JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

DRUGS AND HERBS USED AS ANTIDIABETIC: A REVIEW

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Abstract: Diabetes mellitus is one of the common metabolic disorders. Impaired insulin secretion by the tissue is thought to be common reason contributing to pathophysiology. To provide an up-to-date account of the current trends of antidiabetic pharmaceuticals, this review offers a comprehensive analysis of the main classes. Several options for pharmacologic therapy of lowering blood glucose are currently available, which has revolutionized long-term management for Diabetes mellitus. From the review it was suggested that, the most active plants showing hypoglycemic potential are Allium sativum, Gymnema sylvestre, Moringa oleifera, Javaplum. The review describes some new bioactive drugs and isolated compounds from plants showing significant insulinomimetic and antidiabetic activity. The review also discusses the management aspect of diabetes mellitus using plants and active principles.

Keywords: Diabetes, pathophysiology, Allium sativum, Gymnema sylvestre, Moringa oleifera, Javaplum.

I. INTRODUCTION

1) History:

The term diabetes is the shortened version of the full name diabetes mellitus. DM is derived from the Greek word *diabetes* meaning siphon- to pass through and the Latin word *mellitus* meaning honeyed or sweet. This is often because in diabetes excess sugar is found in blood as well as the urine. It had been known in the 17th century as the "pissing evil". The term diabetes was probably coined by Apollonius of Memphis around 250 BC. Diabetes is first recorded in English, within the form diabetes, during a medical text written around 1425. It had been in 1675 that Thomas Willis added the word "'mellitus'" to the word diabetes. This was due to the sweet taste of the urine.

2) Role of pancreas:

Joseph von Mering and Oskar Minkowski in 1889 discovered the role of pancreas in diabetes. They found that dogs whose pancreas was removed developed all the signs and symptoms of diabetes and died shortly afterwards.

In 1910, Sir Edward Albert Sharpey-Schafer found that diabetes resulted from lack of insulin. He termed the chemical regulating blood glucose as insulin from the Latin "insula", Meaning Island, in regard to the insulin-producing islets of Langerhans in the pancreas.

3) Discovery of insulin: In 1921 Sir Frederick Grant Banting and Charles Herbert Best repeated the work of Von Mering and Minkowski and went ahead to demonstrate that they might reverse induced diabetes in dogs by giving them an extract from the pancreatic islets of Langerhans of healthy dogs. Banting, Best, and their chemist colleague Collip purified the hormone insulin from pancreases of cows at the University of Toronto. This led to the supply of an effective treatment for diabetes in 1922. For this, Banting and laboratory director MacLeod received the Nobel Prize in Physiology or Medicine in 1923; both shared their Prize money with others in the team who were not recognized, in particularly Best and Collip. Banting and Best made the patent available freed from cost so millions of people worldwide could get access to insulin. In 1922 January, Leonard Thompson, 14, a charity patient at the Toronto General Hospital, became the primary person to receive and injection of insulin to treat diabetes. Thompson lived another 13 years before dying of pneumonia at age 27.

4) Types of diabetes

a) Type 1 diabetes
b) Type 2 diabetes
c) Gestational diabetes

a) Type 1 diabetes:

It is a chronic condition in which the pancreas produces little or no insulin. Type 1 diabetes is usually diagnosed in children and young adults, although it can appear at any age. People with type 1 diabetes need to take insulin every day to stay alive.

Causes of Type 1 diabetes: This is an immune system disease. Your body attacks and destroys insulin-producing cells in your pancreas. Absence of insulin allows glucose to enter your cells, glucose builds up in your bloodstream. Genes may also play a role in some patients. Also, a virus may trigger the immune system attack.

b) Type 2 diabetes:

A chronic condition that affects the way the body processes blood glucose (glucose). Type 2 diabetes formerly referred to as adult-onset diabetes. With type 2 diabetes, the body either doesn't produce enough insulin, or it resists insulin. You can develop type 2 diabetes at any age, even during childhood. However, this sort of diabetes occurs most often in middle-aged and older people. Type 2 is that the most common type of diabetes.

Prediabetes: This type is the stage before Type 2 diabetes. Your blood sugar levels are higher than normal but nothing enough to be officially diagnosed with type 2 diabetes. Your body's cells don't allow insulin to figure as it should to let glucose into its cells. Your body's cells became resistant to insulin. Your pancreas can't continue and make enough insulin to overcome this resistance. Glucose levels rise in your bloodstream.

c) Gestational diabetes

Gestational diabetes develops in some women once they are pregnant. Most of the time, this sort of diabetes goes away after the baby is born. However, if you've had gestational diabetes, you've got a greater chance of developing type 2 diabetes later in life. Sometimes diabetes diagnosed during pregnancy is really type 2 diabetes.

