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Review Article

# THERAPEUTICALLY EFFECTS OF VARIOUS PLANT EXTRACT ON DIABETES MELLITUS

Vishal Garg, **Dinesh Jindal***, Ajay Saini and Kriti Gupta

Jaipur School of Pharmacy, MVGU, Jaipur, India

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## ABSTRACT

Diabetes mellitus (DM) is becoming one of the leading causes of death worldwide because of its adverse complications that include cardiovascular related diseases and chronic kidney disease. DM is considered a menace to public health due to the unavailability of adequate drugs to manage this condition, especially in poor developing countries such as those in the African continent. Proper management and treatment of this is lacking, which possibly explains escalating percentages of morbidity and mortality associated with it. In Africa, as a result of poor socio-economic conditions, it is nearly impossible to properly monitor and manage DM. Globally, the commercially available drugs used in diabetes treatment regimens have been associated with drastic side effects and are also mostly unaffordable in some developing countries (particularly in Africa), hence the need to investigate cheap and readily available medicinal plants. It is important to thoroughly investigate the activities of medicinal plants in animal models to identify both their therapeutic and toxic effects. This review paper examines the potential anti-diabetic benefits of some selected plants.

**Keywords:** Diabetes mellitus; Hyperglycemia; Metabolic disarray; Hypoglycemic agents; Herbal formulations.

## INTRODUCTION

A group of metabolic ailments exemplified through hyperglycemia termed as diabetes mellitus fallouts from deficiency in insulin discharge, insulin attainment, or equally [1]. Pancreas, positioned after the abdomen is an appendage where insulin is prepared. The pancreas hold bunch of cells named islets. Inside the islets, beta cells build insulin and liberate it into the blood (Figure 1) [2]. Glucose assembles up within the blood as an alternative of being captivated through cells inside the body if β-cells don't generate adequate insulin, or the body doesn't retort to the insulin that is there, directing to prediabetes or diabetes. Prediabetes is a form during which blood glucose intensity or A1C levels-which reveal normal blood glucose levels-are elevated than usual but not high enough to be analyzed as diabetes. In diabetes, the body's cells be famished of vigor regardless of lofty blood glucose intensity [2].

Diabetes is provoked via as well as linked by means of metabolic impediment that can afterward escort toward untimely fatality [3]. The persistent hyperglycemia of diabetes be related by durable injury, dysfunction, as well as failure of diverse organs, mainly the eyes, kidneys, nerves, heart, and blood vessels [1].

### Etymology

The terms "Diabetes" and "Mellitus" are derivative of Greek "Diabetes" denote "a passer throughout a siphon" while the "Mellitus" denotes "sweet". It is

reflection that the Greeks name it so owing to the extreme amount of urine formed via diabetics attracted flies and bees [3].

## Classification

Diabetes is deviated into two groups: type 1 diabetes and type 2 diabetes. A third type diabetes is Gestational diabetes, its occur only in pregnancy [2].

**Type 1 Diabetes (Moderate Generation Of Insulin) [4,5]**

A lifetime (chronic) ailment with elevated intensity of glucose level in the blood [6]. The production of insulin is faulty hence glucose cannot t ra v e l inside the cells [5]. Type 1 diabetes is occurring at any age. Most often the disease is detected in children, teenagers or young adults [6]. The rate of cell damage is somewhat inconsistent in this type of diabetes being hasty in some persons (chiefly infants and children) and deliberates in others (primarily adults). Several patients, mostly kids and youngsters may begin with ketoacidosis as the first symptom of the disease. Others comprise reserved fasting hyperglycemia that can speedily alter to stern hyperglycemia and/or ketoacidosis in the occupancy of disease or other strain [1].

**Type 2 Diabetes (Weakened Reaction To Insulin Or B-Cell Dysfunction) [4]**

The disease consists of a group of dysfunctions exemplified hyperglycemia from the mixture of resistance to insulin action, insufficient insulin secretion, and extreme or improper glucagon secretion [7].

Greatly frequent and accounts for 90-95% of all diabetes.

Adults are chiefly affected though newly Type 2 has commenced developing in kids.

There is a sturdy connection between Type 2 diabetes, Physical Inactivity and fatness [5].

### Gestational Diabetes

A disease defined by glucose hypersensitivity of inconsistent sternness with beginning of initial identification in pregnancy. Hyperglycemia in pregnancy is found to be related through d i v e r s e motherly as well as prenatal undesirable outcome. Their offspring will contain a lifetime raise possibility of glucose fanaticism, stoutness plus metabolic disorder while the mother will contain an elevated threat of metabolic disorder and diabetes in the future [8].

