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An Appraisal on antidiabetic properties of herbal medicinal plants.

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Abstract –
As the percentage of population having diabetes has been raised from 108 million in 1980 and it has been raised more than half a billion people and it has been noticed that the number could rose upto more than double to 1.3 billion of peoples further next 30 years. The diabetes is of two types TYPE I and TYPE II.
TYPE I which is insulin dependent which mainly means that it is deficient of insulin production whereas, TYPEII affects blood glucose level, this type of diabetes affects the body's consumption of blood sugar(glucose) for energy. It inhibits the proper usage of insulin which can lead to high level of blood sugar in body if not treated early
symptoms can be seen are like, feeling very thirsty, instant urination more oftenly than normally, laziness, weight loss and blurring of the vision which further can damage the vessels of blood in heart, kidneys, nerves and eyes. many people have also been infected by foot ulcers and amputation.
diabetes mainly occurs due to when the pancreas does not secrete enough insulin or the usage of insulin by the body is not done.
basically, insulin is a basic hormone secreted by the pancreatic beta cells which regulates the blood glucose levels in blood serum.
So, this review is for the usage of the insulin mimetic herbal drugs and the herbal drugs which can help for the reduction of increased glucose level. Mostly those drugs belong to the family like Fabaceae, anacardiaceae, liliaceae, maliaceae, zingiberaceae, lamiaceae which contains mainly important chemical constitutes used for treatment of diabetes are hexadecenoic acid, oleic acid, gracillin, galactomannan, mangiferin, anthocyanidin, eugenol, paradols, gingerols, curcuminoids, nimbin, nimbidin, jambolin and carnosol.
So this review has also explained about the mechanism of actions, chemical constitutes of herbal drugs and their active principles in the treatment of the diabetes.

Keywords: diabetes, insulin mimetic, glucose, medicinal plants, pancreas, phytoconstituents.

INTRODUCTION

Diabetes is a disorder which is mainly characterized by imbalance in the serum blood glucose level and insulin. Almost 2.8% of world population is affected by diabetes. Diabetes is mainly classified as Type I and Type II diabetes. Type I diabetes is caused due to the poor production of insulin hence it is also known as insulin dependent diabetes which mainly occurs at early age (also known as juvenile) whereas in Type II diabetes there is sufficient production of insulin but body fails to utilize the insulin therefore, it is also known as insulin independent diabetes. Drugs such as Biguanides, Sulfonylureas, DPP4 inhibitors are usually used to treat diabetes.

Herbal drugs such as Mangifera indica, Aloe vera, Trigonella foenum, Allium sativum are widely used to get rid of diabetes. The main advantage of using herbal drug is that they show potent action with minimum side effects. The herbal drug market for diabetes has reached to 61.87 billion USD in 2022.

1.List of plants having insulin mimetic or insulin secretory action-

Table no. 1- List of insulin mimetic herbal drugs.

Sr No	Botanical name	Common name	Family	Plant part	Mechanism of action
1	*Chamaecostus cuspidatus*	Fiery costus	*Costaceae*	leaf	It shows antidiabetic activity by elevated glucokinase activity.
2	*Trigonella foenum*	methi	*fabaceae*	seed	It decreases glucose absorption in small intestine and also increase serum insulin level.
3	*Mangifera indica*	mango	*anacardiaceae*	fruit	It modulates metabolism of glucose ameliorating insulin resistance.
4	*Cinnamomum zeylanicum*	cinnamon	*lauraceae*	bark	It stimulates release of insulin and increase insulin receptor signalling
5	*Zingiber officinalis*	ginger	*zingiberaceae*	rhizome	inhibition of key enzymes of carbohydrate metabolism-α-glucosidase and α-amylase.
6	*Aloe vera*	aloe	*liliaceae*	leaves	Acts via blocking of pancreatic amylase activity

1.1. Chamaecostus cuspidatus

Chamaecostus cuspidatus, commonly named as fiery costus, is an herbaceous perennial plant belonging to shady rainforest in eastern Brazil. It grows upto 2 to 4 feet in height. The leaves can reach 1.5-2.5" wide 4.5-7" long, and show spiral arrangement along the stems. Terminal clusters of 3-8, bright orange, 1.5-2" wide flowers bloom during the growing season.

The genus name Chamaecostus comes from the ancient Greek khamaí meaning "lowly" or "near the ground" and the genus name Costus, in reference to the growth habit of some members of this genus and their close relation to Costus. It belongs to family Costaceae.

