Afr. J. Traditional, **Complementary and Alternative Medicines**
www.africanethnomedicines.net

Review Paper

ISSN 0189-6016©2008

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

Rahul Gupta[1*], Kumar Gaurav Bajpai[1], Samta Johri[2], A.M. Saxena[3]

[1]Research students, [3]Reader, Department of Zoology, University of Lucknow, Lucknow-226007, Uttar Pradesh, India; [3]Email: anandmsaxena@rediffmail.com; [*]Email: rahulguptalu2007@rediffmail.com
[2]Reader, Department of Zoology, Mahila Degree College, Lucknow, U. P., India.

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

[3] **Corresponding Author: Tel. + 91 9415028759 (Mobile), +91 532 2357057 (Resi.)**

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 ß-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 use 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. LD_{50} (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 (Upadhya *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* bulb, 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 ß-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 ajoene (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 -1 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 impaired estrous 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.	$1\text{-}T_4$	= 1-thyroxine
2.	ANEP	= Accumulation of advanced glycation end products
3.	b.w.	= Body weight
4.	ED_{50}	= Effective dose
5.	gm	= Gram
6.	kg	= Kilogram
7.	LD_{50}	= 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 cystein sulphoxide.
Figure 1.3: S-allyl cystein sulphoxide.
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.

