

## Role of Nutraceuticals in Prevention and Treatment of Diabetes

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**Abstract :** Traditional Indian diets are functional and used both as food and medicine. Although in recent scientific studies these diets are evaluated for rich source of dietary fiber (whole grains and vegetables), antioxidants and other active principles suitable for diabetes. In recent years a wide range of herbal dietary supplements and herbal medicines have scientifically proven to benefit type 2 diabetes mellitus. Primarily, they have been selected and used based on fundamental principles of Ayurveda, such as their Rasa, Guna, Virya, Vipaka, Prabhava, and so on. Reviewing the characteristic properties along with important antidiabetic properties of conventional system of medicine, accentuates the role of these diets in Diabetes. However, as it is difficult to maintain a healthy lifestyle, especially if the individual has a sedentary job, nutraceuticals have recently been marketed to help patients. Nutraceuticals include food or part of food that provides medical or health benefits including the prevention or treatment of a disease. A numerous studies have suggested the potential association of nutraceuticals with diet and health. Bioactive compounds with medicinal value isolated from food/edible materials are accepted as nutraceutical compounds. Other than food/edible materials, medicinal plants which are generally considered safe without toxicity are also considered nutraceuticals by many, but not by all. This article mainly focuses on role of nutraceuticals in prevention and treatment of diabetes.

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**KEYWORDS:** Nutraceuticals, diabetes mellitus; herbal formulations; Ayurveda, hyperglycemia

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Diabetes mellitus is a major and growing health problem in most countries and an important cause of prolonged ill health and early death. It represents a group of heterogeneous metabolic diseases characterized by persistent hyperglycemia and various acute and chronic complications.<sup>1</sup> Diabetes mellitus is syndrome, initially characterized by a loss of glucose homeostasis resulting from defects in insulin secretion, insulin action both resulting impaired metabolism of glucose and other energy yielding fuels such as lipids and protein<sup>2</sup>. As the disease progresses tissue or vascular damage ensues leading to severe diabetic complications such as retinopathy, neuropathy, nephropathy, cardiovascular complications and ulceration.<sup>3</sup> Thus, diabetes covers a wide range of heterogeneous diseases. The characteristic symptoms of diabetes are polyuria (excessive urine production), polydipsia (thirst and increased fluid intake) and blurred vision; these symptoms may be absent; if the blood sugar is only mildly elevated.<sup>4</sup> According to World Health Organization

(WHO) there are three forms of diabetes mellitus: Type 1, Type 2 and gestational diabetes, for which causes are same but have same signs, symptoms and consequences. Ultimately, all forms are due to the beta cells of the pancreas being unable to produce sufficient insulin to prevent hyperglycemia.<sup>5-7</sup> As per WHO, 171 million persons were suffering from diabetes worldwide in 2006, it is estimated that, this number will be doubled till 2030. Diabetes mellitus occurs throughout the world, but most cases are found in the more developed countries. The greatest increase in prevalence is, however, expected to occur in Asia and Africa, where most patients will likely be found by 2030. The increased incidence of diabetes in developing countries follows the trend of urbanisation and lifestyle changes, perhaps most importantly a 'Western-style' diet.<sup>8</sup>

Although many effective allopathic drugs have been developed for treatment of diabetes but recently, the focus of scientific world has shifted to identify herbal effective agents that can be used along with existing drugs to treat this disease synergistically.<sup>9</sup> Nutraceuticals are food or food products that provide health and medical benefits, including the prevention and treatment of disease. A numerous studies have suggested the potential association of nutraceuticals with diet and health. Nutraceuticals is defined as food products, extracts or food derivatives such as vitamins, herbs, amino acids, minerals and enzymes that can potentially exhibit pharmaceutical benefit in addition to their nutritional value. Nutraceuticals are classified as nutrients, herbs and herbal products and dietary supplements. Nutraceuticals are significantly contributing in modulation of the complex mechanisms of disease pathology with a view being that they may be essential in optimizing *in vivo* defences and help in maintaining wellness. The researchers say that nutraceuticals can certainly be used for their natural health-promoting benefits, such as reducing the **occurrence of high blood sugar levels**. However, a healthy diet and lifestyle are the most important things that can reduce the risk of diabetes.<sup>10</sup>

### **The Ayurvedic approach to Diabetes**

Ayurveda, the ancient healing of India recommends a combination of lifestyle management (which includes diet, exercise and medication), and treatment with specific herbs and minerals to cure various diseases. Ayurvedic physicians have treated diabetes for thousands of year using a combination of regulated lifestyle and herbal formulations.<sup>11</sup> According to principles of Ayurveda,

the persons who take the diet and do the activities, which are beneficial to all Dhatus, will never suffer from Diabetes (Prameha). It can be presumed that, Diabetes is mainly caused by heavy food, which increases Kapha, Medas, and others. But also emphasized that, excessive starvation or intake of dry substances will also cause another variety of Prameha (Diabetes). Thus it recommends wholesome diet suitable to all Dhatus (tissues of the body).<sup>12</sup>

