INTERNATIONAL JOURNAL OF PHYTOTHERAPY RESEARCH
ISSN 2278 – 5701

Review article

ANTI DIABETIC POTENTIAL OF HERBAL PLANTS AND POLYHERBAL FORMULATION

Durgeshnandani Sinha, Chandraprakash Dwivedi, Mehendra Kumar Dewangan, Rajni Yadav, S Prakash Rao,Kunal Chandrakar, Shashank Shekhar Singh ,Amit Roy

Columbia Institute of Pharmacy, Tekari, Near Vidhansabha Raipur,C.G., 493111, India

Corresponding Author: Durgeshnandani Sinha, Columbia Institute of Pharmacy, Tekari, Near Vidhansabha Raipur, Chhattisgarh, 493111, India

ABSTRACT:
Diabetes mellitus (DM), both insulin-dependent DM (IDDM) and non-insulin dependent DM (NIDDM) is a common and serious metabolic disorder throughout the world. Traditional plant treatments have been used throughout the world for the therapy of diabetes mellitus. Among many medications and polyherbal plants, several herbs have been known to cure and control diabetes; additionally they have no side effects. Diabetes mellitus is a dreadful disease found in all parts of the world and is becoming a serious threat to mankind health. Diabetes mellitus is a group of metabolic diseases characterized by high blood sugar (glucose) levels thatresult from defects in insulin secretion, or action, or both. Thus, plants are a potential source of anti-diabetic drugs which can be proved by the ethnobotanical information reports about 800 plants that may possess anti-diabetic potential. Although, synthetic oral hypoglycemic agents/insulin is the mainstream treatment of diabetes and effective in controlling hyperglycaemia, they have prominent side effects and fail to significantly alter the course of diabetic complications. This forms the main reason for an increasing number of people finding alternating therapies that may have less severe or no side effects. This article presents a review on some reported antidiabetic medicinal plants (with their botanical name, common name, constituent and mechanism of action for antidiabetic action) and plant based marketed polyherbal herbal formulations

Keywords: Diabetes mellitus, Medicinal plants,glucose , polyherbal plants

INTRODUCTION

Diabetes is a heterogeneous metabolic disorder characterized by altered carbohydrate, lipid and protein metabolism which causes hyperglycemia resulting from insufficient insulin secretion, insulin action or both.[1, 2] It is one of the refractory diseases identified by Indian council of medical research for which an alternative medicine is a need for the treatment. Diabetes mellitus has become a growing problem in the contemporary world.[3]The biochemical parameters (glucose, urea, creatinine, serum cholesterol, serum triglyceride, high density lipoprotein, low density lipoprotein, hemoglobin and glycosylated hemoglobin) of the polyherbal formulation were assessed in diabetic. The product showed its effectiveness in oral glucose tolerance test and Antidiabetic activity,

but it does not produce hypoglycemic effect. Treatment of diabetic rats with the product restored the elevated biochemical parameters significantly. The present study supports the use of this product as an antidiabetic.[4]The number of people with diabetes is increasing day by day the main cause of this problem is aging, urbanisation and increasing privilege of obesity and physical inactivity. Quantifying the prevalence of diabetes and the number of people affected by diabetes, now and in the future it is important to have rational planning and allocation of resources towards treatment and prevention of this disease. Diabetes is a metabolic disorder where in human body does not produce or properly uses insulin, a hormone that is required to convert sugar, starches, and other food into energy.[5] Diabetes results in abnormal levels of glucose in the bloodstream. Herbal plants are very common in use in our day to day life. Either as a nutrient or as a source of food these herbs are being consumed by the patient as well as healthy person. Easy availability, raw consumption, least side effects and low cost makes the herbal preparations the king of all available therapies.[6]

The vast majority of cases of diabetes fall into two broad etiopathogenic categories. In one category, type 1 diabetes, the cause is an absolute deficiency of insulin secretion. In the other, much more prevalent category, type 2 diabetes, the cause is a combination of resistance to insulin action and an inadequate compensatory insulin-secretary response (American Diabetes Association, 2005). Currently available therapies for diabetes include insulin and various oral antidiabetic agents such as sulfonylureas, biguanides and glinides.[7] Many of them have a number of serious adverse effects; therefore, the search for more effective and safer hypoglycemic agents is one of the most important areas of investigation. In diabetes, hyperglycemia generates reactive oxygen species(ROS), which in turn cause lipid peroxidation and membrane damage and these free radicals play an important role in the production of secondary complications in diabetes mellitus(kidney, eye, blood vessel, and nerve damage).[8,9] Antioxidants have been shown to prevent the destruction of ß- cells by inhibiting the peroxidation chain reaction and thus they may provide protection against the development of diabetes.

Plants contain natural antioxidants (tannins, flavonoids, vitamins C and E, etc.) that can preserve ß- cell function and prevent diabetes induced ROS formation. In this present review article an attempt was made to list out the herbal plants possessing antidiabetic activity by one or the other possible mechanisms.[10, 11]Diabetes mellitus is a serious health problem with continuously increasing rates of incidence and mortality. Diabetes mellitus is characterized by elevated plasma glucose concentrations resulting from insufficient insulin and insulin resistance, or both, leading to metabolic abnormalities in carbohydrates, lipids and proteins. If not cured or controlled it may even lead to acute or chronic complications causing ketoacidosis, microangiopathy and other related infections. Different types of reported diabetes mellitus can be classified under following two categories:

Type 1 is insulin-dependent diabetes mellitus (IDDM), in which the body does not produce any Insulin. It most often occurs in children and young adults. Type 1 diabetes accounts for 5–10% of

Diabetes.

Type 2 is noninsulin-dependent diabetes mellitus (NIDDM), in which the body does not produce enough, or improper use of secreted insulin is the most common form of the disease, accounting for 90–95% of diabetes. Type 2 diabetes is nearing epidemic proportions, due to an increased number of elderly people, and a greater prevalence of obesity and sedentary lifestyles.

Basis of Diabetes Mellitus treatment:

- Patient education concerning the disease
- Physical exercise
- Diet and
- Hypoglycemic agents

As a very common chronic disease, diabetes is becoming the third “killer” of the health of mankind along with cancer, cardiovascular and cerebrovascular diseases because of its high prevalence, morbidity and mortality. Therefore once diagnosed, it is well regulated by means of various therapeutically effective drugs. Besides, the therapy based on chemotherapeutic agents, the present century has progressed towards naturopathy. Thus, medical plants have an ever emerging role to play in treatment or management of lifelong prolonging diseases like diabetes mellitus, especially in developing countries where resources are meager. Diabetes mellitus alone is accompanied with several other diseases infecting healthy individuals. The treatment of each of such disease can be done by exploiting the herbal integrity of India. The plants in parts or as full can be used for curing any disorder related with diabetes mellitus. Moreover, in some cases extracts of plants are self capable of treating the related disorders such as polyuria, polydipsia, glucosuria, etc. along with curing the chronic disorders such as diabetes mellitus .