Chemical constituents- The leaf of fiery costus contains hexadecenoic acid, 9, 12-Octadecadienoic acid, ethyl ester, Tetra decanoic acid, Ethyl Oleate, Oleic acid, Leaf Octadecanoic acid, 2-benzenedicarboxylic acid, di-is octyl ester, Squalene, Tigogenin gracillin, Sitosterol, D-Glucose.

Mechanism of action- Lost ß-cell regeneration in diabetes and successfully differentiated human hematopoietic stem cells (HSCs) from functional ß-like cells. Costus leaf extract is known to produce anti-diabetic activity by lowering blood glucose level.
The leaf extract exhibited anti-diabetic property elevated glucokinase activity which catalyzes the rate-limiting step of glucose catabolism in ß-like cells and acts as a sensor for insulin production while decreasing the glucose-6-phosphatase activity. It shows enhanced IBS and GLUT2 gene expression and elevated glucokinase activity in ß-like cells differentiated from HSCs. The extract has potential for use in the dealing of diabetes. It reduces postmeal blood glucose levels and fasting blood glucose levels. Along with the antidiabetic activity, insulin plant decreases the complications associated with diabetes like renal, hepatic parameters to a normal level. It decreases the amount of glycosylated hemoglobin, corrects the lipid profile, increases as insulin level and body weight which shows specific Improvement in the histopathological examination.

1.2. Trigonella foenum

Fenugreek belongs to Fabaceae family. Trigonella in Latin language means “little triangle” due to its yellowish white triangular flower. Synonyms: It is named as Methi (Hindi, Marathi, punjabi) Hulba (Arabic) Moshoseitaro (Greek) Ullwa (Malayalam) and heyseed in English.

Fenugreek (Trigonella foenum-graceum) is the primeval medicinal plant which belongs to Fabaceae family originated in cultural Asia 4000 B.C.

Chemical constituents- It contains Galactomannan which show Anti-Diabetic activity. It has multiple alkaloids, saponins and flavonoids which are responsible for different therapeutic actions of methi. Saponin are in high concentration in Fenugreek seeds.

Mechanism of action- Antidiabetic Activity Fenugreek seeds have antidiabetic effect by increasing gastric emptying time and glucose absorption rate.
Fenugreek seeds have greater amount of fiber that decrease uptake of glucose from small intestine and eventually leads to increased serum insulin level.

1.3. Mangifera indica

Mango (Mangifera indica L.) is a juicy fruit belongs to the family of Anacardiaceae. The Stems, bark, leaves and seeds of mango have a key role in the treatment of diabetes. The WHO suggested the use of traditional herbal medicine for diabetes treatment.
Mango (Mangifera indica L.) is one of the effective plants which is used for treatment of diabetes in different communities.

Chemical Constitutes- Mango fruits are chief source of micronutrients, vitamins, micronutrients, vitamins and other phytochemicals along with it provides energy. Mangiferin, other constituents are selected anthocyanidins including tannins, peonidin, cyanidin, leucoanthocyanins, gallic tannins and catechin. Mango leaf oil is rich in sesquiterpene and also contains mangiferin, d-3-carene, a-gurjunene, ß-selinene and ß-caryophyllene. Mango leaves also contain alkaloids, phenols, flavonoids, saponins and tannins.

Mechanism of action- Mangiferin has also been shown to employ a pro-hypoglycemic role by moderating glucose metabolism and ameliorates resistance of insulin, lowering cholesterol synthesis, and inhibits tumor necrosis factor a and inducible nitric oxide synthase. Leaves, stems, seeds and bark of mango found to have crucial role in the treatment of diabetes. Mango (Mangifera indica L.) is one of the effective plants which is used for treatment of diabetes in different communities.

1.4. Cinnamomum zeylanicum

Cinnamon is an evergreen tree belongs to Lauraceae family, which grows from 20 to 30 feet.

Chemical constituents- The main constituents of cinnamon are cinnamate, cinnamaldehyde, cinnamic acid and numerous essential oils. They all contribute to the odour and to the several biological activities observed with cinnamon. In addition it contains, procyanidins tannins mucilage and a small portion of coumarin. Cinnamaldehyde (trans-cinnamaldehyde) is the main constituent in cinnamon bark. However, the principal component of leaf oil is eugenol.

Mechanism of action- Cinnamon exhibit hypoglycaemic activity may be identified to numerous mechanisms of action, including the stimulation of insulin release and receptor of insulin signalling, the activation and regulation of enzymes involved in carbohydrate metabolism, glycolysis, gluconeogenesis, stimulation of cellular glucose uptake and increased glucose transporter-4 receptors.

Another study shown that Cinna tannin B1, a proanthocyanin isolated from the stem, bark of ceylon cinnamon, stimulates the phosphorylation of the insulin receptor ß-subunit on adipocytes as well as other insulin receptors. 5- Zingiber officinale Ginger are fresh and dried rhizomes belonging to the family Zingiberaceae.

