Phytopharmacology

Inforesights Publishing

Therapeutic potential of antidiabetic nutraceuticals

Uttara Singh[1,*], Sadhana Singh[2], Anita Kochhar[1]

[1] College of Home Science, Punjab Agricultural University, Ludhiana-141004, India
[2]College of Home Science, Narendra Dev University of Agriculture and Technology, Kumarganj, Faizabad, India

*Corresponding Author: usuttarasingh@gmail.com

Received: 31 December 2011, **Revised**: 28 January 2012 **Accepted**: 28 January 2012

Abstract

Diabetes mellitus is a metabolic disorder of endocrine system. This dreadful disease is found in all parts of the world and is becoming a serious threat to mankind health. There are lots of chemical agents available to control and to treat diabetic patients, but now currently several medicinal plants have been investigated for their beneficial use in diabetes. The effects of these plants may delay the development of diabetic complications and correct the metabolic abnormalities. Many chemical constituents are responsible for antidiabetic effects have been isolated from medicinal plants as nutraceuticals. There is growing recognition of the potential role for nutraceuticals and dietary supplements in helping to reduce health risks and improve health quality. In the global marketplace nutraceuticals and functional foods have become a multi-billion dollar industry. Selection for consistent production of high and low productivity of active nutraceutical components within specific ecological regions will lead to development of alternative nutraceuticals and functional foods with distinctive and more reliable health and food properties.

Keywords: Diabetes mellitus; Plants; Herbal medicine; phytochemical

Introduction

Diabetes is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces (WHO 2009). Diabetes is fast becoming a leading cause of morbidity, mortality and disability across the world. Diabetes mellitus is a global metabolic epidemic affecting essential biochemical activities in almost every age group (Gupta et al., 2008). According to International Diabetic Federation the estimated diabetes prevalence for 2010 has risen to 285 million, representing 6.4% of the world‘s adult population, with a prediction that by 2030 the number of people with diabetes will have risen to 438 million corresponding to 7.8% of the adult population (IDF 2011). India has been declared as the “Diabetic capital of world”. Currently 40.9 million people in India suffering from diabetes (IDF 2007) and by 2030 there would be 79.44 million diabetics in India alone (WHO 2007). It is estimated that by the year 2030, diabetes is

likely to be the seventh leading cause of death accounting 3.3 per cent of total deaths in the world (WHO 2008).

Diabetes increases the risk of heart disease and stroke. Fifty per cent of people with diabetes die of cardiovascular disease (primarily heart disease and stroke). Diabetes with reduced blood flow, neuropathy in the feet increases the chance of foot ulcers and eventual limb amputation. Diabetic retinopathy is an important cause of blindness and occurs as a result of long-term accumulated damage to the small blood vessels in the retina. After 15 years of diabetes, approximately 2% of people become blind and about 10% develop severe visual impairment. Diabetes is among the leading causes of kidney failure. Ten to twenty per cent of people with diabetes die of kidney failure. Diabetic neuropathy is damage to the nerves as a result of diabetes and affects up to 50% of people with diabetes. Although many different problems can occur as a result of diabetic neuropathy, common symptoms are tingling, pain, numbness or weakness in the feet and hands. The overall risk of dying among people with diabetes is at least double the risk of their peers without diabetes (WHO 2011). Type 2 diabetes runs in families. Tendency is due to children learning bad habits eating a poor diet, not exercising from their parents. In general, if one has type 2 diabetes, the risk of their child getting diabetes is 1 in 7 if one was diagnosed before age 50 and 1 in 13 if diagnosed after age 50. Child's risk is greater when the parent with type 2 diabetes is the mother. If both have type 2 diabetes then child's risk is about 1 in 2 (Anonymous 2011). Lifestyle factors, genetics and dietary composition are mainly responsible for type 2 diabetes mellitus. Dietary fat is of particular interest because fatty acids influence glucose metabolism by altering cell membrane function, enzyme activity and insulin signaling and gene expression. Replacing saturated fats and trans fatty acids with unsaturated (polyunsaturated and/or monounsaturated) fats has beneficial effects on insulin sensitivity and is likely to reduce risk of type 2 diabetes. Consumption of partially hydrogenated fats should be minimized (Risérus et al., 2009).

These days great attention is being given to management of diabetes with medicinal plants along with dietary restriction. Modern medicine is rooted in ethnobotanical traditions using indigenous flora to treat symptoms of human diseases or to improve specific aspects of the body conditions. Today a great number of modern drugs are still derived from natural sources and 25 per cent of all prescriptions contain one or more active ingredients from plants (Thorfeldt 2005). WHO has estimated that 80 per cent of the population of developing countries still relies on traditional medicines mostly plant drugs for their primary health care needs and ensure patient safety by upgrading the skills and knowledge of traditional medicine providers (WHO 2008).

Nutraceuticals

Nutraceutical is a food with a medical-health benefit, including the prevention and treatment of disease. The term was coined in the late 1980s by Stephen DeFelice. Such foods also commonly are referred to as *functional foods*, signifying they and/or their components may provide a health benefit beyond basic nutrition. Nutraceuticals contain health-promoting ingredients or natural components that have a potential health benefit for the body. Consumer interest in the relationship between diet and health has increased the demand for information on nutraceuticals (NCABR 2007).

The use of nutraceuticals, as an attempt to accomplish desirable therapeutic outcomes with reduced side effects, as compared with other therapeutic agents has met with great monetary success (Nelson 1999 and Whitman 2001). Eastern cultures have a long history of use of traditional medicines associated with health foods in forms of recognized nutritional foods, food supplements, medicinal herbs, and crude powdered drugs derived from plant, animal and marine sources (Datta et al., 2002; Dahanukar et al., 2000). India and China are the two most important countries known for their production of traditional functional food products and nutraceuticals. Both of these countries have large populations, in particular in rural, remote and inaccessible areas which are totally dependent upon herbal remedies and other naturally available bioresources which they use to treat common ailments, and as general preventive and protective medications (Dhanuka et al., 2000).

In India the most common forms of functional foods and nutraceuticals are available as traditional Indian Ayurvedic Medicines (IAM); these are marketed under different brand names (Patwardhan et al., 2005). India is the home of a large number of medicinal herbs, spices and tree species that have a substantially large domestic market with no major foreign competition at present (Datta et al., 2002; Patwardhan et al., 2005). However, it is important to note that there are no strict pharmaceutical regulations on Ayurvedic and nutraceutical health products in India. Most of these products are available to consumers directly over the counter without need for a medical prescription (Patwardhan et al., 2005). India has a large share of the international functional food and nutraceutical market, and exports products to the far east, south-east, west and middle east Asia as well as to parts of north Africa and the EU. However, India's major export destination is the USA and Japan (Patwardhan et al., 2005). Labelling, and strict control over formulations and branding are still not required for most products. In addition cost of production typically is low, making this produce highly competitive in Asian and African markets (World Nutraceuticals, 2006).

Aegle marmelos L.

Aegle marmelos family rutaceae is highly reputed medicinal tree commonly known as the bael. It is medium sized tree growing throughout the forest of India of altitude 1200 meter. It is found all over India, from sub-Himalayan forest, Bengal, central and south India. The different parts of this plant contain number of coumarins, alkaloids, sterols and essential oils. Various parts of this plant such as leaves, fruit and seed possess hypoglycaemic, hypolipidemic and blood pressure lowering property (Vijay et al., 2006). The peel of the fruit which is a very hard shell and green to brown in color depends on ripening stage. The appearance of yellow or orange edible pulp is like a boiled pumpkin, possesses a slightly sweet taste and a characteristic floral, terpene-like aroma, very fragrant and pleasantly flavored. Seeds are surrounded by slimy transparent mucilage (Suvimol and Pranee 2008). Bael (*Aegle marmelos*) is an important medicinal plant of India. Bioactive constituents of bael leaves, fruits and seeds have been used in several diseases like diabetes, cardiovascular and anti-inflammatory (Maity et al., 2009). The most important ingredients present are alkaloids, terpenoids, steriods, phenols glycosides and tannins (Venkatesan et al., 2009). The bael leaf contain 15 compounds, including seven monotorpene hydrocarbons (90.7%), three oxygenated monoterpenes (2.9%), four sesquiterpene hydrocarbons (3.1%) and one phenolic compound (0.2%). Limonene (82.4%) was the main constituent (Kaur et al., 2006).

A. marmelos extract (AME) was found to decrease the levels of FBG, total cholesterol, TBARS, LDH and CK, and increase the levels of GSH, CAT and SOD dose dependently as compared to diabetic control groups. The maximum dose-dependent decrease in TBARS (63.46%), LDH (34.04%), CK (53.14%), and increase in GSH (64.91%), CAT (59.34%), SOD (69.65%) was evident at an optimum dose of 200mg kg-1 (Bhatti et al., 2011). Aegle marmelos fruit aqueous extract (AMF; 250, 500 and 1000 mg/kg) improves insulin resistance, dyslipidemia and β-cell dysfunction in high fat diet fed-streptozotocin (HFD-STZ)-induced diabetic rats by modulating peroxisome proliferator-activated receptor-γ (PPARγ) expression (Sharma et al., 2011).

The effects medicinal plants may delay the development of diabetic complications and correct the metabolic abnormalities. Many phytoconstituents responsible for antidiabetic effects have been isolated from hypoglycaemic plants (Singh et al., 2011). Marmin or (7-(6',7'-dihydroxygeranyl-oxy) coumarin is an active compound isolated from Aegle marmelos Correa. The effects of marmin on the histamine release from rat mast cell. The histamine release from these cells was determined by using HPLC fluorometric method. Marmin succeeded to inhibit the histamine release from RBL-2H3 cell line induced by DNP24-BSA, thapsigargin or ionomycin. In addition, marmin suppressed 45Ca2+ influx on RBL-2H3 cell line induced by thapsigargin. Marmin also succeeded to inhibit the histamine release from RPMCs induced by thapsigargin. However, marmin showed weak inhibitory effects on the histamine release from RPMCs induced by compound 48/80, PMA or ionomycin. The inhibitory effect of marmin on the histamine release from mast cells high depends on the type of mast cell and also involves mechanisms related to intracellular Ca2+ signaling events by blocking Ca2+ influx into mast cells (Nugroho et al., 2011).

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

Anti-hyperglycemic activity of aqueous leaf extract in alloxanized rats (Ponnachan et al., 1993). Antihyperglycemic activity of aqueous leaf extract in streptozotocin induced diabetic rats (Das et al., 1996; Seema et al., 1996). Hypoglycemic and antioxidant activity of leaves in diabetic male albino rats (Upadhyay et al., 2004). Antihyperglycemic and antioxidant activity of the plant in alloxanized rats (Sabu and Kuttan, 2004).