### Symptoms[5]

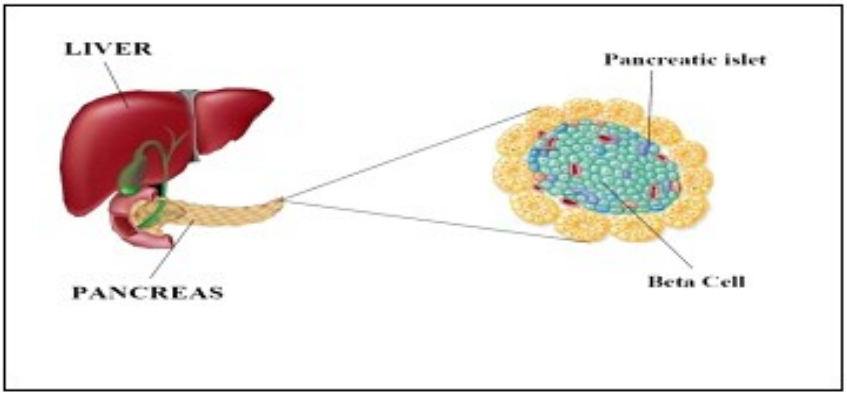
Indistinct visualization
Abnormal dehydration
Recurrent urination
Slow-healing incisions
Baffling weariness
Hasty mass loss (Type 1 diabetes)
Erectile dysfunction
Lack of sensation or itching in hands or feet

### Pathophysiology

Insulin is the key hormone to control the uptake of glucose from the blood into various cells of the body, chiefly liver, muscle, as well as adipose tissue. Therefore, its deficiency or the tactlessness of its receptors depicts a vital task in the entire type of diabetes mellitus. Beta cells (β-cells), found in the islets of Langerhans in the pancreas, release insulin into the blood in response to rising levels of blood glucose, typically after eating. About two third of the body's cells use insulin for glucose absorption from the blood for use as fuel, for conversion to other needed molecules, or for storage. Decreased insulin release from the beta cells and the breakdown of glycogen to glucose is an outcome of lower glucose levels. The hormone glucagon primarily controls this process, which acts in the converse manner to insulin.

If the amount of insulin available is insufficient, if cells respond poorly to the effects of insulin (insulin insensitivity or insulin resistance), or if the insulin itself is defective, then glucose will not be absorbed properly by the body cells that require it, and it will not be stored appropriately in the liver and muscles. The net result is steadily elevated intensity of blood glucose, reduced protein synthesis, plus additional metabolic derangements, such as acidosis. while the glucose concentration in the blood vestiges elevated above time, the kidneys will achieve a portal of reabsorption, excretion in the urine (glycosuria) (Figures 2 and 3) [9].

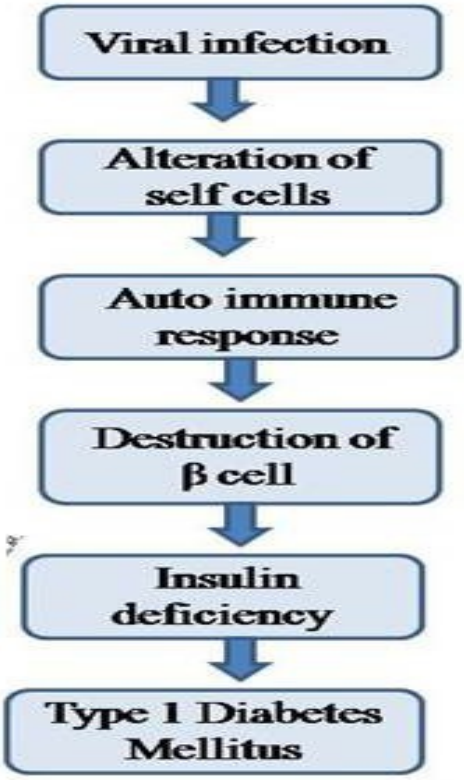
Hasty mass loss (Type 1 diabetes), Erectile dysfunction, Lack of sensation or itching in hands or feet [5].




## Etiology

### Causes Related To Type-1 Diabetes

- Hereditary Vulnerability: Genetics plays an essential part in determining who is likely to develop type 1 diabetes. Genes are passed down from biological parent to child. Genes carry instructions for making proteins that are needed for the body's cells to function. Variations in genes that affect more than 1 percent of a population group are called gene variants (Figure 4) [1].
- Certain gene variants that carry instructions for making proteins called human leukocyte antigens (HLAs) on white blood cells are linked to the risk of developing type 1 diabetes. Some combinations of HLA gene variants predict that a person will be at higher risk for type 1 diabetes, while other combinations are protective or have no effect on risk [2].
- Autoimmune damage of Beta Cells: In this form of diabetes, T cells hit and demolish beta cells. The course of action starts well earlier than diabetes sign emerges and persists following identification. Type 1 diabetes is not identified frequently until major beta cells have by now been damaged. At this peak, an individual wants every day insulin therapy to stay alive [2].
- Ecological aspects: Ecological aspects such as foodstuffs, viruses and pollutants might play a part in the advancement of type 1 diabetes, although the precise character of their function has not been resolute. Few speculations propose that Ecological features prompt the autoimmune damage of beta cells in people with a hereditary vulnerability to diabetes. Further hypothesis imply that ecological features play an enduring part in diabetes, yet subsequent to diagnosis [2].



