Journal of Advance Research in Science and Social Science (JARSSC)
Official Publication of Indian Mental Health & Research Centre

ISSN: 2582-2004
Volume 05, Issue 01

DOI: 10.46523/jarssc.05.01.19
Multidisciplinary, Open Access
Impact Factor: 3.575

Anti-diabetic Activity of Widely Used Medicinal Plants in Indian Traditional Healthcare System

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ABSTRACT

Disorders in the metabolism of various biomolecules have serious implications for health and are of great medical interest. Diabetes is one such condition which affects a large proportion of the global population and is hard to manage because of many reasons. Diabetes involves an unusual elevation of blood glucose levels arising as a consequence of failure in its endocrine regulation. Persistent hyperglycemic condition occurs when the body's mechanisms are unable to keep up with rising blood glucose levels. Medicinal plants have been used for centuries as a source of therapeutic chemicals to treat a wide variety of diseases. Based on the encouraging results of traditional medicinal plants in treating various conditions, medicinal herbals may have a role to play in the treatment of diabetics too. Herbal remedies are becoming more popular among patients due to their low cost, ease of availability, and lack of negative effects associated with their usage. Research shows that medicinal plants use a variety of active chemicals and multiple mechanisms to elicit their therapeutic effects. Several plants found in the Indian subcontinent have been shown to possess hypoglycemic properties. Investigation of the active principles isolated from medicinal plants that have demonstrated significant anti-diabetic benefits in exploratory research should be carried out. This paper takes a close look at some of these chemicals.

Keywords: Hypoglycemic, anti-hyperglycemic, anti-hyperlipidemic, anti-diabetic, Diabetes Mellitus, Insulin, hypoglycemic, anti-hyperlipidemic

Received: 15.12.2021 **Accepted:** 07.01.2022 **Published**: 07.01.2022

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INTRODUCTION:

Blood sugar levels are unusually high in people with diabetes mellitus. Insulin is produced and released by beta cells of the pancreas when blood sugar levels increase. Pathways of carbohydrate and lipid metabolism are critically dependent on insulin and are severely impaired when insulin production is dropped or when insulin fails to elicit its effects (Ramchandran, 2014). Activating muscle and fat cells while lowering glucose metabolism in the liver lowers blood glucose levels.

People with diabetes have increased blood glucose levels at all times which may be a result of reduced glucose uptake by body cells or an outcome of failure to store excess glucose in liver or muscles. Insulin resistance or decreased insulin production from beta cells are the primary causes of diabetes. In some cases, a compromised immune system makes it difficult for people with diabetes to discriminate between their own pancreatic cells and external invaders, resulting in death of beta cells leading to insulin shortage. Gestational diabetes which occurs during pregnancy affects only a tiny percentage of diabetics. Diabetes is a life style disease which often involves lack of responsivity to insulin despite its abundance leading to its famous description as a state of 'starvation amidst plenty'.

The mention of diabetes is found in ancient texts of Ayurveda where it is described as 'madhumeha' and several herbal remedies ate recommended for this condition. Although the efficacy of these traditional drugs is established in certain conditions, the physiological basis of their effect is not yet known. A proper study of the efficacy of herbs in management of diabetes should involve identification, characterization and isolation of active principles having sugar lowering effects.

TYPES OF DIABETES:

Diabetes does not result from a unique cause and the presentation of this disease varies on the basis of its underlying cause. Broadly speaking, there are two major classes of diabetic conditions - Type

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1 and Type 2. However, diabetes may also be associated with pregnancy (gestational diabetes) or drug use.

1. Type 1 Diabetes:

This type of diabetes is relatively less abundant constituting less than 20% of all known cases of the disease. This is early onset and is also called Insulin Dependent Diabetes Mellitus (IDDM) because it is characterised by the loss of insulin-secreting β-cells of the islets of Langerhans present in the pancreas. Obviously, there is no production of insulin in this type of diabetes and hence the hyperglycemic condition can be temporarily cured by administering insulin hormone.

Quite often this condition results from autoimmunity. When the immune system is unable to distinguish between pancreatic self-cells and foreign cells, antibodies are formed against the insulin-producing β-cells of pancreas. Autoantibodies against islet cells, insulin, glutamate decarboxylase, or tyrosine phosphatases cause beta cell to lose its insulin-producing ability in people with type 1 diabetes. Antibodies specific to pancreatic cells are found in high concentrations in the blood of people with Type 1 diabetes. It is speculated that this kind of diabetes may be a result of an HLA gene mutation.

Beta cell apoptosis varies widely among type 1 diabetics. Some individuals give up too soon, while others persevere. Diabetic ketoacidosis is the earliest indication in children and adolescents with type 1 diabetes. There are certain children who have mild hyperglycemia and ketoacidosis and might develop life-threatening diabetes. Adults who utilize exogenous insulin to prevent ketoacidosis for a long period of time have a lower chance of developing it.

