Some Essential Herbal Drugs Use for Treatment of Diabetes mellitus

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A B S T R A C T

From longer period of time herbal drugs are used by human society depending upon nature for treatment and prevention of various diseases including diabetes. It is an important human health problem around the globe as most of the people are suffering with this disease. It is determined as one of the commonest public health hazards; optimal control of which is still not possible. There is a no of synthetic drugs area available in the market but most of the drugs are possess a number of drug related complications and high cost so researchers are focusing to develop substitute for synthetic one. Herbal drugs are inexpensive and simply available and not have toxicity. In this review authors are focussing on the herbal remedies that play the crucial role for the treatment and prevention of morbid disorder like diabetes and their root mechanisms for the blood glucose-lowering action. Authors also focussing on some herbal products already been marketed for the remedial action of diabetes. This review will help for researchers to gather information for antidiabetic research work.
Introduction: Nature has provided a complete store-house of remedies to treat every ailments of mankind. In the past, almost all the medicines used were from the plants. In traditional medicine plants constitute a vital source of new biologically active compounds. In India, plants are widely used by all sections of the population either directly as folk medicine or indirectly in the pharmaceutical preparations of modern medicines. As per World Health Organization (WHO) around 21,000 plants, useful for treatment of various ailments around the world. Among these around 2500 species are available in India and from that 150 species are generally used commercially. Effect of herbal drugs on human health is represented in figure:1 and mechanism of antidiabetic action of different herbal drugs presented in Table:1.

Type 2 diabetes mellitus (T2DM) is a global pandemic, with an estimated 370 million people currently affected. Diabetes mellitus is one of the oldest known diseases. In ancient scripture it was reveal that as early as 700-200 B.C. Sushruta used the term “Madhumeha” for diabetes mellitus in 6th Century. He describes it as a disease of rich, produced by over consumption of rice, flour and sugar. By definition, the term diabetes mellitus describes the metabolic disorder having heterogeneous etiologies which are characterized by chronic hyperglycemia and abnormal of carbohydrate, protein and fat metabolism due to impaired in insulin secretion, resistant to insulin action, or both. This review is an approach to explore therapeutic potential of some indigenously available herbal drugs and formulations.

Figure:1 Effect of herbal drugs on Human health

Acacia arabica: Acacia (Figure:1) is the most essential genus of family: Leguminosae, first of all described by Linnaeus in 1773. about two-third of them local to Australia and rest of spread around tropical and subtropical regions of the world. It is found all over India mainly in the wild habitat. Extract of this plant is responsible for improve insulin secretion. It can cause hypoglycemia in normal control rats but not in alloxan treated animals. Acacia arabica seeds when administered (2,3 and 4 g/kg body weight) to normal rabbits induced hypoglycemic effect by initiating release of insulin from pancreatic β-cells.

Aegle marmelos: Aegle marmelos (Figure:3) is a native plant of India. A. marmelos is included in Rutaceae family and it is famous in the name of wood apple. In India, Hindu people offer it to lord Shiva so found in temple garden. A marmelos is an important medicinal plant with several ethnomedicinal applications in traditional and folk medicinal systems.

Administration of aqueous extract of leaves improve digestion and reduce blood glucose and urea, serum cholesterol in Alloxan administered 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, insulin release effect of A. marmelos leaves similar to Glibenclamide. A. marmelos treatment significantly increased insulin level, and produced similar effects on other biochemical parameters. Histological studies showed the regenerative effect of A. marmelos on the β-cells of diabetic rats.8

**Allium cepa:** Allium, a large genus containing about 4000 species is scattered throughout temperate regions of the world including Europe, Asia, North America and Africa.9 Various ether soluble fractions as well as insoluble fractions of dried onion powder show anti-hyperglycemic activity in diabetic rabbits. *Allium cepa* (Figure:4) is also possess antioxidant and hypolipidaemic property.