***Brassica juncea* L.**

Brassica juncea is higher yielding, more heat and drought tolerant, and more resistant to blackleg (a fungal disease) and less prone to seed loss due to shattering. These attributes

make *B. juncea* well adapted to the semi-arid growing conditions (Gaynor 1999). This is a small herb cultivated throughout India and used as a spice in food and has been reported to exert significant hypoglycemic activity. Hypoglycemic activity of *Brassica juncea* diet (10%, w/w) in normal rats upon oral administration for 60 days reduce glucose level due to increases the concentration of hepatic glycogen and glycogenesis and suppressed the activity of glycogen phosphorylase and gluconeogenic enzymes, lead to reduction in glycogenolysis and gluconeogenesis (Khan et al., 1995). Aqueous extract of *Brassica juncea* (seeds) at a dose of 250, 350 and 450 mg/kg body weight was given to adult male Swiss albino rats of six numbers. The serum insulin levels were recorded a significant depletion in all groups, short term as well as long term diabetic animals, when compared to that of normal animals. A significant dosage dependent augmenting effect of the seed extract on the serum insulin was recorded in both short term as well as long term groups (Thirumalai et al., 2011). Mustard (Brassica juncea) leaf extract (BJLE) on streptozotocin (STZ)-induced diabetic cataract in Wistar rats. A daily oral dose of BJLE at 250 and 500mg/kg body weight was administered to STZ-induced diabetic rats for 8 weeks. Reversal of changes associated with hyperglycemia, delayed cataract progression and maturation were observed with the two doses of the extract, while the higher dose (500mg/kg) gave an increased protection. The results suggest that BJLE can be effective against hyperglycemia-induced oxidative and osmotic stress as well as the subsequent development of diabetic cataract.

Brassica juncea leaf extract (BJLE) delayed the cataract progression along with preventing oxidative and osmotic stress (Valavala et al., 2011). Methanol extract of leaves of mustard in acetic acid-induced gastric pain writhing models in mice, and anti-hyperglycemic effect in oral glucose tolerance tests in glucose-loaded mice. In antinociceptive tests, the methanol extract of leaves demonstrated dose-dependent and significant antinociceptive activity. At a dose of 200 mg leaf extract/kg body weight, writhing induced by acetic acid in Swiss albino mice was inhibited by 43.9%, which was the same as that observed with the standard drug aspirin when administered at a dose of 200 mg/kg body weight. Maximum inhibition of writhing was observed with an extract dose of 400 mg/kg body weight (75.7%). In oral glucose tolerance tests, the methanol extract of leaves also demonstrated significant and dose-dependent glucose lowering activity. The extract, when administered at a dose of 200 mg/kg body weight reduced serum glucose levels in glucose-loaded mice by 46.79% versus 73.40% obtained when mice were administered a standard hypoglycemic drug glibenclamide at a dose of 10 mg/kg body weight (Rahmatullah et al., 2010). Feeding of fructose rich diet for 30 days resulted in rise in blood glucose by 29.4%, insulin by 101.2% and cholesterol by 26.7% indicating development of insulin resistance. However, feeding of a fructose diet containing 10% Brassica juncea seeds powder for 30 days significantly decreased fasting serum glucose, insulin and cholesterol levels but did not normalize them. On the other hand, a diet containing 15% Murraya koenigii leaves powder failed to exert any effect on these parameters. Study suggests that BJ can play a role in management of pre-diabetic state of insulin resistance and should be promoted for use in patients prone to diabetes (Yadav et al., 2004). Ten percent powder of seeds of Brassica juncea (BJ) for 60 days on serum glucose concentrations and kidney functions in streptozotocin (STZ; 100mg/kg) diabetic rats. Serum glucose levels, body weight, urine volume, serum creatinine, and urinary albumin (UAE) levels were monitored on day 0, 10, 25, 40, and 70 of the experiment. After 60 days of STZ administration, urine volume per day and UAE levels were significantly higher ($P<0.0005$) in diabetic controls (DC) as compared to normal controls

(Grover et al., 2003).

***Mangifera indica* L.**

Mangos belong to the genus *Mangifera* of the family Anacardiaceae. The genus *Mangifera* contains several species that bear edible fruit. Most of the fruit trees that are commonly known as mangos belong to the species *Mangifera indica*. The other edible *Mangifera* species generally have lower quality fruit and are commonly referred to as wild mangos. There are over 1000 named mango varieties throughout the world, which is a testament to their value to humankind. Mango is a common garden tree throughout the tropics. Its fruit is also eaten green, processed into pickles, pulps, jams, and chutneys, and is frozen or dried. The fruit is also an important source of sustenance for birds, bats, insects, and mammals. The genus *Mangifera* originates in tropical Asia, with the greatest number of species found in Borneo, Java, Sumatra, and the Malay Peninsula. The most-cultivated *Mangifera* species, *M. indica* (mango), has its origins in India and Myanmar. In India, a drink made from unripe mango fruit is used as a remedy for exhaustion and heat stroke. Half-ripe fruit eaten with salt and honey is used for a treatment of gastro-intestinal disorders, bilious disorders, blood disorders, and scurvy. Ripe mangos are a rich source of vitamin A, and are used to treat vitamin A deficiencies such as night blindness. Diabetes has been treated with a drink made from the infusion of fresh mango leaves. Dried mango seed ground into flour is used to treat diarrhea. Diarrhea and throat disorders are treated by gargling bark extracts mixed with water. In India, fruit sap has been used to treat the pain of bee and scorpion stings. Many of the traditional Indian medicinal uses of mango involve eating unripe fruit. It should be noted that unripe fruit contains a lot of the toxic sap that when eaten in excess can cause throat irritation, indigestion, dysentery, and colic (Bally 2006). Hypoglycemic activity of aqueous leaf extract (1 g/kg p.o.), given along with as well as 60 min before glucose administration in streptozotocin-induced diabetic rats (Aderibigbe et al., 1999). Treatment with Mangifera indica extract produced decrease in alloxan induced glucose, urea, uric acid, and creatinine levels in alloxan induced diabetic rats (Kemasari et al., 2011). Zinjarde et al, (2011) have reported the alpha- amylase inhibitory effect of its crude extract.

Mangiferin is one the major active compounds present in mango. Hypoglycemic activity of Mangiferin (10 and 20 mg/kg, i.p. once daily for 28 days) was observed in STZ-induced diabetic rats. In the same study Mangiferin (Figure 1) revealed improvement in oral glucose glucose tolerance in glucose-loaded normal rats upon chronic administration (10 and 20 mg/kg, i.p.) for 14 days, through intestinal reduction of the absorption of glucose as well

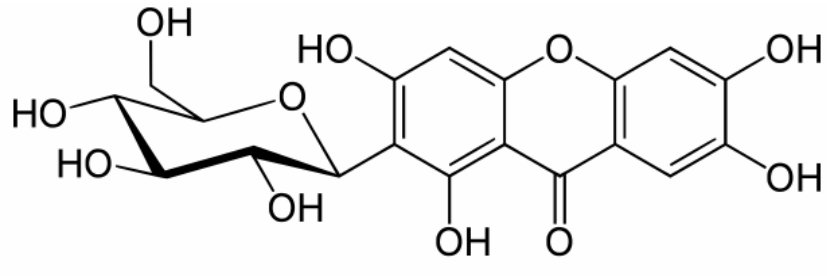

Figure 1. Mangiferin

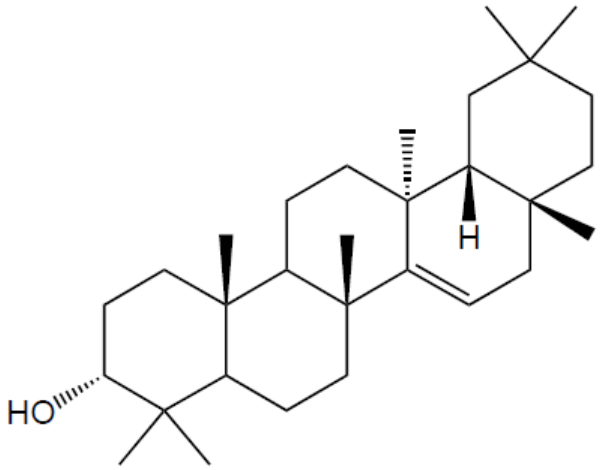

Figure 2. 3β-taraxerol

as pancreatic and extra pancreatic mechanisms (Murugananda et al., 2005). Mangiferin () is also reported for its protective effect in diabetic nephropathy progression in streptozotocin-induced diabetic rats (Li et al., 2010). 3β-taraxerol (Figure 2) is another compound isolated from *Mangifera indica*, which was identified as a PI3K dependent dual activator of glucose transport and glycogen synthesis in 3T3-L1 adipocytes (Sangeetha et al., 2010).

***Hippophae rhamnoides* L.**

Seabuckthorn *(Hippophae rhamnoides* L.*, Elaegnacea)* is a thorny deciduous shrub native to several countries of Europe and Asia. The distribution ranges from Himalaya regions of India, Nepal, Pakistan, Afghanistan, Britain, Germany, Finland and France. All parts of this plant are considered rich source of a large number of bioactive substances with high medicinal and nutritional properties. Seabuckthorn (SBT) seed oils, berries, leaves and bark are well known for their medicinal properties and have been suggested to be due to high contents of antioxidative substances present in this plant. (Negi et al., 2005). Seabuckthorn possess hypoglycemic activity (Zhang et al., 2010). Significant ($P<0.001$) increase in blood glucose level was observed in STZ induced –diabetic rats when compared to normal control rats. Oral administration of SBT at two doses (1 and 2 ml/kg), for 3 weeks reduced the blood glucose level significantly ($P<0.001$) in a dose dependent manner. In the oral glucose tolerance test, SBT significantly reduced the blood glucose level in glucose loaded rats at 30, 60, 90 and 120 min. as compared with control rats, loaded only with glucose (Sharma et al., 2011).It have also reported that the flavonoids from the seed and fruit residue of *Hippophae rhamnoides* L. exhibited hypoglycaemia and hypolipidemic effects (Cao et al., 2003). In a recent study, Chaman et al. (2011), have reported the hypoglycemic activity along with hepato and neuroprotective effects in animals and humans. In diabetes, *H. rhamnoides* Linn. affected not only the lowering of the blood sugar including fasting blood glucose and 2 h postprandial blood glucose, but also in treating the complications. *H. rhamnoides* Linn. had been shown to be effective in cell cultures, animal studies, and clinical practice. Although, H. rhamnoides Linn. had been shown to have positive effects in relieving symptoms, such as fatigue, dry mouth and dry eye in non-diabetic disease, whether it has the therapeutic effect on diabetes symptoms was still unclear. Studies have to be conducted to test and verify the

effect of H. rhamnoides Linn. on symptoms in diabetes patients (Wang et al., 2011). Ten healthy normal-weight male volunteers consumed four study breakfasts, one control (A) and three sea buckthorn meals on four distinct study days. All the meals contained yoghurt and glucose (50 g). The sea buckthorn ingredients used were dried and crushed whole berries (meal B1), supercritical fluid (SF)-carbon dioxide (CO_2)-extracted oil-free berries (meal B2) or ethanol-extracted SF-CO_2-extraction residue (meal B3). Blood samples for glucose, insulin and tumor necrosis factor-α analyses were collected before and during the 6-h study period. Meal B1 suppressed the postprandial peak insulin response when compared with meal A (concentration of 30-min peak value 21.8 mU/l, $P<0.039$), and stabilized postprandial hyperglycemia and subsequent hypoglycemia (concentration of 30-min peak value120-min value 30.4 mU/l, $P<0.036$). Furthermore, meal B2 resulted in a more stable insulin response than the control meal (concentration of 30-min peak value120-min value 25.9 mU/l, $P<0.037$) (Lehtonen et al., 2010).

