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Medicinal plants of India with anti-diabetic potential

J.K. Grover *, S. Yadav, V. Vats

Department of Pharmacology, All India Institute of Medical Sciences, Ansari Nagar, New Delhi-110049, India

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Abstract

Since ancient times, plants have been an exemplary source of medicine. Ayurveda and other Indian literature mention the use of plants in treatment of various human ailments. India has about 45 000 plant species and among them, several thousands have been claimed to possess medicinal properties. Research conducted in last few decades on plants mentioned in ancient literature or used traditionally for diabetes have shown anti-diabetic property. The present paper reviews 45 such plants and their products (active, natural principles and crude extracts) that have been mentioned/used in the Indian traditional system of medicine and have shown experimental or clinical anti-diabetic activity. Indian plants which are most effective and the most commonly studied in relation to diabetes and their complications are: *Allium cepa*, *Allium sativum*, *Aloe vera*, *Cajanus cajan*, *Coccinia indica*, *Caesalpinia bonducella*, *Ficus bengalenesis*, *Gymnema sylvestre*, *Momordica charantia*, *Ocimum sanctum*, *Pterocarpus marsupium*, *Swertia chirayita*, *Syzigium cumini*, *Tinospora cordifolia* and *Trigonella foenum graecum.* Among these we have evaluated *M. charantia*, *Eugenia jambolana*, *Mucuna pruriens*, *T. cordifolia*, *T. foenum graecum*, *O. sanctum*, *P. marsupium*, *Murraya koeingii* and *Brassica juncea*. All plants have shown varying degree of hypoglycemic and anti-hyperglycemic activity. © 2002 Elsevier Science Ireland Ltd. All rights reserved.

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1. Introduction

Diabetes mellitus (DM) is the commonest endocrine disorder that affects more than 100 million people worldwide (6% of the population) and in the next 10 years it may affect about five times more people than it does now (WHO/Acadia, 1992; ADA, 1997). In India, the prevalence rate of diabetes is estimated to be 1–5% (Patel et al., 1986; Verma et al., 1986; Rao et al., 1989). Complications are the major cause of morbidity and mortality in DM.

Historical accounts reveal that as early as 700–200 BC, DM was a well recognized disease in India and was even distinguished as two types; a genetically based disorder and other one resulting from dietary indiscretion (Oubre et al., 1997). In India, indigenous remedies have been used in the treatment of DM since the time of Charaka and Sushruta (6th century BC) (Grover and Vats, 2001).

Plants have always been an exemplary source of drugs and many of the currently available drugs have been derived directly or indirectly from them. The ethnobotanical information reports about 800 plants that may possess anti-diabetic potential (Alarcon-Aguilara et al., 1998). Several such herbs have shown anti-diabetic activity when assessed using presently available experimental techniques (Saifi et al., 1971; Mukherjee et al., 1972; Coimbra et al., 1992; Ajit kar et al., 1999; Jafri et al., 2000). A wide array of plant derived active principles representing numerous chemical compounds have demonstrated activity consistent with their possible use in the treatment of NIDDM (Bailey and Day, 1989; Ivorra et al., 1988; Marles and Farnsworth, 1995). Among these are alkaloids, glycosides, galactomannan gun, polysaccharides, peptidoglycans, hypoglycans, guani-

* Corresponding author. Tel.: +91-11-6594897; fax: +91-11-6862663.

E-mail address: jkgrover@hotmail.com (J.K. Grover).

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dine, steroids, carbohydrates, glycopeptides, terpenoids, amino acids and inorganic ions. Even the discovery of widely used hypoglycemic drug, metformin came from the traditional approach of using *Galega officinalis*. Thus, plants are a potential source of anti-diabetic drugs (and others too) but this fact has not gained enough momentum in the scientific community. The reasons may be many including lack of belief among the practitioners of conventional medicine over alternative medicine, alternative forms of medicine are not very well-defined, possibility of quacks practising such medicine providing alluring and magical cures and natural drugs may vary tremendously in content, quality and safety.

Although, oral hypoglycemic agents/insulin are the mainstay of treatment of diabetes and are effective in controlling hyperglycemia, they have prominent side effects and fail to significantly alter the course of diabetic complications (Rang and Dale, 1991). As the knowledge of heterogeneity of this disorder increases, there is need to look for more efficacious agents with lesser side effects. Though development of modern medicine resulted in the advent of modern pharmacotherapeutics including insulin, biguanides, sulfonylureas and thiazolidinediones, there is still a need to look for new drugs as no drug (except strict glycemic control with insulin) has been shown to modify the course of diabetic complications. In relation to plants also, barring a few studies (Grover et al., 2000; Rathi et al., in press a, Srivastava et al., 1988; Karunanayake et al., 1990, etc.), most of the studies have not assessed the impact of these plants on the course of diabetic complications. The present review circumscribes Indian plants that have been pharmacologically tested and shown to be of some value in DM. Since there was a paucity of journals that published plant related research work, previous work has been published in non-indexed and obscure journals and therefore may have been missed in this article as citations for the present article were taken from Medline database.

2. Plants with anti-diabetic potential

2.1. Acacia arabica or nilotica: Babul (Hindi), Indian Gum Arabic tree (English)

It occurs in wild throughout in India and is also cultivated. Feeding of 94% seed diet to normal rats showed significant hypoglycemic effect versus controls. However, the same diet failed to show any hypoglycemic effect in alloxanized rats (175 mg/kg SC) indicating that plant acts through release of insulin (Singh et al., 1975). Powdered seeds of *Acacia arabica* administered in doses of 2, 3 and 4 gm/kg body weight exerted a significant ($P < 0.05$) hypoglycemic effect in normal rabbits by initiating the release of insulin from pancreatic beta cells. No acute toxicity and behavioral changes were observed at these doses (Wadood et al., 1989).

2.2. Aegle marmelose: Bael or Sirphal (Hindi), Holy Fruit Tree (English)

It is a medium sized, armed deciduous tree found wild, especially in dry forests and is also cultivated throughout India. Oral administration of aqueous decoction of *Aegle marmelose* root bark (1 ml/100 gm) showed hypoglycemic effect which was maximum (44%) at 3 h in normal fasted rats. In addition, the same extract completely prevented peak rise of blood sugar at 1 h in OGTT. The hypoglycemic activity was reduced upon storage of extract (Karunanayake et al., 1984). Aqueous extract of the leaves (1 gm/kg for 30 days) significantly controlled blood glucose, urea, body weight, liver glycogen and serum cholesterol of alloxanized (60 mg/kg IV) rats as compared to controls and this effect was similar to insulin treatment (Ponnachan et al., 1993). When fed as aqueous leaf extract (1 gm/kg/day) to STZ (45 mg/kg IV) diabetic rats for 2 weeks, it decreased malate dehydrogenase levels (an enzyme known to increase in diabetes) in comparison to diabetic controls. The extract was equi-effective in comparison to insulin in restoring blood glucose and body weight to normal levels (Seema et al., 1996). Aqueous leaf extract administered orally for 28 days also normalized STZ (45 mg/kg body weight) induced histo-pathological alterations in the pancreatic and kidney tissues of rats (Das et al., 1996).

2.3. Allium cepa: Pyaj (Hindi) and Onion (English)

It is cultivated throughout India and is an important dietary constituent. Various ether soluble fractions of onion as a single oral dose (0.25 mg/kg) showed significant hypoglycemic effect in normal fasted rabbits. Ethyl ether extract showed most potent hypoglycemic action (Augusti, 1973). Petroleum ether insoluble fraction of the ether extract of dried onion powder (100 mg/kg) given orally for 7 days to alloxanized (180 mg/kg) diabetic rabbits caused a significant anti-hyperglycemic effect (Mathew and Augusti, 1975). Oral administration of 250 mg/kg of ethanol, petroleum, chloroform and acetone extract of powder dried onion showed maximal reduction of 18.57, 8.35, 3.0 and 3.20% in fasting blood glucose of alloxanized (150 mg/kg IP) diabetic rabbit (Jain and Vyas, 1974). In a preliminary study of seven different fractions obtained from onion bulb, only petroleum ether and chloroform extracts significantly lowered blood sugar in OGTT (2 gm/kg) in rabbits (Gupta et al., 1977). Feeding of diet containing 3% freeze-dried onion powder for 8 weeks produced a significant hypoglycemia along with partial reversion

of abnormal plasma albumin, urea, creatinine and inorganic phosphorus in STZ diabetic albino rats. Anti-oxidant and hypolipidemic activity is reported (Babu and Srinivasan, 1997).

Administration a sulfur containing amino acid isolated from *Allium cepa* Linn. called *S*-methyl cysteine sulphoxide (SMCS) (200 mg/kg for 45 days) to alloxanized rats significantly controlled blood glucose and lipids in serum and tissues and normalized the activities of liver hexokinase, glucose 6-phosphatase and HMG CoA reductase. The effect was comparable to that of glibenclamide and insulin (Kumari et al., 1995). Sheela et al. (1995) also showed beneficial effect of SMCS and *S*-allylcysteine sulfoxide (SACS) in alloxanized diabetic rats on glucose intolerance, weight loss and liver glycogen. It also decreased hyperglycemic peak in subcutaneous glucose tolerance tests conducted in rabbits (Roman-Ramos et al., 1995).

Oral single dose of 50 gm of juice expressed onion residue to 3 diabetic patients significantly controlled post-prandial glucose levels (Mathew and Augusti, 1975). Oral administration of 25, 50, 100 and 200 gm of aqueous onion extract to overnight fasted healthy volunteers ($n = 5$/group) 30 min before, after or simultaneously with oral glucose (50 gm) significantly and in a dose-dependent manner increased glucose tolerance and the effect was comparable to tolbutamide. In addition, adrenaline (0.5 ml of 1:1000, SC) induced hyperglycemia was also inhibited in these patients. In the same experiment, there was no difference in the anti-hyperglycemic effect of raw and boiled onion extract in these human volunteers (Sharma et al., 1977). Beneficial effects of fresh onion (3×20 g) as a dietary aid has also been shown in a crossover designed clinical study. The onion diet decreased or maintained blood sugar levels (Tjokroprawiro et al., 1983).

2.4. *Allium sativum: Lahasun (Hindi) and Garlic (English)*

It is a perennial herb cultivated throughout India and is commonly used as a food ingredient. Oral administration of 0.25 gm/kg of ethanol, petroleum ether, ethyl ether extract of *Allium sativum* causes 18.9, 17.9, 26.2% reduction in blood sugar in alloxan-diabetic rabbits (150 mg/kg IV) (Jain and Vyas, 1975). Oral administration of 0.25 gm/kg allicin (isolated from *A. sativum*) produced hypoglycemia comparable to tolbutamide in mildly diabetic rabbits (glucose levels ranging from 180 to 300 mg%) while it showed no such effect in severely diabetic animals (blood sugar > 350 mg%) (Mathew and Augusti, 1973). Aqueous homogenate of garlic (10 ml/kg/day) administered orally to sucrose fed rabbits (10 gm/kg/day in water for 2 months) significantly increased hepatic glycogen and free amino acid contents, decreased fasting blood sugar, triglyceride levels in serum, liver and aorta and protein levels in serum and liver in comparison to sucrose controls (Zacharias et al., 1980). In subcutaneous glucose tolerance test in rabbits, garlic decreased hyperglycemic peak (Roman-Ramos et al., 1995). Pretreatment with aged garlic extract (AGE) (5 and 10 ml/kg, PO) in stress induced hyperglycemia model of mice significantly prevented adrenal hypertrophy, hyperglycemia and elevation of cortisone without altering serum insulin levels. The efficacy of AGE was the same as that of diazepam (5 mg/kg, PO). Thus, AGE may prevent stress-induced risk of DM and its progression (Kasuga et al., 1999).

Daily oral feeding of garlic extract (100 mg/kg) increased cardiovascular functions in STZ rats, prevented abnormality in lipid profile and increased fibrinolytic activities with decreased platelet aggregation. Plasma insulin level increased with concomitant decrease in plasma glucose levels. In addition, daily oral feeding of the same dose for 16 weeks showed anti-atherosclerotic effects in STZ diabetic rats. Thus, garlic may prevent diabetic cardiovascular complications (Patumraj et al., 2000). Ethanolic (95%) extract (45 mg/kg body wt/day for 28 days) of garlic in alloxanized diabetic mice exerted anti-nociceptive effects in tail-flick, hot-plate, allodynia and formalin tests with concomitant decrease in serum glucose levels (Kumar and Reddy, 1999). However, administration of garlic as 6.25% by weight in the diet and as infusions (1 g/400 ml) in place of drinking water for 12 days to normal mice did not alter plasma glucose and insulin concentrations. However, it reduced hyperphagia and polydipsia but not hyperglycemia or hypoinsulinemia in STZ mice (200 mg/kg i.p.) (Swanston-Flatt et al., 1989).

SACS, a sulfur containing amino acid is the precursor of allicin and garlic oil (Sheela and Augusti, 1992). Various studies in experimental diabetes have shown beneficial effect of SACS. Administration of SACS (200 mg/kg) significantly decreased the concentration of serum lipids, blood glucose and activities of serum enzymes like alkaline phosphatase, acid phosphatase and lactate dehydrogenase and liver glucose-6-phosphatase. It also significantly increased liver and intestinal HMG CoA reductase activity and liver hexokinase activity (Sheela and Augusti, 1992). In another study, oral administration of SACS to alloxan-diabetic rats for 1 month ameliorated glucose intolerance, weight loss, depletion of liver glycogen in diabetic rats in comparison to glibenclamide and insulin (Sheela et al., 1995). SACS also controlled lipid peroxidation better than glibenclamide and insulin and ameliorated diabetic condition almost to the same extent as they did. Furthermore, SACS significantly stimulated in vitro insulin secretion from β cells isolated from normal rats (Augusti and Shella, 1996). Hypolipidemic effect has also been described (Augusti and Mathew, 1973).

2.5. *Aloe vera or Aloe barbadensis: Ghee Kunwar and Kumar panthu (Hindi)*

It is cultivated or grows wildly as hedgerows in the drier part of India. It is used in Ayurveda for managing painful conditions and is also mentioned in folk medicine of Arabian Peninsula for management of diabetes. Extracts of aloe gum effectively increased glucose tolerance in both normal and diabetic rats (Al-Awadi and Gumaa, 1987). Chronic but not single administration of the exudate of the leaves of *Aloe barbadensis* (500 mg/kg PO) showed significant hypoglycemic effect in alloxan-diabetic mice. However, single as well as chronic administration of the bitter principle (5 mg/kg IP) showed significant hypoglycemic effect in the same model. The hypoglycemic effect of single dose of the bitter principle was extended over a period of 24 h with maximum hypoglycemia observed at 8 h while chronic administration (exudate twice daily and the bitter principle once a day for 4 days) showed maximum reduction in plasma glucose level at the 5th day. Hypoglycemic effect of aloe and its bitter principle is mediated through stimulation of synthesis and/or release of insulin from the beta-cells of Langerhans (Ajabnoor, 1990).

