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## ETHNO MEDICINAL PLANTS WITH ANTIDIABETIC ACTIVITY: A REVIEW

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**ABSTRACT:** Diabetes is a complex and multifarious group of disorders characterized by hyperglycemia that has reached epidemic proportions in the present century. Several drugs such as biguanides and sulfonylureas are presently available to reduce hyperglycemia in diabetes mellitus. These drugs have side effects and thus searching for a new class of compounds is essential to overcome these problems. Management of diabetes without any side effects is still a challenge to the medical community. There is continuous search for alternative drugs. Therefore, it is prudent to look for options in herbal medicine for diabetes as well.

**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. Human bodies possess enzymatic and non-enzymatic antioxidative mechanisms which minimize the generation of reactive oxygen species, responsible for many degenerative diseases including diabetes. 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. 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.

According to World Health Organization the diabetic population is likely to increase up to 300 million or more by the year 2025.


There are three types of diabetes:

### 1) Type-I Diabetes:

The body does not produce insulin, cause refer to this type as insulin-dependent diabetes, juvenile diabetes or early-onset diabetes. People usually develop type 1 diabetes before their 40th year, often in early adulthood or teenage years. Patients with type 1 diabetes will need to take insulin injections for the rest of their life. They must also ensure proper blood-glucose levels by carrying out regular blood tests and following a special diet.

### 2) Type-II Diabetes:

The body does not produce enough insulin for proper function, or the cells in the body do not react to insulin (insulin resistance). Some people may be able to control their type 2 diabetes symptoms by losing weight, following a healthy diet, doing plenty of exercise, and monitoring their blood glucose levels. However, type 2 diabetes is typically a progressive disease - it gradually gets worse - and the patient will probably end up have

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to take insulin, usually in tablet form. Overweight and obese people have a much higher risk of developing type 2 diabetes compared to those with a healthy body weight. People with a lot of visceral fat, also known as central obesity, belly fat, or abdominal obesity, are especially at risk. Being overweight/obese causes the body to release chemicals that can destabilize the body's cardiovascular and metabolic systems.

### 3) Gestational Diabetes:

This type affects females during pregnancy. Some women have very high levels of glucose in their blood, and their bodies are unable to produce enough insulin to transport all of the glucose into their cells, resulting in progressively rising levels of

glucose. Diagnosis of gestational diabetes is made during pregnancy. The majority of gestational diabetes patients can control their diabetes with exercise and diet. Between 10% to 20% of them will need to take some kind of blood-glucose-controlling medications. Undiagnosed or uncontrolled gestational diabetes can raise the risk of complications during childbirth. Scientists from the National Institutes of Health and Harvard University found that women whose diets before becoming pregnant were high in animal fat and cholesterol had a higher risk for gestational diabetes, compared to their counterparts whose diets were low in cholesterol and animal fats.