For insulin, resistance as well as type 2 diabetes however also for heart plus blood vessel ailment furthermore termed cardiovascular disease (CVD). This surplus "abdomen stout" produces hormones along with additional materials that be able to cause dangerous unremitting consequences inside the body like harm to blood vessels [2]. Insulin Resistance: An ordinary situation in public who are heavy or overweight contain surplus abdominal fat.

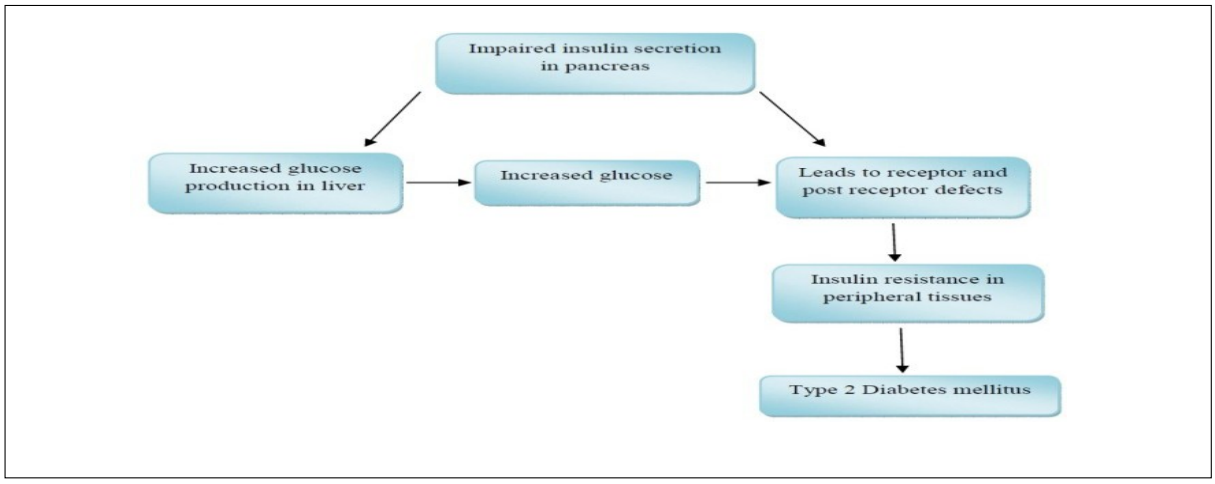
**Causes related to Type-2 diabetes**

Hereditary vulnerability: Genes play a major piece in propensity to type 2 diabetes. Comprising definite genes or mixture of genes might augment or lessen a person's danger for possessing the ailment. The role of genes is recommended by the elevated pace of type 2 diabetes in families and identical twins and extensive deviation in diabetes predominance through traditions. Learnings have revealed that variants of the TCF7L2 gene enhance vulnerability to type 2 diabetes [2].

Fatness and Physical Sluggishness: Physical sluggishness and fatness are stoutly linked via growth of type 2 diabetes. When these hazardous features are nearby the people who are genetically susceptible to type 2 diabetes are more vulnerable. Difference among caloric ingestion along with physical activity can lead to fatness which cause insulin resistance and is frequent within public with type 2 diabetes. Fundamental heaviness, within which an individual have surplus abdominal fat, is a foremost hazard issue not merely for insulin resistance as well as type 2 diabetes however also for heart plus blood vessel ailment furthermore termed cardiovascular disease (CVD). This surplus "abdomen stout" produces hormones along with additional materials that be able to cause dangerous unremitting consequences inside the body like harm to blood vessels [2].

Insulin Resistance: An ordinary situation in public who are heavy or overweight contain surplus abdominal fat, as well as arenot bodily energetic. Muscle, fat, as well as liver cells impede reacting correctly toward insulin, forcing the pancreas to balance through generating superfluous insulin. Blood glucose intensity resides within the usual array, as long as β- cells are capable to generate adequate insulin. However, as insulin production wane since β- cell dysfunction, glucose intensity increases foremost to pre-diabetes or diabetes [2].

Irregular Glucose Production through the Liver: An abnormal increase in glucose production by the liver also contributes to high blood glucose levels in some people with diabetes. Generally, the pancreas discharges the hormone glucagon when blood glucose as well as insulin intensity is small. The liver is stimulated by glucagon and produces glucose which is released into the bloodstream. Glucagon levels drop, when blood glucose and insulin levels are high after a meal and the liver stores surplus glucose intended for later, as needed. In several populaces with diabetes, glucagon intensity resides elevated than required. Elevated glucagon intensity cause the liver to generate unwanted glucose, which throw in to elevated blood glucose intensity [2].



**Complications Acute [10,11]**

Diabetic ketoacidosis
Hyperglycemia hyperosmolar state
Hypoglycemia
Diabetic blackout
Erectile Dysfunction
Respiratory contagion
Periodontal sickness

**Chronic [12]**

Diabetic retinopathy
Diabetic nephropathy
Diabetic neuropathy

**Diagnosis**

Following tests are employed in diagnosing of diabetes:

Random plasma test: This is the simplest test that requires no fasting prior to the test. Blood glucose of 200 or more than 200 mg/ dl possibly specify diabetes but have to be confirmed again [12].