Advantages[14,15]

Mostly herbal drugs are well tolerated by the patient, having fewer unintended consequences and fewer side effects than traditional medicine, and may be safer to use.
2. Herbal drugs are more effective for long-standing health complaints that don't respond well to traditional medicine
3. Cost of herbal drugs is much less than prescription medications. Research, testing, and marketing add considerably to the cost of prescription medicines. Herbs tend to be inexpensive compared to drugs.
4. Herbs are available without a prescription. Simple herbs, such as peppermint and chamomile, can be cultivated at home.

Life style for patient [16, 17]

Some of the home and herbal remedies prescribedby Ayurveda are described below.
1. Include turmeric and cinnamon diets.

2. Avoid oily, fried and starchy foodstuffs.
3. Avoid coffee, sugar, refined flour andalcohol Eat smaller meals (low fat diet) five to six times a day instead of having three large meals.
5. Increase intake of vegetables like spinach, cucumber, tomatoes, onion, sprouts, beans, garlic etc.
6. Refrain from taking stress.
7. Regular exercise. Walk for at least 40 minutes a day.
8. Avoid red meat and excessive salt in you rmeals. Fish and soy can be taken due to their good protein value.
9. Avoid white bread, rice, potatoes, sweet and sugary foods.

Recent Regulatory Developments:

Herbal drugs, as defined by regulatory measures constitute only those traditional medicines, which primarily use medicinal plant preparations for therapy. WHO has recently defined traditional medicine (including herbal drugs) as comprising therapeutic practices that have been in existence, almost for several hundreds of years, before the development and spread of modern medicine and others which are still in use. In recent years FDA and EMEA have took keen interest and also have reviewed the regulatory frameworks governing the development and use of botanical drug. This keen interest has provided a significant fillip to the natural products industry and has significantly lowered the entry barriers for botanicals and related products. These new guidelines more importantly also provide guarantees of market exclusivity for botanicals as well as the acceptance of synergistic combinations of plant derived bioactives products. Developing and developed countries such as India and China have clearly a natural advantage over the others.[18,19]

Mechanism of Action of Herbal Antidiabetics [20, 21]

The antidiabetic activity of herbs depends upon variety of mechanisms. The mechanism of action of herbal anti-diabetic could be grouped as-
• Adrenomimeticism, pancreatic beta cell potassium channel blocking, cAMP (2nd messenger) stimulation
• Inhibition in renal glucose reabsorption
• Stimulation of insulin secretion from beta cells of islets or/and inhibition of insulin degradative processes
• Reduction in insulin resistance
• Providing certain necessary elements like calcium, zinc, magnesium, manganese and copper for the beta-cells
• Regenerating and/or repairing pancreatic beta cells
• Increasing the size and number of cells in the islets of Langerhans
• Stimulation of insulin secretion
• Stimulation of glycogenesis and hepatic glycolysis

• Protective effect on the destruction of the beta cells
• Improvement in digestion along with reduction in blood sugar and urea
• Prevention of pathological conversion of starch to glucose
• Inhibition of β -galactocidase and α–glucocidase
• Cortisol lowering activities
• Inhibition of alpha-amylase

MEDICINAL PLANTS WITH ANTIDIABETIC AND RELATED BENEFICIAL PROPERTIES

Acacia arabica (Mimosaceae)

It occurs in wild throughout 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. Powdered seeds of Acacia Arabica administered in doses of 2, 3 and 4 gm/kg body weight exerted a significant (PB/0.05) hypoglycemic effect in normal rabbits by initiating the release of insulin from pancreatic beta cells. No acute oxicity and behavioural changes were observed at these doses .It is found all over India. The plant extract acts as an antidiabetic agent by acting as secretagouge to release insulin. It induces hypoglycemia in control rats but not inalloxanized animals. Powdered seeds of A. arabica when administered (2, 3 and 4 g/kg body weight) to normal rabbits, induces hypoglycemic effect by initiating release of insulin from pancreatic beta cells.[22, 23]

Achyranthes aspera (Amaranthaceae)

It is distributed throughout the tropical world. Oral administration of *A. aspera* powder produces a significant dose-related hypoglycemic effect in normal as well as in diabetic rabbits. The water and methanol extracts also decreases blood glucose levels in normal and alloxan diabetic rabbits. The acute toxicity study in rabbits does not reveal any adverse or side effects of this folk medicine at dosages up to 8 g/kg orally. The plant could act by providing certain necessary elements like calcium, zinc, magnesium, manganese and copper to the beta-cells.[23, 24]

Allium cepa, onion (Liliaceae)

Allium cepa is known only in cultivation but related wild species occur in Central Asia. Various ether soluble fractions as well as insoluble fractions of dried onion powder show anti-hyperglycemic activity in diabetic rabbits.[25, 26] A. cepa also known to have antioxidant and hypolipidemic activity. Administration of a sulfur containing amino acid, S-methyl cysteine sulphoxide (SMCS) (200 mg/kg for 45 days) to alloxan induced diabetic rats significantly controlled bloodnglucose as well as lipids in serum and tissues.

ISSN 2278 – 5701

It normalizes the activities of liver hexokinase, glucose 6-phosphatase and HMG Co A reductase .[27, 28] When diabetic patients were given single oral dose of 50 g of onion juice, it significantly controlled post-prandial glucose levels.[29, 30]



Fig1: Acacia Arabica **Fig2: Achyranthes Aspera** **Fig3: Allium Cepa**

Allium sativum , garlic (Liliaceae)

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). 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 %). 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 Oral administration of the garlic extract significantly decreases serum glucose, total cholesterol, triglycerides, urea, uric acid, creatinine, AST and ALT levels, while increases serum insulin in diabetic rats but not in normal rats when compared with antidiabetic drug glibenclamide. The antidiabetic effect of the extract was more effective than glibenclamide. It is concluded that the plant must be considered as excellent candidate for future studies on diabetes mellitus .[31, 32]

Aloe barbadensis ,Aloe gibberellins (Liliaceae)

It grows in arid climates and is widely distributed in Africa, India and other arid areas. Aloe vera gel at 200 mg/kg had significant antidiabetic and cardioprotective activity and reduces the increased TBARS and maintains the Superoxide dismutase and Catalase activity up to the normal level and increases reduced glutathione by four times in diabetic rats.[33] The leaf pulp extract showed hypoglycemic activity on IDDM and NIDDM rats, the effectiveness being enhanced for type II diabetes in comparison with glibenclamide. Both Aloe vera and (over a dose range of 2-100 mg/kg) inhibit inflammation in a dose-response manner and improve wound healing in STZ diabetic mice. 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 .[34]

Aloe vera (Liliaceae) is a cactus like plant with green dagger shaped leaves that are fleshy tapering, spiny and filled with clearly viscous gel. The aqueous extract of Aloe vera has the hypoglycemic property which was given orally at a dose of 150mg/kg of body weight. Whole study was performed on the alloxan induced male albino rats ,Treatment of chronic but no single dose of exudates of Aloe barbadensis leaves shows hypoglycemic effect inalloxanized diabetic rats. Single as well as chronic doses of bitter principle of the same plant also show hypoglycaemic effect in diabetic rats. This action is through stimulation of synthesis and/or release of insulin from pancreatic beta cell.[35, 36]