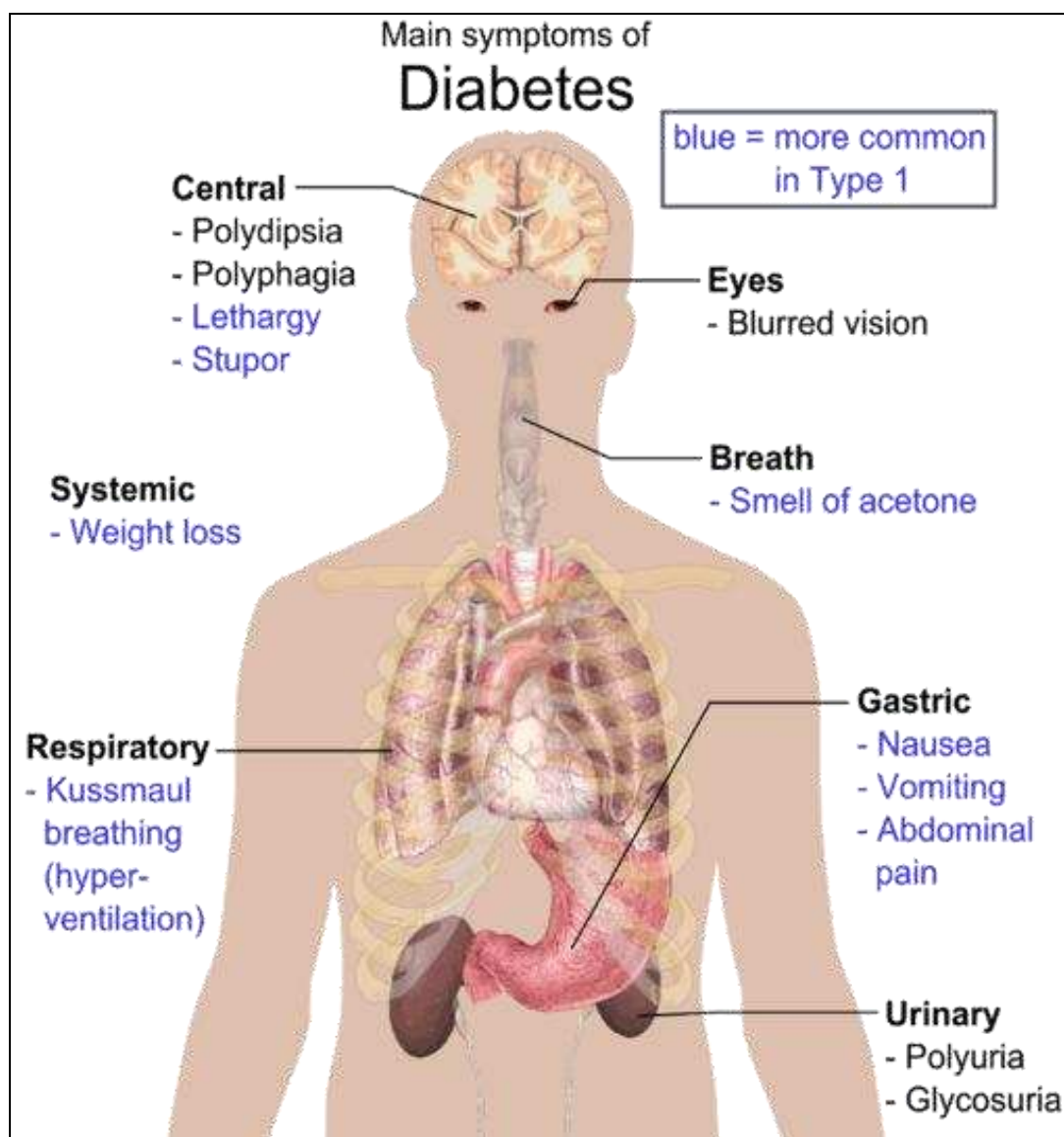


FIG. 1: SYMPTOMS OF DIABETES

TABLE1: ETHNO-MEDICINAL PLANTS USED TO TREAT DIABETES:

Botanical name	Common name	Family
<i>Acorus calamus</i>	Sweet flag	<i>Acoraceae</i>
<i>Salacia oblonga</i>	Saptrangi	<i>Celastraceae</i>
<i>Catharanthus roseus</i>	Rose peri winkle	<i>Apocyanaceae</i>
<i>Acanthopanax senticosus</i>	Siberian ginseng	<i>Araliaceae</i>
<i>Coccinia indica</i>	Tindora	<i>Cucurbitaceae</i>
<i>Tinospora cordifolia</i>	Geloy	<i>Menispermaceae</i>
<i>Costus speciosus</i>	Crepe ginger	<i>Costaceae</i>
<i>Vaccinium bracteatum</i>	Sea bilberry	<i>Ericaceae</i>
<i>Embllica officinalis</i>	Indian Gooseberry	<i>Euphorbiaceae</i>
<i>Senna auriculata</i>	Tanner's cassia	<i>Fabaceae</i>
<i>Cinnamomum zeylanicum</i>	Cinnamon	<i>Lauraceae</i>
<i>Strychnos potatorum</i>	Clearing nut tree	<i>Loganiaceae</i>
<i>Hibiscus rosa sinensis</i>	Chinese hibiscus	<i>Malvaceae</i>
<i>Ficus benghalensis</i>	Indian fig	<i>Moraceae</i>
<i>Syzygium cumini</i>	Java plum	<i>Myrtaceae</i>
<i>Biophytum sensitivum</i>	Siker pud	<i>Oxalidaceae</i>
<i>Punica granatum</i>	Anar	<i>Lythraceae</i>
<i>Aegle marmelos</i>	Bael tree	<i>Rutaceae</i>

### ***Acorus calamus*:**

Oral administration of methanolic extract of *A. calamus* rhizome restored the levels of blood glucose in Streptozotocin induced diabetic rats after 21 days. Further, lipid profile (total cholesterol, LDL and HDL-cholesterol), glucose 6-phosphatase, fructose 1,6 bis Phosphatase levels and hepatic markers enzymes (aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase) were decreased <sup>2</sup>.