Additionally, both *Aloe vera* and *Aloe gibberellin* (over a dose range of 2–100 mg/kg) inhibit inflammation in a dose-response manner and improve wound healing in STZ diabetic mice (Davis and Maro, 1989; Chithra et al., 1998). The dried sap of the plant (half a teaspoonful daily for 4–14 weeks) has shown significant hypoglycemic effect both clinically as well as experimentally (Ghannam et al., 1986).

2.6. *Artemisia pallens: common name: Davana*

It is a shrub endemic to south India especially in Mysore state and is used in folk medicine as a treatment for DM in parts of south India (Subramoniam et al., 1996). Oral administration of methanol extract of aerial parts of *Artemisia pallens* showed a dose-dependent (100, 500 and 1000 mg/kg) anti-hyperglycemic effect in glucose fed hyperglycemic and alloxanized rats (60 mg/kg IV). The effect was moderate in fasted normal rats but more in diabetic rats (Subramoniam et al., 1996). Authors hypothesized that the plant extract increased peripheral glucose utilization or inhibited glucose re-absorption in the proximal tubules (Subramoniam et al., 1996).

2.7. *Areca catechu: Supari (Hindi), Betelnut (English)*

It is a tall slender unbranched tree and is cultivated throughout India. Although, an epidemiological study has shown that nitrosmaines released during betel chewing may contribute to the risk of developing NIDDM (Mannan et al., 2000), subcutaneous administration of alkaloid fraction of *Areca catechu* (0.05–0.5 mg/kg) in alloxanized rabbits (140 mg/kg) showed significant hypoglycemic effect lasting for 4–6 h (Chempakam, 1993).

2.8. *Azadirachta indica: Nim or Neem (Hindi)*

It is a medium to large size tree found throughout India in deciduous forests and is also widely cultivated. Hydroalcoholic extract of *Azadirachta indica* showed hypoglycemic and anti-hyperglycemic effect in normal, glucose fed and STZ diabetic rats (Chattopadhyay et al., 1987a). The plant exerts its pharmacological activity independent of its time of administration i.e. either prior or after alloxan administration (Khosla et al., 2000). The plant blocks the action of epinephrine on glucose metabolism, thus increasing peripheral glucose utilization (Chattopadhyay, 1996). It also increased glucose uptake and glycogen deposition in isolated rat hemidiaphragm (Chattopadhyay et al., 1987b).

2.9. *Beta vulgaris: Chukkander (Hindi), Garden beet (English)*

It is a herb cultivated in many parts of India. Various glycosides isolated from the root extract of *Beta vulgaris* (e.g. beta vulgarosides II, III and IV) have been shown to increase glucose tolerance in OGTT conducted in rats (Yoshikawa et al., 1996). In addition, the extract also inhibited non-enzymatic glycosylation of skin proteins in STZ diabetic rats (Tunali et al., 1998).

2.10. *Biophytum sensitivum: Lajjalu or Laksmana (Hindi)*

It is found throughout tropical parts of India as a weed in moist and shady areas. The leaf extract of this plant has been shown to exert significant anti-hyperglycemic effect in alloxanized rabbits possibly by pancreatic β cells stimulating action as the plant was effective in only mild to moderate and not in severe diabetes (Puri and Baral, 1998).

2.11. *Bombax ceiba: Semul (Hindi) and Red Silk Cotton Tree (English)*

It is found throughout India especially in the forest region up-to an elevation of 1500 m. A C-flavonol glucoside isolated from *Bombax ceiba* leaves called as Shamimin has been shown to exert significant hypoglycemic activity at the dose of 500 mg/kg in rats (Saleem et

al., 1999). The extract was lethal in rats at 500 mg/kg but not in mice even up to 1 gm/kg dose.

2.12. *Brassica juncea: Rai (Hindi)*

It is commonly used spice in various food items in India. Oral feeding of *Brassica juncea* diet (10% w/w) for 60 days to normal rats led to significant hypoglycemic effect. This effect was attributed to stimulation of glycogen synthetase (leading to increase in hepatic glycogen content) and suppression of glycogen phosphorylase and other gluconeogenic enzymes (Khan et al., 1995). Anti-oxidant (Khan et al., 1996a, 1997) and hypolipidemic activity (Khan et al., 1996b) is also described in literature.

2.13. *Caesalpinia bonducella:*

Kantkarej or Kantikaranja (Hindi) and Fever nut or Bonduc nut (English). A thorny shrub found throughout India in planes on wasteland and coastal area. The aqueous and alcoholic extract of *Caesalpinia bonducella* seeds exhibited significant hypoglycemic and anti-hyperglycemic activities in normal and STZ hyperglycemic rats (Simon et al., 1987; Rao et al., 1994). However, aqueous extract (100 mg/kg) was associated with prolonged hypoglycemia as compared to 50% ethanolic extract. Hypolipidemic activity has also been described (Sharma et al., 1997).

2.14. *Cajanus cajan: Tuwar (Hindi) and Red gram or Pigeon pea (English)*

It is cultivated through out India. It is used in Panamanian folk medicine for the treatment of diabetes. A single dose of unroasted seeds of *Cajanus cajan* administration as a 60 and 80% diet to normal and alloxanized mice caused a significant reduction in the serum glucose levels after 1–2 h and a significant rise at 3 h. On other hand, roasted seeds administration caused a significant increase in the serum glucose levels during a 3 h experimental period. Roasting of seeds at high temperature for 30 min resulted in the total loss of hypoglycemic principle but not the hyperglycemic principle present in the seeds (Amalraj and Ignacimuthu, 1998a). Aqueous fraction of the leaves and stems of *C. cajan* (500 and 1000 mg/kg) lacked hypoglycemic effect in normal mice. However, it significantly increased glucose tolerance at 1 and 2 h in OGTT (Esposito Avella et al., 1991). Hypolipidemic effect has also been reported earlier (Prema and Kurup, 1973a,b). Cooked diet of *C. cajan* has also shown significant hypoglycemic effect in healthy human volunteers (Panlasigui et al., 1995).

2.15. *Capparis decidua: Kurel or Pinju (Hindi) and Caper plant (English)*

It is found throughout India especially in dry areas. Oral feeding of diet containing (30%) *Capparis decidua* fruit powder for 3 weeks to alloxanized (80 mg/kg IP) diabetic rats (blood glucose, 450 mg%) showed significant hypoglycemia (blood glucose, 120–130 mg%) (Yadav et al., 1997b). In addition, anti-oxidant (Yadav et al., 1997a,b) and hypolipidemic activity (Agarwal and Chauhan, 1988) has been described in literature.

2.16. *Citrullus colocynthis: Badi Indrayan or Makkal (Hindi) and Bitter apple (English)*

It is an annual herb found in wild as well as cultivated throughout India in the warm areas. The fruit of this plant is traditionally used as anti-diabetic in Mediterranean part of the World. Aqueous extract of its fruit showed dose-dependent increase in insulin release from isolated islets (Abdel-Hassan et al., 2000). Oral administration of aqueous extract (300 mg/kg) in normal rabbits significantly reduced plasma glucose after 1 h and highly significant reduction after 2, 3 and 6 h. Glycosidic extract (50 mg/kg) was more effective in lowering fasting glucose as compared to alkaloidal extract. Graded doses (10, 15 and 20 mg/kg) of saponin also reduced plasma glucose concentration in alloxanized rabbits. Thus, saponins and glycosidic components levels of the rind of *Citrullus colocynthis* are responsible for its hypoglycemic effect (Abdel-Hassan et al., 2000).

2.17. *Coccinia indica: Bimb or Kanturi (Hindi) and Ivy Guard (English)*

It is a perennial tendril climber found throughout India. It is used in Ayurveda and Unani system of medicine for treatment of diabetes, skin eruptions, tongues sore, earache, etc. (Chopra et al., 1956). Feeding of water soluble alkaloid fraction of alcohol extract (1 gm/kg) of *Coccinia indica* leaves to normal fasting guinea pigs showed hypoglycemic activity of short duration and the effect was attributed to the presence of beta sitosterol (Mukherjee et al., 1972). Oral administration (2 gm/kg/day) of pectin isolated from *C. indica* fruit showed a significant hypoglycemic action in normal rats due to stimulation of glycogen synthetase activity and reduction of phosphorylase activity (Kumar et al., 1993).

Oral administration of 500 mg/kg of *C. indica* leaves showed significant hypoglycemia in alloxan-diabetic dogs (45 mg/kg IV) and increased glucose tolerance in normal and diabetic dogs (OGTT and IVGT), respectively, (Singh et al., 1985). Oral administration of ethanolic extract of *C. indica* root (250 mg/kg) to

normal rats significantly lowered blood sugar in fasted model and depressed the peak value in glucose loaded model (Chandrasekar et al., 1989). Oral feeding of ethanol extract of the leaves (200 mg/kg) to 18 h fasted rats and STZ diabetic rats led to lowering of blood sugar by 23 and 27%, hepatic glucose-6-phosphatase by 19 and 32%, hepatic fructose-1,6-bisphosphatase by 20 and 30%, respectively, as compared to controls (Shibib et al., 1993). Oral administration of water soluble alkaloid fraction, chloroform extract and alcoholic fraction (100 mg/kg) reduced fasting blood glucose of guinea pig by 29.3, 34.5 and 36.3%, respectively. Blood glucose was reduced by 25 and 21% by chloroform extract and alkaloid fraction, respectively, in OGTT (1 gm/kg) conducted on rats (Mukherjee et al., 1972).

Beneficial effects of leaves of *C. indica* have also been shown in a double-blind control trial enrolling 16 patients with uncontrolled maturity onset diabetes and 16 controls. Treatment was given for 6 weeks and 10 patients showed marked improvement in their glucose tolerance (Azad Khan et al., 1979; Khan et al., 1980). In a clinical study ($n = 30$), oral administration of dried extract of *C. indica* (500 mg/kg for 6 weeks) significantly restored the raised activity of lipoprotein lipase and the levels of G-6 phosphatase and LDH, which are otherwise increased in the severe diabetics. This action of the plant extract was akin to that of insulin (Kamble et al., 1998). As a single oral dose, the plant extract has been shown to exert beneficial hypoglycemic effect in experimental animals and human diabetic subject possibly through an insulin secreting effect or through influence of enzymes involved in glucose metabolism (Platel and Srinivasan, 1997). Results of Hossain et al. (1992) suggests that the hypoglycemic effect of *C. indica* are partly mediated through suppression of gluconeogenic enzyme glucose-6-phosphatase.

2.18. *Eucalyptus globulus: Safeda (Hindi)*

It is a lofty tree of about 90 m in height and is grown in various part of India. Aqueous extract (0.5 gm/l) of eucalyptus increased peripheral glucose utilization in the mouse abdominal muscle and stepwise enhancement of insulin secretion from the clonal pancreatic beta cell line by 70–160% (Gray and Flatt, 1998). Administration of *Eucalyptus globulus* leaves diet (6.25% w/w) for 12 days to normal rats did not result in hypoglycemia. In addition, STZ administration to these pre-treated rats did not produce hyperglycemia as severely as it was seen in controls. In addition, pre-treated rats also showed less polydypsia and body weight loss (Swanston-Flatt et al., 1990).

2.19. *Eugenia uniflora: Pitanga and Surinam cherry (Vernacular)*

It is a large bushy shrub cultivated in garden. It is also distributed in southern Asia, Africa, and in South America. Oral feeding of ethanol extract of the leaves of *Eugenia uniflora* to mice has been shown to contain plasma glucose levels during OGTT and plasma triglyceride level in oral corn oil tolerance test (Arai et al., 1999).

Few fractions isolated on the basis of polarity and molecular size from the ethanolic extract of the leaves of *E. uniflora* have shown positive effects in OGTT conducted in mice (Arai et al., 1999). In addition all fractions except one showed dose-dependent inhibitory effect on lipase activity and these effects were apparently due to the inhibition of the decomposition of carbohydrates and fats in the intestine (Arai et al., 1999).

2.20. *Ficus bengalenesis: Indian Banyan tree or Bur (Hindi)*

A very large tree distributed throughout India from sea level to 1.200 m. A glucoside isolated from the bark of *Ficus bengalenesis* showed more potent hypoglycemic action as compared to crude ethanolic extract and the activity was half of tolbutamide (Augusti, 1975). Oral administration of bark extract showed significant antihyperglycemic effect in STZ diabetic rats by raising serum insulin levels or inhibiting insulinase activity in liver and kidney (Achrekar et al., 1991). Oral administration of leucopelarogonidin derivative (100 mg/kg) isolated from bark of *F. bengalenesis* exerts significant hypoglycemic activity in normal and moderately alloxanized diabetic dogs (60 mg/kg IV injection) (Augusti et al., 1994). A leucocyanidin derivative (100 mg/kg) isolated from the bark of *F. bengalenesis* was hypoglycemic in normal rats. Combination of single dose of this chemical and low dose insulin controlled diabetes in alloxanized rats as effectively as that of high dose of insulin. In addition, long term treatment with this combination showed equal response to double dose of insulin in respect to body weight, urine and blood sugar along with amelioration of serum cholesterol and triglyceride (Kumar and Augusti, 1994). The other glycoside (pelargonidin derivative) isolated from bark decreased fasting blood glucose by 19% and improved glucose tolerance by 29% in moderately diabetic rats at the dose of 250 mg/kg. In comparison, glibenclamide (2 mg/kg) showed 25 and 66% reduction, respectively, versus controls (Cherian et al., 1992). Treatment with the same glycoside (100 mg/kg/day) for 1 month reduced the fasting blood glucose levels to almost half of the pretreatment levels. Glucose tolerance improved by 15% in glycoside treated group versus 41% in glibenclamide treated group (0.5 mg/kg/day). In addition, pelargonidin

was more potent than leucocyanidin in stimulating in vitro insulin secretion by beta cells (Cherian et al., 1992). Another glycoside, leucopelarogonidin derivative possesses significant hypoglycemic, hypolipidemic and serum insulin raising effects in moderately diabetic rats (Cherian and Augusti, 1993). Upon single administration of 0.2–1.8 gm/kg and 100, 250, 500 mg/kg/day of the extract for 1 month in experimental animals, no lethality and toxic effects were observed (Augusti et al., 1994). Anti-oxidant property of the flavanoid compounds of the bark of this plant has been described (Daniel et al., 1998). Leucodelphinidin (250 mg/kg) also showed hypoglycemic action equal to that of glibenclamide (2 mg/kg) in normal and alloxan-diabetic rats. However, in OGTT, it was less effective as compared to glibenclamide (2 mg/kg) (Geetha et al., 1994).

