AN OVERVIEW OF INDIAN NOVEL TRADITIONAL MEDICINAL PLANTS WITH ANTI-DIABETIC POTENTIALS

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Abstract

Diabetes mellitus is a global metabolic epidemic affecting essential biochemical activities in almost every age group. Indian literatures like Ayurveda have already mentioned herbal remediation for a number of human ailments. Among Indian traditional medicinal plants several potential anti-diabetic plants and herbs are being used as part of our diet since prehistoric time. India has a long list of native medicinal plants with confirmed blood sugar lowering property. Some of these have proved remarkable for cure of diabetes and its complications. The current paper is aimed at providing a review on clinical and experimental studies carried out on the most effective and commonly used hypoglycemic plants and herbs species from traditional Indian flora. This write-up includes hypoglycemic and anti-hyperglycemic activities of plants, active hypoglycemic compounds and constituents along with their available toxicity status.

Key words: Ayurveda, Anti-diabetic, Hypoglycemia, India, Traditional herbs.

Introduction

Diabetes mellitus is the most severe metabolic pandemic of the 21st century, affecting essential biochemical activities in almost every cell in the body and increasing the risk of cardiac problems. It is estimated that in the year 2000, 171 million people had diabetes, and this is expected to double by year 2030 (Boon et al., 2006). Conventionally, insulin-dependant diabetes mellitus is treated with exogenous insulin (Felig et al., 1995) and non insulin-dependant diabetes mellitus with synthetic oral hypoglycemic agents like sulphonylureas and biguanides (Rosac et al., 2002). However the hormone fails as a curative agent for complications of diabetes (Mukherjee et al., 1966) and synthetic oral drugs produce adverse health effects (Raheja, 1977). Different medicinal systems are using the active plant constituents, which discovered as natural hypoglycemic medicine, came from the virtue of traditional knowledge. Herbal drugs are considered free from side effects than synthetic one. They are less toxic, relatively cheap and popular (Momin, 1987). In India, medicinal plants have been used as natural medicine since the days of Vedic glory. Many of these medicinal plants and herbs are part of our diet as spices, vegetables and fruits. Historically, in ‘Atharva-Veda’ (about 200 B.C.) description of medicinal plants was made under a separate chapter ‘Ayurveda’. Sushruta (about 400 B.C.) compiled classification of 700 herbal drugs under 37 classes in ‘Sushruta Samhita’ (A compendium of ancient Indian surgery). Charak (about 600 B.C.) made the scientific classification of herbal drugs based on remedial properties in his renowned treatise ‘Charaka Samhita’ (A compendium of general medicine). In which he described 50 classes of herbal remedies comprising 500 crude drugs (Mukherjee, 1983; Saxena et al., 2006). The medicinal values of plants have been tested by trial and error method for a long time by

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different workers. Even today great opportunities are still open for scientific investigations of herbal medicines for
cure of diabetes and its complications.

Trials for Anti-diabetic Potentials of Medicinal Plants

Recently the plants and herbs are being used as decoctions or in other extracted forms for their blood sugar
lowering potential. There are some useful reviews on Indian medicinal plants having blood sugar lowering potentials
(Mukherjee et al., 1981; Grover et al., 2002; Saxena et al., 2004; Mukherjee et al., 2006). Many useful herbs
introduced in pharmacological and clinical trials have confirmed their blood sugar lowering effect, repair of β-cells
of islets of Langerhans. Details of some potent Indian herbs, their recently reported pharmacological and clinical
hypoglycemic efficacy, active chemical constituents, their mechanism of action and available toxicity status are
described chronologically as follows:

