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A Review on Use of Herbal Plant in Diabetes Mellitus

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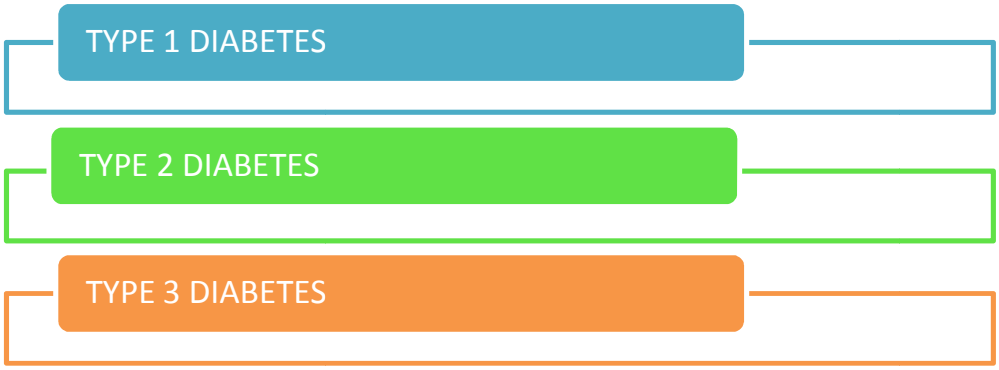
Abstract: *Diabetes mellitus is one of the common metabolic disorders and 2.8% of the population suffers from this disease throughout the world and it may cross 5.4% by the year 2025. Oral hypoglycemic agents like sulphonylureas and biguanides are still the major players in the management of the disease but there is growing interest in herbal remedies due to the side effects associated with the oral hypoglycemic agents. Herbal medicines have been the highly esteemed source of medicine throughout human history. They are widely used today indicating that herbs are a growing part of modern, hightech medicine.*
The medicinal plants, besides having natural therapeutic values against various diseases and considerable works have been done on these plants to treat diabetes mellitus, describes that the antidiabetic activity of medicinal plants is due to the presence of phenolic compounds, flavonoids, terpenoids, coumarins and other constituents which show reduction in blood glucose levels. Some of these herbal plants and their active chemical constituents which have a role in the management of diabetes mellitus are compiled here and discussed in this review.[1,2,3].

Keywords: Diabetes mellitus, hypoglycemic agents, herbal medicines, sulphonylureas, biguanides

I. INTRODUCTION

World health organization (WHO) has defined diabetes as a chronic, metabolic disease characterized by elevated levels of blood glucose (or blood sugar), which leads over time to serious damage to the heart, blood vessels, eyes, kidneys and nerves.Diabetes also known as diabetes mellitus, is a group of common endocrine diseases characterized by sustained high blood sugar levels.Diabetes is due to either the pancreas not producing enough insulin, or the cells of the body not responding properly to the insulin produced.Diabetes, if left untreated, leads to many health complications. Untreated or poorly treated diabetes accounts for approximately 1.5 million deaths per year.[4,5,6]

II. DIABETES



There is no widely-accepted cure for most cases of diabetes.
The most common treatment for type 1 diabetes is insulin replacement therapy (insulin injections)

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Anti-diabetic medications such as metformin and semaglutide, as well as lifestyle modifications, can be used to prevent or respond to type 2 diabetes.

Gestational Diabetes normally resolves shortly after delivery.

As of 2019, an estimated 463 million people had diabetes worldwide accounting for 8.8% of the adult population.

Type 2 diabetes makes up about 90% of all diabetes cases.