Administering the sea buckthorn concentrate for two months to diabetic children, the erythrocyte superoxide dismutase activity was significantly higher ($p<0.05$). Levels of glycated hemoglobin were significantly lower ($p<0.05$). The activity of whole blood glutathione peroxidase was moderately increased but the difference was not statistically significant. C peptide concentration was significantly higher after treatment with this dietary supplement ($p<0.05$). Treatment with this dietary supplement has a beneficial effect in the treatment of type 1 diabetic children and it should be considered as a phytotherapeutic product in the fight against diabetes mellitus (Nemes-Nagy et al., 2008).

***Tamarindus indica* L.**

Tamarindus indica Linn was used as a traditional medicine for the management of diabetes mellitus in human and experimental animals (Maiti et al., 2004; Chatterjee et al., 2009; Maiti et al., 2005; Martinello et al., 2006). *Tamarindus indica* Linn is tree-type of plant belonging to the caesalpiniaceae family (Maiti et al., 2005) grows naturally in tropical and subtropical regions and now is one of the most important plant resources as food materials and is accepted as herbal medicine in parts of the world (Siddhuraju, 2007). It is widely cultivated as an ornamental tree and for its acidic fruits used in making drinks and a popular component of many decoctions used as health remedies (Doughari 2006). *Tamarindus indica* seed coat may play an important role in chemical protection from oxidative damage by possessing endogenous antioxidants such as phenolic compounds. The potential antioxidant activity of Tamarind seeds have already been reported and the isolated antioxidant components are 2-hydroxy-30,40-dihydroxyacetophenone, methyl 3,4- ihydroxybenzoate, 3,4-dihydroxyphenylacetate and epicatechin in addition to oligomeric proanthocyanidins (Siddhuraju, 2007). Phenolic compounds in seeds of Tamarind indica includes Procyanidin B2, Epicatechin, Procyanidin trimer, Procyanidin tetramer, Procyanidin pentamer, Procyanidin hexamer, Polymeric tannins, Polymeric tannins (Sudjaroen et al., 2005). Treatment of diabetic rats with *Tamarindus indica* seed extract, from one week after diabetes induction, compensated hypoglycemia after 6, 4 and 2 weeks, and increased blood insulin (Mahmoudzades-Sagheb et al., 2010). Supplementation of 80mg/0.5ml distilled water/100gm body weight/day of aqueous extract of seed of *Tamarindus indica* after 7 days and 14 days resulted significant diminution of fasting blood glucose level and significant increase of insulin level

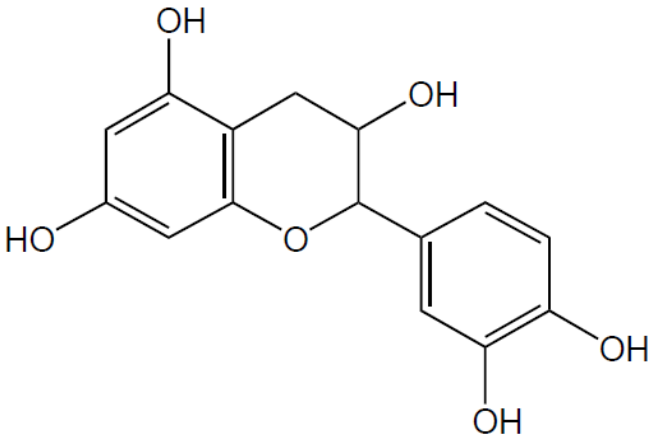

Figure 3. Epicatechin

in respect to diabetic rat, and symptoms like loss of body weight, weakness, polyuria and polyphasia that accompany type-I diabetes mellitus were significantly absent in *Tamarindus indica* treatment diabetic groups (Maiti et al., 2004).

***Eugenia jambolana* L.**

Eugenia jambolana belongs to the family Myrtaceae, is a large evergreen tree growing up to 30 m height, found widely in India and the Asian subcontinent. The seeds of this plant have been reported to possess many medicinal properties in the Ayurveda system of medicine. The fresh seeds are most effective in diabetes as they quickly reduce sugar in urine (Gohil et al., 2010). *E. Jambolana* is established for its antidiabetic potential in ayurveda, as well as in the modern scientific community. *E. jambolana* seeds have hypoglycemic, anti-inflammatory property (Achrekar et al., 1991). *E. jambolana* possibly acts as a hypoglycemic agent by increasing insulin levels rather than just as an antihyperglycemic agent (Bansal et al., 1981). According to investigation by Sridhar et al., (2005), *E. jambolana* seed powder administered for 15 days to STZ-induced diabetic rats revealed an increase in body weight. Hypoglycemic activity of ethanolic whole seeds, kernel (100 mg/kg of body weight) and seed coat extracts in streptozotocin-induced diabetic rats and exhibits normoglycemia and better glucose tolerance (Ravi et al.,2004). Jamun in diet could help in the management of both type 1 and type 2 diabetes (Kaur et al., 2011).

Momordica charantia

Momordica charantia is a very common and well established folkloric remedy for diabetes. Extract of fruit pulp, seed, leaves and whole plant of Momordica charantia has shown hypoglycemic effect in various animal models (Ali et al., 1993). Karunanayake et al. (1984), M. charantia showed hypoglycemic as well as antihyperglycemic activity in laboratory animals. A Polypeptide isolated from fruit, seeds, and tissue of *M. charantia* showed potent hypoglycemic effect when administered subcutaneously to gerbils, langurs, and humans (Khanna et al., 1981).

Aqueous extracts of *M. charantia* improved OGTT after 8 h in normal mice and

reduced hyperglycemia by 50% after 5 h in STZ induced 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). In a similar study, 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) reported the anti-hyperglycemic as well as hypoglycemic effect after administration of ethanolic extract of *M. charantia* (200 mg/kg) in normal and STZ diabetic rats. This occurred possibly due to inhibition of glucose-6-phosphatase and fructose-1,6-bisphosphatase in the liver and stimulation of red-cell and hepatic glucose-6-phosphate dehydrogenase activities. When fed orally, aqueous extract of M. charantia but not ethanolic extract showed anti-hyperglycemic and hypoglycemic effect in cyproheptadine-induced hyperglycemic and normoglycemic mice, respectively, (Cakici et al., 1994). The pulp juice and saponin free methanolic extract of pulp juice exerted significant hypoglycemic effect in fasting and postprandial states of normal and NIDDM rats but not in IDDM rats. Effect was more pronounced in case of saponin free methanol extract. Charantin, a peptide resembling insulin isolated from M. charantia lowered fasting blood sugar in rabbits gradually beginning from 1st and lasting till the 4th h and slowly recovering to the initial level. Charantin (50 mg/kg) administered orally, lowered blood glucose by 42% at the 4th 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 (PB/0.001) of postprandial serum glucose in 86% cases and fasting glucose in 5% cases (Ahmad et al., 1999). Aqueous juice of M. charantia fruit exerted anti-hyperglycemic and antioxidant effect in pancreas of STZ-diabetic mice (Sitasawad et al., 2000). Oral supplementation (0.5, 1 and 3%) with freeze-dried powder of M. charantia for 14 days with and without 0.5% cholesterol and 0.15% bile acid in the diet resulted in a consistent decrease in serum glucose levels in normal rats only in the former group. Experiments in rats showed that 2 important constituents of M. charantia i.e. oleanolic acid 3-*O*-glucuronide exert anti-hyperglycemic effect by inhibiting glucose transport at the brush border of the small intestine (Matsuda et al., 1998). The fruit juice significantly increased the number of beta cells (PB/0.004) in diabetic rats (Ahmed et al., 1998). Oral administration of different M. charantia extracts showed a varying pattern of anti-hyperglycemic effect without altering the insulin response suggesting a mechanism of action which is independent of intestinal glucose absorption and probably involves an extrapancreatic effect (Day et al., 1984).

Oral feeding of *M. charantia* juice to normal rats prior to glucose loading increased hepatic and muscle glycogen content while triglyceride content was not effected. Aqueous extract of unripe fruits of M. charantia has also been shown to partially stimulate insulin release from isolated beta-cell of obese-hyperglycemic mice which differed from D-glucose and other insulin secretagogues agent in the manner that not being suppressed by L-epinephrine and in even being potentiated by the removal of Ca2_suggesting that the insulin-releasing action is the result of perturbations of membrane functions (Welihinda et al., 1982). Daily administration of extract of *M. charantia* fruit (4 gm/kg/) for 2 months to alloxanized diabetic rats (120 mg/kg) delayed development of cataract. Respective blood sugar level in the two groups was 3079/81 and 66.37 mg% (Srivastava et al., 1988). In a clinical trial,

water-soluble extract of the fruits of M. charantia significantly reduced blood glucose concentrations in the 9 NIDDM diabetics on OGTT (50gm). 11β-Hydroxysteroid dehydrogenase type 1 (11β-HSD1) catalyzes the intracellular regeneration of active cortisol from inert cortisone in key metabolic tissues, thus regulating ligand access to glucocorticoid receptors. There is strong evidence that increased adipose 11β-HSD1 activity may be an important aetiological factor in the current obesity and diabetes type 2 epidemics. Hence, inhibition of 11β-HSD1 has emerged as a promising anti-diabetic strategy for new drugs against NIDDM. Recently a compound was isolated from *M. charantia* with significant activity against 11β-Hydroxysteroid dehydrogenase type 1 (11β-HSD1) enzyme, which is an important therapeutic target in NIDDM (Blum et al., 2012).

Momordicine II and 3-hydroxycucurbita-5,24-dien-19-al-7,23- di-*O*-β-glucopyranoside (4), were isolated as saponins from *M. charantia.* Both compounds showed significant insulin releasing activity in MIN6 β-cells at concentration of 10 and 25 μg/ml (Keller et al., 2011). According to Kim and Kim (2011) *M. charantia* extract suppressed the activation of MAPKs including stress-activated protein kinase/c-Jun N-terminal kinase (SAPK/JNK), p38, and p44/42, and the activity of NF-κB. The findings suggest that *M. charantia* protects zpancreatic β-cells through down-regulation of MAPKs and NF-κB in MIN6N8 cells. In a similar study, suggest that *M. charantia* improves the serum and liver lipid profiles and serum glucose levels by modulating PPAR-γ gene expression. To our knowledge, this study for the first time shows that BMS exerts cardioprotective effects by down-regulating the NF-κB inflammatory pathway (Gadang et al., 2011). According to ragasa et al., (2011), clerosterol and 5α-stigmasta-7-en-3β-ol were isolated as sterols from *M. charantia* having significant hypoglycemic effects. *M. charantia* was identified to posses a potent neuroprotective activity against global cerebral ischemia-reperfusion induced neuronal injury and consequent neurological deficits in diabetic mice (Malik et al., 2011). Protein tyrosine phosphatase 1B (PTP1B), a negative regulator of insulin signaling, has served as a potential drug target for the treatment of type 2 diabetes. Hoang et al., (2010) reported the PTP1B inhibitory activity of *M. charantia.*

Ocimum sanctum L.

