A Comprehensive Review on Diabetes Mellitus and the Antidiabetic Potential of Indian Medicinal Plants

Vanshika*[1], Archana Chaudhary*[1], Tarun Kumar Sharma[1], Vinay Pandit[1], M.S. Ashawat[1]

1 Department of Pharmaceutics, Laureate Institute of Pharmacy, VPO-Kathog, Kangra H.P 176031

Corresponding author:
Vanshika
Research Scholar
Laureate Institute of Pharmacy, Kathog
Email Id: *Vanshikadhiman5@gmail.com*[1]

Abstract

Diabetes mellitus is a chronic metabolic disorder characterized by impaired carbohydrate, fat, and protein metabolism due to insufficient insulin production or action. This disorder is classified into several types, including type 1, type 2, and gestational diabetes. Its prevalence is increasing globally, particularly in developing countries. Traditional medicinal plants offer promising antidiabetic properties and are widely used in India. This paper outlines the epidemiology, risk factors, and symptoms of diabetes, and highlights Indian medicinal plants such as *Azadirachta indica* (Neem), *Momordica charantia* (Bitter gourd), and *Allium sativum* (Garlic), emphasizing their hypoglycemic effects and mechanisms of action in diabetes management.

Introduction

Diabetes mellitus is a chronic disorder of carbohydrates, fats and protein metabolism. A defective or deficient insulin secretary response, which translates into impaired carbohydrates (glucose) use, is a characteristic feature of diabetes mellitus, as is the resulting hyperglycemias [1] Diabetes mellitus (DM) is commonly referred to as a “sugar” and it is the most common endocrine disorder and usually occurs when there is deficiency or absence of insulin or rarely, impairment of insulin activity (insulin resistance) [2]. The International Diabetes Federation (IDF) estimates the total number of diabetic subjects to be around 40.9 million in India and this is further set to rise to 69.9 million by the year 2025 [3]. Insulin and glucagon hormones both are secreted by the pancreas. Insulin is secreted by the beta (ß) cells and glucagon is secreted by the alpha (α) cells both are located in the islets of Langerhan’s.

Insulin decreases the blood glucose level by the glycogenesis and transport glucose into the muscles, liver and adipose tissue. Neural tissue and erythrocytes do not required insulin for glucose utilization whereas alpha (α) cells plays an important role in controlling blood glucose by producing the glucagon and it increases the blood glucose level by accelerating the glycogenolysis [4, 5].

The most common forms of diabetes are type 1diabetes (5%), which is an autoimmune disorder, and type 2 diabetes (95%), which is associated with obesity. Gestational diabetes is a form of diabetes that occurs in pregnancy, and other forms of diabetes are very rare and are caused by a single gene mutation [6]. There's no cure for diabetes. But with treatment and lifestyle changes, you can live a long, healthy life [7].

Classification of Diabetes Mellitus

The first mostly accepted classification of diabetes mellitus was published by WHO in the year 1980 [8] and, it is modified in the year 1985 [9]. The most common and important form of Primary or idiopathic diabetes mellitus, which is focus of our discussion. It must be different from secondary diabetes mellitus which includes forms of hyperglycemia associated with identifiable causes in which destruction of pancreatic islets is induced by inflammatory Pancreatic diseases, surgery, tumors, certain drugs, iron overloaded (Hemochromatosis) and certain acquired or genetic endocrinopathies [10]. The classification encompasses both clinical stages and aetiological types of diabetes mellitus and other categories of hyperglycemia [11].

1. Insulin Dependent Diabetes Mellitus (Type1 IDDM) This type of diabetes mellitus is also called autoimmune diabetes and previously known as juvenile-onset or ketosis prone diabetes. The individual may also seek with other autoimmune disorders such as Graves' disease, Hashimoto's thyroiditis, and Addison's disease [12]. Type I diabetes mellitus is also known as insulin- dependent diabetes mellitus (IDDM), this occurs mainly in children and young adults; the onset is usually sudden and can be life threatenin [13].

2. Non-Insulin Dependent Diabetes Mellitus (Type2 NIDDM) Type 2 diabetes mellitus is also known as adult-onset diabetes. The progressive insulin secretary defect on the background of insulin resistance (American Diabetes Association, 2014) [14]. People with this type of diabetes frequently are resistant to the action of insulin [15]. The long-term complications in blood vessels, kidneys, eyes and nerves occur in both types and are the major causes of morbidity and death from diabetes [10]. The causes are multifunctional and predisposing factor includes: Obesity, Sedentary lifestyle, increasing age (affecting middle-aged and older people), Genetic factor (Ross and Wilson 2010), such patients are at increased risk of developing macro vascular and micro vascular complications [16, 17].