2.21. *Gymnema sylvestre: Gudmar or Merasingi (Hindi) and Periploca of the woods (English)*

Anti-hyperglycemic effect of dried leaf powder of *Gymnema sylvestre* was seen in alloxanized rabbits along with decrease in the activity of gluconeogenic enzymes and reversal of pathological changes in the liver initiated during the hyperglycemic phase (Shanmugasundaram et al., 1983). Oral feeding of powdered leaves of *G. sylvestre* (500 mg/rat) for 10 days significantly prevented intravenous beryllium nitrate induced hyperglycemia in rats and normalized it in 4 days in comparison to 10 days in untreated rats. However, no significant hypoglycemia was seen in normal rats who were daily fed with the leaves of *G. sylvestre* for 25 days (Prakash et al., 1986). Oral administration of aqueous extracts of leaves of *G. sylvestre* (20 mg/day) for 20–60 days normalized blood sugar levels of STZ diabetic rats through β cell regeneration (Shanmugasundaram et al., 1990b). Single as well as chronic (32–35 days) oral administration of aqueous extract of *G. sylvestre* leaves (1 g/kg) to 18-h fasted non-diabetic and STZ (30 mg/kg) induced mild diabetic rats showed significant reduction in blood glucose on OGTT (1 g/kg) without any significant effect on immuno-reactive insulin (IRI) levels (Okabayashi et al., 1990). Oral administration of varying doses (50, 100, 200 and 500 mg/kg) of aqueous extract to normal and STZ diabetic rats showed significant dose-dependent hypoglycemic activity (Chattopadhyay, 1999). However, Tominaga et al. (1995) reported no effect of *G. sylvestre* leaves extract (120 mg/kg/day PO) for 7 days on insulin resistance in STZ diabetic rats. Hypolipidemic effect is described in spontaneously hypertensive rats (Preuss et al., 1998).

Various hypoglycemic principles of *G. sylvestre* isolated from the saponin fraction of the plant are referred as gymnemosides and gymnemic acid (Murakami et al., 1996; Yoshikawa et al., 1997a). Its triterpene glycosides isolated from plant inhibited glucose utilization in muscles (Shimizu et al., 1996). Gymnemic fractions also inhibit glucose uptake in the intestine (Shimizu et al., 1997). Alcoholic extract also stimulate insulin secretion from the rat islets of Langerhans and several pancreatic beta cell lines in absence of other stimulus (Persaud et al., 1999). However, triterpene glycosides exhibited little or no inhibitory activity against glucose absorption in OGTT conducted in rats. Gymnemic acid I and gymnemasaponin V lacked anti-hyperglycemic effect (Yoshikawa et al., 1997b). Oral administration of aqueous leaf extract (50, 100, 200 and 400 mg/kg) to normal and STZ diabetic rats showed dose-dependent decrease in blood glucose level (Chattopadhyay, 1999). In another study, water-soluble fraction of alcoholic extract of the plant significantly lowered the hepatic glycogen content of the glucose fed rats (Chattopadhyay, 1998).

Beneficial effects of oral treatment of *G. sylvestre* leaves extract (400 mg) for 18–20 months plus conventional treatment showed beneficial effects in 22 NIDDM patients. Results showed significant reduction in blood glucose, glycosylated haemoglobin and plasma proteins and lowering of conventional drug requirement. Five patients totally discontinued conventional drug therapy and maintained blood glucose homeostasis with plant extract alone. In addition, serum insulin levels were raised suggesting insulin-releasing effect (Baskaran et al., 1990). Oral administration of a water-soluble leaves extract of *G. sylvestre* (400 mg/day) to 27 IDDM patients on insulin therapy lowered fasting blood glucose, glycosylated haemoglobin (HbA1c), glycosylated plasma protein and insulin requirements but it remained higher than controls. In addition, it reduced serum lipid level to near normal levels (Shanmugasundaram et al., 1990a). In a clinical observation of aqueous decoction of *G. sylvestre* leaves (2 gm thrice daily) to 10 healthy persons (10 days) and 6 diabetic patients (15 days) significantly reduced the fasting and OGTT glucose level in all the groups except OGTT in healthy group (Khare et al., 1983).

2.22. *Hibiscus rosa-sinesis: Gudhal or Jasson (Hindi) and Shoe-flower (English)*

It is a shrub cultivated as an ornamental plant throughout India and has been mentioned in Ayurveda for its medicinal value. Single oral administration of 250-mg/kg ethanol extract of *Hibiscus rosa-sinesis* showed mild but significant hypoglycemia at 120 min in glucose loaded rat. Daily administration of same dose for 7 days showed significant hypoglycemic effect at 30, 90, 120 min after glucose loading in normal rats. The action was similar to tolbutamide and possibly due to insulin release by stimulation of pancreatic beta cells or an increase of the glycogen deposition in liver (Sachdeva and Khemani, 1999).

2.23. *Ipomoea batatas: Sakkargand or Mitha Alu (Hindi)*

A trailing herb cultivated for its succulent tuberous roots. Oral administration of *Ipomoea batatas* reduces hyperinsulinemia in Zucker fatty rats by 23, 26, 60 and 50% after 3, 4, 6 and 8 weeks, respectively. In addition, inhibition of blood glucose level after glucose loading was observed after 7 weeks of treatment along with regranulation of pancreatic beta cells and reduction in insulin resistance (Kusano and Abe, 2000). Hypolipidemic activity has also been described (Kusano and Abe, 2000).

2.24. *Lantana camara: Caturang or Ghaneri (Hindi)*

A large aromatic shrub found throughout India. It is mentioned in Ayurveda for treatment of various vitiated body conditions. Once daily administration of *Lantana camara* leaves juice (1500 mg/kg/day for 14 days) showed significant hypoglycemic effect in rats (Garg et al., 1997; Sachdeva and Khemani, 1999). However, the plant is hepatotoxic in nature (Sharma et al., 1992).

2.25. *Mangifera indica: Aam or Amb (Hindi) and Mango (English)*

The tree is found throughout India and traditionally its seeds and fruits are used for treatment of various ailments.

Oral administration of aqueous extract of the leaves (1 gm/kg) failed to alter the blood glucose levels in normoglycemic or STZ induced diabetic rats. However, the extract showed anti-diabetic activity when given 60 min before or concurrently with glucose and this action could be due to reduction in intestinal absorption of glucose (Aderibigbe et al., 1999). However, possibility of other mechanism can not be excluded. *Mangifera indica* has also been shown to exert powerful anti-oxidant activity in vitro (Martinez et al., 2000).

2.26. *Memecylon umbellatum: Anjani or Alli (Hindi)*

It is a small tree found mostly in Southern India, Andaman islands and the coastal region of the Deccan peninsula and eastern part of India. Oral administration of alcoholic extract of the leaves of *Memecylon umbellatum* (250 mg/kg) caused a significant reduction in the serum glucose levels in normal and alloxanized rats at 30, 60 and 90 min after administration (Amalraj and Ignacimuthu, 1998b).

2.27. *Momordica cymbalaria: Kadavanchi and Athalaki (Vernacular)*

It is a perennial trailing plant found in Deccan, Mysore and Konkan region of India and is a commonly used as a vegetable in India. The first report of its hypoglycemic activity came in 1992 by Nagaraju (1992) who showed that oral feeding of powder of the fruit of *Momordica cymbalaria* (250 mg/kg for 15 days) caused significant reduction in fasting blood glucose levels in alloxanized rats (150 mg/kg IP) with no reduction of glucose levels in normal rats possibly by increasing hepatic glycogen (Rao et al., 1999). In addition, hypolipidemic activity has been described in the literature (Rao et al., 1999).

2.28. *Momordica charantia: Karela (Hindi) and Bitter Gourd (English)*

It is a very common folklore remedy for diabetes. Extract of fruit pulp, seed, leaves and whole plant of *Momordica charantia* has shown hypoglycemic effect in various animal models (Sharma et al., 1960; Gupta and Seth, 1962; Jose et al., 1976; Vimla Devi et al., 1977; Kedar and Chakrabarti, 1982; Ali et al., 1993; Rathi et al., in press a).

In a preliminary study by Karunanayake et al. (1984), *M. charantia* showed hypoglycemic as well as antihyperglycemic activity in laboratory animals. Polypeptide-p, isolated from fruit, seeds, and tissue of *M. charantia* showed potent hypoglycemic effect when administered subcutaneously to gerbils, langurs, and humans (Khanna et al., 1981). Aqueous extracts of *M. charantia* improved OGTT after 8 h in normal mice and reduced hyperglycemia by 50% after 5 h in STZ diabetic mice. In addition, chronic oral administration of extract to normal mice for 13 days improved OGTT while no significant effect was seen on plasma insulin levels (Bailey et al., 1985). Ethanolic extract of *M. charantia* (250 mg/kg dose PO) significantly lowered blood sugar in fasted as well as glucose loaded non-diabetic rats (Chandrasekar et al., 1989). Oral administration of acetone extract of fruit powder of *M. charantia* for 15–30 days to alloxan-diabetic rats lowered the blood sugar and serum cholesterol levels to normal range and the blood sugar was found normal even after 15 days of discontinuation of the treatment (Singh et al., 1989). Shibib et al. (1993) showed that ethanolic extract of *M. charantia* (200 mg/kg) showed an anti-hyperglycemic as well as hypoglycemic effect in normal and STZ diabetic rats as evident by 23% ($P < 0.01$) and 27% ($P < 0.001$) decrease in blood sugar, respectively. This occurred possibly due to inhibition of glucose-6-phosphatase and fructose-1,6-bisphosphatase in the liver and stimulation of red-cell and hepatic glucose-6-phosphate dehydrogenase activities. When fed orally, aqueous extract of *M.*

charantia but not ethanolic extract showed anti-hyperglycemic and hypoglycemic effect in cyproheptadine-induced hyperglycemic and normoglycemic mice, respectively, (Cakici et al., 1994). The pulp juice and saponin free methanolic extract of pulp juice exerted significant hypoglycemic effect in fasting and post-prandial states of normal and NIDDM rats but not in IDDM rats. Effect was more pronounced in case of saponin free methanol extract. Charantin, a peptide resembling insulin isolated from *M. charantia* lowered fasting blood sugar in rabbits gradually beginning from 1st and lasting till the 4th h and slowly recovering to the initial level. Charantin (50 mg/kg) administered orally, lowered blood glucose by 42% at the 4^{th} h with a mean fall of 28% during 5 h (Lolitkar and Rao, 1966). Homogenized suspension of the vegetable pulp of *M. charantia* to 100 cases of moderate NIDDM subjects caused a significant reduction ($P < 0.001$) of post-prandial serum glucose in 86% cases and fasting glucose in 5% cases (Ahmad et al., 1999). Aqueous juice of *M. charantia* fruit exerted anti-hyperglycemic and anti-oxidant effect in pancreas of STZ-diabetic mice (Sitasawad et al., 2000). Oral supplementation (0.5, 1 and 3%) with freeze-dried powder of *M. charantia* for 14 days with and without 0.5% cholesterol and 0.15% bile acid in the diet resulted in a consistent decrease in serum glucose levels in normal rats only in the former group. The plant also exerted anti-atherogenic effect (Jayasooriya et al., 2000).

STZ (50 mg/kg IP) diabetic rats fed 0.5% diet containing *M. charantia* for 6 weeks did not show beneficial hypoglycemic effect and neither prevented diabetes related abnormalities in the levels of protein, urea and creatinine (Platel and Srinivasan, 1995). In other study, feeding of 0.02, 0.1 and 0.5% w/w diet containing *M. charantia* for 8 weeks did not affect blood sugar, food intake, growth, organ weights and hematological parameters of normal adult rats. Notably, 0.5% diet caused a significant hypo-cholestrolemic effect (Platel et al., 1993). Single or repeated oral administration of *M. charantia* juice (10 ml/kg for 30 days) did not affect the results of OGTT in STZ diabetic rats. In addition, glycosylated hemoglobin concentration remained unchanged in treated and untreated diabetic rats. Results of this study were suggestive of the fact that viable beta cells are required to manifest the hypoglycemic activity of *M. charantia* (Karunanayake et al., 1990).

Experiments in rats showed that 2 important constituents of *M. charantia* i.e. oleanolic acid 3-*O*-glucuronide and momordin Ic exert anti-hyperglycemic effect by inhibiting glucose transport at the brush border of the small intestine (Matsuda et al., 1998). The fruit juice significantly increased the number of beta cells ($P < 0.004$) in diabetic rats (Ahmed et al., 1998). Oral administration of different *M. charantia* extracts showed a varying pattern of anti-hyperglycemic effect without altering the insulin response suggesting a mechanism of action which is independent of intestinal glucose absorption and probably involves an extra-pancreatic effect (Day et al., 1984). Oral feeding of *M. charantia* juice to normal rats prior to glucose loading increased hepatic and muscle glycogen content while triglyceride content was not effected. In vitro the fruit juice increased glucose uptake by tissues without concomitant increase in tissue respiration (Welihinda and Karunanayake, 1986). Aqueous extract of unripe fruits of *M. charantia* has also been shown to partially stimulate insulin release from isolated beta-cell of obese-hyperglycemic mice which differed from D-glucose and other insulin secretagogues agent in the manner that not being suppressed by L-epinephrine and in even being potentiated by the removal of Ca^{2+} suggesting that the insulin-releasing action is the result of perturbations of membrane functions (Welihinda et al., 1982).

Daily administration of extract of *M. charantia* fruit (4 gm/kg/) for 2 months to alloxanized diabetic rats (120 mg/kg) delayed development of cataract. Respective blood sugar level in the two groups was 307 ± 81 and 66.37 mg% (Srivastava et al., 1988). Anti-oxidant activity has also been described (Dhar et al., 1999).

In a clinical trial, water-soluble extract of the fruits of *M. charantia* significantly reduced blood glucose concentrations in the 9 NIDDM diabetics on OGTT (50 gm). Fried karela fruits consumed as a daily supplement to the diet produced a small but significant improvement in glucose tolerance in diabetic subjects without any increase in serum insulin levels (Leatherdale et al., 1981).

2.29. *Morus alba: Shetut or Tut (Hindi) and White Mulberry (English)*

Chronic subcutaneous administration of the extract of the leaves of *Morus alba* to rabbits led to degranulation of beta-cells of the Langerhans islets (Gulubova and Boiadzhiev, 1975). Single intra-peritoneal dose of 200 mg/kg of ethanol insoluble fraction of hot water extract of *M. alba* leaves exhibited a potent hypoglycemic activity in fasted and non-fasted STZ (150 mg/kg IV) diabetic mice and the glucose level fell by $24.6 \pm 6\%$ and $81.4 \pm 7.9\%$, respectively. Increase in glucose uptake was postulated as the mechanism of hypoglycemic action (Chen et al., 1995). Alkaloids of this plant are known to possess glycosidase inhibitory activity (Asano et al., 1994). Anti-oxidant activity has been described previously (Ohsugi et al., 1999; Kim et al., 1999).

2.30. *Musa sapientum: Kela (Hindi) and Banana (English)*

It is cultivated throughout India and its various parts are used for different medicinal purposes including diabetes. Intragastric administration of fresh flower decoction (4 ml/kg) to hyperglycemic rabbits significantly decreased the hyperglycemic peak and/or the area under the glucose tolerance curve (Alarcon-Aguilara et al., 1998). Oral administration of various doses (150, 200 and 250 mg/kg) of chloroform extract of *Musa sapientum* flowers for 30 days significantly reduced blood glucose and glycosylated hemoglobin and increased total hemoglobin in alloxanized rats (150 mg/kg IP). The effect was highly significant at the dose of 250 mg/kg (Pari and Maheswari, 1999). Anti-oxidant activity (Pari and Maheswari, 2000) and hypolipidemic activity has also been described (Horigome et al., 1992).