**Aegle marmelos** Linn. Coorea (Family: Rutaceae)
Hindi name: Bel; Common name: Holy Fruit Tree

The trees grow throughout deciduous forest of India and ripen fruits are commonly used for delicacy. *Aegle marmelos*
is widely used in Indian Ayurvedic medicine for the treatment of diabetes mellitus (Kamalakkanan et al., 2003). Hypoglycemic effect of root bark decoction (1ml/100mg) has been observed in normal fasted rats
(Karunanayake et al., 1984). Leaf extract produced anti-hyperglycemic activity in alloxan diabetic rats along with
decreased cholesterol and blood urea (Ponnachan et al., 1993). In diabetic rats leaf extract exhibited insulin like
activity (Paulose et al., 1993). Aqueous leaf extract has been shown to improve the functional state of pancreatic
cells in streptozotocin induced diabetic rats (Das et al., 1996). Aqueous leaf extract (250 & 500mg/kg, orally)
produced hypoglycemic effect and increased plasma insulin level of STZ-diabetic rats. LD₅₀ (lethal dose) observed
greater than 10.0g/kg at oral administration to rats (Sharma et al., 1996). Anti-hyperglycemic activity caused by leaf
extract (250mg/kg, orally) in glucose fed hyperglycemic rats (Sachdewa et al., 2001). Aqueous fruit extract
(250mg/kg, twice daily for one month) produces anti-hyperglycemic effect along with decreasing glycosylated
haemoglobin level in STZ induced diabetic albino wistar rats (Kamalakkanan et al., 2003). Hypoglycemic and
antioxidant activity of leaves have been observed in diabetic male albino rats (Upadhyaya et al., 2004). Fruit extract
(125 and 250mg/kg, orally twice daily for 30 days) produced anti-diabetic, anti-hyperlipidaemic and antioxidant
activity in STZ diabetic rats along with partial repair of damaged pancreatic islets (Kamalakkanan et al., 2005).
Treatment of severely (fasting blood glucose level >250 mg/ml) diabetic rats for 14 days with aqueous extract
(250mg/kg, orally) of *Aegle marmelos* seeds reduced the fasting blood glucose by 60.84% and urine sugar by 75%
than their pretreatment levels (Kesari et al., 2006).

**Allium cepa** Linn. (Family: Liliaceae)
Hindi name: Pyaj; Common name: Onion

The plant is cultivated throughout India. Onion bulb and leaves are the important part of diet. Ether soluble
fraction of onion (0.25mg/kg, orally) has been observed to lower blood sugar level in normal rabbits and exhibited
potent antioxidant activity (Auguati, 1973). In a clinical study treatment of diabetic patients by juice of *Allium cepa*
bulp, controlled the blood sugar level (Mathew et al., 1975). Dipropyl disulphide oxide [Fig.1.1] and onion oil
produced significant hypoglycemic effect (Augusti, 1976). Significant blood sugar lowering produced by petroleum
ether extract (2g/kg) from onion bulb in glucose, induced hyper-glycemic rabbits (Gupta et al., 1977). A sulphur
containing amino acid, S-methyl cystein sulphoxide [Fig.1.2] (at a dose of 200mg/kg for 45 days) from onion
showed potent hypoglycemic activity in alloxan induced diabetic rats (Kumari et al., 1995). S-allyl cystein
sulphoxide [Fig.1.3] from onion significantly reduced blood glucose level of alloxan induced diabetic rats (Sheela
et al., 1995). Prolonged administration of freeze dried onion powder (3%) with a diet produced anti-hyperglycemic,
hypolipidemic and antioxidant activity in STZ-diabetic rats (Babu et al., 1997). Onion callus cultures showed
greater hypoglycemic potential over natural onion bulb (Kelkar et al., 2001). Prolonged administration of a diet
containing onion produced hypoglycemic and antioxidant effect in diabetic rats (Campos et al., 2003). *Allium cepa*
juice (0.4g/100g b.w. for 4 weeks) exhibited anti-hyperglycemic and antioxidant effect in alloxan induced diabetic
rats, it also repaired hepatic and renal damage caused by alloxan (El-Demerdash et al., 2005).

**Allium sativum** Linn. (Family: Liliaceae)
Hindi name: Lahsun; Common name: Garlic

The plant is cultivated all over India. It is an important part of dietary ingredients. Allicin [Fig.1.4]
(0.25mg/kg, orally) from garlic exhibited pronounce hypoglycemia in mild diabetic rabbits (Mathew et al., 1973). In
alloxan induced diabetic rabbits ethanol, ethyl acetate and petroleum ether extract (0.25mg/kg, orally) produced anti-hyperglycemic activity (Jain et al., 1975). Treatment of alloxan diabetic rats with the antioxidant s-allyl cysteine sulfoxide isolated from garlic ameliorates the diabetic condition almost to the same extent as did glibenclamide and insulin. It also significantly stimulates in vitro insulin secretion from β-cells isolated from pancreas of normal rats (Augusti et al., 1996). Extract (500mg/kg/day) of Allium sativum bulb proved to be effective for treatment of l-thyroxine (l-T4) induced hyperglycemia in rats (Thailiani et al., 2003). Alloxan induced diabetic rats fed a diet containing Allium sativum (12.5%) for 15 days were able to reduce blood glucose as compare to control group (Jelodar et al., 2005). Oral administration of a laboratory diet containing 0.05% of ajone (derived from garlic) for 8 weeks has been observed to produce anti-diabetic effect in genetically diabetic KK-A(y) mice. The levels of plasma glucose significantly suppressed about 73.8% (Hattori et al., 2005). Two garlic compounds garlic oil (100mg/kg body weight) and diallyl trisulfide [Fig.1.5] (40mg/kg body weight) given every other day for 3 weeks to STZ-diabetic rats significantly raised the basal insulin concentration and increased the insulin sensitivity (Liu et al., 2005). Herbal extract of garlic (20mg 100 g . body weight, orally, daily for 5 weeks) produced hypoglycemia, probably by interfering with food intake of both normal and STZ-diabetic rats (Musabayane et al., 2006). S-allyl cysteine, a key component of aged garlic, found potent antioxidant and inhibited AGEP (accumulation of advanced glycation end products) formation (Ahmad et al., 2006). Bis (allixinato) oxovanadium (IV) [Fig.1.6] from garlic found to be the most potent anti-diabetic agent in type 1 diabetic mice on both intraperitoneal injections and oral administrations (Adachi et al., 2006).