5) Symptoms of diabetes include

- Increased thirst.
- Weak, tired feeling.
- Blurred vision.
- Numbness or tingling within the hands or feet.
- Slow-healing sores or cuts.
- Weight loss.
- Frequent urination.
- Frequent unexplained infections.
- Dry mouth.

Other symptoms:

- In women: Dry and itchy skin, and frequent yeast infections or urinary tract infections.
- In men: Decreased sex drive, erectile dysfunction, decreased muscle strength.

If your blood sugar level remains high over a long period of time, your body's tissues and organscan be seriously damaged. Some complications are often life-threatening over time.

Complications includes:

- Cardiovascular issues including coronary artery disease, chest pain, heart attack, stroke, high blood pressure, high cholesterol, atherosclerosis (narrowing of the arteries).
- Nerve damage (neuropathy) that causes numbing and tingling that starts at toes or fingers then spreads.
- Kidney damage (nephropathy) which will lead to kidney failure or the need for dialysis or transplant.
- Eye damage (retinopathy) which will lead to blindness; cataracts, glaucoma.
- Foot damage including nerve damage, poor blood flow and poor healing of cuts and sores.
- Male Erectile dysfunction.
- Deafness.
- Depression.
- Dementia.
- Dental problems.

6) Established Drug Classes for the Treatment of Diabetes:

6.1 Derivatives of Insulin

Different types of insulin comprise a considerable portion of FDA-approved drugs for diabetes treatment with at least 14 unique analogues and combination regimens. Insulin is probably one of the most studied proteins and has been an integral part of T2DM treatment. Recombinant insulin analogues are developed that act in several different ways. Rapid-acting insulin analogues supply a bolus insulin level needed at mealtimes (prandial insulin) and include **insulin lispro, aspart, and glulisine**. Longer-acting insulins released slowly over a more extended period supply the basal insulin level needed throughout the day and night (basal insulin) and include **detemir, glargine**, and therefore the ultra-long-acting **degludec**. Such a spectrum of insulin analogues enables combinations of various insulin forms, providing an efficient basal-bolus therapy that more closely reflects physiological insulin secretion. In additionally to insulin plus insulin combination regimens, insulin plus glucagon-like peptide-1 (GLP1) receptor agonist combinations have also been approved. Furthermore, basal insulin therapy combinations with other drugs or adjunctive therapies also are prescribed. Although insulin has been an important discovery for the treatment of diabetes, it's rarely used as a first-line treatment. Insulin administration comes with risks of developing severe hypoglycemia, cancer, and cardiovascular complications, and most frequently occurs when patients develop insulin tolerance and the dose administered has to be increased.

6.2 Sulfonylureas (SU)

Until the approval of metformin, sulfonylureas (SU) were the sole approved insulin competitors and were extensively used to treat T2DM. While currently, only three SU drugs are available for the prescription **(glyburide, glipizide, and glimepiride)**. There are at least four additional uniquechemical SU compounds previously approved that are now discontinued. Two SU and metformin combination regimens are FDA-approved that are currently marketed: glyburide/metformin, glipizide/metformin. Combinations of glimepiride and metformin do exist, e.g., Amaryl M and Glimetal Lex, but aren't approved by the FDA or the European Medicines Agency. However, within the FDA approval of Amaryl (Glimepiride, 2021) it's stated that the two drugs can be taken together if monotherapies of each fail to work. The primary SU compounds were discovered in the 1940s and entered the pharmaceutical market in the mid-1950s. Sulfonylureas mimic the effect of ATP in pancreatic beta cells and act as insulin-secreting agents. SU molecules interact with the sulfonylurea receptors (SURs) on the surface of beta cells. As a result, the intracellular concentration of potassium cations increases, resulting in plasma membrane depolarization. Theseconditions stimulate the opening of voltage-gated calcium channels, and an increased concentration of cytosolic calcium cations results in a surge in insulin secretion. SU drugs are extensively prescribed to treat T2DM for more than 50 years. SUs are well-tolerated, and their popularity might be attributed to their low cost and the possibility of use as a monotherapyor in combination with metformin. SUs don't only interact with SURs in pancreatic beta cells, but also in smooth muscle cells and cardiac myocytes. This might explain why SU agents have been linked to a greater prevalence of hypoglycemia and cardiovascular risk however; most reports support the cardiovascular safety of SUs.

