REVIEW ARTICLE

Medicinal Plants: A Source of Antidiabetic Drugs

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Abstract

Introduction: In the recent decades, diabetes mellitus has emerged as a major health problem in the world and it is hampering the development economically and socially. Indeed, about 80% of the masses in the developing countries depend upon ancient systems of herbal formulations for their primary health concerns. Plants-based drugs and their constituents play a pivotal role in prevention and treatment of various diseases and are considered as rich resources that can be used in drug development and synthesis in future. The purpose of this systematic review is to analyze hypoglycemic properties of medicinal plants.

Aim: The study is primarily focused to understand the historical and modern documentation related to treatment of diabetes and also to create the attention of pharmacologists, botanists, and phytochemists for further scientific research in the field.

Results: This present review mainly focuses on 50 medicinal plants with hypoglycemic properties. Various research papers and studies have been reviewed on the role of diverse active chemical biomolecules associated with antidiabetic properties.

Conclusion: Since time immemorial, plants have been the potential source of medicine and therefore the novel form of healthcare known. The hypoglycemic properties of medicinal plants verified by several researchers have confirmed the effective management of diabetes mellitus. This study concluded that the profiles of plant species were generally used for treatment of disease and having antidiabetic properties can be an effective source for the development of safer oral hypoglycemic agents.

Keywords: Chemical constituents, Diabetes mellitus, Medicinal plants, Plant parts.

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Introduction

Medicinal plants are the pillar of traditional medicine and are used to treat various diseases throughout the world. Noncommunicable diseases have always been a curse to the mankind.[1] During the past decades, traditional medicines have acquired an expedient growth obtained from biological, mineral, or marine origins, which gained popularity because of their, less cost, natural origin, and lesser side effects and these traditions are still flourishing. Current estimate recommended by the World Health Organization (WHO) suggests a large proportion of population, around 80%, in developing countries relies on these novel traditional systems of medicine for healthcare needs.[2,3] Since ancient times, medicinal plants have been a potential remedy in management of diabetic mellitus through traditional approaches. These medicinal plants contain chemical moieties with antidiabetic therapeutic properties that act as precursor for synthetic drugs.[4,5] A large number of antidiabetic medicines are available in the pharmaceutical market with unwanted side effects, thus creating a demand for a novel sustainable approach.[6,7] Recently, the herbal medicines have gain attention because of their effective remedial properties associated with least or no side effects both in developing and developed countries.[8–10] The management of diabetes is a global concern and successful treatment is highly sought as it accounts for majority of deaths in the world.[11] This article highlights the significance and the interest of medicinal plants in the effective and enduring treatment of chronic disease, i.e., antidiabetes mellitus.

Diabetes Mellitus

The word "diabetes" ("*dia*" means through; "*betes*" means pass) was coined by the Greek physician Aeretaeus. Diabetes mellitus is a chronic ailment associated with abnormally elevated levels of glucose in the blood and caused by a deficiency in the secretion or action of insulin. Therefore, inadequacy of insulin secretion due to its receptors' insensitivity is the primary reason for all forms of diabetes mellitus.[12]

The first widely accepted classification of diabetes mellitus was published by WHO in 1980[13] and, in modified form, in 1985.[14] There are two main clinical types of diabetes:

Type I (Juvenile-onset) Insulin-dependent Diabetes Mellitus

The disease starts very early in life and shiftly becomes severe and it requires lifelong insulin therapy and intake of balanced diet.

Type II (Maturity-onset) Noninsulin-dependent Diabetes Mellitus

This is a condition in which the regulatory action of insulin is defective. It is generally characterized by insulin resistance. The symptoms are milder and frequently goes undiagnosed at first and the individuals with this disorder become insulin-resistant.

Diabetes mellitus is a disease that affects almost all the body systems and disturbs their normal function and it can lead to microvascular and macrovascular complications such as neuropathy, retinopathy, cardiomyopathy, nephropathy, exocrine

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gland insufficiency, and several other complications and eventually to death.[15]

Prevalence and Incidence of Diabetes Mellitus

Approximately 425 million people are facing diabetes in the world; by 2045, this will rise to 629 million and India will become the country with second largest number of type 2 diabetes cases at 73 million (international Diabetes Federation, 2017). The most important reasons behind this drastic increase are urbanization, Westernization diet and related lifestyle changes, increase in life expectancy at birth, physical inactivity, obesity, and possibly a genetic background.[4,16] Different ethnic and racial groups have also been found to play an important role in the diabetic epidemiology in diverse populations within the same region.[17–19]

Current Status of Drugs Used in Diabetes

Currently approved oral hypoglycemic drugs such as sulfonylureas, glucosidase inhibitors, biguanides, troglitazone, and glinides are available for treatment of type 2 diabetes; they produce various serious adverse side effects such as kidney failure, liver problems, lactic acidosis, and diarrhea.[20,21] Thus, the effective and safe treatment of diabetes mellitus is considered as an unsolved global problem and the successful treatment without any side effects is still a challenge.