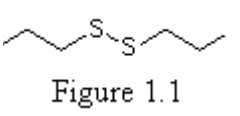

Figure 1.1

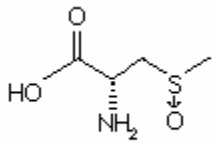

Figure 1.2

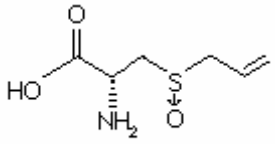

Figure 1.3

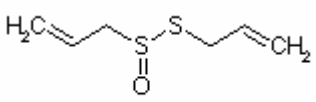

Figure 1.4

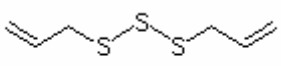

Figure 1.5

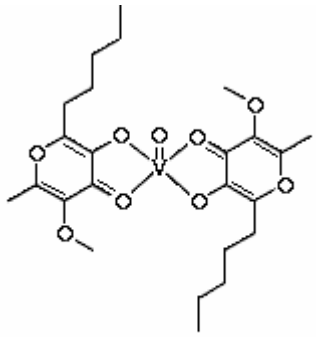

Figure 1.6

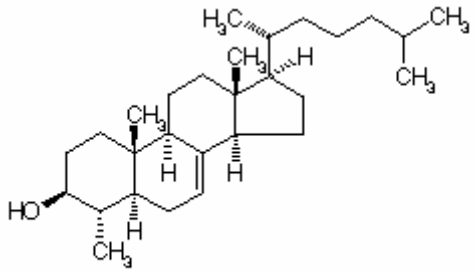

Figure 1.7

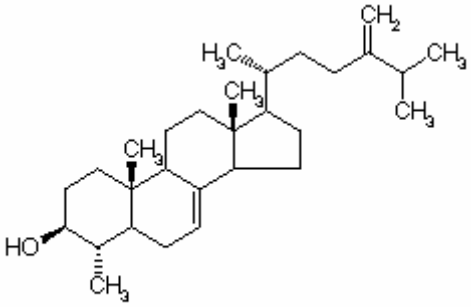

Figure 1.8

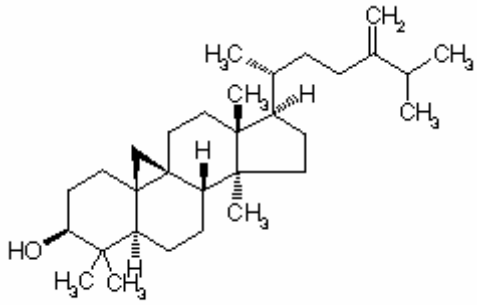

Figure 1.9

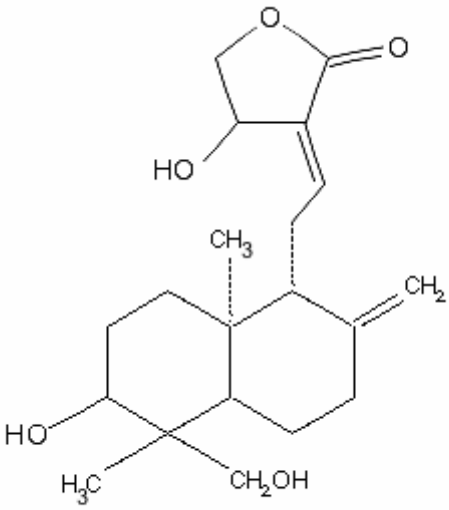

Figure 1.10

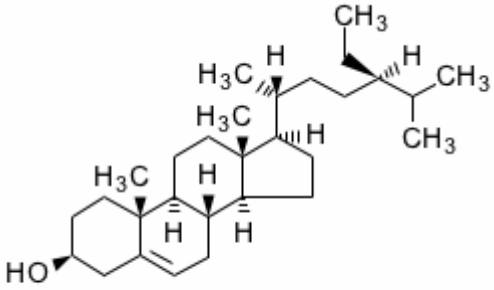

Figure 1.11

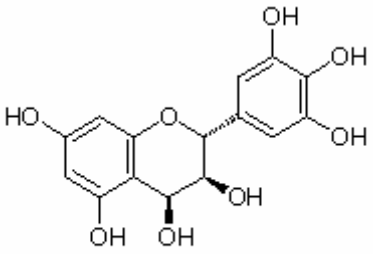

Figure 1.12

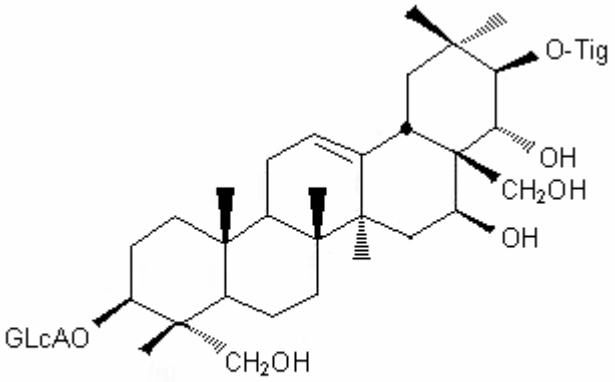

Figure 1.13

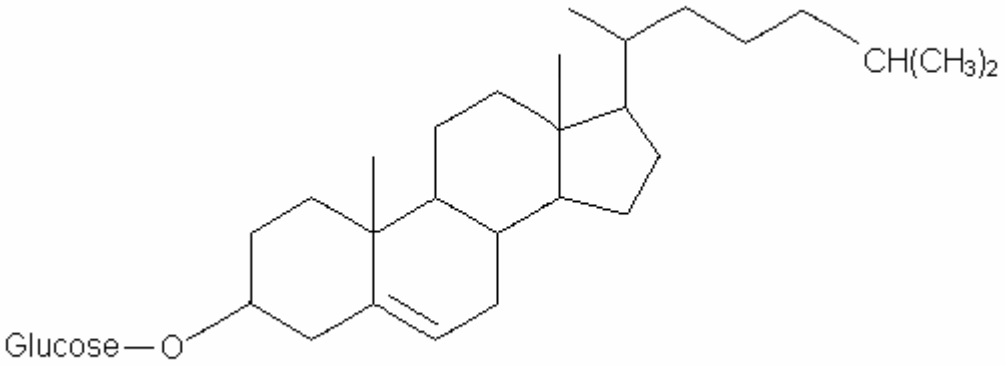

Figure 1.14

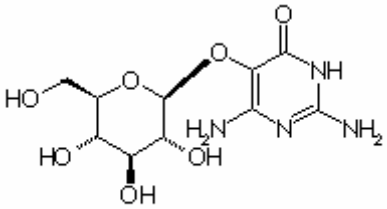

Figure 1.15

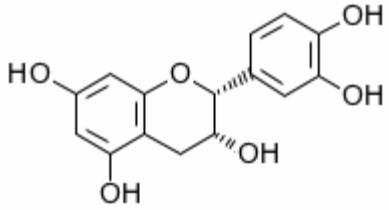

Figure 1.16

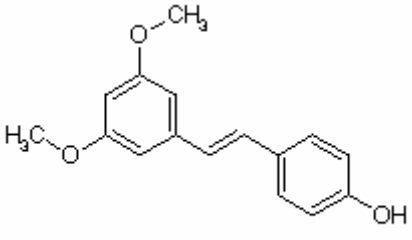

Figure 1.17

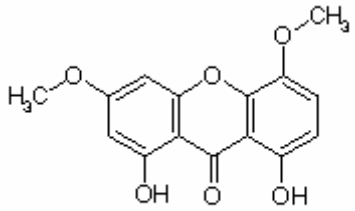

Figure 1.18

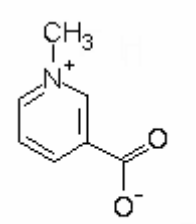

Figure 1.19

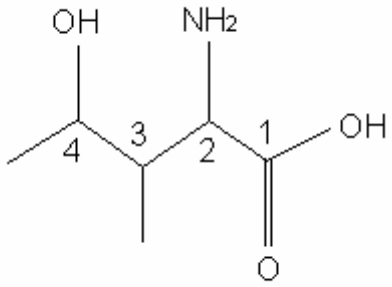

Figure 1.20

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.

Ficus bengalensis Linn. (Family: Moraceae)
Hindi name: Bargad; Common name: Indian Banyan Tree

Plants grow throughout India and in the Indian tradition it is considered as a holy tree (Mukherjee *et al.,* 2006). In a chronic toxicity test extract (25 & 250mg/kg), produced reversible hepatic damage while the acute LD_{50} (lethal dose) found to be 9.47g/kg body weight when given intraperitoneally (Joglekar *et al.,* 1962). Leucocyanidin (3-O-ß-D-galactosylcellobioside) a dimethoxy derivative isolated from bark, lowered blood sugar level and increased serum insulin in normal and moderate diabetic rats (Kumar *et al.,* 1989). It also inhibits the degradation processes of insulin (Kumar *et al.,* 1989). Alcoholic extract of stem bark at a dose of 25, 50 & 75mg/day/100g, b.w. lowered the blood sugar level 47 to 70%, and also restored the normal levels of serum urea, cholesterol and total protein of alloxan diabetic albino rats (Singh *et al.,* 1992). Glucoside of leucopelargonidin isolated from bark has been reported to induce hypoglycemic, hypolipidemic and serum insulin raising effect in moderately diabetic rats (Cherian *et al.,* 1993). 3-O-alfa-L-rhamnoside (250mg/kg, single dose study & 100mg/kg/day, long term study), a dimethoxy derivative isolated from bark, lowered blood sugar in fasted and glucose induced hyperglycemic rats (Cherian *et al.,* 1992), along with enhanced insulin secretion from ß-cells (Augusti *et al.,* 1994). Leucodelphinidine [Fig.1.12] derivative isolated from bark exhibited hypoglycemic activity in normal and alloxan diabetic rats (Geetha *et al.,* 1994). 3-O-α-L-rhamnoside isolated from the bark has been showed its median effective dose (ED_{50}) as 100mg/kg with 12% hypoglycemic action in normal rats (Cherian *et al.,* 1995). Hypoglycemic and hypercholesterolemic effect of aqueous bark extract was observed in alloxan induced mild and severe diabetic rabbits. Lethal dose (LD_{50}) of this was found to be 1gm/kg, when administered orally for 3 months in rats (Gupta *et al.,* 2002). Leucopelrgonin (100mg/kg/day for one month) isolated from bark lowered the fasting blood sugar (34%) and glycosylated haemoglobin (28%) of alloxan diabetic dogs (Daniel *et al.,* 2003).

Gymnema sylvestre (Willd) R. Br. (Family: Ascelpiadaceae)
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 ß-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 ß-cells (Chatopadhyay *et al.,* 1993). In rats the insulin secretion from islets of Langerhans and several pancreatic ß-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 potentially 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, glycosylated hemoglobin, lactate dehydrogenase, glucose-6-phosphatase, fructose-1,6-bisphosphatase 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 ß-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 ß-cells damage in albino rats (Chakroborty *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 ß-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). A 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 ß-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 (Villasenor *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.,* 1974). 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 ß-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.