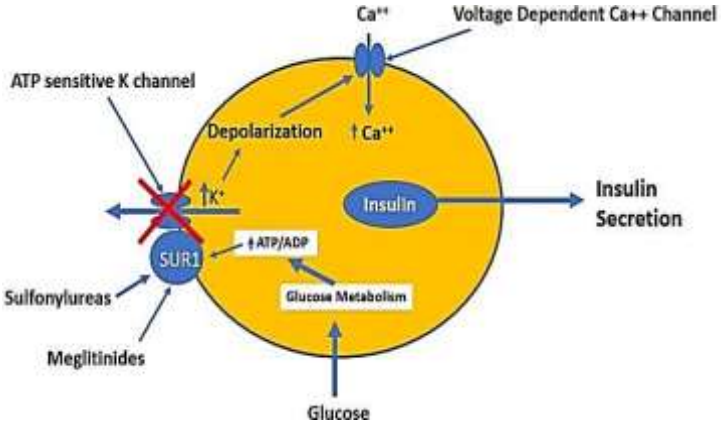

Fig No.1: Mechanism by which SU and Meglitinides stimulate secretion of insulin by beta-cells.

6.3 Biguanides

The approval of the biguanide **metformin** in 1995 significantly changed T2DM therapy and is thatthe only FDA-approved antihyperglycemic agent in this drug class. Metformin selectively inhibits the mitochondrial isoform of glycerophosphate dehydrogenase, indirectly activates adenosine monophosphate-activated protein kinase (AMPK), and reduces cytosolic dihydroxyacetone phosphate while raising cytosolic NADH/NAD ratio. This leads to decreased plasma glucose and lactate levels, reduced liver gluconeogenesis, hepatic glucose secretion, and endogenous glucose production. Moreover, metformin can increase insulin sensitivity in muscle tissues.

6.4 Alpha-Glucosidase Inhibitors

The first alpha-glucosidase inhibitor (AGI), **acarbose**, was approved by the FDA as an antihyperglycemic agent in 1995 and therefore the second AGI, **miglitol**, followed in 1996. Theseare the sole two AGIs approved for the United States market, although another AGI, **voglibose**, was approved by the Pharmaceuticals and Medical Devices Agency in Japan (Oki et al., 1999). Inclinical development, the chewable tablet BTI-320 (PAZ320) recently completed a proof-of- concept study that showed low dose BTI-320 attenuated postprandial rise in blood sugar and reduced body weight modestly in pre-diabetic subjects.

6.5 Thiazolidinediones:

Thiazolidinediones (TZDs) act as insulin sensitizers which activate peroxisome proliferator- activated receptors (PPARs), a broad family of nuclear receptors. The primary TZD drug, **troglitazone**, was approved by the FDA in 1997; however, it had been discontinued in 1999 due to severe hepatotoxicity. Currently, there are two marketed TZD, **rosiglitazone** and **pioglitazone**, which were FDA-approved in 1999. TZD use has previously been limited thanks to concerns with safety issues and side effects. In additionally, there was some controversy over cardiovascular toxicity with rosiglitazone and a rise in bladder cancer with pioglitazone. However, recent studiesshow not significant issues.

ADVANTAGES OF THIAZOLIDINEDIONE	DISADVANTAGES OF THIAZOLIDINEDIONE
Once a day administration	Edema
No hypoglycemia	CHF
Increase HDL and decreased triglycerides	Osetoporosis

Table No .1: Advantages and disadvantages of thiazolidinedione.

6.6 Incretin-Dependent Therapies (GLP1 Receptor Agonists and DPP4 Inhibitors)

In 2005 and 2006, the primary incretin dependent T2DM therapies were approved, and that they have become increasingly popular as monotherapies and in combination regimens since then. Incretin-depending treatments include glucagon-like peptide-1 (GLP1) mimetics which act as GLP1 receptor agonists and DPP4 inhibitors. Six injectable GLP1 receptor agonists were approved, including **exenatide, liraglutide, dulaglutide, albiglutide, lixisenatide, andsemaglutide**. They differ within their lifetime in the bloodstream and in their ability to treat hyperglycemia. Incretin therapies account for 30% of antidiabetic drugs in clinical development, with GLP1R agonists comprising the foremost significant proportion (20%). The clinical outcomeof GLP1R agonists is strong, with 21 agents in clinical trials and therefore the majority of them inphase I and II trials. Fifteen of those receptor agonists target just GLP1R, four agents also target the glucagon receptor (GCGR), one drug targets GLP1R plus GCGR plus the gastric inhibitory polypeptide receptor (GIPR), and one drug targets GLP1R and GIPR. There are currently four DPP4 inhibitors that are FDA-approved**: sitagliptin, saxagliptin, linagliptin, and alogliptin**.