Chemical constituent- Ginger is abundant in active constituents, such as phenolic and terpene compounds. The phenolic compounds in ginger are mainly paradols, shogaols, and gingerols. In fresh ginger, the major polyphenols are gingerols, such as 6-gingerol, 8-gingerol, and 10-gingerol.

Mechanism of action- Mechanism proposed is the inhibition of key enzymes of carbohydrate metabolism-a-glucosidase and a-amylase by phenolic compounds (gingerols and shogaols) present in ginger. Ginger also elevates muscle and liver glycogen stores by enhancing peripheral utilization of glucose, thus limiting gluconeogenesis in the kidney and liver in a manner similar to insulin.

1.5. Aloe vera

Aloe vera is a species of Aloe that is known and famous particularly for its medicinal properties. The Aloe vera name comes from the Arabic word Alloeh meaning “shining bitter substance,” while Vera in Latin means “true”.
It belongs to family Liliaceae.

Chemical constituents- Water is the major constituent of Aloe vera gel, and it comprises of about 98% of leaf matter. The soluble solids are 0.60% and total solid content of Aloe vera gel is 0.66%. Aloe gel consists of proteins (8%), minerals (15%), lipids (5%), sugars (17%) phenolic compounds (2%), and polysaccharides (50%) on dry matter basis. Aloe vera consist 200 active constituents potentially: amino acids, lignin, sugars enzymes, vitamins, minerals, saponin, salicylic acids, and which are accountable for the Aloe multifunctional activity.

Mechanism of action- Lowers fasting blood glucose levels and reduces weight as well as the body fat. The use of Aloe vera is known to reduce the levels of HbA1c which in turn helps to lower the blood glucose levels in diabetic patient. Some studies of Aloe vera extract shows that Aloe can act as a hypoglycaemic agent via inhibition of pancreatic amylase action. This action decreases the breakdown of

starch and offers good postprandial glycaemic control.

2. List of drugs lowering glucose level –

Table no. 2 List of glucose level decreasing herbal drugs.

Sr no	Botanical name	Common name	Family	Plant part	Mechanism of action
1	*Curcuma longa*	Turmeric	*zingiberaceae*	Rhizome	inhibiting α-glucosidase, lowers absorption of glucose.
2	*Ocimum sanctum*	tulsi	*lamiaceae*	Leaf	alpha-glucosidase inhibitors, and the oral dipeptidyl-peptidase-4 inhibitor sitagliptin
3	*Azadirachta indica*	neem	*meliaceae*	Leaf, bark, oil	reduced the glucose uptake through up-regulation of glucose transporter 4 (GLUT4) and inhibition of glucosidases
4	*Syzgium cumini*	jamun	*myrtaceae*	Fruit	Reduce the excess oxidative stress.
5	*Salvia rosmarinus*	rosemary	*lamiaceae*	Leaf ,shrub	Increases consumption of glucose in HepG2 cells

2.1. Curcumin

Turmeric is a rhizomatous medicinal perennial plant (Curcuma longa) that has a rich history of use in Asian countries, including China and South East Asia.
Turmeric or Curcuma longa is a flowering plant in the ginger family Zingiberaceae.

Chemical constituents- Turmeric powder is consists of 1-6% curcuminoids,2-6% dietary fibres, 3-7% essential oils,3-7% dietary minerals, 5-10% fats ,6-8% proteins, 6-13% water, 60-80% carbohydrates. Curcumin imparts golden yellow colour to turmeric. Approximately 34 essential oils are present in turmeric, among which atlantone, turmerone, zingiberene and turmerone are prime constituents.
Phytochemical constituents of turmeric comprise diarylheptanoids, include a class innumerable curcuminoids such as bisdemethoxycurcumin, dimethoxycurcumin and curcumin.

Mechanism of action- Curcumin pre-treatment significantly reduced serum glucose levels and increased insulin levels, glucose clearance and pancreatic glucose transporter 2 (GLUT2) messenger ribonucleic acid (mRNA) levels.

2.2. Ocimum sanctum

Ocimum sanctum commonly called as holy basil, tulsi or Tulasi, and tamole, damole, or domole in Fiji, is an everlasting plant in the family Lamiaceae.

Chemical constituents-
carvacrol, estragol, rosmarinic acid, cirsimaritin, ursolic acid, linalon, eugenol, caryphyllin are the important compound present in the leaves of Ocimum sanctum.