Andrographis paniculata (Acanthaceae)

It is a herbaceous plant native to India, Sri Lanka and widely cultivated in southern Asia. Oral administration of andrographis significantly increases the activity of SOD and Catalase. Also decreases blood glucose levels due to its antioxidant properties. The ethanolic extract of A. paniculata possesses antidiabetic property and may be attributed at least in part to increase glucose metabolism. Its hypotriglyceridemic effect is also beneficial in the diabetic state .[37,38]



Fig4: Allium Sativum **Fig5: Aloe Barbadensis** **Fig6: Andrographis Paniculata**

Annona squamosa (Annonaceae)

It is a small well-branched tree or shrub, grows at lower altitudes. Administration of 15 mg/kg/day of isolated juercetin-3-O-glucoside from Annona squamosa leaves for 10 consecutive days to the hyperglycemic animals reverse these effects and simultaneously inhibits the activity of hepatic GIucose-6-phosphatase. Aqueous extract of A. squamosa root (at a dose of 250 mg/kg and 500 mg/kg bw) when given to STZ- induced diabetic rats reduced the blood glucose level from 285.52 to 208.81 mg/dl, 6 hours after oral administration of extract.It further decreases the hepatic and renal lipid peroxidation with a concomitant increase in the activities of antioxidative enzymes, such as Catalase and Superoxide dismutase as well as glutathione content, indicating its safe and antiperoxidative effects.[39, 40]

Azadirachta-indica (Meliaceae)

Commonly known as Neem. It is a tree native to India, Burma, Bangladesh, Sri Lanka, Malaysia and Pakistan, growing in tropical and semi-tropical regions. A low (0.5g tid) and high (2g tid) doses of powdered part, aqueous extract and alcoholic extract of A. indica shows significant hypoglycemic activity in high dose and can be successfully combined with oral hypoglycemic agents in type-2 diabetic patients whose diabetes is not controlled by these agents.[41]

Bryonia alba (Cucurbitaceae)

It is a flowering plant native to western Eurasia and adjacent regions, such as North Africa, the Canary Islands and South Asia. Administration of trihydroxyoctadecadienoic acids obtained from the roots of the native Armenian plant B. alba L. (0.05 mg/kg/day for 15 days. Lin.) restores the disordered lipid metabolism of alloxan-diabetic rats. Metabolic changes induced in diabetes significantly restores towards their normal values with the exception of diminished triglyceride content of muscle which does not restores. Thus, they can influence the profile of the formation of stable prostaglandins by actions downstream of prostaglandin endoperoxides .[42]


Fig7: Annona Squamosa


Fig: 8Azadirachta-Indica


Fig9: Bryonia Alba

Catharanthus roseus (Apocynaceae)

Oral administration at dose-dependent of 0.5, 0.75 and 1.0 mL/kg body weight reduced the blood glucose of bothnormal and diabetic rabbits comparable with that of the standard drug, glibenclamide. The results indicate a prolonged action in reduction of blood glucose by C. Roseus and the mode of action of the active compound(s) is probably mediated through enhance secretion of insulin from the betacells of Langerhans or through extra pancreatic mechanism.[44]

Momordica charantia L. (Cucurbitaceae)

M. charantia (bitter melon) is commonly known as vegetable insulin. An oral sucrose tolerance test reveals that administration of aqueous extract (AE), methanol fraction (MF) or methanol insoluble fraction (MIF) each significantly suppresses plasma glucose levels at 30 min as compared with control. In addition, the plasma insulin level at 30 min also lowers after MF administration than the control in the oral sucrose tolerance test, these results demonstrates that bitter melon suppresses postprandial hyperglycemia by inhibition of α glucosidase activity.[45]

Fig10: Catharanthus roseus Fig11: Momordica charantia Fig12: Mangifera indica

Panax ginseng (Araliaceae)

The roots are taken orally in the treatment of type II diabetes. Extracts of ginseng species shows antihyperglycemic activity associated with increased peroxisome proliferator-activated receptor gamma expression and adenosine monophosphate-activated protein kinase phosphorylation in liver and muscle. Oral administration of P. ginseng root improves insulin sensitivity and may be used as an adjuvant therapy for treating diabetic patients with insulin resistance.[46, 47, 48,]

Ocimum sanctum L. (Lamiaceae)

It is commonly known as Tulsi. Since ancient times, this plant is known for its medicinal properties. [49,50]The aqueous extract of leaves shows significant reduction in blood sugar level in both normal and alloxan induced diabetic rats .Significant reduction in fasting blood glucose, uronic acid, total amino acid, total cholesterol, triglyceride and total lipid indicate the hypoglycemic and hypolipidemic effects of tulsi in diabetic rats .[51, 52] Oral administration of plant extract (200 mg/kg) for 30 days leads to decrease in the plasma glucose level. Renal glycogen content increases 10 fold while skeletal muscle and hepatic glycogen levels decreases by 68 and 75% respectively in diabetic rats as compared to control. This plant also shows antioxidant, antibacterial, antifungal, antiviral, antiasthemitic, antistress, antitumor, gastric antiulcer activity, antimutagenic and immunostimulant activities.[53, 54]

Mangifera indica (Anacardiaceae)

The aqueous extract produces reduction of blood glucose level in normoglycemic and glucose-induced hyperglycemia, but does not have any effect on streptozotocin-induced diabetic mice under the same conditions when compared with that of an oral dose of chlorpropamide. The result indicates that the aqueous extract of the leaves of M. indica possess hypoglycemic activity.[53, 54]

Tinospora cordifolia (Menispermaceae)

ISSN 2278 – 5701

Commonly known as Guduchi, an herbaceous vine indigenous to the tropical areas of India, Myanmar and Sri Lanka. Oral administration of an aqueous T. cordifolia root extract to alloxan diabetic rats causes a significant reduction in blood glucose and brain lipids. Though the aqueous extractat a dose of 400 mg/kg could elicit significant antihyperglycemic effect in different animal models, its effect is equivalent to only one unit/kg of insulin.[55, 56]



Fig13:Panax ginseng **Fig14:Tinospora cordifolia** **Fig15:Ocimum sanctum**

Ougeinia oojeinensis (FABACEAEA)

The ethanolic extract of O. oojeinensis (200 mg/kg) bark significan tly decreased the blood glucose level, triglycerides, LDL, VLDL and total cholesterol and increased high density lipoprotein level in alloxan induced diabetic rats.[57]

Solanum xanthocarpum (SOLANACEAE)

The methanolic extract of both the leaves (field and in vitro raised) of S. xanthocarpum at a dose of 200 mg/kg given orally, significantly reduced the blood glucose level, urea, uric acid and creatinine level and increased the serum insulin level in alloxan induced diabetic rats.[58]