2.31. *Mucuna pruriens: Kavach (Hindi) and Cowitch (English)*

It is a twinning herb found all over tropical parts of India. It has been reported to be anti-diabetic (Dhawan et al., 1980). Feeding of *Mucuna pruriens* seed diet (96.5 gm seed powder per 100 gm of the total constituents) for 1 week to normal albino rat showed 39 and 61% reduction in fasting blood glucose and cholesterol level, respectively (Pant et al., 1968). Administration of powdered seeds (0.5, 1 and 2 g/kg) significantly decreased the blood glucose levels of normal rabbits while 1 and 2 g/kg caused a significant fall in alloxan-diabetic rabbits. Hypoglycemic principles of *M. pruriens* seeds may be both organic and mineral, which seem to act indirectly by stimulating the release of insulin and/or by a direct insulin-like action (Akhtar et al., 1990).

2.32. *Murraya koeingii*

Kurry patta (Hindi) and curry leaf tree (English). It is cultivated for its aromatic leaves and used extensively as a flavoring agent in curries and chutneys in India. Oral feeding of *Murraya koeingii* leaves diet (10% w/w) for 60 days to normal rats showed hypoglycemic effect associated with increased hepatic glycogen content due to increased glycogenesis and decreased glycogenolysis and gluconeogenesis (Khan et al., 1995). Dietary supplement with curry leaves has been shown to increase lecithin cholesterol acyl transferase activity activity (Khan et al., 1996a).

Curry leaves powder supplementation (12 g providing 2.5 g fiber) for a period of 1 month in 30 NIDDM patients showed reduction in fasting and post-prandial blood sugar levels at 15-day period with no significant changes in serum glycosylated protein levels, glycosylated low density lipoprotein cholesterol fraction, serum lipids, lipoprotein cholesterol levels, uronic acid and total amino acids (Iyer and Mani, 1990).

2.33. *Nelumbo nucifera: Kamal (Hindi) and Lotus (English)*

An aquatic herb found throughout India, up to an altitude of 1.800 m. Oral administration of ethanolic extract of *Nelumbo nucifera* rhizome (400 mg/kg) significantly reduced the blood sugar level of normal, glucose fed hyperglycemic and STZ induced diabetic rats after 1 h. The extract also improved glucose tolerance and potentiated the action of exogenously injected insulin. The activity of extract was 73 and 67% of that of tolbutamide in normal and diabetic rats, respectively (Mukherjee et al., 1997). Hypolipidemic activity has been described (La Cour et al., 1995).

2.34. *Ocimum sanctum: Tulsi (Hindi) and Holy basil (English)*

A herb found throughout India, up to an altitude of 1.800 m. in the Himalayas and its cultivated in temples and gardens. Dhar et al. (1968) reported hypoglycemic effect of ethanolic extract (50%) of leaves. The ethanol (70%) leaves extract of *Ocimum sanctum* has been shown to cause significant reduction of blood glucose level in normal, glucose fed hyperglycemic and STZ (50 mg/kg IP) induced diabetic rats. This effect was 91.55 and 70.43% of that of tolbutamide in normal and diabetic rats, respectively, (Chattopadhyay, 1993). Diet containing leaf powder (1%) fed to normal and diabetic rats for 1 month significantly reduced fasting blood sugar, uronic acid, total amino acids, total cholesterol, triglycerides and total lipids (Rai et al., 1997). The plant has also demonstrated anti-oxidant (Kelm et al., 2000) and hypolipidemic effect (Sarkar et al., 1994).

Results of a randomized, placebo-controlled, cross-over, single blind clinical trial of leaf extract of *O. album* showed significant decrease in fasting, post-prandial blood levels and mean total cholesterol levels in treated subjects as compared to controls (Agrawal et al., 1996).

2.35. *Picrorrhiza kurroa: Kutki (Hindi)*

It is small herb found in the Himalayan region from Kashmir to Sikkim. Alcoholic extract of *Picrorrhiza kurroa* (75 mg extract/kg) reduced serum glucose that was maximum 2 h after the dose. It also showed anti-hyperglycemic effect in alloxanized diabetic rats. Serum glucose decreased by 43 and 60% with 75 and 150 mg/kg of the extracts, respectively (Joy and Kuttan, 1999). Anti-oxidant activity is also described in the literature (Joy and Kuttan, 1999).

2.36. *Phyllanthus niruri: Jangli Amla (Hindi)*

It is used traditionally in management of dropsy and other ailments and has been mentioned in Ayurveda as a potential diuretic, hypotensive and hypoglycemic drug. In a clinical observation, oral administration of a preparation of the whole plant of *P. amarus* (syn. *Phyllanthus niruri*) (5 gm/day in divided doses) for 10 days to 9 mild hypertensives (4 with DM) reduces blood glucose (5–50 mg) in diabetic as well as non-diabetic subjects along with significant reduction in systolic blood pressure No harmful side effects were noted in this study (Srividya and Periwal, 1995).

2.37. *Pterocarpus marsupium: Vijayasar or Bijasal (Hindi) and Indian Malabar (English)*

A moderate to large tree commonly found in hilly region throughout India. Numerous studies conducted by various authors have shown hypoglycemic activity of the wood extract in different animal models (Gupta, 1963; Trivedi, 1963; Shah, 1967; Saifi et al., 1971). Pterostilbene (a constituent derived from wood of *Pterocarpus marsupium*) caused hypoglycemia in dogs (at the dose of 10 mg/kg IV). Higher dose (20, 30 and 50 mg/kg) caused initial hyperglycemia followed by hypoglycemia lasting for nearly 5 h (Haranath et al., 1958). Joglekar et al. (1959) associated its hypoglycemic effect to the presence of tannates in the extract. Oral administration of the bark decoction (1 gm/100 gm body weight for 10 days) showed a hypoglycemic action in alloxanized diabetic rats (Pandey and Sharma, 1976). Chronic administration of the infusion of the wood powder for 5 days inhibited the rise in blood glucose level in rats after glucose loading (Khandre et al., 1983). Flavonoid fraction of *P. marsupium* has been shown to cause pancreatic beta cell regranulation and may explain the anti-diabetic mechanism of the plant (Chakravarthy et al., 1980). Epicatechin, a pure flavonoid isolated from the ethanol extract of *P. marsupium* bark has also been shown to possess significant anti-diabetic effect (Chakravarthy et al., 1982b,a; Sheehan et al., 1983). Epicatechin has been shown to enhance insulin release and conversion of proinsulin to insulin in vitro (Sheehan et al., 1983). Phenolic constituents such as marsupin and pterostilbene significantly lowered blood glucose level in STZ diabetic rats and the effect was comparable to metformin (Manickam et al., 1997). Hypolipidemic effect has also been described (Jahromi and Ray, 1993).

An Indian open multicentric study assessing Vijayasar in the treatment of newly-diagnosed or untreated NIDDM showed that the extract controlled fasting and post-prandial blood glucose levels in 67 out of 97 patients (69%) by the 12th week at the dose of 2, 3 and 4 g in 73, 16 and 10% patients, respectively. Four patients were withdrawn from treatment due to excessively high post-prandial blood glucose levels. No significant change was observed in the mean levels of lipids. Other laboratory parameters remained stable during the designated treatment period of 12 week (ICMR, 1998).

2.38. *Punica granatum: Anar (Hindi) and Pomegranate (English)*

A shrub or small tree grows wild in the warm valleys and outer hills of the Himalayas and also cultivated throughout India. The flowers of *Punica granatum* are used as anti-diabetic in Unani medicine called Gulnar farsi. Oral administration of aqueous-ethanolic extract (50% v/v) led to significant blood glucose lowering effect in glucose fed hyperglycemic and alloxanized diabetic rats with the maximum effect at the dose of 400-mg/kg-body weight (Jafri et al., 2000). Anti-oxidant activity has been described in the literature (Schubert et al., 1999).

2.39. *Salacia reticulata: Vairi or Pitica (Vernacular)*

It is found throughout in the forest region of India. Oral administration of aqueous decoction (1 ml/rat/day) of *Salacia reticulata* root bark to over night fasted rats caused 30% reduction in glucose levels at 3 h (Karunanayake et al., 1984). Potent natural α-glycosidase inhibitors such as kotalanol and salacinol isolated from the roots and stems of the plant exert potent inhibitory activity against sucrase (Yoshikawa et al., 1998).

2.40. *Salacia oblonga: Ponkoranti (Vernacular)*

Aqueous extract of the root bark has shown hypoglycemic activity (Karunanayake et al., 1984). Two biologically active fractions from the petroleum ether extract of the root bark has been shown to exert hypoglycemic effect of about 60 and 76% potency of an equal dose of tolbutamide (250 mg/kg) in albino rats (Augusti et al., 1995). Petroleum ether extract of the bark of the root has been shown to prevent STZ (65 mg/kg) induced hyperglycemia and hypoinsulinemia in rats. The aqueous-methanolic extract of the roots inhibited increase in serum glucose level in sucrose and maltose loaded rats. The water-soluble and ethyl acetate soluble portions of the same extract showed inhibitory activities on alpha-glucosidase and aldose reductase (Matsuda et al., 1999). Further, salacinol and kotalanol with nine other sugar related component were isolated from the water soluble portion while, a new triterpene, kotalagenin 16-acetate along with known diterpene and triterpenes isolated from the ethyl acetate portion were found to be responsible component for the inhibitory activity on aldolase reductase (Matsuda et al., 1999). In addition, the extract has shown significant anti-oxidant activity (Krishnakumar et al., 1999).

2.41. *Swertia chirayita: Chirata (Hindi)*

It is mainly found in temperate Himalayas between the height of 1200 and 1300 m. Various crude extracts and its isolated fractions have shown hypoglycemic activity in various animal models. Oral administration of ethanolic extracts (95%) and hexane fraction of *Swertia chirayita* (10, 50 and 100 mg/kg) to normal, glucose fed and STZ induced diabetic rats significantly lowered blood glucose in all groups of animals. Out of 95% ethanol extract and its four fractions (each 250 mg/kg) tested in fasted, fed, glucose-loaded and tolbutamide-pretreated animal models, hexane fraction caused a maximum lowering of blood sugar in all but fasted rats (Sekar et al., 1987). Single oral dose of the plant's hexane fraction (250 mg/kg) to normal rats significantly reduced blood sugar and increased plasma IRI simultaneously without influencing hepatic glycogen content. However, when administered for 28 days, it significantly increased hepatic glycogen content in conjunction with other effects probably by releasing insulin (Chandrasekar et al., 1990). In a study, Swerchirin (a xanthone isolated from hexane fraction of the plant) showed significant blood sugar lowering effect in fasted, glucose loaded and tolbutamide pre-treated albino rats. Oral ED50 of Swerchirin for 40% blood sugar reduction in male albino rats is 23.1 mg/kg (Bajpai et al., 1991). Force feeding of Swerchirin (35 and 65 mg/kg IV) to STZ diabetic rats (50 mg/kg) showed significant anti-hyperglycemic effect at 0, 1, 3 and 7 h after the dose both in healthy as well as STZ rats (35 mg/kg) but not in the group treated with STZ (65 mg/kg) (Saxena et al., 1991). Single oral administration of Swerchirin (50 mg/kg) to rats caused a 60% fall in blood glucose at 7 h post-treatment with marked depletion of aldehyde-fuchsin stained beta-granules and immunostained insulin in the pancreatic islets. In vitro, glucose uptake and glycogen synthesis by muscle (diaphragm) was significantly enhanced by the serum of Swerchirin-treated rat. Swerchirin at 100, 10 and 1 μM concentration greatly enhanced glucose (16.7 mM) stimulated insulin release from isolated islets (Saxena et al., 1993).

2.42. *Syzigium cumini (Eugenia jambolana): Jamun (Hindi) and Black Berry (English)*

It is widely distributed throughout India and Indian folk medicine mentions its use for the treatment of DM (Chopra et al., 1958; Nandkarni, 1992). Preliminary studies on *Syzigium cumini* seeds have also shown hypoglycemic effect (Mahapatra et al., 1985). Decoction of dry leaves of *S. cumini* has shown hypoglycemic effect (Coimbra et al., 1992). Oral feeding of *Eugenia jambolana* (170, 240 and 510 mg/rat for 15 days) caused 50% reduction in blood glucose of normal fasted rats while chlorpropamide showed 52% reduction. In addition, there was a 2.4–6.8-fold and 9.2-fold increase in cathepsin B activity (proteolytic conversion of proinsulin to insulin) by plant extract and chlorpropamide, respectively, (Bansal et al., 1981). Oral administration of pulp extract of the fruit of *S. cumini* to normoglycemic and STZ induced diabetic rats showed hypoglycemic activity in 30 min possibly mediated by insulin secretion. In addition, the extract inhibited insulinase activity from liver and kidney (Achrekar et al., 1991). Oral administration of dried alcoholic extract of the seeds caused hypoglycemia and reduced glycosuria (Indira and Mohan Ram, 1992). Oral administration of the aqueous extract of seeds of *S. cumini* (2.5 and 5.0 gm/kg for 6 weeks) showed hypoglycemic (> glibenclamide) and anti-oxidant activity. The hypoglycemic effect was most prominent at the dose of 5.0 gm/kg while no significant effect was observed at 7.5 gm/kg dose (Prince et al., 1998). Daily administration of lyophilized powder of *E. jambolana* (200 mg/kg) showed maximum reduction of 73.51, 55.62 and 48.81 as compared to their basal values in mild (plasma sugar > 180 mg/dl, duration 21 days), moderate (plasma sugar > 280 mg/dl, duration 120 days) and severe (plasma sugar > 400 mg/dl, duration 60 days) diabetic rats. In addition, the treatment also partially restored altered hepatic and skeletal muscle glycogen content and hepatic glucokinase, hexokinase, glucose-6-phosphate and phosphofructokinase levels (Grover et al., 2000).

2.43. *Trigonella foenum graecum: Methi or Mutti (Hindi) and Fenugreek (English)*

It is found as a wild plant and also cultivated in Northern India. The hypoglycemic effect of fenugreek seeds has been demonstrated in experimentally induced diabetic rats, dogs, mice and healthy volunteers (both IDDM and NIDDM) (Ribes et al., 1984; Riyad et al., 1988; Alarcon-Aguilara et al., 1998).