Immunodeficiency may be a result of genetic abnormalities. The autoimmune disorders Vitiligo, Celiac scurvy, and myasthenia gravis are also included in Hashimoto's thyroiditis, which is more common in those with Type 1 diabetes. Ketoacidosis is more likely to occur in patients who have insulinopenia, a disease in which the body produces insufficient amounts of the hormone.

2. Type 2 Diabetes:

Type 2 diabetes, which accounts for 90% to 95% of all cases, is characterized by insulin resistance and insulin insufficiency. It is alternatively called non-insulin dependent diabetes mellitus (NIDDM). As a result, insulin injections will no longer be required for these people. Obesity and

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decreased insulin sensitivity are two major complications of type 2 diabetes. Type 2 diabetes may lead to ketoacidosis, a potentially fatal condition, if the patient is sick or stressed. Those with type 2 diabetes are more likely to have both macrovascular and microvascular problems. Despite the use of medications and lifestyle changes such as weight loss, insulin resistance is seldom entirely cured. Overweight, hypertensive, and sedentary people over the age of 40 are more prone to have type 2 diabetes.

3. Gestational diabetes:

This the third type of diabetes which occurs during pregnancy and leads to the birth of children with high sugar levels. Compared to other forms of diabetes, gestational diabetes affects just a tiny proportion of diabetics (between 5-10%).

Because gestational diabetes tends to run in families, there is no substantial association between HLA and the condition. Ketoacidosis is more common in certain people than in others. This is owing to the fact that their insulin levels may vary significantly. Diabetes during pregnancy may need a change in insulin dosage.

4. Drug-induced diabetes:

Diabetes may also develop as a result of elevated blood sugar levels caused by the use of glucocorticoids. Blood sugar levels return to normal once glucocorticoids are withdrawn. People who have been using thiazide medicines for a long period run the risk of developing diabetes later in life.

OVERIEW OF GLUCOSE METABOLISM:

Glucose is the body's most important source of energy. Many distinct pathways of carbohydrate metabolism are involved in the maintenance of optimum blood glucose levels. Tricarboxylic acid (TCA) cycle uses pyruvate, a three-carbon compound that enters the mitochondria and is used in oxidative phosphorylation to make ATP. When blood glucose levels get too high, glucose is stored as glycogen or fat in the body.

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It is necessary to release insulin in order to maintain proper blood glucose levels. Insulin stimulates insulin-dependent GLUT-4 transporters in muscle and adipose tissues to facilitate the transfer of glucose from the blood to the tissue.

Conversion of glucose to glycogen in the hepatocytes of the liver and the muscle cells utilizes glycogenetic pathway which decreases blood glucose levels. Glucose can however be generated in times of need from the stored glycogen through glycogenolytic pathway.

The action of insulin is primarily antagonized by another pancreatic hormone 'glucagon', which is produced by the α-cells of the islets of Langerhans in the pancreas. Alpha cells in the Langerhans islets release glucagon when blood glucose levels are low, which causes the glycogen stores to be emptied. Lipids and proteins may be depleted by glucagon when blood glucose levels go too low.

Regulation of Blood Glucose:

In order to keep up with the body's needs, blood glucose levels vary. Between 70 to 110 mg/dl of blood glucose is considered optimal for the body's metabolic system. It is possible to boost blood sugar levels by diet, glycogen depletion, and hepatic glucose production. A person's blood sugar levels rise when they consume carbohydrates because of the greater glycemic index and faster digestion and absorption that occur. GLUTs are the only transporters that can move glucose across cell membranes. There are a total of six different kinds of GLUT transporters (GLUT 1-5, 7). Of these transporters, GLUT 1 and 3, have a high affinity for glucose. Transporters that deliver glucose in a concentration gradient from the blood to cells are abundant in cells with a high demand for glucose. Insulin isn't required for these transporters to operate. GLUT-2 transporters in the pancreas and liver allow insulin and glucose to go in both directions. Insulin regulates the insulin-sensitive transporter GLUT-4. In adipose tissues, the expression of GLUT-4 receptor increases when blood glucose levels rise, allowing fat to be used as a storage form of excess glucose. GLUT-5 are the fructose-sensitive transporters and are specially abundant in the sperms, testicles and intestines. The smooth endoplasmic reticulum, which contains GLUT-7 receptors, is required for insulin synthesis.

The liver is where the majority of glucose is produced in the body. When the body is starving, it releases glucose from glycogen, which helps to keep blood glucose levels normal. The liver

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synthesizes glucose from the intermediates that emerge from the breakdown of carbs, protein, and lipids.

Insulin Synthesis:

Insulin is released into the bloodstream by beta cells located in the islets of Langerhans of the pancreas which represent its endocrine part. The insulin gene is located on the 11th chromosome in man. Transcription produces insulin polypeptides from mRNA, which is translated in the cytoplasm before being delivered to the cell. Splicing two mRNA introns results in the production of a 110-amino-acid protein during translation. It is the principal translation product of insulin although it is inactive and is called Preproinsulin. Proteases in the endoplasmic reticulum break the first component of preproinsulin, enabling it to be transformed into proinsulin. Tripeptide proinsulin is made up of peptide chains A, B, and C. The C-chain is also called the connecting peptide.