Administration of a amino acid containing S from *Allium cepa*, S-methyl cysteine sulfoxide (SMCS) (200 mg/kg for 45 days) to Alloxan induced diabetic rats significantly controlled blood glucose level as well as lipids in serum and tissues and normalized the activities of liver hexokinase, glucose 6-phosphatase and HMG CoA reductase.10,11 Administration of single oral dose of 50 g of onion juice, it significantly able to control post-prandial glucose levels.12

*Aegle marmelos*:

**Allium sativum:** *Allium sativum* L. (Figure:5) (Garlic) are bulbous herbs belonging to family: Alliaceae and are commercially cultivated worldwide. This is a perennial herb cultivated all over India. Allicin, contain sulphur containing compound is liable for its strong odour and it is responsible for its hypoglycaemic action.13 This effect is thought to be due to improved hepatic metabolism, improved insulin release from pancreatic β-cells and/or insulin sparing effect.14 Aqueous extract of garlic (10 ml/kg/day) when administered orally rabbits given sucrose (10 g/kg/day in water for two months) it was observed a significant increased hepatic glycogen and free amino acid level, decreased fasting blood glucose level, and triglyceride levels in serum with respect to sucrose controls.15 S-allyl cysteine sulfoxide (SACS), the precursor of allicin in garlic oil, is a S containing amino acid, it control lipid peroxidation better than glibenclamide and insulin. It also improved diabetic conditions. SACS also stimulated in vitro insulin secretion from β cells isolated from normal rats.16 Apart from this, *Allium sativum* also exhibits antimicrobial, anticancer and cardio protective activities. Allicin chemically known as 2-propene-1-sulfinothioic acid S-2-propenyl ester; thio-2-propene-1-sulfonic acid S-allyl ester (Merck Index, 1989). Discovered by Cavallito and Bailey in 1944.17 Recently, it is accounted that the hypoglycemic action of garlic, garlic oil and its organosulfur constituents especially di-allyl-trisulfide, result in higher insulin secretion and insulin sensitivity in streptozotocin-induced diabetic rats.18
**Aloe vera and Aloe barbadensis:** The Biological name of *Aloe vera* (Figure:6) is *Aloe barbadensis miller* which belongs to family: Liliaceae. It is a shrubby, perennial, xerophytic, succulent plant. It is found generally in Africa, Asia, Europe and America. In India, it is found in Rajasthan, Andhra Pradesh, Gujarat, Maharashtra and Tamil Nadu. 

Aloe, a popular houseplant, has a long history as a versatile folk therapy. It can be separated into: gel and latex. *Aloe vera* gel is the leaf flesh or mucilage, commonly known as “aloe juice,” is bitter yellow exudates from the pericyclic tubules just beneath the outer skin of the leaves. Extracts of aloe gum efficiently increases glucose tolerance in both normal and diabetic rats. Treatment of chronic but no single dose of exudates of *Aloe barbadensis* leaves showed hypoglycaemic effect in alloxanized diabetic rats. Single as well as multiple doses of bitter principle of *Aloe vera* shows 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 β-cells.  

**Azadirachta indica:** It is popularly known as Neem tree (Figure:7) which belongs to the family: Meliaceae. It is found in abundance in tropical and semitropical regions like India, Pakistan, Bangladesh and Nepal. It grows fast with 20–23 m tall and trunk has diameter of around 4-5 ft. *Azadirachta indica* L. (Figure:7) Presence of various active ingredients responsible for its therapeutic potential. The chief active constituent is azadirachtin and the others like: nimbin, nimbin, nimbidin, nimbidol, salannin, and quercetin etc. Leaves also contain ingredients like: nimbin, nimbanene, 6-desacylnimbininene, nimbandiol, nimbolide, ascorbic acid, n-hexacosanol and amino acid, 7-desacetyl-7-benzoylazadiradione, 7-desacetyl-7-benzoylgedunin, 17-hydroxyazadiradione, and nimbiol. 

