and is related to high cholesterol level and high blood pressure. Type 2 DM therapy aims at decreasing the insulin conflict and increasing secretion of insulin.
Gestational diabetes is a form of diabetes that found in pregnant women with hyperglycemia. It typically occurs in the 2nd or 3rd trimester in 2-4 percent pregnancies [8].

Diagnosis of Diabetes Mellitus
Random plasma test: This is the easiest test, and before taking the rest, it does not require fasting. If blood sugar is 200 or more than 200 mg / dl, it is most likely to suggest diabetes but must be reconfirmed.
Fasting plasma glucose test: Before taking the test, there should be eight hours of fasting. A diagnosis of diabetes is confirmed by glucose greater than 130 mg/dl on performed two or more than two tests on entirely separate days [9].
Oral glucose tolerance test: If the value is 160-200 mg / dl for random plasma glucose test and 110-125 mg/dl for the fasting plasma test then this test is carried out. This blood test assesses the reaction to glucose in the body. This

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test requires at least eight hours of fasting, but not more than 16 hours. If the amount of glucose is determined for fasting, then 75gm of glucose and 100gm for pregnant women are given. Then the blood is checked for two to three hours every thirty minutes to one hour. If level of glucose is below 140 mg/dl for two hours, this test is normal. The diagnosis of diabetes is indicated by a fasting level of 130 mg/dl or above and a level of glucose 200 mg/dl or above for two hours [9].

Antidiabetic drugs

It is possible to avoid diabetes mellitus disease by controlling blood sugar levels with different medications, acquiring various exercise or yoga therapies or diet plans [10]. Actually available diabetes mellitus therapies include insulin therapy for the type 1 DM and some other oral hypoglycemic medicines i.e. peptide analogues, thiazolidinediones and sulphonylureas for type 2 diabetes treatment [11,12]. Different side effects like sickness, malignant anaemia, vomiting, swelling, dysentery, migraine and faintness are associated with synthetic drugs used for diabetes care, so the need of herbal medicines created [13]. In ancient times, traditional plants with therapeutic value were used by physicians and lay public for the treating various diseases i.e. Cardiac disease, cancer, skin diseases and diabetes etc. Traditional plants used to regulate diabetes have a long history in India and China. Several books are available like CharakaSamhita and SusrutaSamhita that describe the phytopharmacology characteristics of diabetes and its adverse effect [14]. The details of some drugs with their class, action and disadvantages are summarized in table 1.

Table 1: Representative antidiabetic agents used in the treatment of T2DM patients

Drug (s)	Class	Action	Disadvantages	References
Acarbose/ Miglitol/ Voglibose	*AGIs*	Decrease absorption of carbohydrate	GI side effects and high dose frequency	[15]
Metformin	Biguanides	Enhance sensitivity of insulin, decreases risk of cardiovascular and hypoglycemia.	Side effects of Gastrointestinaland too much lactic acid produces in the body	[16]
Repaglinide (Prandin) Nateglinide (Starlix)	Meglitinides	Stimulate the release of insulin	Decreases blood glucose level and increases body weight	[17]
Pioglitazone/Roziglitazone/ Troglitazone	*TZDs*	High sensitivity of insulin and low risk of hypoglycemia	Increases risk of cancer and weight of body	[18,19]
Saxagliptin (Onglyza) Sitagliptin (Januvia) Linagliptin (Tradjenta) Alogliptin	Dipeptidyl-peptidase 4 (DPP-4) inhibitors	Enhances insulin release and inhibits glucose release	Infection of upper respiratory tract, headache and pharyngitis	[20,21]
Liraglutide/ Exenatide	Glucagon like peptide -1 receptor agonists	Increases secretion of insulin and decreases secretion of glucagon	Side effects of gastrointestinal tract, renal dysfunction and acute pancreatitis	[15,22]
Empagliflozin/ Dapagliflozin/ Canagliflozin	Sodium-glucose transporter 2 inhibitors	Inhibits reabsorption of glucose	Nausea or vomiting	[23]
Glyburide/ Glipizide/ Gliclazide/ Glimepiride	*Sulfonylureas*	Incresease secretion of insulin	Hypoglycemia weight gain	[15,23]
Colesevelam (Welchol)	Bile acid sequestrants	Reduces level of cholesterol and blood glucose	Flatulence Constipation Indigestion	[22]

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Pramlintide (Symlin)	Amylin mimetics	help in controlling level of blood sugar	Hypoglycemia Nausea or vomiting	[24]

Role of herbs in the treatment of Diabetes Mellitus

Due to fewer bad effects and adverse effects, natural medications have proven to be a safer option over prescription drugs.

