

Antidiabetic Potential of Herbal Drugs Current Status and Future Prospective

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Abstract

Diabetes is an important human ailment affecting many from various walks of life in different countries. The limitations of currently-available oral antidiabetic medication either in terms of efficacy and safety coupled with the emergence of the disease into a worldwide epidemic have encouraged effort to discover newer phytomedicines that can be used to manage diabetes more efficiently. Many plants around us have been reported to possess antidiabetic properties. During the last few years, bioactive drugs have been isolated from plants showing anti-diabetic potential. Many studies have been carried out to prove the benefits of medicinal plants with hypoglycemic effects for managing diabetes. Here a list of medicinal plants with proven antidiabetic and related beneficial effects is reviewed and compiled.

Keywords: - Antidiabetic, Hypoglycemic, Clinically, Complications.

INTRODUCTION

Diabetes is a chronic disorder of carbohydrate, fat and protein metabolism characterized by increased fasting and post prandial blood sugar levels. Over the past 30 year, the status of diabetes has changed from being considered as a mild disorder of the elderly to one of the major causes of

morbidity and mortality affecting the youth and middle aged people.

Diabetes is a disease of global distribution affecting individuals of all ages with widely varying prevalence rates of 150 million in 2010 which is predicted to double by 2025 to 300 million. It is

estimated to have diabetes globally and this number expected to increase to near about 450 million by 2030 [1] [2].

The therapeutic measurements include use of insulin and other agents like amylin analogues, sulphonyl ureas, biguanides, and alpha glycosidase inhibitors like acarbose, miglitol and voglibiose for the treatment of hyperglycemia. These drugs also have certain adverse effects like causing hypoglycemia at higher doses, liver problems, lactic acidosis and diarrhoea. Oral agents and delivery measures only partially correct the multiple disturbances [3].

In ancient literature, more than 800 plants are reported to have antidiabetic properties [4]. Ethanopharmacological surveys indicate that more than 1200 plants are used in traditional medicine for hypoglycemic activity [5]. Ancient Indian medicine has mentioned numerous dravyas (things which has biological functions and properties) have been reported effective in madhumeha (Diabetes) [6].

The use of herbs in the management of Diabetes mellitus has been prevalent in Indian society from a long time. From the

ethnobotanical information, about 800 plants possessing antidiabetic potential have been found. The popularity of herbal usage can be attributed to its fewer side effects compared to the synthetic hypoglycemic agents and also their safety, effectiveness, and availability.

Further, herbal action may delay the development of diabetic complications and correct the metabolic abnormalities. During the last few years, bioactive drugs have been isolated from plants showing anti-diabetic potential. Many studies have been carried out to prove the benefits of medicinal plants with hypoglycemic effects for managing the Diabetes mellitus. Herbal drugs are prescribed widely because of their effectiveness, less side effects and relatively low cost. Therefore, investigation on such agents from traditional medicinal plants has become more important. [3] [7].

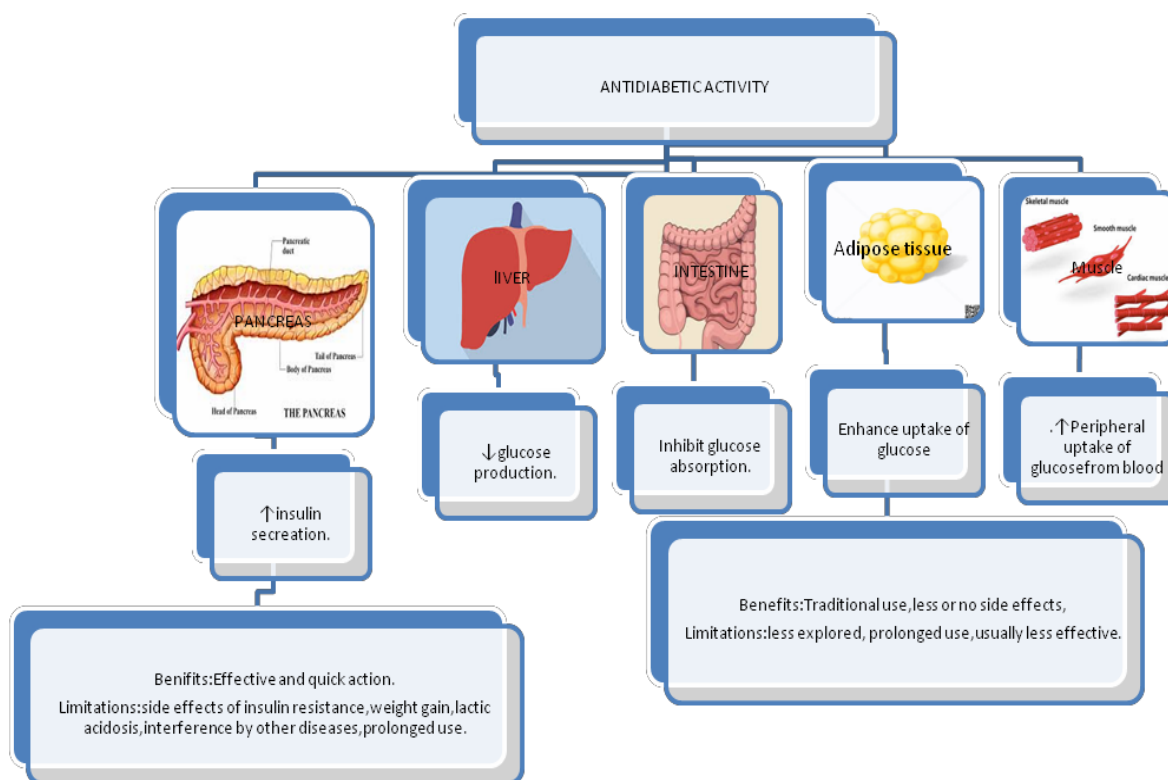


Figure.1 Antidiabetic Activity

Phytoconstituents with hypoglycemic potentials. Researchers have proved that the anti-diabetic activity of medicinal plants is due to the presence of phenolic compounds, flavonoids, terpenoids, coumarins and other ingredients which show hypoglycemic activity. However lots of investigations are needed for the evaluation of mechanism of action of medicinal plants with antidiabetic activity. Compound with different structure but with the same therapeutic activity isolated from different plant species act as active moieties for the treatment of various diseases. Some of these active principles

originate from edible plants and their inclusion in the diet would undoubtedly be of some value because of their hypoglycemic potential. Several phytomolecules including flavonoids, alkaloids, glycosides, saponins, glycolipids, dietary fibres, polysaccharides, peptidoglycans, carbohydrates, amino acids and others obtained from various plant sources have been reported as potent hypoglycemic agent[8].

