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A Review on Antidiabetic Activity of Indian Medicinal Plant

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Abstract: *Diabetes mellitus is one of the common metabolic disorders acquiring around 9.3% of adults worldwide in 2019.Since long back herbal medicines have been the highly esteemed source of medicine therefore, they have become a growing part of modern, high-tech medicine. In view of the above aspects the present review provides profiles of plants (65 species) with hypoglycemic properties, available through literature source from various database with proper categorization according to the parts used, mode of reduction in blood glucose (insulin mimetic or insulin secretagogues activity) and activephytoconstituents having insulin mimetics activity.*

The treatment of diabetes is mainly based on the long-term use of pharmacological agents, often expensive and causing unpleasant side effects. There is an alarming increase in the number of pharmaceuticals taken in Europe. The aim of this paper is to concisely collect information concerning the few antidiabetic or hypoglycemic raw plant materials that are present in the consciousness of Indian and relatively easily accessible to them on the market and sometimes even grown on Indian plantations.The following raw materials are discussed in this mini-reviewBoerhaavia diffusa Linn. (Nyctaginaceae),Annona squamosa Linn. (Annonaceae),Bougainvillea spectabilis Linn. (Nyctaginaceae),Cassia kleinii Wight & Arn. (Caesalpiniaceae),Coscinium fenestratum Colebr. (Menispermaceae),Ficus hispida Linn. (Moraceae),Murraya koenigii Linn. (Rutaceae),White Mulberry (Morus alba L.), Acacia arabica: (Babhul), Aegle marmelos: (Bengal Quince, Bel or Bilva), Allium cepa: (onion), Allium sativum: (garlic), Aloe vera and Aloe barbadensis, Azadirachta indica: (Neem), Eugenia jambolana: (Indian gooseberry, jamun), Mangifera indica: (Mango), Momordica charantia: (bitter gourd), Ocimum sanctum: (holy basil).

Keywords: Diabetes mellitus, Herbal medicinal plant, Insulin, Hypoglycemia.

I. INTRODUCTION

Diabetes mellitus, one of the most common endocrine metabolic disorders has caused significant morbidity and mortality due to microvascular (retinopathy, neuropathy, and nephropathy) and macrovascular (heart attack, stroke and peripheral vascular disease) complications[1]. Human bodies possess enzymatic and non-enzymatic antioxidative mechanisms which minimize the generation of reactive oxygen species, responsible for many degenerative diseases including diabetes[2]. The disease is rapidly increasing worldwide and affecting all parts of the world. Due to deficiency of the insulin people suffering from diabetes have high blood glucose level[3]. Type 2 diabetes or non-insulin-dependent diabetes mellitus, is the most common form of the disease, accounting for 90%–95% of cases in which the body does not produce enough insulin or properly use it[4]. According to World Health Organization the diabetic population is likely to increase up to 300 million or more by the year 2025[5]. Currently available therapies for diabetes include insulin and various oral antidiabetic agents such as sulfonylureas, biguanides and glinides. Many of them have a number of serious adverse effects; therefore, the search for more effective and safer hypoglycemic agents is one of the important areas of investigation[6]. Diabetes mellitus is a serious metabolic disorder. The reason for chronic hyperglycemia can be: (1) a lack of production of an adequate amount of insulin or (2) the impossibility of peripheral tissues to react to the presence of insulin [7].Diabetes mellitus spreads rapidly. In 2019, 9.3% of the global adult population were found to be diabetic [8]. The International Diabetes Federation in 2017 reported that the risk of type 2 diabetes concerned 352 million people. According to health forecasts, 439 million adults will have been affected by diabetes by the year 2030 [9]. Mortality from diabetes in 2010 ranged from 6% of all deaths in Africa to 15.7% of all

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deaths recorded in North America [10], and a meta-analysis of studies conducted during the COVID-19 pandemic showed that diabetes increases mortality in patients with COVID-19 [11].

Boerhaavia diffusa Linn. (Nyctaginaceae), distributed widely all over in India, is a small perennial creeping herb, commonly known as ìRed hogweedî. The root and the whole plant are used as an Ayurvedic medicine in India and Unani medicine for the treatment of diabetes, stress, dyspepsia, abdominal pain, inflammation, jaundice, enlargement of spleen, congestive heart failure and bacterial infections [12-14]. Aqueous leaf extract of the plant has been studied for its antidiabetic effect in alloxan-induced diabetic rats [15, 16]. The antidiabetic activity of the chloroform extract of the plant leaves on chronic treatment of streptozotocin induced NIDDM (non insulin dependent diabetes mellitus) model diabetic rats was evaluated and the herb possesses antidiabetic activity. The herb mainly acts by reducing blood glucose level and increasing insulin sensitivity [17].