FIG. 2: ACORUS CALAMUS

***Salacia oblonga*:** Aqueous extract of the root bark has shown hypoglycemic activity <sup>3</sup>. Two biologically active fractions from the petroleum ether extract of the root bark has been shown to exert hypoglycemic effect of about 60 and 76% potency of an equal dose of tolbutamide (250

mg/kg) in albino rats <sup>4</sup>. Petroleum ether extract of the bark of the root has been shown to prevent streptozotacin (65 mg/ kg) induced hyperglycemia and hypoinsulinemia in rats. The aqueous-methanolic extract of the roots inhibited increase in serum glucose level in sucrose and maltose loaded rats. The water-soluble and ethyl acetate soluble portions of the same extract showed inhibitory activities on alpha-glucosidase and aldose reductase <sup>5</sup>.



FIG. 3: SALACIA OBLONGA

### ***Catharanthus roseus*:**

The administration of *C. roseus* leaf powder (100 mg/kg b.w.) lowered the plasma glucose and increased the plasma insulin were observed after 15 days in streptozotacin induced diabetic rats. The significant enhancement in plasma total cholesterol, triglycerides, LDL and VLDL cholesterol, and the atherogenic index of diabetic rats were normalized in extract treated diabetic rats <sup>6</sup>.





FIG. 4: CATHARANTHUS ROSEUS

***Acanthopanax senticosus:***

A hot water extract (85-95°C) of *A. senticosus* stem bark significantly decreased the plasma glucose level without affecting plasma insulin levels and inhibited  $\alpha$ -glucosidase activity in diabetic mice. The addition of *A. senticosus* extract inhibited  $\alpha$ -glucosidase activity but not  $\alpha$ -amylase activity. Thus it would be useful as an ingredient of functional foods to improve postprandial hyperglycemia and prevent type II diabetes mellitus<sup>7</sup>.



FIG. 5: ACANTHOPANAX SENTICOSUS

***Coccinia indica:***

It is a perennial tendril climber found throughout India. It is used in Ayurveda and Unani system of medicine for treatment of diabetes, skin eruptions, tongues sore, earache, etc.<sup>8</sup>. Feeding of water soluble alkaloid fraction of alcohol extract (1 gm/kg) of *Coccinia indica* leaves to normal fasting guinea pigs showed hypoglycemic activity of short duration and the effect was attributed to the presence of beta sitosterol<sup>9</sup>. Oral administration (2 gm/kg/day) of pectin isolated from *C. indica* fruit showed a significant hypoglycemic action in normal rats due to stimulation of glycogen

synthetase activity and reduction of phosphorylase activity<sup>10</sup>.



FIG. 6: COCCINIA INDICA

***Tinospora cordifolia:***

It is found in forests throughout India and is widely used in Ayurveda as tonic, vitalizer and as a remedy for DM and metabolic disorders<sup>11,12</sup>. Oral administration of the water extract of *Tinospora cordifolia* root (2.5, 5 and 7.5 mg/kg) caused a significant reduction in blood glucose, brain lipid level, hepatic glucose-6-phosphatase, serum acid phosphatase, alkaline and lactate dehydrogenase and increase in body weight, total hemoglobin and hepatic hexokinase in alloxanized diabetic rats (150 mg/kg, IP)<sup>13</sup>. Oral administration of 400 mg/kg of aqueous extract of TC for 15 weeks of treatment showed maximum hypoglycemia of 70.37, 48.81 and 0% in mild (plasma sugar /180mg/dl), moderate (plasma sugar / 280mg/dl) and severe (plasma sugar /400mg/dl) diabetic rats, respectively. Hypoglycemic effect depended upon the functional status of the pancreatic beta cells<sup>14</sup>.



FIG.7: TINOSPORA CORDIFOLIA

***Costus speciosus:***

Oral administration of Eremanthin (a compound isolated from the plant *C. speciosus* rhizome) decreased the HbA1c, serum total cholesterol,



triglyceride, LDL-cholesterol level and at the same time markedly increased plasma insulin, tissue glycogen, HDL-cholesterol and serum protein of streptozotacin induced diabetic rats. It also restored the plasma enzyme levels to near normal. Thus it – possessed a significant hypoglycemic and hypolipidemic activities and hence it could be used as a drug for treating diabetes<sup>15</sup>.