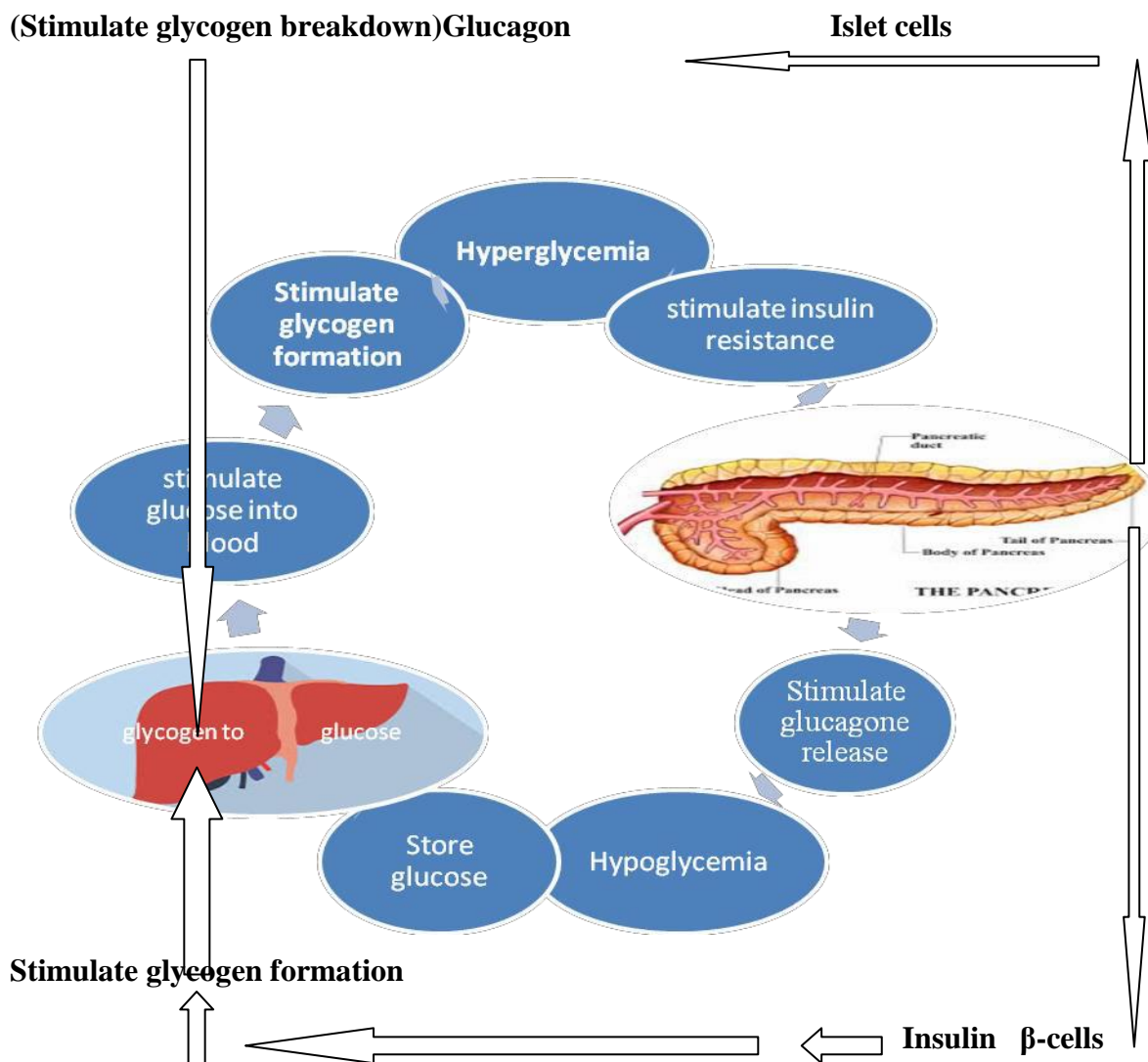


Figure .2 Differentiate between Hyperglycemic & Hypoglycemia.

Table 1: Here a list of herbs with proven hypoglycemic effect have been reviewed

Plant name	Family	Source	Antidiabetic & other beneficial effects in	Reference
Aegle marmelos	Rutaceae	Leaf	Decrease elevated glucose & glycosylated haemoglobin	Vertrichelvan.Tet al;2002 Rajesh.Ret al;2012
Aerva lanata	Amaranthaceae	Herb	Decrease blood sugar level	Thomsom.M et al;2007
Allium sativum	Liliaceae	Fruit	Decrease blood sugar level	Kar. A, 2003

