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REVIEW ON ANTIDIABETIC ACTIVITY OF MEDICINAL PLANTS

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ABSTRACT

Diabetes mellitus is one of the common metabolic disorders affecting a huge number of populations in the world. It is mainly characterized by chronic hyperglycemia, resulting from defects in insulin secretion or insulin action. It is predicted that the number of diabetes patients in the world could reach up to 366 million by the year 2030. Even though the cases of diabetes are increasing day by day, except insulin and oral hypoglycemic drugs no other way of treatment has been successfully developed so far. Thus, the objective of this review is to provide an insight over the pathological and etiological aspects of diabetes. The review also contains brief idea about diabetes mellitus and the list of herbal medicinal plants which shows the antidiabetic activity. Among this list of antidiabetic medicinal plants, five medicinal plants such as

syzygium cumini, aloe vera, momordica charantia, azadiracta indica, and annona squamosa are well described. Active chemical constituents, plants parts to be used, and chemical tests for determination of presence of active constituents in the prepared extract are also included in this review. The plants having antidiabetic activity is mainly due to the presence of the secondary metabolites. So, the information provided in this review will helps to the researchers for the development of an alternative methods and medicines rather than insulin and oral hypoglycemic agents for the treatment of diabetes mellitus, which will minimize the complications associated with the diabetes and related disorder.

KEYWORDS: Diabetes mellitus, antidiabetic medicinal plants, chemical tests, animal study.

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder, resulting from insulin deficiency, characterized by abnormal increase in the blood sugar level, altered metabolism of carbohydrates, proteins and lipids, and an increased risk of vascular complications. As per world health organization, DM is a chronic metabolic disorder characterized by common features of chronic hyperglycemia with disturbance of carbohydrate, fat, protein metabolism. This includes autoimmune destruction of the β -cells of the pancreas which leads to consequent insulin deficiency and abnormalities that result in resistance to insulin action.

SIGNS AND SYMPTOMS

Signs and symptoms of hyperglycemia include weight loss, blurred vision, polyuria, polydipsia, polyphagia, hypotension, wasting, tachycardia, fatigue, headache and poor wound healing. The development of foot ulcer, renal impairment and retinopathy may be considered as long term complications of long-standing diabetes in a patient.

ETIOLOGY

Classification of diabetes

Type 1: type 1 diabetes mellitus (T1DM) is typically characterized by an absolute insulin deficiency attributed to an autoimmune distruction of the β -cells of the islets of langerhans.

Type 2: type 2 diabetes mellitus (T2DM) is the most common form of DM and is typically identified in individuals over the age of 30 years; however, it has become a prominent diagnosis in adolescents of certain ethnic origins

Gestational diabetes mellitus: gestational diabetes mellitus (GDM) is a condition in which woman first exhibit levels of elevated plasma glucose during pregnancy.

Pre-diabetes: individuals who have elevated blood glucose levels that do not meet diagnostic criteria for diabetes, but that are too high to be considered normal, are classified as having pre-diabetes. It is high risk category for the future development of T2DM.

EPIDEMIOLOGY

In the united states, an estimated 8.3% of the population has DM and 35% of adults (age 20 years and older) have pre-diabetes. Disparities exists in the diagnosis of diabetes across ethnic groups and minority populations, with native Americans and Alaska natives having the

highest rates of diagnosed diabetes (16.1%), followed by blacks (12.6%) and Hispanics (11.8%). T2DM accounts for more than 90% of the cases of diabetes.^[1]

TOP 10 COUNTRIES HAVING DM COUNTRY NO.OF ADULTS WITH DM

- 1. China 98.4%
- 2. India 65.1%
- 3. USA 24.4%
- 4. Russia 10.9%
- 5. Mexico 8.7%
- 6. Indonesia 8.5%
- 7. Germany 7.6%
- 8. Egypt 7.5%
- 9. Japan 7.2%
- 10. Saudi Arabia 24.6%