Aegle marmelos (RUTACEAE)

The methanolic extract of leaf and callus powder of A. marmelos significantly decreased the blood sugar level of STZ induced diabetic rabbits. A. marmelos would act like insulin in the restoration of blood sugar and body weight to normal levels in rat and was therefore recommended as a potential hypoglycaemic agent.[59]

ISSN 2278 – 5701



Fig16: Ougeinia oojeinensis **Fig17: Solanum xanthocarpum** **Fig18:Aegle marmelos**

Table1.LIST OF HERBAL PLANTS WITH ANTIDIABETIC EFFECT

Botanical Name	**Extract, Part**	**Drug induced Diabetes animal model**	**Mechanism of action**
Acacia auriculiformis (Leguminosae)[60]	Acetone, bark, pods	Alloxan - rat	↑ insulin secre on ↑ insulin secretion
Amaranthus viridis (Amaranthaceae)[61]	MeOH, whole plant	Alloxan - rat	↓ in blood glucose and lipid profile
Acacia Arabica (Leguminosae)[62]	Chloroform, bark	Alloxan - rat	↑ insulin secretion
Aegle marmelos (Rutaceae)[63]	AE, plant	STZ - rat	Direct stimulation of glucose uptake by insulin secretion
Agrimony eupatoria (Rosaceae)[64]	AE, plant		
Alangium salvifolium (Alangiacea)[65]	MeOH, leaves	Dexamethasone - rat	Insulinotropic effect
Allium sativum (Alliacea)[66]	Ethyl, ether, EtOH	Alloxan- rat	↑ insulin secretion
Aloe vera (Lilaceae)[67]	EtOH, leaves	EtOH, leaves	↑ insulin secretion
Annona squamosa (Annonaceae) [68]	AE, EtOH, leaves	STZ - rat	↑ insulin secretion increasing utilization of glucose in muscle and inhibiting the glucose

			output from liver
Caffeine[69]	Caffeine	Pancreatectomized rats	↓ body weight, fats, and ↓ insulin resistance, enhanced glucose stimulated first – and second – phase insulin secretion and beta – cell hyperplasia
Camellia sininsis (Theaceae)[70]	Green tea	STZ –rat	Epigallocatechin gallate increases insulin activity
Capsicum frutescens (Solanaceae)[71]	Red chilli	STZ – Sprague Dawley rat	Insulinotropic
Catharanthus roseus (Apocynacea)[72]	Dichloromethane –EtOH leaves and twigs	STZ - rat	Enhance secretion of insulin
Coccinia indica (cucurbitacea)[72]	EtOH, Leaves	STZ – male rats	Insulin secreting effect or through influence of enzymes involved in glucose metabolism
Ephedra distachya (Ephedraceae)[66]	Aqueous MeOH, AE, Crude drug	Alloxan - mice	Regeneration and restoration of atrophied Pancreatic islets that induces the secretion of insulin.
Eucalyptus globules (Myrtacea)[73]	AE, Leaves	STZ - mice	↑ insulin secretion from the clonal pancreatic beta Cell
Eucalyptus citriodora (Myrtaceae)[73]	AE, leaves	Alloxan - rat	↓ the blood glucose level
Nigella sativa oil (Ranunculaceae)[74]	Oil	STZ-nicotinamide hamster rat	Insulinotropic property
Radix rehmanniae (Scrophulariaceae)[64]	EtOH, rhizome	STZ - mice	↑ insulin secretion, ↓ the glycogen content
Rehmania glutinosa (Scrophulariaceae)[66]	EtOH, rhizome	Alloxan - rat	↑ insulin secretion, ↓ the glycogen content
Rosmarinus officinalis(Lamiaceae)	EtOH, leaves	Alloxan- rat	↑ insulin secre on
Pongamia pinnata (Fabaceae)	EtOH, leaves	Alloxan – rats	↓ blood glucose levels and prevented body weight loss

ISSN 2278 – 5701

Solanum xanthocarpum (Solanaceae)[59]	AE, leaves	Alloxan – rat, mice	Insulin like activity
Semen coicis (Gramineae)[66]	seeds	Alloxan- rat	Prevention of pancreatic beta – cells injury
Solanum nigrum (Solanaceae)[66]	AE, leaves	Alloxan - rats	↓ blood sugar levels
Sphenostylis stenocarp (Leguminosae)[66]	MeOH seeds	Alloxan – rat	↓ blood by blood glucose levles
Tribuluks terrestris (Zygophyllaceae) [66]	Saponin from decoction of plant	Alloxan - mice	Increases serum insulin release
Terminalia superb (Combretaceae)[75]	MeOH, CH2 CL2, stem barks	STZ -rat	↓ blood glucose levels
Vernonia amygdalina (Asteraceae)[76]	AE, leaves	STZ - rats	Antioxidant activity, ↓ triglyceride levels
Zizyphus mauritiana (Rhamnaceae)[77]	Petroleum ether, AE, seed	Alloxan - mice	Restored the elevated biochemical parameters like glucose, urea, creatinine, total cholesterol, triglycride, High density lipoprotein, low density lipo protein, hemoglobin and glycosylated hemoglobin

ISSN 2278 – 5701

Table 2: Some plants having hypoglycemic activities[77]

Sn.	Common name	Botanical name and family	Parts used	Therapeutic action
1	Asiatic ginseng	Panax ginseng (Araliac)	Roots	Lowers blood glucose by decreasing the rate of carbohydrate absorption, increasing glucose transport and modulation of insulin secretion
2	Ashvagandha, winter cherry	Withania somnifera (Solanaceae)	Roots	Decrease in blood glucose Level
3	Asiatic sweet-leaf	Symplocos Paniculata (Symplocaceae)	Leaves Stems	Inhibits protein tyrosine phosphatase 1B (PTP1B) 1 and 2
4	Banana	Musa sapientum Kuntz(Musaceae)	Fruits/Flower	Decreases blood glucose and glycosylated haemoglobin level
5	Banyan tree	Ficus bengalensis (Moraceae)	Bark	Inhibits insulinase activity from liver and kid-ney, stimulates insulin secretion
6	Barbados	Aloe barbadensis Mill. (Liliaceae)	Leaves	Stimulates synthesis and/or release of insulin from -cells
7	Betel, Betel vine	Piper betle (Piperaceae	Leaf	Antihyperglycemic, glucose metabolism
8	Bilwa, bael fruit	Aegle marmelos (Rutaceae)	Leaf extract	Decreases blood urea & cholesterol
9	Bitter-kola, false kola	Garcinia kola (Clusiaceae)	Seed	Hypoglycaemic and Hypolipidemic
10	Black tea	Camellia sinensis L.(Theaceae)	Leaves	Decreases blood glucose level
11	Common fig	Ficus carica L. (Moraceae)	Leaves	Decreases hyper-glycaemia and level of total cholesterol
12	Custard apple, sugar apple	Annona squamosa (Annonaceae)	Fruit pulp	Decreased urine sugar, urine protein and gly-co-haemoglobin

Herbal drug formulation

Diabecon manufactured by 'to increase peripheral utilization of glucose, increase hepatic and muscle glucagon contents, promote B cells repair and regeneration and increase c peptide level.