Aloe barbadensis	Aloaceae	Leaf	Hypoglycemic.	Kumar.GP, 1993 Mallick. C 2007 Rejesh.R 2012
Andrographis paniculata	Acanthaceae	Herb	Decrease blood glucose	Xu.j 2012
Azadiracta indica	Meliaceae	Leaf	Hypoglycemic.	Chattopadhyay.RR,1987 Chattopadhyay.RR 1996
Coccinia India	Cucurbitaceae	Fruit	Reduced blood glucose	Mallick c, et al;2005
Costus speciosus	Zingiberaceae	Rhizome	Reduced blood glucose	Xu, et al;
Euphorbia hirta	Euphorbiaceae	Leaf	Significant hypoglycemic & antihyperlipidemic effect.	Chattopadhyay. RR 1996
Gymnema	Asclepidaceae	Leaf	Anti-hyperglycemic & hypolipidemic.	Vessal M, et al;2003
Mangifera indica	Anacardeaceae	Leaf	Reduced blood glucose	Kumar GP et al;1993
Momordica charantia	Cucurbitaceae	Fruit	Potent blood glucose level	Maslick C et al;2005
Pterocarpus	Leguminosae	Bark	Reduced blood sugar level	Abesundar KJet al;2004
Stevia rebaudiana	Asteraceae	Leaf	Reduced blood sugar level	Vanek Tet al;2001
Syzygium cumini	Myrtaceae	Fruit	Hypoglycemic.	Bekele T et al;2008
Tinospora cordifolia	Menispermaceae	Leaf	Potent hypoglycemic.	Ravi K et al;2004
Trigonella foenumfraecu	Fabaceae	Seed	Anti-hyperglycemic & hypolipidemic.	RajalakshmiMet al;2009
Chloroxylin swietenia	Rutaceae	Bark	Antidiabetic activity	Shani J et al;1974
Guar gum	Fabaceae	Bean	Hypoglycemic	Karthik D et al;2011
Kyllinga triceps	Cyperaceae	Bark	Hypoglycemic	M,et.al;2013
Anacardium	Anacardeaceae	Leaf	Hypoglycemic.	Jayaprasad J et al;2016
Zanthoxylum	Rutaceae	Root	curative rather than palliative	M.R.Nasryet al;2013

Cinnamomum	Lauraceae	Bark	Reduced blood	Mukul et al., 2008
zeylanicum			glucose level	
Emblica officinalis	Phyllanthaceae	Fruit	Reduced blood	Shikha et al;2009 Ahad
Mangifera indica	Anacardeaceae	Leaf	Hypoglycemic	Aderibigbe et al., 1999 Bhowmilk et al., 2009
<u>Panax ginseng</u>	Araliaceae	Roots	Hyperglycemic & anti obese effect.	Attele et al;2002
Paseolus vulgaris	Leguminosae	Bean	Hypoglycemia.	Helmstadter et al;2010
Plantago ovata	Plantagonaceae	Seed	Control blood sugar level	Freitas et al;2002
Prunus dulci	Rosaceae	Flowers	Reduced blood sugar level	Singh etal;2002
Vaccinium myrtillus	Ericaceae	Leaf	Reduced blood sugar level	Zohary et al;2000
Aegle marmelos	Rutaceae	Leaf	Decrease elevated glucose & glycosylated haemoglobin levels.	Vertrichelvan.Tet al;2002 Rajesh.Ret al;2012
Chloroxylon swietenia	Rutaceae	Bark	Decrease blood glucose level	Shani J et al;1974
Zanthoxylum chalybeum	Rutaceae	Root	curative rather than palliative	M.R.Nasryet al;2013
Citrus reticulates	Rutaceae	Fruit	Decrease Glucose	Kar A etal;2003
Acacia arabica	Fabaceae	Seed, Bark	_____	Yasir et al; 2010
Cassia articulate	Fabaceae	Flower	Hypoglycemic	Kumar GP etal;1997
Tamarindus indica	Leguminosae	Seed,Fruit	Decrease Glucose	Xu J.etal;2012
Xanthocercis zambisiaca	Fabaceae	Leaf	Potent blood glucose level	Chattopadhyay R etal;1996

Neem	Meliaceae	Leaf, seed	Hypoglycemic	Moses etal;2016
Brassica juncea	Brassicaceae	Seed, leaf	Decrease blood glucose level	Aderibigbe etal;1999
Lipidium sativum	Cruciferae	Leaf	Decrease blood glucose level Decrease lipid	Bhowmilk etal;2009
Raphanus sativus	Brassicaceae	Whole plant	Potent for blood sugar level	Kar A etal;2003
Momordica charantia	Cucutbitaceae	Whole plant	Decrease Glucose, Decrease lipid	Karunanayake etal;1984
Coccinia India	Cucurbitaceae	Fruit	Reduced blood glucose level	Mallick c, et al;2005
Mangifera indica	Anacardeaceae	Leaf	Reduced blood glucose level	Kumar GP et al;1993
Anacardium occidentale	Anacardeaceae	Leaf	Hypoglycemic	Jayaprasad J et al;2016
Rhus ciriaria	Anacardeaceae	Fruit	Decrease Glucose	Mohammadis etal;2010

Although a lot of pharmacological investigations have been carried out based on the ingredients present but a lot more can still be explored, exploited and utilized. A summary of the findings of these studies is presented below.

Aegle marmelos (Family: Rutaceae) A moderate sized tree found throughout the deciduous forests of India. Different extracts obtained from the leaves, bark and

fruit of this plant have been investigated for possible hypoglycemic activity in various experimental animal models of diabetes like streptozotocin and alloxan induced diabetes along with possible mechanism of action. It increases utilization of glucose; either by direct stimulation of glucose uptake or via the mediation of enhanced insulin secretion and also decreases the elevated glucose and glycosylated haemoglobin levels. The

leaves have antihyperglycemic activity in glucose induced hyperglycemic rat at an oral dose equivalent to 250 mg/kg [17]. Antihyperglycemic activity of aqueous fruit extract (250 mg/kg, twice daily for 1 month) in streptozotocin induced female albino Wistar diabetic rats also have been reported [18].

Aerva lanata (Family: Amaranthaceae) It is a branched herb widely used in Indian folk medicine for the treatment of Diabetes mellitus. The effect of an alcoholic extract of *Aerva lanata* on blood glucose and other biochemical parameters in alloxan-induced diabetic rats was studied and it was observed that the extract reduced the increase of blood sugar in alloxanized rats by 42% at 375 mg/kg and 48% at 500 mg/kg body weight [19]. The methanolic and aqueous extract also reduced blood sugar level of streptozotocin induced rats significantly upon chronic administration (400mg/kg) for 2 weeks [20].

Allium sativum L. (Family: Liliaceae) Garlic (*Allium sativum*), a member of the Liliaceae family, is a common food for flavour and spice and it is one of the herbs most commonly used in modern folkloric medicine to reduce various risk factors associated with cardiovascular diseases.