In order to make active insulin, many enzymes must first cleave the C-chain of proinsulin from the insulin A and B chains. These granules, which are found in the beta cell, are discharged into the circulation from there. When glucose reaches the granules, the exocytosis of glucophages and the release of insulin are both increased.

The two chains A & B make up the insulin molecule. After the connecting peptide is removed, the two chains A&B remain joined by two disulfide bridges. Among the A-chain residues, there is a third disulfide bridge that links residues 6 and 11.

Insulin Secretion: Insulin is released when the pancreas detects an increase in blood glucose levels, as explained above. A number of steps are required for insulin to be secreted from beta cells. The following is the order in which events take place in beta cells during the production of insulin:

- Type 2 glucose transporters (GLUT-2) move glucose from the blood to cells by following the concentration gradient. The enzymes Hexokinase and Glucokinase, which are found in cells that deal with high concentrations of glucose, quickly phosphorylate glucose to glucose-6-phosphate once it is inside. Even in cells with just a modest quantity of glucose, the enzyme

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hexokinase works quickly. Glucokinase, on the other hand, is a sluggish enzyme that can only be activated in cells with high levels of glucose. Hexokinase has a lower K_m and V_{max} than glucokinase, according to scientific standards, and vice versa. Because normal cells seldom reach high glucose concentrations, cells with low K_m and V_{max} are sought for by almost all organisms. High K_m and V_{max} values for glucokinase are required in liver cells because the cells' hepatocytes must deal with a high glucose concentration to make use of the enzyme.

- Through the Glycolysis-TCA Cycle Oxidative Phosphorylation Pathway, glucose is broken down into the energy molecules ATP.
- Increased ATP levels in cells enable ATP to bind to ATP-sensitive potassium channels in the beta cell membrane, resulting in an increase in beta cell function. To prevent K^+ ions from exiting the beta cells, ATP binds to the potassium channels and shuts them.
- Beta cells depolarize owing to intracellular positivity caused by an increase in K^+ concentration.
- Calcium ions (Ca^{2+}) flood the cell via voltage-sensitive channels.
- By way of exocytosis, a rise in intracellular calcium concentration causes insulin to be released.

Two phases of insulin release occur when blood sugar levels increase. During the first phase, secretory granules, which are pre-packed with insulin, release insulin instantly. Following this, insulin release decreases temporarily. After a short delay in the first phase of insulin release, new insulin is released in the second phase. As blood glucose levels rise, the release of insulin causes a biphasic insulin response.

ANTI-DIABETIC DRUGS:

There exist a number of drugs to treat hyperglycemia in diabetic patients. Despite their efficacy in achieving this goal, they only provide temporary relief and therefore have to be taken regularly. Here is a description of some of the more important hypoglycemic drugs:

Metformin:

Hepatic gluconeogenesis is inhibited by metformin, a hypoglycemic drug that lowers blood glucose levels. Metformin treatment also decreases or delays sugar absorption in the intestines.

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After 4-6 weeks of metformin therapy, patients' LDL and VLDL cholesterol levels drop while HDL levels rise. Metformin's side effects include weight loss and a lower risk of cardiovascular disease and death. If metformin is used by individuals with congestive heart failure, they are more likely to have severe lactic acidosis due to metformin's side effects. Metformin and other antihyperglycemic medications may cause hypoglycemia..

Nateglinide:

It belongs to the family of hypoglycemic medicines known as meglitinides. Unlike the sulfonylureas, it can bind to ATP-sensitive K^+ channels, although it has a lower affinity for them. Because they increase insulin production by generating intracellular depolarization, they work similar to sulfonylureas to boost insulin secretion with quicker onset and longer duration of effect. It has a positive impact on insulin release in both the pre- and post-prandial periods. Compared to sulfonylurea, it causes less hypoglycemia because of its brief duration of action. CYP3A4 inhibitors extend its effect, whereas CYP3A4 promoters shorten it. Severe hypoglycemia may occur when gembifrozil and repaglinide are used together.

Pioglitazone:

Peroxisome proliferator-activated receptor (PPAR) may be triggered by pioglitazone. Three pathways in obesity are all under the control of PPAR antagonists, which have been shown to be effective. This medication, pioglitazone, enhances insulin's ability to reach fat, liver, and muscle cells. It is possible that hyperglycemia and triglyceride levels may decrease and HDL levels will increase after administration. Pioglitazone users have an increased chance of developing fat deposits beneath the skin. Hepatotoxicity, which may be deadly, is one of the side effects. Those who are taking pioglitazone should have their liver functions evaluated at regular intervals.

Miglitol:

The oligosaccharide derivative Miglitol slows down the digestion and absorption of carbohydrates when taken before meals. Miglitol inhibits the enzyme glucosidase, which is located in the intestinal brush borders. Diarrhea, flatulence, and cramping are some of the negative effects of this medication. It's not advised to be taken by anybody with a gastrointestinal disorder.

