

**Review Article****Anti-Diabetic Effects of Some Medicinal Plants In Experimental Animals: A Review****Imran Gani, Mudasir Maqbool\*, Mohmad Amin Dar**

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**ABSTRACT**

Diabetes is a chronic endocrine disease with global prevalence and increasing incidence. Diabetes presents with a major health issue in all age groups in the present times owing to its multisystem involvement and serious complications. In spite of drug development and therapeutic interventions, successful treatment of diabetes still remains a challenge and worldwide research is focused on finding alternative modalities. By conducting sizable amount of analytical work, numerous traditional medicines have been found for diabetes. Substances and extracts isolated from completely different natural resources particularly plants have perpetually been a fashionable arsenal for dominant and treating polygenic disorders downside and complication arising because of it. Many medicinal plants have shown promising effects in experimental animals which can be extrapolated to humans also. In this paper, we will review various medicinal plants showing anti-diabetic activity in experimental animals.

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**INTRODUCTION**

Diabetes mellitus is a modern epidemic increasing alarmingly worldwide and is defined as the abnormal glucose tolerance which affects pancreatic beta cells functions and sensitivity leading to progression of diabetes and its associated complications. It is a chronic disease of carbohydrate, fat and protein metabolism manifested by increased fasting and post prandial blood sugar level and an enhanced risk of vascular complications. It is the most common endocrine disorder in men and women, and the major public health concern of epidemic proportions, once assumed to be a disease of the west, is changing to an endemic in modernizing and urbanizing population in our country. From the ancient times, Ayurvedic literature reveals that since the time of Charak and Sushrut, many herbal plants in different oral formulations have been used in Madhumeha (diabetes mellitus) and confident claims of cure are on record<sup>1</sup>. Diabetes Mellitus (DM) has become the most common endocrine dysfunction in the world

caused by defect in insulin dynamics. It is estimated by year 2030 more than 439 million people are believed to be affected by diabetes. India is one of the hubs of the global DM pandemic. In Addition, diabetes is a fast growing potential epidemic syndrome in India with more than 62 million diabetic patients currently diagnosed every year. It is assumed that by the year 2030 such cases may increase up to 79.4 million, posing potential risk imposed by diabetes<sup>2</sup>. A vast number of herbal plants with potential antidiabetic activity have been studied, which may include: *Azadirachta indica* (leaves, stem bark and seeds) possess hypoglycemic activity via increasing insulin secretion from pancreatic beta-cells, *Grewia asiatica* (its antioxidant and radical scavenging activity), *Eugenia jambolana* (seed kernel extracts) inhibits alpha-glucosidase activity, *Cinamomum zeylanicum* (chief active constituent cinnamaldehyde) increases serum insulin level, *Allium sativum* (active compound allicin) shows significant hypoglycemic activity, *Allium cepa*

(active constituent S-methyl cysteine sulfoxide) significantly controls blood glucose levels and others like *Aegle marmelos*, *Aralia elata*, *Phyllanthus amarus* and *Tinospora cordifolia*<sup>3</sup>. Recently, the World Health Organization (WHO) suggested the use of medicinal plants for the management of Diabetes Mellitus and further encouraged the expansion of the frontiers of scientific evaluation of anti-diabetic properties of diverse plant species. Consequently, current estimates showed that over 70% of the Global population applies resources derived from traditional plant derived medicines for the management and alleviation of DM and its complications exponential growth in the field of traditional herbal medicine and these drugs are becoming popular both in developing and developed countries because of their natural origin and lesser side effects. Many traditional medicines used are derived from medicinal plants, minerals and organic matter. The World Health Organization (WHO) has listed 21,000 plants, which are being used for medicinal purpose around the world<sup>4</sup>.

#### **Plants with hypoglycemic/antidiabetic effects in experimental animal**

##### ***Aegle marmelos* Corr. (Rutaceae)**

A significantly high level of metabolic enzyme, malate dehydrogenase was observed in STZ induced diabetic rats compared to control. Insulin as well as the leaf extract of *A. marmelos* treatment brought about a reversal of the Km values of these enzyme to near normal. Moreover, *A. marmelos* was found to be as effective as insulin in restoration of blood glucose and body weight to normal levels<sup>5</sup>. Another study shows that *A. marmelos* extract effectively reduced the oxidative stress induced by alloxan as it significantly decreased lipid peroxidation, conjugated diene and hydroperoxidase levels in serum as well as in liver<sup>6</sup>.