Herbal formulations can be purchased without prescription. These are safe natural drugs i.e. no adverse effects are present. Herbal preparations include natural herbs and extracts of fruits and vegetables that are effective without harmful effects in the treatment of multiple diseases. In the other hand, chemicals are synthetically prepared, which also have side effects. Herbal formulations compared with allopathic drugs are inexpensive. Herbal formulations are Enviroment friendly because these are made from normal products whereas allopathic drugs are made from substances which are chemically modified. Herbal preparations are available without prescription while most allopathic medicines required prescription [25-26].

Herbal antidiabetic drugs

The medicinal plants and herbs are currently used for their anti-diabetic activity in extract forms and restore the action of pancreatic β- cells [27]. Flavonoids, tannins, phenolics, and alkaloids are the basic most usual herbal active ingredients used in the diabetes treatment [28]. The continuation of these substances implies the significance of the anti-diabetic properties of these plants [29]. Tannin, for instance, increases the function of beta cells of pancrease and enhance insulin discharge. Quercetin is an antioxidant that interacts with many oxygen radicals removal pathways, preventing peroxidation of lipid and chelation of metal ion [29]. In fact, the mechanisms of actions for hypoglycemic plants include: increase in the secretion of insulin, increase in the absorption by muscle and adipose tissues, from the intestine preventing the incorporation of glucose, and preventing the output of glucose by the cells of liver [30]. The reduction or removal of diabetes complications is mainly responsible for these factors and the medicinal plants list used for antidiabetic activity is given in table 2, while marketed herbal formulations for antidiabetic activity are enlisted in table 3.

Table 2: List of herbal plants used in diabetes mellitus

S. No.	Plant species	Family	Common Name	Plant Part	Main Chemical constituents	Mechanism of action	Ref
1.	*Aeglemarmelos*	Rutaceae	Golden apple	Leaves extracts	Aeglemarmelosine	Enhance the functional condition of pancreatic β-cells	[31]
2.	*Allium cepa*	Lilliaceae	Pyaaz	Bulbs	Allyl propyl disulphide and diallyldisulphide	Improve antioxidant activity	[32]
3.	*Allium sativum*	Lilliaceae	Garlic	Petroleum ether exract of bulbs	Allylpropyldisulphide oxide, allicin	Improve plasma lipid metabolism and plasma antioxidant activity	[33]
4.	*Aloe barbadensis*	Asphodelaceae	Ghikanwar	Leaf pulp extract	β- sitosterol, campesterol	Improvement in impaired glucose tolerance	[34]
5.	*Andro-graphispaniculata*	Acanthaceae	Kalmegh	Ethanolic extract of plant	Kalmeghin	Increases the glucose utilization and lower plasma glucose	[35]
6.	*Annonasquamosa*	Annonaceae	Sharifa	Leaves	Borneol, camphor, eugenol	Improve tolerance of glucose	[36]
7.	*Azadirachtaindica*	Meliaceae	Margosa	Leaf extract	Nimbin, quercetin	Glycogenolytic effect was blocked because of epinephrine action	[37]

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8.	*Brassica juncea*	Brassicaceae	Mustard	Aqueous extract	Sulforaphane	Enhances Glycogen synthetase activity	[38]
9.	*Cajanuscajan*	Leguminosae	Pigeon pea	Seeds	2'-2' methyl cajanone, isoflavones, cajanin, cahanones	Substantialdecrease in serum glucose level	[39]
10.	*Carica papaya*	Caricaceae	Papaya	Aqueous seed extract	Papain, chymopapain	Lowered fasting blood sugar, triglyceride, total cholesterol	[40]
11.	*Carumcarvi*	Apiaceae	Caraway	Aqueous extract of seed	Furfurol, carvone	Substantial decrease in blood glucose level	[41]
12.	*Cassia auriculata*	Leguminosae	Tanner's cassia	Aqueous extract of seed	Limonene, terpinol	Enhances the activity of hepatic hexokinase, phosphor-fructokinase	[42]
13.	*Catharanthu sroseus*	Apocynaceae	Vinca	Hot water decoction of leaves	Catharanthine, vincristine, vinblastine	Lowering of glycemia	[43]
14.	*Cocciniaindi ca*	Cucurbitacea e	Baby water-melon	Ethanolic extract of whole plant	Glutamic acid, Asparagine	Lesser blood glucose level because of suppressed glucose synthesis	[44]
15.	*Coriandrum sativum*	Apiaceae	Coriander	Seed extract	p-cymene, linalool	Enhancing the activity of β-cells and decrease serum glucose	[45]
16.	*Cinnamomu m cassia*	Lauraceae	Cinnamon	Bark	Cinnam-aldehyde, eugenol	Increases the sensitivity of insulin receptor	[46]
17.	*Cinnamomu m tamala*	Lauraceae	Tejpatta	Leaf extract	Linalool, β-caryophyllene	Insulin release from pancreatic β-cells	[47]
18.	*Curcuma longa*	Zingiberaceae	Turmeric	Rhizomes	Curcuminoids, bisdemethoxy -curcumin, dimethoxy-curcumin	Reduces blood sugar level, Improves metabolism of glucose	[48]
19.	*Eugenia jambolana*	Myrtaceae	Jambolan	Fruit pulp	Oleanolic acid, gallic acid	Decreases blood glucose level	[49]
20.	*Ficusbengal ensis*	Moraceae	Bargad	Alcoholic extract of stem bark	Leucodelphinidi n	Enhanced insulin secretion from β-cells	[50]
21.	*Ficushispida*	Moraceae	Daduri	Alcoholic extract of leaves	Ficustriol, O-methyltylophori nidine	Reduces level of blood glucose and improved level of serum insulin	[51]
22.	*Gymnemasyl vestre*	Asclepidacea e	Gudmar	Dried leaves	Gymnemic acid, dammarene	Decreases blood glucose level	[52]
23.	*Mangiferain dica*	Anacardiacea e	Mango	Extract of leaves	Mangiferin	Reduces intestinal absorption of glucose	[53]
24.	*Momordicac harantia*	Curcubitacea e	Bitter gourd	Fresh green leaves	Charantin, sterol	Activates PPARs alpha a nd lowers plasma apo β100 in high-fat diet mice	[54]
25.	*Musa*	Musaceae	Banana	Flower	Tryptophan,	Reduces blood	[55]