PATHOPHYSIOLOGY OF DIABETES MELLITUS

Pathophysiology of diabetes mellitus is depends upon carbohydrates metabolism and insulin action. Carbohydrates from the food are broken down into glucose molecules in the gut and this glucose is absorbed into the bloodstream, elevating the blood glucose levels which results in the secretion of insulin from the pancreatic beta cells. Insulin binding to specific cellular receptors facilitates entry of glucose into the cell. The cell uses glucose for energy production. The increased insulin secretion from the pancreas and the subsequent cellular utilization of glucose results in lowered of blood glucose levels. If insulin production and secretion are altered by diseases, blood glucose dynamics will also change. The decrease in insulin production may inhibit glucose entry into the cells resulting in hyperglycemia. Inadequate utilization of pancreatic insulin by the cells also leads to abnormal increase in the blood sugar level. When there is an elevation in the insulin secretion, blood glucose level becomes low as large amounts of glucose enter the cells and little remains in the bloodstream.

Excess glucose is stored in the liver and muscles as glycogen. Later, when energy is needed, glycogenolysis converts stored glycogen back to glucose. Triglycerides also formed from excess glucose and stored in adipose tissue which may subsequently undergo lipolysis, yielding glycerol and free fatty acids. The liver also produces glucose from proteins and fat through a process called gluconeogenesis. Normal homeostasis is achieved through a balance

of the metabolism of glucose, free fatty acids and amino acids, which maintains a blood glucose level, sufficient to provide an uninterrupted supply of glucose to the brain. The counter-regulatory hormones such as glucagon, catecholamine, growth hormones, thyroid hormones and glucocorticoids also affect the normal blood glucose level.

Nowadays, different treatments, such as insulin therapy, pharmacotherapy, and diet therapy, are available to control diabetes. There are several types of glucose-lowering drugs that exert anti-diabetic effects through different mechanisms. These mechanisms include stimulation of insulin secretion by sulfonylurea and meglitinides drugs, increasing of peripheral absorption of glucose by biguanides and thiazolidinediones, delay in the absorption of carbohydrates from the intestine by alpha-glucosidase, and reduction of hepatic gluconeogenesis by biguanides. In the past three decades, despite the significant progress made in the treatment of diabetes, the results of treatment in patients is still far from perfect. These treatments have some disadvantages, including drug resistance (reduction of efficiency), side effects, and even toxicity. For example, sulfonylureas lose their effectiveness after 6 years of treatment in 44% of patients. It is also said that the glucose-lowering drugs are not able to control hyperlipidemia. In addition, the side effects of medicines and their interactions with each other in vitro must be considered by medical staff. Today, many treatments that involve the use of medicinal plants are recommended.

Most plants used as antidiabetic plants and they contains carotenoids, flavonoids, terpenoids, alkaloids, glycosides. The anti-hyperglycemic effects that results from treatment with plants are often due to their ability to improve the performance of pancreatic tissue, which is done by increasing insulin secretions or reducing the intestinal absorption of glucose. The number of people with diabetes today has been growing and causing increasing concerns in medical community and the public. The main purpose of this article is to introduce a number of effective antidiabetic medicinal plants to treat diabetes and other plant compounds used to reduce glucose levels and increase insulin secretion. [4]

Table 1: List of Antidiabetic Medicinal Plants. [2-3]