Acknowledgement

The authors are thankful to Honorable Vice-Chancellor Professor. R.P. Singh, University of Lucknow and Prof. Nirupama Agarwal, Head, Department of Zoology, University of Lucknow, for their constant encouragement in the subject. Authors are also thankful to Dr. Joy Sarkar, Senior Lecturer, Department of Chemistry, University of Lucknow, for his in-put on the chemistry aspects of the manuscript.

References

1. Abdel Barry, J.A., Abdel Hassan, I.A. and Al-Hakiem, M.H. (1997). Hypoglycaemic and antihyperglycaemic effect of *T. foenum graecum* leaf in normal and alloxan induced diabetic rats. J. Ethnopharmacology, 58: 149-155.
2. Achrekar, S., Kakliji, G.S., Pote, M.S. and Kelkar, S.M. (1991). Hypoglycemic activity of *Eugenia jambolana* and *Ficus bengalenesis*: Mechanism of action. *In Vivo*, 5: 143-147.
3. Adachi, Y., Yoshida, J., Kodera, Y., Katoh, A., Takada, J. and Sakurai, H. (2006). Bis(allixinato)oxovanadium(IV) complex is a potent anti-diabetic agent: studies on structure-activity relationship for a series of hydroxypyrone-vanadium complexes. J. Med. Chem., 49: 3251-3256.
4. Ahmad, F., Khan, M.M., Rastogi, A.K., Chaubey, M. and Kidwai, J.R. (1991). Effect of (-)-epicatechin on cAMP content, insulin release and conversion of proinsulin to insulin in immature and mature rat islets in vitro. Ind. J. Exp. Biol., 29: 516-520.
5. Ahmad, M.S. and Ahmad N. (2006). Antiglycation properties of aged garlic extract: possible role in prevention of diabetic complications. J. Nutr., 136: 796-799.
6. Anuradha, C.V. and Ravikumar, P. (2001). Restoration on tissue antioxidants by fenugreek seeds (*Trigonella foenum graecum*) in alloxan–diabetic rats. Ind. J. Physiol. Pharmacol., 45: 408-420.

7. Augusti, K.T. (1973). Studies on the effects of a hypoglycemic principle from *Allium cepa* Linn. Ind. J. Med. Res., 61: 1066-1071.
8. Augusti, K.T. and Sheela, C.G. (1996). Antiperoxide effect of S-allyl cysteine sulfoxide, an insulin secretagogue, in diabetic rats. Experientia, 52: 115-120.
9. Augusti, K.T., Rajisuan, Cherian, D.S., Sheeta, C.G. and Nair, C.R. (1994). Effect of leucopelargonin derived from *Ficus bengalensis* (Linn.) on diabetic dogs. Ind. J. Med. Res., 99: 82-86.
10. Augusti, N.T. (1976). Gas chromatographic analysis of onion principles & a study on their hypoglycemic action. Ind. J. Exp. Biol., 14: 110-112.
11. Babu, P.S. and Srinivasan, K. (1997). Influence of dietary capsaicin and onion on the metabolic abnormalities associated with streptozotocin induced diabetes mellitus. Mole. Cell. Biochem., 175: 49-57.
12. Bajpai, M.B., Asthan, R.K., Sharma, N.K., Chatterjee, S.K. and Mukherjee, S.K. (1991). Hypoglycemic effect of Swerchirin from the hexane fraction of *Swertia chirayta*. Planta Medica, 57: 102-104.
13. Boon, N.A., Colledge, N.R. and Walker, B.R. (2006). Davidson's principles and practice of medicine: Diabetes mellitus, 20th ed. Elsevier, London, 805-847.
14. Borhanuddin, M., Shamsuzzoha, M., Hussain, A.H. (1994). Hypoglycemic effect of *Andrographis paniculata* Nees on non-diabetic rabbits. Bang. Med. Res. Coun. Bull., 20: 24-26.
15. Campos, K.E., Diniz, Y.S., Cataneo, A.C., Faine, L.A., Alves, M.J. and Novelli, E.L. (2003). Hypoglycemic and antioxidant effect of onion, *Allium cepa*: dietary onion addition, antioxidant effect and hypoglycemic effects on diabetic rats. Int. J. Food Sci. Nutr., 54: 241-246.
16. Chakroborty, B.K., Gupta, S., Gambhir, S.S. and Gode, K.D. (1980). Pancreatic ß-cells regeneration- a novel anti-diabetic mechanism of *Pterocarpus marsupium* Roxb. Ind. J. Pharmacol., 12: 123-127.
17. Chandola, H.M., Tripathi, S.N. and Udupa, K.N. (1980). Hypoglycemic response of *Cinnamonum tamala* in patients of maturity onset (NIDDM) diabetes. J. Res. Ayurv. Sidha, 1: 275-290.
18. Chandrasekar, B., Bajpai, M.B. and Mukherjee, S.K. (1990). Hypoglycemic activity of *Swertia chirayita* (Roxb. ex Flem.) Karst. Ind. J. Exp. Biol., 28: 616-618.
19. Chandrasekar, B., Mukherjee, B. and Mukherjee, S.K. (1989). Blood sugar lowering potentiality of selected Cucurbitaceae plants of Indian origin. Ind. J. Med. Res., 90: 300-305.
20. Chatopadhyay, R.R., Medda, C., Das, S. and Basu, T.K. (1993). Hypoglycemic and antihyperglycemic effect of *Gymnema sylvestre* leaf extract in rats. Fitoterapia, 64: 450-454.
21. Chattopadhyay, R.R. (1993). Hypoglycemic effect of *Ocimum sanctum* leaf extract in normal and streptozotocin diabetic rats. Ind. J. Exp. Biol., 31:891-893.
22. Chattopadhyay, R.R. (1999). A comparative evaluation of some blood sugar lowering agents of plant origin. J. Ethnopharmacology, 67: 367-372.
23. Chattopadhyay, R.R., Chattopadhyay, R.N., Nandy, A.K., Poddar, G. and Maitra, S.K. (1987b). The effect of fresh leaves of *Azadirachta indica* on glucose uptake and glycogen content in the isolated rat hemi diaphragm. Bull. Calcutta Sch. Trop. Med., 35: 8-12.
24. Chattopadhyay, R.R., Chattopadhyay, R.N., Nandy, A.K., Poddar, G. and Maitra, S.K. (1987a). Preliminary report on antihyperglycemic effect of a fraction of fresh leaves of *Azadirachta indica* (Beng. Neem). Bull. Calcutta Sch. Trop. Med., 35: 29-33.
25. Cherian, S. and Augusti, K.T. (1993). Hypoglycemic effects of a glycoside of leucopelargonidin isolated from *Ficus bengalenesis* Linn. Ind. J. Exp. Biol., 31: 26-29.
26. Cherian, S. and Augusti, K.T. (1995). Insulin sparing action of leucopelargonitin derivative isolated from the *Ficus bengalensis*. Ind. J. Exp. Biol., 33: 608-611.
27. Cherian, S., Kumar, R.V., Augusti, K.T. and Kidwai, J.R. (1992). Hypoglycemic effect of a glycoside of pelargonidin isolated from the bark of *Ficus bengalenesis* Linn. Ind. J. Biochem. Biophy., 29: 380-382.
28. Daniel, R.S., Devi, K.S., Augusti, K.T. and Nair, C.R.S. (2003). Mechanism of action of antiatherogenic & related effects of *Ficus bengalensis* (Linn.) flavonoids in experimental animals. Ind. J. Exp. Biol., 41: 296-303.
29. Das, A.V., Padayathi, P.S. and Paulose, C.S. (1996). Effect of leaf extract of *Aegle marmelose* (L.) Correa ex Roxb. on histological and ultra structural changes in tissue of streptozotocin induced diabetic rats. Ind. J. Exp. Biol., 34: 341-345.
30. El-Demerdash, F.M., Yousef, M.I. and El-Naga, N.I. (2005). Biochemical study on the hypoglycemic effects of onion and garlic in alloxan–induced diabetic rats. Food Chemi. Toxicol., 43: 57-63.
31. Felig, G., Bergman, M. and Felig, C. (1995). The Endocrine Pancreas: Diabetes mellitus, 3rd ed. MacGraw-Hill, New York. 1107-1250.
32. Geetha, B.S., Mathew, B.C. and Augusti, K.T. (1994). Hypoglycemic effects of leucodelphinidin derivative isolated from *Ficus bengalensis* (Linn.). Ind. J. Phy. Phar., 38: 220-222.