Aloe vera (Linn.) Burm. f. (Family: Liliaceae)
Hindi and Common name: Aloe

The herbs are cultivated throughout India for its variety of medicinal properties. Dry sap of plant produced prominent anti-hyperglycemic response in type 2 diabetic patients (½ teaspoonful, orally for 4-14 weeks), and in alloxan induced diabetic Swiss albino mice (500mg/kg, twice daily for 5 days) (Ghannam et al., 1986). In a clinical study, it was reported that oral administration of aloe might be a useful adjuvant for lowering of blood glucose in diabetic patients (Vogler et al., 1999). Aloe vera leaf pulp extract showed hypoglycemic activity on type 1 and type 2 diabetic rats, the effect being enhanced in type 2 diabetes as compared with glibenclamide (Okyar et al., 2001). Plant extract (200 and 300mg/kg, orally) produced hypoglycemic activity along with controlled carbohydrate metabolizing enzymes in normal fasted, oral glucose fed and STZ-diabetic rats (Rajsekaran et al., 2004). Oral administration of ethanolic extract (300mg/kg b.w.) to STZ-diabetic rats for 21 days resulted in a prominent reduction of fasting blood glucose along with improved plasma insulin level of diabetic rats (Rajsekaran et al., 2005). Administration of the five phytosterols from Aloe vera namely, lophenol [Fig.1.7], 24-methyl-lophenol [Fig.1.8], 24-ethyl-lophenol, cycloartanol and 24-methylene-cycloartanol [Fig.1.9] to severe type 2 diabetic mice for 28 days decreased the fasting blood glucose levels 64%, 28%, 47%, 51%, and 55% respectively (Tanaka et al., 2006). Oral administration of Aloe vera gel extract (300mg/kg b.w. per day for 21 days) to STZ-diabetic rats resulted in a significant reduction of fasting blood glucose and improved the plasma insulin level (Rajsekaran et al., 2006).

Andrographis paniculata (Burm. f.) Nees (Family: Acanthaceae)
Hindi name: Kalmegha; Common name: King of Bitter

This is an annual herb that grows throughout India. Plant extract effectively produced hypoglycemic and anti-hyperglycemic activity in normal rats (Borhanuddin et al., 1994). Different doses (0.1, 0.2, and 0.4g/kg b.w.) of plant extract effectively reduced the fasting serum glucose level of STZ-diabetic rats (Zhang et al., 2000a). Anti-hyperglycemic and antioxidant activity of plant extract (400mg/kg b.w, twice a day for 14 days), has also been reported in diabetic rats (Zhang et al., 2000b). The andrographolide [Fig.1.10] from plant increases the glucose utilization and lowers plasma glucose in diabetic rats lacking insulin (Yu et al., 2003). Significant reduction in blood glucose level (52.90%) observed when hyperglycemic rats treated with 50mg/kg body weight aqueous extract of Andrographis paniculata. This effect enhanced when freeze-dried material used at a dose of 6.25 mg/kg body weight, it reduced 61.81% blood glucose level (Husen et al., 2004). The anti-diabetic potentials of plant restored the impairestrous cycle in alloxan-induced diabetic rats (Reyes et al., 2006).