Fasting plasma glucose test: The test requires eight hours fasting. More than 126 mg/dl blood glucose on two or more tests carried out on diverse days confirm a diabetes diagnosis [12].

Oral glucose tolerance test: This test is carried out when random plasma glucose test is 160-200 mg/dl and the fasting plasma test is 110-125 mg/dl. This blood test estimates body's response to glucose is estimated. Fasting of at least eight but not more than 16 hrs is required in this test. Fasting not bodily energetic. Muscle, fat, as well as liver cells impede reacting correctly toward insulin, forcing the pancreas to balance through generating superfluous insulin. Blood glucose intensity resides within the usual array, as long as β- cells are capable to generate adequate insulin. However, as insulin production wane since β- cell dysfunction, glucose intensity increases foremost to pre-diabetes or diabetes [2].

Eight but not more than 16 hrs is required in this test. Fasting glucose intensity is resolute furthermore provide 75 gm of glucose, 100 gm for pregnant women. Every 30 minutes to one hr for two or three hrs the blood is tested. If the glucose level at two hrs is less than 140 mg/dl, then this test is normal. A diabetes diagnosis is confirmed with the fasting level of 126 mg/dl or greater and two-hour glucose level of 200 mg/dl or Higher [12].

HbA1C (A1C or glycated hemoglobin test): This test can be used for the diagnosis of both prediabetes and diabetes. Average blood glucose control for the past 2 to 3 months is measured. Moreover, this test is more convenient as no fasting is required. When the A1C is 6.5% or higher, diabetes is diagnosed [13,14].

Fructosamine test: The main component of plasma proteins is albumin. Since albumin too includes open amino clusters, non- enzymatic response among glucose within plasma occurs. Thus, glycated albumin be able to equally serve up like a indicator to examine blood glucose. Glycated albumin is generally taken to present a fair measure of regular blood glucose concentration greater than a time of 1 to 3 weeks [12].

**Management**

Diabetes mellitus being a persistent ailment for which there is no identified treatment excluding very explicit situation. Maintaining blood sugar levels since close toward normal being the attention towards management, exclusive of causing stumpy blood sugar. This be able to generally consummate by means of a well diet, work out, mass loss, along with employment of suitable drugs (insulin during the case of type 1 diabetes; oral drugs, as well as probably insulin, during type 2 diabetes) [9].

Apparently, the cornerstone in the management of diabetes mellitus is life style. In the prevention of diabetes and cardiovascular disease life style management is recognized as being an essential part. The dietetic managing of diabetes mellitus being an accompaniment of lifestyle management and has a affirmative result on long term fitness along with quality of life. Dietetic managing seeks on best metabolic control with creating equilibrium among food ingestion, bodily motion in addition to medicine in the direction of evading problems. The dietary objective in type 2 diabetes is for improved glycemic and lipid levels and weight loss as appropriate [3].

**Treatment**

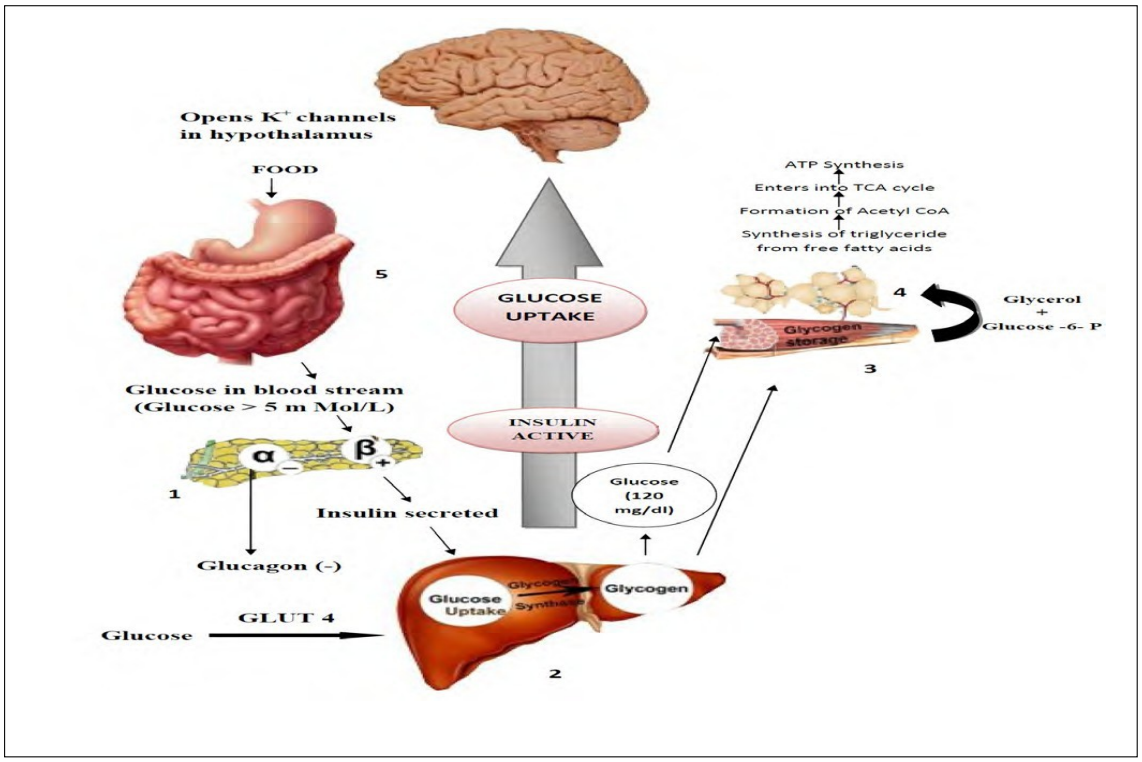
Medicines employed to extravagance diabetes act consequently through lessening blood sugar levels. Here are a number of diverse classes of anti-diabetic medicines (Figure 5) [9].