Aloe Vera	Medicago sativa	Securinegra virosa	Mucuna pruriens
Milk thistle	Averrhova bilimbi	Agrimony eupatoria	Nigella sativa oil
Banaba	Azadiracta indica	Alangium salvifolium	Panax ginseng
Cinnamon	Aegle marmelose	Annona muricata	Pandanus odorus
Green tea	Biophytum sensitivum	Asparagus racemosus	Parinari excelsa
Gymnema sylvestre	Barleria prionitis	Bauhinia variegata	Prunella vulgaris
Momordica charantia	Brassica nigra	berberine	Psidium guajava
Pterocarpus marsupium	Bryonia alba	Boerhaavia diffusa	Pterocarpus marsupium
Allium cepa	Caesalpinia bonducella	Bougainvillea spectabilis	Radix rehmanniae
Guggul	Carum carvi	caffeine	Rehmania glutinosa
Loquat	Cajanus cajan	Camellia sinensis	Ricinus communis
Garcinia kola	Casearia esculenta	Capsicum frutescens	Syzygium cumini
Garlic	Cichorium intybus	Catharanthus roseus	Sarcopoterium spinosum
Licorice	Chamaemelum nobile	Coccinia indica	Salvia lavandifolia
Juniper berry	Citrulus colocynthis	Cornus officinalis	Selaginella tamariscina
Valeriana wallichii	Coriandrum sativum	Elephantopus scaber	Semen coicis
Yarrow flower	Dorema aucheri	Enicostemma litterale	Smallanthus sonchifolius
Cayenne pepper	Eclipta alba	Ephedra distachya	Stevia rebaudiana
Fenugreek	Fraxinus excersior	Eriorbotrya japonica	Swertia chirayita
Okra	Helicteres isora	Eucalyptus globulus	Swertia punicea
Ginger	Myrcia bella	Ficus bengalensis	Tabernanthe iboga
Acacia arabica	Hypoxis hemerocallidea	Fermented unsalted soybeans	Teucrium polium
Achyranthes aspera	Lepidium sativum	Genistein	Tinospora crispa
Acosmium panamense	Mangifera indica	Ginkgo biloba	Tribuluks terrestris
Andrographis paniculata	Nigella sativa	Radix glycyrrhizae	Trigonella foenum -graecum
Annona squamosa	Origanium vulgare	Helicteres isora	Zizyphus spina -christi
Argyreia nervosa	Ocimum sanctum	Hibiscus rosa sinensis	Salacia reticulata
Artemisia herba	Phyllanthus amarus	Hordeum vulgare	Prangos ferulacea (L.) Lindl,

Table 3: Detail Information of Five Most Useful Medicinal Plants Which Shows Anti-Diabetic Activity.

Sr.no	Plant botanical name	Family	Parts to be used	Active chemical constituents	Chemical constituents which shows anti-diabetic activity
1	Syzygium cumini	Myrtaceae	Seeds, leaves, flower	Anthocyanins, glucoside, ellagic acid, isoquercetin, flavonoids, kaempferol, myricetin, mycaminose	Mycaminose, flavonoids
2	Aloe vera	Liliaceae	leaves	Vitamins, enzymes, minerals, saponins, lignin, aloin, barbaloin, aloe emodin, glucosamines, anthraquinone glycosides, Lophenol, 24-methyl lophenol, 24-ethyl-lophenol, 24-methylene-cycloartanol	Phytosterols, lophenol, cycloartanol, saponins, flavonoids, anthraquinones
3	Momordica charantia	Cucurbitaceae	fruits	Momordicin, charantin, galactose, Glycosides, saponins, alkaloids, resins, cycloartenols, charine, cucurbitins, galacturonic acid, gentisic acid, lanosterol, Fixed oil, acids	Polypeptide-P, charantin, Triterpene, proteid, lipid, Steroid, alkaloid, phenolic compounds

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4	Azadiracta indica	Meliaceae	Leaves, bark	Azadiractin, nimbin, nimbolinin, nimbidin, nimbidol, quercetin, nimbanene, polyphenolic flavonoids	Flavonoids, Triterpenoid, Glycosides
5	Annona squamosa	Annonaceae	leaves	Anonaine, anolobine, aporphine, carvone, linalool, limonene, squamosin, quercetin, diterpenes, alkaloids, Cyclopeptides, phenolic substances	Alkaloids, saponin, terpenes, tannins

1. Syzygium cumini (jamun) -Commonly known as Malabar plum, java plum, or black plum. It is an evergreen tropical tree belongs to the family of **Myrtaceae**. The original home of syzygium cumini is India. It is also found in Thailand, Philippines, Madagascar and some other countries.