The prevalence of the disease continues to increase, most dramatically in low- and middleincome nations. Rates are similar in women and men, with diabetes being the 7th-leading cause of death globally. The global expenditure on diabetes-related healthcare is an estimated USD760 billion a year.[7,8]

Signs And Symptoms Of Diabetes Mellitus :

- Frequent urination (polyuria)
- Increase thirst(polydipsia)
- Increase hunger(polyphagia)
- Blurred vision
- Fatigue
- Headache[9,10]

III. PATHOPHYSIOLOGY

The principal hormone that regulates the uptake of glucose from the blood into most cells of the body, especially liver, adipose tissue and muscle, except smooth muscle, in which insulin acts via the IGF-1. Therefore, deficiency of insulin or the insensitivity of its receptors play a central role in all forms of diabetes mellitus.[11,12]

The body obtains glucose from three main sources

1) The intestinal absorption of food; the breakdown of glycogen (glycogenolysis),

2) The storage form of glucose found in the liver

3) Gluconeogenesis, the generation of glucose from non-carbohydrate substrates in the body. Insulin plays a critical role in regulating glucose levels in the body. Insulin can inhibit the breakdown of glycogen or the process of gluconeogenesis, it can stimulate the transport of glucose into fat and muscle cells, and it can stimulate the storage of glucose in the form of glycogen.

Insulin is released into the blood by beta cells (β-cells), found in the islets of Langerhans in the pancreas, in response to rising levels of blood glucose, typically after eating. Insulin is used by about two-thirds of the body's cells to absorb glucose from the blood for use as fuel, for conversion to other needed molecules, or for storage. Lower glucose levels result in decreased insulin release from the beta cells and in the breakdown of glycogen to glucose. This process is mainly controlled by the hormone glucagon, which acts in the opposite manner to insulin. If the amount of insulin available is insufficient, or if cells respond poorly to the effects of insulin (insulin resistance), or if the insulin itself is defective, then glucose is not absorbed properly by the body cells that require it, and is not stored appropriately in the liver and muscles. The net effect is persistently high levels of blood glucose, poor protein synthesis, and other metabolic derangements, such as metabolic acidosis in cases of complete insulin deficiency.

When glucose concentration in the blood remains high over time, the kidneys reach a threshold of reabsorption, and the body excretes glucose in the urine (glycosuria). This increases the osmotic pressure of the urine and inhibits reabsorption of water by the kidney, resulting in increased urine production (polyuria) and increased fluid loss. Lost blood volume is replaced osmotically from water in body cells and other body compartments, causing dehydration and increased thirst (polydipsia). In addition, intracellular glucose deficiency stimulates appetite leading to excessive food intake (polyphagia).[13,14]

Tests for type 1 and type 2 diabetes and prediabetes:

A1C test. This blood test, which doesn't require not eating for a period of time (fasting), shows your average blood sugar level for the past 2 to 3 months. It measures the percentage of blood sugar attached to hemoglobin, the oxygen-carrying protein in red blood cells. It's also called a glycatedhemoglobin test.

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The higher your blood sugar levels, the more hemoglobin you'll have with sugar attached. An A1C level of 6.5% or higher on two separate tests means that you have diabetes. An A1C between 5.7% and 6.4% means that you have prediabetes. Below 5.7% is considered normal.

Random blood sugar test. A blood sample will be taken at a random time. No matter when you last ate, a blood sugar level of 200 milligrams per deciliter (mg/dL) — 11.1 millimoles per liter (mmol/L) — or higher suggests diabetes.

Fasting blood sugar test. A blood sample will be taken after you haven't eaten anything the night before (fast). A fasting blood sugar level less than 100 mg/dL(5.6 mmol/L) is normal. A fasting blood sugar level from 100 to 125 mg/dL(5.6 to 6.9 mmol/L) is considered prediabetes. If it's 126 mg/dL (7 mmol/L) or higher on two separate tests, you have diabetes.

Glucose tolerance test. For this test, you fast overnight. Then, the fasting blood sugar level is measured. Then you drink a sugary liquid, and blood sugar levels are tested regularly for the next two hours.