33. Ghannam, N., Kingston, M., Al-Meshaal, I.A., Tariq, M., Parman, N.S. and Woodhouse N. (1986). The hypoglycemic activity of aloes: preliminary clinical and experimental observations. Hormo. Res., 24: 288-294.
34. Gholap, S. and Kar, A. (2003). Effects of *Inula racemosa* root and *Gymnema sylyestre* leaf extracts in the regulation of corticosteroid induced diabetes mellitus: involvement of thyroid hormones. Pharmazie, 58: 413-415.
35. Gholap, S. and Kar, A. (2004). Hypoglycaemic effects of some plant extracts are possibly mediated through inhibition in corticosteroid concentration. Pharmazie, 59: 876-878.
36. Grover, J.K., Rathi, S.S. and Vats, V. (2002b). Amelioration of experimental diabetic neuropathy and gastropathy in rats following oral administration of plant extracts. Ind. J. Exp. Biol., 40: 273-276.
37. Grover, J.K., Vats, V. and Yadav, S.S. (2005). *Pterocarpus marsupium* extract (Vijayasar) prevented the alteration in metabolic patterns induced in the normal rat by feeding an adequate diet containing fructose as sole carbohydrate. Diab. Obes. Metab., 7: 414-420.
38. Grover, J.K., Yadav, S. and Vats, V. (2002). Medicinal plants of India with hypoglycemic potentials. J. Ethnopharmacology, 81: 81-100.
39. Gupta, R.K., Gupta, S. and Samuel, K.C. (1977). Blood sugar lowering effect of various fractions of onion. Ind. J. Exp. Biol., 15: 313-314.
40. Gupta, R.K., Kesari, A.N., Murthy, P.S., Chandra, R., Tandon, V. and Watal, G. (2005). Hypoglycemic and antihyperglycemic effect of ethanol extract of leaves of *Annona squamosa* L. in experimental animals. J. Ethnopharmacology, 99: 75-81.
41. Gupta, R.K., Kesari, A.N., Watal, G., Murthy, P.S., Chandra, R. and Tandon, V. (2005). Nutritional and hypoglycemic effect of fruit pulp of *Annona squamosa* in normal healthy and alloxan-induced diabetic rabbits. Ann. Nutr. Metab., 49: 407-413.
42. Gupta, S., Kataria, M., Gupta, P.K., Murganandan, S. and Yashory, R.C. (2004). Protective role of extract of neem seeds in diabetes caused by Streptozotocin in rats. J. Ethnopharmacology, 90:185-189.
43. Gutpa, S., Shukla, R., Prabhu, K.M., Agarwal, S., Rusia, U. and Murthy, P.S. (2002). Acute and chronic toxicity studies on partially purified hypoglycemic preparation from water extract of bark of *Ficus bengalensis*. Ind. J. Cli. Biochem., 17: 56-63.
44. Hannan, J.M., Marenah, L., Ali, L., Rokeya, B., Flatt, P.R. and Abdel-Wahab, Y.H. (2006). *Ocimum sanctum* leaf extracts stimulate insulin secretion from perfused pancreas, isolated islets and clonal pancreatic ß-cells. J. Endocrinol., 189:127-136.
45. Hannan, J.M., Rokeya, B., Faruque, O., Nahar, N., Mosihuzzaman, M., Azad Khan, A.K. and Ali, L. (2003). Effect of soluble dietary fibre fraction of *Trigonella foenum graecum* on glycemic, insulinemic, lipidemic and platelet aggregation status of Type 2 diabetic model rats. J. Ethnopharmacology, 88: 73-77.
46. Harinantenaina, L., Tanaka, M., Takaoka, S., Oda, M., Mogami, O., Uchida, M. and Asakawa, Y. (2006). *Momordica charantia* constituents and anti-diabetic screening of the isolated major compounds. Chem. Pharm. Bull., 54: 1017-1021.
47. Hattori, A., Yamada, N., Nishikawa, T., Fukuda, H. and Fujino T. (2005). Anti-diabetic effects of ajoene in genetically diabetic KK-A(y) mice. J. Nutr. Sci. Vitaminol., 51: 382-384.
48. Hossain, M.Z., Shibib, B.A. and Rahman, R. (1992). Hypoglycemic effects of *Coccinia indica*: Inhibition of key gluconeogenic enzyme, glucose-6- phosphatase. Ind. J. Exp. Biol., 30: 418-420.
49. Husen, R., Pihie, A.H. and Nallappan, M. (2004). Screening for antihyperglycaemic activity in several local herbs of Malaysia. J. Ethnopharmacology, 95: 205-208.
50. Jain, R.C. and Vyas, C.R. (1975). Garlic in alloxan-induced diabetic rabbits. Ame. J. Clin. Nutr., 28: 684-685.
51. Jelodar, G.A., Maleki, M., Motadayen, M.H. and Sirus, S. (2005). Effect of fenugreek, onion and garlic on blood glucose and histopathology of pancreas of alloxan-induced diabetic rats. Ind. J. Med. Sci., 59: 64-69.
52. Joglekar, G.V., Shrotri, D.S., Aiman, R. and Balwani, J.H. (1962). Further studies on *Ficus bengalensis* Linn.; Part: Toxicity Tests. Ind. J. Med. Res., 50: 737-740.
53. Kaleem, M., Asif, M., Ahmed, Q.U. and Bano, B. (2006). Anti-diabetic and antioxidant activity of *Annona squamosa* extract in streptozotocin-induced diabetic rats. Singapore Med. J., 47: 670-675.
54. Kamalakkanan, N. and Prince, P.S. (2003). Hypoglycaemic effect of water extract of *Aegle marmelos* fruit in streptozotocin diabetic rats. J. Ethnopharmacol., 87: 207-210.
55. Kamalakkanan, N. and Prince, P.S. (2005). The effect of *Aegle marmelos* fruit extract in streptozotocin diabetes: a histopathological study. J. Herb Pharmacother., 5: 87-96.
56. Kamalakkann, N., Rajadurai, M. and Prince, P.S. (2003). Effect of *Aegle marmelos* fruits on normal and streptozotocin-diabetic Wistar rats. J. Med. Food, 6: 93-98.

