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.

Introduction

Medical 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. 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. 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. 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. 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. The management of diabetes is a global concern and successful treatment is highly sought as it accounts for majority of deaths in the world. 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 Aerataeus. 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.

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

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

The disease starts very early in life and shiftsly 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
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.¹⁴,¹⁶ 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 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.

### 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.

### 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 | 28   |
| 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 | 12 and 30 |
| 4     | Amaryllidaceae  | Allium cepa L. | Onion | Bulb | Allyl propyl disulphide, S-methyl cysteine sulfoxide | Antioxidant and antihyperglycemic effects | 12, 30 and 31 |
|       |                  | Allium sativum L. | Garlic | Root | Diallyl disulphide oxide, Ajoene, allyl propyl disulphide, S-allyl cysteine, S-allylmercaptocysteine | Suppresses hyperglycaemia and hypertriglyceridemia | 31   |
| 5     | Asparagaceae    | Aloe vera (L.) Burm.f. | Barbados aloe | Leaf | Pseudoprototinosaponin, prototinosaponin | Decreases glycosylated hemoglobin | 12 and 32 |

Contd...
## Medicinal Plants: A Source of Antidiabetic Drugs

| 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     | Amaranthaceae| *β vulgaris* L.         | Beetroot        | Whole plant| Sugar beet pectin, Polydextrose                        | Reduce blood glucose level by regeneration of β cells     | 12 and 34 |
| 8     | Leguminosae  | *Canavan cajan* (L.) Milsp. | Pigeon pea      | Seed       | (7R*,9as*)-7-phenylotachydroquinolinizin-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                             | Increases in β cells                                      |       |
|       |              | *Xanthocercis zambesiaca* (Baker) Dumaz-le-Grand | Nyala tree | Leaf      | Fagomine, 4-O-β-D-glucopyranosylfagomine, Castanospermine | Anti hyperglycemic 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-     | 12 and 42 |
|       |              |                         |                 |            |                                                        | dehydrogenase, succinate dehydrogenase and malate    |       |
|       |              |                         |                 |            |                                                        | dehydrogenase                                           |       |
|       |              |                         |                 |            |                                                        | Hypoglycemic, hypolipidemic decreases glycated         | 12, 43–45 |
|       |              |                         |                 |            |                                                        | hemoglobin (HbA1c),                                     |       |
|       |              |                         |                 |            |                                                        | Reduction in blood glucose levels                      |       |
|       |              |                         |                 |            |                                                        | Insulin secretion by hyper polarized B-cells           | 12, 46 and 47 |
|       |              |                         |                 |            |                                                        | Reduction in hyperglycemia and glucosuria              |       |
| 11    | Lauraceae    | *Cinnamomum zeylanicum* Blume | Cinnamon        | Leaf, bark | Cinnamaldehyde                                         | Hypoglycemic, hypolipidemic decreases glycated hemoglobin (HbA1c), | 12, 43–45 |
|       |              |                         |                 |            |                                                        | Reduction in blood glucose levels                      |       |
|       |              | *Persea americana* Mill. | Avocado         | Fruit      | Fat, protein, vitamin, mineral                          | Insulin secretion by hyper polarized B-cells           | 12, 46 and 47 |
| 12    | Apiaceae     | *Coriandrum sativum* L. | Coriander       | Leaf       | Alanine                                                | Reduction in hyperglycemia and glucosuria              |       |
|       |              | *Cuminum-cyminum* L.   | Cumin seed      | Seed       | Aldehyde                                              |                                                        |       |
| 13    | Zingiberaceae| *Curcuma longa* L.      | Turmeric        | Root       | Curcuminoid and 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, isostictinin, pedunculagin, polysaccharide | Hypoglycemic and hypotensive effects                     |       |
|       |              | *Syzygium cordatum* Hochst. Ex Krauss | Jambolan       | Fruit      | Anthocyanin, citric, malic, gallic acid                | Increased hepatic glycogen content                    |       |

Contd…
### Medicinal Plants: A Source of Antidiabetic Drugs

| 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, Gymnemic acids I–IV and Gymnemasaponin V | Insulin secretion by β-cells                              | 12, 38, 52 and 53 |
| 16    | Asclepiadaceae       | Gymnema sylvestre (Retz.) Schult | Sugar destroyer              | Leaf       |                                                                                             | Insulin-releasing action                                  | 54         |
| 17    | Poaceae              | Triticum vulgare VIII.      | Wheat                        | Whole plant| Albumin                                                                                     | Reduces hemoglobin A1c 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, Momordin, 19-epoxy-3β,25-dihydroxycurcubita-6,23(ĕ)-diene and 3β,7β,25-trihydroxycurcubita-5,23(ĕ)-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 Nelumboroside 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           | Chamaemulum nobile (L.) All. | Chamomil                     | Leaf       | 3-hydroxy-3-methylglutaric acid, flavonoid, glucoside Chamaemeloside                        | Hyopglycaemic 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.\(^6\) 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.\(^7\) 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 रोगी 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 प्रायोगिक स्वास्थ्य संबंधी विकारों हेतु वास्तविक औषधियों की पुरातन पद्धति पर निर्भर हैं। विभिन्न रोगों के निवारण और उपचार में पाद्य-आधारित औषधियां और उनके कोलोनिट्रांस महत्वपूर्ण भूमिका निभाते हैं और इनका उपयोग भविष्य में औषधि विकास और संशोधन हेतु एक महत्वपूर्ण संसाधन के रूप में किया जा सकता है। इस व्यवस्थित समीक्षा का उद्देश्य औषधीय पादपों की हाइपोग्लाइसेमिक गुणकार्य का विश्लेषण करना है।

उद्देश्य: यह अध्ययन मुख्य रूप से मधुमेह से संबंधित उपचार के ऐतिहासिक और आधुनिक प्रक्रियाओं को समझाते एवं इस क्षेत्र में और अधिक वैज्ञानिक अनुसंधान हेतु फार्माकोलोजिस्ट्स, बोटेनिस्ट्स और फाइटोकेमिस्ट्रिस के ध्यानाकर्षण पर केंद्रित है।

परिणाम: मुख्यतः यह वर्तमान समीक्षा हाइपोग्लाइसेमिक गुणकर्म वाले 50 औषधीय पादपों पर केंद्रित है। मधुमेह रोगी विशेषताओं से संबंद्ध विविध एक्टिव केमिकल बायोमॉलिक्युलर की भूमिका पर विभिन्न शोध पत्रों और अध्ययनों की समीक्षा की गई।

निष्कर्ष: पुरातन काल से, पादप औषधियों के सशक्त स्रोत हैं, और जात स्वास्थ्य देखभाल के एक नूतन रूप में हैं। विभिन्न अनुसंधानकार्यों के प्रमाणित औषधीय पादपों की हाइपोग्लाइसेमिक विशेषता संबंधी मधुमेह के प्रभावकारी उपचार की पुष्टि की। अध्ययन से यह निष्कर्ष लिखला है कि पादप जाति की प्रोफाइल्स का समानांतर उपयोग रोगों का उपचार करने में होता है और इसकी मधुमेह रोगी विशेषता सुरक्षित अभ्यंतर हाइपोग्लाइसेमिक एजेंस का विकास करने हेतु एक प्रभावी स्रोत हो सकता है।

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