Annona squamosa Linn. (Annonaceae)
Hindi name: Sharifa; Common name: Sugar apple tree

The plants grow throughout India and commonly use by tribal communities of Northern India for the treatment of diabetes. Aqueous leaf extract produces hypoglycemic activity in streptozotocin-nicotinamide induced diabetic rats (Shirwaikar et al., 2004). Ethanolic leaf-extract (350mg/kg b.w., orally 10-day) administration to STZ-
List of Abbreviations
1. 1-T4 = 1-thyroxine
2. ANEP = Accumulation of advanced glycation end products
3. b.w. = Body weight
4. ED50 = Effective dose
5. gm = Gram
6. kg = Kilogram
7. LD50 = Lethal dose
8. mg = Milligram
9. ml = Milliliter
10. SDF = Soluble dietary fibre
11. STZ = Streptozotocin

Figure legends
Figure 1: Active hypoglycemic constituents of plants
Figure 1.1: Dipropyl disulphide oxide.
Figure 1.2: S-methyl cysteine sulfoxide.
Figure 1.3: S-allyl cysteine sulfoxide.
Figure 1.4: Allicin.
Figure 1.5: Diallyl trisulphide.
Figure 1.6: Bis(allixinato) oxovanadium(IV).
Figure 1.7: Lophenol.
Figure 1.8: 24-methyl lophenol.
Figure 1.9: 24-methylene cycloartanol.
Figure 1.10: Andrographolide.
Figure 1.11: Beta-sitosterol.
Figure 1.12: Leucodelphinidine.
Figure 1.13: Gymnemic acid (IV).
Figure 1.14: Charantin.
Figure 1.15: Vicine.
Figure 1.16: (-)-Epicatechin.
Figure 1.17: Pterostilbene.
Figure 1.18: Swerchirin.
Figure 1.19: Trigonellin.
Figure 1.20: 4-hydroxyisoleucine: 5.

diabetic rats has been shown to lower fasting blood glucose level to (73.3%), and treatment of severely diabetic rabbits with leaf-extract (350mg/kg, for 15 days) reduced fasting blood glucose by 52.7% and urine sugar by 75% (Gupta et al., 2004). Annona squamosa fruit pulp extract (2.5 and 5.0g/kg b.w.) has been observed to improve the glucose tolerance of alloxan diabetic rats (Gupta et al., 2005). Further more, fruit pulp (5g/kg b.w.) brought down urine sugar, urine protein and glycol-hemoglobin in diabetic rabbits (Gupta et al., 2005). Oral administration of aqueous leaf-extract to diabetic rats for 30 days significantly reduced the levels of blood glucose and increased the activity of plasma insulin and antioxidant enzymes (Kaleem et al., 2006).

Azadirachta indica A. Juss. (Family: Meliaceae)
Hindi name: Neem; Common name: Indian lilac tree
This is an evergreen tree grows throughout India. Aqueous extract is known to produce antihyperglycemic and hypoglycemic activity in diabetic dogs (Satyanarayan et al., 1978). Fresh leaves decoction induced anti-hyperglycemic activity (Chattopadhyay et al., 1987a) and increased the peripheral glucose utilization in normal rats (Chattopadhyay et al., 1987b). Leaf extract of Azadirachta indica has been reported to produce the hypoglycemic activity in normal rats without altered serum cortisol level (Chattopadhyay et al., 1999). Crude ethanol extract (250mg/kg, for 2 weeks) potentially lowered the blood sugar level of alloxan diabetic rats (Kar et al., 2003). Leaf extract has been observed to produce anti-hyperglycemic activity in streptozotocin diabetic rats without altered serum cortisol level (Gholap et al., 2004). Petroleum ether extract of seed kernel (2gm/kg b.w.) & seed husk (0.9gm/kg b.w.) restricted oxidative stress in heart and erythrocytes caused by streptozotocin in diabetic rats (Gupta et al., 2004). Dianex, a polyherbal formulation consists of the aqueous extract of Azadirachta indica has been well tolerated in laboratory animals at higher doses (up to 10 g/kg in mice, acute toxicity; up to 2.5 g/kg in rats, sub-acute toxicity studies for 30 days) without any toxic manifestation (Mutalik et al., 2005). Beta-sitosterol [Fig.1.11], a steroid obtained from Azadirachta indica, may be responsible for its hypoglycemic property (Mukherjee et al., 2006). In a clinical study of type 2 diabetes powdered part, aqueous extract and alcoholic extract of Azadirachta indica at high dose for 14 days exhibited hypoglycemic activity (Waheed et al., 2006).