Hydroalcoholic extracts of Neem shows antihyperglycemic activity in streptozotocin induced diabetic rats and because it increases in glucose uptake and glycogen deposition in isolated rat hemidiaphragm. Glucosidase are normally present in the pancreas and gut of small intestine and play an important role in the digestion of dietary carbohydrates. The inhibitors of α-glucosidase, in result retard the use of dietary carbohydrates to suppress postparendial hyperglycaemia in diabetes. *A. indica* is reported as a pancreatic; glucosidase inhibitor. *A. indica* may play a significant role in the management of type-2 diabetes mellitus, by improving the insulin signalling molecules and glucose utilization in the skeletal muscle.
glycogen content. Extract increase secretion of insulin from isolated islets. Various extracts of*C. bonducella* seeds shown antihyperglycemic and hypolipidemic activities in STZ induced diabetic rats. The antihyperglycemic action is due to the blocking of glucose absorption. The drug has the potential to act as antidiabetic as well as antihyperlipidemic.

*Ocimum sanctum*: It is commonly known as Tulsi (Figure: 9) belongs to the family Lamiaceae. From ancient periods people are using this plant for its medicinal properties. The aqueous extract of leaves of *Ocimum sanctum* significantly reduce in blood sugar level in both normal and alloxan induced diabetic rats. Oral administration of plant extract (200 mg/kg) for 30 days led to decrease in the plasma glucose level. It also shows anti-asthmatic, anti-stress, antimicrobial, antineoplastic, antiulcer activity, antioxidant, immunostimulant activities. Whole plant is used as a therapeutic agent against several ailments. *O. sanctum* is reported to grow globally. Its nutritional and chemical components make it important. Eugenol, the active constituent present in *O. sanctum* L., has been found to be responsible for its healing potential. Major bioactive constituents present in the leaves and stems of holy basil include flavonoids, saponins, tannins, triterpenoids, rosmarinic acid, apigenin, isothymusin.

*O. sanctum* leaves oil contains eugenol, carvacrol, linalool, limatrol, ursolic acid and caryophyllene along with eugenol. Seeds oil also contains fatty acids and sitosterol. While seed mucilage contains some sugars. Anthocyanins are present in green leaves. Furthermore, *O. sanctum* is also rich in vitamins, minerals, chlorophyll, and many other phytonutrients. Antidiabetic properties of *O. sanctum* were appreciated in Ayurveda. A significant fall in blood glucose, glycosylated haemoglobin, and urea along with a simultaneous increase in glycogen, hemoglobin, and protein in STZ induced diabetic rats has been observed when rats were supplemented with ethanolic extract of *O. sanctum*. Chloroform extracts of *Ocimum sanctum* shows beneficial effect in alloxan induced diabetic rats. The extract significantly decreased elevated level of serum glucose and also reversed the cholesterol, triglyceride, and LDL values. Various studies reported that oral administration of alcoholic extract of leaves of *O. sanctum*L. significantly decrease blood glucose level in normal, glucose induced hyperglycemic, and streptozotocin induced diabetic rats. Improvement in the action of exogenous insulin in normal rats has also been recorded. Mixed extract of *P. marsupium* and *O. sanctum* has been recorded to not only rectify dyslipidemia but also restore the endogenous antioxidant levels in alloxan-induced diabetic rats.
Philippines, Java and Spain. Both hydro-alcoholic and aqueous extracts of *Tamarindus indica* seeds possess potential anti-diabetic, hypolipidemic effect. Hydro alcoholic and aqueous extracts of *Tamarindus indica* leaves possess antidiabetic and hypolipidemic potential.

*Figure:10 Tamarindus indica*

**Cyperus rotundus:** *Cyperus rotundus* (Figure: 11) generally known as Nagarmotha is found all over the India. It belongs to the family Cyperaceae. The genus name *Cyperus* is derived from *Cyperus*, which was the ancient Greek name for the genus, *rotundus* is Latin word for round and refers to the tuber. The experimental findings of the present study concluded that ethanolic extract is capable of exhibiting significant anti-hyperglycemic activity in STZ-induced diabetic mice.

*Figure:11 Cyperus rotundus*

**Curcuma longa:** *Curcuma longa* (Figure:12) is a rhizome and belonging to the ginger family Zingiberaceae. It is native to tropical South Asia. As many as 133 species of *Curcuma* have been identified worldwide. Pancreatic β-cell possess glucose sensor which automatically produce insulin and in type –II diabetic people’s pancreatic β-cells are unable to produce sufficient amount of insulin. Curcumin act on pancreatic β- cell to stimulate the secretion of insulin. It stimulates pancreatic β-cells which is responsible for depolarization of the cell membrane potential, the generation of electrical activity, and an increase in insulin release.