57. Kamble, S.M., Kamlakar, P.L., Vaidya, S. and Bambole, V.D. (1998). Influence of *Coccinia indica* on certain enzymes in glycolytic and lipolytic pathway in human diabetes. Ind. J. Med. Sc., 52:143-146.
58. Kar, A., Choudhary, B.K. and Bandyopadhyay, N.G. (2003). Comparative evaluation of hypoglycaemic activity of some Indian medicinal plants in alloxan diabetic rats. J. Ethnopharmacology, 84:105-108.
59. Karunanayake, E.H., Welihinda, J., Sirimanne, S.R. and Sinnadorai, G. (1984). Oral hypoglycemic activity of some medicinal plants of Sri Lanka. J. Ethnopharmacology, 11: 223-231.
60. Kelkar, S.M., Kaklij, G.S. and Bapat, V.A. (2001). Determination of hypoglycemic activity in *Allium cepa* (onion) tissue cultures. Ind. J. Biochem. Biophy., 38: 277-279.
61. Kesari, A.N., Gupta, R.K., Singh, S.K., Diwakar, S. and Watal, G. (2006). Hypoglycemic and antihyperglycemic activity of Aegle marmelos seed extract in normal and diabetic rats. J. Ethnopharmacology, 107: 374-379.
62. Khan, A.K.A., Akhtar, S. and Mahatab, H. (1980). Treatment of diabetes mellitus with *Coccinia indica*. Brit. Med. J., 280: 1044.
63. Khanna, P., Jain, S.C., Panagariya, A. and Dixit, V.P. (1981). Hypoglycemic activity of polypeptide-p from a plant source. J. Nat. Prod., 44: 648-655.
64. Kimura, I. (2006). Medical benefits of using natural compounds and their derivatives having multiple pharmacological actions. Yakugaku Zasshi, 126: 133-143.
65. Kohli, K.R. and Singh, R.H. (1993). A clinical trial of Jambu (*Eugenia jambolana*) in Non Insulin Dependent Diabetes Mellitus. J. Res. Ayurveda Siddha, 14: 89-97.
66. Krawinkel, M.B. and Keding, G.B. (2006). Bitter gourd (*Momordica charantia*): A dietary approach to hyperglycemia. Nutr. Rev., 64: 331-337.
67. Kumar, G.P., Sudheesh. S. and Vijayalakshmi, N.R. (1993). Hypoglycemic effect of *Coccinia indica*: Mechanism of action. Planta Medica, 59: 330-332.
68. Kumar, R.V. and Augusti, K.T. (1989). Hypoglycemic effect of a leucocyanidin derivative isolated from the bark of *Ficus bengalensis* Linn. Ind. J. Biochem. Biophy., 31: 73-76.
69. Kumari, K., Mathew, B.C. and Augusti, K.T. (1995). Hypoglycemic and hypolipidemic effects of S-Methyl Cysteine sulfoxide isolated from *Allium cepa* Linn. Ind. J. Biochem. Biophy., 32: 49-54.
70. Liu, C.T., Hse, H., Lii, C.K., Chen, P.S. and Sheen, L.Y. (2005). Effects of garlic oil and diallyl trisulfide on glycemic control in diabetic rats. Eur. J. Pharmacol., 516: 165-173.
71. Lolitkar, M.M., Rao, M.R.R. (1966). Pharmacology of a hypoglycemic principle isolate from fruit of *Momordica charantia* Linn. Ind. J. Pharmacy, 28:129-133.
72. Manickam, M., Ramanathan, M., Johromi, M.A., Chansouria, J.P. and Ray, A.B. (1997). Anti-hyperglycemic activity of phenolics from *Pterocarpus marsupium*. J. Nat. Prod., 60: 609-610.
73. Mathew, P.T. and Augusti, K.T. (1973). Studies on the effect of allicin (diallyl disulphide-oxide) on alloxan diabetes. Hypoglycemic action and enhancement of serum insulin effect and glycogen synthesis. Ind. J. Biochem. Biophy., 10: 209-212.
74. Mathew, P.T. and Augusti, K.T. (1975). Hypoglycemic effect of onion, *Allium cepa* (Linn.) on diabetes mellitus. Ind. J. Physiol. Pharmacol., 19: 213-217.
75. Matsuda, H., Li, Y., Murakami, T., Matsumura, N., Yamahara, J. and Yoshikawa, M. (1988). Anti-diabetic principles of natural medicines-III. Structure related inhibitory activity & action mode of oleanolic acid glycosides on hypoglycemic activity. Chem. Pharma. Bull., 46:1399-1403.
76. Miura, T., Itoh, Y., Iwamoto, N., Kato, M. and Ishida, T. (2004). Suppressive activity of the fruit of *Momordica charantia* with exercise on blood glucose in type 2 diabetic mice. Biol. Pharm. Bull., 27: 248-250.
77. Momin, A. (1987). Role of indigenous medicine in primary healthcare. In: Proceedings of first international seminar on Unani medicine. New Delhi, India, 54.
78. Mukherjee, B., Sekar, B.C. and Mukherjee, S.K. (1988). Blood Sugar lowering effect of *Coccinia indica* root and whole plant, in different experimental rat models. Phytoterapia, 59: 207-210.
79. Mukherjee, P.K., Maiti, K., Mukherjee, K. and Houghton, P.J. (2006). Leads from Indian medicinal plants with hypoglycemic potentials. J. Ethnopharmacology, 106: 1-28.
80. Mukherjee, S.K. (1981). Indigenous Drugs in Diabetes mellitus. J. Diab. Asso. Ind., 21: 97-108.
81. Mukherjee, S.K. and Mukherjee, S.S. (1966). Therapeutic advance in diabetes mellitus through ages. J. Res. Ind. Med., 1: 91-112.
82. Mukhtar, H.M., Ansari, S.H., Ali, M., Bhat, Z.A. and Naved, T. (2005). Effect of aqueous extract of *Pterocarpus marsupium* wood on alloxan-induced diabetic rats. Pharmazie, 60: 478-479.