Cinnamomum tamala (Hamm.) Nees. & Eberm. (Family: Lauraceae)
Hindi name: Tejpat; Common name: Bayberry
The plant is cultivated in different parts of India and use as spice (Saxena et al., 2006). Aqueous leaf extract induced potential blood sugar lowering effect in 18 hours fasted and glucose induced hyperglycemic rabbits at a dose of 500mg/kg (Tripathi et al., 1979). Oral administration of powdered leaves (20gm for 15 days) exhibited hypoglycemic effect in patients of type 2 diabetes mellitus along with insulin released from pancreatic ß-cells (Udupa et al., 1980). In a clinical study, leave powder produced hypoglycemic response in type 2 diabetic patients (Chandola et al., 1980). Ethanolic extract (210mg/kg) of leaves induced potential hypoglycemic effect in 18 hours fasted albino rats (Tripathi et al., 1990). Alcoholic extract of leaves produced hypoglycemic activity in alloxan induced diabetic rats when administered orally for two weeks at a dose of 250mg/kg (Kar et al., 2003)

Coccinia grandis (Linn.) Voigt (Family: Cucurbitaceae)
Syn. Coccina indica (White & Arn); Hindi name: Kunderi; Common name: Ivy Guard
The plants are wild creepers grow in many parts of India (Saxena et al., 2006). Blood sugar lowering effect has been observed in patients treated with homogenized freeze dried leaves (Khan et al., 1990). Ethanol extract (250mg/kg) of whole plant produced hypoglycemic activity in fasted, glucose fed and diabetic albino rats (Mukherjee et al., 1988). Hypoglycemic effect of alcoholic extract (250mg/kg, orally) of Coccinia indica was observed in fasted and glucose fed hyperglycemic male albino rats (Chandrasekar et al., 1989). Alcoholic leaf extract produced hypoglycemic effect in normal fed and 48 hours fasted rats, response mediated by suppression of gluconeogenic enzyme glucose-6-phosphatase (Hossain et al., 1992). Pectin (200mg/100gm/day) isolated from fruits, exhibited blood sugar lowering effect and an increase in the glycogen content of liver in normal rats (Kumar et al., 1993). Ethanol (60%) leaf extract (200mg/kg, orally) lowered the blood sugar level of diabetic rats due to suppressed glucose synthesis, through depression of glucose-6-phosphatase, fructose-1-6-biphosphatase and enhanced glucose oxidation by shunt pathway through activation of glucose-6-phosphate dehydrogenase (Shibib et al., 1993). Leaf extract was produced hypoglycemic, and insulin secretogouge activity in diabetic patients (Platel et al., 1997). Dried extract (500mg/kg, p.o. for 6 weeks), of plant exhibited anti-hyperglycemic activity in diabetic patients. Extract mimic insulin like activity and improved the functional status of enzymes in glycolytic pathway and lypolytic pathway (Kamble et al., 1998). Potent antioxidant (Venkateswaran et al., 2003) and hypolipidemic activity (Pari et al., 2003) exhibited by ethanolic leaf extract administered at a dose of 200mg/kg for 45 days to streptozotocin induced diabetic rats.

**Gymnema sylvestre** (Willd) R. Br. (Family: Asclepiadaceae)

Hindi name: Gudmar; Common name: Periploca of the wood

Plants are grown in tropical regions of India and used as household remedy for diabetes (Kar et al., 2003). Oral administration of a water soluble fraction G-54 isolated from Gymnema sylvestre administered to 27 type 2 diabetic patients reduced their insulin requirement, lowered the fasting blood sugar and glycosylated haemoglobin content (Shanmugasundaram et al., 1990a). Two water soluble fractions (GS-3 and GS-4) obtained from leaves were found to double the pancreatic islets and β-cell numbers in diabetic rats (Shanmugasundaram et al., 1990b). Alcoholic leaf extract (500mg/kg, orally) lowered maximum blood sugar in fasted, glucose fed and diabetic rats along with insulin released from pancreatic β-cells (Chatopadhyay et al., 1993). In rats the insulin secretion from islets of Langerhans and several pancreatic β-cell lines induced by alcoholic extract in absence of other stimulus (Persaud et al., 1999). Gymnemic acid IV [Fig.1.13], isolated from leaves produced potent hypoglycemic effect in STZ-diabetic mice (Sugihara et al., 2000). Leaf extract has been observed to produce anti-hyperglycemic (Gholap et al., 2003) and hypoglycemic (Gholap et al., 2004) effects of in corticosteroid-induced diabetes mellitus, without altered serum cortisol concentration. A polyherbal formulation containing aqueous extracts of Gymnema sylvestre produced prominent hypoglycemic activity in normal and diabetic rats at a dose of 100-500mg/kg/day, orally for
acute, 6 hours and for long-term, 6 weeks studies (Mutalik et al., 2005). Gymnemic acid IV isolated from the leaves has been observed to produce hypoglycemic, anti-hyperglycemic, glucose uptake inhibitory and gut glycosidase inhibitory effects (Kimura, 2006).