In traditional systems of medicine, different parts (leaves, stem, flower, root, seeds and even whole plant) of *Ocimum sanctum Linn* (Tulsi), a small herb seen throughout India, have been recommended for the treatment of bronchitis, bronchial asthma, malaria, diarrhea, dysentery, skin diseases, arthritis, painful eye diseases, chronic fever, insect bite etc. The *Ocimum sanctum* L. has also been suggested to possess antifertility, anticancer, antidiabetic, antifungal, antimicrobial, hepatoprotective, cardioprotective, antiemetic, antispasmodic, analgesic, adaptogenic and diaphoretic actions. Eugenol (l-hydroxy-2-methoxy-4-allylbenzene), the active constituent present in *Ocimum sanctum L.,* has been found to be largely responsible for the therapeutic potentials of Tulsi (Prakash and Gupta 2005). Aqueous decoction of whole plant lowers blood glucose level and is said to control diabetes mellitus (Nargarjun 1989). Ethanolic extract of O. sanctum L. significantly decreases the blood glucose, glycosylated hemoglobin and urea with a concomitant increase in glycogen, hemoglobin and protein in streptozotocin-induced diabetic rats (Narendhirakannan 2006). Treatment with O. sanctum L. extract for 30 days to normal rats fed with fructose for 30 days significantly lowered serum glucose level (Grovel et al., 2005). Mechanism of glucose-

lowering activity of *O. sanctum* L. in male mice. The study suggested that O. sanctum L. decreases the serum concentration of both cortisol and glucose and also exhibited antiperoxidative effect. Therefore O. sanctum L. may potentially regulate corticosteroid- induced diabetic mellitus (Ghosap et al., 2004). Administration of O. sanctum L. extracts 200 mg/kg for 30 days lead to decrease in plasma glucose levels by approximately 9.06 and 24.4% on 15th and 30th day. O. sanctum L. significantly decreased renal but not liver weight (expressed as % of body weight) O. sanctum L. glycogen content in any tissue; also O. sanctum L. partially corrected the activity of glucokinase (gk), hexokinase (hk) and phosphofructokinase (PFK) distributed in the diabetic control (Luthra 2010).

Terminalia chebula

Terminalia chebula RETZ. (Combretaceae), a native plant in India and Southeast Asia, is extensively cultivated in Taiwan. Its dried ripe fruit, also called as medicinal terminalia fruit, has traditionally been used to treat various ailments in Asia (Perry 1980). *Terminalia chebula* (Kadukkai) is one of the traditional Ayurvedic medicines that have found to posses various qualities on curing different kinds of diseases. *T. chebula* has been reported to exhibit a variety of biological activity, including anticancer, antidiabetic, antimutagenic, antibacterial, antifungal, and antiviral activities, etc (Cheng et al., 2003). *T. chebula* extract showed stimulatory effect on on the insulin secretion activity of rat pancreatic INS-1 β-cells and glucose consumption in mouse 3T3-L1 adipocytes (Kaur et al., 2011). Kim et al., (2011) reported that administration of *T. chebula* extract reduced the levels of blood glucose and serum lipids, decreased malondialdehyde concentrations of serum and thoracic aorta in diabetic rats, and significantly improved serum biochemical values and the pathomorphological changes of the liver and kidney in diabetic rats. Also, HEETC decreased the advanced glycation end products (AGEs) distribution in testis seminiferous tubules.

T. chebula extract showed considerable inhibitory effect on α-amylase (Zinjarde et al., 2011) revealing its potential as potential antidiabetic agent. Glycation is one of the major factors associated with Diabetes militis. Kusirisin et al., (2009) have reported the antiglycation effect of *T. chebula* extract.

P*anax ginseng*

Panax ginseng is used medicinally for thousands of years in China, Korea, and Japan,1 is well known as an adaptogen and a restorative tonic that is widely used in traditional Chinese medicine (TCM) and Western herbal preparations (Duke 2000 and Blumenthol 2003). *Panax ginseng* belongs to the Araliaceae family and is found throughout East Asia and Russia.5,6 Eclectic uses for *Panax ginseng* include fatigue, infertility, liver disease, amnesia, colds, menopause and erectile dysfunction and diabetes (Duke 2000 and Weiss 1988). Eclectic medicine texts reference *Panax ginseng* for its beneficial use in blood sugar regulation (Hoffman 2003). In a double-blind RCT of *Panax ginseng* in newly diagnosed type 2 diabetics (Sotaniemi 1995). Parameters measured included physical performance, mood, serum lipids, fasting blood glucose, hemoglobin A1c (HbA1c), aminoterminal propeptide (PIIINP) concentration and body weight. PIIINP serum levels are associated with coronary artery disease and were used as a safety parameter in this study. The study participants (n=36) were given 100 mg ginseng extract, 200 mg ginseng extract, or placebo daily for eight

weeks. Compared to the placebo group, the 200-mg ginseng group experienced elevated mood, improved physical performance, and reduced fasting blood glucose. The authors concluded ginseng warrants further study as an adjuvant to diabetes management. A 2005 double-blind, crossover RCT examined the effects of *Panax ginseng* on blood glucose levels and cognitive performance during sustained mental activity (Reay et al.,2005). Healthy young adults (n=30) took a 10-minute test battery for baseline results, then were given 200 mg G115, 400 mg G115, or placebo. One hour later the test battery was repeated six times in rapid succession. Blood sugar levels were assessed at baseline and twice during the testing procedure. The 200-mg and 400-mg G115 doses reduced blood glucose levels significantly ($p<0.005$). Significant improvement was also noted in the ability to complete the serial sevens subtraction task after taking 200 mg G115 ($p<0.05$). The authors concluded *Panax ginseng* improves mental performance, possibly by regulating glucose metabolism. A double-blind, 12-week RCT examined the effect of red *Panax ginseng* on HbA1c levels in 19 subjects with well-controlled type 2 diabetes (Vuksan et al.,2008). Study participants received 2 g ginseng or placebo three times daily before meals. Plasma glucose and insulin, insulin sensitivity, and oral glucose tolerance were secondary measures of efficacy, while blood pressure checks and liver and kidney function tests assessed safety. Although no change was seen in HbA1c levels with ginseng, the participants remained well controlled throughout the study without pharmaceutical intervention with average levels of HbA1c of 6.5 percent. A significant 8 to 11 percent decrease in glucose on the oral glucose tolerance test and 33 percent decrease in plasma insulin ($p<0.05$) was seen in the ginseng group compared to placebo (Anonymous 2009).

Various bioactive compounds isolated from *P. ginseng* have been reported. Li et al., (2012), the hypoglycemic and insulin-sensitizing capabilities of Compound K (CK) isolated from *P. ginseng* have considerable inhibitory effect on type 2 diabetes induced by HFD/STZ via down-regulation of Phosphoenolpyruvate carboxykinase (PEPCK) and Glucose-6-phosphatase (G6Pase), expression in liver. Ginsenoside Rb2 is an active compound found in *P. ginseng* showed inhibition of palmitate-induced gluconeogenesis via AMP-activated protein kinase (AMPK)-induced small heterodimer partner (SHP by relieving ER stress, a cause of gluconeogenesis

Moringa oliefera

Moringa oleifera is the most widely cultivated species of a monogeneric family, the Moringaceae, that is native to the sub-Himalayan tracts of India, Pakistan, Bangladesh and Afghanistan. This rapidly-growing tree (also known as the horseradish tree, drumstick tree, benzolive tree, kelor, marango, mlonge, moonga, mulangay, nébéday, saijhan, sajna or Ben oil tree), was utilized by the ancient Romans, Greeks and Egyptians; it is now widely cultivated and has become naturalized in many locations in the tropics. It is a perennial softwood tree with timber of low quality, but which for centuries has been advocated for traditional medicinal and industrial uses. Moringa preparations have antibiotic, antitrypanosomal, hypotensive, antispasmodic, antiulcer, anti-inflammatory, hypo-cholesterolemic, and hypoglycemic activities (Fahey 2005).

Graded doses of the leaves extract (250 and 500 mg/kg i.p.) were separately administered to groups of fasted normal and fasted STZ diabetic rats. The hypoglycemic effect of the

ethanolic leaves extract was compared with that of insulin 6 i.u/kg in fasted normal and STZ diabetic rats. Moderate to high doses of *Moringa oleifera* (250 and 500 mg/kg i.p.) produced a dose-dependent, significant reduction ($p<0.05$) in blood glucose levels of fasted STZ diabetic rats only. A significant decrease in the blood glucose levels after 1-7 h of administration with the doses of 250 and 500 mg/kg was observed in the STZ diabetic group when compared to control. As regards to the dose of 250 and 500 mg/kg for the fasted normal rats, there was significant increase in the blood glucose levels when compared to control. In conclusion the ethanolic extract of the leaves of *Moringa oleifera* possesses hypoglycemic activity in STZ induced diabetic Wistar rats only. (Tende et al., 2011).

Ziziphus Jujuba

Zizyphus jujuba commonly called, Red date, Chinese date or Bera (Pushto), belongs to family *Rhamnaceae*. This family consists of 50 genera and more than 900 species; it is almost cosmopolitan and found mainly in subtropical to tropical areas. The bark, leaves and fruit of several species of *Rhamnaceae* have been used as laxatives, notably *Rhamnaceae cathartica* and *Rhamnaceae frangula*. Many *Ziziphus* species yield edible fruit, among these are: *Z. jujuba* (Chinese jujube) and *Ziziphus mauritiana* (Indian jujube) which are cultivated on a commercial scale (Yilin and Carsten 2007). Z. Jujuba extract has significantly reduced glucose level from 767.82 mg/dl to 250.94 mg /dl (Shirdel et al., 2009). Four-five fresh leaves are chewed daily to lower blood glucose level (Ahmad et al., 2009).

Azadirachta indica A.

Azadirachta indica A. Juss., commonly referred as the neem tree, is a broad-leaved evergreen tree with a height of 20–30m and a trunk girth of 2.5 m, found throughout India and is widely recognized as potent insecticide. Hypoglycemic activity of hydro alcoholic *Azadirachta indica* extract in normal rats and hypoglycemic activity in glucose fed and streptozotocin induced diabetic rats (Chattopadhyay et al.,1987a; Chattopadhyay, 1996). Hypoglycemic and antihyperglycemic activities of leaf extract in normal and streptozotocin-induced diabetic rat (Chattopadhyay, 1999; Gholap and Kar, 2004). Hypoglycemic activity of crude ethanolic extract of the plant in alloxan diabetic albino rats (Kar et al., 2003). The plant exerts its pharmacological activity independent of its time of administration i.e. either prior or after alloxan administration (Khosla et al., 2000). *Azadirachta indica's* possible mechanism is to inhibits action of epinephrine on glucose metabolism, resulting in increased utilization of peripheral glucose (Chattopadhyay et al., 1987b; Chattopadhyay, 1996) and exhibits hypoglycaemic activity without altering the serum cortisol concentration (Chattopadhyay, 1999; Gholap and Kar, 2004).