Epinsulin

Marketed by Swastik formulations, contains epicatechin, a benzopyran, as an active principle. Epicatechin increases the cAMP content of the islet, which is associated with increased insulin release. It plays a role in the conversion of proinsulin to insulin by increasing cathepsin activity. Additionally it has an insulin-mimetic effect on osmotic fragility of human erythrocytes and it inhibits Na/K ATPase activity from patient's erythrocytes. It corrects the neuropathy, retinopathy and disturbed metabolism of glucose and lipids. It maintains the integrity of all organ systems affected by the disease. It is reported to be a curative for diabetes, Non Insulin Dependent Diabetes Mellitus (NIDDM) and a good adjuvant for Insulin Dependent Diabetes Mellitus (IDDM), in order to reduce the amount of needed insulin. It is advised along withexisting oral hypoglycemic drugs and is known to prevent diabetic complications. It has gentle hypoglycemic activity and hence induces no risk of being hypoglycemic. [79]

Polyherbal Formulations Annona squamosa and Nigella sativa

Plant formulation and combined extracts of plants are used a drug of choice rather than individual. Various herbal formulations such as diamed, coagent db, Diasulin. .Polyherbal formulation of Annona squamosa and Nigella sativa on blood glucose, plasma insulin, tissue lipid profile, and lipidperoxidation in streptozotocin induced diabetic rats.(Fig19,20)Aqueous extract of Polyherbal formulation of was administered orally (200 mg/kg body weight) for 30 days. [21]The different doses of Polyherbal formulation on blood glucose and plasma insulin in diabetic rats were studied and the levels of lipid peroxides and tissue lipids were also estimated in streptozotocin induced diabetic rats. The effects were compared with tolbutamide. Treatment with Polyherbal formulation and tolbutamide resulted in a significant reduction of blood glucose and increase in plasma insulin. [79, 80]

Fig19: Annona squamosa

Fig20: Nigella sativa

ISSN 2278 – 5701

Polyherbal Formulation of Kaishore Guggulu

Triphala and giloya are cut into small pieces manually or into a pulverizer. They are dipped overnight into water. In the morning, this water is boiled until 1/4th of water is left. Then, decoction is prepared by filtering this water. In this decoction of triphala and giloya, purified guggul gum is added and this mixture is heated slowly so that we get syrup like liquid of hard consistency. Now, powders of herbs (number 4 to 11) are added and this mixture is pounded (stricken again and again) either by hand or in a mortar and pestle or in chattu machine. Processing this mixture for some hours decreases the particle size and increases the bioavailability of the mixture. Thereafter, tablets are made from this gum like mixture either by hand or by tablet machine. The average size varies between 250-500 mg per tablet. It is taken with milk or water or herbal decoction.

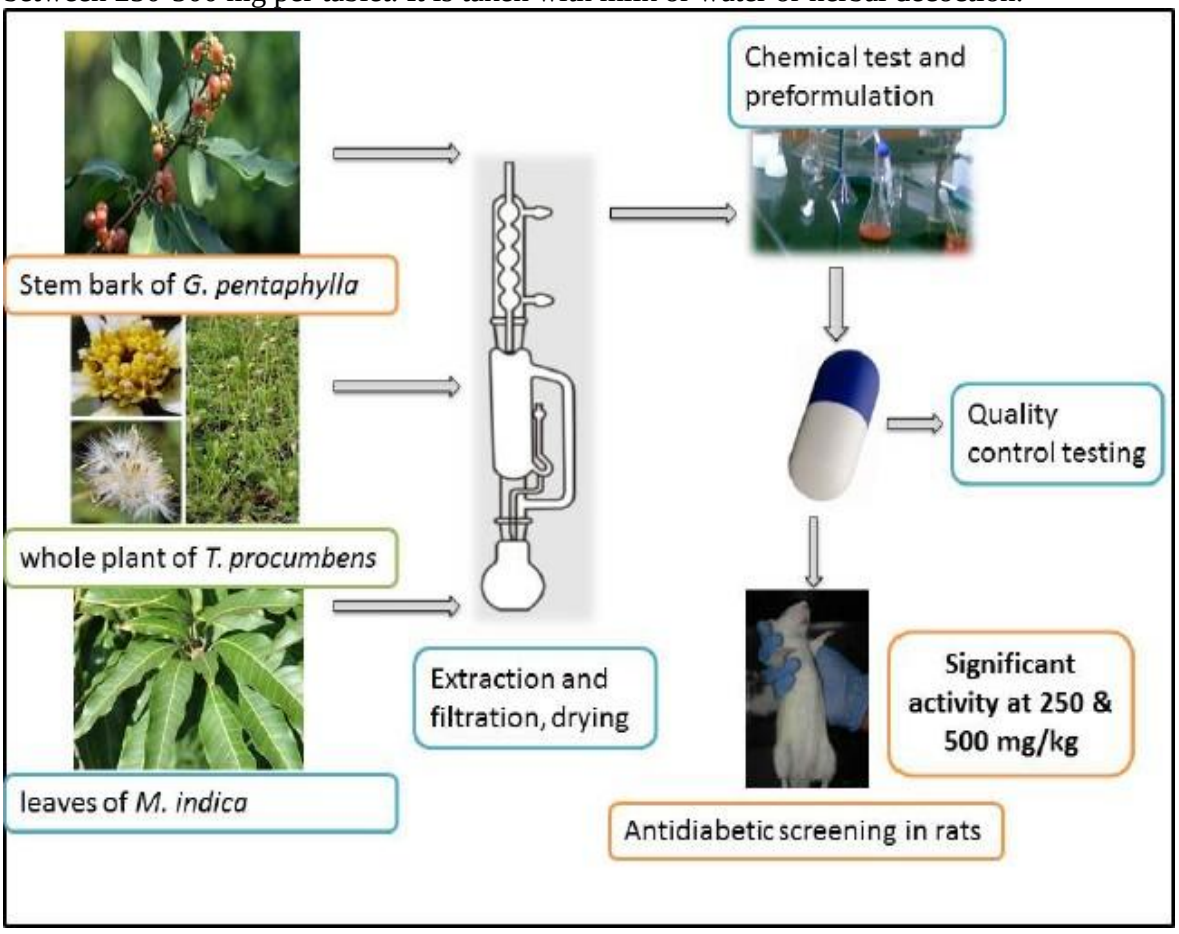

Fig21: Polyherbal formulation through Antidibetic screening in rats [90]