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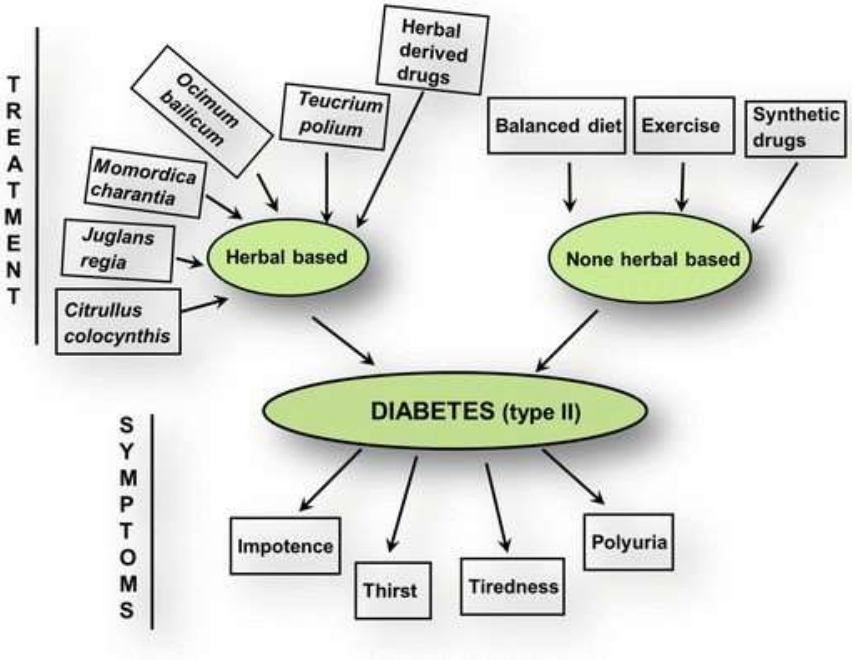
Glimipride:

It is a long acting sulfonylurea which acts by inhibiting ATP-sensitive K^+ channels. It's similar to meglitinides in how it works, but it lasts a lot longer. It increases insulin binding to target cells and decreases glucagon release. Weight gain, insulin resistance, and hypoglycemia are all possible side effects. Insufficient hepatic and renal function results in the buildup of glimepiride, which increases the risk of hypoglycemia.



IMPORTANCE OF HERBAL MEDICINES

Natural remedies have been used to heal a broad variety of problems since the beginning of time. Natural medicines are still widely used to cure a broad variety of ailments. A wide variety of civilizations throughout the world rely on plants for their active therapeutic components. Because of its accessibility, low cost, and lack of side effects, complementary and alternative medicine is a viable option for treating sickness in countries where the contemporary medical system is still in its infancy. Many active compounds from medicinal plants have been shown to be effective in the treatment of a broad variety of illnesses. In traditional medicine, the antidiabetic characteristics of a variety of plant species are being explored and used. Before the discovery of insulin, both types

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of diabetes were often treated using traditional botanicals. Following is a description of some popular medicinal plants recommended as antidiabetic:

Acacia arabica:

Traditional Indian medicine makes use of a plant called *Acacia arabica* to treat and manage diabetes (babul). Alloxanized rats were not hypoglycemic after receiving doses of 2, 3, or 4g/kg powdered seeds extract (Wadood et al., 1989). Beta cells must be active in order for the plant extract to serve as a secretagogue. Beta cells produce insulin in response to plant extracts.

Adansonia digitata:

Traditional African medicine uses the leaves, bark, and fruits of the Adansonia digitata plant to treat diabetes. Many people use the herb as a supplement. A frequent moniker for this tree is 'the tiny pharmacy or pharmacist tree' in reference to its many medicinal properties. Treatment of diabetic Wistar rats with its methanolic stem bark extract resulted in comparable outcomes to those of healthy rats (Tanko et al., 2008). The hypoglycemic effects of the extract were changed when the dosage was increased. After only 1, 3, 5, and 7 hours of delivering 100 mg/kg of this extract, blood glucose levels declined significantly. Blood glucose levels dropped dramatically after three, five, and seven hours of treatment with a dosage of 200 mg/kg. Moreover, seven hours after treatment with 400 mg/kg of glucose, hypoglycemia symptoms were still present, compared to the average saline dosage. Plant extracts have been demonstrated to have hypoglycemic properties.

Adhatoda vasica:

The methanolic extract of *Adhatoda vasica* leaves was shown to inhibit sucrase, an enzyme that transforms sucrose into glucose. Sucrose inhibition may be achievable in the presence of the chemicals vasicine and vascinol, with IC50 values of 125 millimoles and 250 millimoles for these two medicines, respectively. A comprehensive pharmacokinetic investigation found that glucosidase slowed the inhibitory effects of these two drugs. Competing for binding were drugs with K_i values of 82 and 183 nM. According to these investigations, an extract of the plant that contains vasicine and vascinol may have anti-diabetic properties (Gao et al., 2000). It's time to investigate these two chemicals as possible hypoglycemic agents.