The plant contains anthocyanins, glucosides, ellagic acid, isoquercetin, kaempferol and myricetin. The significant amount of **flavonoid** in syzygium cumini seed is responsible for antidiabetic properties. S. cumini seed extract significantly decrease the blood glucose, blood urea, serum cholesterol and serum triglyceride levels in alloxan induced diabetic rats. Flavonoids are bioactive compounds found in plants that have been shown to enhance insulin release and regeneration of pancreatic beta cells.^[6-7]





Fig. 1: Syzygium cumini seeds and fruits.

Sample preparation

Firstly washed the Jamun fruit and then fruits and seeds were separated. Then dried the fruits and seeds in tunnel drier at 40 °C for 24 h. The dried fruits and seeds were ground to a fine powder using a grinder (PHILIPS 600W Type HR 2068). The resultant powders were packed in air tight glass jars and stored in laboratory cabinet at room temperature of 25-30 °C for further investigations.^[5]

Preparation of jamun extracts

The Jamun extracts are prepared using binary solvent i.e. aqueous ethanol (50% v/v). About 50 g of sample added in volumetric flasks followed by the addition of solvent. Then the volumetric flasks are placed in orbital shaker operating at 280 rpm and 50 °C at temperature for a time length of 45 min. after that, all extracts are filtered. The filtrate then evaporated using Rotary Evaporator (Eyela, Japan) at 40 °C under reduced pressure for the removal of solvent. The extracts were then stored in sealed bottles for future use. ^[5]

Chemical test for determination of flavonoids present in the extract

In a test tube containing 0.5 ml of alcoholic extract of the samples, 5 to 10 drops of diluted HCl and small amount of Zn or Mg are added and the solution is boiled for few minutes. Appearance of reddish pink or dirty brown colour indicated the presence of flavonoids.^[6]

Animal study

The study was carried out on 40 Sprague Dawley rats procured from National Institute of Health (NIH), Islamabad for model feeding trials. International guidelines for the use of laboratory animals were followed during rodent feed trial. All the rats were housed in well ventilated metal cages and provided normal diet for two weeks before the experiment for acclimatization and to ensure the normal growth and behavior. They were fed on normal diet and tap water ad libitum. At the commencement of study, some rats were slaughtered to get baseline values. For efficacy trials, the research was carried out in two categories; normal and hyperglycemic. For studies, three groups of rats were planned to have five rats in each. One group was given control diet, while other two groups were fed on respective test diets respectively, during sixty days trial period. During entire study time, the animal room was maintained at a temperature of (23 \pm 2) °C and relative humidity of 55% \pm 5%, with 12 h light/dark cycle. At the culmination of the study, the overnight fasted rats were slaughtered to probe the effect of respective treatments on the selected parameters including glucose & insulin levels as well as hematological studies. And for an initial period of one week, basal diet was given to the rats to acclimatize them to the environment. Later, the diets containing jamun fruit and seed extracts were fed for sixty days. The experimental diet consisted of flour (82%), corn oil (10%), casein (4%), mineral mix (3%) and vitamin mix (1%). In Study II, high sucrose diet containing 40% sucrose was provided to the normal rats to determine the effect on serum glucose and insulin levels. And Simultaneously, the effect of fruit and seed extracts containing diets on the induced trait in relevant groups of rats was also assessed.

Nutraceutical (SE) and Nutraceutical (FE) diets were prepared by adding 3% extracts of seed and fruit in normal diet, respectively.^[5]

2. Aloe vera- Aloes is the dried juice of the leaves of the Aloe barbadensis miller, known as Curacao aloes; or of Aloe perryi Baker, known as Socotrine aloes; or Aloe ferox miller belongs to the family **Liliaceae**. Aloe vera contains the chemical constituents such as vitamins, enzymes, minerals, lignin, saponins, salicylic acids and amino acids. It also contains anthraquinone glycosides, aloin, barbaloin, aloe emodin, resins, homonataloin, aloesone, galactouronic acid, and glucosamines. The compounds were identified such as lophenol, 24-methyl-lophenol, 24- ethyl- lophenol, cycloartenol, and 24-methylene-cycloartanol which show the antihyperglycemic effect. These five phytosterols are evaluated for their antihyperglycemic effects in type 2 diabetes.^[8]





Fig. 2: Aloe Vera plant and leaf.