FIG. 8: *COSTUS SPECIOSUS*

#### ***Vaccinium bracteatum*:**

Intragastric administration of the aqueous and ethanolic extract of *V. bracteatum* leaves significantly ameliorated the body weight, blood glucose, insulin and plasma lipid levels of streptozotacin induced diabetic mice<sup>15</sup>. The effect of *V. bracteatum* aqueous extract on the diabetic mice was superior to that of *V. bracteatum* ethanolic extract<sup>16</sup>.



FIG. 9: *VACCINIUM BRACTEATUM*

#### ***Emblia officinalis*:**

Amla is a small to medium sized deciduous tree, found in throughout India, Pakistan, Uzbekistan, Sri Lanka, South East Asia, China and Malaysia. It grows about 8-18m height with thin light grey bark,

leaves are simple, light green, sub-sessile, closely set along the branchlets looks like pinnate leaves; flowers are greenish yellow; fruits are globose, fleshy, pale yellow with six obscure vertical furrows enclosing six trigonous seeds in two seeded three crustaceous cocci. Amla is highly nutritious and is one of the richest sources of Vitamin-C, amino acids and minerals. It contains several chemical constituents like tannins, alkaloids and phenols. Oral administration of ethanolic extract of seed powder of *E. officinalis* decreased the blood glucose level and serum cholesterol level in alloxan induced diabetic rats<sup>17</sup>.



FIG. 10: *EMBLICA OFFICINALIS*

#### ***Senna auriculata*:**

Oral administration of the ethanolic extract of *S. auriculata* (at a dose of 150 mg/kg of bw) leaf significantly reduced the blood glucose level, SGOT, SGPT, ALP, total cholesterol, triglyceride and low density lipoprotein-cholesterol (LDL-C) levels to the normal level and significantly increased HDL-C and phospholipid (PL) level in alloxan induced diabetic rats<sup>18</sup>. *S. auriculata* leaf gained much importance in diabetic control as it has been used as a traditional medicine for diabetes; since the phytochemical analysis has shown the presence of potent phytochemicals like flavonoids, terpenoids, glycosides, steroids, saponin and phenols.



FIG. 11: *SENNA AURICULATA****Cinnamomum zeylanicum*:**

A compound Cinnamaldehyde isolated from *C. zeylanicum* bark. The oral administration of a Cinnamaldehyde compound (20mg/kg) significantly decreased the HbA1C, serum total cholesterol, triglyceride levels and at the same time markedly increased plasma insulin, hepatic glycogen and high density lipoprotein cholesterol levels in streptozotacin-induced diabetic rats<sup>19</sup>. It also restored the plasma enzyme reduction in blood glucose level<sup>20</sup>.

FIG. 12: *CINNAMONUM ZEYLANICUM****Strychnos potatorum*:**

Oral administration of the ethanolic extract of *S. potatorum* plant material significantly decreased the AST, ALT and ALP level along with reduction of blood glucose level of alloxan induced diabetic rats<sup>21</sup>. The alloxan treated rat shows reduced body (26%) and liver (40%) weight. The blood glucose level falls by 53% with extract treatment, demonstrating the antidiabetic potential of the plant. The serum enzymes AST and ALT were increased from 24 and 18 IU/l to 60 and 65 IU/l respectively whereas ALP was decreased to 5 IU/l

from 14 IU/l. The total serum protein level also increased up to 5 mg/ml in the extract treated animal. The insulin level also increased up to 61µg/ml within 30 days of extract treatment compared to control with 51µg/ml. The plant extract efficiently decreased the initial cholesterol 219 µg/ml level into 170µg/ml. In liver, the AST, ALT and ALP enzymes were decreased to 160, 60, and 140 IU/l from 178, 79, and 156 IU/ml respectively<sup>22</sup>.

FIG. 13: *STRYCHONOUS POTATORUM****Hibiscus rosa sinensis*:**

Treatment with the aqueous extract of *H. rosa sinensis* (500 mg kg<sup>-1</sup>) aerial part reduced the blood glucose level, urea, uric acid and creatinine but increased the activities of insulin, C-peptide, albumin, albumin/globulin ratio and restored all marker enzymes to near control levels of streptozotacin-induced diabetic rats. Thus, it exhibited an antihyperglycaemic effect and consequently may alleviate liver and renal damage associated with streptozotacin-induced diabetes mellitus in rats<sup>23</sup>.