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Aegle marmelos:

Traditional Indian medicine depends on *Aegle marmelos* leaf extract for the treatment and control of diabetes. Diabetic mice given methanolic extract of the plant's leaves had substantial reductions in blood glucose levels (Sabu & Ramadasan, 2001). There were positive effects following a six-day course of hypoglycemic extract treatment. Glucose levels reduced by 54% after 12 days of extract treatment. According to the research, the plant extract may also have antioxidant properties in addition to its excellent antidiabetic benefits.

Aloe barbadensis:

A wide range of ailments, including burns and wounds, have traditionally been treated using *Aloe vera* in folk medicine (Ajabnoor, 1990). Gel and latex are two of its most important components. The pericyclic tubules beneath the leaf's outer surface produce a bitter yellow fluid, unlike the *Aloe vera* gel. When aloe gum extracts were fed to diabetic and non-diabetic rats, their glucose tolerance increased. Alloxanized diabetic rats' blood glucose levels decreased when *Aloe barbadensis* exudate therapy was continued. The plant extract in question is considered to have secretagogue actions on beta cells in the pancreas. There was a drop in glucose levels in diabetic rats that received bitter plant components.

Andrographis paniculata:

An extract of *Andrographis paniculata* root chloroform demonstrated substantial antihyperglycemic properties in diabetic rats (Rao, 2006). Glucose levels decreased significantly in both acute and chronic tests. Researchers found that an extract from the plant helped to lower levels of albuminuria, proteinemia, and uremia when administered to mice. The plant's roots have been shown to have an antidiabetic impact in this investigation.

Anthocephalus indicus:

The Ayurvedic medicinal system has long utilized *Anthocephalus indicus* as a diarrhoea cure, aphrodisiac, and cleanser. Extracts from plant roots were examined for their antidiabetic, antioxidant, and antilipidemic activities in rats that had been alloxanized (Kumar et al., 2009). There were 500 mg per kilogram of the medication supplied during the research period. Phospholipids, glycated triglycerides, and total cholesterol decreased significantly following

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therapy. Antioxidant properties have also been revealed in the plant. For both enzyme and non-enzymatic systems, taking root extract at a 100-400 g/kg dosage reduced the formation of superoxide anions and hydroxl radicals *in vitro*. The results of the study may provide evidence of this plant's capacity to lower cholesterol and prevent diabetes.

Artanema sesamoides:

An *Artanema sesamoides* methanolic extract was employed in tests on diabetic rats. After extract treatment, diabetic rats demonstrated lower blood glucose levels and more liver glycogen than controls (Selvan et al., 2008). After taking the medication, the liver's and blood's levels of alkaline phosphatase decreased as well. The herb may also act as an antioxidant, as shown by the research. A research found that the plant has an antidiabetic effect. The extraction and identification of anti-diabetic components will need additional investigation.

Azadirachta indica:

Diabetic rats administered hydroalcoholic extracts of the Indian herb *Azadirachta indica* (Neem) saw their blood sugar levels drop (Chattopadhyay et al., 1987). In the rat hemi diaphragm, after treatment with extract, glucose uptake and glycogen storage were increased Research into the plant's anti-inflammatory, antibacterial, and antibiotic properties has made encouraging progress.

Boerhavia diffusa:

Uses for Punarnava's diuretic and liver-protective properties are many in Indian medicine. In rats fed 200 mg/kg of *Boerhavia diffusa* leaves for four weeks, the aqueous extract exhibited a substantial decline in blood glucose levels (Pari & Satheesh, 2004). Significant reductions were also seen in the levels of liver enzymes. It was discovered that rats fed with the extract had a substantially higher tolerance for glucose than control rats. Glibenclamide (600 mg/kg) was shown to be less effective in treating type 2 diabetes than extracts.

Butea monosperma:

Butea frondosa, as it's known, may be found throughout India. Antihelmintic, anticonvulsant, and hepatoprotective properties were reported in a seed methanol extract (Deore et al., 2008). According to legend, the herb may assist in the treatment of diabetes. The medication resulted in

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significant reductions in blood glucose levels in both healthy and diabetic animals. Scientists have discovered that the plant contains anti-diabetic properties.

Caesalpinia bonducella:

This plant may be found in great abundance across the tropics, including India and other nations. Seed kernel extracts (containing petroleum ether, gasoline, and ether) lowered blood sugar levels in both healthy rats and diabetic animals induced with alloxan. In diabetic rats, ethyl acetate and water extracts lowered insulin levels (Parameshwar et al., 2002). There were similar outcomes with the standard hypoglycemic medication, glibenclamide. Therapy with polar extracts also helped to restore diabetic-induced changes in lipid profiles and liver function. In the absence of antidiabetic activity, the non-polar extracts were discovered. The polar extract included triterpenoids and glycosides following a phytochemical screening.