Mechanism of action- Eugenol is capable of reducing blood glucose levels by 38% by inhibition of a-glucosidase whereas insulin and glycated haemoglobin levels remain the same. The caffeic acid, polyphenols, p-coumaric acid of aqueous extracts of tulsi leaves show anti-diabetic effect. alpha-glucosidase inhibitors, and the oral dipeptidyl-peptidase-4 inhibitor sitagliptin can only be used for patients with type 2 diabetes.

They are mainly used to replace the insulin deficiency or to enhance the action of insulin or decrease the insulin resistance for dealing with diabetes and management of its complications.

2.3. Azadirachta indica

Azadirachta indica popularly known as neem, neem tree, margosa, or Indian lilac, is a plant in the mahogany family Meliaceae.

Chemical constituents- Neem root bark contains terpenoids like nimbin and nimbidin. Nimbidin is having antidiabetic activity. The seed oil contains nimbolide, glycerides, triterpenes, diverse polyphenols and beta-sitosterol. The oil is yellow in colour with bitter taste, garlic like odour and constitute about 2% of limonoid compounds.
The leaves contain vitamin C, quercetin, carotenes and catechins.

Mechanism of action- Neem also reduced the glucose uptake through up-regulation of glucose transporter 4 (GLUT4) and inhibition of key intestinal enzymes such as glucosidases. Neem leaf extract dilate the blood vessels in diabetic patients and the neem leaves and seed is found to reduce the amount of insulin required to be administered to a diabetic patient.

2.4. Syzygium cumini

Syzygium cumini popularly known as jaman, Java plum, jambul, Malabar plum, black plum jambolana, jamun is an evergreen tropical plant in the blossoming plant family Myrtaceae, and favored for its, ornamental value fruit and timber.

Chemical constituents- glycosides, flavonoids, Terpenoids, saponins, phenols, and other chemical components are responsible for inhibition of glucose. Jamun contains an essential glycoside called as Jambolin, which has a mechanism of inhibition of starch from being biotransformed into sugar and so helps in blood sugar regulation.

Mechanism of action- The Jamun bark contains ethanol whose extract has been also found to reduce blood glucose levels. The aqueous leaf extract of Jamun alleviated the adenosine deaminase activity and glucose level in the serum of diabetic patients.
The hypoglycemic and hypolipidemic action of Jamun may be due scavenging of free radicals as diabetes is caused by surplus glutathione-s-transferase oxidative stress, increased activities of catalase glutathione-s-transferase and elevated formation of glutathione coupled with decrease in lipid peroxidation. Jamun may have activated PPAR and PPARa genes that suppressed the transcription of NF-B, COX, iNOS, TNF- a and other inflammatory cytokines followed by the upregulation of Nrf2.

2.5. Salvia Rosmarinus

Salvia rosmarinus commonly identified as rosemary, which is a shrub with fragrance, evergreen, and presence of needle-like leaves and purple, pink, white or blue colored flowers, native to the South European region.
It was known by the scientific name Rosmarinus officinalis, which presently is synonym. It belongs to the sage family Lamiaceae.

Chemical constituents- Rosemary consists a number of phytochemicals, including rosmarinic acid, camphor, caffeic acid, ursolic acid, betulinic acid, carnosic acid, and carnosol. Rosemary essential oil contains 10–20% camphor. Rosemary extract, specifically the type mainly consisting of carnosol and carnosic acid carnosol, is approved as a food antioxidant preservative in several countries.

Mechanism of action- rosemary extract and its phenolic ingredients especially, carnosol, carnosic acid, and rosmarinic acid, could significantly treats the diabetes mellitus by regulating anti- oxidation lipid metabolism, anti-inflammation, and, glucose metabolism showing enormously high research value.
Rosemary extract significantly increase glucose uptake in HepG2 cells. The phosphorylation of AMP-activated protein kinase (AMPK) and its substrate, acetyl-CoA carboxylase (ACC), is amplified by rosemary extract. Rosemary extract also transcriptionally control the genes associated in breakdown including SIRT1, PPAR coactivator 1a (PGC1a), glucose-6-phosphatase (G6Pase), low-density lipoprotein receptor (LDLR) and ACC. Furthermore, the PPAR-specific antagonist GW9662 weakened rosemary's effects on glucose utilization. Overall, rosemary potentially elevates fatty acid oxidation and liver glycolysis by activation of AMPK and PPAR pathways.

3.Future prospective

Research and investigation studies should be carried out for the use of herbal medicinal plants from the countries having rich herbal resources. Herbal medicines have less side effects and potent action in the treatment of diabetes. there are lesser harmful effects

associated with traditional medicine than that of chemically derived treatments, the use of traditional plants along with allopathic medicine will give a more promising result.

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