Garlic is stated to possess many therapeutic benefits. Garlic's strong odour is largely due to sulphur-containing compounds (S-allyl cysteine sulphoxide), which are believed to account for most of its medicinal properties. Garlic has been found to be effective in lowering blood glucose level in STZ-induced diabetic rats as a response of administration of 500mg/kg of aqueous extract [21]. However, garlic treatment did not reduce glucose level of diabetic animals to normal levels. But the study strongly suggests that garlic may be very useful in the alleviation of diabetic complications. ~ 167 ~ Journal of Medicinal Plants Studies.

Aloe barbadensis (Family: Aloaceae) Aloes have long been used all over the world for their various medicinal properties. The extract of aloe gum is effective in enhancing glucose tolerance in normal as well as diabetic rats [18]. Several other works have revealed the hypoglycemic activity of this plant along with possible mode of action. Oral administration of Aloe gel significantly reduced the fasting blood glucose, hepatic transaminases, plasma and tissue cholesterol, triglycerides, free fatty acids and phospholipids. It significantly increases plasma insulin levels [22]. The

hypoglycemic activity of leaf pulp extracts (200 and 300 mg/kg) in streptozotocin-induced diabetic rat was also reported [23]. Leaf pulp juice of 10–20 ml is used to control diabetes in humans.

Andrographis paniculata (Family: Acanthaceae) It is an erect annual herb commonly known as Kalmegh or ‘King of Bitters’, found throughout India and cultivated in many states of India. A number of studies have shown that *Andrographis paniculata* extract and the active metabolite andrographolide can exert potent antihyperglycemic activity. A water-soluble polysaccharide (APP) was isolated from *Andrographis paniculata* and the synergistic effect of APP in combination with andrographolide on renal complication in streptozotocin (STZ) induced diabetic mice was investigated. APP and/or andrographolide were administered to diabetic mice continuously for two weeks. APP plus andrographolide decreased the levels of blood glucose in diabetic rats, as well as the relative kidney weight. In summary, APP plus andrographolide can improve the metabolic abnormalities of diabetic mice and prevent or delay the progression of diabetic renal complications, which may be useful as a therapeutic agent for

inhibiting the progression of diabetic nephropathy [24].

Acacia Arabica (Babul): The plant extract acts as an antidiabetic agent by acting as secretagogue to release insulin. It induces hypoglycemia in control rats but not in alloxanized animals. Powdered seeds of *Acacia arabica* when administered (2,3 and 4 g kg⁻¹ b.wt.) to normal rabbits induced hypoglycemic effect by initiating release of insulin from pancreatic beta cells Oral administration of cold water extract of *Acacia arabica* bark to diabetic and normal rats at a dose of 400 mg kg⁻¹ b.wt. Resulted in significant reduction of **blood glucose**, cholesterol and triglycerides [21].

Azadirachta indica (Family: Meliaceae) *Azadirachta indica* commonly referred as the neem tree is a broad-leaved evergreen tree found throughout India and is widely recognized as a potent insecticide. Hypoglycemic activity of hydro alcoholic *Azadirachta indica* extract in normal rats and hypoglycemic activity in glucose fed and streptozotocin induced diabetic rats has been reported [13] [25]. Hypoglycemic activities of leaf extract in normal and streptozotocin-induced diabetic rat. Crude ethanolic extract of neem inhibited action

of epinephrine on glucose metabolism, resulting in increased utilization of peripheral glucose in alloxan diabetic albino rats [26].

Coccinia indica (Family: Cucurbitaceae) A creeper grows wildy in many parts of the Indian subcontinent and is well known as a hypoglycemic herb. Hypoglycemic activity of Pectin, isolated from the fruit of *Coccinia indica* was studied in normal rats at a dose of 200 mg/100 g/day upon oral administration and it showed significant reduction in blood glucose and an increase in the liver glycogen level [27]. Aqueous methanolic (40:60) extract of leaf of *Coccinia indica* significantly reduced the blood glucose level [28]

Costus speciosus (Family: Zingiberaceae) It is a rhizomatous herbaceous plant. It has a very wide distribution in India and widely used in several indigenous system of medicine for the treatment of various ailments. The rhizomes are used as an alternative source for diosgenin, tigogenin and saponins. Aqueous and methanolic extract of *Costus speciosus* have shown significant decrease in fasting blood glucose level in diabetic rats. As a response of administration of 200 mg/kg of both the extract there was drastic and

significant reduction in blood glucose level starting from 30 min and is maintained till 240 min and is highly significant [24].

Euphorbia hirta (Family: Euphorbiaceae) It is a slender- stemmed, annual hairy plant with many branches from the base to top, spreading upto 40 cm in height, reddish or purplish in color. *Euphorbia hirta* has been studied by various workers and a number of active constituents like Afzelin, Quercitrin, and Myricitrin have been isolated. Ethanolic extract of *Euphorbia hirta* leaves have hypoglycemic activity in STZ induced diabetic wistar rats [25].

Ethanolic extract of *Euphorbia hirta* leaves was administered to streptozotocin induced rats. Glibenclamide was used as a standard drug. Blood glucose levels were determined after oral administration of a dose of *Euphorbia hirta* (400 mg/kg b. wt) in diabetic groups. Blood glucose levels were determined on 0, 7th, 14th and 21st day after oral administration and was found to reduce blood sugar in diabetic rats. Reduction in blood sugar could be seen from 7th day after continuous administration of the extract. These results indicated that *Euphorbia hirta* possesses significant hypoglycemic and antihyperlipidemic effect.

Gymnema sylvestre (Family: Asclepiaceae) *Gymnema sylvestre* is one of the Asclepiad strains, native to the tropical regions of India and commonly known as the “sugar destroyer” because the leaves effectively block sweet tastes in the mouth when chewed. The plant has been used in the treatment of Diabetes mellitus for a long time in India and reported by different workers for its blood glucose lowering activity both invitro and in vivo. Aqueous leaf extract of *Gymnema sylvestre* significantly reduced the fasting blood glucose in diabetic rats [26]. Treatment with *Gymnema sylvestre* powder significantly reduced the glucose and triglycerides levels [10]. The study revealed the anti-diabetic effect in stomach of albino wistar rats using *Gymnema sylvestre* herbal powder. The different concentration of *Gymnema sylvestre* treated were 5, 10, 15, 20/gms/25 days. Treatment with *Gymnema sylvestre* reduced the stomach weight of animals and reduced levels of insulin, protein, triglycerides, cholesterol and glucose significantly. Thus it could be recommended that *Gymnema sylvestre* could be used in various ailments in limited dosage on the advice of a physician.