Cassia auriculata:

C. auriculata, which grows in the wild in several Asian nations, is an important ingredient in Ayurvedic treatment. Traditional Indian medicine uses its extract as a tonic, astringent, and therapy for illnesses such as conjunctivitis, ophthalmitis, and diabetes. The Ayurvedic formulation 'Avaaraipanchagachooranam' contains it as a component in the treatment of type 2 diabetes in humans (Hakkim et al., 2007). Plant aqueous and ethanolic extracts effectively lowered blood glucose levels in Alloxan-induced diabetic rats (0.25-0.5g/kg). Using mice with diabetes produced by streptozotocin, researchers discovered that the herb possesses both antihyperlipidemic and antidiabetic effects. A phytochemical screening revealed flavonoids and phenolics in the plant extract. The antidiabetic potency of ethanolic vs. aqueous extracts varied. Clinical investigations revealed that it has hypolipidemic and anti-diabetic benefits.

Cocinia indica:

In dogs that had been alloxanized, a 500 mg/kg dose of *Cocinia indica* leaf extract caused significant hypoglycemia when administered orally. Plant extract enhanced glucose tolerance in both normal and diabetic dogs (Kamble et al., 1998).

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Eugenia jambolana:

According to recent findings by researchers in India, the herb *Eugenia jambolana* has long been used to treat diabetes. A broad variety of natural goods also include supplements for diabetes. Their alcoholic and watery extracts have shown substantial anti-hyperglycaemic properties. Intermediate diabetics (plasma sugar >180 mg/dL) had a 75% decrease in glucose levels (Ravi et al., 2004). Glucose levels decreased by 55% and 17% in people with mild and severe diabetes, respectively, according to this study. Within 30 minutes of dosing, a plant pulp extract demonstrated considerable hypoglycemic action in streptozotocin-induced diabetic mice. After 24 hours, the extract of the seed was found to have hypoglycemic effect. Tests in vitro have shown that Langerhans islets from healthy and diabetic rats produce hormones when exposed to plant extracts. The treatment also lowered insulinase activity in liver and kidney cells.

Ficus bengalensis:

In addition to being recognized as the banyan tree, the bark of *Ficus bengalensis* has long been used to treat diabetes in India (Sharma et al., 2007). When compared to other ethanolic extracts, the ethanolic extract of *Ficus bengalensis* was substantially more successful in lowering blood glucose than the other extracts. It was observed that ethanolic fruit extracts delivered at levels of 120 mg/kg were more efficient against diabetes than root or bark extracts. The extract's hypoglycemic efficacy was equivalent to that of a routinely prescribed medication. glibenclamide.

Ficus racemosa:

The methanolic extract of *Ficus racemosa* stem bark showed significant hypoglycemic effects in both groups of diabetic rats given 200 mg/kg and 400 mg/kg of the extract, respectively (Rao et al., 2002). The novel medication performed similarly to glibenclamide, the standard treatment for type 2 diabetes. According to this analysis, the plant's antidiabetic capabilities were confirmed.

Hibiscus rosa-sinesis

Blooming trees known as Gudhal may be found throughout the nation. To test the antidiabetic properties of plant extracts, both acute and subacute models were used. A study used 250 mg/kg and 500 mg/kg of floral ethanolic extract on rats to see what impact it had on their behavior. Both animals exhibited a considerable drop in blood sugar levels. Glucose levels in the acute model

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were lowered after 1, 3, and 5 hours of extract treatment. Glucose levels dropped after only one, three, five, and seven days of extract therapy treatment in a subacute animal model. Using ethanolic plant extract to treat diabetes, both acute and chronic, was shown to be a viable treatment option in this study's results (Venkatesh et al., 2008).

Holarrhena antidysenterica

Indians refer to this plant's genus and species as kurchi, which is short for *Holarrhena antidysenterica*. Albino rats were used to evaluate the hypoglycemic effects of the plant's seeds. Excessive doses of extract were given to diabetic rats, whereas healthy rats were given 350 mg per kg of body weight. Glucose levels began to fall after the seventh day of extract administration. Blood glucose levels were considerably lower both before and after the meal, indicating better control of blood glucose levels. The glucose levels in the rats used as a control also dropped. The 7th day of the trial showed a drop in fasting glucose levels. After seven days, diabetic rats' lipid profiles had improved even though there had been no noticeable improvement in the control groups' lipid profiles. There was a significant drop in cholesterol levels as early as day fourteen.

Lawsonia inermis:

In India, the plant *Lawsonia inermis* is often referred to as mehndi. It has long been used as a treatment for diabetes. Using alloxanized rats, researchers were able to establish the validity of the claim (Syamsudin & Winarno, 2008). 800 mg/kg of a plant leaf extract was administered to rats in both normal and diabetic conditions. Glucose levels began to fall on the experiment's fourteenth day. Normal glucose levels were restored from 194 mg/dl. Reduced lipid profiles have been seen as well.

Lepidium sativum:

The hypoglycemic effects of *Lepidium sativum* seed extracts were investigated. In their experiment, scientists used both healthy and diabetic rats. A dosage of 20 mg/kg effectively lowered blood glucose levels in both acute and chronic tests (Eddouks et al., 2008). The blood sugar levels returned to normal after taking the extracts for two weeks. Glucose levels in normal rats were significantly reduced in studies conducted over short and extended periods of time.