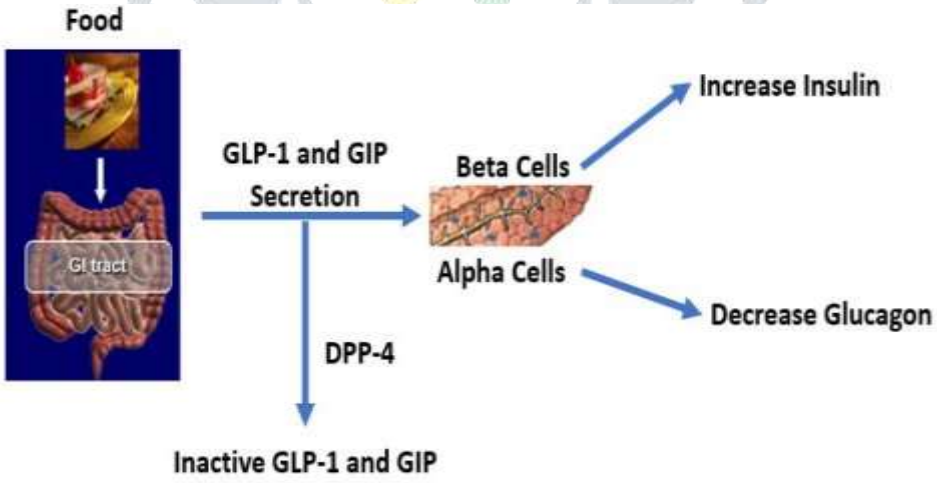

Fig no. 2: Mechanism of GLP 1 Receptor agonist and DPP4 inhibitors.

6.7 Meglitinides

Two meglitinides are FDA-approved: **nateglinide** in 2009 and **repaglinide** in 2013. Currently, there are not any meglitinides in clinical trials. Meglitinides shares an identical mechanism of action to sulfonylurea agents in that they increase insulin secretion in the pancreas. They bind to SURs in pancreatic beta cells but at a binding site different than SUs and induce the identical reaction cascade that

leads to insulin secretion. In contrast to SUs, meglitinides, nateglinide particularly, exhibit glucose-sensitive action whereby their potency increases at higher glucose concentrations. Meglitinides are short-acting and related to lower hypoglycemia risks, weight gain, and chronic hyperinsulinemia than sulfonylurea drugs.

ADVANTAGES OF MEGLITINIDES	DISADVANTAGES OF MEGLITINIDES
Flexible dosing	Hypoglycemia
Relatively inexpensive	Weight gain
Short acting	Frequent dosing

Table No. 2: Advantages and Disadvantages of meglitinides.

6.8 Sodium-Glucose Cotransporter Type 2 Inhibitors

The most modern and promising drug class is SGLT2 inhibitors. The primary SGLT2 inhibitors, **canagliflozin, and dapagliflozin** were approved in 2013, followed by additional monotherapy agents including **empagliflozin** in 2014 and **ertugliflozin** in 2017. Additionally, SGLT2 inhibitors are popular together regimens with metformin and DPP4 inhibitors and combinations of all three and TZD drugs. SGLT2 inhibitors are the second largest group of antidiabetic agents in clinical trials (12%) after incretin therapies. Three of the twelve drugs in phase II, III, and IV clinical trialshave been previously approved by other regulating agencies. Five other agents are in phase III trials, indicating that new SGLT2 inhibitors could also be approved soon.

6.9 Drug Combinations

The different types of approved oral combinations have steadily increased, together with the proportion of combinations being approved in comparison to monotherapies. Nearly 40% of the approved antidiabetic drugs are combination regimens. FDA-approved combinations of antihyperglycemic drugs are often divided into two generations. First-generation combinations were mixtures of various insulin isoforms, where they differed within the method of preparation, natural source, duration of action, or concentrations. They consisted mainly of medicine that require oral administration, and in most cases, one among the components was metformin. The primary triple combination regimen was approved in 2019, consisting of metformin, saxagliptin, and dapagliflozin. Another triple combination approval for metformin, linagliptin, and empagliflozin followed in 2020.

DRUG 1	DRUG 2	BRAND NAME
Glyburide	Metformin	Glucovance
Glipizide	Metformin	Metaglip
Glimepiride	Pioglitazone	Duetact
Saxagliptin	Metformin	Kombiglyze
Repaglinide	Metformin	PrandiMet
Alogliptin	Metformin	Kazano

Table No. 3: Drug combinations

7) NEW DRUGS IN APPROVAL FOR THE TREATMENT.