Isolated fibers, saponins and other proteins from fenugreek seeds given with meals for 21 day to alloxan-diabetic dogs showed significant anti-hyperglycemic and anti-glycosuric effect along with reduction in high plasma glucagon and somatostatin (Ribes et al., 1986). Oral administration of 2 and 8 g/kg of plant extract produced dose-dependent fall ($P < 0.05$) in blood glucose both in the normal as well as diabetic rats (Khosla et al., 1995). 4-hydroxyisoleucine, a novel amino acid has been extracted and purified from fenugreek seeds. It increased glucose-induced insulin release (ranging from 100 μmol/l to 1 mmol/l) through a direct effect on the isolated islets of Langerhans in both rats and humans. This pattern of insulin secretion was biphasic, glucose dependent, occurred in the absence of any change in pancreatic alpha and delta cell activity and without interaction with other agonists of insulin secretion (such as leucine, arginine, tolbutamide, glycer-

aldehyde) (Sauvaire et al., 1998). Oral administration of aqueous leaf extract (0.06, 0.2, 0.5, 1 g/kg, i.p. and 1, 2, 8 g/kg PO) to normal and alloxanized diabetic rats showed significant hypoglycemic and anti-hyperglycemic effect while (50%) ethanolic extract significantly reduced blood glucose concentration ($P < 0.02$) at 2 and 24 h when given i.p. (0.8 g/kg) (Abdel-Barry et al., 1997). Seed powder normalized the altered creatinine kinase activity in heart, skeletal muscle and liver of diabetic rats to almost control values (Genet et al., 1999). It also normalized alteration in hepatic and renal glucose-6-phosphatase and fructose-1,6-bisphosphatase activity (Gupta et al., 1999). Anti-oxidant (Ravikumar and Anuradha, 1999) and hypocholesterolemic activity (Stark and Madar, 1993) is described in the literature.

In a clinical trial administration of fenugreek seed powder (50 gm each with lunch and dinner) in insulin-dependent (Type I) diabetic patients for 10 days significantly reduces fasting blood sugar and improved OGTT along with 54% reduction in glycosuria. In addition, it also showed significant hypolipidemic effect (Sharma et al., 1990).

2.44. *Tinospora cordifolia: Amarta or Guduci (Hindi)*

It is found in forests throughout India and is widely used in Ayurveda as tonic, vitalizer and as a remedy for DM and metabolic disorders (Nandkarni, 1954; Chopra et al., 1958). Oral administration of 400 mg/kg of aqueous extract of TC for 15 weeks of treatment showed maximum hypoglycemia of 70.37, 48.81 and 0% in mild (plasma sugar $>$ 180 mg/dl), moderate (plasma sugar $>$ 280 mg/dl) and severe (plasma sugar $>$ 400 mg/dl) diabetic rats, respectively. Hypoglycemic effect depended upon the functional status of the pancreatic beta cells (Grover et al., 2000). Oral administration of the water extract of *Tinospora cordifolia* root (2.5, 5 and 7.5 mg/kg) caused a significant reduction in blood glucose, brain lipid level, hepatic glucose-6-phosphatase, serum acid phosphatase, alkaline and lactate dehydrogenase and increase in body weight, total hemoglobin and hepatic hexokinase in alloxanized diabetic rats (150 mg/kg, IP) (Stanely et al., 2000). Anti-oxidant (Prince and Menon, 1999) and hypolipidemic activity is described (Stanely et al., 1999).

2.45. *Vinca rosea (Catharanthus roseus): Sadabahar (Hindi) and Madagascar periwinkle (English)*

It is found throughout India in wastelands and is also cultivated. Oral administration of water-soluble fraction of ethanolic extract of *Vinca rosea* leaves (100, 250, 500 and 1000 mg/kg) showed significant dose-dependent reduction in blood sugar at 4 h by 26.22, 31.39, 35.57 and 33.37%, respectively, in normal rats. In addition, oral administration of 500 mg/kg 3.5 h before OGTT (10 gm/kg) and 72 h after STZ administration (50 mg/kg IP) in rats showed significant anti-hyperglycemic effects. No gross behavioral changes and toxic effect were observed up to 4 gm/kg IP (Chattopadhyay et al., 1991).

3. Conclusion

Due to economic constraints, providing modern medical healthcare in developing countries such as India is still a far-reaching goal. The most commonly used drugs of modern medicine such as aspirin, anti-malarials, anti-cancers, digitalis, etc. have originated from plant sources. Out of an estimated 250 000 higher plants, less than 1% have been screened pharmacologically and very few in regard to DM. Therefore, it is prudent to look for options in herbal medicine for diabetes as well. We have been working continuously towards establishing the scientific basis of use of certain plants in DM. We have previously shown that *M. charantia* and *E. jambolana* are very effective in controlling glucose levels in chemically induced mild to severe model of DM in rodents and seem to work by stimulating kinases involved in peripheral utilization of glucose (Grover et al., 2000; Rathi et al., in press a). In addition, both these plants have shown excellent positive outcomes in respect to diabetic complications such as diabetic nephropathy (Grover et al., 2001), fructose induced insulin resistance (Vats et al., 2001) and cataract (Rathi et al., in press b). The 2 plants also partially prevented diabetic neuropathy (Grover et al., 2002). Recently we have taken up work in assessing the efficacy of *Trigonella foenum graecum*, *O. sanctum*, *P. marsupium*, *M. koeingii* and *B. juncea* in DM and its related complications. Although all these plants have shown varying degree of hypoglycemic and anti-hyperglycemic activity (Vats et al., 2002), not all (notably *M. pruriens*, *T. cordifolia*, *M. koeingii* and *B. juncea*) were effective in severe experimental diabetes and its related complications. A novel anti-hyperglycemic amino acid has been extracted and purified from Fenugreek seeds (4-hydroxyleucine) which reportedly increases glucose-induced insulin release. *A. vera* has been shown to improve wound healing in STZ diabetic mice (Davis and Maro, 1989; Chithra et al., 1998) and *A. sativum* prevented diabetic cardiovascular complications (Patumraj et al., 2000). The apparent benefit of drinking water in the glass made out of the bark of Vijayasar by diabetic patients have been proven to be true by an Indian open multicentric study. Results of this study showed that the Vijayasar extract could control fasting and post-prandial blood glucose levels in 69% of patients ($n = 97$) (ICMR, 1998). Such an ethnomedical approach for diabetes is a practical, cost-effective and a logical for its treatment. The goals of medicine no matter to which group it belongs, are the same i.e. the welfare of the patient. One can look

towards a future of integrated medicine and hope that research in alternative medicine will help identify what is safe and effective rather than marginalising, unorthodox medical claims and findings.

References

Abdel-Barry, J.A., Abdel-Hassan, I.A., Al-Hakiem, M.H. 1997. Hypoglycemic and antihyperglycemic effects of *Trigonella foenum-graecum* leaf in normal and alloxan induced diabetic rats. Journal of Ethnopharmacology 58 (3), 149–155.

Abdel-Hassan, I.A., Abdel-Barry, J.A., Tariq Mohammeda, S. 2000. The hypoglycemic and antihyperglycemic effect of *Citrullus colocynthis* fruit aqueous extract in normal and alloxan diabetic rabbits. Journal of Ethnopharmacology 71 (1–2), 325–330.

Achrekar, S., Kaklij, G.S., Pote, M.S., Kelkar, S.M. 1991. Hypoglycemic activity of *Eugenia jambolana* and *Ficus bengalenesis*: mechanism of action. In Vivo 5 (2), 143–147.

ADA, 1997. Clinical practice recommendation 1997, Screening for diabetes. Diabetes care 20(1), 22-24.

Aderibigbe, A.O., Emudianughe, T.S., Lawal, B.A. 1999. Antihyperglycemic effect of *Mangifera indica* in rat. Phytotherapy Research 13 (6), 504–507.

Agarwal, V., Chauhan, B.M. 1988. A study on composition and hypolipidemic effect of dietary fibre from some plant foods. Plant Foods and Human Nutrition 38 (2), 189–197.

Agrawal, P., Rai, V., Singh, R.B. 1996. Randomized placebo-controlled, single blind trial of holy basil leaves in-patients with non insulin-dependent diabetes mellitus. International Journal of Clinical Pharmacology and Therapy 34 (9), 406–409.

Ahmad, N., Hassan, M.R., Halder, H., Bennoor, K.S. 1999. Effect of *Momordica charantia* (Karella) extracts on fasting and postprandial serum glucose levels in NIDDM patients. Bangladesh Medical Research Council Bulletin 25 (1), 11–13.

Ahmed, I., Adeghate, E., Sharma, A.K., Pallot, D.J., Singh 1998. Effects of *Momordica charantia* fruit juice on islet morphology in the pancreas of the streptozotocin-diabetic rat. Diabetes Research and Clinical Practice 40 (3), 145–151.

Ajabnoor, M.A. 1990. Effect of aloes on blood glucose levels in normal and alloxan diabetic mice. Journal of Ethnopharmacology 28, 215–220.

Ajit kar, Choudhary, B.K., Bandhopadhyay, N.G. 1999. Preliminary studies on the inorganic constituents of some indigenous hypoglycemic herbs on oral glucose tolerance test. Journal of Ethnopharmacology 64, 179–184y.

Akhtar, M.S., Qureshi, A.Q., Iqbal, J. 1990. Antidiabetic evaluation of *Mucuna pruriens*, Linn. seeds. The Journal of Pakistan Medical Association 40 (7), 147–150.

Alarcon-Aguilara, F.J., Roman-Ramos, R., Perez-Gutierrez, S., Aguilar-Contreras, A., Contreras-Weber, C.C., Flores-Saenz, J.L. 1998. Study of the anti-hyperglycemic effect of plants used as antidiabetics. Journal of Ethnopharmacology 61 (2), 101–110.

Al-Awadi, F.M., Gumaa, K.A. 1987. Studies on the activity of individual plants of an antidiabetic plant mixture. Acta Diabetologica Latina 24, 37–41.

Ali, L., Khan, A.K., Mamun, M.I., Mosihuzzaman, M., Nahar, N., Nur-e-Alam, M., Rokeya, B. 1993. Studies on hypoglycemic effects of fruit pulp, seed and whole plant of *Momordica charantia* on normal and diabetic model rats. Planta Medica 59 (5), 408–412.

Amalraj, T., Ignacimuthu, S. 1998a. Hypoglycemic activity of *Cajanus cajan* (seeds) in mice. Indian Journal of Experimental Biology 36, 1032–1033.

Amalraj, T., Ignacimuthu, S. 1998b. Evaluation of the hypoglycemic effect of *Memecylon umbellatum* in normal and alloxan diabetic mice. Journal of Ethnopharmacology 62 (3), 247–250.

Arai, I., Amagaya, S., Komatsu, Y., Okada, M., Hayashi, T., Kasai, M., Arisawa, M., Momose, Y. 1999. Improving effects of the extracts from *Eugenia uniflora* on hyperglycemia and hypertriglyceridemia in mice. Journal of Ethnopharmacology 68 (1–3), 307–314.

Asano, N., Oseki, K., Tomioka, E., Kizu, H., Matsui, K. 1994. N-containing sugars from *Morus alba* and their glycosidase inhibitory activities. Carbohydrate Research 259 (2), 243–255.

Augusti, K.T. 1973. Studies on the effects of a hypoglycemic principle from *Allium Cepa* Linn. Indian Journal of Medical Research 61 (7), 1066–1071.

Augusti, K.T., Mathew, P.T. 1973. Effect of long term feeding of the aqueous extracts of Onion (*Allium cepa* Linn.) and garlic (*Allium sativum* Linn.) on normal rats. Indian Journal of Experimental Biology 11, 239–241.

Augusti, K.T. 1975. Hypoglycemic action of bengalenoside, a glucoside isolated from *Ficus bengalenesis* Linn., in normal and alloxan diabetic rabbits. Indian Journal of Physiology and Pharmacology 19 (4), 218–220.

Augusti, K.T., Daniel, R.S., Cherian, S., Sheela, C.G., Nair, C.R. 1994. Effect of leucopelargonin derivative from *Ficus bengalenesis* Linn. on diabetic dogs. Indian Journal of Medical Research 99, 82–86.

Augusti, K.T., Joseph, P., Babu, T.D. 1995. Biologically active principles isolated from *Salacia oblonga* wall. Indian Journal of Physiology and Pharmacology 39 (4), 415–417.

Augusti, K.T., Shella, C.G. 1996. Antiperoxide effect of *S*-allyl cysteine sulfoxide, an insulin secretagogue, in diabetic rats. Experientia 52, 115–120.

Azad Khan, A.K., Akhtar, S., Mahtab, H. 1979. *Coccinia indica* in the treatment of patients with diabetes mellitus. Bangladesh Medical Research Council Bulletin 5 (2), 60–66.

Babu, P.S., Srinivasan, K. 1997. Influence of dietary capsaicin and onion on the metabolic abnormalities associated with streptozotocin induced diabetes mellitus. Molecular and Cellular Biochemistry 175 (1–2), 49–57.

Bailey, C.J., Day, C. 1989. Traditional plant medicines as treatment for diabetes. Diabetes Care 12, 553–564.

Bailey, C.J., Day, C., Turner, S.L., Leatherdale, B.A. 1985. Cerasee, a traditional treatment for diabetes. Studies in normal and streptozotocin diabetic mice. Diabetes Research 2 (2), 81–84.

Bajpai, M.B., Asthana, R.K., Sharma, N.K., Chatterjee, S.K., Mukherjee, S.K. 1991. Hypoglycemic effect of Swerchirin from the hexane fraction of *Swertia chirayita*. Planta Medica 57 (2), 102–104.

Bansal, R., Ahmad, N., Kidwai, J.R. 1981. Effects of oral administration of *Eugenia jambolana* seeds and chloropropamide on blood glucose level and pancreatic cathepsin B in rat. Indian Journal of Biochemistry and Biophysics 18 (5), 377.

Baskaran, K., Kizar Ahamath, B., Radha Shanmugasundaram, K., Shanmugasundaram, E.R. 1990. Antidiabetic effect of a leaf extract from *Gymnema sylvestre* in non-insulin-dependent diabetes mellitus patients. Journal of Ethnopharmacology 30 (3), 295–300.

Cakici, I., Hurmoglu, C., Tunctan, B., Abacioglu, N., Kanzik, I., Sener, B. 1994. Hypoglycemic effect of *Momordica charantia* extracts in normoglycemic or cyproheptadine-induced hyperglycemic mice. Journal of Ethnopharmacology 44 (2), 117–121.

Chakravarthy, B.K., Gupta, S., Gambhir, S.S., Gode, K.D. 1980. Pancreatic beta cell regeneration. A novel antidiabetic mechanism of *Pterocarpus marsupium* Roxb. Indian Journal of Pharmacology 12, 123–127.

Chakravarthy, B.K., Gupta, S., Gode, K.D. 1982a. Functional beta-cell regeneration in the islets of pancreas in alloxan induced diabetic rats by (−) epicatechin. Life Science 31, 2693–2697.

Chakravarthy, B.K., Gupta, S., Gode, K.D. 1982b. Antidiabetic effect of (−) epicatechin. Lancet 2, 272–273.

Chandrasekar, B., Mukherjee, B., Mukherjee, S.K. 1989. Blood sugar lowering potentiality of selected Cucurbitaceae plants of Indian origin. Indian Journal of Medical Research 90, 300–305.

Chandrasekar, B., Bajpai, M.B., Mukherjee, S.K. 1990. Hypoglycemic activity of *Swertia chirayita* (Roxb ex Flem) Karst. Indian Journal of Experimental Biology 28 (7), 616–618.

Chattopadhyay, R.R., Sarkar, S.K., Ganguly, S., Banerjee, R.N., Basu, T.K. 1991. Hypoglycemic and antihyperglycemic effect of leaves of *Vinca rosea* Linn. Indian Journal of Physiology and Pharmacology 35 (3), 145–151.