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

Hindi name: Karela; Common name: Bitter gourd

The plant is an annual climber grown mostly in tropical India and commonly use as vegetable (Saxena et al., 2006). Charantin (50mg/kg, orally) isolated from *Momordica charantia* has been resembled insulin lower blood sugar level (maximum 42% at 4th hour) of rabbits (Lolitkar et al., 1966). In a clinical study of type 1 and type 2 diabetic patients the polypeptide-p isolated from fruit, seeds and tissue exhibited hypoglycemic activity without any side effect. The subcutaneous injection of (0.5unit/kg) lowered the blood sugar in gerbils and langurs (Khanna et al., 1981). Charantin [Fig.1.14] obtained from *Momordica charantia* induced hypoglycemic effect (Ng et al., 1986a) and also stimulated the insulin release and blocked the formation of glucose in blood stream (Ng et al., 1986b). Hypoglycemic effect and delayed cataract development was reported in alloxan diabetic rats treated with fruit extract (4g/kg/Day orally for 2 months) (Srivastava et al., 1988). Ethanolic extract (200mg/kg) of *Momordica charantia* was produced hypoglycemic activity in normal and streptozotocin diabetic rats; this was occurred possibly due to inhibiting glucose-6-phosphatase and fructose-1,6-biphosphatase in liver, and stimulating hepatic glucose-6-phosphate dehydrogenase activities (Shibib et al., 1993). Oleanolic acid and momordin from plant, produced anti-hyperglycemic effect by inhibiting glucose transport in intestine of rat (Matsuda et al., 1988). Fruit aqueous extract (200mg/kg, orally for 6 weeks), and exercise potential lowered blood sugar of type 2 diabetic and hyperinsulinemic (insulin resistance) rats (Miura et al., 2004). Seed aqueous extract produced prominent reduction in blood glucose, glycyslated hemoglobin, lactate dehydrogenase, glucose-6-phosphatase, fructose-1,6-biphosphatase and glycogen phosphorylase along with increased hemoglobin, glycogen content and hexokinase, glycogen synthase activity (Sekar et al., 1987). Anti-diabetic properties of plant such as charantin, vicine [Fig.1.15] and polypeptide-p have the potential to be a part of dietary supplement for patients of diabetes (Krawinkel et al., 2006). From *Momordica charantia* the major compounds, 5b,19-epoxy-3b,25dihydroxycucurbita-6,23(E)-diene(4) and 3b-7b,25dihydroxycucurbita-5,23(E)-dien-19-al(5) administered at a dose of 400mg/kg produced hypoglycemic effect in ddY mice strain (Harinantenaina et al., 2006).

**Ocimum sanctum** Linn. (Family: Lamiaceae)

Hindi name: Tulasi; Common name: Holy Basil

It is a tropical annual herb grown all over India and use for household remediation (Mukherjee et al., 2006). Oral administration of alcoholic extract of leaves of *Ocimum sanctum* lowered blood sugar level in normal; glucose fed hyperglycemic and STZ-diabetic rats, along with increased insulin release (Chattopadhyay, 1993). *Ocimum sanctum* leaf powder was produced potent hypoglycemic and hypolipidemic effect in normal and diabetic rats (Ravi et al., 1997). Alcoholic extract of leaves significantly lowered the blood glucose in normal and alloxan diabetic rats (Vats et al., 2002). Administration of plant extract 200mg/kg in STZ-diabetic rats for 30 days led to decreased in plasma glucose level by 26.4% (Vats et al., 2004). Plant extract lowered blood glucose level along with inhibited cortisol level (Gholap et al., 2004). From leaf extract the aqueous butanol and ethylacetate fractions stimulated insulin secretion from perfuse rat pancreas, isolated rat islets and a clonal rat β-cell line in a concentration-dependent manner (Hannan et al., 2006).

