

**OVERVIEW OF HERBAL TREATMENTS IN INDIA FOR DIABETES: A
SYSTEMATIZED REVIEW**Rasika D. Bhalke^{1*}, Mahendra A. Giri², Yash S. Lodha¹, Aditya S. More¹ and Pranjal S. Dange¹¹Sanjivani College of Pharmaceutical Education and Research Kopargaon, Maharashtra, India 423603.²Rajashri Shahu College of Pharmacy, Buldana.

Received on: 22/03/2021

Revised on: 11/04/2021

Accepted on: 01/05/2021

*Corresponding Author

Rasika D. Bhalke

Sanjivani College of
Pharmaceutical Education and
Research Kopargaon,
Maharashtra, India 423603.**INTRODUCTION**

Diabetes Mellitus (DM) is a metabolic disorder characterized by the presence of chronic hyperglycemia accompanied by greater or lesser impairment in the metabolism of carbohydrates, lipids, and proteins. DM is probably one of the oldest diseases known to man. It was first reported in an Egyptian manuscript about 3000 years ago. In 1936, the distinction between type 1 and type 2 DM was made. Type 2 DM was first described as a component of metabolic syndrome in 1988. The origin and etiology of DM can vary greatly but always include defects in either insulin secretion or response or both at some point in the course of the disease. Most patients with diabetes mellitus have either type 1 diabetes (which is immune-mediated or idiopathic) Type 2 DM (formerly known as non-insulin dependent DM) is the most common form of DM characterized by hyperglycemia, insulin resistance, and relative insulin deficiency. Type 2 DM results from the interaction between genetic, environmental, and behavioral risk factors. Diabetes also can be related to the gestational hormonal environment, genetic defects, other infections, and certain drugs.^[1]

Epidemiology

Estimates of diabetes for 2019 and projections to 2030 and 2045: In 2019, a total of 463 million people are estimated to be living with diabetes, representing 9.3% of the global adult population (20–79 years). This number is expected to increase to 578 million (10.2%) in 2030 and 700 million (10.9%) in 2045. The prevalence of diabetes in women in 2019 is estimated to be 9.0%, and 9.6% in men. The increase of diabetes prevalence with age leads to a prevalence of 19.9% (111.2 million) in people aged 65–79 years. Diabetes prevalence differed by World Bank Income group, with a higher prevalence among high-income countries (10.4%) and middle-income countries (9.5%) compared to low-income countries (4.0%). In 2045, diabetes prevalence is projected to reach 11.9%, 11.8%, and 4.7% in high-, middle- and low-income countries, respectively. Of all people living with diabetes, 67.0% are living in urban areas. Although prevalence is still higher in urban than in rural areas (10.8% vs. 7.2%), this difference is less marked than that reported in previous editions of the Atlas reflecting, no doubt, a degree of urbanization or “westernization” of rural areas. As an example, a recent study in Pakistan has reported the prevalence of diabetes to be only slightly higher in urban (28.3%) than in rural (25.3%) areas. At a country level, China (116 million), India (77 million), and the United States of America (31 million) are those with the high- est numbers of people living with diabetes in 2019. In 2030, China, India, and the United States of America will remain at the top of the list with 140, 101, and 34 million people with diabetes, respectively. In 2045, the top three countries with the

highest number of people with diabetes are expected to be China, India, and Pakistan, with 147, 134, and 37 million, respectively.^[2]

Types of Diabetes**Type 1 diabetes mellitus**

Type 1 diabetes mellitus (juvenile diabetes) is characterized by beta cell destruction caused by an autoimmune process, usually leading to absolute insulin deficiency. Type 1 is usually characterized by the presence of anti-glutamic acid decarboxylase, islet cell, or insulin antibodies which identify the autoimmune processes that lead to beta cell destruction. Eventually, all type1 diabetic patients will require insulin therapy to maintain normoglycemia.

Type 2 diabetes mellitus

The relative importance of defects in insulin secretion or the peripheral action of the hormone in the occurrence of DM2 has been and will continue to be cause for discussion. DM2 comprises 80% to 90% of all cases of DM. Most individuals with Type 2 diabetes exhibit intra-abdominal (visceral) obesity, which is closely related to the presence of insulin resistance. Besides, hypertension and dyslipidemia (high triglyceride and low HDL-cholesterol levels; postprandial hyperlipidemia) often are present in these individuals. This is the most common form of diabetes mellitus and is highly associated with a family history of diabetes, older age, obesity, and lack of exercise. It is more common in women, especially women with a history of gestational diabetes, and in Blacks, Hispanics, and Native Americans.