Natural Medicines Used for Diabetes Therapy

There has been resurgence of ethnomedicine and folk medicines, which are regarded as quite safer and well-practiced.[22–25] From the long time, medicinal plants have been well documented for their value as a source of new drugs with therapeutic potential and are still significant as an important tool for the identification of molecules, which leads to effective and novel pharmacologically active drugs. Major multinational pharmaceutical companies search for various bioactive compounds from medicinal plants. Mostly drugs are derived from plants through direct and indirect approach. Medicinal plants have been instrumental in lowering the blood sugar level and thereby used widely as antidiabetic remedies. It includes delaying the diabetes-related complications and metabolic abnormalities.

After an extensive literature search and application of traditional knowledge, it is observed that plant-derived constituents display different kinds of pharmacological activities; among these, alkaloids, carbohydrates, glycosides, gallic acid, glycopeptides, hypoglycans, polysaccharides, peptidoglycans, steroids, terpenoids, tannins, amino acids, and inorganic ions have exhibited hypoglycemic activity. The list of the medicinal plants, different parts used, and the mode of action are presented in Table 1.

Results and Discussion

Diabetes mellitus is chronic disorder associated with metabolic disorder due to insufficient secretion of insulin. It is now emerging as an epidemic worldwide and its cure is yet to be found. The inexpensive and novel properties associated with herbal drugs are the main reason behind the immense use in clinical research. The present review has highlighted 50 medicinal plants belonging to various families and different plant parts used against diabetes mellitus with primary emphasis on the role of the active biomolecules with diverse active chemical structures. This work can serve as a potential basis for further research on curative potential of medicinal plants against diabetes.

Table 1: Medicinal plants having active hypoglycemic constituents

S. no	*Family*	*Botanical name*	*Common name*	*Parts used*	*Active chemical constituents*	*Mechanism of action*	*Ref.*
1	Malvaceae	*Helicteres isora* L.	East Indian screw tree	Root	Steroid, terpenoid, alkaloid, carbohydrate, phenolics	Reduction in blood glucose, total cholesterol and triglycerides	20
2	Fabaceae	*Acacia arabica* (Lam.) Wild.	Indian gum Arabic	Seed, bark	Polyphenol, tannin	Initiate release of insulin	12, 26 and 27
		Cassia auriculata (L.) Roxb.	Tanner's cassia	Flower	β Sitosterol, flavonoids, triterpenoid, tannins	Increase utilization of glucose through increase glycolysis	
3	Rutaceae	*Aegle marmelos* (L.) Correa	Golden apple	Fruit	Aegeline 2, Coumarin, flavonoid, alkaloid	Increase glucose tolerance of ethanolic extract	12, 28 and 29
		Murraya koenigii (L.) Spreng.	Curry-leaf tree	Leaf, fruit	Carbazole, alkaloid	Reduces in the serum cholesterol, glucose, hypoglycaemic and hepatoprotective effects	
4	Amaryllidaceae	*Allium cepa* L.	Onion	Bulb	Allyl propyl disulphide, S-methyl cysteine sulphoxide	Antioxidant and antihyperglycemic effects	12, 30 and 31
		Allium sativum L.	Garlic	Root	Diallyldisulphide oxide, Ajoene, allyl propyl disulfide, S-allyl cysteine, S-allylmercaptocysteine	Suppresses hyperglycemia and hypertriglyceridemia	
5	Asparagaceae	*Aloe vera* (L.) Burm.f.	Barbados aloe	Leaf	Pseudoprototinosaponin, prototinosaponin	Decreases glycosylated hemoglobin	12 and 32