GENERIC/ CODE NAME	INDICATION	PHASE
DPP4 INHIBITORS		
Alogliptin/ SYR-322	Type 2 diabetes	2
KRP-204/ N-5984	Type 2 diabetes	2
Vildagliptin	Type 2 diabetes	NDA Submitted
Saxagliptin /BMS-477118	Type 2 diabetes	NDA Submitted
Dutogliptin /PHX1149	Type 2 diabetes	3
GLP-1 ANALOGS		
Albiglutide /GSK716155	Type 2 diabetes	2
AVE0010/ ZP-10	Type 2 diabetes	3
Exenatide LAR	Type 2 diabetes	3
Liraglutide /NN2211	Type 2 diabetes	NDA Submitted
BIGUANIDES		
Metformingum /buccal	Type 2 diabetes	2
THIAZOLIDINEDIONES		
Balaglitazone / DRF-2593	Type 2 diabetes	3
Mitoglitazone / MDSC 0160	Type 2 diabetes	2
Rivoglitazone / CS-011	Type 2 diabetes	3
PPAR AGONIST		
Aleglitazar / RI439	Type 2 diabetes	2
Indeglitazar	Type 2 diabetes	2
INSULINS		
Inhaled technosphere insulin	Type 1 and type 2 diabetes	3
Oral insulin spray	Type 1 and type 2 diabetes	3
Recombinant human hyaluronidase	Type 1 diabetes	2

Table No. 4: New drugs in approval for treatment.

I) HERBS HAVING ANTIDIABETIC ACTIVITY

The diabetes is rapidly increasing worldwide and affecting all parts of the planet. DM in Ayurveda is known as Madhu-meha. People having deficiency of the insulin suffering from diabetes have high blood glucose level. Human bodies possess enzymatic and non-enzymatic antioxidative mechanisms which minimize the generation of reactive oxygen species, liable for many degenerative diseases including diabetes. Type 2 diabetes is that the most common form of the disease. 90% – 95% of cases during which the body does not produce enough insulin. Currently available therapies for diabetes include insulin and various oral antidiabetic agents like sulfonylureas, biguanides and glinides. Many of them variety of serious adverse effects; therefore, the look for more effective and safer hypoglycemic agents is one of the important areas of investigation. The hypoglycemic effect of several plants used as antidiabetic remedies

has been confirmed, and therefore the mechanisms of hypoglycemic activity of these plants are being studied.

This review also focuses on the role of traditional therapeutic and natural medicines from medicinal plants for diabetes. Traditional medicines from readily available medicinal plants offer great potential for the invention of new antidiabetic property. Antihyperglycemic activity of the plants is mainly due to their ability to restore the function of pancreatic tissues by causing an increase in insulin secretion or inhibit the intestinal absorption of glucose or to the facilitation of metabolites in insulin dependent processes. Looking for new antidiabetic drugs from natural plants is still attractive because they contain substances which demonstrate alternative and safe effects on diabetes mellitus. Most of plants contain glycosides, alkaloids, terpenoids, flavonoids, carotenoids, *etc*., that are frequently implicated as having antidiabetic effect.

1. MORINGA OLEIFERA

Family :- Moringaceae

Synonyms :- Guilandina moringa , Hyperanthera moringa

Morphology:-

- **Colour :-** Green
- **Odour :-** Characteristic
- **Taste :-** Characteristic
- **Shape :-** Long , slender
- **Size :-**Height is 10 -12 m and diameter is 45 cm

Fig. No. 3 : *Moringa Oleifera*

Moringa leaves have the antidiabietic property. *Moringa oleifera* Lam. may be a perennial tropical tree with high economic and pharmaceutical value. As an edible plant, *M. oleifera* Lam. is rich in nutrients, like proteins, amino acids, mineral elements and vitamins. Besides, it also contains an important number of bioactive phytochemicals, like polysaccharides, flavonoids, alkaloids, glucosinolates and isothiocyanates. *M. oleifera* for long has been used as a natural anti-diabetic herb in India and other Asian

Countries. Thus, the anti-diabetic properties of Moringa plant have evolved highly attention to the researchers. Leaf extracts had significantly good antidiabetic activity. Variations were observed within the total phenolic, condensed tannins and flavonoid contents among the various plant partstested. The leaf extracts exhibited the very best amount of total phenolics, while the lateral roots had higher amounts of condensed tannins and flavonoid contents. The roots are often used as a better source of antioxidants than the leaves. All the leaf extracts had significantly good antidiabetic and antimicrobial activity as compared to the roots. *Moringa oleifera* is an Indian and it's referred to as "drum stick tree" or the "horse riding tree". The therapeutic use of *M. oleifera* leaves has been evaluated in diabetes due to their possible capacity to decrease blood glucose concentrations after ingestion because they contains polyphenols such as quercetin-3-glycoside, rutin, kaempferol and glycoside. It also contains flavanoids, phenolic acid, glucosinolate and isothiocyanate (mainly distributed within the leaves), alkaloids and sterols (distributed within the leaves, roots, and seeds), and terpene (all distributed within the pods).