Gestational Diabetes Mellitus (GDM)

Gestational diabetes mellitus is an operational classification (rather than a pathophysiologic condition) identifying women who develop diabetes mellitus during gestation. Women who develop Type 1 diabetes mellitus during pregnancy and women with undiagnosed asymptomatic Type 2 diabetes mellitus that is discovered during pregnancy are classified with Gestational Diabetes Mellitus (GDM). In most women who develop GDM; the disorder has its onset in the third trimester of pregnancy.

Pathogenesis and Pathophysiology of Diabetes

There is a direct link between hyperglycemia and physiological & behavioral responses. Whenever there is hyperglycemia, the brain recognizes it and sends a message through nerve impulses to the pancreas and other organs to decrease its effect.

Type 1 diabetes mellitus

Type 1 Diabetes is characterized by autoimmune destruction of insulin-producing cells in the pancreas by CD4+ and CD8+ T cells and macrophages infiltrating the islets. Several features characterize type 1 diabetes mellitus as an autoimmune disease.

1. Presence of immuno-competent and accessory cells in infiltrated pancreatic islets.
2. Association of susceptibility to disease with the class II (immune response) genes of the major histocompatibility complex (MHC; human leukocyte antigens HLA)
3. Presence of islet cell-specific autoantibodies.
4. Alterations of T cell-mediated immunoregulation, in particular in CD4+ T cell compartment.
5. The involvement of monokines and TH1 cells producing interleukins in the disease process.
6. Response to immunotherapy.
7. Frequent occurrence of other organ-specific autoimmune diseases in affected individuals or their family members.

Approximately 85% of patients have circulating islet cell antibodies, and the majorities also have detectable anti-insulin antibodies before receiving insulin therapy. Most islet cell antibodies are directed against glutamic acid decarboxylase (GAD) within pancreatic B cells.

The autoimmune destruction of pancreatic β -cells leads to a deficiency of insulin secretion which results in the metabolic derangements associated with T1DM. In addition to the loss of insulin secretion, the function of pancreatic α -cells is also abnormal and there is excessive secretion of glucagons in T1DM patients. Normally, hyperglycemia leads to reduced glucagon secretion, however, in patients with T1DM, glucagon secretion is not suppressed by hyperglycemia. The resultant inappropriately elevated glucagon levels exacerbate the metabolic defects due to insulin deficiency. Although insulin deficiency is the primary defect in T1DM, there is also leads to uncontrolled lipolysis and elevated levels

of free fatty acids in the plasma, which suppresses glucose metabolism in peripheral tissues such as skeletal muscle. This impairs glucose utilization and insulin deficiency also decreases the expression of several genes necessary for target tissues to respond normally to insulin such as glucokinase in the liver and the GLUT 4 class of glucose transporters in adipose tissue explained that the major metabolic derangements, which result from insulin deficiency in T1DM are impaired glucose, lipid and protein metabolism.

Type 2 diabetes mellitus

In type 2 diabetes these mechanisms break down, with the consequence that the two main pathological defects in type 2 diabetes are impaired insulin secretion through a dysfunction of the pancreatic β -cell, and impaired insulin action through insulin resistance. In situations where insulin resistance predominates, the mass of β -cells transforms capable of increasing the insulin supply and compensating for the excessive and anomalous demand. In absolute terms, the plasma insulin concentration (both fasting and meal stimulated) usually is increased, although "relative" to the severity of insulin resistance, the plasma insulin concentration is insufficient to maintain normal glucose homeostasis. Keeping in mind the intimate relationship between the secretion of insulin and the sensitivity of hormone action in the complicated control of glucose homeostasis, it is practically impossible to separate the contribution of each to the etiopathogenesis of DM2.

Insulin resistance and hyperinsulinemia eventually lead to impaired glucose tolerance. Except for maturity-onset diabetes of the young (MODY), the mode of inheritance for type 2 diabetes mellitus is unclear. MODY inherited as an autosomal dominant trait, may result from mutations in the glucokinase gene on chromosome 7p. MODY is defined as hyperglycemia diagnosed before the age of twenty-five years and treatable for over five years without insulin in cases where islet cell antibodies (ICA) are negative.