Mangifera indica (Family: Anacardiaceae) It is a well-known perennial tree commonly known as Mango, distributed and widely cultivated throughout India. The aqueous leaf-extract (1 g/kg) exert hypoglycemic activity in - induced diabetic rats upon oral administration [27]. The glucose lowering effect of mangiferin, a xanthoneglucoside, isolated from the leaves of *Mangifera indica* was also studied and possible mode of action could be through the intestinal reduction of absorption of glucose as well as pancreatic and extra pancreatic mechanisms.

Momordica charantia (Family: Cucurbitaceae) It's a slender, climbing annual vine commonly known as 'bitter gourd' grows in India and other tropical countries. Several earlier and recent studies have indicated the ~ 168 ~ Journal of Medicinal Plants Studies hypoglycemic activity of various parts of this plant. Fruit powder and aqueous fruit extract of *Momordica charantia* was investigated for its effect on blood glucose and other biochemical parameters in alloxan-induced diabetic rats and found to exert potent blood glucose lowering effect. Alcoholic extract of fruits of *Momordica charantia* decreases the blood sugar level

significantly. Blood glucose once lowered by this treatment remained static even after discontinuation of drug for 15 days [28].

Pterocarpus marsupium (Family: Leguminosae) It is a small tree attaining a height of 7.5m and traditionally used in the treatment of diabetes, bleeding piles, dysentery and in all skin inflammations. It is a well-known plant commonly known as Vijaysar, found throughout India.

In folk medicine the plant is used as hypoglycemic, which was proved by some earlier studies. Different parts of the plant like bark, latex, etc. were investigated and reported to have hypoglycemic activity [21] [29]. Various active components like epicatechin, marsupsin, pterosupin and pterostilbene, isolated from the bark and heartwood of the plant, were also found to possess blood sugar lowering activity.

Stevia rebaudiana (Family: Asteraceae) Stevia, one of the genera of the Asteraceae Family is a genus of more than 200 species. Members of Stevia comprise mostly of herbs but also shrubs and trees. It is a non-calorie sweetener (250-300 times sweeter than sucrose at 0.4% solution) in medicinal green teas for treating heart burn and other ailments [30].

The alkaloids Stevioside & Rebaudioside present in leaves is responsible for its antidiabetic action [31] reported that the crude aqueous extract of Stevia rebaudiana lowered elevated blood glucose level in alloxan induced diabetic mice. The fasting mean blood glucose level of diabetic mice treated with crude aqueous extract (300 mg/kg and 500 mg/kg body weight), and crude ethanol extract (300 mg/kg and 500 mg/kg body weight) was reduced significantly compared to diabetic control (positive control) mice. The effect was more pronounced in the case of crude aqueous extract compared to crude ethanol extract. The result of the ethanol extract did not show dose-dependence whereas the aqueous extract showed a dose-dependent reduction of blood glucose levels.

Syzygium cumini (Family: Myrtaceae) Large evergreen tree of Indian subcontinent, commonly known as 'Jamun'. In India, the decoction of kernels of *Eugenia jambolana* is used as a household remedy for diabetes. Hypoglycemic activity of ethanolic whole seeds, kernel and seed coat extracts (100 mg/kg) in streptozotocin induced diabetic rats has been reported [32]. The seeds and decoction of dry leaves were found to produce hypoglycemic effect.

Tinospora cordifolia (Family: Menispermaceae) It is a large climbing shrub found throughout India and used in various ailments. Various extracts of the leaves of this plant were investigated for their blood sugar lowering activity in normal and alloxanized rats in graded doses and the findings have proved that the plant has potent hypoglycemic activity. Supplementation of methanol extract of *Tinospora cordifolia* significantly reduced the fasting blood glucose level and glucose-6-phosphatase activity [33]. The oral administration of various extracts (Hexane, Ethyl acetate and Methanol) of *Tinospora cordifolia* stem (TCS) were found to have potent antidiabetic activity that reduces blood sugar level in streptozotocin-(STZ) induced diabetic rats. In this study, the chronic (100 days) Antihyperglycemic effect of the extracts at a dose of 250 mg/kg TCS were investigated. Insulin was used as a reference drug at a dose of 3 I.U/kg.

Trigonella foenumgraecum (Family: Fabaceae) Fenugreek is a well-known hypoglycemic agent used in traditional Indian medicines. Various extracts of different parts of this plant; fibres, proteins and saponins isolated from the seeds were investigated and found to possess

significant hypoglycemic activity. Fenugreek seeds and the major alkaloid component, Trigonelline, exerted a mild hypoglycemic effect on streptozotocin- induced diabetic rat [34] [35] reported the antidiabetic activity of Ethanolic extract of *Cynadon dactylon* (450mg) on blood glucose level. Regular intake of *Ipomea digitata* tuber root powder is reported to be beneficial to persons suffering from or prone to diabetic and coronary disease [36].

Based on our present experimental data, it can be suggested that PHPE may prevent hyperglycemia and hyperlipidemia in STZ induced diabetic rats by its blood glucose lowering effect which can be due to various mechanisms like insulinomimetic property, β -cell regeneration, increased insulin secretion, increased peripheral glucose utilization and decreased intestinal glucose absorption.