### **Medicinal Herbs**

Although several therapies are in use for treatment, there are certain limitations due to high cost and side effects such as development of hypoglycemia, weight gain, gastrointestinal disturbances, and liver toxicity. Medicinal plants are being looked up once again for the treatment of diabetes. Many conventional drugs have been derived from prototypic molecules in medicinal plants. Metformin exemplifies an efficacious oral glucose-lowering agent. Its development was based on the use of *Galega officinalis* to treat diabetes. *Galega officinalis* is rich in guanidine, the hypoglycemic component. Because guanidine is too toxic for clinical use, the alkyl biguanides synthalin A and synthalin B were introduced as oral anti-diabetic agents in Europe in the 1920s, but were discontinued after insulin became more widely available. However, experience with guanidine and biguanides prompted the development of metformin. To date, over 400 traditional plant treatments for diabetes have been reported, although only a small number of these have received scientific and medical evaluation to assess their efficacy. The hypoglycemic effect of some herbal extracts has been confirmed in human and animal models of type 2 diabetes. The World Health Organization Expert Committee on diabetes has recommended that traditional medicinal herbs be further investigated.<sup>13</sup>

### **Important medicinal plants having antidiabetic potential**

There are many herbal remedies suggested for diabetes and diabetic complications. Medicinal plants form the main ingredients of these formulations.

#### ***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 secretagogue 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.<sup>14</sup>

#### ***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.<sup>15</sup>

#### ***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.<sup>16,17</sup>

#### ***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.<sup>18</sup> This effect is thought to be due to increased hepatic metabolism, increased insulin release from pancreatic  $\beta$  cells and/or insulin sparing effect.<sup>19</sup>

#### ***Aloe vera* and *Aloe barbadensis***

Aloe, 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.<sup>20</sup>

#### ***Azadirachta indica*: (Neem)**

Hydroalcoholic extracts of this plant showed antihyperglycemic activity in streptozotocin treated rats and this effect is because of increase in glucose uptake and glycogen deposition in isolated rat hemidiaphragm.<sup>21</sup>

### ***Caesalpinia bonducella***

*Caesalpinia bonducella* is widely distributed throughout the coastal region of India and used ethnically by the tribal people of India for controlling blood sugar. Both the aqueous and ethanolic extracts showed potent hypoglycemic activity in chronic type II diabetic models. These extracts also increased glycogenesis thereby increasing liver glycogen content.<sup>22</sup>

### ***Capparis decidua***

This is found throughout India, especially in dry areas. Hypoglycemic effect was seen in alloxanized rats when the rats were fed with 30% extracts of *Capparis decidua* fruit powder for 3 weeks. This extract also reduced alloxan induced lipid peroxidation significantly in erythrocytes, kidney and heart. *Capparis deciduas* was also found to alter superoxide dismutase and catalase enzyme levels to reduce oxidative stress.<sup>23</sup> *Capparis deciduas* additionally showed hypolipidaemic activity.<sup>24</sup>

### ***Coccinia indica***

Dried extracts of *Coccinia indica* (500 mg/kg body weight) were administered to diabetic patients for 6 weeks. These extracts restored the activities of enzyme lipoprotein lipase (LPL) that was reduced and glucose-6- phosphatase and lactate dehydrogenase, which were raised in untreated diabetics.<sup>25</sup>

### ***Cucurbita Maxima (Pumpkin)***

In a recent report, the low molecular weight fraction in pumpkin juice at the dose of 300 mg/kg produced significant reductions in plasma glucose at the end of treatment. Pumpkin extract could also reduce or eliminate the need for insulin injections in Type 1 diabetics by increasing insulin production and regenerate damaged pancreatic cells.<sup>26</sup>

### ***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.<sup>27</sup>

### **Ginseng**

Both Panax ginseng and American ginseng have been used to manage diabetes. Panax ginseng has been found to remarkably reduce blood sugar levels in normal and hyperglycaemic mice. Two 8-week trials following patients with T2D found American ginseng significantly decreased fasting blood glucose, haemoglobin and post-prandial blood glucose levels.<sup>28</sup>

### **Gymnema Sylvestre (Gurmarbooti, Gurmar)**

*Gymnema sylvestre* is an herb widely used in Ayurveda. Few non-randomised controlled clinical trials confirmed improved glycaemic control in patient after receiving extract of *Gymnema* over those who received conventional treatment alone. Patients using insulin were able to decrease their insulin requirements.<sup>29</sup>