ISSN 2278 – 5701

Table 3: Marketed herbal Antidiabetic products

SN	Product	Manufacturer	Mechanism	Ref.
1	Sharang Dyab-Tea(Fig. 22)	Plant Med. Lab Pvt. Ltd	Stimulate insulin production	[81]
2	Herbal hills jambu(Fig. 23)	Isha Agro Developers	Reduce blood and urine sugar level	[82]
3	Stevia-33(Fig. 24)	Vitalize Herbs Pvt. Ltd.	Stimulate β cells of pancreas	[83]
4	Diab-FIT(Fig. 25)	Herbal FIT	Maintain proper blood sugar level	[84]
5	Madhumar capsule(Fig. 26)	Kangrd Hills Care & Products	Control chronic Cure diabetes mellitus	[85]
6	Daya Stone Powder (Fig. 27)	Jignesh and Co.	Lower the blood glucose level and tone up β Cells of	[86]
7	Blue berry Al (Fig. 28)	Hikma FZCO	Antidiabetic	[87]
8	Episulin (Fig. 29)	Varuna Biocell Pvt. Ltd	Antidiabetic	[88]

Fig 22: Sharang Dyab-Tea

Fig 23: Herbal Hills Jambu

Fig 24: Stevia-33

ISSN 2278 – 5701

Fig 25: Diab-FIT **Fig 26: Madhumar Capsule** **Fig 27: Daya Stone powder**

Fig 28: Blue berry **Fig 29: Episulin**

ACKNOWLEDGMENT: I am very thankful to Principal, Columbia College of pharmacy Raipur Chhattisgarh and my teachers for their valuable guidance. I am also thankful to my colleagues for their time to time support.

CONCLUSION

Diabetes mellitus is the most common endocrine disorder, affecting more than 300 million people worldwide. For this, therapies developed along the principles of western medicine (allopathic) are often limited in efficacy, carry the risk of adverse effects and are often too costly, especially for the developing world. The prevalence of diabetes mellitus continues to rise worldwide and treatment with oral hypoglycemic drugs ends with numerous side effects and huge monetary expenditure. There is increasing demand by patients to use the natural products with antidiabetic activity. This paper has presented various anti-diabetic plants that have been pharmacologically tested and shown to be of some value in treatment of Diabetes Mellitus. The effects of these plants may delay the development of diabetic complications and correct the metabolic abnormalities. However,

more investigations must be carried out to evaluate the mechanism of action of medicinal plants with antidiabetic effect

The aim of present review is to establish the use of plants, plant parts or extract in curing Diabetes mellitus. It also collates available data on plants with hypoglycemic effects. In the present investigation, interest is focused on experimental studies performed on hypoglycemic
Plants and their bioactive components. A brief description is given about the, type of diabetes,related physiological disorders and available herbal plants which can be further exploited for antidiabetic activity. Overall, this review presents the profiles of plants with hypoglycaemic properties, reported in the literature. All the herbal drugs discussed .

REFERENCES

1. Joseph B, Jini D. An insight in hypoglycemica effect of traditional Indian herbs used in the treatment of diabetes, Research Journal of Medicinal plant. 2011; 5:352-376.
2. Tanaka K, Nishizono S, Makino N, Tamaru S, Terai O, Ikeda I. Hypoglycemic activity of Eriobotrya japonica seeds in type 2 diabetic rats and mice.Biosci Biotechnol Biochem 2008, 72, 686-693.
3. C.K .Kokate, A.P .Purohit Pharmacognosy,Published By Nirali Prakashan ,Vol 1&2, 47th Edition, 2008 .
4. Deb L, Dutta A. Diabetes mellitus its possible pharmacological eveluation techniques and naturopathy. Int J Green Pharmacy 2006;1:7-28.
5. Murray, M.T.: (1995). Healing power of Herbs. 2nd edition, Gramercy Books NY, pp: 357.
6. Grover J K, Yadav S, Vats V, Medicinal plants of India with anti-diabetic potential, J Ethnopharmacol , 81 (2002) 81.
7. Shukla R, Sharma S B, Puri D, Prabhu K M & Murthy P S , Medicinal plants fortreatment of diabetes mellitus, Indian Journal of Clinical Biochemistry, 15(Suppl.) (2000) 169.
8. Mutalik S, Sulochana B, Chetana M, Udupa N, Uma Devi UP. Preliminary studies on acute and sub acute toxicity of an antidiabetic herbal preparation, Dianex. Indian Journal of Experimental Biology. 2003; 4:316- 320.
9. Piyush MP, Natvarlal MP, Ramesh KG. Holistic classification of herbal antidiabetics: A review. Pharma Times, 2006; 38: 19-25.
10. Sharma R, Arya V. A Review on Fruits Having Anti-Diabetic Potential. Journal of Chemical and Pharmaceutical Research. 2011; 3(2):204-212.
11. Rao MU, Sreenivasulu M, Chengaiah B, Reddy KJ, Chetty CM. Herbal Medicines for Diabetes Mellitus: A Review. International Journal of PharmTech Research. July-Sept 2010; 2(3): 1883-1892.
12. Dahanukar SA, Kulkarni RA, Rege NN. Pharmacology of Medicinal Plants and Natural Products (1994–98), Indian J Pharmacol. 2000; 32:S81–S118.
13. Edwin Jarald, Siddaheswar Balakrishnan Joshi and Dharam Chandra Jain. Diabetes and Herbal Medicines. Iranian Journal of Pharmacology and Therapeutics, 2008; 7: 97-106
14. Dahanukar SA, Kulkarni RA, Rege NN. Pharmacology of Medicinal Plants and Natural Products (1994–98),Indian J Pharmacol. 2000; 32:S81–S118.
15. Pulok KM, Kuntal M, Kakali M, Peter JH. Leads from Indian medicinal plants with hypoglycemic potentials. J Ethnopharmacol 2006; 106:1–28.
16. Pritesh Patel, Pinal Harde, Jagath Pillai, Nilesh Darji and Bhagirath Patel Sat Kaival Pharmacophore 2012; 3: 18-29.
17. Eddouks M, Maghrani M. Phlorizin-like effect of Fraxinus excelsior in normal and diabetic rats. JEthnopharmacol 2004; 9:149-54.