Insulin resistance and hyperinsulinemia eventually lead to impaired glucose tolerance, Except for maturity-onset diabetes of the young (MODY), the mode of inheritance for type 2 diabetes mellitus is unclear. MODY inherited as an autosomal dominant trait, may result from mutations in the glucokinase gene on chromosome 7p. MODY is defined as hyperglycemia diagnosed before the age of twenty-five years and treatable for over five years without insulin in cases where islet cell antibodies (ICA) are negative.^[1]

HERBAL DRUGS USED IN DIABETES

Aegle Marmelose (Bael)

Aegle Marmelose is commonly known as bael belongs to the family Rutaceae. *Aegle marmelos* is native across the Indian subcontinent and Southeast Asia and is cultivated throughout Sri Lanka, Tamilnadu, Thailand, and Malesia. Bhavani R et.al. evaluated the hyperglycemic

effect of aqueous extract of *A. marmelos* leaves on diabetic rats. An ethanolic extract of *A. marmelos* was found to be reducing the blood sugar in alloxan-induced diabetic rats. This might be due to restoration of delays insulin response or inhibition of intestinal absorption of glucose due to reduction in the activity of intestinal glycosidases like sucrose, maltase, and lactase in the small intestine. On administration of *A. marmelos* extract to diabetes rats restore the protein level almost equal to group treated with Glibenclamide. It might be due to the increased uptake of glucose by the cell by stimulating the insulin receptor. This may inhibit the protein catabolism leads to positive nitrogen balance. The diabetic rat shows a significant decrease in plasma insulin. Extract treated group restore the plasma insulin significantly compares to Glibenclamide treated Group.^[3]

Allium sativum L (Garlic)

Allium sativum is commonly known as garlic belongs to the family Liliaceae. Allium species are native to the Northern Hemisphere, being spread throughout the holarctic region, from dry subtropics to the boreal zone, predominantly in Asia. The antidiabetic effect of garlic ethanolic extract (*Allium sativum L.*) was investigated by Eidi A et.al. in normal and streptozotocin-induced diabetic rats. Oral administrations of the garlic extract significantly decreased serum glucose, total cholesterol, triglycerides, urea, uric acid, creatinine, AST, and ALT levels, while increased serum insulin in diabetic rats but not in normal rats. A comparison was made between the action of garlic extract and glibenclamide (600 mg/kg) and result shown that antidiabetic effect of the extract was more effective than that observed with glibenclamide.^[4]

Annona Squamosa (sweetsop)

Annona Squamosa is commonly known as sweetsop belongs to the family Annonaceae. It is native to Argentina, Brazil, Chile, Islands, Bangladesh, Cambodia, China and India. Sangala R et.al. studied the hypoglycemic activity of methanolic and ethanolic extracts 200 mg/kg b.wt. of seeds of *Annona squamosa* and observed significant hypoglycemic activity in both normal and Alloxan induced diabetic rats due to the presence of more than one antihyperglycemic principles. On the 7th day of post-administration of methanol and ethanol extracts, the percentage of blood glucose-lowering potential was observed as 45.99% and 43.96% respectively; while standard Glibenclamide caused 59.21% reduction blood glucose in the untreated group appear to be higher than that in the treated group. It can be suggested that the methanol and ethanol extracts of *Annona squamosa* may exhibit dose-dependent action in a similar mechanism as Glibenclamide i.e., by stimulation of surviving β -cells to release more insulin.^[5]

Artocarpus Heterophyllus (Jackfruit)

Artocarpus Heterophyllus is commonly known as Jackfruit and belongs to the family Moraceae. It is native to the Western Ghats of southern India and the

rainforests of Malaysia. Shahin N et.al. investigated the hypoglycemic effect of the leaves of *Artocarpus heterophyllus* in normal and streptozotocin-induced diabetic rats. Treatment with extract of the leaves at dose 250 mg/kg to diabetic rats resulted in a significant reduction of serum glucose, total cholesterol, whereas a significantly increased level of high-density lipoprotein was observed.^[6]

Azadirachta indica (Indian lilac)

Azadirachta indica is commonly known as Indian lilac. It is native to Afghanistan, Pakistan, India, Sri Lanka, Bangladesh, Myanmar, and China. The anti-diabetic efficacy of *Azadirachta indica* in Alloxan monohydrate induced albino rats. The *Azadirachta indica* leaves shows similar effect like insulin treatment in alloxan monohydrate administered animal model. It is stated that *Azadirachta indica* leaves might have some ingredients to increase the output of insulin by binding to the receptors of the Beta cells of the Langerhans located in the pancreas. Once they bind to the Sulphonyl urea receptors, the K⁺-ATP channels are probably, closed and therefore the membrane is depolarized and insulin production is stimulated.^[7]

Bambusa vulgaris(Common Bamboo)

Bambusa vulgaris also known as Common Bamboo belongs to the family Poaceae. It is native to Indochina and the province of Yunnan in southern China. Senthilkumar MK studied the anti-diabetic activity of petroleum ether extract of *Bambusa vulgaris* leaves (PEBV) in Streptozotocin-induced diabetic rats. The results showed that the PEBV significantly lowered the fasting blood sugar level of hyperglycemic rats in a dose-dependent manner and it was also comparable to that of the standard drug Glibenclamide. The plant may act by either a pancreatic or extra-hepatic mechanism or both mechanisms.^[8]