Annona squamosa Linn. (Annonaceae), commonly called custard apple in English and sharifa in Hindi. It is cultivated throughout India. The pharmacological active ingredients are present in seeds, leaves and aerial parts of the plant [18]. The research reveals that the plant possesses both hypoglycemic and antidiabetic activity. It acts by enhancing insulin level from the pancreatic islets, increases utilization of glucose in muscle and inhibits the glucose output from liver. Its margin of safety is high. The extract obtained from leaves of this plant is useful in maintaining healthy blood sugar and cholesterol levels [19].

Bougainvillea spectabilis Linn. (Nyctaginaceae), is a very familiar ornamental plant commonly grown in Indian gardens. Bougainvillea is a genus of flowering plants native to South America from Brazil west to Peru and south to southern Argentina. The traditional plant has the antidiabetic potential. The blood glucose lowering potential of Bougainvillea spectabilis Willd leaf extract in streptozotocin-induced type I diabetic albino rats was reported. The ethanolic extract of the leaves has antihyperglycemic activity probably due to increased uptake of glucose by enhanced glycogenesis in the liver and also due to increase in insulin sensitivity [20].

Cassia kleinii Wight & Arn. (Caesalpiniaceae), is the medical remedy for the folk diabetic practitioners in South India. The traditional systems like Ayurveda and Siddha systems donít use this plant. The alcoholic extracts of leaves seem to show promising results for the development of phytomedicines by exhibiting the antihyperglycemic activity on glucose feed hyperglycemic and alloxan-induced diabetic rats. The leaf extract of Cassia kleinii may not act by potentiation of insulin but it could be used in insulin independent diabetes because drug exhibited antihyperglycemic effect but not hypoglycemic effect in fasted rats. The action of drug may be mimicking some or all of the action of insulin on the metabolism of glucose [21].

Coscinium fenestratum Colebr. (Menispermaceae), commonly known as tree in Western Ghats (India) and Sri Lanka. The plant has been mainly used for diabetes mellitus in the traditional, Ayurvedic and Siddha systems of medicine. Alcoholic stem extract of this plant regulates metabolism and improves antioxidant status in streptozotocin, nicotinamide-induced diabetic rats. The alcoholic extract regulates glucose homeostasis and decreased gluconeogenesis by C. fenestratum. The drug also has protective action on cellular antioxidant defense [22].

Ficus hispida Linn. (Moraceae), also known as Daduri for the treatment of diabetes. This small tree may be found throughout India. Different workers have reported for the hypoglycemic effects of different compounds obtained from F. bengalensis [23- 25]. The hypoglycemic activity of F. bengalensis Linn. (bark) in normal and diabetic albino rats concluded that the water-soluble fraction of the alcoholic extract of Ficus hispida significantly decreases fasting blood glucose levels in normal and alloxan-induced diabetic rats. The extract has direct peripheral action on β cells but drug interaction can occur between Ficus hispida bark extract and insulin if given together [26].

Murraya koenigii Linn. (Rutaceae), is commonly known as Curry patta and is widely used condiment and spice in India. In normal and alloxan diabetes the aqueous extract of the leaves of M. koenigii produced hypoglycemic effect [27]. Oral feeding of this plant for 60 days diet to normal rats showed an increase in the concentration of hepatic glycogen due to hypoglycemic activity [28]. It has been reported that feeding different doses of M. koenigii leaves to diabetic rats play a role in control of mild diabetic rats to moderate, severe and type I diabetes [29]. It suppresses blood glucose level and was found to have beneficial effect on carbohydrate metabolism [30].

White Mulberry (Morus alba L.)Mulberry is a fast-growing, deciduous plant from the *Moraceae* family that is found at various geographical latitudes, i.e., in climates from tropical to moderate [31]. White mulberry originates from China, Japan, and India, and historical sources have revealed that all its parts, i.e., fruits, leaves, and bark, were already used in

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medicine in 3000 B.C. It was brought to Europe in the 11th century with silkworm caterpillars. It is also very common in other countries of Asia, Europe, and America [32]. White mulberry is also grown in Europe due to low agrotechnical requirements, relatively easy and cheap cultivation, and the possibility of using it in the food industry [33,34,35,36].