Action on pancreas through jamming K+ ions in β-cells to stimulate insulin emission: Meglitinides, Sulphonylureas.

Reduce Gluconeogenesis by action on liver: Biguanide and Thiazolidine diones.

Action on muscle along with adipose tissue to enhance marginal glucose uptake: Biguanide Metformin.

Insulin sensitivity is augmented through activation of receptors: Thiazolidine diones.Delays glucose absorption by acting on intestine: α-glucosidase inhibitors.




## Herbal Treatment for Diabetes

Herbal drugs have been employed from the time of the beginning of human beings on this earth and as a consequence is approximately as old as time itself [15]. Even though here are numerous synthetic medications designed for patients, however it is the reality that it has in no way been account that someone had recovered completely from diabetes. The present oral hypoglycemic agents generate adverse consequence. Therefore, during the recent times great consideration have been aimed on the antidiabetic potential of therapeutic foliage plus their herbal formulation in the management of ailment [16]. Substitute to these synthetic agents various herbal plants with hypoglycemic assets are identified since crosswise the planet. 21,000 plants have been listed by the World Health Organization (WHO), which are utilized for therapeutic rationale around the world [17-24]. Several therapeutic plants with possible antidiabetic actions accounted with their promising mode of action have been listed below (Table 1) [16].

### Polyherbal Formulation for Diabetes Dihar

A polyherbal formulation holding eight diverse herbs *Syzygium* cumini, Momordica charantia, Emblica officinalis, Gymnema sylvestre, Enicostemm, Azadirachta indica, Tinospora cordifolia and Curcuma longa.

Literatures revealed that combination of these eight herbs shows effective Anti-hyperglycemic activity in Streptozotocin (STZ,45 mg/kg iv single dose) induced type 1 diabetic rats.

**Diasol**

Holds plant extracts of Eugenia jambolana, Foenum graceum, Terminalia chebula, Quercus, infectoria, Cuminum cyminum, Taraxacum officinale, Emblica officinalis, Gymnea sylvestre, Phyllanthus nerui and Enicostemma littorale.

Previous investigation showed Diasol produced 63.4% reduction of blood glucose level in a dose of 125 and 250 mg/kg b.w i.p and proved to be effective antidiabetic polyherbal formulation.

**Dia-Care**

Containing Sanjeevan Mool; Himej, Jambu beej, Kadu, Namejav, Neem chal is a herbal formulation alleged to be efficient for together Type 1, Type 2 diabetes surrounded by 90 days of treatment and heals within 18 months.

With 1/2 glass of water, approx. 5 grams (1 tea spoon) powder is blend stirred well set aside overnight and filtered. The filtrate is taken in the morning on empty stomach.

**Table 1:** Herbal plants possessing antidiabetic activity with their mode of action

| Botanical Name | Common Name | Part Used | Active Constituent | Mode of Action |
|---|---|---|---|---|
| Aegle marmelos [16] | Bael [18] | Leaf [19] | Aegelin [24] | Augments consumption of glucose each via straight stimulation of glucose uptake otherwise via the arbitration of improved insulin discharge and have strong antioxidant activity, which can account for the hypoglycemic potential [16] |
| Allium cepa [16] | Onion [20] | Bulb [21] | Quercetin [24] | Lessens oxidative strain as well as conserve pancreatic beta cell reliability [24] |
| Azadirachta indica [23] | Neem [22] | Leaf and bark [23] | Quercetin, rutin, and nimbidin [23] | β cells rejuvenation [16] |
| Brassica juncea [16] | Indian mustard [24] | Seed [24] | Isothiocyanate glycoside singrin [15] | Hepatic glycogen and glycogenesis mass is increased and the activity of glycogen phosphorylase and gluconeogenic enzymes is repressed, directs the reduction in glycogenolysis and gluconeogenesis [16] |
| Cajanus cajan [20] | Pigeonpea [21] | Leaves [21] | Two globulins, cajanin and concajanin [20] | Plasma glucose extent is lowered [16] |
| Eucalyptus globules [22] | Blue gum [23] | Leaves [22] | Polyphenols, proanthocyanidins, anthocyanins [22] | Hamper α-glucosidase [23] |
| Aloe vera [24] | Aloe [24] | Gel from leaves [24] | Barbaloin [24] | Stimulate production and/or discharge of insulin from pancreatic beta cells [17] |
| Catharanthus roseus [16] | Madagascar periwinkle | Leaf [16] | Indole alkaloid (vincristine) [15] | Raise mobilization of glucose [16] |