Chloroxylon swietenia (Family: Rutaceae) Ceylon satinwood East Indian satinwood *Chloroxylon swietenia* bark methanol and aqueous extracts have proved to possess antidiabetic activity in STZ induced diabetic rats, which might be due to increase in plasma insulin levels, and this would be responsible for the restoration of

carbohydrate metabolizing enzymes and liver glycogen and results of (CSBMEt) *Chloroxylon swietenia* bark methanol extract (250 mg/kg) are more effective and comparable to the standard drug glibenclamide.[34]

Guar gum or cluster bean, with the botanical name **Cyamopsis tetragonoloba**, (Family: Fabaceae) Guar gum decreased STZ induced hyperglycemia and ameliorated oxidative stress, similar to gliclazide alone. Its antidiabetic activity may be related to increased insulin secretion and antioxidant activity [35]

Kyllinga triceps (Family: Cyperaceae) Streptozotocin is well known for its selective pancreatic islets β cell cytotoxicity and has extensively used to induce diabetes in experimental rat model. The folkloric use of *Kyllinga triceps* in different ethnic communities of Manipur, Madhya Pradesh and Chhattisgarh. It may be concluded that *Kyllinga* extract possess hypoglycemic activities and the plant extract may be used as hypoglycemic agent. The plants should be considered as an excellent candidature for further studies on diabetes mellitus [36]

Anacardium occidentale (Family: Anacardeaceae) results signify that the n- STZ diabetic animal group developed a moderate type 2 diabetes; nevertheless the animals were in better conditions (with lower blood-sugar concentrations); which confirms that the (n-STZ) model is appropriate for study on type 2 diabetes. It can be concluded that the traditional use of Anacardeaceae as a hypoglycaemic agent is justified. The extracts from the leaves of this plant show a significant activity which is comparable to the standard hypoglycemic drug pioglitazone [37].

Zanthoxylum chalybeum (Family: Rutaceae) *Zanthoxylum chalybeum* to alloxan-induced diabetic rats improves their glucose tolerance, an important finding in the control of diabetes. This suggests that *Zanthoxylum chalybeum* is useful in protection and amelioration of diabetic complications through enhancement of regeneration of β -cells of the islets of Langerhans. Therefore, the effects of *Zanthoxylum chalybeum* appear to be curative rather than palliative. Further studies are needed to define the active agents present and their mode of activity [38]

Cinnamomum zeylanicum (Cinnamon) It has Insulin-like properties, which able to decrease blood glucose levels as well as triglycerides and cholesterol, all of which are important especially for type II diabetes patients. Just half a teaspoon of Cinnamon into the daily diet of a diabetic can significantly reduce blood glucose levels. Oral administration of ethanolic extract in the doses of 100,150 and 200 mg kg-1b.wt to white Wistar albino rats significantly reduced their blood sugar level in alloxan induced diabetic rats under acute and sub acute studies [42]

Camellia sinensis (White tea) to evaluate the effect of WTE on reducing fasting blood glucose levels in diabetic rats administration of WTE for 14 days showed decreased fasting blood glucose level in diabetic rats. The dose of 100 mg/kg BW of WTE has the highest effect on reducing fasting glucose level significantly compared to negative control group ($p < 0.05$). The content of flavonoids, especially catechin compounds are suspected to play a role in lowering fasting blood glucose levels. The administration of WTE for 14 days has potentially antidiabetic activity in diabetic rats induced streptozotocin-nicotinamide [43].

Emblica officinalis (Amla): It is rich in Vitamin C. Amla stimulates the Pancreas to secrete Insulin (Ahad et al., 2010). The aqueous extract of *Emblica officinalis* seeds was investigated for its anti-diabetic activity in Streptozotocin induced type 2 diabetes animal models. The dose of 300 mg kg-1 of aqueous seed extract in sub- and mild-diabetic animals produced a maximum fall of glucose level in the blood [44]

Mangifera indica (Mango): The leaves of this plant are used as an antidiabetic agent in Nigerian folk medicine, although when aqueous extract given orally did not alter blood glucose level in either normoglycemic or streptozotocin induced diabetic rats. However, antidiabetic activity was seen when the extract and glucose were administered simultaneously and also when the extract was given to the rats 60 min before the glucose. The results indicate that aqueous extract of *Mangifera indica* possess hypoglycemic activity. This may be due to an intestinal reduction of the absorption of glucose [45] The ethanol extracts of stem-barks reduced glucose absorption gradually during the whole perfusion period in type 2 diabetic rats[46].

Panax ginseng (Ginseng): It has been shown to enhance the release of Insulin from the pancreas and to increase the number of Insulin receptors. It also has a direct blood sugar-lowering effect. Therapeutic dosage is 100-200 mg daily. The antihyperglycemic and anti-obese effects of Panax ginseng berry extract and its major constituent, ginsenoside The obese diabetic mice and their lean littermates was evaluated [47]

Phaseolus vulgaris (Kidney Bean): In addition to lowering cholesterol, kidney bean's high fiber content prevents blood sugar levels from rising too rapidly after a meal, making these beans an especially good choice for individuals with diabetes, Insulin resistance or hypoglycemia. It seems that Phaseolus preparations should not be considered the first choice in phytopharmaceutical treatment of diabetes or lead structure research. To be effective, fairly high doses of aqueous extracts need to be given. Because of their fiber content and an α -amylase inhibitory effect, beans might be more useful as food components in preventing or ameliorating type 2 diabetes [48]

Plantago ovata (Ispaghula): It can be taken in the form of seeds/husk In case of diabetics, it controls blood sugar by inhibiting the excessive absorption of sugar from the intestine. [49]

Prunus dulcis (Almond): The fixed Oil of Almonds is extracted from both Bitter and Sweet They have a special dietary value (containing about 20% of proteins); they contain practically no starch, and are therefore often made into flour for cakes and biscuits for patients suffering from diabetes.[50]

Vaccinium myrtillus (Blue Berry): Blue berry is a natural source of lowering blood sugar levels and results have shown the leaves have an active ingredient with a remarkable ability to get rid the body of excessive sugar in the blood.[51]

Cucurbita pepo (Pumpkin) Cucurbita pepo, is mainly known for its improvement in prostatic hiperplasia (BPH), urinary dysfunction and cytotoxic properties, also has also been used extensively as a hypoglycaemic agent.

Many pharmacological studies have demonstrated hepato protection, inhibit benign prostatic hiperplasia, antioxidant, anticancer, antimicrobial, antiinflammatory,

antidiabetic, and antiulcer activities supporting its traditional uses [60].