A blood sugar level less than 140 mg/dL(7.8 mmol/L) is normal. A reading of more than 200 mg/dL(11.1 mmol/L) after two hours means you have diabetes. A reading between 140 and 199 mg/dL (7.8 mmol/L and 11.0 mmol/L) means you have prediabetes[15,16]

Need and Scope of Alternative Remedies

Regardless of the type of diabetes, patients are required to control their blood glucose with medications and/or by adhering to an exercise program and a dietary plan.

Insulin therapy by injection is given to those with type 1 DM and also to some patients with type 2 DM when oral hypoglycaemic drugs fail to lower blood glucose .

Due to modernization of lifestyle, non-insulin dependent diabetes mellitus is becoming a major health problem in developing countries.

Patients with type 2 DM are usually placed on a restricted diet and are instructed to exercise, the purpose of which primarily is weight control.

If diet and exercise fail to control blood glucose at the desired level, oral antidiabetic medication is prescribed.[17,18]

Oral antidiabetic agents exert their effects by various mechanisms:

(1) stimulation of beta cells in the pancreas to produce more insulin (sulfonylureas and meglitinides)

(2) increasing the sensitivity of muscles and other tissues to insulin (thiazolidinediones),

(3) decreasing gluconeogenesis by the liver (biguanides)

(4) delaying the absorption of carbohydrates from the gastrointestinal tract (alpha-glucosidase inhibitors)

These treatments have their own drawbacks, ranging from the developing of resistance and adverse effects to lack of responsiveness in large segment of patients population.

Sulfonylureas lose effectiveness for 44% of patients within six years.

Also, these treatments are associated with side effects or even toxic effects (e.g., thiazolidinediones may cause liver toxicity; sulphonylureas might worsen heart disease, lower the glucose below the normal range and increase the body weight gain; bloating, flatulence,diarrhea and abdominal discomfort and pain are the major complaints with glucosidase inhibitors).

According to literature, two-thirds of medications prescribed for use in children have not been proven safe or effective for this patient population.

The limitations of currently-available oral antidiabetic agents either in terms of efficacy/safety coupled with the emergence of the disease into a global epidemy have encouraged a concerted effort to discover drugs that can manage type 2 diabetes more efficiently.[19,20]

Herbal Remedies:

As per ancient literature, more than 800 plants are reported to have antidiabetic properties.

Ethnopharmacological surveys indicate that more than 1200 plants are used in traditional medicine for their alleged hypoglycemic activity.

Medicinal plants, since times immemorial, have been used in virtually all cultures as a source of medicine.

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Ayurvedicantidiabetic herbs improve digestive power, increase one of the Rasas (gastric secretions); being Laghu, get easily digested in the body; and being Ruksha, decrease output of overall body fluids e.g. urine, sweat etc. Food items, which are 'madhumehaghna' (antidote), are an important underlying principle of therapy for the prameha (diabetes) patient.

Indian materiamedica has mentioned numerous dravyas which have been reported effective in Madhumeha.

Plants-based products have been popular all over the world for the centuries. In diabetes, some herbal alternatives are proven to provide symptomatic relief and assist in the prevention of the secondary complications of the disease. Some herbs have also been proven to help in the regeneration of ß-cells and in overcoming resistance.

In addition to maintaining normal blood sugar level, some herbs are also reported to possess antioxidant activity and cholesterol-lowering action. The management of type 2 diabetes mellitus (NIDDM) is possible with the drugs that can lower the blood sugar level in one hand and restore the liver glycogen level on the other.

In modern system of medicine, there is no drug, which is reported to posses both of these properties . However, the hypoglycemic effect of some herbal extracts have been confirmed in human and animal models of type 2 diabetes and conventional drugs have been derived from the active molecules of these medicinal plants.