3. Gestational Diabetes Mellitus The glucose intolerance occurring for the first time or diagnosed during pregnancy is referred to as gestational diabetes mellitus (GDM) [2]. Women who develop Type1 diabetes mellitus during pregnancy and women with

undiagnosed asymptomatic Type 2 diabetes mellitus that is discovered during pregnancy are classified with Gestational Diabetes Mellitus (GDM) [16]. Gestational diabetes mellitus (GDM) (diabetes diagnosed during pregnancy that is not clearly over diabetes) [17].

Symptoms of Diabetes Mellitus

Diabetes symptoms are caused by rising blood sugar.

General Symptoms

The general symptoms of diabetes include:

- increased hunger
- increased thirst
- weight loss
- frequent urination
- blurry vision
- extreme fatigue sores that don't heal.

Type 1 Diabetes

Symptoms of type 1 diabetes can include:

Extreme hunger, increased thirst, unintentional weight loss, frequent urination, blurry vision tiredness

Type 2 Diabetes

Symptoms of type 2 diabetes can include:

increased hunger, increased thirst, increased urination, blurry vision, tiredness sores that are slow to heal.

It may also cause recurring infections. This is because elevated glucose levels make it harder for the body to heal [18].

- **Gestational-Diabetes**
- Fatigue
- Blurred vision
- Extreme thirst
- Nausea Frequent bladder
- vaginal, or skin infections
- Frequent urination
- Sugar in the urine

Risk Factors

Although persons are at higher risk above the age of 45 (primarily for T2DM), the prevalence is particularly high among those aged 65 and above. Having a family history of diabetes is a risk factor for both T1DM and T2DM. Genetic susceptibility is not due to single genes, however. Multiple genetic loci have been implicated using modern "GWAS"

techniques for both T1DM and T2DM (19, 20) Studies are consistent that lifestyle characteristics, including being overweight, having insufficient physical activity, smoking, and poor dietary patterns are potent risk factors for diabetes, either via direct effects or their effects on obesity (21, 22) There is also clinical trial evidence that weight-loss focused lifestyle interventions reduce the risk of T2DM among people at high risk for the disease (23, 24). Diabetes is associated with an increased risk of all cause mortality. The excess risk has been reported to be at least twofold or greater (compared to those without diabetes) in diverse regions of the world, such as Europe (25, 26) Asia, (27, 28) and Latin America as well as in the United States (29, 30).

Epidemiology

It is estimated that 366 million people had DM in 2011 by 2030 this would have risen to 552 million. The number of people with type 2 DM is increasing in every country with 80 % of people with DM living in low- and middle-income countries. DM caused 4.6 million deaths in 20118 (33). It is estimated that 439 million people would have type 2 DM by the year 2030.The incidence of type 2 DM varies substantially from one geographical region to the other as a result of environmental and lifestyle risk factors (34). It is predicted that the prevalence of DM in adults of which type 2 DM is becoming prominent will increase in the next two decades and much of the increase will occur in developing countries where the majority of patients are aged between 45 and 64 years (35).

Indian Medicinal Plants with Antidiabetic and Related Beneficial Effects

Acacia arabica: (Babhul) It is found all over India mainly in the wild habitat. The plant extract acts as an antidiabetic agent by acting as secretagouge to release insulin. It induces hypoglycemia in control rats but not in alloxanized animals. Powdered seeds of Acacia arabica when administered (2,3 and 4 g/kg body weight) to normal rabbits induced hypoglycemic effect by initiating release of insulin from pancreatic beta cells (36).

Aegle marmelos: (Bengal Quince, Bel or Bilva) Administration of aqueous extract of leaves improves digestion and reduces blood sugar and urea, serum cholesterol in alloxanized rats as compared to control. Along with exhibiting hypoglycemic activity, this extract also prevented peak rise in blood sugar at 1h in oral glucose tolerance test (37).