83. Musabayane, C.T., Bwititi, P.T. and Ojewole, J.A. (2006). Effects of oral administration of some herbal extracts on food consumption and blood glucose levels in normal and streptozotocin-treated diabetic rats. Methods Find. Exp. Clin. Pharmacol., 28: 223-228.
84. Mutalik, S., Chetana, M., Sulochana, B., Devi, P.U. and Udupa, N. (2005). Effect of Dianex, an herbal formulation on experimentally induced diabetes mellitus. Phytotherapy Research, 19: 409-415.
85. Nadkarni K.M. (1976). Indian Materia Medica, Vol. I, Popular Prakashan, Bombay.
86. Narender, T., Puri, A., Shweta, Khaliq, T., Saxena, R., Bhatia, G. and Chandra, R. (2006). 4-hydroxyisoleucine an unusual amino acid as antidyslipidemic and antihyperglycemic agent. Bioorg. Med. Chem. Lett., 16: 293-296.
87. Ng, T.B., Wong, C.M., Li, W.W. and Yeung, H.W. (1986a). Insulin-like molecules in *Momordica charantia* seeds. J. Ethnopharmacology, 15: 107-117.
88. Ng, T.B., Wong, C.M., Li, W.W. and Yeung, H.W. (1986b). Isolation and Characterization of a galactose binding lectin with insulinomimetic activities from the seeds of the bitter gourd *Momordica charantia* (Family: Cucurbitaceae). Intrnational J. Peptide Protein Research, 28: 163-172.
89. Okyar, A., Can, A., Akev, N., Baktir, G., Sutulupinar, N. (2001). Effect of *Aloe vera* leaves on blood glucose level in type I and type II diabetic rat models. Phytother. Res., 15: 157-161.
90. Pandey, M.C. and Sharma, V.P. (1975). Hypoglycemic effect of bark of *Pterocarpous marsupium* Roxb. (Bijaka) on alloxan induced diabetes. Med. Surg., 15: 21.
91. Pari, L. and Venkateswaran, S. (2003). Protective effect of *Coccinia indica* on changes in the fatty acid composition in streptozotocin induced diabetic rats. Pharmazie, 58: 409-412.
92. Paulose, C.S., Ponnachan, P.T.C. and Panikkar, K.R. (1993). Effect of leaf extract of *Aegle marmelose*. Ind. J. Exp. Biol., 31: 345-347.
93. Persaud, S.J., Al-Majed, H., Raman, A. and Jones, P.M. (1999). *Gymnema sylvestre* stimulates insulin release in vitro by increased membrane permeability. J. Endocrinology, 163: 207-212.
94. Platel, K. and Srinivasan, K. (1997). Plant foods in the management of diabetes mellitus: vegetables as potential hypoglycemic agents. Die. Nahrung, 41: 68-74.
95. Ponnachan, P.T., Paulose, C.S. and Panikkar, K.R. (1993). Effect of leaf extract of *Aegle marmelose* in diabetic rats. Ind. J. Exp. Biol., 31: 345-347.
96. Prince, P.S.M., Menon, V.P. and Pari, L. (1997). Effect of *Syzygium cumini* extracts on hepatic hexokinase and glucose-6-phasphatase in experimental diabetes. Phytotherapy Research, 11: 529-531.
97. Prince, P.S.M., Menon, V.P. and Pari, L. (1998). Hypoglycaemic activity of *Syzygium cumini* seeds: effect on lipid peroxidation in alloxan diabetic rats. J. Ethnopharmacology, 61: 1-7.
98. Purohit, A. and Daradka, H.M.M. (2000). Anti-diabetic activity of *Syzygium cumini* seeds extract in alloxan induced diabetic mice. Hamdard medicus, 43: 33-34.
99. Raheja, B.S. (1977). Oral hypoglycemic agent in the management of Maturity-Onset Diabetes-A: Reprint. Reassessment. Journal J. J. Group Hospitals Grant Medical College, 22: 1-9.
100. Rai, V., Iyer, U. and Mani, U.V. (1997). Effect of Tulasi (*Ocimum sanctum*) leaf powder supplementation on blood sugar levels, serum lipids and tissue lipids in diabetic rats. Plant Foods Hum. Nutr., 50: 9-16.
101. Rajasekaran, S., Ravi, K., Sivagnanam, K. and Suramanian S. (2006). Beneficial effects of *Aloe vera* leaf gel extract on lipid profile status in rats with streptozotocin diabetes. Clin. Exp. Pharmacol. Physiol., 33: 232-237.
102. Rajasekaran, S., Sivagnanam, K. and Suramanian, S. (2005). Modulatory effects of *Aloe vera* leaf gel extract on oxidative stress in rats treated with streptozotocin. J. Pharm. Pharmacol., 57: 241-246.
103. Rajsekaran, S., Sivagnanam, K., Ravi, K. and Subramanian, S. (2004). Hypoglycemic effect of *Aloe vera* gel on streptozotocin-induced diabetes in experimental rats. J. Med. Food, 7: 61-66.
104. Ravi, K., Rajasekaran, S. and Subramanian, S. (2005). Antihyperlipidemic effect of *Eugenia jambolana* seed kernel on streptozotocin-induced diabetes in rats. Food Chem. Toxicol., 43: 1433-1439.
105. Ravi, K., Ramachandra, B., Subramanian, S. (2004). Protective effect of *Eugenia jambolana* seed kernel on tissue antioxidants in streptozotocin induced diabetic rats. Biol. Pharm. Bull., 27: 1212-1217.
106. Reyes, B.A., Bautista, N.D., Tanquilut, N.C., Anunccado, R.V., Leung, A.B., Sanchez, G.C., Magtoto, R.L., Castronuevo, P., Tsukamura, H. and Maeda, K.I. (2006). Anti-diabetic potentials of *Momordica charantia* and *Andrographis paniculata* and their effects on estrous cyclicity of alloxan-induced diabetic rats. J. Ethnopharmacology, 105: 196-200.
107. Rosac, C. (2002). The pathophysiological basis of efficacy and clinical experience with the new oral anti-diabetic agents. J. Diab. Compli., 16: 123-132.