Basella Rubra(Malabar spinach)

Basella Rubra is commonly known as Malabar spinach belongs to the family Basellaceae. It is native to southern parts of India. Nirmala an et.al. investigated the beneficial effects of *Basella rubra* in streptozotocin-induced diabetic rats. They observed in pancreatic sections of diabetic rats fed with *B. Rubra*, the islets normal compared to diabetic control rats (insulinitis was observed). In the liver, the change caused after induction of diabetes was global microvesicular steatosis. The portal tracts appeared normal and central veins appeared congested, which was brought back to normal after feeding with *B. rubra*. While, in the kidney sections, of diabetic control rats and diabetic rats fed with *B. rubra* no histopathological changes were noticed. The results demonstrate that the leaf pulp of *B. rubra* possesses a strong hypoglycemic effect in streptozotocin-induced diabetic rats. Hypoglycemic action of *B. rubra* in diabetic rats may be possible through the insulin-mimetic action or by another mechanism such as stimulation of glucose uptake by peripheral tissue, inhibition of

endogenous glucose production, or activation of gluconeogenesis in liver and muscle.^[9]

Beta vulgaris (Beet)

Beta vulgaris is commonly known as a beet belongs to the family Amaranthaceae. It is native to India. Kumar S et.al. studied the anti-diabetic and haematonic properties of *Beta vulgaris* juice in an alloxan-induced experimental animal model. *Beta vulgaris* juice was found less effective than that of the insulin treatment group. The result indicates that *Beta vulgaris* juice has the property to lowers blood glucose levels. Alloxan monohydrate facilitates the production of free radicals and causes tissue damage. The beta cells of the pancreas are susceptible to such damage. It appears from the this investigation that the *Beta vulgaris* juice might have tissue repairable and restorative capacities.^[10]

Biophytum Sensitivum (Mukkutti)

Biophytum Sensitivum is commonly known as Mukkutti belongs to the family Oxalidaceae. It is commonly found in the wetlands of Nepal, tropical India, and other Southeast Asian countries. Chitravel R et.al. studied effect of oral administration of aqueous, ethanol, and ethyl acetate extracts of *B. sensitivum* to diabetic rats at a dose of 200 mg/kg body weight. Results reveals significant reduction in blood glucose in streptozotocine induced diabetic rats at different treatment period. *B. sensitivum* extracts treated diabetic rats were significantly recovered from a diabetic condition such as, polyphagia, polyurea, and hypoglycemia. *B. sensitivum* treatment decreased the blood glucose and Glycosylated hemoglobin level, and increased serum insulin level which were more or less similar to the diabetic treated rats treated with glibenclamide and control rats. The administration of the aqueous ethanolic extract, ethyl acetate extract, and ethanolic extract of *Biophytum Sensitivum* whole plant increased the serum insulin level which may be due to increased pancreatic secretion from existing β cells.^[11]

Boerhaavia diffusa (Punarnava)

Boerhaavia diffusa is commonly known as Punarnava belongs to the family Nyctaginaceae. It is native to India. Nalamolu RK et.al. studied the glucose-lowering activity of the leaf extract was studied in streptozotocin-induced (65 mg/kg, i.v.) NIDDM model diabetic rats after oral administration of the extract at daily doses. the leaf extract of *B. diffusa*. The chloroform extract of *B. diffusa* has significant antidiabetic activity and this supports the traditional usage of the plant by Ayurvedic physicians for the control of diabetes. *B.diffusa* produced a dose-dependent reduction in blood glucose in streptozotocin-induced NIDDM rats comparable to that of glibenclamide. The results indicate that the reduction in blood glucose produced by the extract is probably through rejuvenation of pancreatic β -cells or extrapancreatic action.^[12]

Bouvardia Terniflora (Firecracker bush)

Bouvardia Terniflora is commonly known as Firecracker bush belongs to the family Rubiaceae. It is native to Mexico, the range extending south into Honduras and north into the southwestern United States. Perez GRM et.al. Studied Hypoglycemic effect of activity-guided fraction which on chemical analysis led to the isolation of two triterpenes (Ursolic acid and oleanolic acid) from the chloroform extract of the dried stem of *B. terniflora*. The compounds lowered blood sugar levels in normal and alloxan diabetic mice. compounds isolated from the active fraction were tested for their hypoglycemic and antihyperglycemic activities. Ursolic acid and oleanolic acid were administered intra peritonically at doses of 25,50, 75 mg/kg to alloxan diabetic and normal mice. Both substances reduced blood glucose levels and a dose-dependent manner. The maximum blood sugar lowering is seen in identical amounts of ursolic acid (blood sugar lowering is seen 61.25%) and tolbutamide (blood sugar lowering is seen 63.70%).^[13]