##### ***Allium cepa* Linn. (Liliaceae)**

Onion oil and synthetic dipropyl disulphide oxide produces significant hypoglycemic effect in mice<sup>7</sup>. Petroleum ether and chloroform extract of the bulb reduces blood sugar during the glucose tolerance test<sup>8</sup>.

##### ***Azadirachta indica* Juss. (Maliaceae)**

Significant antidiabetic and antihyperlipaemic effect was reported with neem seed kernel powder in alloxan diabetic rats<sup>9</sup>. Possible mechanism of antihyperglycemic effect of neem leaf extract was studied in normal and STZ induced diabetic rabbits. The reduction in peripheral utilization of glucose and glycogenolytic effect due to epinephrine action was blocked by the extract almost completely in diabetic rabbits and to certain extent in normal ones<sup>10</sup>.

##### ***Caesalpinia bouducella* Roxb. (Leguminosae):**

Aqueous and ethanolic extracts of *Caesalpinia bouducella* seeds produced hypoglycemic effect in normal rats and antihyperglycemic activity in STZdiabetic rats. The drug also showed a hypolipidemic activity in diabetic rats<sup>11</sup>.

##### ***Capparis deciduas* (Capparaceae) :**

Antidiabetic treatment with powdered fruit of *Capparis decidua* lowered alloxan induced lipid peroxidation and altered erythrocyte superoxide dismutase and catalase enzymes to reduce oxidative stress in alloxan diabetic rats<sup>12</sup>.

##### ***Catharanthus roseus* L. (Apocynaceae):**

Dichloromethane-methanol (DCMM) extract of leaves and twigs of *C. roseus* shows protective effects against STZ-diabetes rats and action on lipid peroxidation. Antidiabetic activity seems to be a result of increase of glucose utilization<sup>13</sup>.

##### ***Coccinia indica*:**

Ethanolic and aqueous extract of defatted roots produces significant hypoglycemic effect in alloxan-diabetic rats and in rabbits compare to tolbutamide<sup>14</sup>. In a clinical double-blind controlled trial, a significant improvement in the glucose tolerance was seen in 10 of 16 type 2 DM patients who received *Coccinia indica* leaf preparation<sup>15</sup>.

##### ***Ficus bengalensis*:**

A glycoside of leucopelargonidin isolated from the bark of FB showed significant hypoglycemic, hypolipidemic and serum insulin-raising effects in moderately diabetic rats which was similar to that of glibenclamide<sup>16</sup>.

##### ***Gymnema slyvestra* Roxb. (Asclepiadaceae):**

Powder or decoction of leaves reduces the urine glucose in humans. Oral administration of aqueous or alcoholic extract of leaves reduced blood sugar level in diabetic rabbits<sup>17</sup>, in diabetic dogs<sup>18</sup> and in diabetic humans. It been shown to stimulate the secretion or release of insulin in vitro and in vivo<sup>19</sup>. It also has partial protective effect on the pancreas against potent pancreatic toxins like beryllium<sup>20</sup>. Study also suggest it may be promoting the regeneration of islet cells destroyed by STZ in rats<sup>21</sup>. One study showed that it increases the activity of enzymes responsible for the utilization of glucose by insulin dependent pathway, as increase in phosphorylase activity, and a decrease in gluconeogenic enzymes and sorbitol dehydrogenase<sup>22</sup>.

##### ***Momordica charantia* Linn. (Cucurbitaceae):**

Aqueous extract of fruit inhibited hyperglycemia probably by influencing the glucose tolerance in albino rats and hypoglycemic activity was observed in alloxan-diabetic rabbits<sup>23</sup>. Several studies report that increased secretion or release of insulin as a mechanism of hypoglycemic activity<sup>24,25</sup>. Biochemical effects, such as the reduction in lipid peroxidation reported in STZ-DM rat pancreas and islet cells may contribute to hypoglycemic activity. Another biochemical studies showed that hepatic glucose-6-phosphatase and fructose-1, 6-biphosphatase activities are increased and decrease in hepatic glucose-6-phosphate dehydrogenase activity in STZ-DM rats<sup>26</sup>. Two hypoglycemic chemicals isolated from plants (i) the oleanolic acid 3-Omonodesmoside, momordin Ic, and (ii)

oleanolic acid 3-O-glucuronide showed dose response effect in inhibiting the increase in serum glucose level in oral glucose-loaded rats. Both chemicals were found to suppress gastric emptying time and inhibits glucose uptake in small intestine in vitro<sup>27</sup>.