FIG. 14: *HIBISCUS ROSA SINENSIS****Ficus benghalensis* :**



*Ficus benghalensis* is native to India where it grows from low altitudes to 2000 ft (610 m), especially in dry regions. It is native to a wide area of Asia from India through Myanmar (Burma), Thailand, Southeast Asia, Southern China and Malaysia. Stem bark contains a number of anthocyanidin derivatives (methyl ethers of leucodelphinidin-3-O-L-rhamnoside, leucopelargonidin-3-O-L-rhamnoside, leucocyanidin-3-O-D-galactosylcellobioside) and aliphatic long chain ketones (pentatriacontan-5-one, tetratriacont-20-en-2-one, heptatriacont-6-en-10-one), besides-beta-sitosterol glucoside and meso inositol.

The leaves contain 9.63% crude protein, 26.84% crude fibres, 2.53% calcium oxalate and 0.4% phosphorous. The various qualitative chemical tests of ethanol extract and aqueous extract of leaves contain sterols, flavanoids, phenol, tannins, and saponins in large amount whereas aromatic acids, carbohydrates, triterpenoids, gums, mucilage, and volatile oils were totally absent in this plant. The aqueous extract of *F. benghalensis* stem bark significantly reduced the blood glucose level of streptozotacin induced diabetic rats<sup>24</sup>.

FIG. 15: *FICUS BENGHALENSIS*

### **Syzygium cumini:**

Mycaminose a compound isolated from the plant *S. cumini* seed extract. Oral administration of a compound (50 mg/kg), ethyl acetate (200 mg/kg) and methanol extracts (400 mg/kg) of fruits and leaves of *S. cumini* reduced the blood glucose level of streptozotacin-induced diabetic rats<sup>25</sup>. *S. cumini* seed powder and ethanol extract *S. cumini* seed have potential antihyperlipidemic effect in type 2 diabetic model rats<sup>26</sup>.

FIG. 16: *SYZYGium CUMINI*

### **Biophytum sensitivum:**

*B. sensitivum* shows hypoglycemic activity in alloxan-diabetic rabbits, initial dose-response studies showed that a dose of 200 mg/kg body weight (b.wt.) was optimum for hypoglycemia. A single administration of this dose to 16-h fasted non-diabetic rabbits brought about a 16.1% fall in fasting plasma glucose (FPG) level at the end of 1 h and 2 h, and the hypoglycemic effect persisted at the end of 6 h (13.8% fall). The study also showed rise in serum insulin levels in the treated animals, suggesting a pancreatic mode of action (i.e. insulinotropic effect) of *B. sensitivum*<sup>27</sup>.

Hypoglycemic effect was studied in the alloxan diabetic male rabbits of different severities: subdiabetic (alloxan recovered; AR), mild diabetic (MD) and severely diabetic (SD). Following single dose administration, there was fall in 1 h and 2.5 h glucose values by 25.9% and 27.4%, respectively, in the subdiabetic rabbits, and by 36.9% and 37.7%, respectively, in the mild diabetic rabbits<sup>28</sup>. Oral administration of the ethanolic extract of *B. sensitivum* whole plant significantly decreased the blood glucose level, serum cholesterol level and increased the total protein level of alloxan induced diabetic rats<sup>29</sup>.

FIG.17: *BIOPHYTUM SENSITIVUM*

### **Punica granatum:**

A shrub or small tree grows wild in the warm valleys and outer hills of the Himalayas and also cultivated throughout India. The flowers of *Punica granatum* are used as anti-diabetic in Unani medicine called Gulnar farsi. Oral administration of aqueous-ethanolic extract (50% v/v) led to significant blood glucose lowering effect in glucose fed hyperglycemic and alloxanized diabetic rats with the maximum effect at the dose of 400-mg/kgbody weight<sup>30</sup>. Anti-oxidant activity has been described in the literature<sup>31</sup>.



FIG. 18: *PUNICA GRANATUM*

#### *Aegle marmelos*:

Antidiabetic potential of the leaves and callus of *A. marmelos* was reported in streptozotocin induced diabetic rabbits. All the extracts reduced the blood sugar level in streptozotocin diabetic rabbits, however, among the various extracts, the methanol extracts of the leaf and callus brought about the maximum anti-diabetic effect. The methanolic extract of leaf and callus powder of *A. marmelos* significantly decreased the blood sugar level of streptozotocin induced diabetic rabbits<sup>32</sup>. *A. marmelos* would act like insulin in the restoration of blood sugar and body weight to normal levels in rat and was therefore recommended as a potential hypoglycemic agent<sup>32</sup>.



FIG. 19: *AEGLE MARMELOS*

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