***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 [37].

***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 [38].

***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 antioxidant 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 [39, 40]. When diabetic patients were given single oral dose of 50 g of onion juice, it significantly controlled post-prandial glucose levels [41].

***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 [42]. This effect is thought to be due to increased hepatic metabolism, increased insulin release from pancreatic beta cells and/or insulin sparing effect [43]. 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 [44].

S-allyl cystein sulfoxide (SACS), the precursor of allicin and garlic oil, is a sulfur containing amino acid, which controlled lipid peroxidation better than glibenclamide and insulin. It also improved diabetic conditions. SACS also stimulated *in vitro* insulin secretion from beta cells isolated from normal rats [45]. Apart from this, *Allium sativum* exhibits antimicrobial, anticancer and cardioprotective activities.

Aloe vera and Aloe barbadensisAloe, a popular houseplant, has a long history as a multipurpose 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 [46]. Treatment of chronic but not single dose of exudates of *Aloe barbadensis* leaves showed hypoglycemic 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 [47]. This plant also has an anti-inflammatory activity in a dose dependent manner and improves wound healing in diabetic mice [48].

***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 [49, 50]. Apart from having anti-diabetic activity, this plant also has anti-bacterial, antimalarial, antifertility, hepatoprotective and antioxidant effects [51].

***Eugenia jambolana*: (Indian gooseberry, jamun)**In India decoction of kernels of *Eugenia jambolana* is used as household remedy for diabetes. This also forms a major constituent of many herbal formulations for diabetes. Antihyperglycemic effect of aqueous and alcoholic extract as well as lyophilized powder shows reduction in blood glucose level. This varies with different level of diabetes. In mild diabetes (plasma sugar >180 mg/dl) it shows 73.51% reduction, whereas in moderate (plasma sugar >280 mg/dl) and severe diabetes (plasma sugar >400 mg/dl) it is reduced to 55.62% and 17.72% respectively [52]. The extract of jamun pulp showed the hypoglycemic activity in streptozotocin induced diabetic mice within 30 min of administration while the seed of the same fruit required 24 h. The oral administration of the extract resulted in increase in serum insulin levels in diabetic rats. Insulin secretion was found to

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be stimulated on incubation of plant extract with isolated islets of Langerhans from normal as well as diabetic animals. These extracts also inhibited insulinase activity from liver and kidney [53].

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 [54].

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 [55]. 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 [56].

***Ocimum sanctum*: (holy basil)**It is commonly known as Tulsi. Since ancient times, this plant is known for its medicinal properties. The aqueous extract of leaves of *Ocimum sanctum* showed the significant reduction in blood sugar level in both normal and alloxan induced diabetic rats [57]. Significant reduction in fasting blood glucose, uronic acid, total amino acid, total cholesterol, triglyceride and total lipid indicated the hypoglycemic and hypolipidemic effects of tulsi in diabetic rats [58]. Oral administration of plant extract (200 mg/kg) for 30 days led to decrease in the plasma glucose level by approximately 9.06 and 26.4% on 15 and 30 days of the experiment respectively. Renal glycogen content increased 10 fold while skeletal muscle and hepatic glycogen levels decreased by 68 and 75% respectively in diabetic rats as compared to control [59].

II. CONCLUSION

Diabetes mellitus is a syndrome, initially characterized by loss of glucose homeostasis resulting from defects in insulin secretion, insulin action both resulting in impaired metabolism of glucose and other energy-yielding fuels such as lipids and proteins . Currently, many countries face large increases in the number of people suffering from diabetes. The World Health Organization estimated that about 30 million people suffered from diabetes in 1985 and the number increased to more than 171 million in 2000. It is estimated that the number will increase to over 366 million by 2030 and that large increases will occur in developing countries, especially in people aged between 45 and 64 years.

Experimental diabetes in animals has provided considerable insight into the physiological and biochemical derangement of the diabetic state. Many of these derangements have been characterized in hyperglycemic animals. Significant changes in structure and lipid metabolism occur in diabetes. In these cases the structural changes are clearly oxidative in nature and are associated with development of vascular disease in diabetes.

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