Brassica nigra (Black mustard)

Brassica nigra is commonly known as black mustard belongs to the family Brassicaceae. It is native to probably native to northern Africa, western and central Asia, and parts of Europe. Anand P et.al. studied the effect of oral administration of AEBN for two months on glycolytic and gluconeogenic enzymes in liver and kidney tissues of rats with streptozotocin (STZ) induced diabetes mellitus. They observed higher gluconeogenic enzymes activities and decreased glycolytic enzymes in both the liver and kidney tissues during diabetes. However, in diabetic rats treated with AEBN for two months, a decrease of serum glucose, increase of serum insulin. Insulin and release of insulin from the pancreas (shown in vitro from the isolated pancreas) along with the restoration of key regulatory enzyme activities of carbohydrate metabolism and glycogen content were observed. The therapeutic role of AEBN in STZ induced diabetes as exemplified and can be attributed to the release of insulin from the pancreas and the change of glucose metabolizing enzyme activities to normal levels, thus stabilizing glucose homeostasis in the liver and kidney.^[14]

Brassica Juncea (Brown Mustard)

Brassica Juncea is commonly known as Brown Mustard belongs to the family Brassicaceae. It is native to India. Valavala VK et.al. investigated the effect of *Brassica juncea* leaf extract (BJLE) on streptozotocin-induced diabetic cataract in Wistar rats. Results suggest that *Brassica juncea* leaf extract can be effective against hyperglycemia-induced oxidative and osmotic stress as well as the subsequent development of diabetic cataracts. A combination of glycemic control, aldose reductase inhibition, and antioxidant potential could be the mechanism in delaying the cataract formation by BJLE.^[15]

Cassia auriculata (Avaram)

Cassia auriculata is commonly known as avaram belongs to the family Fabaceae. It is native to India and Sri Lanka. Kumar JSP et.al. studied the protective effect of *Cassia auriculata* L. flower extract (CAE) in a high-fat diet and streptozotocin-induced type 2 diabetes (T2DM) rats. T2DM rats showed significantly elevated glucose and reduced c-peptide levels in serum. Also, there was a significant increase in serum marker enzymes of liver toxicity-alanine transaminase (SGPT), aspartate transaminase (SGOT), and alkaline phosphatase (ALP) along with a significant reduction in liver glycogen and increase in lipid peroxidation levels. There was also deregulation in lipid levels in plasma and liver and a significant reduction in antioxidant enzymes in plasma, liver, and pancreas. Treatment with *Cassia auriculata* extracts caused significant improvement in the glucose, insulin, lipid levels in plasma, and the antioxidant status of the liver and pancreas.^[16]

Caesalpinia bonducella F (Grey Nicker)

Caesalpinia bonducella F. is commonly known as Nata Karanja belongs to the family Fabaceae. It is native to India, Sri Lanka, and Andaman, and the Nicobar Islands. Chakrabarti S et.al. studied the antidiabetic effect of aqueous and ethanolic extracts of the seeds in both type 1 and 2 diabetes mellitus in Long Evans rats. Significant blood sugar lowering effect (PB/0.05) of *C. bonducella* was observed in the type 2 diabetic model. The activity of *C. bonducella* (aqueous and ethanolic extract) in both type 1 and 2 models is due to increase uptake of glucose for the formation of glycogen by enhanced glycogenesis. This may be the probable mechanism for the hypoglycemic action, as the drug has no role in gut sugar absorption.^[17]

Carica papaya (Papaya)

Carica papaya is commonly known as Papaya belongs to the family Caricaceae. It is native to India. Solikhah TI et.al. studied the effect of *Carica papaya* leaf ethanolic extract on the blood sugar level of diabetic mice induced by alloxan at a dose of 1000 mg/kg body weight. The administration of papaya leaf ethanol extract with 3 doses and glibenclamide at a dose of 2 mg/kg body weight could reduce blood glucose levels in diabetic Wistar mice induced by alloxan. The administration at a dose of 1000 mg/kg body weight of papaya leaf ethanol extract is more effective in reducing blood glucose levels in diabetic Wistar mice compared to 2 mg/kg body weight of glibenclamide. *Carica papaya* leaf ethanol extract also had several chemical substances, including saponins, flavonoids, terpenoids, tannins, and alkaloids, which causes hypoglycemia. Flavonoids, terpenoids, saponins, and tannins give antioxidant activities, which can capture free radicals produced by the oxidation reaction of alloxan. The active substance contained in papaya leaf also acts in stimulating the release of insulin from beta-pancreatic cells and the release of somatostatin and suppresses the secretion of glucagon and reduce oxidative stress. Alkaloids and saponins can stimulate

the secretion of insulin from pancreatic beta cells. Terpenoids, like triterpenoids, can increase the absorption of glucose by copying the function of insulin and as an insulin sensitizer.^[18]