18. Mohamed B, Abderrahim Z, Hassane M, Abdelhafid T, Abdelkhaleq L. Medicinal plants with potential antidiabetic activity-A review of ten years of herbal medicine research (1990-2000). Int J Diabetes Metabol 2006; 14:1-25.
19. Manisha Modak, Priyanjali Dixit, Jayant Londhe, Saroj Ghaskadbi, and Thomas Paul A. Indian Herbs and Herbal Drugs Used for the Treatment of Diabetes., J. Clin. Biochem. Nutr.2007; 40: 163–173.
20. Ghosh MN. Fundamentals of experimental Pharmacology. 3rd ed. Hilton and Company; 2005. P. 190 – 7.
21. Dwivedi Chandraprakash, Daspaul Swarnali, Antidiabetic Herbal Drugs and Polyherbal Formulation Used For Diabetes: A Review, The Journal of Phytopharmacology 2013; 2 (3): 1-7
22. Wadood, A., N. Wadood and S.A. Shah, 1989. Effects of Acacia Arabica and Caralluma edulis on blood glucose levels of normal and alloxan diabetic rabbits. JPMA. The Journal of Pakistan Medical rabbits. JPMA. The Journal of Pakistan Medical Association, 39(8): 208-12.
23. Mukesh Rawat, Namita Parmar, Medicinal Plants with Antidiabetic Potential - A Review, American-Eurasian J. Agric. & Environ. Sci., 13 (1): 81-94, 2013.
24. Akhtar, M.S. and J. Iqbal, 1991. Evaluation of the hypoglycaemic effect of Achyranthes aspera in normal and alloxan-diabetic rabbits J. Ethnopharmacol., 31: 49-57.
25. Kumari, K., B.C. Mathew and K.T. Augusti, 1995. Antidiabetic and hypoHpidaemic effects of S-methyl cysteinesulfoxide, isolated from Allium cepa Linn. Ind. J. Biochem. Biophys, 32: 49-54.
26. Gupta, D., J. Raju, N.Z. Baquer, 1999. Modulation of some gluconeogenic enzyme activities in diabetic rat liver and kidney: effect of antidiabetic compounds. Indian J. Expt. Biol., 37: 196-99.
27. Kirtikar KR, Basu BD. Indian Medicinal Plants, Indian Press, Allahabad, India, 1933: 1052-1054.
28. Hlebowicz J, Darwiche G, Bjorgell O, Almer LO. Am J Clin Nutr 2007; 85:1552–1556?
29. Dey L, Attele AS, Yuan C. Alternative therapies for Type 2 Diabetes Review. Alternative Medicine Review.2002; 7(1): 45-58.
30. Roman-Ramos, R., J.L. Flores-Saenz and F.J. Alarcon-Aguilar, 1995. Antihyperglycemic effect of some edible plants. J. Ethnopharmacol., 48: 25-32
31. Gupta, D., J. Raju, N.Z. Baquer, 1999. Modulation of some gluconeogenic enzyme activities in diabetic rat liver and kidney: effect of antidiabetic compounds Indian J. Expt. Biol., 37: 196-99.
32. Zacharias, N.T., K.L. Sebastian, B. Philip and K.T. Augusti, 1980. Hypoglycemic and hypolipidemic effects of garlic in sucrose fed rabbits. Indian Journal of Physiology and Pharmacology, 24: 151-54.
33. Ajabnoor, M.A., 1990. Effect of aloes on blood glucose levels innormal and alloxan diabetic mice. J. Ethnopharmacol., 28: 215-20.
34. Ghannam, N., M. Kingston, I.A. Al-Meshaal, M. Tariq, N.S. Parman and N. Woodhouse, 1986. M. Tariq, N.S. Parman and N. Woodhouse, 1986. and experimental observations. Hormone Research, 24: 288-94.
35. Noor A, Gunasekaran S, Soosai A, Minicab, Vijayalakshmi MA. Antidiabetic activity of Aloe vera and histology of organs in streptozotocin induced diabetic rats. Current science 2008; 94:1070-1076.
36. Rehman SU, Jafri SA, Hassan S, Ishtiaq N, Muhammad N. Study on antidiabetic effect of Aloe vera extract on alloxan induced diabetic rats. Libyan Agriculture Research Center Journal International 2011; 2: 29-32.
37. Zhang, X.F. and Tan, B.K. (2000b). Antihyperglycemic and antioxidant properties of Andrographis paniculata in normal and diabetic rats. Clin. Exp. Pharm. Phy., 27: 358-363.
38. Yu, B.C., Hung, C.R., Chen, W.C. and Cheng, J.T. (2003). Antihyperglycemic effect of andrographolide in streptozotocin-induced diabetic rats. Planta Med., 69:1075-1079.
39. Teonard, L., T. Dimo and D. Paul, 2006. Title …??? Afr. J. Tradit. Complement. Altern. Med., 3: 23.
40. Mohd M, Alam K S, Mohd A, Abhishek M, & Aftab A, Antidiabetic activity of the aqueous extract of Annona squamosa in Streptozotocin inducedhyperglycemic rats, T. Pharm. Res, 2 (2009) 59.
41. Waheed, A., G.A. Miana and S.I. Ahmad, 2006, Clinical investigation of hypoglycemic effect of seeds of Azadirachta-inidca in type-2(NIDDM) diabetes mellitus. Pak. J. Pharm. Sci., 19: 322-25.
42. Sokeng, S.D., B. Rokeya and M. Mostafa, 2005 Title …??? Afr. J. Tradit. Complement. Altern. Med., 2: 94.
43. Singh S.N., Vats P., Suri S., et al.: J. Ethnopharmacol.76, 269 (2001).
44. Rasineni K, Bellamkonda R, Singareddy S R, Desireddy S, Antihyperglycemic activity of Catharanthus roseus leaf powder in streptozotocin-induced diabetic rats, Phcog. Res, 2 (2010) 195