Chattopadhyay, R.R. 1993. Hypoglycemic effect of *Ocimum sanctum* leaf extract in normal and streptozotocin diabetic rats. Indian Journal of Experimental Biology 31 (11), 891–893.

Chattopadhyay, R.R. 1996. Possible mechanism of antihyperglycemic effect of *Azadirachta indica* leaf extract. Part IV. General Pharmacology 27 (3), 431–434.

Chattopadhyay, R.R. 1998. Possible mechanism of antihyperglycemic effect of *Gymnema sylvestre* leaf extract, part I. General Pharmacology 31 (3), 495–496.

Chattopadhyay, R.R. 1999. A comparative evaluation of some blood sugar lowering agents of plant origin. Journal of Ethnopharmacology 67 (3), 367–372.

Chattopadhyay, R.R., Chattopadhyay, R.N., Nandy, A.K., Poddar, G., Maitra, S.K. 1987a. Preliminary report on antihyperglycemic effect of a fraction of fresh leaves of *Azadirachta indica* (Beng. Neem). Bulletin of the Calcutta School of Tropical Medicine 35, 29–33.

Chattopadhyay, R.R., Chattopadhyay, R.N., Nandy, A.K., Poddar, G., Maitra, S.K. 1987b. The effect of fresh leaves of *Azadirachta indica* on glucose uptake and glycogen content in the isolated rat hemi diaphragm. Bulletin of the Calcutta School of Tropical Medicine 35, 8–12.

Chempakam, B. 1993. Hypoglycemic activity of arecoline in betel nut *Areca catechu* L. Indian Journal of Experimental Biology 31 (5), 474–475.

Chen, F., Nakashima, N., Kimura, I., Kimura, M. 1995. Hypoglycemic activity and mechanisms of extracts from mulberry leaves (folium mori) and cortex mori radicis in streptozotocin-induced diabetic mice. Yakugaku Zasshi 115 (6), 476–482.

Cherian, S., Kumar, R.V., Augusti, K.T., Kidwai, J.R. 1992. Antidiabetic effect of a glycoside of pelargonidin isolated from the bark of *Ficus bengalenesis* Linn. Indian Journal of Biochemistry and Biophysics 29 (4), 380–382.

Cherian, S., Augusti, K.T. 1993. Antidiabetic effects of a glycoside of leucopelargonidin isolated from *Ficus bengalenesis* Linn. Indian Journal of Experimental Biology 31 (1), 26–29.

Chithra, P., Sajithlal, G.B., Chandrakasan, G. 1998. Influence of *Aloe vera* on the healing of dermal wounds in diabetic rats. Journal of Ethnopharmacology 59, 195–201.

Chopra, R.N., Nayar, S.L., Chopra, I.C., 1956. Glossary of Indian Medicinal Plants. CSIR, New Delhi.

Chopra, R.N., Chopra, I.C., Handa, K.L., Kapur, L.D., 1958. Indigenous Drugs of India, second ed., UN Dhar and sons Pvt. Ltd, Calcutta.

Coimbra, T.C., Danni, F.F., Blotta, R.M., da Periara, C.A., Guedes, M.D., Graf, R.G. 1992. Plants employed in the treatment of diabetes mellitus; results of an ethnopharmacological survey in Porto Alegre, Brazil. Fitoterapia 63 (4), 320–322.

Daniel, R.S., Mathew, B.C., Devi, K.S., Augusti, K.T. 1998. Antioxidant effect of two flavonoids from the bark of *Ficus bengalenesis* Linn. in hyperlipidemic rats. Indian Journal of Experimental Biology 36 (9), 902–906.

Das, A.V., Padayatti, P.S., Paulose, C.S. 1996. Effect of leaf extract of *Aegle marmelose* (L.) Correa ex Roxb. on histological and ultrastructural changes in tissues of streptozotocin induced diabetic rats. Indian Journal of Experimental Biology 34 (4), 341–345.

Davis, R.H., Maro, N.P. 1989. *Aloe vera* and *gibberellin*. Anti-inflammatory activity in diabetes. Journal of American Pediatric Medical Association 79, 24–26.

Day, C., Cartwright, T., Provost, J., Bailey, C.J., Karunanayake, E.H., Welihinda, J., Sirimanne, S.R., Sinnadorai, G. 1984. Oral hypoglycemic activity of some medicinal plants of Sri Lanka. Journal of Ethnopharmacology 11 (2), 223–231.

Dhar, M.L., Dhar, M.M., Dhawan, B.N., Mehrotra, B.N., Ray, C. 1968. Screening of Indian plants for biological activity. Indian Journal of Experimental Biology 6 (4), 232–247.

Dhar, P., Ghosh, S., Bhattacharyya, D.K. 1999. Dietary effects of conjugated octadecatrienoic fatty acid (9 *cis*, 11 *trans*, 13 *trans*) levels on blood lipids and nonenzymatic in vitro lipid peroxidation in rats. Lipids 34 (2), 109–114.

Dhawan, B.N., Dubey, M.P., Mehrotra, B.N., Rastogi, R.P., Tandon, J.S. 1980. Screening of Indian plants for biological activity. Part 9. Indian Journal of Experimental Biology 18, 594–606.

Esposito Avella, M., Diaz, A., de Gracia, I., de Tello, R., Gupta, M.P. 1991. Evaluation of traditional medicine: effects of *Cajanus cajan* L. and of *Cassia fistula* L. on carbohydrate metabolism in mice. Revista Medica de Panama 16, 39–45.

Garg, S.K., Shah, M.A., Garg, K.M., Farooqui, M.M., Sabir, M. 1997. Antilymphocytic and immunosuppressive effects of *Lantana camara* leaves in rats. Indian Journal of Experimental Biology 35 (12), 1315–1318.

Geetha, B.S., Mathew, B.C., Augusti, K.T. 1994. Hypoglycemic effects of leucodelphinidin derivative isolated from *Ficus bengalenesis* (Linn.). Indian Journal of Physiology and Pharmacology 38 (3), 220–222.

Genet, S., Kale, R.K., Baquer, N.Z. 1999. Effects of vanadate, insulin and fenugreek (*Trigonella foenum graecum*) on creatinine kinase levels in tissues of diabetic rat. Indian Journal of Experimental Biology 37 (2), 200–202.

Ghannam, N., Kingston, M., Al-Meshaal, I.A., Tariq, M., Parman, N.S., Woodhouse, N. 1986. The antidiabetic activity of aloes: preliminary clinical and experimental observations. Hormone Research 24, 288–294.

Gray, A.M., Flatt, P.R. 1998. Antihyperglycemic actions of *Eucalyptus globulus* (Eucalyptus) are associated with pancreatic and extrapancreatic effects in mice. Journal of Nutrition 128 (12), 2319–2323.

Grover, J.K., Vats, V., Rathi, S.S. 2000. Anti-hyperglycemic effect of *Eugenia jambolana* and *Tinospora cordifolia* in experimental diabetes and their effects on key metabolic enzymes involved in carbohydrate metabolism. Journal of Ethnopharmacology 73 (3), 461–470.

Grover, J.K., Vats, V. 2001. Shifting Paradigm "from conventional to alternate medicine." An introduction on traditional Indian medicine. Asia Pacific Biotechnology News 5 (1), 28–32.

Grover, J.K., Vats, V., Rathi, S.S., Dawar, R. 2001. Traditional Indian anti-diabetic plants attenuate renal hypertrophy, urine volume and albuminuria in streptozotocin induced diabetic mice. Journal of Ethnopharmacology 76 (3), 233–238.

Grover, J.K., Rathi, S.S., Vats, V. 2002. Amelioration of experimental diabetic neuropathy and gastropathy in rats following oral administration of plant extracts. Indian Journal of Experimental Biology, 40 (3) 273–276.

Gulubova, R., Boiadzhiev, T.S. 1975. Morphological changes in the endocrine pancreas of the rabbit after the administration of a *Morus alba* extract. Eksperimentalna meditsina i morfologiia 14 (3), 166–171.

Gupta, D., Raju, J., Baquer, N.Z. 1999. Modulation of some gluconeogenic enzyme activities in diabetic rat liver and kidney: effect of antidiabetic compounds. Indian Journal of Experimental Biology 37 (2), 196–199.

Gupta, R.K., Gupta, S., Samuel, K.C. 1977. Blood sugar lowering effect of various fractions of onion. Indian Journal of Experimental Biology 15 (4), 313–314.

Gupta, S.S. 1963. Effect of *Gymnema sylvestre* and *Pterocarpus marsupium* on glucose tolerance in albino rats. Indian Journal of Medical Research 51, 716–724.

Gupta, S.S., Seth, C.B. 1962. Effect of *Momordica charantia* Linn. (Karela) on glucose tolerance in albino rats. Journal of Indian Medical Association 39, 581–584.

Haranath, P.S.R.K., Ranganatharao, K., Anjaneyulu, C.R., Ramanathan, J.D. 1958. Studies on the hypoglycemic and pharmacological actions of some stilbenes. Indian Journal of Medical Science 12, 85–89.

Horigome, T., Sakaguchi, E., Kishimoto, C. 1992. Hypocholesterolemic effect of banana (*Musa sapientum* L. var. Cavendishii) pulp in the rat fed on a cholesterol-containing diet. British Journal of Nutrition 68 (1), 231–244.

Hossain, M.Z., Shibib, B.A., Rahman, R. 1992. Hypoglycemic effects of *Coccinia indica*: inhibition of key gluconeogenic enzyme, glucose-6-phosphatase. Indian Journal of Experimental Biology 30 (5), 418–420.

Indian Council of Medical Research (ICMR) Collaborating Centres, New Delhi, 1998. Flexible dose open trial of Vijayasar in cases of newly diagnosed non-insulin-dependent diabetes mellitus. Indian Journal of Medical Research (108), 24–29.

Indira, G., Mohan Ram, M., 1992. Fruits, National Institute of Nutrition, Indian council of Medical Research, Hyderabad, India, pp. 34–37.

Ivorra, M.D., Paya, M., Villar, A. 1988. Hypoglycemic and insulin release effect of tormentic acid: a new hypoglycemic natural product. Planta Medica 54, 282–286.

Iyer, U.M., Mani, U.V. 1990. Studies on the effect of curry leaves supplementation (*Murraya koeingii*) on lipid profile, glycated proteins and amino acids in non-insulin-dependent diabetic patients. Plant Foods and Human Nutrition 40 (4), 275–282.

Jafri, M.A., Aslam, M., Javed, K., Singh, S. 2000. Effect of *Punica granatum* Linn. (flowers) on blood glucose level in normal and alloxan-induced diabetic rats. Journal of Ethnopharmacology 70 (3), 309–314.

Jahromi, M.A., Ray, A.B. 1993. Antihyperlipidemic effect of flavonoids from *Pterocarpus marsupium*. Journal of Natural Products 56 (7), 989–994.

Jain, R.C., Vyas, C.R. 1974. Letter: hypoglycemia action of onion on rabbits. British Medical Journal 2 (921), 730.

Jain, R.C., Vyas, C.R. 1975. Garlic in alloxan-induced diabetic rabbits. American Journal of Clinical Nutrition 28, 684–685.

Jayasooriya, A.P., Sakono, M., Yukizaki, C., Kawano, M., Yamamoto, K., Fukuda, N. 2000. Effects of *Momordica charantia* powder on serum glucose levels and various lipid parameters in rats fed with cholesterol-free and cholesterol-enriched diets. Journal of Ethnopharmacology 72 (1–2), 331–336.

Joglekar, G.V., Chaudhary, N.Y., Aiaman, R. 1959. Effect of Indian medicinal plants on glucose absorption in mice. Indian Journal of Physiology and Pharmacology 3, 76–77.

Jose, M.P., Cheeran, J.V., Nair, K.P.D. 1976. Effect of selected indigenous drug on the blood sugar level in dogs. Indian Journal of Pharmacology 8, 86.

Joy, K.L., Kuttan, R. 1999. Anti-diabetic activity of *Picrorrhiza kurroa* extract. Journal of Ethnopharmacology 67 (2), 143–148.

Kamble, S.M., Kamlakar, P.L., Vaidya, S., Bambole, V.D. 1998. Influence of *Coccinia indica* on certain enzymes in glycolytic and lipolytic pathway in human diabetes. Indian Journal of Medical Science 52 (4), 143–146.

Karunanayake, E.H., Welihinda, J., Sirimanne, S.R., Sinnadorai, G. 1984. Oral hypoglycemic activity of some medicinal plants of Sri Lanka. Journal of Ethnopharmacology 11 (2), 223–231.

Karunanayake, E.H., Jeevathayaparan, S., Tennekoon, K.H. 1990. Effect of *Momordica charantia* fruit juice on streptozotocin-induced diabetes in rats. Journal of Ethnopharmacology 30 (2), 199–204.

Kasuga, S., Ushijima, M., Morihara, N., Itakura, Y., Nakata, Y. 1999. Effect of aged garlic extract (AGE) on hyperglycemia induced by immobilization stress in mice. Nippon Yakurigaku Zasshi 114, 191–197.

Kedar, P., Chakrabarti, C.H. 1982. Effects of bittergourd (*Momordica charantia*) seed and glibenclamide in streptozotocin induced diabetes mellitus. Indian Journal of Experimental Biology 20 (3), 232–235.

Kelm, M.A., Nair, M.G., Strasburg, G.M., DeWitt, D.L. 2000. Antioxidant and cyclooxygenase inhibitory phenolic compounds from *Ocimum sanctum* Linn. Phytomedicine 7 (1), 7–13.

Khan, A.K., Akhtar, S., Mahtab, H. 1980. Treatment of diabetes mellitus with *Coccinia indica*. British Medical Journal 280 (6220), 1044.

Khan, B.A., Abraham, A., Leelamma, S. 1996a. Biochemical response in rats to the addition of curry leaf (*Murraya koeingii*) and mustard seeds (*Brassica juncea*) to the diet. Plant Foods and Human Nutrition 49 (4), 295–299.

Khan, B.A., Abraham, A., Leelamma, S. 1996b. Role of *Murraya koeingii* (curry leaf) and *Brassica juncea* (Mustard) in lipid peroxidation. Indian Journal of Physiology and Pharmacology 40 (2), 155–158.

Khan, B.A., Abraham, A., Leelamma, S. 1995. Hypoglycemic action of *Murraya koeingii* (curry leaf) and *Brassica juncea* (mustard): mechanism of action. Indian Journal of Biochemistry and Biophysics 32 (2), 106–108.

Khan, B.A., Abraham, A., Leelamma, S. 1997. Anti-oxidant effects of curry leaf, *Murraya koeingii* and mustard seeds, *Brassica juncea* in rats fed with high fat diet. Indian Journal of Experimental Biology 35 (2), 148–150.

Khandre, S.S., Rajwade, G.G., Jangle, S.N. 1983. A study of the effect of bija and jamun seed extract on hyperglycaemia induced by glucose load. Maharashtra Medical Journal 30, 117.

Khanna, P., Jain, S.C., Panagariya, A., Dixit, V.P. 1981. Hypoglycemic activity of polypeptide-p from a plant source. Journal of Natural Products 44 (6), 648–655.