108. Sachdewa, A., Raina, D., Srivastava, A.K. and Khemani, L.D. (2001). Effect of *Aegle marmelos* and *Hibiscus rosa sinensis* leaf extract on glucose tolerance in glucose induced hyperglycemic rats (Charles foster). J. Environ. Biol., 22: 53-57.
109. Satyanarayan, K., Murthy, D., Narayan Rao, D., Krishna, R. and Gopal, L.B. (1978). A preliminary study on hypoglycemic and antihyperglycemic effect of *Azadiracta indica*. Ind. J. Pharmacol., 10: 247-250.
110. Sauvaire, Y., Petie, P., Broca, C., Manteghetti, M., Baissac, Y., Fernandez-Alvarez, J., Gross, R., Roye, M., Leconte, A., Gomis, R. and Ribes, G. (1998). 4-Hydroxyisoleucine: a novel amino acid potentiator of insulin secretion. Diabetes, 47: 206-210.
111. Saxena, A. and Vikram, N.K. (2004). Role of selected Indian plants in management of type 2 diabetes: a review. J. Alt. Comple. Med., 10: 369-378.
112. Saxena, A.M., Bajpai, M.B. and Mukherjee, S.K. (1991). Swerchirin induced blood sugar lowering of streptozotocin treated hyperglycemic rats. Ind. J. Exp. Bio., 29: 674-675.
113. Saxena, A.M., Bajpai, M.B., Murthy, P.S. and Mukherjee, S.K. (1993). Mechanism of blood sugar lowering by a Swerchirin-containing hexane fraction (SWI) of *Swertia chirayita*. Ind. J. Exp. Biol., 31: 178-181.
114. Saxena, A.M., Mukherjee, S.K. and Shukla, G. (2006). Progress of diabetes research in India during 20th century. National Institute of Science and Communication (CSIR), New Delhi, 1-104
115. Saxena, A.M., Murthy, P.S.R. and Mukherjee, S.K. (1996). Mode of action of three structurally different hypoglycemic agents: A comparative study. Ind. J. Exp. Biol., 34: 351-355.
116. Sekar, B.C., Mukherjee, B., Chakravarti, R.B. and Mukherjee, S.K. (1987). Effect of different fractions of *Swertia chirayita* on the blood sugar level of albino rats. J. Ethnopharmacology, 21: 175-181.
117. Sekar, D.S., Sivagnanam, K. and Subramanian, S. (2005). Hypoglycemic activity of *Momordica charantia* seeds on streptozotocin induced diabetic rats. Pharmazie, 60: 283-387.
118. Shani, J., Goldsehmied, A., Joseph, B., Ahronson, Z. and Sulman, F.G. (1974). Hypoglycaemie effect of *Trigonella foenum graecum* and *Lupinus termis* (Leguiminosae) Seeds and their major alkaloids in alloxan-diabetic and normal rats. Arch. Int. Pharm. Thera., 210: 27-37.
119. Shanmugasundaram, E.R.B., Gopinath, K.L., Shanmugasundaram, K.R. and Rajendran, V.M. (1990b). Possible regeneration of islets of Langerhans in streptozotocin-diabetic rats given *Gymnema sylvestre* leaf extracts. J. Ethnopharmacology, 30: 265-279.
120. Shanmugasundaram, E.R.B., Rajeswari, G., Bhaskaran, K., Rajesh Kumar, B.R., Raja, K. and Kijar Ahmad (1990a). Use of *Gymnema sylvestre* leaf extract in the control of blood glucose in insulin dependent diabetes mellitus. J. Ethnopharmacology, 30: 281-294.
121. Sharma, S.B., Nasir, A., Prabhu, K.M. and Murthy, P.S. (2006). Antihyperglycemic effect of the fruit-pulp of *Eugenia jambolana* in experimental diabetes mellitus. J. Ethnopharmacology, 104: 367-373.
122. Sharma, S.B., Nasir, A., Prabhu, K.M., Murthy, P.S. and Dev, G. (2003). Hypoglycaemic and hypolipidemic effect of ethanolic extract of seeds of *Eugenia jambolana* in alloxan-induced diabetic rabbits. J. Ethnopharmacology, 85: 201-206.
123. Sharma, S.R., Dwivedi, S.K., Varshney, V.P. and Swarup, D. (1996). Antihyperglycemic and insulin release effect of *A. marmelos* leaves in streptozotocin diabetic rats. Phytotherapy Research, 10: 426-428.
124. Sheehan, E.W., Zemaitis, M.A., Slatkin, D.J. and Schiff Jr, P.L. (1983). A constituent of *Pterocarpus marsupium* (-)-epicatechin, as a potential hypoglycemic agent. J. Natural Products, 46: 232-234.
125. Sheela, C.G., Kumud, K. and Augusti, K.T. (1995). Anti-diabetic effects of onion and garlic sulfoxide amino acids in rats. Planta Medica, 61: 356-357.
126. Shibib, B.A., Khan, L.A. and Rahman, R. (1993). Hypoglycemic activity of *Coccinia indica* and *Momordica charantia* in diabetic rats depression of the hepatic gluconeogenic enzymes glucose-6-phosphatase and fructose-1,6- bisphosphatase and elevation of both liver and red-cell shunt enzyme glucose-6-phosphate dehydrogenase. Biochem. J., 292: 267-270.
127. Shirwaikar, A., Rajendra, K., Dinesh Kumar, C. and Bodla, R. (2004). hypoglycemic activity of aqueous leaf extract of *Annona squamosa* in streptozotocin-nicotinamide type 2 diabetic rats. J. Ethnopharmacology, 91: 171-175.
128. Singh, N., Tyagi, S.D. and Agarwal, S.C. (1992). Study on anti-diabetic effect of alcoholic extract of *Ficus bengalensis* (Linn.) on alloxan diabetic albino rats. J. Res. Ayurveda Siddha, 13: 56-62.
129. Srivastava, Y., Venkatakrishna-Bhatt, H. and Verma, Y. (1988). Effect of *Momordica charantia* Linn. pomous aqueous extract on cataractogenesis in murrin alloxan diabetics. Pharmacol. Res. Commun., 20: 201-209.