**Pterocarpus marsupium** Roxb. (Family: Fabaceae)

Hindi name: Vijayasar; Common name: Indian Malabar

Plants grow throughout India and are use as hypoglycemic plant in folklore medicine (Mukherjee et al., 1996). Aqueous bark extract lowered blood sugar and improved glucose tolerance of diabetics with no side effects observed (Pandey et al., 1975). From alcoholic extract of bark the ethyl acetate soluble fraction caused blood sugar lowering and repaired the alloxan induced pancreatic β-cells damage in albino rats (Chakroverty et al., 1980). From plant the (-)-epicatechin (30mg/kg, i.p.) produced anti-hyperglycemic effect in alloxan induced diabetic rats (Sheehan et al., 1983). The (-) epicatechin [Fig.1.16], from bark increased the cAMP content of the pancreatic islets associated with increased insulin release, conversion of proinsulin to insulin and cathepsin B activity in rats (Ahmad et al., 1991). Marsupin and pterostilbene [Fig.1.17], two phenolic constituents of plant potentially lowered blood glucose at same level as compared to metformin in STZ-diabetic rats (Manickam et al., 1997). Aqueous extract (1g/kg, orally) of bark has been observed to produce anti-cataract activity in alloxan diabetic rats (Vats et al., 2004). Plant extract was prevented the hyper-triglyceridaemia and hyper-insulinaemia (insulin resistance) in type 2 diabetic
patients (Grover et al., 2005). Aqueous extract (250mg/kg, orally) of dried wood has been reported to produce hypoglycemic effect in acute and sub-acute study (Mukhtar et al., 2005).

**Swertia chirayita** (Roxb. ex Flam) Karst. (Family: Gentianaceae)

Hindi name: Kirayat Chirata; Common name: Bitter Stick

The herbs grow abundantly in Himalayan regions of India and are used for treatment of various ailments by the tribes (Grover et al., 2002). 95% ethanol extract (250mg/kg) of plant potentially lowered the blood sugar level in fasted, glucose fed and tolbutamide pretreated animals (Sekar et al., 1987). Hexane fraction (250mg/kg, b.w. orally for 28 days) of plant, lowered blood sugar of albino rats with increased glycogen content of liver and insulin released from pancreatic β-cells (Chandrasekhar et al., 1990). Swerchirin (50mg/kg, orally) isolated from hexane fraction of plant exerted potent hypoglycemic activity in normal and STZ-diabetic albino rats (Saxena et al., 1991). An xanthone isolated from the hexane fraction of *Swertia chirayita* identified as swerchirin (1,8-dihydroxy-3,5-dimethoxyxanthone) [Fig.1.18] exhibited blood sugar lowering effect in fasted, fed, glucose fed hyperglycemic and tolbutamide pretreated albino rats. Effective dose (ED$_{50}$) of *Swertia chirayita* has been reported to be 23.1mg/kg/oral, lower maximum 40% blood sugar level of male albino rats of body weight 140-165g (Bajpai et al., 1991). Swerchirin (50mg/kg, b.w. orally) isolated from crude extract lowered maximum 60% blood glucose at 7 hour post-treatment, along with depleted aldehyde-fuchsin stained b-granules and immunostained insulin of islets of Langerhans (Saxena et al., 1993). Swerchirin isolated from plant was found to be superior blood sugar lowering agent over tolbutamide (Saxena et al., 1996). Alcoholic extract (250mg/kg, once daily for two weeks) exhibited hypoglycemic effect in alloxan induced diabetic rats (Kar et al., 2003).

**Syzygium cumini** Linn. (Family: Myrtaceae)

Syn. *Eugenia jambolana* (Linn.); Hindi name: Jamun; Common name: Black Berry

Plants grow in different parts of India. The ripe fruits are used as part of dietary component (Nadkarni,1976). Oral administration of fruit pulp induced hypoglycemic activity in normal and STZ-diabetic rats along with insulin released from β-cells (Achrekar et al., 1991). Seed powder provided good symptomatic relief to 30 patients of diabetes (type 2) and regulated blood sugar level (Kohli et al., 1993). Increased activity of hexokinase and decreased activity of glucose-6-phosphate in liver produced blood sugar lowering effect at oral administration of aqueous seed extract (2.5g/kg, b.w. for one month) to alloxan diabetic rats (Prince et al., 1997). Aqueous seed extract (2.5 & 5g/kg, b.w. for 6 weeks) has been observed to produce hypoglycemic and antioxidant activity, and increase in haemoglobin content in rats (Prince et al., 1998). Alcoholic seed extract injection (20mg, intraperitoneally) reduced the blood sugar level to 37.17% at 3 hour and 46.68% at 6 hour of administration in alloxan diabetic mice along with enhanced insulin secretion (Purohit et al., 2000). Decreased plasma glucose concentrations in STZ-induced diabetic mice was observed at oral administration of fruit extract (200mg/kg, for 50 days) (Grover et al., 2002). Blood sugar lowering, hypolipidemic activity, increased serum insulin, increased glycogen content of liver and muscles and a fall in glycosylated haemoglobin level produced by ethanolic extract (100mg/kg b.w. orally) of seed (Sharma et al., 2003). Ethanolic seed kernels extract (100gm/kg b.w.) has been observed to improve glucose tolerance (Ravi et al., 2004), and produce hypoglycemic and hypolipidemic effect (Ravi et al., 2003) in STZ-diabetic rats. *Syzygium cumini* was produced prominent fall of blood sugar in mice (Villansenor et al., 2006). Aqueous and ethanolic extracts of the fruit-pulp has been reported to produce anti-hyperglycemic effect in alloxan diabetic rats, and 24.4% raise in plasma insulin level in mild diabetic and 26.3% in severely diabetic rabbits (Sharma et al., 2006).