Preparation of A.vera leaf pulp extract

Aloe vera leaves, over 3 years old, were washed, weighed, peeled and the leaf pulp was scratched with a spoon. The pulp was homogenized with a homogenizer, mixed with an equal volume of phosphate buffered saline (0.1 M, PH= 7), homogenized again, kept at 4°C overnight then filtered through cloth. The clear filtrate was kept at -20°C in small portions until use. The yield of fresh aloe pulp was about 35% v/w in terms of starting fresh leaf weight. [9]

Animal study

Ethanol extract of A.vera leaf gel shows significant antihyperlipidaemic effect in streptozotocin induced diabetic rats at 300 mg/ kg for 21 days. The treatment of A. Vera in diabetic rats showed a marked increase in body weight, liver glycogen, decreased blood and urine glucose levels and normalized serum lipids. Oral administration of processed A.vera gel for 8 weeks in diet induced non insulin dependent diabetes mellitus in mice inhibits significantly plasma glucose level. Oral administration of polyphenol-rich A.vera extracts (350 mg/kg) with known concentrations of aloin (181.7 mg/g) and aloe- emodin (3.6 mg/g) for 4 weeks to insulin resistant ICR mice decreases significantly both body weight and blood glucose levels. The lophenol and cycloartanol, phytosterols isolated from A.vera gel inhibits blood glucose level at 25 g/kg/day respectively for 44 days in animal model of type- 2 diabetes.^[10]

Chemical Tests for determination of presence of phenolic compounds, free anthraquinones, saponins and flavonoids

- **1. Gelatin test-** 2ml of 1% solution of gelatin containing 10% NaCl is added to 1 ml of the extract. White precipitate indicates the presence of phenolic compounds.
- **2. Lead acetate test-** 3ml of 10% lead acetate solution was added to 1ml of the extract. Appearance of bulky white precipitate confirms the presence of phenolic compounds.
- **3. Ammonium hydroxide test-** 1ml of chloroform extract introduced into a test tube in addition to 1 ml of diluted NH₄OH and stirs the red colour which indicates the presence of free anthraquinones.
- **4. Foam test** About 1ml of the sample extract was boiled in 20ml of distilled water in a water bath and filtered; 10 ml of the filtrate was mixed with the 5 ml of the distilled water and mixed vigorously for 15 min to form a stable persist ant froth. The presence of froth after 5 min taken as an indication of presence of saponins.
- **5. Ammonia test** –A few drops of 1% NH₃ solution was added to 1ml of the extract in a test tube. Observation of yellow colour indicates the presence of flavonoids.^[11]
- **3. Momordica charantia** A well known plant bitter melon belonging to the family **Cucurbitaceae**. It is widely used for the treatment of diabetes. Oral administration of the fruit juice or seed powder resulted in a significant decline in FBG and pronounced amelioration of glucose tolerance exerting both insulin secretagogue and insulin mimetic activities. This potent antidiabetic activity mainly attributed due to the presence of insulin

like polypeptide known as polypeptide-P, similar in structure to the bovine insulin. It reduces plasma sugar levels when injected subcutaneously into type I diabetic patients and appears to inhibit gluconeogenesis. It also improves glucose tolerance in type II diabetes. Other hypoglycemic agents isolated from M. charantia comprise the sterol glucoside mixture charantin isolated from fruit and the pyrimidine nucleoside vicine abundant in the seeds.^[12]





Fig. 3: Momordica charantia fruit and seeds.