### **Lagerstroemia Speciosa (Banaba)**

The leaves of the Banaba plant contain corosolic acid, which exhibit anti-diabetic properties. Two placebo-controlled crossover trials demonstrated that Gluco Trim a product containing, corosolic acid 1% lowers blood glucose levels.<sup>30</sup>

### ***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.<sup>31</sup>

#### ***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 *Momordica charantia* showed significant hypoglycemic effect when administered subcutaneously to langurs and humans.<sup>32</sup>

#### ***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.<sup>33</sup> 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.<sup>34</sup>

#### ***Phyllanthus amarus*: (Bhuiawala)**

It is a herb of height up to 60 cm, from family Euphorbiaceae. It is commonly known as Bhuiamala. It is scattered throughout the hotter parts of India, mainly Deccan, Konkan and south Indian states. Traditionally it is used in diabetes therapeutics. Methanolic extract of *Phyllanthus amarus* was found to have potent antioxidant activity. This extract also reduced the blood sugar in alloxanized diabetic rats.<sup>35</sup>

#### ***Pterocarpus marsupium***

It is a deciduous moderate to large tree found in India mainly in hilly region. Pterostilbene, a constituent derived from wood of this plant caused hypoglycemia in dogs showed that the hypoglycemic activity of this extract is because of presence of tannates in the extract.<sup>36</sup> Flavonoid fraction from *Pterocarpus marsupium* has been shown to cause pancreatic  $\beta$  cell regranulation.<sup>37</sup>

#### ***Trigonella foenum graecum*: (Fenugreek)**

It is found all over India and the fenugreek seeds are usually used as one of the major constituents of Indian spices. 4-hydroxyisoleucine, a novel amino acid from fenugreek seeds increased glucose stimulated insulin release by isolated islet cells in both rats and humans.<sup>38</sup> Oral administration of 2 and 8 g/kg of plant extract produced dose dependent decrease in the blood glucose levels in both normal as well as diabetic rats.<sup>39</sup>

### ***Tinospora cordifolia*: (Guduchi)**

It is a large, glabrous, deciduous climbing shrub belonging to the family Menispermaceae. It is widely distributed throughout India and commonly known as Guduchi. Oral administration of the extract of *Tinospora cordifolia* roots for 6 weeks resulted in a significant reduction in blood and urine glucose and in lipids in serum and tissues in alloxan diabetic rats. The extract also prevented a decrease in body weight.<sup>40</sup>

### **Mineral Supplementation**

The treatment of diabetes requires nutritional supplementation, as these patients have a greatly increased need for many nutrients. Supplying the diabetic with additional key nutrients has been shown to improve blood sugar control as well as help prevent or ameliorate many major complications of diabetes.<sup>41</sup>

### ***Chromium:***

Chromium is an essential micronutrient for humans. Considerable experimental and epidemiological evidence now indicates that chromium levels are a major determinant of insulin sensitivity, as it functions as a cofactor in all insulin regulating activities.<sup>42</sup> Chromium facilitates insulin binding and subsequent uptake of glucose into the cell. Supplemental chromium has been shown to decrease fasting glucose levels, improve glucose tolerance, lower insulin levels, and decrease total cholesterol and triglycerides, while increasing HDL cholesterol in normal, elderly, and type 2 diabetic subjects. Without chromium, insulin's action is blocked and glucose levels are elevated.<sup>43</sup>

### ***Vanadium:***



Prior to the discovery of insulin in 1922, vanadium was used for the control of blood sugar. Studies have confirmed the effectiveness of vanadyl sulfate at a dose of 100 mg/day in improving insulin sensitivity.<sup>44</sup>

### ***Magnesium:***

A deficiency of magnesium is significantly more common in type 2 diabetics than in the general population. Magnesium deficiency has been associated with complications of diabetes, retinopathy in particular.<sup>45</sup>

### **Conclusion:**

Nowadays, nutraceuticals have received considerable interest due to its potential to improve health, delay the aging process, prevent chronic diseases, or support the structure or function of the body. In the present review effort has been devoted to provide their role in treatment and prevention of diabetes mellitus. Nutraceuticals is one of the promising approach for prevention and treatment of diabetes mellitus. In spite of availability of synthetic drugs for treatment of diabetes, extensive efforts are taken on finding a new approach for treatment and prevention of diabetes. Along with many herbal drugs dietary supplements viz. vitamins, minerals, amino acids, anti-oxidants and fatty acids, are considered as armature for new therapies for type 2 diabetes and insulin resistance. Use of nutraceuticals along with synthetic drugs can lead to development of new synergistic combinations for effective treatment and prevention of diabetes and could revolutionize the treatment of diabetes.

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