**Trigonella foenum-graecum** Linn. (Family: Fabaceae)

Hindi name: Methi; Common name: Fenugreek

Plants are commonly cultivated throughout India. The leaves are used as vegetable and seeds as spice (Nadkarni,1976). Major alkaloid trigonellin [Fig.1.19] from fenugreek seeds produced hypoglycemic activity (Shani et al., 1998). Ethanol extract (0.8g/kg, i.p.) of leaves has been observed to reduce blood glucose concentration in alloxan induced diabetic rats. Lethal doses (LD$_{50}$) of aqueous leaf extract were 1.9g/kg at intra-peritoneal and 10g/kg at oral administration (Abdel Barry et al., 1997). 4-Hydroxyisoleucine, an insulinotropic compound isolated from seeds increased the insulin release in glucose fed hyperglycemic rats and humans (Sauvaire et al., 1998). Seeds powder treatment normalized the enhanced lipid peroxidation and reduced the susceptibility to oxidative stress associated with depletion of antioxidants in liver of rats (Anuradha et al., 2001). Maximum 46.64% decrease in blood sugar level of diabetic rats was observed at oral administration of seed extract (1g/kg, for one month) (Vats et al., 2003). From fenugreek seeds, the soluble dietary fibre (SDF) fraction at (0.5g/kg, orally administered twice daily, for 28 days) inhibited platelets aggregation in type 2 diabetic rats and produced beneficial effect in
dyslipidemia (Hannan et al., 2003). Restored activity of glutamate dehydrogenase, NAD linked isocitrate dehydrogenase and D-b-hydroxybutyrate dehydrogenase reported at oral administration of seed powder (5%, for 3 weeks) in alloxan diabetic rats. It also repaired the liver and kidney damage caused by alloxan (Thakran et al., 2004). 4-hydroxyisoleucine:5 [Fig.1.20], an amino acid, isolated from seeds, produced anti-hyperglycemic effect and decreased the 33% plasma triglyceride, 22% total cholesterol (22%) and 14% free fatty acids (Narender et al., 2006).

**Active hypoglycemic constituents from plants**

Many active compounds have been isolated from the plant and herb species of India. These active principles are dietary fibres, alkaloids, flavonoids, saponins, amino acids, steroids, peptides and others. These have produced potent hypoglycemic, anti-hyperglycemic and glucose suppressive activities (Saxena et al., 2006). The above effects achieved by either insulin release from pancreatic β-cells, inhibited glucose absorption in gut, stimulated glycogenesis in liver or increased glucose utilization by the body (Grover et al., 2002; Saxena et al., 2004). These compounds also exhibited their antioxidant, hypolipidemic, anticataract activities, restored enzymatic functions, repair and regeneration of pancreatic islets and the alleviation of liver and renal damage (Mukherjee et al., 2006). Some active constituents have been obtained from plants possess insulin like activity and could be provide alternate for insulin therapy. Chemical structures (Figure-1) of few active compounds having anti-diabetic potentials from above mentioned plants are provided.

**Conclusion**

Metabolic imbalance causing diabetes mellitus is a characteristic of materialistic world. Differences in social structure, psychic stress, obesity, hormonal imbalance and heredity are optimizing the growth of pandemic. Increasing population with diabetes has a huge requirement of effective remediation. The Indian flora has a vast variety of medicinal plants, which are used traditionally for their anti-diabetic property. However, careful assessment including sustainability of such herbs, ecological and seasonal variation in activity of phyto-constituents, metal contents of crude herbal anti-diabetic drugs, thorough toxicity study and cost effectiveness is required for their popularity. These efforts may provide treatment for all and justify the role of novel traditional medicinal plants having anti-diabetic potentials.

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**References**