Catharanthus roseus (Periwinkle)

Catharanthus roseus is commonly known as Periwinkle belongs to the family Apocynaceae. The plant is also naturalized throughout subtropical Asia, Africa, and America. Leena M et.al. studied antidiabetic effect of the leaf extracts of *Catharanthus roseus* in alloxan-induced diabetic rats. Results revealed significantly ($P < 0.001$) decreased blood glucose levels and has brought down TC, LDL, VLDL, and TG close to a normal level. In control rats, fed with the experimental leaves did not show any hypoglycemia effect and no significant body weight changes were found. Aqueous extract of leaves of *Catharanthus roseus* appear to be inhibiting glucose-6-phosphate dehydrogenase thus controlling the elevated blood glucose levels.^[19]

Cinnamomum Tamala (tezapatta)

Cinnamomum Tamala is commonly known as Tez Patta belongs to the family Lauraceae. It is native to India, Bangladesh, Nepal, Bhutan, and China. Chakraborty U et.al. evaluated the anti-hyperglycemic activity of the aqueous extracts of *Cinnamomum Tamala* (CTLEt) leaves on the blood glucose of albino rats. CTL was administered at doses of 125 and 250 mg/kg body weight respectively on streptozotocin-induced diabetic rats for 3 weeks. Results suggest that *Cinnamomum Tamala* extract induces antihyperglycemic as well as antioxidant activities in STZ-diabetic rats.^[20]

Citrus Maxima (Pomelo)

Citrus Maxima is commonly known as Pomelo. native to Southeast Asia. It belongs to family Rutaceae. Islam A et.al. studied *in vitro* antioxidant capacity and *in vivo* antidiabetic property of *Citrus maxima* leaf. To explore the *in vivo* antidiabetic property methanol extract of *Citrus maxima* leaf and ethanolic extract of *Citrus maxima* leaf were used in diabetic mellitus (DM) induced Swiss albino mice by a single intraperitoneal injection of alloxan. This study suggests *Citrus maxima* leaf possesses significant antioxidant and antidiabetic properties and they might play a potential role to prevent diabetic mellitus and diabetic mellitus associated complications. In this current study, methanol extract of *Citrus maxima* leaf and ethanolic extract of *Citrus maxima* leaf represented significant hypoglycemic potentiality in alloxan induced diabetic mice. Increased serum levels of TC, TG, LDL and VLDL in diabetic mice were also ameliorated after 28 days of treatment with methanol extract of *Citrus maxima* leaf and ethanolic extract of *Citrus maxima* leaf. Treatment with both extracts also restored the decreased levels of serum HDL in diabetic mice. Increased levels of SGPT, SGOT and CRP were also observed in alloxan induced diabetic mice compared to that of normal control mice.^[21]

Cocos Nucifera (Coconut)

Cocos Nucifera is commonly known as Coconut. It is native to India. It belongs to family Arecaceae. The hypoglycaemic effects of *Cocos nucifera* (Coconut) Husk was studied on alloxan-induced diabetic female rats. *Cocos nucifera* husk tea has a significant hypoglycemic and anti-diabetic effects in alloxan-induced diabetes. The histopathological study of diabetic treated group indicated increased volume density of islets and increased percentage of beta cells, in the diabetic rats that received the extracts (coconut husk tea) which may be a sign of regeneration of β cells and potentiating of insulin secretion from surviving β cells of the islets of Langerhans.^[22]

Coriandrum Sativum L (Coriander)

Coriandrum Sativum L is commonly known as Coriander belongs to family Apiaceae. This plant is native to India, Egypt, and Morocco, Holland, Argentina, Eastern Europe, China, Russia, and Bangladesh Coriandrum. Coriander has been used as an herbal medicine for diabetes mellitus, particularly the seed. Alicia W et. al. evaluated the activity of coriander leaves as an antidiabetic agent, utilizing both in vivo and in vitro method. In in vivo method, the extract was orally administered to the insulin deficiency mice model (alloxan induced at dose of 65 mg/kg bw iv) with dose of 200, 400, and 800 mg/kg bw for 14 days. At the end of the in vivo study, the pancreas was isolated. The ethanolic extract of coriander leaves had the antidiabetic activity at dose of 400 mg/kg bw by improving and regenerating the β cell in pancreas and inhibiting the α -glucosidase enzyme in small intestine.^[23]

Curcuma longa (Turmeric)