Supported the phytochemical analysis, phenols and alkaloids are more abundantwithin the leaves than in the seeds, while flavonoids, saponins, and anthocyanins are more abundant within the seeds. Flavonoids, a gaggle of hydroxylated phenolic substances known to bepotent free radical scavengers, have attracted an incredible interest as possible therapeutics againstfree radical mediated diseases, particularly DM flavonoids may act on biological targets involved in type 2 DM such as α-glycosidase and DPP-4. Being a radical scavenger, flavonoids can effectively prevent and/or manage type 2 DM. *Moringa oleifera*, with few reported side effects, has a long history for curing diseases and is aninexpensive and credible natural medicine.

Uses of *Moringa oleifera*:

a. Antidiabetic agent

b. Treat hyperthyroidism

c. Treat asthma

d. Reduce blood pressure

e. Reduce cholesterol

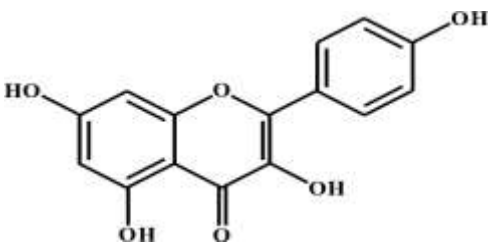

Fig. No.4: Structure of kaempferol

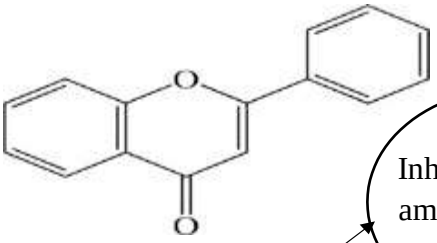

Fig. No. 5: Structure of flavonoid

Fig. No. 6: Mechanism of *Moringa oleifera*

2. JAVA PLUM

Family: Myrtaceae

Synonyms :- Malabar plum, Black plum

Fig. No. 7: Java Plum

Java plum is widely used medicinal plant having the antidiabetic property. The plant has been viewed as an antidiabetic plant since it became commercially available several decades ago. During last four decades, numerous folk medicine and scientific reports on the antidiabetic effectsof this plant are cited in the literature. The amount of literatures revealed that the extracts of different parts of jambolan showed significant pharmacological actions. Hence identification of such active compounds is beneficial for producing safer drugs in the treatment of various ailmentsincluding diabetes. Jambolan is widely used as

traditional healer for the treatment of varied diseases especially diabetes and related complications. The plant has many important compounds which confer the foremost of the characteristics of the plant. It is widely distributed throughout India and ayurvedic medicine (Indian folk medicine) mentions its use for the treatment of diabetes mellitus. Various traditional practitioners in India use the varied parts of the plant in the treatment of diabetes, blisters in mouth, cancer, colic, diarrhea, digestive complaints, dysentery, piles, pimples and stomachache. In Unani medicine various parts of jambolan act as liver tonic, enrich blood, strengthen teeth and gums and form good lotion for removing ringworm infection. *Syzygium cumini* (*S. cumini*).

The synonyms of *S. cumini* are *Eugenia jambolana* Lam., *Myrtus cumini* Linn., *Syzygium jambolana* DC., *Syzygium jambolanum* (Lam.) DC., *Eugenia djouant* Perr., *Calyptranthes jambolana* Willd., *Eugenia cumini* (Linn.) Druce and *Eugenia caryophyllifolia* Lam. It is commonly known as jambolan, black plum, jamun, java plum, Indian blackberry, Portuguese plum, Malabar plum, purple plum, Jamaica and damson plum. Jamun fruit decrease sugar in blood of human body and helps in the prevention of diabetes. Jamun contain the glycoside is consider to keep antidiabetic properties. Jamun seeds and pulp controls the blood glucose level and decrease the diabetic complications including neuropathy and cataracts. Jamun is known as adjuvant therapy in type 2 diabetes. The seeds are claimed to contain alkaloid, jambosine, and glycoside jambosine or antimellin, gallic acid, ellagic acid, beta sitosterol which avoid the conversion of starch into sugar and seed extract has lowered vital sign by 34.6 %. The seed are reported to be rich in flavonoids, a well-known antioxidant, which accounts for the scavenging of free radicals and protective effect on antioxidant enzymes and also found to possess high total phenolics with significant antioxidant activity and are fairly rich in protein and calcium. Java plums are rich in sugar, mineral salts, vitamins C. Fruit pulp contain the Anthocyanins, delphinidin, petunidin, malvidin- diglucosides.