Allium (*Allium sativum* and *Allium cepa*)

Allium species such as onions and garlic are used as foodstuff, condiment, flavoring, and folk medicine. Garlic has attracted particular attention of modern medicine because of its widespread health use around the world, and the cherished belief that it helps in maintaining good health, warding off illnesses and providing more vigor. The biological responses of garlic have been largely attributed to (i) reduction of risk factors for cardiovascular diseases and cancer, (ii) stimulation of immune function, (iii) enhanced detoxification of foreign

compound, (iv) hepatoprotection, (v) antimicrobial effect and (vi) antioxidant effect (Banerjee and Maulik, 2002). Onion was also a popular folk remedy. It is rich in flavonoids such as quercetin and sulfur compounds, such as allyl propyl disulphide that have perceived benefits to human health (Griffiths et al., 2002). In addition, onion and garlic are rich in sulfur containing compounds mainly in the form of cysteine derivatives, viz.S-alkyl cysteine sulfoxides which are decomposed the enzyme allinase into a variety of volatile compounds such as thiosulfinates and polysulfides during extraction. These compounds possess antidiabetic, antibiotic, hypocholesterolaemic, fibrinolytic, and various other biological effects. In addition to volatile substances in alliums, there are nonvolatile sulfur-containing peptides and proteins which have been shown to have potential health benefits (Augusti, 1996).

A dose of 1ml of either onion or garlic juices/100g body weight (equivalent to 0.4 g/100gBW) was orally administered daily to alloxan-diabetic rats for four weeks. The levels of glucose, urea, creatinine and bilirubin were significantly ($p < 0.05$) increased in plasma of alloxan-diabetic rats compared to the control group. Aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), and alkaline and acid phosphatases (AlP, AcP) activities were significantly ($p < 0.05$) increased in plasma and testes of alloxan-diabetic rats, while these activities were decreased in liver compared with the control group. Brain LDH was significantly ($p < 0.05$) increased. The concentration of thiobarbituric acid reactive substances and the activity of glutathione S-transferase in plasma, liver, testes, brain, and kidney were increased in alloxandiabetic rats. Treatment of the diabetic rats with repeated doses of either garlic or onion juices could restore the changes of the above parameters to their normal levels. The present results showed that garlic and on ion juices exerted antioxidant and antihyperglycemic effects and consequently may alleviate liver and renal damage caused by alloxan-induced diabetes (El-Demerdash et al., 2005).

Cinnamomum cassia

Cinnamon (*Cinnamomum cassia*) has insulin like activity and it contains an active ingredient water soluble polephenol compound MHCP (methyl hydroxi chalcon polymer). It initiate insulin, triggers its receptors and work synergistically with insulin cells. Cinnamon also reduced cholesterol level and improves lipid metabolism (Jarvill and Karjee 2003). The fasting blood sugar reduced from 148.73±3.69 mg/dl (initial value) to 134.0± 3.12 mg/dl at 20 days after intervention and continued to reduce to 120.66±4.70 mg/dl and reduction in post prandial blood glucose value was 172.93±3.51 mg/dl at the mid (20th day) of the intervention and further reduced to 163.6±5.09mf/dl at the end of the intervention (40th day) after supplementation of cinnamon (Soni and Bhatnagar 2009). Three groups receiving 1, 3, 6 g of cinnamon/day for 40 days reduced blood glucose level (Khan et al., 2003). Significant reduction in both fasting and post prandial blood glucose after 4 g cinnamon supplementation for 90 days (Anuradha and Devi 2004).

Glycine max

Glycine max (Soybean) belongs to the family Leguminosae or Fabaceae, which contains vegetable protein, oligo- saccharides, dietary fibre, phytochemicals (especially isoflavones) and minerals. The Food and Drug Administration (FDA) USA approved the role of soybean in reducing coronary heart disease and lowers cholesterol level. Also, it has anti-

inflammatory and anti-carcinogenic effects on digestive system (Aparicio et al., 2008). Male rabbits were divided into four different groups including, Normal control, Diabetic control, treated with soybean chloroform extract and soybean alcohol extract, with 3 rabbits in each group. The extracts were given orally for 24 days, 50ml extract per rabbit per day. At every 3rd day blood sample was collected, serum separated and glycemic level, total cholesterol level, urea level, uric acid level were determined by kit method. The body weight was recorded on every 6th day's interval. The data obtained revealed that soybean chloroform and alcohol extracts reduced the glucose level, 42.53% and 49.78% respectively. The treatment with these extracts also reduced the cholesterol level, urea level significantly and increased uric acid level and body weight as compared with normal and diabetic groups. Therefore, it is concluded that the soybean possess significant antidiabetic activity (Khushk et al., 2010).

Trigonella foenum-graecum

Trigonella foenum-graecum, commonly known as fenugreek, is extensively used in many preparations of Ayurveda and also against antiulcer action5 and hypocholesterolaemic effects(Singhal and Augusti, 1982; Sharma 1984; Sharma et al., 1996). Fenugreek (*Trigonella foenum-graecum*) is commonly used as a condiment and seasoning in food preparations; is assumed to possess nutritive and restorative properties9 and has been used in folk medicine for centuries for a wide range of diseases including diabetes, fever and abdominal colic as a poultice for abscesses, boils, and carbuncles(Sharma 1986). The hypoglycemic property of fenugreek was observed in diabetic patients (Al- Shamony et al., 1994). Fenugreek (*Trigonella Foenum-Graecum*) found in nature and is cultivated in India and Pakistan is a well known medicinal plant having properties of reducing blood sugar level (Raghuram et al., 1994). Oral administration of ethanolic extract of *T. foenum-graecum* seed powder (50mg/100g bodyweight) for 48 days on the blood glucose level, serum cholesterol level, SGOT and SGPT level in normal and alloxaninduced diabetic rats were evaluated. Administrations of the herbal extract decreased blood glucose, serum cholesterol, SGOT and SGPT levels. (Renuka et al.,2009). Twenty-five patients with newly diagnosed type 2 diabetes received either 1 g daily of a hydroalcoholic extract of fenugreek seeds or "usual care" (dietary discretion and exercise). After two months, mean fasting blood glucose levels were reduced in both groups without significant differences between groups (148.3 mg/dL to 119.9 mg/dL in the fenugreek group versus 137.5 mg/dL to 113.0 mg/dL in the "usual care" group) (Gupta et al., 2001).

Streptozotocin-induced diabetic rats were administrated by oral intragastric intubation separately with low dose (0.44 g/kg.d), middle dose (0.87 g/kg.d), high dose (1.74 g/kg.d) of *Trigonella foenum-graecum* extract, and Metformin HCl (0.175 g/kg.d) for 6 weeks. Compared with diabetic group, rats treated with *Trigonella foenum-graecum* extract had an increase in body weight and a decrease in kidney /body weight ratio ($p<0.05$). Compared with diabetic group, rats treated *Trigonella foenum-graecum* extract had lower blood glucose, glycated hemoglobin, triglycerides, total cholesterol and higher higher-density-lipoprotein-cholesterol in a dose-dependent manner ($p<0.05$). The plasma viscosity, whole blood viscosity of high shear rate (200 s -1) and low shear rate (40 s-1), erythrocyte sedimentation rate, whole blood reduction viscosity and platelet conglutination were significantly reduced in diabetic rats treated with high and middle doses of *Trigonella foenum-graecum* extract, but not in those treated with low dose of

Trigonella foenum-graecum extract. It may be concluded that *Trigonella foenum-graecum* extract can lower kidney /body weight ratio, blood glucose, blood lipid levels and improve hemorheological properties in experimental diabetic rats following repeated treatment for 6 weeks (Xue et al., 2007).

Ipomoea batas L.

Ipomoea batatas (L.) Lam. from the family Convolvulaceae is the world's sixth largest food crop which is widely grown in tropical, subtropical and warm temperate regions (Scott 1992). The tuber of *Ipomoea batatas* is commonly known as sweet potato. It is also called kamote, lapni, yams and tugi in various parts of the world. The boiled tubers are consumed as a vegetable globally. The tuber is often long and tapered and the skin may be red, purple, or brown and white in color. The flesh may be white, yellow, orange or purple. The *I. batatas* plant has been used extensively in traditional medicines for various ailments (Miyazaki et al., 2005; Cambie R C, Ferguson 2003). The effects of flavone extracted from *Ipomoea batatas* leaf (FIBL) on body weight, blood glucose, serum lipid profiles, serum insulin and free radicals in rats with non-insulin dependent diabetes mellitus (NIDDM) were studied. FIBL treatment (25, 50, 100 mg kg^{-1}) for 2 weeks resulted in a significant decrease in the concentration of plasma triglyceride (TG), plasma cholesterol (TC) and weight in NIDDM rats. Furthermore, FIBL markedly decreased fasting plasma insulin level, blood glucose (FBG) level, low-density lipoprotein cholesterol (LDL-C), and malondialdehyde (MDA) levels and significantly increased the Insulin Sensitive Index (ISI) and superoxide dismutase (SOD) level in NIDDM rats. In addition, flavone extracted from *I. batatas* leaf did not show any physical or behavioural signs of toxicity. More significantly, our data demonstrate the FIBL at the dose of 50 mg kg^{-1} body weight exhibited the optimal effect. The above results suggest that flavone extracted from *I. batatas* leaf could control blood glucose and modulate the metabolism of glucose and blood lipid, and decrease outputs of lipid peroxidation and scavenge the free radicals in non-insulin dependent diabetic rats (Zhao et al., 2007).

Citrullus colosynthis

Plant drugs are frequently considered to be less toxic and free from side effects than synthetic ones**.** The World Health Organization has also recommended the evaluation of the effectiveness of plants in conditions where safe modern drugs are beyond the reach of general people **(**Upadhayay and Pandey, 1984). Theplant *Citrullus colocynthi*s claims to possess hypoglycemic property as reviewed from various literatures (Abdel-Hassana et al., 2000, Fatma et.al.,(2004)). Eighty wistar rats were divided into three groups containing six rats in each group. Group T1 was maintained as normal control, whereas groups T2 and T3 received aqueous extract of *Citrullus colocynthis* @ 50 and 100 mg/kg body weight for 28 days. Haematological and Biochemical estimations were done at the end of experiment i.e. on 29th day by using standard kits. Rats were then sacrificed and histopathological examinations were done. The results obtained showed that *Citrullus colocynthis* is safe at its antidiabetic dose and is safe for use as an antidiabetic remedy (Atole et al., 2009).

Future perspectives

As the people are becoming aware of the potency and side effect of synthetic drugs,

there is an increasing interest in the natural product remedies with a basic approach towards the nature. Throughout the history of mankind, many infectious diseases have been treated with herbals. A number of scientific investigations have highlighted the importance and the contribution of many plant families i.e. Asteraceae, Liliaceae, Apocynaceae, Solanaceae, Caesalpinaceae, Rutaceae, Piperaceae, Sapotaceae used as medicinal plants. Medicinal plants play a vital role for the development of new drugs. The bioactive extract should be standardized on the basis of active compound. Almost, 70% modern medicines in India are derived from natural products. Medicinal plants play a central role not only as traditional medicines but also as trade commodities, meeting the demand of distant markets. India has a very small share (1.6%) of this ever-growing global market. To compete with the growing market, there is urgency to expeditiously utilize and scientifically validate more medicinally useful plants. Diabetes is a disorder of carbohydrate, fat and protein metabolism attributed to diminished production of insulin or mounting resistance to its action. Herbal treatments for diabetes have been used in patients with insulin-dependent and non-insulin-dependant diabetes, diabetic retinopathy, diabetic peripheral neuropathy, etc. Several Indian plant species has proved the efficacy of the botanicals in reducing the sugar level. So all these plant materials help to control diabetes.