Khare, A.K., Tandon, R.N., Tewari, J.P. 1983. Hypoglycemic activity of an indigenous drug (*Gymnema sylvestre*, 'Gurmar') in normal and diabetic persons. Indian Journal of Physiology and Pharmacology 27 (3), 257–258.

Khosla, P., Gupta, D.D., Nagpal, R.K. 1995. Effect of *Trigonella foenum graecum* (Fenugreek) on blood glucose in normal and diabetic rats. Indian Journal of Physiology and Pharmacology 39 (2), 173–174.

Khosla, P., Bhanwra, S., Singh, J., Seth, S., Srivastava, R.K. 2000. A study of hypoglycemic effects of *Azadirachta indica* (Neem) in normal and alloxan diabetic rabbits. Indian Journal of Physiology and Pharmacology 44 (1), 69–74.

Kim, S.Y., Gao, J.J., Lee, W.C., Ryu, K.S., Lee, K.R., Kim, Y.C. 1999. Antioxidative flavonoids from the leaves of *Morus alba*. Archieves of Pharmacal Research 22 (1), 81–85.

Krishnakumar, K., Augusti, K.T., Vijayammal, P.L. 1999. Hypoglycemic and anti-oxidant activity of *Salacia oblonga* Wall. extract in streptozotocin-induced diabetic rats. Indian Journal of Physiology and Pharmacology 43 (4), 510–514.

Kumar, G.P., Sudheesh, S., Vijayalakshmi, N.R. 1993. Hypoglycemic effect of *Coccinia indica*: mechanism of action. Planta Medica 59 (4), 330–332.

Kumar, R.V., Augusti, K.T. 1994. Insulin sparing action of a leucocyanidin derivative isolated from *Ficus bengalenesis* Linn. Indian Journal of Biochemistry and Biophysics 31 (1), 73–76.

Kumar, G.R., Reddy, K.P. 1999. Reduced nociceptive responses in mice with alloxan induced hyperglycemia after garlic (*Allium*

sativum Linn.) treatment. Indian Journal of Experimental Biology 37, 662–666.

Kumari, K., Mathew, B.C., Augusti, K.T. 1995. Antidiabetic and hypolipidemic effects of *S*-methyl cysteine sulfoxide isolated from *Allium cepa* Linn. Indian Journal of Biochemistry and Biophysics 32 (1), 49–54.

Kusano, S., Abe, H. 2000. Antidiabetic activity of white Skinned potato (*Ipomoea batatas*) in obese Zucker fatty rats. Biological and Pharmaceutical Bulletin 23 (1), 23–26.

La Cour, B., Molgaard, P., Yi, Z. 1995. Traditional Chinese medicine in treatment of hyperlipidemia. Journal of Ethnopharmacology 46 (2), 125–129.

Leatherdale, B.A., Panesar, R.K., Singh, G., Atkins, T.W., Bailey, C.J., Bignell, A.H. 1981. Improvement in glucose tolerance due to *Momordica charantia* (karela). British Medical Journal (Clinical Research Edition) 282 (6279), 1823–1824.

Lolitkar, M.M., Rao, M.R.R. 1966. Pharmacology of a hypoglycemic principle isolated from the fruits of *Eugenia jambolana* Linn. Indian Journal of Pharmacy 28 (5), 129–133.

Mahapatra, P.K., Pal, M., Chaudhauri, A.K.N., Chakarborty, D., Basu, A. 1985. Preliminary studies on glycemic effect of *Syzigium cumini* seeds. IRCS. Medical Science Biochemistry 13 (7), 631–632.

Manickam, M., Ramanathan, M., Jahromi, M.A., Chansouria, J.P., Ray, A.B. 1997. Antihyperglycemic activity of phenolics from *Pterocarpus marsupium*. Journal of Natural Products 60 (6), 609–610.

Mannan, N., Boucher, B.J., Evans, S.J. 2000. Increased waist size and weight in relation to consumption of *Areca catechu* (betel-nut); a risk factor for increased glycemia in Asians in east London. British Journal of Nutrition 83 (3), 267–275.

Marles, R.J., Farnsworth, N.R. 1995. Antidiabetic plants and their active constituents. Phytomedicine 2, 133–189.

Martinez, G., Delgado, R., Perez, G., Garrido, G., Nunez Selles, A.J., Leon, O.S. 2000. Evaluation of the in vitro antioxidant activity of *Mangifera indica* L. extract. Phytotherapy Research 14 (6), 424–427.

Mathew, P.T., 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. Indian Journal of Biochemistry and Biophysics 10, 209–212.

Mathew, P.T., Augusti, K.T. 1975. Hypoglycemic effects of onion, *Allium cepa* Linn. on diabetes mellitus—a preliminary report. Indian Journal of Physiology and Pharmacology 19 (4), 213–217.

Matsuda, H., Li, Y., Murakami, T., Matsumura, N., Yamahara, J., Yoshikawa, M. 1998. Antidiabetic principles of natural medicines. III. Structure-related inhibitory activity and action mode of oleanolic acid glycosides on hypoglycemic activity. Chemical and Pharmaceutical Bulletin (Tokyo) 46 (9), 1399–1403.

Matsuda, H., Murakami, T., Yashiro, K., Yamahara, J., Yoshikawa, M. 1999. Antidiabetic principles of natural medicines. IV. Aldose reductase and alpha-glucosidase inhibitors from the roots of *Salacia oblonga* Wall. (Celastraceae): structure of a new friedelane-type triterpene, kotalagenin 16-acetate. Chemical and Pharmaceutical Bulletin (Tokyo) 47 (12), 1725–1729.

Mukherjee, K., Ghosh, N.C., Datta, T. 1972. *Coccinia indica* Linn. as potential hypoglycemic agent. Indian Journal of Experimental Biology 10 (5), 347–349.

Mukherjee, P.K., Saha, K., Pal, M., Saha, B.P. 1997. Effect of *Nelumbo nucifera* rhizome extract on blood sugar level in rats. Journal of Ethnopharmacology 58 (3), 207–213.

Murakami, N., Murakami, T., Kadoya, M., Matsuda, H., "Yamahara, J., Yoshikawa, M. 1996. New hypoglycemic constituents in gymnemic acid from *Gymnema sylvestre*. Chemical and Pharmaceutical Bulletin (Tokyo) 44 (2), 469–471.

Nagaraju, N., 1992. Biochemical studies on some medicinal plants of Rayalaseema region. Ph.D. thesis, S.V. University, Tirupathi.

Nandkarni, A.K. 1992. Indian Materia Medica, vol. 1. Popular Prakashan, Bombay, p. 157.

Nandkarni, A.K. 1954. *Tinospora cordifolia*. Indian Materia Medica, third ed.. Popular Prakashan, Bombay, p. 1221.

Ohsugi, M., Fan, W., Hase, K., Xiong, Q., Tezuka, Y., Komatsu, K., Namba, T., Saitoh, T., Tazawa, K., Kadota, S. 1999. Active-oxygen scavenging activity of traditional nourishing-tonic herbal medicines and active constituents of Rhodiola sacra. Journal of Ethnopharmacology 67 (1), 111–119.

Okabayashi, Y., Tani, S., Fujisawa, T., Koide, M., Hasegawa, H., Nakamura, T., Fujii, M., Otsuki, M. 1990. Effect of *Gymnema sylvestre*, R.Br. on glucose homeostasis in rats. Diabetes Research and Clinical Practice 9 (2), 143–148.

Oubre, A.Y., Carlson, T.J., King, S.R., Reaven, G.M. 1997. From plant to patient: an ethnomedical approach to the identification of new drugs for the treatment of NIDDM. Diabetologia 40 (5), 614–617.

Pandey, M.C., Sharma, P.V. 1976. Hypoglycemic effect of bark of *Pterocarpus marsupium* ROXB. (Bijaka) on alloxan induced diabetes. Medicine and Surgery 16 (7), 9.

Panlasigui, L.N., Panlilio, L.M., Madrid, J.C. 1995. Glycemic response in normal subjects to five different legumes commonly used in the Philippines. International Journal of Food Science and Nutrition 46 (2), 155–160.

Pant, M.C., Uddin, I., Bhardwaj, U.R., Tewari, R.D. 1968. Blood sugar and total cholesterol lowering effect of *Glycine soja* (Sieb and Zucc.), *Mucuna pruriens* (D.C.) and *Dolichos biflorus* (Linn.) seed diets in normal fasting albino rats. Indian Journal of Medical Research 56 (12), 1808–1812.

Pari, L., Maheswari, J.U. 1999. Hypoglycemic effect of *Musa sapientum* L. in alloxan-induced diabetic rats. Journal of Ethnopharmacology 68 (1–3), 321–325.

Pari, L., Maheswari, J.U. 2000. Antihyperglycemic activity of *Musa sapientum* flowers: effect on lipid peroxidation in alloxan diabetic rats. Phytotherapy Research 14 (2), 136–138.

Patel, M., Jamrozik, K., Allen, O., Martin, F.I., Eng, J., Dean, B. 1986. A high prevalence of diabetes in a rural village in Papua New Guinea. Diabetes Research and Clinical Practice 2 (2), 97–103.

Patumraj, S., Tewit, S., Amatyakul, S., Jaryiapongskul, A., Maneesri, S., Kasantikul, V., Shepro, D. 2000. Comparative effects of garlic and aspirin on diabetic cardiovascular complications. Drug Delivery 7, 91–96.

Persaud, S.J., Al-Majed, H., Raman, A., Jones, P.M. 1999. *Gymnema sylvestre* stimulates insulin release in vitro by increased membrane permeability. Journal of Endocrinology 163 (2), 207–212.

Platel, K., Shurpalekar, K.S., Srinivasan, K. 1993. Influence of bitter gourd (*Momordica charantia*) on growth and blood constituents in albino rats. Die Nahrung 37 (2), 156–160.

Platel, K., Srinivasan, K. 1995. Effect of dietary intake of freeze-dried bitter gourd (*Momordica charantia*) in streptozotocin induced diabetic rats. Die Nahrung 39 (4), 262–268.

Platel, K., Srinivasan, K. 1997. Plant foods in the management of diabetes mellitus: vegetables as potential hypoglycemic agents. Die Nahrung 41 (2), 68–74.

Ponnachan, P.T., Paulose, C.S., Panikkar, K.R. 1993. Effect of leaf extract of *Aegle marmelose* in diabetic rats. Indian Journal of Experimental Biology 31 (4), 345–347.

Prakash, A.O., Mathur, S., Mathur, R. 1986. Effect of feeding *Gymnema sylvestre* leaves on blood glucose in beryllium nitrate treated rats. Journal of Ethnopharmacology 18 (2), 143–146.

Prema, L., Kurup, P.A. 1973a. Effect of protein fractions from *Cajanus cajan* (redgram) and *Dolichos biflorus* (horsegram) on the serum, liver and aortic lipid levels in rats fed a high-fat-cholesterol diet. Atherosclerosis 18, 369–377.

Prema, L., Kurup, P.A. 1973b. Hypolipidemic activity of the protein isolated from *Cajanus cajan* in high fat-cholesterol diet fed rats. Indian Journal of Biochemistry and Biophysics 10, 293–296.

Preuss, H.G., Jarrell, S.T., Scheckenbach, R., Lieberman, S., Anderson, R.A. 1998. Comparative effects of chromium, vanadium and *Gymnema sylvestre* on sugar-induced blood pressure elevations in SHR. Journal of the American College of Nutrition 17 (2), 116–123.

Prince, P.S., Menon, V.P., Pari, L. 1998. Hypoglycemic activity of *Syzigium cumini* seeds: effect on lipid peroxidation in alloxan diabetic rats. Journal of Ethnopharmacology 61 (1), 1–7.

Prince, P.S., Menon, V.P. 1999. Antioxidant activity of *Tinospora cordifolia* roots in experimental diabetes. Journal of Ethnopharmacology 65 (3), 277–281.

Puri, D., Baral, N. 1998. Hypoglycemic effect of *Biophytum sensitivum* in the alloxan diabetic rabbits. Indian Journal of Physiology and Pharmacology 42 (3), 401–406.

Rai, V., Iyer, U., Mani, U.V. 1997. Effect of Tulsi (*Ocimum sanctum*) leaf powder supplementation on blood sugar levels, serum lipids and tissue lipids in diabetic rats. Plant Foods and Human Nutrition 50 (1), 9–16.

Rang, H.P., Dale, M.M. 1991. The Endocrine System Pharmacology, Second ed.. Longman Group Ltd, UK, pp. 504–508.

Rao, P.V., Ushabala, P., Seshiah, V., Ahuja, M.M., Mather, H.M. 1989. The Eluru survey: prevalence of known diabetes in a rural Indian population. Diabetes Research and Clinical Practice 7 (1), 29–31.

Rao, B.K., Kesavulu, M.M., Giri, R., Appa Rao, C. 1999. Antidiabetic and hypolipidemic effects of *Momordica cymbalaria* Hook. fruit powder in alloxan-diabetic rats. Journal of Ethnopharmacology 67 (1), 103–109.

Rao, V.V., Dwivedi, S.K., Swarup, D. 1994. Hypoglycemic effect of *Caselpinia bonducella* in rabbits. Fitoterpia 65, 245–247.

Rathi, S.S., Vats, V., Grover, J.K. Anti-hyperglycemic effects of *Momordica charantia* and *Mucuna pruriens* in experimental diabetes and their effect on key metabolic enzymes involved in carbohydrate metabolism. Phytotherapy Research, in press a.

Rathi, S.S., Grover, J.K., Vats, V. Prevention of experimental diabetic cataract by Indian Ayurvedic plant extracts. Phytotherapy Research, in press b.

Ravikumar, P., Anuradha, C.V. 1999. Effect of fenugreek seeds on blood lipid peroxidation and antioxidants in diabetic rats. Phytotherapy Research 13 (3), 197–201.

Ribes, G., Sauvaire, Y., Baccou, J.C., Valette, G., Chenon, D., Trimble, E.R., Loubatieres-Mariani, M.M. 1984. Effects of fenugreek seeds on endocrine pancreatic secretions in dogs. Annuals of Nutrition and Metabolism 28 (1), 37–43.

Ribes, G., Sauvaire, Y., Da Costa, C., Baccou, J.C., Loubatieres-Mariani, M.M. 1986. Antidiabetic effects of subfractions from fenugreek seeds in diabetic dogs. Proceedings of the Society for Experimental Biology and Medicine 182 (2), 159–166.

Riyad, M.A., Abfdul-Salam, S.A., Mohammad, S.S. 1988. Effect of Fenugreek and lupine seeds on the development of experimental diabetes in rats. Planta Medica 54 (4), 286–290.

Roman-Ramos, R., Flores-Saenz, J.L., Alarcon-Aguilar, F.J. 1995. Anti-hyperglycemic effect of some edible plants. Journal of Ethnopharmacology 48, 25–32.

Sachdeva, A., Khemani, L.D. 1999. A preliminary investigation of the possible hypoglycemic activity of *Hibiscus rosa-sinensis*. Biomedicine and Environmental Science 12 (3), 222–226.