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S. no	*Family*	*Botanical name*	*Common name*	*Parts used*	*Active chemical constituents*	*Mechanism of action*	*Ref.*
6	Meliaceae	*Azadirachta indica* A. Juss.	Neem	Leaf, seed	Nimbidin	Glycogenolytic effect due to epinephrine action was blocked	33
7	Amaran-thaceae	*β vulgaris* L.	Beetroot	Whole plant	Sugar beet pectin, Polydextrose	Reduce blood glucose level by regeneration of β cells	12 and 34
8	Leguminosae	*Cajanus cajan* (L.) Milsp.	Pigeon pea	Seed	(7R*,9as*)-7-phenyloctahydro-quinolizin-2-one	Reduction in the serum glucose levels	12, 35–38
		Butea monosperma (Lam.) Taub.	Bastard teak	Fruit	Butein, palasonin, stigmasterol-3 β-D-glucopyranoside	Reduction in blood glucose	
		Glycine max (L.) Merr.	Soya beans	Seed	3-O-methyl-D-chiro-inositol	Reduces blood glucose	
		Xanthocercis zambesiaca (Baker) Dumaz-le-Grand	Nyala tree	Leaf	Fagomine, 4-O-β-D-glucopyranosylfagomine, Castanospermine	Antihyperglycemic action	
9	Solanaceae	*Withania somnifera* (L.) Dunal	Winter cherry	Leaf	Withanolide alkaloid	Decrease blood sugar level	12, 39–41
		Lycium barbarum L.	Chirchita	Fruit	Polysaccharide	Improvement of insulin resistance and antioxidant ability	
		Capsicum annuum. L.	Chilli	Seed	Capsaicin	Elevation in plasma insulin levels	
10	Apocynaceae	*Catharanthus roseus* (L.) G. Don	Red periwinkle	Whole plant	Vinculin, alkaloid	Decreases glycogen synthase, glucose 6-phosphate-dehydrogenase, succinate dehydrogenase and malate dehydrogenase	12 and 42
11	Lauraceae	*Cinnamomum zeylanicum* Blume	Cinnamon	Leaf, bark	Cinnamaldehyde	Hypoglycemic, hypolipidemic de-creases glycosylated hemoglobin (HbA_{1C}),	12, 43–45
		Persea americana Mill.	Avocado	Fruit	Fat, protein, vitamin, mineral	Reduction in blood glucose levels	
12	Apiaceae	*Coriandrum sativum* L.	Coriander	Leaf	Alanine	Insulin secretion by hyperpolarized B-cells	12, 46 and 47
		Cuminum-cyminum L.	Cumin seed	Seed	Aldehyde	Reduction in hy-perglycaemia and glucosuria	
13	Zingiberaceae	*Curcuma longa* L.	Turmeric	Root	Curcuminoidand turmeric essential oil	Control blood glucose levels and abdominal adipose tissue masses	12, 48 and 49
		Zingiber officinale Roscoe	Ginger	Bulb	Gingerol	Effect of enhancement against insulin-sensitivity	
14	Myrtaceae	*Eucalyptus globulus* Labill.	Blue gum	Leaf	Calytoside	Increase insulin secretion from clonal pancreatic β line	12, 38, 50 and 51
		Psidium guajava L.	Guava	Leaf, fruit	Terpen, flavonoid, strictinin, isostrictinin, pedunculagin, polysaccharide	Hypoglycemic and hypotensive effects	
		Syzygium cordatum Hochst. Ex Krauss	Jambolan	Fruit	Anthocyanin, citric, malic, gallic acid	Increased hepatic glycogen content	

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S. no	*Family*	*Botanical name*	*Common name*	*Parts used*	*Active chemical constituents*	*Mechanism of action*	*Ref.*
15	Moraceae	*Ficus benghalensis* L.	Banyan tree	Bark	Leucopelargonidin, Perlargonidin 3-O-α-L rhamnoside,	Insulin secretion by β-cells	12, 38, 52 and 53
16	Asclepiadaceae	*Gymnema sylvestre* (Retz.) Schult	Sugar destroyer	Leaf	Gymnemic acids I–IV and Gymnemasaponin V	Insulin-releasing action	54
17	Poaceae	*Triticum vulgare* Vill.	Wheat	Whole plant	Albumin	Reduces hemoglobin A_1c levels	55 and 56
		Hordeum vulgare L.	Barley	Seed	β-glucan	Improve glucose control	
18	Cucurbitaceae	*Ibervillea sonorae* (S. Watson) Greene	Huereque	Root	Monoglyceride (MG) fatty acids	Reduces glucose level	12, 39, 57 and 58
		Momordica charantia L.	Bitter gourd	Whole plant	Charantin, Momordicin, 19-epoxy-3β,25-dihydroxycucurbita-6,23(*E*)-diene and 3β,7β,25-trihydroxycucurbita-5,23(*E*)-dien-19-al	Hypoglycaemic effects.	
19	Phyllanthaceae	*Phyllanthus emblica* L.	Amla	Fruit	Tannoid compounds	Antioxidative effect and antidiabetic property	12, 39 and 59
20	Anacardiaceae	*Mangifera indica* L.	Mango tree	Leaf, stem bark, fruit	Mangiferin, polyphenolics, flavonoids, triterpenoids	Anti-inflammatory, analgesic, and hypoglycemic effects	12, 39 and 60
21	Musaceae	*Musa sapientum* L.	Sweet banana	Flower	Flavonoid, Steroid, Glycoside	Blood sugar reduction	12, 39 and 61
22	Lamiaceae	*Ocimum sanctum* L.	Holy basil	Leaf	Eugenol (1-hydroxy-2-methoxy-4-allylbenzene)	Antidiabetic, hepatoprotective, hypotensive, hypolipidmic	62
23	Piperaceae	*Piper betle* L.	Pan	Leaf	Quercetin	Reduction in blood glucose and glycosylated hemoglobin	63
24	Nymphaeaceae	*Nelumbo nucifera* Gaertn.	Sacred lotus	Flower	Nelumboroside A Nelumbroside B	Improvement of glucose tolerance	12 and 64
25	Ranunculaceae	*Nigella sativa* L.	Roman coriander	Whole plant	Thymoquinone	Decreases serum glucose	12 and 65
26	Asteraceae	*Chamaemelum nobile* (L.) All.	Chamomil	Leaf	3-hydroxy-3-methylglutaric acid, flavonoid, glucoside Chamaemeloside	Hypoglycaemic activity	66 and 67
		Baccharis trimera (Less.) DC.	Carqueja	Leaf	Flavonoids and chlorogenic acids	Reduces the glycaemia	
27	Rubiaceae	*Hintonia latiflora* (Sesse & Moc. Ex DC.) Bullock	Copalchi	Stem bark	Coumarins	Decreases in blood glucose levels	68