| | | | | |
|---|---|---|---|---|
| | [17] | | | |
| Cryptolepis Sanguinolenta [15] | Anantmul [15] | Stem [18] | Cryptolepine [15] | Glucose uptake is enhanced by 3T3-L1 cells [15] |
| Olea europia [15] | Olive [15] | Leaf [19] | Oleuropeoside [15] | Potentiates glucose, stimulation of insulin discharge and escalates peripheral uptake of glucose [15] |

.

**Diabeta**

A formulation obtainable in the capsule type is an anti-diabetic among mixture of verified anti-diabetic equipped with strong immunomodulators, antihyperlipidemics, anti-stress and hepato-protective of plant source include *Gymnema sylvestre, Vinca rosea, Curcuma longa, Azadirachta indica, Pterocarpus marsupium, Momordica charantia, Syzygium cumini, Acacia arabica, Tinospora cordifolia,* and *Zingiber officinale*.

**Karmin plus**

Holds Momordica charantia, Azadirachta indica, Picrorrhiza kurroa, Ocimum sanctum and Zinziber officinale is a local polyherbal formulation.

Banger et al. estimated its antidiabetic action and established that on two dosage stage by 200 mg/kg and 400 mg/kg body weight product confirmed efficacy for antidiabetic action [16].

**Examples Of Some Medicinal Plants Used In The Treatment Of Dm**

The following plants have been reported to treat DM and they are mainly used in the Eastern Cape region of South Africa. They include: *Artemisia afra*, *Vernonia amygadalina*, *Bulbine frutes- cens* and *Catharanthus roseus*[24].

**Artemisia afra**

*Artemisia afra* is a medicinal plant frequently used in to treat DM. *A. afra* is a shrub that usually reaches 2m in height with hairy, leafy stems. Studies carried out by Afolayan and Sunmonu,[24] showed this plant's ability to reverse diabetic oxidative stress in the pancreas of streptozotocin (STZ)-induced diabetic rats. They concluded that this was due to the reduction of lipid peroxidation that was accompanied by an increase in activity of antioxidant enzymes[24].

The plant has been studied by the same authors[25] to substanti- ate its anti-diabetic effects. In a 15 day experimental study, rats were divided into 6 groups where group 1 and group 2 were normal and diabetic controls respectively. Groups 3 to 5 were diabetic rats treated with aqueous extracts of (50, 100 and 200 mg/kg) of *A. afra* respectively. The 6th group consisted of dia-betic rats treated with glibenclamide, a standard drug for DM.

The results highlighted that the effects of the 200 mg/kg dosage had almost the same effects as glibenclamide. The effect of the plant on blood glucose levels showed a significant reduction with the greatest reduction seen in the 200 mg/kg concentra- tion. The oral glucose tolerance test indicated an equivalent blood glucose reduction between the plant extract and gliben- clamide. The study also monitored water/feed intake and weight changes. The results highlighted that *A. afra* prevented the pro- gression of the symptoms of diabetes namely polydipsia and polyphagia in*A. afra* treated diabetic groups when compared to the diabetic controls, which consumed higher quantities of water and feed [25].

**Bulbine frutescens**

*frutescens* is is well known for its use as a topical ointment as well as a digestive tonic[26,27]. Apart from the above mentioned uses, the plant has been used as a hypoglycaemic agent in the treatment of diabetes by traditional healers in the Nelson Man-dela Metropole of South Africa. To support these claims, van Huyssteen et al investigated the effects of *B. frutescens* in C2 and C12 muscle cell lines and in Chang liver cells by assessing glucose utilisation in treated cell lines. They reported that

aque- ous plant extract improved the glucose utility/uptake in these cell lines when compared to insulin [27]. A synergistic effect of ethanolic extract of *B. frutescens* with insulin on glucose utilisa- tion was also reported.

**Catharanthus roseus**

*roseus* or *Vinca rosea* is a shrub with distinct purple or white flowers that has its origin in Madagascar[26]. The hypoglycaemic nature of the plant was associated with the presence of various phytochemicals distributed throughout the plant. *C. roseus* was reported to be an anti-hyperglycemic plant [28] rather than a hy-poglycaemic plant as it increases glycolysis and glucose oxida- tion (via the Pentose phosphate shunt pathway). A 77.7% blood glucose reduction in treated diabetic rats was noted after 60 days of treatment. To validate earlier findings, other authors ob- served an increase in the activity of glucose metabolic enzymes as well as a decrease in lipid peroxidation, a driving factor in the development of diabetic complications [29]. An increase in glucose utilisation in hepatocytes was also reported [30].