Tamarix gallica (Family: *Tamaricaceae*) **Alzheimer's (AD) and type 2 diabetes (T2D)**. Ten antioxidant flavonoids isolated from the medicinal halophyte *Tamarix gallica* were tested for their amyloid aggregation inhibition potential. Glucuronosylated flavonoids show relatively strong inhibitory activity of

Amyloid β ($A\beta$) and human islet amyloid polypeptide (hIAPP) aggregation compared to their aglycone analogs. Structure–activity relationship of the flavonoids suggests that the catechol moiety is important for amyloid aggregation inhibition, while the methylation of the carboxyl group in the glucuronide moiety and of the hydroxyl group in the aglycone flavonoids decreased it [69].

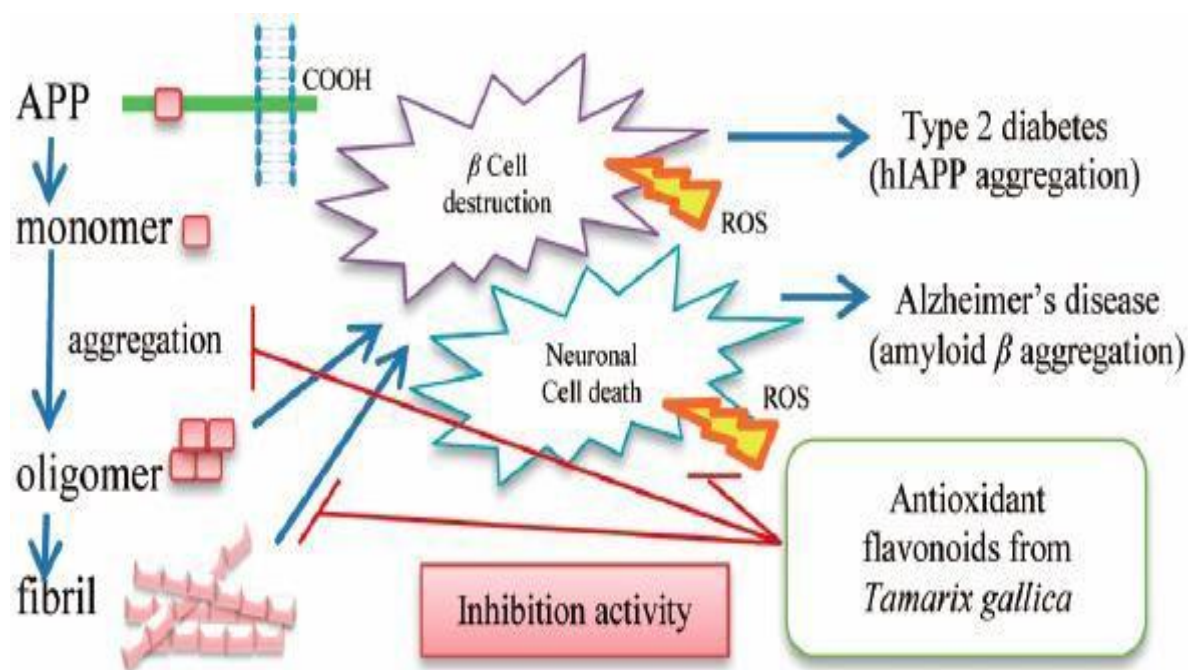


Figure .2 [69]

**CLINICALLY PROVED
ANTIDIABETIC ACTIVITY**

Kalanchoe pinnata (Family: Anacandaceae)

Diabetes mellitus was induced in rats by a single administration of streptozotocin (60 mg/Kg). Diabetic rats were then treated with aqueous *Kalanchoe pinnata* for 30 days. Serum glucose, proteins, lipid composition, liver and kidney function indices, inflammatory markers, and key enzymes of hepatic carbohydrate and lipid metabolism were determined. The aqueous preparation of *Kalanchoe pinnata* preparation consumption may be beneficial in the management of diabetes mellitus. The observed adverse effect on alkaline phosphatase activity may be due to the combined effect of streptozotocin-induced diabetes and *Kalanchoe pinnata* preparation administration. *Kalanchoe pinnata* may accrue some benefits in the management of diabetes, further studies are needed to evaluate the long-term effects of *Kalanchoe pinnata* preparation versus a positive control drug currently used in the treatment of diabetes mellitus on serum ALP activity. The phytochemical result showed that the aqueous extracts contained tannins, flavonoids, alkaloids, sterols, and saponins. The antidiabetic activity showed could be due to the

presence of some phytochemicals present which have antidiabetic activity. *Kalanchoe pinnata* preparation may protect against cardiovascular risk associated with diabetes mellitus. [52]

Piper Capence (Family: Piperaceae) Diabetes was induced by administration of 186.9 mg/kg weight of 10% alloxan monohydrate intraperitoneally. The control animals were administered normal saline intraperitoneally. At 48 hours after induction of diabetes blood sugar level was measured with a glucometer. Only those mice which were considered diabetic and standard methods were used to determine the phytochemical of alkaloids, flavonoids, saponins, tannins, and sterols present in *Piper capence* extracts decrease in body weight, and hypoglycemic and hypocholesterolemic activities which are beneficial in the management of diabetes.[53]

Alpinia galanga (family: Zingiberaceae) The results of preliminary phytochemical studies showed the presence of alkaloids, triterpenes, steroids, polyphenols and carbohydrates in methanolic extract of aerial parts of *Alpinia galanga*. Among them polyphenolics are the most reported phytoconstituents showing a wide range of

pharmacological effects including antidiabetic activity.[22,23] The presence of polyphenols or other phytoconstituents may be responsible for the promising antidiabetic activity of methanolic extract of aerial parts of *A. galanga*. The plant may be further explored for its phytochemical profile to recognize the active constituents responsible for its antidiabetic activity. [57]

Capparis spinosa (family:capparaceae) *Capparis spinosa* root extract on diabetic metabolic disorders have been studied in experimental diabetes. Diabetic rats receiving 0.2, 0.4 g/kg of plant extract or 0.6 mg/kg glibenclamide (groups D0.2, D0.4 or DG respectively). A normal group of rats was also designed to receive 0.2 g/kg of plant extract. Rats were rendered diabetic (streptozotocin 60 mg/kg, i.p.) and treated with 0.2, 0.4 g/ kg of plant extract or glibenclamide for four weeks. Glucose levels were measured at the first and fourth week and lipid profiles, insulin and liver enzymes at the end of the study. Glucose levels significantly decreased after treating with plant extract (p=0.003). However, insulin levels did not increase in any treating groups. Plant extract could significantly raise HDL and reduce levels of LDL and liver enzymes (ALT and

ALP). *C. spinosa* root extract could improve diabetic related metabolic derangement such as hyperglycemia, dyslipidemia, and elevated liver markers in an insulin-independent manner [70].