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	Paradisia				tannin, serotonin	glucose and glycosylated haemoglobin levels	
26.	*Ocimum sanctum*	Labiateae	Tulsi	Whole plant	Eugenol	Increases release of insulin	[56]
27.	*Panax ginseng*	Araliaceae	Ginseng	Root extract	Ginsenosideprotopanaxdiol	Inhibit activity of α-glycosidase and reduces absorption of glucose	[57]
28.	*Phyllanthus emblica*	Euphorbiaceae	Amla	Entire plant	Alkaloids	Reduces level of blood glucose	[58]
29.	*Punicagrantum*	Puniaceae	Pomegranate	Seeds	Gallic acid, protein, tannin, vitamin C	Decreases the blood glucose level	[59]
30.	*Swertiachirata*	Gentinaceae	Chirata	Whole plant	Gentianine, Xanthonemangiferin, Methyl swertianin	Reduces level of blood glucose	[60]
31.	*Terminaliaarjuna*	Combretaceae	Arjuna	Bark and stem	Arjunolic acid, arjunic acid	Decreases blood glucose level and Glucose-6-Phosphate activity	[61]
32.	*Terminaliacatappa*	Combretaceae	Almond	Petroleum ether fruit extract	Omega-9-ftty acid	Reduction in blood glucose level	[62]
33.	*Tinosporacardifolia*	Menispermaceae	Giloy	Aqueous extract of root	Tinosporone, tinosporic acid	Declineinglycemia as well aslipids of brain	[63]
34.	*Trigonellafoenum*	Fabaceae	Methi	Seeds	Fat, volatile oil, carbohydrate, protein	Stimulating insulin relea se, reducing insulin resistance, and reducing blood sugar levels	[64]
35.	*Zingiberofficinalis*	Zingiberaceae	Sunth	Rhizome	Gingerol	Insulin level improved	[65]

Table 3: Antidiabetic herbal formulation marketed in India [66]

Sr. No.	Brand Name	Manufecturer	Ingredients
1.	Diabecon	Himalaya	*Asparagus racemosus, Balsamodendronmukul, Trikatu, Aloe vera, Casearіaesculenta, Gymnemasylvestre, Ocimum sanctum, Swertiachirata, Abutilon indicum, Tribulusterrestris*, Shilajit, *Gmelinaarborea, Berberisaristata, Boerhaaviadiffusa, Sphaeranthusindicus*,powders of *Momordicacharantia, Eugenia jambolana, Piper nigrum, Tinosporacordifolia, Curcuma longa, Rumexmaritimus, Phyllanthusamarus, Gossypiumherbaceum, Pterocarpusmarsupium.*
2.	Pancreatic tonic 180 cp	Ayurvedic herbal supplement	*Aeglemarmelos, Cinnamomumtamala, Ficusracemosa, Momordicacharantia, Azadirachtaindica, Gymnemasylvestre, Trigonellafoenumgraceum,Syzygiumcumini, Pterocarpusmarsupium*
3.	Bitter gourd powder	Garry and Sun natural Remedies	*Momordicacharantia*
4.	Diasulin		*Curcuma longa, Cassia auriculata, Momordicacharantia,*