**Vernonia amygadalina**

*Vernonia amygadalina*, also known as the bitter leaf, grows wildly in the KwaZulu Natal, Mpumalanga and the Eastern and Northern Cape regions of South Africa [23]. In folk medicine the plant was and still is being used to treat parasitic infections in- cluding malaria, diabetes and eczema. In attempts to confirm its anti-diabetic nature, several *in vivo* tests were carried out. *V. amygadalina* also reverses diabetic oxidative stress [31]. The abil- ity of the plant to curb diabetic oxidative stress was assessed in a series of experiments carried out in 3 groups of rats namely: normal control, STZ-induced non-treated and STZ-induced dia- betic treated with 200 mg/kg of the plant extract. Malondialde- hyde, glucose and lipid parameters were measured in all groups and the results indicated the hypolipidemic, hypoglycaemic and antioxidant effects of *V. amygadalina* in the diabetic treated group. The significant fall of triglyceride levels was associated with the delay of CVD progression [31]. These results collaborated the findings in which a reduction of low density lipoproteins, triglycerides and cholesterol was observed in diabetic Albino rats [32]. A dose related reduction in blood glucose levels after *V. amygadalina* extract induction was reported in adult alloxan- ised rabbits [33]. In normal treated rabbits a fall from 96 mg/dL-48 mg/dL was observed while a 520 mg/dL-300 mg/dL fall in al- loxanised treated rabbits was reported [33]. The mode of action of this plant was suggested to be associated with insulin produc- tion and correction of carbohydrate metabolism [31]. abundant in Southern Africa. In South Africa, the African potato mainly grows in the Eastern Cape and all the way to the KwaZulu Natal area. It is also native in some parts of Lesotho, Mozambique and Zimbabwe. The plant is character- ised by strap shaped leaves and thick green hairy stems that are unbranched. The stems hold stalks supporting 2-12 yellow, star shaped flowers. At the base of the plant (just above the ground) lies the corm – a tuberous root stalk, that is wrongly referred to as the potato [23,36,37,38,39].

The tuberous part of the *H. hemerocallidea* is believed to pos- sess medicinal effects.[23,40] In folk medicine, the African potato was used for centuries to treat various ailments including the following: arthritis, cancer, diabetes mellitus, high blood pres- sure, psoriasis, gastric ulcers, wounds, tuberculosis, urinary tractinfections, asthma, central nervous system disorders and epi-lepsy.[23,35,36,37,38] Most of these were just anecdotal claims, how- ever scientific studies indicated that *H.hemerocallidea* possess anti-diabetic, anti-inflammatory, antioxidant, anti-nociceptive, antibacterial, anticancer and anti-diarrhoeal effects [36,37,40,41]. Previous reports highlighted that the African potato has the abil- ity to boost immunity in HIV infected patients; however, the plant was also linked to the suppression of the bone marrow. For this reason, the use of the plant in HIV infected patients has been terminated in South Africa [23,40].

These medicinal effects of the African potato are attributed to the presence of sterols, starols, sterolins, norlignan, daucos- terols and hypoxides

[35,39,41]. Amongst these phytochemicals; daucosterols, beta sitosterol and hypoxide are associated with its therapeutic activities. Hypoxide is the major component iso- lated from the corm. Hypoxide is a glycosylated norlignan that is derived from cinamic acid. In its natural form, hypoxide is in- active but can be converted to rooperol by beta glucosidase en- zyme. This conversion occurs in the gut in humans; in animals bacterial beta glucosidase catalyses the conversion. Rooperol is a bioactive compound that has powerful antioxidant properties in human blood [35,39,40,41,42].

**Anti-diabetic activities of H. hemerocallidea in experimental studies**

In reference to experimental studies carried out by several authors; *H. hemerocallidea* was shown to be an anti-diabetic plant [36,42,43,44]. In a study carried out by Ojewole,[36] STZ-induced diabetic rats were divided into 7 groups made up of 8 rats per group. Five groups were subjected to different concentrations of aqueous plant extract (50, 100, 200, 400 and 800 mg/kg). Depending on the group; the other 2 groups were treated with either chlorpropamide (a reference drug) or distilled water (in diabetic control). After STZ administration, animals were fasted for 16 hours, after fasting; rats were orally treated with respec- tive dosages of the aqueous plant extract. Blood glucose levels were measured at 1, 2, 4 and 8 hours post treatment. The results indicated that all extracts significantly reduced blood glucose levels and the reduction was dose dependent. The greatest reduction of 41% was observed in the group that was treated with 800 mg/kg. In addition; treatment with chlorpropamide decreased blood glucose levels by 65%. Therefore the 800 mg/ kg of the plant extract had almost the same effect on blood glucose reduction as chlorpramide.[36] In another study; treat- ment of fasted normal and STZ-induced diabetic rats with 800 mg/kg aqueous extract of *H. hemerocallidea* caused respective reductions in blood glucose levels by 30, 20% and 48, 54%.[42] The results obtained from this study indicate that *H. hemerocal- lidea* has hypoglycemic effects since a 30% reduction in normal fasted non-diabetic rats was observed. The presence of phyto- sterols was, however, linked to the hypoglycaemic action [42]. The hypoglycemic effect of *H. hemerocallidea* was also com- pared to the activities of glibenclamide in diabetic rats where the reduction was 55, 32% and 68, 71% respectively. Although *H. hemerocallidea* is less potent than glibenclamide, the plant still possess hypoglycemic effects, validating its folkloric use in South Africa [44].

