

Review

Blood glucose lowering potential of some herbal plants

Uttara Singh^{1*}, Anita Kochhar² and Sadhana Singh³

¹College of Home Science, Punjab Agricultural University, Ludhiana-141004, India.

²Punjab Agricultural University, Ludhiana-141004, India.

³College of Home Science, Narendra Deva University of Agriculture and Technology, Kumarganj, Faizabad, India.

Accepted 9 March, 2011

Diabetes mellitus is a metabolic disorder in the endocrine system. This dreadful disease is found in all parts of the world and is becoming a serious threat to mankind health. There are lots of chemical agents available to control and to treat diabetic patients, but nowadays several medicinal plants have been investigated for their beneficial use in diabetes. The effects of these plants may delay the development of diabetic complications and correct the metabolic abnormalities. Many phytoconstituents responsible for antidiabetic effects have been isolated from hypoglycaemic plants.

Key words: Diabetes mellitus, plants, herbal medicine, phytoconstituents.

INTRODUCTION

Diabetes is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces (WHO, 2009). Diabetes is fast becoming a leading cause of morbidity, mortality and disability across the world. Diabetes mellitus is a global metabolic epidemic affecting essential biochemical activities in almost every age group (Gupta et al., 2008).

According to International Diabetic Federation the estimated diabetes prevalence for 2010 has risen to 285 million, representing 6.4% of the world's adult population, with a prediction that by 2030 the number of people with diabetes will have risen to 438 million (IDF, 2010). India has been declared as the "Diabetic capital of world". Currently 40.9 million people in India suffering from diabetes (IDF, 2007) and by 2030 there would be 79.44 million diabetics in India alone (WHO, 2007). It is estimated that by the year 2030, diabetes is likely to be the seventh leading cause of death accounting 3.3% of total deaths in the world (WHO, 2008).

Far from being a disease of higher income nations, diabetes is very much a disease associated with poverty, with the major burden borne by the low- and middle-

income countries and disproportionately affecting the lower socio-economic groups, the disadvantage and the minorities in the richer countries. The largest age group currently affected by diabetes is between 40 to 59 years. By 2030 this "record" is expected to move to the 60 to 79 age groups with 196 million cases. Diabetes is one of the major causes of premature illness and death worldwide. Non-communicable diseases including diabetes account for 60% of all deaths worldwide (IDF, 2010).

High levels of physical activity, a healthy diet, did not smoke, and consumed alcohol in moderation had an 82% lower rate of diabetes (Mozaffarian et al., 2009). A positive correlation has been found between the concentration in the urine of bisphenol A, a constituent of some plastics, and the incidence of type 2 diabetes (Lang et al., 2008). Hypertension, elevated cholesterol, acromegaly elevate, Cushing's syndrome, thyrotoxicosis, chronic pancreatitis, cancer, drugs, aging (Jack et al., 2004) and high-fat diets found to increase the risk of type 2 diabetes (Lovejoy, 2002). A person with first-degree relatives with type 2 diabetes have a much higher risk of developing type 2 diabetes. Concordance among monozygotic twins is close to 100%, and about 25% of those with the disease have a family history of diabetes. Genes significantly associated with developing type 2 diabetes, include *TCF7L2*, *PPARG*, *FTO*, *KCNJ11*, *NOTCH2*, *WFS1*, *CDKAL1*, *IGF2BP2*, *SLC30A8*, *JAZF1*,

*Corresponding author. E-mail: usuttarasingh@gmail.com.

and *HHEX* (Lyssenko et al., 2008; McCarthy, 2010).

Bael (*Aegle marmelos* (L.) Correa (Family: Rutaceae)

Aegle marmelos family rutaceae is highly reputed medicinal tree commonly known as the bael. It is medium sized tree growing throughout the forest of India of altitude 1200 m. It is found all over India, from sub-Himalayan forest, Bengal, central and south India. The different parts of this plant contain number of coumarins, alkaloids, sterols and essential oils. Various parts of this plant such as leaves, fruit and seed possess hypoglycaemic, hypolipidemic and blood pressure lowering property (Vijay et al., 2006).

The peel of the fruit which is a very hard shell and green to brown in color depends on ripening stage. The appearance of yellow or orange edible pulp is like a boiled pumpkin, possesses a slightly sweet taste and a characteristic floral, terpene-like aroma, very fragrant and pleasantly flavored. Seeds are surrounded by slimy transparent mucilage (Suvimol and Pranee, 2008).

Bael (*A. marmelos*) is an important medicinal plant of India. Biochemical compounds of bael leaves, fruits and seeds have been used in several diseases like diabetes, cardiovascular and anti-inflammatory (Maity et al., 2009). The most important ingredients present in plants are alkaloids, terpenoids, steriods, phenols glycosides and tannins (Venkatesan et al., 2009). The bael leaf contain 15 compounds, including seven monoterpene hydrocarbons (90.7%), three oxygenated monoterpenes (2.9%), four sesquiterpene hydrocarbons (3.1%) and one phenolic compound (0.2%). Limonene (82.4%) was the main constituent (Kaur et al., 2006).