Curcuma longa is commonly known as Turmeric. It is native to India. It belongs to family Zingiberaceae. Olatunde A. et al. studied the anti-diabetic activity of aqueous extract of *Curcuma longa* rhizome in both normal and alloxan induced diabetic rats. They reported that the possible mechanism by which aqueous extract from plants brings about their hypoglycemic action may be by induction of pancreatic insulin secretion from β cells of islets of Langerhans or due to enhanced transport of blood glucose to peripheral tissue. Reducing insulin resistance and inhibition of intestinal glucose absorption are also possible mechanisms. This study has demonstrated that aqueous extract of *Curcuma longa* rhizome significantly reduces blood glucose, LDL, TG, TC and increase body weight, total protein and albumin in experimentally induced diabetic rats. Therefore, the plant has hypoglycaemic, hypolipidaemic effects at the dosage and duration of study. Further studies are needed to be carried out to isolate and identify the active principle(s) in the extract as well as elucidate its mode of action and toxicity for enhanced Phytotherapy.^[24]

Dalbergia Sissoo (Rosewood)

Dalbergia Sissoo (DS) is commonly known as Rosewood belongs to the family Fabaceae. It is Native to

the Indian subcontinent and southern Iran. Niranjana S et al. studied the hypoglycemic effect of ethanolic extract of *Dalbergia sissoo* L. leaves in alloxanized diabetic rats. Results suggested that the ethanolic extract of plant *Dalbergia sissoo* leaves is 12 % more effective in reducing the BGL compare to standard drug (Glibenclamide). Study Indicated that sissoo ethanolic extract produced antihyperglycemic effects in experimental diabetes by providing a regenerative modification against damage caused by alloxan to endocrine cells of the pancreas.^[25]

Decalepis hamiltonii (Maredu Kommulu)

Decalepis Hamiltonii is commonly known as Maredu Kommulu belongs to the family Apocynaceae. It is native to India. Manickam D et al. studied the antidiabetic activity of methanolic extracts of the root of *Decalepis hamiltonii* in normal and alloxan-induced diabetic rats. The methanolic extract of *D. hamiltonii* at 200 mg and 400 mg and glibenclamide at 7 mg/kg was administered to normal and alloxan-induced diabetic rats. Results showed significant reduction in blood glucose in the normal rats and alloxan-induced diabetic rats. Also, the administration of extract significantly decreased serum total cholesterol, triglyceride, and AST and ALT levels and at the same time increased liver glycogen content. The antidiabetic activity of methanolic extract of *D. hamiltonii* may be due to its promotion of insulin secretion by the closure of K_p -ATP channels, membrane depolarization, and stimulation of calcium influx.^[26]

Dillenia indica (elephant apple)

Dillenia Indica is commonly known as the Elephant apple belongs to the family Dilleniaceae. It is native to southeastern Asia, from India and Sri Lanka east to southwestern China and Vietnam, and south through Thailand to Malaysia and Indonesia. Kumar S et al. studied antidiabetic and antihyperlipidemic effects of *Dillenia indica* methanolic leaves extracts in streptozotocin-induced diabetic Wistar rats by administering graded oral doses. The extract showed significant antidiabetic activity. Extract treatment also showed to enhance serum insulin level in diabetic rats as compared to the diabetic control group. They proposed one possible anti-diabetic mechanism of *D. indica* extract may be stimulation of insulin secretion. *D. indica* leaves are rich in polyphenols and have an in vitro antioxidant effect. Treatment with *Dillenia indica* methanolic leaves extracts significantly increased the HDL cholesterol level. This suggests that the extract may inhibit the pathway of bad cholesterol synthesis.^[27]

Dodonaea viscosa (Hop-Bushes)

Dodonaea Viscosa is commonly known as Hop-Bushes belongs to the family Sapindaceae. The plant is originated from Australia and native to western America.

Muthukumaran P et al. studied effect of aqueous-ethanol and butanol extracts of the *Dodonaea viscosa* by glucose tolerance test in normal rats and alloxan-induced diabetic

rats for its anti-diabetic activity. Both aqueous-ethanol and butanol extracts have reduced the glucose levels to 51% and 69% respectively, in a prolonged treatment study and shown a significant ($P < 0.001$) increase in glucose tolerance. The blood glucose levels were reduced considerably within 60 minutes of the drug administration. The drug may be acting by potentiating the pancreatic secretion or increasing the glucose uptake.^[28]