Curcumin combined with metformin may act synergistically on dyslipidemia and oxidative stress, as well as increase paraoxonase 1 (PON 1) levels. Therefore, it might be a promising strategy for combating diabetic complications, mainly the cardiovascular events.

**Table:**

<table>
<thead>
<tr>
<th>Sl No</th>
<th>Plant Name</th>
<th>Action</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><em>Aegle marmelos</em></td>
<td>Glucose utilization increase; both by direct stimulation of glucose uptake or enhanced insulin secretion. It has potent antioxidant activity.</td>
<td>45</td>
</tr>
<tr>
<td>2</td>
<td><em>Allium cepa</em></td>
<td>decrease blood glucose level, antioxidant activity</td>
<td>46</td>
</tr>
<tr>
<td>3</td>
<td><em>Allium sativum</em></td>
<td>Increased the insulin like activity of plasma</td>
<td>47</td>
</tr>
<tr>
<td>4</td>
<td><em>Aloe vera</em></td>
<td>Maintains glucose homeostasis by controlling the carbohydrate metabolizing enzymes</td>
<td>48,49</td>
</tr>
<tr>
<td>5</td>
<td><em>Andrographis paniculata</em></td>
<td>Prevents glucose absorption from gut</td>
<td>50</td>
</tr>
<tr>
<td>6</td>
<td><em>Annona squamosa</em></td>
<td>Hypoglycemic and anti-hyperglycemic effect, increased plasma insulin level</td>
<td>51,52,53</td>
</tr>
<tr>
<td>7</td>
<td><em>Artemisia pallens</em></td>
<td>Increases peripheral glucose utilization or inhibits glucose reabsorption</td>
<td>54,55</td>
</tr>
<tr>
<td>8</td>
<td><em>Areca catechu</em></td>
<td>Hypoglycemic</td>
<td>56</td>
</tr>
<tr>
<td>No.</td>
<td>Herb</td>
<td>Mechanism of Action</td>
<td>Table 1: Mechanism of action of some important anti-diabetic herbs</td>
</tr>
<tr>
<td>-----</td>
<td>-------------------------------</td>
<td>-------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------</td>
</tr>
<tr>
<td>9</td>
<td>Azadirachta indica</td>
<td>Reduce blood glucose level by regeneration of β cells</td>
<td>litorale activity. Decrease glucose 6-phosphatase and fructose 1,6-bisphosphatase activities.</td>
</tr>
<tr>
<td>10</td>
<td>Beta vulgaris</td>
<td>Increases glucose tolerance in OGTT</td>
<td>57</td>
</tr>
<tr>
<td>11</td>
<td>Boerhavia diffusa</td>
<td>Increase in hexokinase activity, decrease in glucose-6-phosphatase and fructose-bisphosphatase activity, increase plasma insulin level, antioxidant</td>
<td>58,59</td>
</tr>
<tr>
<td>12</td>
<td>Bombax ceiba</td>
<td>Hypoglycemic</td>
<td>60,61, 62,63</td>
</tr>
<tr>
<td>13</td>
<td>Brassica juncea</td>
<td>Increases the concentration of hepaticglycogen and glycogenesis and suppressed the activity of glycogen phosphorylase and gluconeogenetic enzymes, lead to reduction in glycogenolysis and gluconeogenesis</td>
<td>63</td>
</tr>
<tr>
<td>14</td>
<td>Butea monosperma</td>
<td>Anti-hyperglycemic</td>
<td>64</td>
</tr>
<tr>
<td>15</td>
<td>Camellia sinensis</td>
<td>Anti-hyperglycemic activity, antioxidant</td>
<td>65,66</td>
</tr>
<tr>
<td>16</td>
<td>Cassia auriculata</td>
<td>Increased utilization of glucose through increased glycolysis</td>
<td>67,68</td>
</tr>
<tr>
<td>17</td>
<td>Caesalpinia bonducella</td>