Metformin, a less toxic biguanides and potent oral glucose-lowering agent, was developed from Galegaofficianalis and used to treat diabetes . Out of dozens of oral medications for diabetes, only one medication (metformin) is approved for use in children and it has been originated from herbs.[21,22]

Important medicinal plants having antidiabetic potential

Allium sativa (Garlic)

Common name :- Garlic

Family :-Amaryllidaceae

Main chemical constituent :-Allyl propyl disulphide, allicin.[23]

Pharmacological study :-

1) When the aqueous extract of garlic is given orally to sucrose-fed rabbits, it considerably improved hepatic glycogen and free amino acid content, reduced fasting blood glucose and triglyceride levels in serum

2) Also, garlic extract administered to streptozotocin-diabetic rats not only decreased the blood glucose level but also inhibited the lipid peroxidation and inhibited the superoxide formation.

This study has also recommended its long-term use in preventing diabetic complications.

However, the extrapolation of these results to humans needs further research Most recent findings have also proposed that aged garlic extract inhibits the generation of glycation -derived free radicals and AGEs in vitro.

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S -allyl cysteine, a chief ingredient of aged garlic, is a potent antioxidant that can inhibit AGEs synthesis and, thus, deserves more attention Evidence also proposes that the antioxidative, anti -inflammatory and antiglycative properties of garlic are accountable for its role in preventing diabetes and its complications.[24,25]]

Camellia sinesis :

Common name :- Green Tea.
Family :-Theaceae.
Main chemical constituent/Phytoconstituent :- caffeine and catechins.[26]


Pharmacological study :

Camellia sinensis, commonly known as green tea, is a medicinal plant traditionally used to treat various health conditions, including diabetes, arthritis, bacterial infections and hyperlipidaemia.

C. sinensis has been demonstrated to decrease total and low-density lipoprotein (LDL) cholesterol as well as triacylglyceride levels, and increase high-density lipoprotein (HDL) cholesterol, thus lowering the risk of developing CVD.

C. sinensis can inhibit DPP-IV enzyme activity and has blood-glucose-lowering and insulin secretory properties.

Recent studies have reported that C. sinensis contains phytochemicals such as epicatechin, isoquercitrin, rutin, catechin, epicatechingallate, quercetin, kaempferol, epigallocatechingallate, ellagic acid, myricetin and gallic acid.

Among these, kaempferol, rutin, isoquercitrin, epicatechin, quercetin, gallic acid and catechin have been previously observed to have DPP-IV enzyme inhibitory properties.

Additionally, studies have shown that kaempferol, rutin, isoquercitrin, epicatechin, quercetin, ellagic acid and epigallocatechingallate can lower blood glucose levels, enhance insulin secretion and improve β-cell function.[27,28]

Beta vulgaris:
Common name :- beet
Family :-Amaranthaceae
Main chemical constituent/Phytoconstituent :-Phenolics, betacyanins.[29]


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Pharmacological study:-

The vitexin-200O-rhamnoside, its demethylated form 200-xylosylvitexin, isorhamnetin 3- gentiobioside, and rutin of phenolic fraction, obtained from B. vulgaris showed no toxicity to human lymphocytes and slight toxicity to macrophages.

Vitexin-200O-rhamnoside strongly inhibited DNA synthesis in MCF-7 cells, whereas 200- xylosylvitexin and isorhamnetin 3-gentiobioside were activators.

Combinations of activators and inhibitors maintained the over-all inhibitory effect[30,31]

IV. CONCLUSION

Herbal therapy for diabetes has been followed all over the World successfully. Herbs are used to manage Type 1 and Type II diabetes and their complications.For this, therapies developed along the principles of western medicine (allopathic) are often limited in efficacy, carry the risk of adverse effects, and are often too costly, especially for the developing world.The abovementioned plants have been considered for their possible hypoglycemic actions and the researchers have carried out some preliminary investigations. Scientific validation of several Indian plant species has proved the efficacy of the botanicals in reducing the sugar level could be considered as of possible therapeutic value. Thus many different plants have been used individually or in formulations for treatment of diabetes.[32,33]

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