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			Tinosporacordifolia, Syzygiumcumini, Gymnemasylvestre, Scopariadulcis, Cocciniaindica, Emblicaofficinalis, Trigonellafoenumgraecum
5.	Dia-care	Admark Herbals Limited	Himej, Neemchal, Kadu, Namejav, Jambubeej, SanjeevanMool
6.	Diabetes-daily care	Nature's Health Supply	*Momordicacharantia* extract, *Gymnemasylvestre*extract, Chromax, Alpha Lipoic acid, Vanadium, Fenugreek extract, Cinnamon exract, Liquorice Root extract
7.	Gurmar powder	Garry and Sun Natural Remedies	*Gymnemasylvestre*
8.	Ayurveda alternative herbal formula to Diabetes	Chakrapani Ayurveda	*Azadirachtaindica, Tinosporacordifolia, Trigonellafoenumgraecum, Inularacemosa, Syzigiumcumini, Gymnemasylvestre, Momordicacharantia*
9.	Epinsulin	Swastik Formulations	*Pterocarpusmarsupium*
10.	Diabeta	Ayurvedic cure Ayurvedic Herbal Health Products	*AzadirachtaIndica, Momordicacharantia, Acacia arabica, Curcuma longa, Vincarosea, Gymnemasylvestre, Pterocarpusmarsipium, Tinosporacordifolia, Syzigiumcumini, Zingiberofficinale*
11.	Syndrex	Plethico Laboratories	Germinated Fenugreek seed extract
12.	Diabecure	Nature beautesanté	*Taraxacum, Erythereacentaurium, Berberis vulgaris, Juglansregia, Millefolium,*
13.	MahumehaKusumakara Rasa	Shree Dhoothapapeshwar Limited	*Aeglemarmelos, Curucma longa, Pterocarpusmarsupium, Vasantkusumakar Rasa, Emblicaofficinalis,*ShudhShilajit, Yashadabhasma, *Enicostemmalittorale, Tinosporacordifolia, Vasantkusumakar Rasa*
14.	Zypter	Om Pharmaceuticals Limited	Vijayasar, Haridra, Bibhitaki, Amalaki, Guduchi and Gurmar, Haritaki, JasadBhasma, Chtak, Dalchini
15.	HypoNIDD	CharakPharma	Shilajit, *Curcuma longa,Meliaazadirachta, Emblicaofficinalis, Momordicacharantia, Eugenia jambolana, Gymnemasylvestre, Pterocarpusmarsupium, EnicostemmalittoraleTinosporacordifolia, Cassia auriculata, Swertiachirata, YashadBhasma*
16.	DaburMadhuRakshak	Dabur	*Eugenia jambolana, Piper nigrum, Terminaliachebula, Pterocarpusmarsupium, Gymnemasylvestre, Azadirachtaindica, Phyllanthusemblica, Trigonellafoenum-graecum,* BhavanaDravyas, ShudhShilajit, *MomordicaCharantia, Cinnamomumtamala, Terminaliabelerica*
17.	Ojamin	Tates remedies	*Aeglemarmelos, Meliaazadirachta, Gymnemasylvestre, Carumcarvi, Terminaliachebula, Curcuma longa, Eugenia jambolana, Picrorrhizakurroa, Trigonellafoenum-graecum, Emblicaofficinalis, Terminaliabelarica, Swertiachirata, Salaciachinensis, Tinosporacordifolia*
18.	Madhumehari Granules	Baidyanath	*Aeglemarmelos, Azadirachtaindica, Emblicaofficinalis, Curcuma longa, PicrorrhizaKurroa, Gymnemasylvestre, Tinosporacordifolia, Syzygiumcumini, Momordicacharantia, Acacia catechu, Cinnamomumtamala, ShilajitAsphaltum, Ficusglomerata, Plumbagozeylanica, Pterocarpusmarsupium, Trigonellafoenum-graecum*

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Conclusion

Diabetes mellitus, which affects millions of individuals worldwide, is the most common endocrine condition. There are so many compounds that assist in the treatment of diabetes, but as such no fixed therpy is there that can cure a patient completely from this disease. After doing a large number of trials, several modern medicines have been reported for diabetes. Isolated constituents and extracts from various ordinary resources, mainly plants have various constituests that results in control and treatment of diabetes problems and complications. Plants, partially because of their antidiabetic compounds, such as flavonoids,tannins, phenolics, and alkaloids are natural antioxidants and powerful herbal medicines. This review paper plays a very important role in the design of drugs and the treatment of diabetes mellitus hyperglycemic issues and it can be useful to establish result based different medicines using herbal preparation to cure different types of diabetes problem for health practitioners, scientists and scholars.

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