The antioxidant capacity of rooperol (a bioactive compound of *H. hemerocallidea*) was also extensively evaluated using the thiobarbituric acid reactive substances assay, trolox equivalent antioxidant capacity and the ferric reducing antioxidant power assays [37,41]. Accumulation of reactive oxygen species instigates the rate of shrinkage of cells, chromatin condensation, DNA fragmentation as well as cellular apoptosis (programmed cell death) [44]. These cellular changes play an essential role in the pathogenesis of diabetic complications.

Hyperglycaemia causes tissue injury via 4 major mechanisms:

(1) increased glucose flux through the polyol pathway; (2) increased intracellular formation of AGEs (advanced glyca- tion end products); (3) activation of the protein kinase (PK)C pathway and (4) increased activity of the hexosamine pathway. Scientific evidence has shown that all four mechanisms are triggered by a particular upstream event that points to mito- chondrial overproduction of ROS [45]. The ability of rooperol to inhibit lipid peroxidation was compared to the activity of green tea and rooperol caused higher inhibition [41]. Rooperol has the ability to scavenge hydroxyl radicals and hence reducing mem- brane lipo-oxidation [41]. Therefore, the high antioxidant power of rooperol contributes immensely to its hypoglycaemic effects.

Our laboratory conducted further investigations into the ac- tivities of *H. hemerocallidea* in the liver and kidney tissue of diabetes-induced rats. Our findings correlated with the results obtained by [36,42,44] where significant decreases in

fasting glu- cose levels were also observed. Two dosages of 200 and 800 mg/kg of the aqueous extract were administered to diabetic groups and to a non-diabetic group (for toxicity evaluation). Based on our results, treatment of diabetic rats with a high dose of 800 mg/kg resulted in abnormal kidney function, which was indicated by abnormally elevated relative kidney weights when values were compared to the normal controls. The increase in relative kidney weights was linked to hyper filtration, aggrega- tion of lymphocyte, fat filtration and glomerular hypertrophy. The antioxidant evaluation of the kidneys of the group treated with 800 mg/kg of the plant extract did not differ significantly to the results obtained from the diabetic controls. These abnormal kidney function results are in agreement with the results ob- served by [47] who reported that *H. hemerocallidea* impairs kid- ney function by decreasing urinary sodium output, glomerular filtration rate and also increases plasma creatinine levels. Potent antioxidant activities of the plant were observed in the liver of treated groups which were assessed by measuring the oxygen radical absorbance capacity, ferric reducing antioxidant power, catalase, superoxide dismutase and reduced glutathione ac- tivities. It was concluded that *H. hemerocallidea* demonstrated excellent hypoglycemic and antioxidant effects especially in the liver with possible negative effects on the kidneys [43].

## LIMITATIONS AND RECOMMENDATIONS

DM incidence is rising in all regions of Africa even in the poorest of societies, inflicting a heavy burden on the limited resources available in these poor societies. The pathogenesis of DM portrays a serious therapeutic challenge. Despite all the efforts in DM research, no drug has been found that can cure diabetes or totally reverse its complications. Orthodox drugs have been linked to serious side effects, hence the call for medicinal plants in the treatment and management of DM. despite all the compelling.

Medicinal plants have shown significant potential to counteract the hyperglycaemic effects as they contain phytochemicals with minimum side effects. The use of medicinal plants in the treatment of DM has not gained much global recognition, despite all the compelling.

experimental evidence of hundreds of plants with anti-diabetic activities. Further research studies on medicinal plants are therefore recommended in African settings since it is almost im- possible for poor citizens to purchase the costly orthodox drugs. High throughput screening tests are necessary to isolate active compounds that may be developed into clinical agents either as natural products or maybe synthetically modified to enhance their clinical action. In previous studies, we successfully evalu- ated the effects of *Hypoxis hemerocallidea* in the liver and kidneys of STZ-induced rats. *H. hemerocallidea* significantly reduced hyperglycemic-induced oxidative damage in the liver tissue, however at higher concentrations negative effects were observed in the kidneys. We recommend that further tests to be done on hypoxide and rooperol the active compounds that are speculated to be responsible for both antioxidant and antidi- abetic effects.

## CONCLUSION

In recent years, diabetes has become a major health problem worldwide, affecting people across all ages, sex, ethnicities, and races, and its prevalence has been increasing at an alarming rate. The associated complications of synthetic drugs have lead to a shift towards locating natural resources showing anti diabetic activity. Thus, many different plants have been used individually or in formulations for treatment of diabetes and its complications. The above-mentioned plants have been considered for their possible hypoglycemic actions and the researchers have carried out some preliminary investigations. It is important to know the active component and their molecular interaction, which will help to analyze therapeutic efficacy of the product and also to standardize the product. Efforts are now being made to investigate mechanism of action of some of these plants using model systems.

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