130. Sugihara, Y., Nojima, H., Matsuda, H., Murakami, T., Yoshikawa, M. and Kimura, I. (2000). Antihyperglycemic effects of gymnemic acid IV: A compund derived from *Gymnema sylvestre* leaves in streptozotocin diabetic mice. J. Asi. Natur. Product. Res., 2: 321-327.
131. Tahiliani, P. and Kar, A. (2003). Mitigation of thyroxine-induced hyperglycaemia by two plants extracts. Phytother. Res., 17: 294-296.
132. Tanaka, M., Misawa, E., Ito, Y., Habara, N., Nomaguchi, K., Yamada, M., Toida, T., Hayasawa, H., Takase, M. and Inagaki Higuchi, R. (2006). Identification of five phytosterols from *Aloe vera* gel as anti-diabetic compounds. Biol. Pharm. Bull., 29: 1418-1422.
133. Thakran, S., Siddiqui, M.R. and Baquer, N.Z. (2004). *Trigonella foenum graecum* seed powder protects against histopahological abnormalities in tissues of diabetic rats. Mole. Cellular Biochem., 266: 151-159.
134. Tripathi, S.N., Chandola, H.M., Singh, B.C. and Chadha, A.N. (1990). Study on hypoglycemic fraction *of C. tamala* and *T. belerica*. Ayurveda, 11: 1-12.
135. Tripathi, S.N., Tiwari, C.M., Upadhyay, B.N. and Singh, R.S. (1979). Screening of hypoglycemic action in certain indigenous drugs: Short research communication. J. Res. Ind. Med. Yoga. Homeo., 14: 3-4.
136. Udupa, K.N., Tripathi, S.N. and Chandola, H.M. (1980). Effect of *C. tamala* on plasma insulin vis-à-vis blood sugar in patients of diabetes mellitus. J. Res. Ayu. Siddha, 1: 345-357.
137. Upadhya, S., Shanbhag, K.K., Suneetha, G., Balachandra Naidu, M. and Upadhya, S. (2004). A study of hypoglycemic and antioxidant activity of *Aegle marmelos* in alloxan induced diabetic rats. Ind. J. Physiol. Pharmacol., 48: 476-480.
138. Vats, V., Grover, J.K. and Rathi, S.S. (2002). Evaluation of anti-hyperglycemic and hypoglycemic effect of *Trigonella foenum-graecum* Linn, *Ocimum sanctum* Linn and *Pterocarpus marsupium* Linn in normal and alloxanized diabetic rats. J. Ethnopharmacology, 79: 95-100.
139. Vats, V., Yadav, S.P. and Grover, J.K. (2003). Effect of *T. foenum graecum* on glycogen content of tissue and the key enzymes of carbohydrate metabolism. J. Ethnopharmacology, 85: 237-242.
140. Vats, V., Yadav, S.P. and Grover, J.K. (2004). Ethanolic extract of *Ocimum sanctum* leaves partially attenuates streptozotocin-induced alterations in glycogen content and carbohydrate metabolism in rats. J. Ethnopharmacology, 90: 155-160.
141. Vats, V., Yadav, S.P., Biswas, N.R. and Grover, J.K. (2004). Anti-cataract activity of *Pterocarpus marsupium* bark and *Trigonella foenum-graecum* seeds extract in Alloxan-diabetic rats. J. Ethnopharmacology, 93: 289-294.
142. Venkateswaran, S. and Pari, L. (2003b). Effect of *Coccinia indica* leaves on antioxidant status in streptozotocin–induced diabetic rats. J. Ethnopharmacology, 84: 163-168.
143. Villasenor, I.M. and Lamadrid, M.R. (2006). Comparative anti-hyperglycemic potentials of medicinal plants. J. Ethnopharmacology, 104:129-131.
144. Vogler, B.K. and Ernst, E. (1999). *Aloe vera*: a systematic review of its clinical effectiveness. Br. J. Gen. Pract., 49: 823-828.
145. Waheed, A., Minana, G.A. and Ahmad, S.I. (2006). Clinical investigation of hypoglycemic effect of seeds of *Azadirachta inidca* in type-2 (NIDDM) diabetes mellitus. Pak. J. Pharm. Sci., 19: 322-325.
146. Yu, B.C., Hung, C.R., Chen, W.C. and Cheng, J.T. (2003). Antihyperglycemic effect of andrographolide in streptozotocin-induced diabetic rats. Planta Med., 69:1075-1079.
147. Zhang, X.F. and Tan, B.K. (2000a). Anti-diabetic property of ethanolic extract of *Andrographis paniculata* in streptozotocin-diabetic rats. Acta. Pharmacol. Sin., 21:1157-1164.
148. Zhang, X.F. and Tan, B.K. (2000b). Antihyperglycemic and antioxidant properties of *Andrographis paniculata* in normal and diabetic rats. Clin. Exp. Pharm. Phy., 27: 358-363.