Saifi, A.Q., Shinde, S., Kavishwar, W.K., Gupta, S.R. 1971. Some aspects of phytochemistry and hypoglycemic actions of *Pterocarpus marsupium*. Journal of Research in Indian Medicine 6 (2), 205–207.

Saleem, R., Ahmad, M., Hussain, S.A., Qazi, A.M., Ahmad, S.I., Qazi, M.H., Ali, M., Faizi, S., Akhtar, S., Hussein, S.N. 1999. Hypotensive, hypoglycemic and toxicological studies on the flavonol C-glycoside shamimin from *Bombax ceiba*. Planta Medica 65 (4), 331–334.

Sarkar, A., Lavania, S.C., Pandey, D.N., Pant, M.C. 1994. Changes in the blood lipid profile after administration of *Ocimum sanctum* (Tulsi) leaves in the normal albino rabbits. Indian Journal of Physiology and Pharmacology 38 (4), 311–312.

Sauvaire, Y., Petit, P., Broca, C., Manteghetti, M., Baissac, Y., Fernandez-Alvarez, J., Gross, R., Roye, M., Leconte, A., Gomis, R., Ribes, G. 1998. 4-Hydroxyisoleucine: a novel amino acid potentiator of insulin secretion. Diabetes 47 (2), 206–210.

Saxena, A.M., Bajpai, M.B., Mukherjee, S.K. 1991. Swerchirin induced blood sugar lowering of streptozotocin treated hyperglycemic rats. Indian Journal of Experimental Biology 29 (7), 674–675.

Saxena, A.M., Bajpai, M.B., Murthy, P.S., Mukherjee, S.K. 1993. Mechanism of blood sugar lowering by a Swerchirin-containing hexane fraction (SWI) of *Swertia chirayita*. Indian Journal of Experimental Biology 31 (2), 178–181.

Schubert, S.Y., Lansky, E.P., Neeman, I. 1999. Antioxidant and eicosanoid enzyme inhibition properties of pomegranate seed oil and fermented juice flavonoids. Journal of Ethnopharmacology 66 (1), 11–17.

Seema, P.V., Sudha, B., Padayatti, P.S., Abraham, A., Raghu, K.G., Paulose, C.S. 1996. Kinetic studies of purified malate dehydrogenase in liver of streptozotocin-diabetic rats and the effect of leaf extract of *Aegle marmelose* (L.) Correa ex Roxb. Indian Journal of Experimental Biology 34 (6), 600–602.

Sekar, B.C., Mukherjee, B., Chakravarti, R.B., Mukherjee, S.K. 1987. Effect of different fractions of *Swertia chirayita* on the blood sugar level of albino rats. Journal of Ethnopharmacology 21 (2), 175–181.

Shah, D.S. 1967. A preliminary study of the hypoglycemic action of heartwood of *Pterocarpus marsupium* roxb. Indian Journal of Medical Research 55 (2), 166–168.

Shanmugasundaram, K.R., Panneerselvam, C., Samudram, P., Shanmugasundaram, E.R. 1983. Enzyme changes and glucose utilization in diabetic rabbits: the effect of *Gymnema sylvestre*, R.Br. Journal of Ethnopharmacology 7 (2), 205–234.

Shanmugasundaram, E.R., Rajeswari, G., Baskaran, K., Rajesh Kumar, B.R., Radha Shanmugasundaram, K., Kizar Ahmath, B. 1990a. Use of *Gymnema sylvestre* leaf extract in the control of blood glucose in insulin-dependent diabetes mellitus. Journal of Ethnopharmacology 30 (3), 281–294.

Shanmugasundaram, E.R., Gopinath, K.L., Radha Shanmugasundaram, K., Rajendran, V.M. 1990b. Possible regeneration of the islets of Langerhans in streptozotocin-diabetic rats given *Gymnema sylvestre* leaf extracts. Journal of Ethnopharmacology 30 (3), 265–279.

Sharma, K.K., Gupta, R.K., Gupta, S., Samuel, K.C. 1977. Anti-hyperglycemic effect of onion: effect on fasting blood sugar and induced hyperglycemia in man. Indian Journal of Medical Research 65 (3), 422–429.

Sharma, O.P., Vaid, J., Pattabhi, V., Bhutani, K.K. 1992. Biological action of lantadene C, a new hepatotoxicant from *Lantana camara* var. aculeata. Journal of Biochemistry and Toxicology 7 (2), 73–79.

Sharma, R.D., Raghuram, T.C., Rao, N.S. 1990. Effect of fenugreek seeds on blood glucose and serum lipids in type I diabetes. European Journal of Clinical Nutrition 44 (4), 301–306.

Sharma, S.R., Dwivedi, S.K., Swarup, D. 1997. Hypoglycemic, antihyperglycemic and hypolipidemic activities of *Caesalpinia bonducella* seeds in rats. Journal of Ethnopharmacology 58 (1), 39–44.

Sharma, V.N., Sogani, R.K., Arora, R.B. 1960. Some observations on hypoglycemic activity of *Momordica charantia*. Indian Journal of Medical Research 48, 471–477.

Sheehan, E.W., Zemaitis, M.A., Slatkin, D.J., Schiff, P.L., Jr. 1983. A constituent of *Pterocarpus marsupium*, (−)-epicatechin, as a

potential antidiabetic agent. Journal of Natural Products 46 (2), 232–234.
Sheela, C.G., Augusti, K.T. 1992. Antidiabetic effects of *S*-allyl cysteine sulphoxide isolated from garlic *Allium sativum* Linn. Indian Journal of Experimental Biology 30, 523–526.
Sheela, C.G., Kumud, K., Augusti, K.T. 1995. Anti-diabetic effects of onion and garlic sulfoxide amino acids in rats. Planta Medica 61 (4), 356–357.
Shibib, B.A., Khan, L.A., 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. Biochemistry Journal 292 (Part 1), 267–270.
Shimizu, K., Abe, T., Nakajyo, S., Urakawa, N., Atsuchi, M., Yamashita, C. 1996. Inhibitory effects of glucose utilization by gymnema acids in the guinea-pig ileal longitudinal muscle. Journal of Smooth Muscle Research 32 (5), 219–228.
Shimizu, K., Iino, A., Nakajima, J., Tanaka, K., Nakajyo, S., Urakawa, N., Atsuchi, M., Wada, T., Yamashita, C. 1997. Suppression of glucose absorption by some fractions extracted from *Gymnema sylvestre* leaves. The Journal of the Veterinary Medical Science 59 (4), 245–251.
Simon, O.R., Singh, N., Smith, K., Smith, J. 1987. Effect of an aqoues extract of Nichol (*Caesalpinia bounduc*) in blood glucose concentration: evidence of an antidiabetic action presented. Journal of Science Research Council 6, 25–32.
Singh, K.N., Chandra, V., Barthwal, K.C. 1975. Letter to the editor: hypoglycemic activity of *Acacia arabica*, *Acacia benthami* and *Acacia modesta* leguminous seed diets in normal young albino rats. Indian Journal of Physiology and Pharmacology 19 (3), 167–168.
Singh, N., Singh, S.P., Vrat, S., Misra, N., Dixit, K.S., Kohli, R.P. 1985. A study on the anti-diabetic activity of *Coccinia indica* in dogs. Indian Journal of Medical Science 39 (2), 27–29.
Singh, N., Tyagi, S.D., Agarwal, S.C. 1989. Effects of long term feeding of acetone extract of *Momordica charantia* (whole fruit powder) on alloxan diabetic albino rats. Indian Journal of Physiology and Pharmacology 33 (2), 97–100.
Sitasawad, S.L., Shewade, Y., Bhonde, R. 2000. Role of bittergourd fruit juice in STZ-induced diabetic state in vivo and in vitro. Journal of Ethnopharmacology 73 (1–2), 71–79.
Srivastava, Y., Venkatakrishna-Bhatt, H., Verma, Y. 1988. Effect of *Momordica charantia* Linn. pomous aqueous extract on cataractogenesis in murrin alloxan diabetics. Pharmacology Research and Communication 20 (3), 201–209.
Srividya, N., Periwal, S. 1995. Diuretic, hypotensive and hypoglycemic effect of *Phyllanthus amarus*. Indian Journal of Experimental Biology 33 (11), 861–864.
Stanely, Mainzen, Prince, P., Menon, V.P., Gunasekaran, G. 1999. Hypolipidemic action of *Tinospora cordifolia* roots in alloxan diabetic rats. Journal of Ethnopharmacology 64 (1), 53–57.
Stanely, P., Prince, M., Menon, V.P. 2000. Hypoglycemic and other related actions of *Tinospora cordifolia* roots in alloxan-induced diabetic rats. Journal of Ethnopharmacology 70 (1), 9–15.
Stark, A., Madar, Z. 1993. The effect of an ethanol extract derived from fenugreek (*Trigonella foenum-graecum*) on bile acid absorption and cholesterol levels in rats. British Journal of Nutrition 69 (1), 277–287.
Subramoniam, A., Pushpangadan, P., Rajasekharan, S., Evans, D.A., Latha, P.G., Valsaraj, R. 1996. Effects of *Artemisia pallens* Wall. on blood glucose levels in normal and alloxan-induced diabetic rats. Journal of Ethnopharmacology 50 (1), 13–17.
Swanston-Flatt, S.K., Day, C., Flatt, P.R., Gould, B.J., Bailey, C.J. 1989. Glycemic effects of traditional European plant treatments for diabetes. Studies in normal and streptozotocin diabetic mice. Diabetes Research 10 (2), 69–73.
Swanston-Flatt, S.K., Day, C., Bailey, C.J., Flatt, P.R. 1990. Traditional plant treatments for diabetes. Studies in normal and streptozotocin diabetic mice. Diabetologia 33 (8), 462–464.
Tjokroprawiro, A., Pikir, B.S., Budhiarta, A.A., Pranawa, Soewondo, H., Donosepoetro, M., Budhianto, F.X., Wibowo, J.A., Tanuwidjaja, S.J., Pangemanan, M. 1983. Metabolic effects of onion and green beans on diabetic patients. Tohoku Journal of Experimental Medicine 141 (Suppl.), 671–676.
Tominaga, M., Kimura, M., Sugiyama, K., Abe, T., Igarashi, K., Igarashi, M., Eguchi, H., Sekikawa, A., Ogawa, A., Manaka, H. 1995. Effects of seishin-renshi-in and *Gymnema sylvestre* on insulin resistance in streptozotocin-induced diabetic rats. Diabetes Research and Clinical Practice 29 (1), 11–17.
Trivedi, C.P. 1963. Observations on the effects of some Indigenous drug on blood sugar level of normal and diabetic rabbits. Indian Journal of Physiology and Pharmacology 7, S11–12.
Tunali, T., Yarat, A., Yanardag, R., Ozcelik, F., Ozsoy, O., Ergenekon, G., Emekli, N. 1998. The effect of chard (*Beta vulgaris* L. var. cicla) on the skin of streptozotocin induced diabetic rats. Die Pharmazie 53 (9), 638–640.
Vats, V., Grover, J.K., Tandon, N., Rathi, S.S. 2001. Treatment with extracts of *Momordica charantia* prevents hyperglycemia and *Eugenia jambolana* prevents hyperglycemia and hyperinsulinemia in fructose fed rats. Journal of Ethnopharmacology 76 (2), 139–143.
Vats, V., Grover, J.K., Rathi, S.S. 2002. Evaluation of antihyperglycemic and hypoglycemic effect of *Trigonella foenum graecum*, *Ocimum sanctum* and *Pterocarpus marsupium* in normal and alloxanized diabetic rats. Journal of Ethnopharmacology 79 (1), 95–100.
Verma, N.P., Mehta, S.P., Madhu, S., Mather, H.M., Keen, H. 1986. Prevalence of known diabetes in an urban Indian environment: the Darya Ganj diabetes survey. British Medical Journal 293 (6544), 423–424.
Vimla Devi, M., Venkateswarlu, M., Krishana Rao, R.V. 1977. Hypoglycemic activity of the leaves of *Momordica charantia*. Indian Journal of Pharmacology 39, 167–169.
Wadood, A., Wadood, N., Shah, S.A. 1989. Effects of *Acacia arabica* and *Caralluma edulis* on blood glucose levels of normal and alloxan diabetic rabbits. JPMA. The Journal of Pakistan Medical Association 39 (8), 208–212.
Welihinda, J., Arvidson, G., Gylfe, E., Hellman, B., Karlsson, E. 1982. The insulin-releasing activity of the tropical plant *Momordica charantia*. Acta Biologica et Medica Germanica 41 (12), 1229–1240.
Welihinda, J., Karunanayake, E.H. 1986. Extra-pancreatic effects of *Momordica charantia* in rats. Journal of Ethnopharmacology 17 (3), 247–255.
WHO/Acadia, 1992. Rapport de la Journe Internationale de, diabetes 14 octobre.
Yadav, P., Sarkar, S., Bhatnagar, D. 1997a. Action of *Capparis decidua* against alloxan-induced oxidative stress and diabetes in rat tissues. Pharmacological Research 36 (3), 221–228.
Yadav, P., Sarkar, S., Bhatnagar, D. 1997b. Lipid peroxidation and antioxidant enzymes in erythrocytes and tissues in aged diabetic rats. Indian Journal of Experimental Biology 35 (4), 389–392.
Yoshikawa, M., Murakami, T., Kadoya, M., Matsuda, H., Muraoka, O., Yamahara, J., Murakami, N. 1996. Medicinal foodstuff. III. Sugar beet. Hypoglycemic oleanolic acid oligoglycosides, betavulgarosides I, II, III, and IV, from the root of *Beta vulgaris* L. (Chenopodiaceae). Chemical and Pharmaceutical Bulletin (Tokyo) 44 (6), 1212–1217.
Yoshikawa, M., Murakami, T., Matsuda, H. 1997a. Medicinal foodstuffs. X. Structures of new triterpene glycosides, gymnemosides-c, -d, -e, and -f, from the leaves of *Gymnema sylvestre* R.Br.: influence of gymnema glycosides on glucose uptake in rat small intestinal

fragments. Chemical and Pharmaceutical Bulletin (Tokyo) 45 (12), 2034–2038.

Yoshikawa, M., Murakami, T., Kadoya, M., Li, Y., Murakami, N., Yamahara, J., Matsuda, H. 1997b. Medicinal foodstuffs. IX. The inhibitors of glucose absorption from the leaves of *Gymnema sylvestre* R.BR. (Asclepiadaceae): structures of gymnemosides a and b. Chemical and Pharmaceutical Bulletin (Tokyo) 45 (10), 1671–1676.

Yoshikawa, M., Murakami, T., Yashiro, K., Matsuda, H. 1998. Kotalanol, a potent alpha-glucosidase inhibitor with thiosugar sulfonium sulfate structure, from antidiabetic Ayurvedic medicine *Salacia reticulata*. Chemical and Pharmaceutical Bulletin (Tokyo) 46 (8), 1339–1340.

Zacharias, N.T., Sebastian, K.L., Philip, B., Augusti, K.T. 1980. Hypoglycemic and hypolipidemic effects of garlic in sucrose fed rabbits. Indian Journal of Physiology and Pharmacology 24, 151–154.