Allium cepa: (onion) Various ether soluble fractions as well as insoluble fractions of dried onion powder show anti-hyperglycemic activity in diabetic rabbits. Allium cepa is also known to have anti oxidant and hypolipidaemic activity. Administration of a sulfur containing amino acid from Allium cepa, S-methyl cysteine sulphoxide (SMCS) (200 mg/kg for 45 days) to alloxan induced diabetic rats significantly controlled blood glucose as well as lipids in serum and tissues and normalized the activities of liver hexokinase, glucose 6-phosphatase and HMG Co A reductase(38, 39). When diabetic patients were given single oral dose of 50 g of onion juice, it significantly controlled post-prandial glucose levels (40).

Allium sativum: (garlic) This is a perennial herb cultivated throughout India. Allicin, a sulfur-containing compound is responsible for its pungent odour and it has been shown to have significant hypoglycemic activity [41]. This effect is thought to be due to increased hepatic metabolism, increased insulin release from pancreatic beta cells and/or insulin sparing effect [42]. Aqueous homogenate of garlic (10 ml/kg/day) administered orally to sucrose fed rabbits (10 g/kg/day in water for two months) significantly increased hepatic glycogen and free amino acid content, decreased fasting blood glucose, and triglyceride levels in serum in comparison to sucrose controls [43].

Aloe vera and Aloe barbadensis Aloe, a popular houseplant, has a long history as a multi purpose folk remedy. The plant can be separated into two basic products: gel and latex. Aloe vera gel is the leaf pulp or mucilage, aloe latex, commonly referred to as “aloe juice,” is a bitter yellow exudate from the pericyclic tubules just beneath the outer skin of the leaves. Extracts of aloe gum effectively increases glucose tolerance in both normal and diabetic rats [44]. Treatment of chronic but not single dose of exudates of Aloe barbadensis leaves showed hypo glycemic effect in alloxanized diabetic rats. Single as well as chronic doses of bitter principle of the same plant also showed hypoglycemic effect in diabetic rats. This action of Aloe vera and its bitter principle is through stimulation of synthesis and/or release of insulin from pancreatic beta cells [45]. This plant also has an anti-inflammatory activity in a dose dependent manner and improves wound healing in diabetic mice [46].

Azadirachta indica: (Neem) Hydroalcoholic extracts of this plant showed anti hyperglycemic activity in streptozotocin treated rats and this effect is because of increase in glucose uptake and glycogen deposition in isolated rat hemidiaphragm [47, 48]. Apart from having anti-diabetic activity, this plant also has anti-bacterial, antimalarial, antifertility, hepatoprotective and antioxidant effects [49,50].

Mangifera indica: (Mango) The leaves of this plant are used as an antidiabetic agent in Nigerian folk medicine, although when aqueous extract given orally did not alter blood glucose level in either normoglycemic or streptozotocin induced diabetic rats. However, antidiabetic activity was seen when the extract and glucose were administered simultaneously and also when the extract was given to the rats 60 min before the glucose. The results indicate that aqueous extract of Mangifera indica possess hypoglycemic activity. This may be due to an intestinal reduction of the absorption of glucose [51].

Momordica charantia: (bitter gourd) Momordica charantia is commonly used as an antidiabetic and antihyperglycemic agent in India as well as other Asian countries. Extracts of fruit pulp, seed, leaves and whole plant was shown to have hypoglycemic effect in various animal models. Polypeptide p, isolated from fruit, seeds and tissues of M. charantia showed significant hypoglycemic effect when administered subcutaneously to langurs and humans [52]. Ethanolic extracts of M. charantia (200 mg/kg) showed an antihyperglycemic and also hypoglycemic effect in normal and STZ diabetic rats. This may be because of inhibition of glucose-6-phosphatase besides fructose-1, 6 biphosphatase in the liver and stimulation of hepatic glucose 6-phosphate dehydrogenase activities [53].

Conclusion

Diabetes mellitus poses a significant and growing health burden worldwide, especially in low- and middle-income countries. With rising prevalence and limited curative treatments, management focuses on controlling blood glucose levels and preventing complications. Indian medicinal plants play a valuable role in the complementary treatment of diabetes. Plants such as *Acacia arabica*, *Aegle marmelos*, *Allium cepa*, *Allium sativum*, *Aloe vera*, *Azadirachta indica*, *Mangifera indica*, and *Momordica charantia* have demonstrated significant hypoglycemic activity in various studies. Their mechanisms often involve enhancement of insulin secretion, improved glucose uptake, and inhibition of gluconeogenic enzymes, making them potential candidates for natural antidiabetic therapies.

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