The bark is acrid, sweet and contains tannins and carbohydrates. It is astringent to the bowels, anthelmintic and used for the treatment of sore throat, bronchitis, asthma, thirst, biliousness, dysentery and ulcers. It is also a good blood purifier. The fruit is sweet, cooling and astringent to the bowels and removes bad smell form mouth, stomachic, astringent, diuretic and antidiabetic. The fruit has a very long history of use for various medicinal purposes and currently has a large market for the treatment of chronic diarrhea and other enteric disorder. The seed is sweet, astringent to the bowels and good for diabetes. The ash of the leaves is used for strengthening the teeth and gum. Traditional medical healers in Madagascar have been using the seeds of jambolan for the treatment of diabetes. The seed extract is used to treat cold, cough, fever and skin problems such as rashes and the mouth, throat, intestines and genitourinary tract ulcer.

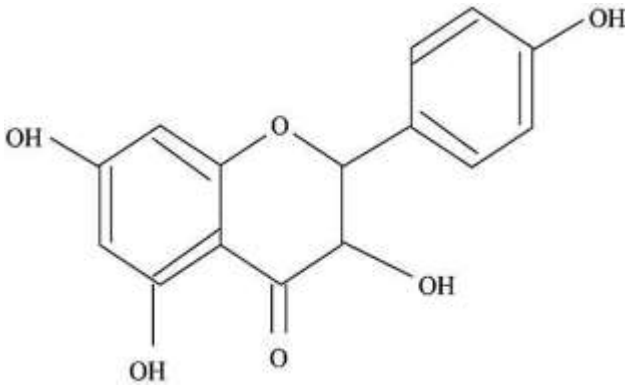

Fig. No. 8: Structure of Jambosine

Use –

- Antidiabetic effect
- Cardioprotective effect
- Anti-inflammatory activity
- Antiviral activity
- Antiallergic activity
- CNS activity

Out of all the pharmacological effect Antidiabetic activity is most important. It has been demonstrated to be the most promising neutraceutical value as reported by several research workers.

3. *Gymnema sylvestre*

Family:- Asclepiadaceae

Synonyms :- Gurmar booti, Madhunashini

Fig. No. 9: *Gymnema sylvestre*

Gymnema sylvestre showed significant prospects in major health problems like diabetes, cardiovascular disorders, obesity, osteoporosis, antioxidant activity and asthma. Gymnema sylvestris (Gurmar), which suggest sugar destroyer, could even be a member of the family Asclepiadaceae. It's also known as madhunashini. It's a wild plant that grows well in vivid agro-climatic conditions in tropical and subtropical region. In traditional medicine the plant particularty is used as hypoglycemic, hypolipidemic,

antiviral, diuretic, antiallergic, antibiotic, in stomach pains and in rheumatism. G. sylvestre contains quite 20 triterpene saponins that form molecular complexes with proteins, lipids, sterols and tannins.

G. sylvestre is well known for its sweet taste suppressing activity and found to be useful for the treatment of diabetes mellitus and obesity. It had been proved that, the leaves extractof G. sylvestre will inhibit the absorption of glucose within the small intestine, and have inhibitory action against glucan synthesis by glucosyltransferase. A spread of gymnema products such as gymnema capsules, gymnema tea, bioshape, and diaxinol are developed and using for thetreatment of various diseases.

The plant is large; more or less pubescent, woody. It is a potent antidiabetic plant and used in folk, ayurvedic and homeopathic systems of medicine. Sushruta describes *Gymnema sylvestre*, as a destroyer of madhumeha (glycosuria) and other urinary disorders. On account of its property of abolishing the taste of sugar it has been given the name of gurmar meaning sugar destroying and it is believed therefore that it might neutralize the excess of sugar present in the body in Diabetes mellitus. The *G. sylvestre* leaves contain phytin, pentriacontane, hentriacontane, alpha and beta chlorophyll, resin, tartaric acid, formic acid, butyric acid, mucilage inositol, d- quercitol, gymnemic acid, antraquinone derivative. The major active component is 'gymnemic acid'. It is a complex mixtureof closely related acidic glycosides. Gymnemic acid is a mixture of at least nine closely related acidic glycosides fractionated by successive extraction with different solvent. Ethyl acetate fraction of such gymnemic acid mixture has a paralyzing effect on taste glands.