Conflict of interest

There is no conflict of interest associated with the authors of this paper.

References

Abdel-Hassan IA, Abdel-Barry JA and Tariq MS (2000). The hypoglycaemic and antihyperglycaemic effect of *Citrullus colocynthis* fruit aqueous extract in normal and alloxan diabetic rabbits. *Journal of Ethnopharmacology* 71, 325-330.

Achrekar B, Kakij GS, Pote MS and Kelkar SM (1991). Hypoglycaemic activity of *Eugenia jambolana* and *Ficus bengalensis*. *In vivo* 5, 143-147.

Aderibigbe AO, Emudianughe TS and Lawal BA (1999). Antihyperglycaemic effect of *Mangifera indica* in rat. *Phytotherapy Research* 13, 504-507.

Ahmad N, Hassan MR, Halder H and Bennoor KS (1999). Effect of *Momordica charantia* (Karella) extracts on fasting and postprandial serum glucose levels in NIDDM patients.

Ahmad M, Qureshi R, Arshad A, Khan MA and Zafar M (2009). Traditional herbal remedies used for the treatment of diabetes from district Attock (Pakistan). *Pakistan Journal of Botany* 41(6): 2777-2782.

Al- Shamony L, Al- Khazraje, SM and Twaiji HA (1994). Journal of Ethnopharmacology 43, 167-171.

Anuradha V and Devi A (2004). Hypoglycemic effect of Cinnamon and Cumin seed powder on type 2 Diabetes.The Indian Journal of Nutrition and Dietetics. 49, 370-374.

Aparicio MI, Cuenca AR, Suarez MJV and Revilla MZA (2008). Soybean, a promising health source. Nutr. Hosp. 23, 305-312.

Atole SK, Jangde CR, Philip P, Rekhe DS, Aghav DV, Waghode HJ and Chougule AM (2009). Safety Evaluation Studies of *Citrullus Colocynthis* for diabetes in Rats. Veterinary World. 2, 423-425.

Augusti KT (1996). Therapeutic values of onion (Allium cepa L.) and garlic (*Allium sativum* L.). Indian Journal of Experimental Biology. 34: 634-640.

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

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

Anonymous (2009). *Panax ginseng,* Alternative Medicine Review Vol. 14, Number 2.

Anonymous (2011). Diabetes Basics, Genetics of Diabetes. American Diabetes Association (http://www.diabetes.org/diabetes-basics/genetics-of-diabetes.html.

Bally ISE (2006). *Mangifera indica* (mango), Species Profiles for Pacific Island Agroforestry 1-25.

Banerjee SK and Maulik SK (2002). Effect of garlic on cardiovascular disorders: a review. *Nutrition Journal*. 1, 1-14.

Bansal R, Ahmad N and Kidwai JR (1981). Effect of oral administration of *Eugenia jambolana* seeds and chlorpropamide on blood glucose level and pancreatic cathepsin B in rat. *Indian Journal of Biochemistry and Biophysics* 18, 377-383.

Bailey CJ, Day C, Turner SL and Leatherdale BA (1985). Cerasee, a traditional treatment for diabetes. Studies in normal and streptozotocin diabetic mice. *Diabetes Research*. 2, 81-84.

Bhatti R, Sharma S, Singh J and Ishar MPS (2011). Ameliorative effect of Aegle marmelos leaf extract on early stage alloxan-induced diabetic cardiomyopathy in rats, *Pharmaceutical Biology* 49, 1137-1143.

Birnbaum M J (2005). Rejoinder: Genetic Research into the Causes of Type 2 Diabetes Mellitus. *Anthropology and Medicine* 12, 129-134.

Blumenthal M (2003). *The ABC Clinical Guide to Herbs*.New York, NY: Theime. 211-225. Blum A, Loerz C, Martin HJ, Staab-Weijnitz CA and Maser E (2012). Momordica charantia extract, a herbal remedy for type 2 diabetes, contains a specific 11β-hydroxysteroid dehydrogenase type 1 inhibitor. (2012) *Journal of Steroid Biochemistry and Molecular Biology* 128, 51-55.

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

Cao QH, Qu WJ, Deng YX, Zhang ZC, Niu W and Pan YF (2003). Effects of flavonoids from the seed and fruit residue of *Hippophae rhamnoides* L. on glycometabolism in mice. *Zhong yao cai Zhongyaocai Journal of Chinese Medicinal Materials* 26, 735-737.

Cambie RC and Ferguson LR (2003). Potential functional foods in the traditional Maori diet. *Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis*. 523-524, 109-117.

Centers for Disease Control and Prevention (CDC) (2004). Prevalence of overweight and obesity among adults with diagnosed diabetes—United States, 1988–1994 and 1999–2002. MMWR. Morbidity and Mortality Weekly Report. 53, 1066-8.

Chaman S, Syed NH, Danish Z, Ahmad M and Khan FZ (2011). Hepato and nephro protective as well as hypoglycemic effects of sea buckthorn berries (Hippophae rhamnoides L.) in rabbits and humans. (2011) *Latin American Journal of Pharmacy*. 30, 1780-1784.

Chandrasekar B, Mukherjee B and Mukherjee SK (1989). Blood sugar lowering potentiality of selected Cucurbitaceae plants of Indian origin. *Indian Journal of Medical Research* 90, 300-305.

Chatterjee K, Ali KM, Mallick C and Ghosh D (2009). Antihyperglycaemic, antioxidative activities of a formulated polyherbal drug MTEC (Modified) in streptozotocin-induced diabetic rat. *Journal of Medicinal Plants Research* 3, 468-480.

Chattopadhyay RR, Chattopadhyay RN, Nandy AK, Poddar G and Maitra SK (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 RR (1996). Possible mechanism of antihyperglycemic effect of *Azadirachta indica* leaf extract, part IV. *General Pharmacology.*27, 431-434.

Chattopadhyay RR, Chattopadhyay RN, Nandy AK, Poddar G and Maitra SK (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.

Chattopadhyay RR (1999). A comparative evaluation of some blood sugar lowering agents of plant origin. *Journal of Ethnopharmacology.* 67, 367-372.

Cheng HY, Lin TC, Yu KH, Yang CM and Lin CC (2003). Antioxidant and Free Radical Scavenging Activities of Terminalia Chebula. *Biololgical and Pharmaceutical Bulletine* 26, 1331-1335.

Dahanukar SA, Kulkarni RA and Rege NN (2000). Pharmacology of medicinal plants and natural products. *Indian Journal of Pharmacology*.32, S81-S118.

Datta Banik S and Basu SK (2002). Environmental perspectives and human responses National Service Scheme 2000-01: Government of India. S. Graphics, Kolkata, India.

Das AV, Padayatti PS and Paulose CS (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, 341-345.

Day C, Cartwright T, Provost J, Bailey CJ, Karunanayake EH,Welihinda J, Sirimanne SR and Sinnadorai G (1984). Oral hypoglycemic activity of some medicinal plants of Sri Lanka. *Journal of Ethnopharmacology*.11, 223-231.

Doughary JH (2006). Antimicrobial Activity of *Tamarindus indica* Linn. *Tropical Journal of Pharmaceutical Research*.5, 597-603.

Duke J (2000). The Green Pharmacy Herbal Handbook: Your Comprehensive Reference to the Best Herbs for Healing. Emmaus, PA: Rodale. 115-116.

El-Demerdash FM, Yousef MI and El-Naga NIA (2005). Biochemical study on the hypoglycemic effects of onion and garlic in alloxan-induced diabetic rats. *Food and Chemical Toxicology*.43, 57-63.

Fahey JW (2005). *Moringa oleifera*: a review of the medical evidence for its nutritional, therapeutic, and prophylactic properties. Part 1.Trees for Life Journal a forum on beneficial trees and plants, http://www.TFLJournal.org/article.php/2005120112493-1586

Fatma Al-Ghaithi, Mamdouh RE, Ernest A and Mohamed HA (2004). Biochemical effects of *Citrullus colocynthis* in normal and diabetic rat. *Molecular and Cellular Biochemistry*.26, 143-149.

Gadang V, Gilbert W, Hettiararchchy N, Horax R, Katwa L and Devareddy L (2011). Dietary bitter melon seed increases peroxisome proliferator-activated receptor-γ gene expression in adipose tissue, down-regulates the nuclear factor-κB expression, and alleviates the symptoms associated with metabolic syndrome. *Journal of Medicinal Food*.14, 86-93.

Gaynor P (1999). Food Approval of Low Erucic Acid Rapeseed Oil (Canola Oil) Derived from Canola-Quality *B. juncea.* Canola Council of Canada. 1-23.

Gholap S and Kar A (2004). Hypoglycaemic effects of some plant extracts are possibly mediated through inhibition in corticosteroid concentration. *Pharmazie*. 59, 876-878.

Gohil T, Pathak N, Jivani N, Devmurari V and Patel J (2010). Treatment with extracts of *Eugenia jambolana* seed and *Aegle marmelos* leaf extracts prevents hyperglycemia and hyperlipidemia in alloxan induced diabetic rats. *African Journal of Pharmacy and Pharmacology* 4,:270-275.

Griffiths G, Trueman L, Crowther T and Thomas B (2002). Onions: a global benefit to health. *Phytotherapy Research*.17, 603-615.

Grover JK, Vats V and Yadav SS (2005). Pterocarpus marsupium extract (Vijayasar) prevented the alteration in metabolic patterns induced in the normal rat by feeding an adequate diet containing fructose as sole carbohydrate. *Diabetes, Obesity and Metabolism* 7, 414-20.

Gupta A, Gupta R and Lal B (2001). Effect of *Trigonella foenum-graecum* (fenugreek) seeds on glycaemic control and insulin resistance in type 2 diabetes mellitus: a double blind placebo controlled study. *J Association of Physicians of India*. 49, 1057-1061.

Gupta R, Bajpai KG, Johri S and Saxena AM (2008). An:Overview of Indian novel traditional medicinal plants with antidiabetic potentials. *African Journal of Traditional, Complimentary and Alternative Medicine* 5, 1-17.

Grover JK, Yadav SP and Vats V (2003). Effect of feeding Murraya koeingii and Brassica juncea diet kidney functions and glucose levels in streptozotocin diabetic mice. *Journal of Ethnopharmacology* 85, 1-5.

Hoang DM, Trung TN, Hien PTT, Ha DT, Van Luong H, Lee M and Bae K (2010). Screening of protein tyrosine phosphatase 1B inhibitory activity from some Vietnamese medicinal plants. *Natural Product Sciences* 16, 239-244.

Hoffman D (2003). Medical Herbalism: The Science and Practice of Herbal Medicine. Rochester, VT: Healing Arts Press. 570.

IDF (2011) Diabetes Atlas. *4th edition* (http://www.diabetesatlas.org/content/foreword-0) IDF (2007) Diabetes Atlas 3. (http://www.eatlas.idf.org).

Jack L, Boseman L and Vinicor F (2004). Aging Americans and diabetes: A public health and clinical response. *Geriatrics* 59, 14-7.

Jarvill J, Karjee T (2003). A hydroxy chalcone derived from cinnamon, function as mimetric to insulin in 3T3 XT adipocytes. http.//.diabetesjournal.