COMPLICATIONS OF ANTIDIABETIC ACTIVITY

Ocimum sanctum: To determine by phytochemical test present findings provide an experimental justification to the traditional use of this plant for the management of hyperglycemia and provide preliminary insight into the possible mechanisms through which *Ocimum sanctum* may aid to overcome diabetes and associated complications. Plant extract exhibited good antioxidant and anti-inflammatory properties which may result in preventing diabetic complications that are generally attributed to excessive oxidative and inflammatory stress during hyperglycemia. Further antidiabetic effect of *Ocimum sanctum* may be attributed to its strong inhibitory effect on α -glucosidase enzyme and presence of rosmarinic acid, stigmasterol, linalool, bieuugenol, and aesculin, which were predicted to be potentially antidiabetic moieties of this plant. [54]

Triterpenes Natural products: The plants described above containing triterpene compounds are used in various countries in traditional medicine as antidiabetic remedies. The Selected triterpenes could become important remedies for curing diabetes mellitus and are promising compounds for the development of new multi target bioactive drugs. The use of triterpenes as AGEs inhibitors may be a potentially effective strategy to prevent diabetic complications. Their activity has been demonstrated in a number of in vitro studies and on animal models, but continuous clinical research does not exist. [55]

Mangifera Indica: The present study shows that *Mangifera Indica* extract brings back the fasting blood glucose levels to normal in alloxan - induced diabetic rats shows hypoglycemic activity and the chemical compounds responsible for this effect is flavonoids, tannins, steroids and trepenoids and the aqueous extract of the leaves contains higher level of phenols and flavonoids which exhibit greater antioxidant activity there by lowering the diabetic complications [56]

Viscum articulatum: (Santalaceae) has been traditionally used in different parts of

the world for treatment of various ailments. Almost all the parts such as leaves, root, stem and bark are having medicinal values and are reported for their uses in Ayurvedic and Chinese system of medicine for the management of various diseases. Modern scientific studies demonstrate efficacy of this plant against hypertension, ulcer, epilepsy, inflammation, wound, nephrotoxicity, HIV, cancer, etc. Major bioactive phytochemicals include oleanolic acid, betulinic acid, eriodictyol, naringenin, b-amyryn acetate, visartisides.

Safranal: Recent studies have been indicated that safranal can affect hyperglycemia in a variety of experimental models [66, 67]. One of the main mechanisms involved in the anti-diabetic effects of safranal is inhibitory effect on free radical production [61]. The radical scavenging activity of safranal is related to donate hydrogen atoms for 2, 2- diphenyl-1-picrylhydrazyl (DPPH) radical stabilization [63,62]. Safranal modulated antioxidant gene expression and upregulate mitochondrial anti-oxidant genes, leading to a lower mitochondrial oxygen radical generation, which may be responsible at least in part for the improved hyperglycemia, hyperlipidemia

and oxidative stress in experimental diabetic model. It was also reported that safranal may be effective in the treatment of diabetes by modulating of oxidative stress in STZ diabetic rats [64]. The antihyperglycemic activity of safranal was also confirmed in alloxan diabetic rats [65]. The findings of one study indicated that safranal may have anti-hyperglycemic effects without hepatic and renal toxicities in the alloxan diabetic rats [62]. Based on these results, the protective effect of safranal on pancreas of diabetic rats might be related to its scavenging activity this review indicated the anti-diabetic effects of safranal related to its antioxidant and anti-inflammatory activities. [59].

Rhus coriaria (Family: Anacardiaceae)

The effects of ethanolic extract of Rhus coriaria fruits were measured on blood glucose, lipids and antioxidant enzymes by commercial kits. mRNA levels of insulin (INS) and glucose transporter type-4 (GLUT-4) genes were investigated by RT-PCR (Reverse transcription-Polymerase chain reaction) technique. Moreover, its effects on intestinal α -glucosidases was measured using an in vitro method significantly lower (by 26%) compared to diabetic control group. The plant extract raised markedly serum High-density

lipoprotein (HDL) by 34% and also reduced low-density lipoprotein (HDL) by 32%. Also it had noticeable antioxidant effects by elevating superoxide dismutase (SOD) and catalase (CAT) activities by 46% and 77%, respectively. However it did not show a strong effect on glutathione peroxidase (GPX) activity. The extract inhibited maltase and sucrase activities by 44% and 27%, respectively. However it made no changes in the transcript levels of INS and GLUT-4 genes. It can be concluded that constituents of Rhus coriaria fruits have effective components which can be utilized as useful herb for alleviation of diabetes complications [68].

CONCLUSION

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. Therefore, treating Diabetes mellitus with plant derived compounds which are accessible and do not require laborious pharmaceutical synthesis seems highly attractive. Conclusively, it appears that we are approaching a 'new era' in the drug development from higher plants and

indeed, from natural sources in general. Now a day it is an urgent need to target the drugs with anti-diabetic potentials as diet to cure the causes and restrict the diabetes at the edge of new millennium where we can move ahead with a health and healthy living. The collective efforts of ethno botanists, phytochemists, pharmacognostists & pharmacologists are needed to document and evaluate the usefulness and safety of the claim. Major hindrance in amalgamation of herbal medicine in modern medical practices is lack of scientific and clinical data proving their efficacy and safety. There is a need for conducting clinical research in herbal drugs, developing simple bioassays for biological standardization, pharmacological and toxicological evaluation, and developing various animal models for toxicity and safety evaluation. It is also important to establish the active components from these plant extracts.

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