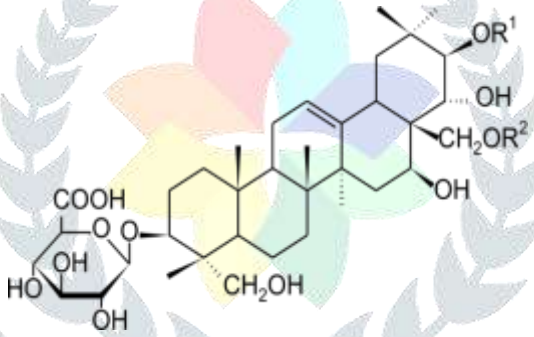

Fig. No.10 : Structure of Gymnemic acid

Mechanism of Action of Gymnemic Acids: The gymnemic acids are the important constituents of gymnema. The gymnemic acids are shown to have antidiabetic, antilipidemic and anti-inflammatory properties. The phytochemical delays the absorption of glucose into the blood. Therefore, gymnemic acids fill the receptors within the taste bud and prevent the activation of sugar molecules that are present in consumed food. Additionally, the gymnemic acids fill the receptors located within the absorptive external layers ofthe intestine so as to prevent the absorption of glucose by the intestines results in low blood sugar level. Additionally, the acids are found to stimulate the pancreas to produce insulin which is required for glycemic control and treating adult onset diabetes mellitus. The acids also increase the excretion of cholesterol in faeces and may act as a laxative, cough suppressant and a diuretic. The gymnemic acids are shown to interfere with the ability of the taste buds present on the tongueto taste sweet or bitter. Researchers believe that the power of the acids to inhibit the sweet taste means that it also inhibits the intake of glucose. However, this has not been proved by research evidence.

The gymnemic acids even have antioxidant properties capable of scavenging reactive oxygen species and other free radicals. The possible mechanisms by which the leaves extract of *G. sylvestre* possess its hypoglycemic acid effects are:

1. It increases secretion of insulin
2. It promotes regeneration of islet cells
3. It causes inhibition of glucose absorption from intestine
4. It increases utilization of glucose because it increases the activities of enzymes responsible for utilization of glucose by insulin-dependent pathway.

Scientific investigation of the biological effect of oral administration of the leaves powder revealed that G. sylvestre therapy also increased the activities of the enzymes affording the utilization of glucose by insulin dependent pathways: it controls phosphorylase level gluconeogenic enzymes and sorbitol dehydrogenase.

Uses:

- Antidiabetic
- Stomachic
- Stimulant
- Laxative
- Diuretic

Dental plaque and caries are prevented by gymnemic acids. Recently drug has received world attention due to weight lowering property.

Interaction with herbs:

Combination of gymnema sylvestre and some herbs increase its hypoglycemic activity like ,

- *Eleutherococcus senticoses*
- *Zingiber officinale*
- *Panax ginseng*
- *Pueraria lobata*

Substitute of *Gymnema*: Leaves of *G. hirsutum* and *G. montanum* of Western Ghats.

4. MODE OF ACTION OF DIFFERENT ANTIDIABETIC HERBS

Sr. No.	Mode of action	Plant Drug
1	Insulin mimic effect	*Aegle marmelos* [Indian bael] *Coccinia indica* [Ivy gourd]
2	Increase insulin secretion	*Allium cepa* [onion] *Ocimum sanctum* [tulsi] *Allium sativum* [garlic]
3	Modifying glucose utilization	*Zingiber officinale* [ginger] *Azadirachta indica* [neem]
4	Alpha amylase and alpha glucosidase inhibitory effects	*Aegle marmelos* [Indian bael] *Tinospora cordifolia* [Guduchi] *Coccinia indica* [Ivy gourd]

Table No. 5: Mode of action of different antidiabetic herbs

II) CURRENT AFFAIRS: INDIAN ONION LOWERS BLOOD GLUCOSE LEVEL

According to The Independent, the findings were presented at The Endocrine Society's 97th annual meeting in San Diego on August 25 and revealed that the **extract of an onion bulb could "strongly lower" high blood sugar** and total cholesterol levels when given alongside the anti- diabetic drug Metformin. The lead study author, Anthony Ojieh of Delta State University, in Abraka, Nigeria, was quoted as saying, "Onion is reasonable and available and has been used as anutritional supplement. It's the potential for use in treating patients with diabetes.

III) CONCLUSION

Diabetes is a serious chronic medical condition that requires a multidisciplinary team approach, consisting of health care professionals, patient educators, patients. In this review we endeavor to outline the current management principles, including the spectrum of medications that are currently used for pharmacologic management, for lowering the blood glucose level. Several antidiabetic drugs have complications which are taken into consideration. The present review also presents comprehensive details of plants having antidiabetic activity. These plant derivatives offer a potential for cost effective management of diabetes. The presence of bioactive chemicals is mainly responsible for the antidiabetic action however more investigation must be carried out to evaluate their mechanism of action.

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