#### **Pterocarpus marsupium Roxb.:**

Pterostilbene, isolated from the wood, produces a fall in blood sugar in dogs. Decoction of the bark lower the blood sugar in diabetic human being and increases tolerance. Alcoholic extract of heartwood significantly lower the blood sugar in and improve the glucose tolerance in rabbits<sup>28</sup>. Three phenolic constituents from Vijayasar showed significant antihyperglycemic activity in STZ-diabetic rats<sup>29</sup>. The study of insulin mimetic effect of (-) epicatechin, a benzopyran extract from bark of Vijaysar, showed that insulin and (-) epicatechin act by different mechanism of action while eliciting protective effects on human red cell osmotic fragility<sup>30</sup>.

#### **Syzgium cumini (Caesalpinaceae):**

Aqueous extract of Jamun showed hypoglycemic and antioxidant property in alloxan diabetic rats. Further the alcoholic extract of seeds at a dose of 100- mg/kg body weight significantly reduces blood glucose, urine sugar and lipid in serum and tissue in alloxan diabetic rats. The extract also increases total hemoglobin<sup>31</sup>.

#### **Trigonella foenum graecum:**

Trigonella foenum graecum (fenugreek) produced a significant does related fall in blood glucose level both in the normal as well as diabetic rats and also significantly reduced various serum lipids in normal rats and decreased the increased level of lipid and HDL cholesterol in the diabetic rats<sup>32</sup>.

#### **Zingiber officinale Rosc. (Zingiberaceae)**

Juice of *Z. officinale* significantly prevented the hyperglycemia and hypoinsulinaemia in 5-HT induced hyperglycemic rats. Treatment with *Z. officinale* produced significant increase in insulin level and decrease in fasting

glucose levels in STZ-diabetic rats. In oral glucose tolerance test, treatment with *Z. officinale* found to decrease significantly the area under curve of glucose and to increase the area under curve of insulin in STZ-diabetic rats. *Z. officinale* also causes a decrease in serum cholesterol, serum triglyceride and blood pressure in diabetic rats<sup>33</sup>.

#### **Zizyphus jujube Linn. (Rhamnaceae)**

The aqueous extract of *Zizyphus jujube* showed hypoglycemic activity in alloxan induced diabetic rats<sup>34</sup>. D-400: The herbal formulation D-400, which is the combination of *Eugenia jambulana*, *Pterocarpus marsupium*, *Ficus glomerulata* and *Ocimum sanctum* with other herbs, showed a favorable response to alloxan induced hyperglycemia and renal damage in rabbits<sup>35</sup>. The increased glucose level, suppressed glycogen level and in vitro decrease in 14C-glucose uptake by liver slices in diabetic rats were brought to within normal levels by D-400. The glucose tolerance of D-400 was also studied in STZ-induced diabetic rats<sup>36</sup>.

#### **Ayush-82:**

Ayush-82 is mixture of four herbs: seeds of *Mangifera indica*, *Syzygium cumini*, and *Momordica Charantia* and the leaves of *Gymnema sylvestre*. In a clinical trial on 350 type 2 DM patients on a basis of a physician's rating scale reported that 61% of the patients had a good response to Ayush-82 when given with Shuddha shilajit. After the treatment, FBS and PPBS levels were found to be significantly reduced<sup>37</sup>.

#### **MA-471:**

MA-471 is mixture of: *Enicostema littorale*, *Phyllanthus niruri*, *Eugenia jambolana*, *Melia azadirachta*, *Terminalia arjuna*, *Aegle marmelos* and shilajit. This mixture were found to produce a significant hypoglycemic activity and hypolipidemic activity in patients resistant to an oral hypoglycemic agent. The authors suggest that it can be used in conjunction with oral hypoglycemic agents<sup>38</sup>.

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