45. Uebanso, T., H. Arai, Y. Taketani, M. Fukaya, H. Yamamoto, A. Mizuno, K. Uryu and T. Hada, 2007. H. Yamamoto, A. Mizuno, K. Uryu and T. Hada, 2007. postprandial hyperglycemia in rats. Nutr. Sci, Vitaminol. (Tokyo), 53: 482-88.
46. Vitaminol. (Tokyo), 53: 482-88. Improvement of insulin resistance by panax ginseng in fructose-rich chow-fed rats. Horm. Metab Res., 37: 146-51.
47. Panax ginseng Monograph. Alternative Medicine Review. 2009; 14(2): 172-176.
48. Mishra R, Shuaib M, Shravan, Mishra PS. A review on herbal antidiabetic drugs. Journal of Applied Pharmaceutical Science. 2011; 1(6): 235-237.
49. Tripathi AK, Bhoyar PK, Baheti JR, Biyani DM, Khalique M, Kothmire MS, et al. Herbal Antidiabetics: A Review. International Journal of Research in Pharmaceutical Sciences.2011; 2(1): 30-37.
50. Grover JK, Yadav S, Vats V. Medicinal plants of India with anti-diabetic potential.
51. Romila Y, Mazumder PB, Choudhary MD. A Review on Ant diabetic Plants used by the People of Manipur Charactirized by Hypoglycemic Activity. Assam University Journal of Science & Technology: Biological and Environmental Sciences. 2010;6(1):167-175.
52. Kumar AS, Kavimani S, Jayaveera KN. A review on medicinal Plants with potential antidiabetic activity. International Journal of Phytopharmacology. 2011; 2(2): 53-60.
53. Journal of Ethnopharmacology. 2002; 81: 81-100
54. Martinez, G., R. Delgado, G. Perez, G. Garrido Nunez A.J. Selles and O.S. Leon, 2000. Evaluation of the in vitro antioxidant activity of Mangifera indica L. extract. Phytotherapy Research, 14(6): 424-27.
55. Chandraprakash et al, indian herbal medicines used for treatment of dementia: an overview, world journal of pharmaceutical research, volume 3, issue 6, 344-382.
56. Rai PK, Jaiswal D, Mehta S, Watal G, Anti-hyperglycaemic potential of Psidium guajava raw fruit peel. Indian J Med Res. 2009; 129: 561-565.
57. Velmurugan C, Sundaram T, Sampath Kumar R, Vivek B, Sheshadri Sekar D & Ashok kumar B S, Anti Diabetic and Hypolipidemic Activity of Bark of Ethanolic Extract of Ougeinia Oojeinensis (ROXB.), Med J Malaysia, 66 (2011) 22.
58. Seema P V, Sudha B, Padayatti S P, Abraham A, Raghu K G & Paulose C S, Kinetic studies of purified malate dehydrogenase in liver of streptozotocin-diabetic rats and the effect of leaf extract of Aegle marmelos (L.) Corr, Indian J Exp Biol, 34 (1996) 600.
59. Poongothai K, Ponmurugan P, Ahmed K S Z, Kumar S B & Sheriff S A, Antihyperglycemic and antioxidant effects of Solanum xanthocarpum leaves (field grown & in vitro raised) extracts on alloxan induced diabetic rats, Asian Pac. J. Trop. Med, 4 (2011) 778.
60. Arumugam sathy, Perumal Siddhuraju, Protetive effect of bark and empty pod extracts from acacia auriculiformis against paracetamol intoxicated liver injury and alloxan induced type II diabetes, Food and tocicology, 56, 2013, 162-170.
61. B,S,Ashok Kumar, Antidiabetic, antihyperlipidemic and antioxidant activities of methanolic extract of amaranthus viridis Linn in alloxan induced diabetic rats, Experimental and toxicologic pathology, 64, 2012, 75-779.
62. Patil RN, Patil RY, Ahirwar A, Ahirwar D, Evaluation of antidiabetic and related actions of some Indian medicinal plants in diabetic rats, Asian Pac J Trop Med, 4, 2011, 20-23.
63. Ayodhya S, Kusum S, Anjali S, Hypoglycemic activity of different extracts of various herbal plants Singh, Int J Ayurveda Res Pharm, 1(1), 2010, 212-224.
64. Bnouham M, Ziyyat A, Mekhfi H, Tahri A, Legsyer A, Medicinal plants with potential antidiabetic activity- a review of ten years of herbal medicine research, (1990-2000), Int J Diabetes metab, 14, 2006, 1-25.
65. K shirsagar RP, Darade SS, Takale V, Effect of Alangium salvifolium (Alangiaceae) on dexamethasone induced insulin resistance in rats, J Pharm Res, 3(11), 2010, 271-276.
66. Chauhan A, Sharma PK, Srinivastava P, Kumar N, Duehe R, Plants having potential antidiabetic activity, A review, Der pharm let, 2(3), 2010, 2(3), 369-387.
67. Singh LW, Traditional medicinal plants of Manipur as antidiabetics, J Med Plant Res, 5(5), 2011, 677-687.
68. Malviya N, Jain S, Malviya S, Antidiabetic potential of medicinal plants, Acta Pol Pharm, 67(2), 2010, 113-118.

69. Park S, Jang JS, Hong SM, Long – term consumption of caffeine improves glucose homeostasis by enhancing insulinotropic action through islet insulin/insulin – like growth factor 1 signaling in diabetic rats, Metabolism, 29(1), 2007, 599-607.
70. Islam MS, Choi H, Green tea, anti- diabetic or diabetogenic, a dose response study, Biofactors, 29(1), 2007, 45-53.
71. Islam S, Choi H, Dietary red chilli (Capsicum frutescns L) is insulinotropic rather than hypoglycemic in type 2 diabetes model of rats, Phytother Res, 22(8), 2008, 1025-1029.
72. Dallak M, Al- khateeb M, abbas M, Elessa R, al- hashem F, basher N, Et al, In vivo, acute, normo – hypoglycemic, antihyperglycemic, insulinotropic actions of orally administered ethanol extract of citrullus colocynthis(L) Scharb pulp, Am J BIochem BIotechnol, 5(3), 2009, 119-126.
73. Arjyun P, Shivesh J, Sahu An, Antidiabetic activity of aqueous extract of Eucalyptus citriodora hook in alloxan induced diabetic rats, Pharmacogn Mag, 5, 2009, 51-54.
74. Fararh KM, Atoji Y, shmizu Y, takewaki T, Insulintropic properties of Nigella sativa oil in streptozotocin plus nicotinamide diabetic hamster, Res Vet Sci, 73(3), 2002, 279-28.
75. Fararh KM, Atoji Y, shmizu Y, takewaki T, Insulintropic properties of Nigella sativa oil in streptozotocin plus nicotinamide diabetic hamster, Res Vet Sci, 73(3), 2002, 279-28.
76. Meenakshi P, Bhuvaneshwari R, Rathi MA, Thiruoorthi L, Guravaiah DC, Jiji MJ, et al, Antidiabetic activity of ethanolic extract of Zaleya decandra in alloxan- induced diabetic rats, Appl Biochem Biotechnol, 162, 2010, 1153-1159.
77. Abdl- zaher Ao, Salim SY, Assaf MH, Abdel- Hady RH, Teucrium polium antidiabetic activity and toxicity of Zizyphus spina – Christi leaves, J Ethnopharmocolgy, 101(1-3), 2005, 129-138.
78. Pravin K. Bhoyar et al., Herbal Antidiabetics: A Review Int. J. Res. Pharm. Sci., 2(1), 2011, 30-37
79. Rajesham V. V et al A review on medicinal plant and herbal drug formulation used I diabetes mellitus, Indo American Journal of Pharmaceutical Research. 2012; :2 (10).
80. Basavaraj K. Nanjwade Polyherbal Formulations for Diabetes. 7th September 2011 in 14th Asian Chemical Congress.
81. http://www.alibaba.com/product-gs/357477619/diabetic herbaltea.html (accessed July 11, 2011)
82. http://www.alibaba.com/product-tp/109604143/Herbaldiabetesproduct.html(accessed July 11, 2011)
83. http://www.alibaba.com/productfree/103220828/Stevia33DiabetesHerbal_Medicine.html (accessed July 11, 2011).
84. http://www.alibaba.com/productfree/252036161/DiabFITHerbalFITforDiabetes.html (accessed July 11, 2011)
85. http://www.alibaba.com/product-free/11942265/HerbalDiabetes.
86. http://www.alibaba.com/product-free/111557110/dayastonpowderfordiabetes.html (accessed July 12, 2011)
87. http://www.alibaba.com/product-free/108363205/herbalmedicine.html (accessed July 12, 2011)
88. http://www.alibaba.com/product-free/109219085/KumariSaar.html (accessed July 12, 2011
89. Journal of Ethnopharmacology. 2002; 81: 81-100, Journal of Ethnopharmacology. 2002; 81: 81-100.
90. www.jtcm.org