Conclusion

Diabetes is the seventh leading cause of death, affecting more than 100 million people each year.[69] Diabetes mellitus is a disorder represented with loss of glucose homeostasis generally due to insulin deficiency, resulting in impaired metabolism of glucose and other energy-yielding fuels such as lipids and proteins.[70] In the present scenario, the recasting of lifestyle has made diabetes a dreadful disease to the world especially developing countries. Several authors have reviewed the significance of medicinal plants as hypoglycemic agents.[71] The beneficial effects of medicinal plants are shown in different hypoglycemic experiments. A wide range of plant-associated chemical constituents are found to have potential against the treatment of diabetes mellitus,[72] thereby centralizing world's attention toward phytomedicines that cure this dreadful disease with less toxic side effects.

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हिंदी सारांश

औषधीय पादप: मधुमेह रोधी औषधियों का स्रोत

भूमिका: वर्तमान सदी में, मधुमेह विश्व में एक मुख्य स्वास्थ्य संबंधी समस्या के रूप में उभरी है और यह आर्थिक और सामाजिक रूप से विकास में बाधा उत्पन्न कर रहा है। वास्तव में, विकासशील देशों की लगभग 80% जनसंख्या प्राथमिक स्वास्थ्य संबंधी विकारों हेतु वानस्पतिक औषधयोगों की पुरातन पद्धति पर निर्भर हैं। विभिन्न रोगों के निवारण और उपचार में पादप-आधारित औषधियां और उनके कोन्स्टिटूएंट्स महत्वपूर्ण भूमिका निभाते हैं और इनका उपयोग भविष्य में औषध विकास और संश्लेषण हेतु एक समृद्ध संसाधन के रूप में किया जा सकता है। इस व्यवस्थित समीक्षा का उद्देश्य औषधीय पादपों की हाइपोग्लाइसेमिक गुणकर्म का विश्लेषण करना है।

उद्देश्य: यह अध्ययन मुख्य रूप से मधुमेह से संबंधित उपचार के ऐतिहासिक और आधुनिक प्रलेखन को समझने एवं इस क्षेत्र में और अधिक वैज्ञानिक अनुसंधान हेतु फ़ार्माकॉलोजिस्टों, बोटेनिस्ट्स और फाइटोकेमिस्ट्स के ध्यानाकर्षण पर केंद्रित है।

परिणाम: मुख्यतया यह वर्तमान समीक्षा हाइपोग्लाइसेमिक गुणकर्म वाले 50 औषधीय पादपों पर केंद्रित है। मधुमेह रोधी विशेषताओं से संबद्ध विविध एक्टिव केमिकल बायोमोलिक्युल्स की भूमिका पर विभिन्न शोध पत्रों और अध्ययनों की समीक्षा की गई।

निष्कर्ष: पुरातन काल से, पादप औषधि के सशक्त स्रोत हैं, अत: ज्ञात स्वास्थ्य देखभाल के एक नूतन रूप में हैं। विभिन्न अनुसंधानकर्ताओं ने प्रमाणित औषधीय पादपों की हाइपोग्लेमिक विशेषता संबंधी मधुमेह के प्रभावकारी उपचार की पुष्टि की। अध्ययन से यह निष्कर्ष निकलता है कि पादप जाति की प्रोफाइल्स का समान्यतया उपयोग रोगों का उपचार करने में होता है और इसकी मधुमेह रोधी विशेषता सुरक्षित अभ्यंतर हाइपोग्लाइसेमिक एजेंट्स का विकास करने हेतु एक प्रभावी स्रोत हो सकता है।

मुख्य शब्द: केमिकल कोन्स्टिटूएंट्स, मधुमेह, औषधीय पादप, पादप भाग।