<td>Hypoglycemic, insulin secretagogue, hypolipidemic</td>
<td>69,70</td>
</tr>
<tr>
<td>18</td>
<td>Camellia sinensis</td>
<td>Epigallocatechin gallate, present in tea increases insulin activity and prevent oxidative damages, responsible for the hypoglycaemic activity</td>
<td>71,72</td>
</tr>
<tr>
<td>19</td>
<td>Cinnamomum zeylanicum</td>
<td>Decrease glucose synthesis, by depression of gluconegenic enzymes glucose-6-phosphatase and fructose-1,6-bisphosphatase and enhances glucosoexidation activation of f enzyme glucose-6-phosphatedehydrogenase</td>
<td>73</td>
</tr>
<tr>
<td>20</td>
<td>Coccinia indica</td>
<td>Decrease blood glucose level</td>
<td>74,75,76</td>
</tr>
<tr>
<td>21</td>
<td>Eriocostema</td>
<td>Increase hexokinase</td>
<td>77</td>
</tr>
<tr>
<td>22</td>
<td>Eucalyptus globulus</td>
<td>Increase insulin secretion from islet-pancreatic beta line</td>
<td>78</td>
</tr>
<tr>
<td>23</td>
<td>Ficus bengalensis</td>
<td>Inhibits insulin degradation</td>
<td>79</td>
</tr>
<tr>
<td>24</td>
<td>Gymnema sylvestre</td>
<td>Anti-hyperglycemic effect, hypolipidemic</td>
<td>80,81</td>
</tr>
<tr>
<td>25</td>
<td>Hibiscus rosasinesis</td>
<td>Initiates insulin release from pancreatic β-cells</td>
<td>82,83</td>
</tr>
<tr>
<td>26</td>
<td>Ipomoea batatas</td>
<td>Reduces insulin resistance</td>
<td>84,85</td>
</tr>
<tr>
<td>27</td>
<td>Momordica cymbalaria</td>
<td>Hypoglycemic</td>
<td>86</td>
</tr>
<tr>
<td>28</td>
<td>Musa sapientum</td>
<td>Anti-hyperglycemic</td>
<td>87</td>
</tr>
<tr>
<td>29</td>
<td>Ocimum sanctum</td>
<td>Hypoglycemic and hypolipidemic effect in normal and diabetic rats</td>
<td>88</td>
</tr>
<tr>
<td>30</td>
<td>Salacia reticulata</td>
<td>Inhibitory activity against sucrase α-glucosidase inhibitor</td>
<td>89</td>
</tr>
<tr>
<td>31</td>
<td>Swertia chirayita</td>
<td>Stimulates insulin release from islets</td>
<td>90</td>
</tr>
<tr>
<td>32</td>
<td>Tamarindus indica</td>
<td>Hypoglycemic and anti-hyperglycemic</td>
<td>91,92</td>
</tr>
<tr>
<td>33</td>
<td>Terminalia belerica</td>
<td>hypoglycemic</td>
<td>93</td>
</tr>
<tr>
<td>34</td>
<td>Terminalia chebula</td>
<td>hypoglycemic</td>
<td>94</td>
</tr>
<tr>
<td>35</td>
<td>Tinospora crispa</td>
<td>stimulates insulin release from islets</td>
<td>95</td>
</tr>
<tr>
<td>36</td>
<td>Trigonella foenumaceum</td>
<td>Decrease blood glucose concentration</td>
<td>96,97</td>
</tr>
<tr>
<td>37</td>
<td>Vinca rosea</td>
<td>Hypoglycemic</td>
<td>98</td>
</tr>
<tr>
<td>38</td>
<td>Withania somnifer a</td>
<td>β-cell rejuvenation, regeneration, stimulation</td>
<td>99</td>
</tr>
<tr>
<td>39</td>
<td>Zingiber officinale</td>
<td>Decrease blood glucose level.</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 1: Mechanism of action of some important anti-diabetic herbs

Available online at http://www.advbiomol.com
Different herbal formulations for treatment of diabetes mellitus: There are large number of herbal formulations are available for treatment of diabetes and its complications. Herbs are the active ingredients of these formulations. A list of Indian herbal formulations with their ingredients are given in Table: 2