Aegeline 2 present in leaves of *A. marmelos* have antihyperglycemic activity as evidenced by lowering the blood glucose levels, decreased the plasma triglyceride, total cholesterol and free fatty acids accompanied with increase in HDL-C and HDL-C/TC ratio (Narender et al., 2007). Bael leaf enhances ability to utilize the external glucose load in the body by stimulation of glucose uptake similar to insulin. Bael extract significantly lowers blood urea, reduction in lipid peroxidation and cholesterol and increased levels of super dioxide dismutase, catalase, glutathione peroxidase and glutathione level in serum as well as in liver in experimental diabetic animals (Sharma et al., 2007). *A. marmelos* fruit extract have protective effect on pancreatic beta (β) cells that leads to increased insulin level associated with a significant decrease in blood glucose in STZ induced diabetic rats (Kamalakkannan and Prince, 2005).

Antihyperglycemic activity of aqueous leaf extract in alloxanized rats (Ponnachan et al., 1993). Antihyperglycemic activity of aqueous leaf extract in streptozotocin induced diabetic rats (Das et al., 1996; Seema et al., 1996). Hypoglycemic and antioxidant activity of leaves in diabetic male albino rats (Upadhyaya

et al., 2004). Antihyperglycemic and antioxidant activity of the plant in alloxanized rats (Sabu and Kuttan, 2004).

Neem (*Azadirachta indica* A.) Juss. (Family: Meliaceae)

A. indica A. Juss., commonly referred as the neem tree, is a broad-leaved evergreen tree with a height of 20 to 30 m and a trunk girth of 2.5 m, found throughout India and is widely recognized as potent insecticide.

Hypoglycemic activity of hydro alcoholic *A. indica* extract in normal rats and hypoglycemic activity in glucose fed and streptozotocin induced diabetic rats (Chattopadhyay et al., 1987a; Chattopadhyay, 1996). Hypoglycemic and antihyperglycemic activities of leaf extract in normal and streptozotocin-induced diabetic rat (Chattopadhyay, 1999; Gholap and Kar, 2004). Hypoglycemic activity of crude ethanolic extract of the plant in alloxan diabetic albino rats (Kar et al., 2003). The plant exerts its pharmacological activity independent of its time of administration that is either prior or after alloxan administration (Khosla et al., 2000). *A. indica*'s possible mechanism is to inhibits action of epinephrine on glucose metabolism, resulting in increased utilization of peripheral glucose (Chattopadhyay et al., 1987b; Chattopadhyay, 1996) and exhibits hypoglycaemic activity without altering the serum cortisol concentration (Chattopadhyay, 1999; Gholap and Kar, 2004).

Brown mustard (*Brassica juncea* (L.) Czern. (Family: Brassicaceae)

This is a small herb cultivated throughout India and used as a spice in food and has been reported to exert significant hypoglycemic activity. Hypoglycemic activity of *B. juncea* diet (10%, w/w) in normal rats upon oral administration for 60 days reduce glucose level due to increases the concentration of hepatic glycogen and glycogenesis and suppressed the activity of glycogen phosphorylase and gluconeogenic enzymes, lead to reduction in glycogenolysis and gluconeogenesis (Khan et al., 1995).

***Mangifera indica* L. (Family: Anacardiaceae)**

Hypoglycemic activity of aqueous leaf extract (1 g/kg p.o.), given along as well as 60 min before glucose administration in streptozotocin-induced diabetic rats (Aderibigbe et al., 1999). Hypoglycemic activity of Mangiferin (10 and 20 mg/kg, i.p. once daily for 28 days) in STZ induced diabetic rats and improvement in oral glucose tolerance in glucose-loaded normal rats upon chronic administration (10 and 20 mg/kg, i.p.) for 14 days,

through intestinal reduction of the absorption of glucose as well as pancreatic and extra pancreatic mechanisms (Murugananda et al., 2005).

Jamun (*Eugenia jambolana* Lam.) (Family: Myrtaceae)

Hypoglycemic activity of ethanolic whole seeds, kernel (100 mg/kg of body weight) and seed coat extracts in streptozotocin-induced diabetic rats and exhibits normoglycemia and better glucose tolerance.

Gudhal (*Hibiscus rosa sinensis* L.) (Family: Malvaceae)

Alcoholic leaf extract of *H. rosa sinensis* (250 mg/kg p.o. for seven consecutive days) in glucose induced hyperglycemia model in rats and single dose of ethanol extract of the plant in glucose-loaded rats at 120 min and blood glucose lowering effect after repeated administration for seven consecutive days at 30, 90 and 120 min after glucose loading (Sachdewa et al., 2001b). It stimulates insulin secretion from pancreatic beta cells and increases utilization of glucose, either by direct stimulation of glucose uptake or through the mediation of enhanced insulin secretion (Sachdewa and Khemani, 1999).