Received: 15.12.2021 **Accepted:** 07.01.2022 **Published**: 07.01.2022

Journal of Advance Research in Science and Social Science (JARSSC)
Official Publication of Indian Mental Health & Research Centre
ISSN: 2582-2004
Volume 05, Issue 01
DOI: 10.46523/jarssc.05.01.19
Multidisciplinary, Open Access
Impact Factor: 3.575

Diabetic and non-diabetic rats had the same baseline plasma insulin levels, showing that the drug's impact was not reliant on the amount of insulin produced.

Momordica Charantia:

Bitter melons, also known as *Momordica charantia* in India and other Asian countries, have long been used to treat diabetes and hyperglycemia. Studies on animals have shown the hypoglycemic properties of fruit pulp, seed, leaves, and the whole plant. Polypeptide produced from its fruit, seeds, and tissues has been shown to have significant hypoglycemic effects in both langurs and humans when administered subcutaneously (Cakici et al., 1994). At a dose of 200 mg/kg, the ethanol extract of the plant had substantial benefits on diabetic rats in terms of lowering their blood sugar levels and preventing hyperglycemia. Inhibiting or stimulating fructose-1,6-bisphosphatase may be a probable mechanism for this plant's activities.

Myristica fragrans:

Traditional medicine has long turned to *Myristica fragrans*, sometimes known as nutmeg, to treat a variety of gastrointestinal disorders and sleep disorders. In normal, alloxanized, and glucose-fed rats, petroleum ether extract from seeds was administered at 200 mg/kg. The number of rats in each group was n=5. Glucose concentrations in normal rats were much lower. One dose of alloxan therapy lowered the percentage of diabetic rats in the oral glucose tolerance test (OGTT), when compared to rats given control glucose (Somani & Singhai, 2008). The extract was applied to the skin every day for the following two weeks. Additionally, the use of extract treatment resulted in a decrease in body weight. Rats treated with adiponectin had better lipid profiles and hemoglobin levels.

Ocimum sanctum:

Ocimum sanctum (also known as holy basil) is a plant that has a wide range of applications. Since ancient times, people have relied on it to treat a broad variety of health issues. Researchers have found evidence that the leaves of the plant may lower blood sugar levels in diabetic rats and humans. Research on the entire ethanolic extract and different fractions (aqueous, butanol, ethyl acetate) of the leaves extract looked at the mechanism of action and the impact on insulin secretion. Extracted ethanolic portions of it boosted insulin production in diabetic rat beta cells and islets

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Impact Factor: 3.575

(Hannan et al., 2006). Tolbutamide and isobutylemethylxanthine (IBMX) were shown to improve the stimulatory effects of extraction. The diazoxide and verapamil slowed the synthesis of insulin. It was found that the cell viability of chloroform and hexane had been decreased. A number of studies have indicated that this has a stimulating effect on cells. Both verapamil and diazoxide had no impact on the results at all! In the BRIN-BD11 cell line, verapamil was demonstrated to suppress intracellular Ca^{2+} increases in part. According to this research, *Ocimum sanctum's* secretagogue action on islet cells seems to have an anti-diabetic effect.

Onion (Allium cepa):

The onion, which originated in Eurasia, has now spread around the globe. All countries eat plants from this genus at least once a week. Insulin breakdown may be prevented by the plant's bulb, which contains an active ingredient known as allyl propyl disulphide (APDS). The entire elevation in blood insulin levels may exercise its anti-diabetic potential because of the higher insulin production in the pancreas (Augusti, 1973).

Phyllanthus niruri:

A wild plant native to the Indian subcontinent is known by the term "bhuiamla" as a common name. This plant is used to treat a wide range of ailments in Indian traditional medicine. With and without insulin dependency, diabetics were tested for the plant's anti-diabetic properties against type 2 diabetes (NIDDM). After ingesting an alcoholic plant extract, lipid metabolism and antioxidant activities were studied. Hypoglycemia may occur in rats infected with the IDDM virus. All animals had lipid-lowering and antioxidant properties (Jasmin & Narasimhacharya, 2007). Antidiabetic and lipid-lowering effects of the plant were discovered independently of the medicine.

Pterocarpus marsupium:

Hilly portions of India's subcontinent are home to this huge tree. *Pterocarpus marsupium* has a number of phytoconstituents that have been isolated and identified. When a plant's flavonoid fraction was supplied, beta cells began to degranulate. In the flavonoid fraction, the tree's extracts of Marsupin, Pterosupin, and Liquiritigenin have enhanced the lipid profile. Epicatechin, a compound derived from the plant, has been demonstrated to have insulinogenic effects.

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Impact Factor: 3.575

Epicatechin has been shown to enhance the amount of glycogen in the diaphragm of the rat in a dose-dependent way by stimulating the absorption of Oxygen into fat cells.