Kamalakkannan N and Prince PS (2005). The effect of *Aegle marmelos* fruit extract in streptozotocin diabetes: A histopathological study. *Journal of Herbal Pharmacotherapy*. 5, 87-98.

Kar A, Choudhary BK and Bandyopadhyay NG (2003). Comparative evaluation of hypoglycaemic activity of some Indian medicinal plants in alloxan diabetic rats. *Journal of Ethnopharmacology* 84, 105-108.

Kaur HP, Garg SN, Sashidhara KV and Yadav A (2006). Chemical Composition of the Essential Oil of the Twigs and Leaves of *Aegle marmelos* (L.) Correa. *Journal of Essential Oil Research*: JEOR.

Kaur L, Han KS, Bains K and Singh H (2011). Indian culinary plants enhance glucose induced insulin secretion and glucose consumption in INS-1 β-cells and 3T3-L1 adipocytes. *Food Chemistry* 129, 1120-1125.

Keller AC, Ma J, Kavalier A, He K, Brillantes AMB and Kennelly EJ (2011). Saponins from the traditional medicinal plant *Momordica charantia* stimulate insulin secretion in vitro. *Phytomedicine* 19, 32-37.

Kemasari P, Sangeetha S, Venkatalakshmi P (2011). Antihyperglycemic activity of *Mangifera indica* linn. In alloxan induced diabetic rats. Journal of Chemical and Pharmaceutical Research. 3(5): 653-659.

Khanna P, Jain SC, Panagariya A and Dixit VP (1981). Hypoglycemic activity of polypeptide from a plant source. *Journal of Natural Products*. 44(6): 648-655.

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

Khan A, Safdar M, Khan HMA, Khallak KN and Richard A (2003). Cinnamon improves glucose and lipid of people with type 2 diabetes. *Pakistan Journal of Nutrition*. 2(5): 312-319.

Khosla P, Bhanwra S, Singh J, Seth S and Srivastava RK (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.

Khushk I, Dahot MU, Baloach SA and Bhutto MA (2010).The Evaluation of Soybean Extracts in Alloxan-Induced Diabetic Rabbits. *World Applied Sciences* (Special Issue of Biotechnology & Genetic Engineering). 22-25.

Kim K and Kim HY (2011). Bitter melon (*Momordica charantia*) extract suppresses cytokineinduced activation of MAPK and NF-κB in pancreatic β-cells. *Food Science and Biotechnology*. 20(2): 531-535.

Kim JH, Hong CO, Koo YC, Kim SJ and Lee KW (2011). Oral administration of ethyl acetate soluble portion of *Terminalia chebula* conferring protection from streptozotocin- induced diabetic mellitus and its complications. *Biological and Pharmaceutical Bulletin*. 34, 1702-1709.

Knol M, Twisk J, Beekman A, Heine R, Snoek F and Pouwer F (2006). Depression as a risk factor for the onset of type 2 diabetes: a meta-analysis. *Diabetologia* 49, 837-845.

Kumari M, Head J and Marmot M (2004). Prospective Study of Social and other risk factors for incidence of type 2 diabetes in the Whitehall II Study. *Archives of Internal Medicine* 164, 1873-1880.

Kusirisin W, Srichairatanakool S, Lerttrakarnnon P, Lailerd N, Suttajit M, Jaikang C and Chaiyasut C (2009). Antioxidative activity, polyphenolic content and anti-glycation effect of some Thai medicinal plants traditionally used in diabetic patients. *Medicinal Chemistry* 5, 139-147.

Lang IA, Galloway TS and Scarlett A (2008). Association of urinary bisphenol concentration with medical disorders and laboratory abnormalities in adults". *JAMA.* 300, 1303–1310.

Lehtonen HM, Järvinen R, Linderborg K, Viitanen M, Venojärvi M, Alanko H and Kallio H (2010). Postprandial hyperglycemia and insulin response are affected by sea buckthorn (*Hippophaë rhamnoides ssp.turkestanica*) berry and its ethanol-soluble metabolites. *European Journal of Clinical Nutrition*. 64, 1465-1471.

Li X, Cui X, Sun X, Li X, Zhu Q and Li W (2010). Mangiferin prevents diabetic nephropathy progression in streptozotocin-induced diabetic rats. *Phytotherapy Research* 24, 893-899.

Li W, Zhang M, Gu J, Meng ZJ, Zhao LC, Zheng YN, Chen L and Yang GL (2012). Hypoglycemic effect of protopanaxadiol-type ginsenosides and compound K on Type 2 Diabetes mice induced by High-Fat Diet combining with Streptozotocin via suppression of hepatic gluconeogenesis. *Fitoterapia*. 83, 192-198.

Lolitkar MM and Rao MRR (1966). Pharmacology of a hypoglycemic principle isolated from the fruits of *Eugenia jambolana* Linn. *Indian Journal of Pharmacy*. 28, 129-133.

Lovejoy JC (2002). The influence of dietary fat on insulin resistance. *Current Diabetes Reports* 2, 435-40.

Lyssenko V, Jonsson A and Almgren P (2008). Clinical risk factors, DNA variants, and the development of type 2 diabetes. *The New England Journal of Medicine*. 359, 2220-2232.

Mahmoudzades-Sagheb H, Heidari Z, Shahraki M And Moudi B (2010). A stereological study of effects of aqueous extract of *Tamarindus indica* seeds on pancreatic islets in Streptozotocin-induced diabetic rats. *Pakistan Journal of Pharmaceutical Sciences*. 23, 427-434.

Maiti R, Jana D, Das UK and Ghosh D (2004). Antidiabetic effect of aqueous extract of seed of *Tamarindus indica* in streptozotocin-induced diabetic rats. *Journal of Ethnopharmacology* 92, 85-91.

Maiti R, Das UK and Ghosh D (2005). Attenuation of Hyperglycemia and Hyperlipidemia in Streptozotocin- Induced Diabetic Rats by Aqueous Extract of Seed of *Tamarindus indica*. *Biological & Pharmaceutical Bulletin* 28, 1172-1176.

Maity P, Hansada D, Bandyopadhyay U and Mishra DK (2009). Biological Activities of crude extracts and chemical constituents of Bael, *Aegle marmelos* (L) Corr#. *Indian Journal of Experimental Biology* 47, 849-961.

Malik ZA, Singh M and Sharma PL (2011). Neuroprotective effect of *Momordica charantia* in global cerebral ischemia and reperfusion induced neuronal damage in diabetic mice. *Journal of Ethnopharmacology* 133, 729-734.

Martinello F, Soaresm SM and Franco JJ (2006). Hypolipidemic and antioxidant activities from *Tamarindus indica* L. pulp fruit in hypercholestromic hamsters. *Food and Chemical Toxicology* 44, 810-818.

Matsuda H, Li Y, Murakami T, Matsumura N, Yamahara J and 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* 46, 1399-1403.

McCarthy MI, Feero WG and Guttmacher AE (2010). Genomics, Type 2 Diabetes, and Obesity. *The New England Journal of Medicine*. 363, 2339-2350.

Miyazaki Y, Kusano S, Doi H and Aki O (2005). Effects on immune response of antidiabetic ingredients from white-skinned sweet potato (*Ipomoea batatas* L.). *Nutrition* 21, 358-362.

Mooy J M, De Vries H, Grootenhuis P A, Bouter L M and Heine R J (2000). Major stressful life events in relation to prevalence of undetected type 2 diabetes: The Hoorn Study. *Diabetes Care* 23, 197-201.

Mozaffarian D, Kamineni A, Carnethon M, Djoussé L, Mukamal KJ and Siscovic D (2009). Lifestyle risk factors and new-onset diabetes mellitus in older adults: the cardiovascular health study. *Archives of Internal Medicine* 169, 798-807.

Murugananda S, Srinivasan K, Gupta S, Gupta PK and Lal J (2005). Effect of *Mangifera indica* on hyperglycemia and atherogenicity in streptozotocin diabetic rats. *Journal of Ethnopharmacology* 97, 497-501.

Nagarajun S, Jain HC and Aulakh GS (1989). Indigenous plants used in the control of Diabetes. In: Cultivation and utilization of medicinal plants. 584.

Narender T, Shweta S, Tiwari P, Papi RK, Khaliq T, Prathipati P, Puri A, Srivastava A, Chander R, Agarwal SC and Raj K (2007). Antihyperglycemic and antidyslipidemic agent from *Aegle marmelos. Bioorganic and Medicinal Chemistry Letters* 17, 1808-1811.

Narendhirakannan RT, Subramanian S and Kandaswamy M (2006). Biochemical evaluation of antidiabetogenic properties of some commonly used Indian plants on streptozotocin-induced diabetes in experimental rats. *Clinical and Experimental Pharmacology and Physiology* 33, 1150-7.

Negi PS, Chauhan AS, Sadia GA, Rohinishree YS and Ramteke RS (2005). Antioxidant and antibacterial activities of various seabuckthorn *(Hippophae rhamnoides* L.) seed extracts. *Food Chemistry* 92, 119-124.

Nelson NJ (1999). Purple carrots, margarine laced with wood pulp, Nutraceuticals move into the supermarket. *Journal of the National Cancer Institute* 91, 755-757.

Nemes-Nagy E, Szocs-Molnár T, Dunca I, Balogh-Sămărghiţan V, Hobai Ş, Morar R, Pusta DL and Crăciun EC (2008). Effect of a dietary supplement containing blueberry and sea buckthorn concentrate on antioxidant capacity in type 1diabetic children. *Acta Physiologica Hungarica* 95, 383-393.

Nugroho AE, Riyanto S, Sukari MA and Maeyama K (2011). Anti-allergic effects of Marmin, a coumarine isolated from *Aegle marmelos* Correa: In vitro study. *International Journal of Phytomedicine* 3, 84-97.

Patwardhan, B, D Warude, P Pushpangadan and N Bhatt, 2005. Ayurveda and Traditional Chinese Medicine: a comparative overview. *Evidence Based Complimentry and Alternative Medicine* 2, 465-473.

Perry LM (1980). Medicinal Plants of East and Southeast Asia-Attributed Properties and Use. The Massachusetts Institute of Technology Press 80-81.

Ponnachan PT, Paulose CS and Panikkar KR (1993). Effect of leaf extract of *Aegle marmelose* in diabetic rats. *Indian Journal of Experimental Biology* 31, 345-347.

Pouwer F, Kupper N and Adriaanse MC (2010). Does emotional stress cause Type 2 Diabetes Mellitus A review from the European Depression in Diabetes (EDID) Research Consortium. *Discovery Medicine* 9, 112-118.

Prakash and Gupta (2005). Therapeutic uses of *Ocimum sanctum linn* (tulsi) with a note on eugenol and its pharmacological actions: a short review. *Indian Journal of Physiology and Pharmacology* 49, 125-131.

Ragasa CY, Alimboyoguen AB, Shen CC, Del Fierro RS and Raga DD (2011). Hypoglycemic effects of tea extracts and sterols from *Momordica charantia* . *Journal of Natural Remedies* 11, 44-53.

Raghuram TC, Sharma RD, Sivakumar B and Sahay BK (1994). Effect of fenugreek seeds on intravenous glucose disposition in non-insulin dependent diabetic patients. *Phytotherapy Research* 8, 83-86.