Karela (*Momordica charantia*)

It is a very common folklore remedy for diabetes. Extract of fruit pulp, seed, leaves and whole plant of *M. charantia* has shown hypoglycemic effect in various animal models (Ali et al., 1993). Karunanayake et al. (1984), *M. charantia* showed hypoglycemic as well as antihyperglycemic activity in laboratory animals. Polypeptide, isolated from fruit, seeds, and tissue of *M. charantia* showed potent hypoglycemic effect when administered subcutaneously to gerbils, langurs, and humans (Khanna et al., 1981). Aqueous extracts of *M. charantia* improved OGTT after 8 h in normal mice and reduced hyperglycemia by 50% after 5 h in STZ diabetic mice. In addition, chronic oral administration of extract to normal mice for 13 days improved OGTT while no significant effect was seen on plasma insulin levels (Bailey et al., 1985). Ethanolic extract of *M. charantia* (250 mg/kg dose PO) significantly lowered blood sugar in fasted as well as glucose loaded non-diabetic rats (Chandrasekar et al., 1989). Oral administration of acetone extract of fruit powder of *M. charantia* for 15/30 days to alloxan-diabetic rats lowered the blood sugar and serum cholesterol levels to normal range and the blood sugar was found normal even after 15 days of discontinuation of the treatment (Singh et al., 1989). Shibib et al. (1993) showed that ethanolic extract of

M. charantia (200 mg/kg) showed an anti-hyperglycemic as well as hypoglycemic effect in normal and STZ diabetic rats as evident by 23% (PB/0.01) and 27% (PB/0.001) decrease in blood sugar, respectively. This occurred possibly due to inhibition of glucose-6-phosphatase and fructose-1,6-bisphosphatase in the liver and stimulation of red-cell and hepatic glucose-6-phosphate dehydrogenase activities. When fed orally, aqueous extract of *M. charantia* but not ethanolic extract showed anti-hyperglycemic and hypoglycemic effect in cyproheptadine-induced hyperglycemic and normoglycemic mice, respectively, (Cakici et al., 1994). The pulp juice and saponin free methanolic extract of pulp juice exerted significant hypoglycemic effect in fasting and postprandial states of normal and NIDDM rats but not in IDDM rats. Effect was more pronounced in case of saponin free methanol extract. Charantin, a peptide resembling insulin isolated from *M. charantia* lowered fasting blood sugar in rabbits gradually beginning from 1st and lasting till the 4th hour and slowly recovering to the initial level. Charantin (50 mg/kg) administered orally, lowered blood glucose by 42% at the 4th hour with a mean fall of 28% during 5 h (Lolitkar and Rao, 1966).

Homogenized suspension of the vegetable pulp of *M. charantia* to 100 cases of moderate NIDDM subjects caused a significant reduction (PB/0.001) of postprandial serum glucose in 86% cases and fasting glucose in 5% cases (Ahmad et al., 1999). Aqueous juice of *M. charantia* fruit exerted anti-hyperglycemic and antioxidant effect in pancreas of STZ-diabetic mice (Sitasawad et al., 2000). Oral supplementation (0.5, 1 and 3%) with freeze-dried powder of *M. charantia* for 14 days with and without 0.5% cholesterol and 0.15% bile acid in the diet resulted in a consistent decrease in serum glucose levels in normal rats only in the former group.

Experiments in rats showed that two important constituents of *M. charantia* that is oleanolic acid 3-O-glucuronide and momordin Ic exert anti-hyperglycemic effect by inhibiting glucose transport at the brush border of the small intestine (Matsuda et al., 1998). The fruit juice significantly increased the number of beta cells (PB/0.004) in diabetic rats (Ahmed et al., 1998). Oral administration of different *M. charantia* extracts showed a varying pattern of anti-hyperglycemic effect without altering the insulin response suggesting a mechanism of action which is independent of intestinal glucose absorption and probably involves an extrapancreatic effect (Day et al., 1984). Oral feeding of *M. charantia* juice to normal rats prior to glucose loading increased hepatic and muscle glycogen content while triglyceride content was not effected. Aqueous extract of unripe fruits of *M. charantia* has also been shown to partially stimulate insulin release from isolated beta-cell of obese-hyperglycemic mice which differed from D-glucose and other insulin secretagogues agent in the manner that not being suppressed by L-epinephrine and in even being potentiated by the removal of Ca₂ suggesting that the

insulin-releasing action is the result of perturbations of membrane functions (Welihinda et al., 1982).

Daily administration of extract of *M. charantia* fruit (4 gm/kg) for 2 months to alloxanized diabetic rats (120 mg/kg) delayed development of cataract. Respective blood sugar level in the two groups was 3079/81 and 66.37 mg% (Srivastava et al., 1988). In a clinical trial, water-soluble extract of the fruits of *M. charantia* significantly reduced blood glucose concentrations in the 9 NIDDM diabetics on OGTT (50 g).

CONCLUSION

Diabetes is a disorder of carbohydrate, fat and protein metabolism attributed to diminished production of insulin or mounting resistance to its action. Herbal treatments for diabetes have been used in patients with insulin-dependent and non-insulin-dependant diabetes, diabetic retinopathy, diabetic peripheral neuropathy, etc. Several Indian plant species has proved the efficacy of the botanicals in reducing the sugar level. So all these plant materials help to control diabetes.

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