<table>
<thead>
<tr>
<th>Brand name</th>
<th>Dosage form</th>
<th>Manufacturer</th>
<th>Ingredient mechanism</th>
<th>Ingredient</th>
<th>remedy</th>
<th>resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>BGR-34</td>
<td>Tablet</td>
<td>Aimil Pharmaeutical</td>
<td></td>
<td>Berberis aristata, Pterocarpus marsupium, Gymnemasyl vestre, Rubia cordifolia, Trigonella foenum graecum, Tinospora cordifolia</td>
<td>DPP 4 inhibitor</td>
<td></td>
</tr>
<tr>
<td>Diabecon</td>
<td>Tablet</td>
<td>Himalayan</td>
<td>Gymnemasyl vestre, pterocarpus marsupium, glycyrrhiza glabra, syczygium cumini, Boerhaviadiffusa, Phyllanthes amara, Tinospora cordifolia, piper nigrum, Ocimum sanctum, triphala, Curcuma longa, Shilajeet</td>
<td>Insulin secretagogues, alpha glucosidase inhibitors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diacare</td>
<td>Powder</td>
<td>Admark herbals limited</td>
<td></td>
<td>Sanjeevaanmol, himej, jambubeej, kadu, namejav, Neem chal</td>
<td>Reduce insulin resistance</td>
<td></td>
</tr>
<tr>
<td>Gurmar</td>
<td>Powder</td>
<td>Garry and sun natural remedy</td>
<td></td>
<td>Gymnemasyl vestre</td>
<td>Maintain blood glucose</td>
<td></td>
</tr>
<tr>
<td>Diabeta</td>
<td>Tablet</td>
<td>Ayurvedic cureayurvedic health products</td>
<td></td>
<td>Gymnemasyl vestre, vinca rosea, Carcuma longa, Azadirachta indica, Tinospora cordifolia, Zingiber officinallis</td>
<td>Release of insulin</td>
<td></td>
</tr>
<tr>
<td>Pancreatic tonic</td>
<td>Liquid</td>
<td>Dr. Morse cellular botanical</td>
<td></td>
<td>Tinospora cordifolia, Syczygium cumini, Melia azadirachta, Momordica charantia, Gymnemasyl vestre, Aegle marmelos,</td>
<td>Regeneratin g pancreatic β-cells</td>
<td></td>
</tr>
<tr>
<td>Sharangdyab tea</td>
<td>Powder</td>
<td>Plants med laboratoriey pvt.ltd</td>
<td></td>
<td>Green coffee beans, cinnamon, Boerhaviadiffusa</td>
<td>Stimulate insulin production</td>
<td></td>
</tr>
<tr>
<td>Spenai</td>
<td>Powder</td>
<td>Shriji herbal products</td>
<td></td>
<td>Karela, jamun, chirayata, methi, kaljiira, indrayav, kutki</td>
<td>Antidiabetic</td>
<td></td>
</tr>
<tr>
<td>Shilajeet</td>
<td>Capsule</td>
<td>Ayurveda rasashala Pune</td>
<td></td>
<td>Shudhashilajeeet</td>
<td>Stimulate insulin secretion</td>
<td></td>
</tr>
<tr>
<td>Triphala guggul</td>
<td>Tablet</td>
<td>Ayurveda rasashala Pune</td>
<td></td>
<td>Triphala guggul</td>
<td>Lower triglyceride level</td>
<td></td>
</tr>
</tbody>
</table>

Table:2 Different herbal antidiabetic formulation uses for treatment of diabetes mellitus

Conclusion: Diabetes mellitus is a most common endocrine-metabolic disorder which is affecting millions of people worldwide. It consists of a group of metabolic disorder characterized by

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hyperglycaemia resulting from defect in insulin secretion and action or both. Allopathic drugs available in market generally possess many side effects and also responsible for unwanted hypoglycaemic effect which drawing attention of researcher towards traditional herbal drugs which is available easily and responsible for larger bioactivity. It also does not require lab for synthesis. This article will help researcher to get information to developed herbal based formulations.

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