Rahmatullah M, Shefa TF, Hasan L, Hossain MT, Ahmed S, Mamun AA, Islam MR, Rahman S, Chowdhury MH (2010). A study on antinociceptive and anti-hyperglycemic activity of methanol extract of *Brassica juncea* (l.) Czern. leaves in mice. *Advances in Natural and* Applied Sciences 4, 221-225.

Rana J, Tricia Y Li, Manson J E and Frank B Hu (2007). Adiposity Compared With Physical Inactivity and Risk of Type 2 Diabetes in Women. *Diabetes Care* 30, 53-58.

Ravi K, Ramachandran B and Subramanian S (2004). Protective effect of *Eugenia jambolana* seed kernel on tissue antioxidants in streptozotocininduced diabetic rats. *Biological and Pharmaceutical Bulletin*. 27, 1212-1217.

Reay JL, Kennedy DO and Scholey AB (2005). Single doses of *Panax ginseng* (G115) reduce blood glucose levels and improve cognitive performance during sustained mental activity. *Journal of Psychopharmacology* 19, 357-365.

Renuka C, Ramesh N and Saravanan K (2009). Evaluation of the antidiabetic effect of *Trigonella foenum-graecum* seed powder on alloxan induced diabetic albino rats. *International Journal of PharmTech Research* 1, 1580-1584.

Sabu MC and Kuttan R (2004). Hypoglycemic activity of *Aegle marmelos* and its relationship with its antioxidant properties. *Indian Journal of Physiology and Pharmacology* 48, 81-88.

Sangeetha KN, Sujatha S, Muthusamy VS, Anand S, Nithya N, Velmurugan D, Balakrishnan A and Lakshmi BS (2010). 3β-taraxerol of *Mangifera indica*, a PI3K dependent dual activator of glucose transport and glycogen synthesis in 3T3-L1 adipocytes. *Biochimica et Biophysica Acta - General Subjects.* 1800, 359-366.

Scott GJ (1992). Transforming traditional food crops: Product Development for Roots and Tuber Crops, vol. 1, International workshop on Root and Tuber crop Processing, Marketing and Utilization in Asia. International Potato Center (CIP), Lima, Peru: 3–20.

Seema PV, Sudha B, Padayatti PS, Abraham A, Raghu KG and Paulose CS (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, 600-602.

Sharma AK, Bharti S, Goyal S, Arora S, Nepal S, Kishore K, Joshi S, Kumari S, Arya DS (2011).Upregulation of PPARγ by *Aegle marmelos* ameliorates insulin resistance and β-cell dysfunction in high fat diet fed-streptozotocin induced type 2 diabetic rats. *Phytotherapy Research* 25, 1457-1465.

Sharma RD, Sarkar A, Hazra DK. (1984) Hypocholestrimic activity of fenugreek seed An experimental study in rats. *Nutrition Research* 33, 669-677.

Sharma RD. (1986). Effect of fenugreek seeds and leaves on blood glucose and serum insulin responses in human subjects. *Nutrition Research* 6, 1353-1364.

Sharma RD, Sarkar A, Hazra DK. (1996) Use of fenugreek seed powder in the management of non-insulin dependent diabetes mellitus. *Nutrition Research* 16, 1331-1339.

Sharma PC, Bhatia V, Bansal N and Sharma A (2007). A review on Bael Tree. *Natural Product Radiance*. 6, 171-178.

Sharma M, Siddique MW, Shamim AK, Shukla G and Pillai KK (2011). Evaluation of Antidiabetic and Antioxidant Effects of Seabuckthorn (*Hippophae rhamnoides* L.) in Streptozotocin-Nicotinamide Induced Diabetic Rats. *The Open Conference Proceedings Journal* 2, 53-58.

Shibib BA, Khan LA and Rahman R (1993). Hypoglycemic activity of *Coccinia indica* and *Momordica charantia* in diabetic rats: depression of the hepatic gluconeogenic enzymes glucose-6-phosphatase and fructose-1,6-bisphosphatase and elevation of both liver and red-cell shunt enzyme glucose-6-phosphate dehydrogenase. *Biochemistry Journal* 292: 267-270.

Shirdel Z, Madani H and Mirbadalzadeh R (2009). Investigation into the hypoglycemic effect of hydroalcoholic extract of *Ziziphus Jujuba* Leaves on blood glucose and lipids in Alloxan-Induced diabetes in rats. *Iranian Journal of Diabetes and Lipid Disorders* 3-19.

Siddhuraju P (2007) Antioxidant activity of polyphenolic compounds extracted from defatted raw and dry heated *Tamarindus indica* seed coat. *LWT Food Science and Technology* 40, 982-990.

Singh N, Tyagi SD and Agarwal SC (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, 97-100.

Singh U, Kochhar A and Singh S (2011).Blood glucose lowering potential of some herbal plants. *Journal of Medicinal Plant Research* 5, 4691-4695.

Sitasawad SL, Shewade Y and Bhonde R (2000). Role of bittergourd fruit juice in STZ induced diabetic state in vivo and in vitro. *Journal of Ethnopharmacology* 73, 71-79.

Soni R and Bhatnagar V (2009). Effect of Cinnamon (*Cinnamomum Cassia*) intervention on Blood Glucose of Middle Aged Adult Male with Non Insulin Dependent Diabetes Mellitus (NIDDM). *Ethno-Medicine* 3, 141-144.

Sotaniemi EA, Haapakoski E and Rautio A (1995). Ginseng therapy in non-insulin-dependent diabetic patients. *Diabetes Care* 18, 1373-1375.

Sridhar SB, Sheetal UD, Pai MRSM and Shastri MS (2005). Preclinical evaluation of the antidiabetic effect of *Eugenia jambolana* seed powder in streptozotocin-diabetic rats. *Brazilian Journal of Molecular Biology Research* 38, 463-468.

Srivastava Y, Venkatakrishna-Bhatt H and Verma Y (1988). Effect of *Momordica charantia* Linn. pomous aqueous extract on cataractogenesis in murrin alloxan diabetics. *Pharmacology Research and Communication* 20, 201-209.

Sudjaroen Y, Haubner R, Wu¨rtele G, Hull WE, Erben G, Spiegelhalder B, Changbumrung S, Bartsch H and Owen RW (2005). Isolation and structure elucidation of phenolic antioxidants from Tamarind (*Tamarindus indica* L.) seeds and pericarp. *Food and Chemical Toxicology*. 43, 1673-1682.

Suvimol C and Pranee A (2008). Bioactive compounds and volatile compounds of Thai bael fruit (*Aegle marmelos* (L.) Correa) as a valuable source for functional food ingredients. *Inter Food Research Journal.* 15, 1-9.

Tende JA, Ezekiel I, Dikko AAU and Goji ADT (2011). Effect of Ethanolic Leaves Extract of *Moringa oleifera* on Blood Glucose Levels of Streptozocin-Induced Diabetics and Normoglycemic Wistar Rats, *British Journal of Pharmacology and Toxicology* 2, 1-4.

Thorfeldt S (2005) Herbs in diabetes mellitus. *Alternative Medicne Review* 9, 13-18.

Thirumalai T, Therasa SV, Elumalai EK and David E (2011). Hypoglycemic effect of *Brassica juncea* (seeds) on streptozotocin induced diabetic male albino rat. *Asian Pacific Journal of Tropical Biomedicine* 1, 323-325.

Upadhayay, V. P.; and Pandey, K. (1984): Ayurvedic approach to diabetes mellitus and its management by indigenous resources. In Bajaj, J. S. (Ed.) *Diabetes mellitus in developing countries*. Interprint,. New Delhi. 375-377.

Upadhyay S, Shanbhag KK, Suneetha G, Balachandra Naidu M and Upadhya S (2004). A study of hypoglycemic and antioxidant activity of *Aegle marmelos* in alloxan induced diabetic rats. *Indian Journal of Physiology and Pharmacology* 48, 476-480.

Valavala VK, Vangipurapu RK, Banam VR, Pulukurthi UMR and Turlapati NR (2011). Effect of mustard (*Brassica juncea*) leaf extract on streptozotocin-induced diabetic cataract in wistar rats. *Journal of Food Biochemistry* 35, 109-124.

Venkatesan D, Karrunakarn CM, Kumar SS and Swamy PTP (2009). Identificati-on of Phytochemical Constituents of *Aegle marmelos* Responsible forAn imicrobial Activity against Selected Pathogenic Organisms. *Ethnobotanic-al Leaflets*. 13, 1362-72.

Vijay A AK, Thakur A and Sinha K (2006). The Metabolic Syndrome – Its Prevalence and Association with Coronary Artery Disease in Type 2 Diabetes. *Journal, Indian Academy of Clinical Medicine* 7, 32-38.

Vuksan V, Sung MK and Sievenpiper JL (2008). Korean red ginseng (*Panax ginseng*) improves glucose and insulin regulation in well-controlled, type 2 diabetes: results of a randomized, double-blind, placebocontrolled study of efficacy and safety. *Nutrition*, *Metabolism & Cardiovascular* Diseases. 18, 46-56.

Wang B, Lin L, Ni Q and Su CL (2011). *Hippophae rhamnoides* linn. for treatment of diabetes mellitus: A review. *Journal of Medicinal Plant Research* 5, 2599-2607.

Weiss R (1988). *Herbal Medicine*. Gothenburg, Sweden:Beaconsfield Publishers LTD:176-177.

Welihinda J, Arvidson G, Gylfe E, Hellman B and Karlsson E (1982). The insulin releasing activity of the tropical plant *Momordica charantia* . *Acta Biologica et Medica Germanica* 41, 1229-1240.

Whitman M (2001).Understanding the perceived need for complementary and alternative nutraceuticals: lifestyle issues. *Clinical Journal of Oncology in Nursing* 5, 190-194.

World Nutraceuticals (2006). Industry Study with Forecasts to 2010 & 2015. The Freedonia Group,Cleveland, USA.

Xue WL, Li XC, Zhang J, Liu YH, Wang ZL Zhang RJ (2007). Effect of *Trigonella foenum-graecum* (fenugreek) extract on blood glucose, blood lipid and hemorheological properties in streptozotocin-induced diabetic rats. *Asia Pacific Journal of Clinical Nutrition* 16, 422-426.

Yadav SP, Vats V, Ammini AC, Grover JK (2004). *Brassica juncea* (Rai) significantly prevented the development of insulin resistance in rats fed fructose-enriched diet. *Journal of Ethnopharmacology*. 93, 113-116.

Yilin C and Carsten S (2007). Flora of China. 12, 115- 355.

Zhang W, Zhao J, Wang J, Pang X, Zhuang X, Zhu X and Qu W (2010). Hypoglycaemic effect of aqueous extract of seabuckthorn *(Hippophae rhamnoides* L.) seed residues in streptozotocin-induced diabetic rats. *Phytotherapy Research* 24, 228-232.

Zhao R, Li Q, Long L, Li J, Yang R and Gao D (2007). Antidiabetic activity of flavone from *Ipomoea Batatas* leaf in non-insulin dependent diabetic rats. *International Journal of Food Science & Technology* 42, 80–85.

Zinjarde PS, Bhargava SS, Kumar SY (2011). Potent α-amylase inhibitory activity of Indian Ayurvedic medicinal plants (2011). *BMC Complementary and Alternative Medicine*, 11, Art. No. 5. .