Preparation of crude extracts of M. charantia

About 1 kg of pulverized crude extract of M. charantia fruit was suspended in 10 L of double-distilled water and extracted by the 100% ddH₂ with an extraction temperature of 20-22°C, extraction frequency of 40 kHz, and extraction time of 0.5 h, which was provided by the Mesophase technologies, Inc. after the extraction, the size of residual powder particles was determined to be 70-300 nm using a laser particle size analyser and so as to determine its steroidal saponin contents (charantin) by spectrophotometry. The charantin rich extract of MC was then concentrated and dehydrated through the process of spray drying. All dried MCaqueous extracts (35% w/w) charantin were combined, and subsequently used for experimental study.^[13]

Animal study

The 6-week-old male KK/HIJ mice, weighing 19–22 g, were purchased from the Jackson Laboratory (Biolasco, Taiwan), and the 6-week-old male ICR mice, weighing 27–31 g, were from the National Laboratory Animal Center in Taipei, Taiwan. All animals were maintained in laminar flow cabinets under specific pathogen-free (SPF) conditions in facilities approved for Accreditation of Laboratory Animal Care and in accordance with Institutional Animal

Care and Use Committee (IACUC) of the Animal Research Committee in Chi-Mei Medical Center, Tainan, Taiwan. The two groups of mice were housed separately and maintained on a 12-h light/dark cycle, temperature 23 ± 3 C, and humidity $55 \pm 15\%$. The KK/HIJ mice (n = 16) were given a high-fat diet consisting of 40% (wt/wt) fat, orally, for 8 consecutive weeks (an average weight of 43 g) to establish a type 2-like diabetic mice model while the control group of KK/HIJ mice (n = 8) was given standard laboratory diet (GAFCO, Tema, Ghana). To setup a type 1-like diabetic mice model, ICR mice (n = 24) were given a single intra peritoneal injection of 150 mg/kg of streptozotocin, STZ (in citrate phosphate buffer). The extract of whole fruit of MC (200 mg/kg/day) was administered (4 and 8 weeks) orally to diabetic KK/HIJ (n = 8) and ICR mice (n = 8), respectively; while tolbutamide (3 mg/kg/day) was administered orally to ICR mice (n = 8) once a week as a positive control. [13]

Chemical test for characterization of charantin

- **1. Libermann- Burchard test**: Giving a play of colours changing from violet to blue to green and yellow with libermann -burchard test.
- 2. Decolourising dilute potassium permanganate and bromine water. [17]
- **4. Azadiracta indica-** It belongs to the family **Meliaceae**. It has been used for a long time in traditional medicine in treating several ailments, including diabetes. Its leaves stem bark and seeds possess hypoglycemic activity via increasing insulin secretion from the beta cells of the pancreas. Its leaves are characterized by the presence of high fibre content that is potent in diabetes management and controlling of post-prandial hyperglycemia through delaying gastric emptying, increasing viscosity of GIT content thus, suppressing digestion and absorption of carbohydrate with no risk of hypoglycemia, hyperinsulinemia and undesirable weight gain. The most important active constituents are azadirachtin and the others are nimbolinin, nimbin, nimbidin, nimbidol, sodium nimbinate, gedunin, salannin, and quercetin. Neem leaves contains flavonoids, triterpenoid, antiviral compounds and glycosides, which may help to manage blood glucose level. [12]





Fig. 4: Azadiracta indica leaves and seeds.

Preparation of extract

- 1. Boil about 20 neem leaves in half a litre of water for about 5 minutes. Then the leaves have begun to appear soft. The water will turn to deep green in colour. Strain and store this water in a container. And drink this decoction at least twice a day.
- 2. The paste of leaf extracts prepared with water is taken at a dose of 2-3 teaspoons daily in empty stomach.