Rubia cordifolia

Rubia cordifolia is a common medicinal herb in many cultures. The word 'majit' is often used to characterize it. *Rubia cordifolia* aqueous roots extract increased blood glucose reduction in diabetic mice. The root extract reduced serum transaminases and hence improved liver function. The extract had no effect on hypercholesterolemia, a common complication of heart disease. Researchers discovered that this herb has hepatoprotective and anti-diabetic capabilities in addition to its antihyperlipidemic ones.

Terminalia chebula:

Terminalia chebula, which is also known as hard or hartiki in India, is typically referred to as sugar lowering herb. With frequent use, it has a positive effect on diabetic patients.

Strepozotocin-induced diabetes in rats was used to assess the anti-diabetic effects of Terminalia in humans. Ethanolic extract from the plant's fruit needed 30 days to administer to mice. Diabetic rats had lower levels of glycosylated hemoglobin (HbA1C) and glucose, and this drop was statistically significant. Evidence of insulin-stimulating activity was found in plasma insulin levels (Kumar et al., 2006). Normalization of carbohydrate-metabolizing enzymes was achieved by extracting for 30 days. Histological abnormalities were determined to have returned to normal at the end of the experiment.

Tinospora cordifolia:

Climbing shrubs known as Guduchi may be found across the Indian subcontinent. After six weeks of treatment with an aqueous extract (400 mg/kg), the blood and urine glucose levels of Alloxan-induced diabetic rats were dramatically reduced (Stanley et al., 2000). The serum and tissue lipid profiles improved as a consequence of these alterations. The patient's weight loss returned to normal after the therapy. Hypoglycemic impact was equal to one unit of insulin per kilogram of body weight. Improved glucose tolerance and reduced glucose levels have been seen in rats as a result of this treatment.

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Trigonella foenum-graceum:

The Indian subcontinent uses fenugreek, also known as foenum-graecum, as a meal and spice. The herb and spice (seeds) of the plant are utilized all over the globe. Diabetic patients' blood sugar levels were lowered by giving them fibre-rich seed fractions. When diabetic individuals were given a dosage of 5-30g of plant seeds, their lipid profiles improved to some degree. Patients who take seeds may have moderate stomach upset as a side effect. People with diabetes and, to a lesser degree, those with high cholesterol may benefit from fenugreek seeds' fiber-rich fraction (Zia et al., 2001). As an added bonus, fenugreek's soluble fiber content may promote weight loss. In general, a dosage of 5 to 30 g is given three times day, with food. Mild gastrointestinal discomfort is one of the known negative effects of high dosages. The use of fenugreek by women who are pregnant or breast-feeding is prohibited.

Withania somnifera:

Traditional medicine depends on Ashwagandha, or Indian gooseberry, to treat and manage a broad range of ailments. Withanolides, steroidal lactones found in the roots of the plant, are the herb's primary active ingredient. Alloxan-induced diabetic mice treated for eight weeks with *Withania somnifera* leaf and root extracts showed remarkable hypoglycemic and lipid-lowering effects (Kumar et al., 2009). Glibenclamide, a commonly prescribed medication, was shown to have similar results. At the conclusion of the experiment, all of the serological markers and blood glucose levels reverted to normal.

CONCLUSION:

Since the beginning of time, medicinal plants have been employed to sustain human health. With no or minimum side effects, plant-based medicines are becoming more popular with the general population. Several phytoconstituents isolated from diverse plants have been shown to be interesting medicinal possibilities. In addition to their potential to heal ailments with the fewest possible side effects, natural medicines are becoming more popular owing to their low cost, convenience of availability, and acceptance based on historical promises. Even under a rational or contemporary medical system, many individuals believe that natural treatments may heal ailments that would otherwise be untreatable. Multiple biological targets are simultaneously attacked using

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Impact Factor: 3.575

multi-target techniques by medicinal plants. A disease treatment strategy can't fail since plants have the potential to target several targets.

Diabetes is a metabolic disorder that affects blood sugar levels. Type-1 and type-2 diabetes may both be treated with insulin replacement treatment and hypoglycemic drug delivery. Diabetic treatment regimens involve a variety of methods for controlling the disease. As of right now, there is no medication that can treat diabetes at its root and end the condition once and for all. Herbal principles, according to conventional medical wisdom, may be used to cure diabetics. Experts in the area scrutinize all possible treatment options for diabetes, including those derived from plants. It has been shown that the great majority of plants investigated have the ability to reduce blood sugar levels, enhance lipid profiles, and improve liver function. As well as treating many different ailments, medicinal plants have the ability to slow or stop disease development by interfering with many different processes.

If carefully studied, plants may be a limitless supply of active principles that can treat illnesses and afflictions while causing the least amount of harm. Pharmacological candidates that show a significant anti-diabetic impact in early studies should be found in medicinal plants that have anti-diabetic effects.

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Received: 15.12.2021 **Accepted:** 07.01.2022 **Published**: 07.01.2022

ISSN: 2582-2004
Volume 05, Issue 01
DOI: 10.46523/jarssc.05.01.19
Multidisciplinary, Open Access
Impact Factor: 3.575

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Received: 15.12.2021 **Accepted:** 07.01.2022 **Published**: 07.01.2022