Animal study

Administration of leaf extract of neem possesses antihyperglycemic and antidyslipidemic activity. And helps to normalizing blood glucose level and lipid parameters in streptozotocin induced diabetic rats. The polyherbal formulation containing neem and bitter leaf possesses significant antidiabetic and antihyperlipidemic activity at 400 mg/kg. The combined leaf extracts of Vernonia amygdalina and A. indica cause increase in insulin level and show antihyperglycemic action in diabetic rats.^[10]

Chemical Test for detection of terpenoids and flavonoids

Salkowski test- 1ml of each extract was mixed with 0.5 ml of chloroform and 1 ml of concentrated H_2SO_4 was carefully added to form a layer. A reddish brown coloration of the interface formed to show positive results for the presence of terpenoids.

Ammonia test- A few drops of 1 % NH₃ solution was added to 1 ml of the extract in a test tube. A yellow coloration was observed for the presence of flavonoids.^[11]

5. Annona Squamosa- It is a small, well-branched tree or shrub from the family **Annonaceae** that bears edible fruits called sugar-apples. The chemical constituents such as

anonaine, anolobine, aporphine are isolated from the parts of the plant. The plant also contains carvone, linalool, limonene, squamosin, and quercetin. Plant possesses antidiabetic activity and acts by promoting insulin release from the pancreatic islets, increasing utilization of glucose in muscle and inhibiting the glucose output from liver. Quercetin-3-O-glucoside isolated from Annona squamosa leaf inhibits glucose 6 phosphatase activity in the liver and lowers blood glucose level. Annona squamosa leaf extract also decreased blood triacylglycerol and total cholesterol levels in diabetic animals.^[16]





Fig. 5: Annona squamosa plant and leaves.

Preparation of plant extract

Leaves of annona squamosa were collected in the month of April and May from the gardens. The leaves were washed with water and shade dried. About 500 gm of crushed leaves were extracted twice with 5 L of boiling ethanol for 6 h. the resulting extract was cooled and filtered. The filtrate was evaporated in vaccum to give a residue.^[14]

Animal study

The aqueous extract of this plant leaf have many antioxidant effects. The blood glucose, hemoglobin, glycosylated hemoglobin, plasma insulin, antioxidant enzymes, lipid peroxidation in liver and kidneys were examined in STZ- induced diabetic rats. Oral administration of Annona squamosa aqueous extract for 30 days caused a significant reduction in the blood glucose, lipids, and lipid peroxidation, but the activity of the plasma insulin and antioxidant enzymes, like catalase and superoxide dismutase, increased. On the other hand, the activity of glutathione and glutathione peroxidase decreased. Generally, the

aqueous extract of this plant is useful for controlling blood glucose levels and improving plasma insulin and lipid metabolism. In addition, this extract is effective in preventing diabetic complications caused by lipid peroxidation and antioxidant systems in experimental diabetic rats.^[2]

Chemical tests for determination of presence of flavonoids and alkaloids

Flavonoids– **Shinoda's test** – A few mg of the Various AS extracts were dissolved in a few ml of methanol and Magnesium powder was added, followed by 5M HCl. Flavonoids gave a pink colour. Flavonoids are a group of about 4000 naturally occurring poly phenolic compounds, found universally in foods of plant origin.

Detection of alkaloids

Wagner's test - To a few ml of filtrate, few drops of Wagner's reagent are added by the side of the test tube, a reddish brown precipitate confirms the tests as positive.

Wagner's reagent- Iodine (1.27g) and Potassium Iodide (2g) were dissolved in 5ml of distilled water and the solution was made up to 100 ml with distilled water was added to a little of the extract dissolved in methanol. Alkaloids gave brown flocculent precipitate.^[15]

CONCLUSION

In this review we discussed about five medicinal plants for the treatment of diabetes mellitus. This review includes the information of active chemical constituents of the plants and chemical tests for detection of presence of chemical constituents which shows the antidiabetic activitiy. In the present review an attempt has been made to investigate the antidiabetic medicinal plants and may be useful to the health professionals, scientists and scholars working in the field of pharmacology and therapeutics to develop antidiabetic drugs.

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