***Enicostemma littorale* (Indian Whitehead)**

Enicostemma littorale is commonly known as Indian Whitehead belongs to the family Gentianaceae. Maroo J et.al. studied the glucose-lowering and antioxidant effect of a methanol extract of *Enicostemma littorale* Blume in alloxan-induced diabetic rats. *E. littorale* increased the serum insulin levels of diabetic rats and improved the antioxidant status of diabetic rats. Extract treatment to the diabetic rats significantly increased reduced glutathione levels and decreased erythrocyte catalase activity and lipid peroxidation. Extract treatment caused an increase in the serum insulin levels of the diabetic rats. This plant extract might have some compound(s) that potentiate the glucose-induced insulin release from the β -cell and cause a decrease in blood glucose levels of extract-treated diabetic rats.^[29]

***Ficus carica* (Anjeer)**

Ficus carica is commonly known as Anjeer belongs to the family Moraceae. It is native to India. Ahmad ZM et.al. studied the effect of methanolic extract of *Ficus carica* L. (Moraceae) stem bark on fasting blood sugar levels and serum biochemical analysis in streptozotocin-induced diabetic rats were investigated. The resulted extract had shown significant protection and lowered the blood glucose levels to normal in glucose tolerance test. The *F. carica*, has beneficial effects on blood glucose levels in STZ-induced diabetes, as well as in improving hyperlipidemia due to diabetes. The active ingredient(s) present here may recover the disorders in carbohydrate metabolism noted in diabetic state by stimulating existing β -cell or by increasing the rate of β -cell regeneration or by modulating intracellular glucose utilization. Meanwhile, the actual mechanism of such antidiabetogenic activity is not clear.^[30]

***Ginkgo Biloba* (maidenhair tree)**

Ginkgo Biloba is commonly known as the maidenhair tree belongs to the family Ginkgoaceae. It is native to China. Sailaja Rao P et.al. evaluated the antidiabetic activity of *Ginkgo biloba* in Albino Wistar rats with streptozotocin-induced diabetes. *Ginkgo biloba* in a high dose of 100 mg/kg produced a significant reduction in FBS of 31% and an increase in blood GSH (57.6%) that is however much less than the fall in FBS produced by troglitazone (47%). However, treatment with troglitazone and *Ginkgo biloba* at both doses did not alter the serum ceruloplasmin levels significantly. The antidiabetic activity of *Ginkgo biloba* may be attributed to its antioxidant activity without having a role in metal ion-

mediated lipid peroxidation.^[31]

***Gongronema latifolium* (Arokeke)**

Gongronema latifolium is commonly known as Arokeke belongs to the family Asclepiadaceae. It is a native of southeastern Nigeria. The fractions were evaluated by Akah PA et.al. for antidiabetic effect in alloxan-induced diabetes in rats. The effect of aqueous extract on the blood sugar level of glycemic rats showed a gradual decrease in the blood sugar level from 0 hour to 32 hours. The decrease seems to be significant ($p < 0.05$) in the 800 mg/kg dose. There was no significant decrease in the blood sugar level of normoglycaemic rats treated with *G. latifolium* aqueous extract. *G. latifolium* could be inducing pancreatic cell regeneration. The phytochemical result showed that MF was very rich in terpenoids, saponins, flavonoids, glycosides, and carbohydrates. Literature showed that saponins and flavonoids are good antidiabetic metabolites. The result of this present study therefore justifies the local use of *G. latifolium* leaves in the treatment of diabetes mellitus.^[32]

***Gymnema sylvestre* (Gurmar)**

Gymnema Sylvestre is commonly known as Gurmar belongs to the family Apocynaceae. It is native to Saudi Arabia, India, Sri Lanka, Vietnam, and southern China. Verma N et.al. studied the antidiabetic activity of alcoholic extract of leaf of *Gymnema Sylvestre* in streptozotocin-induced diabetic rats Oral administration of alcoholic extract of leaves of *G. sylvestre* showed significant hypoglycemic effect on blood glucose level in normal fasted rats. Effects of alcoholic extract of *Gymnema sylvestre* on glucose tolerance has been shown in . At 1 h after glucose administration, the blood glucose levels were found to be increased. The blood glucose was measured prior to, 2, 4 and 6 h of administration of extracts. The test for alcoholic extract of *Gymnema sylvestre* have shown significant hypoglycemic activity in streptozotocin induced rats as compared to reference antidiabetic drug glibenclamide (dose 5 mg/kg). The results were statistically significant as against glycemic effect in streptozotocin induced rats.^[33]

Karuppusamy C et.al. studied the potential ability of *Gymnema sylvestre* to regenerate pancreatic β -cells. In the current investigation, an active extract of *Gymnema sylvestre* with the dose of 200 and 400mg/kg was administered orally to streptozotocin induced diabetic rats for 40 days. These results indicate that *Gymnema sylvestre* extract shows significant change in the all above said biochemical parameters when compared to control group. The histopathological study shows the significant recovery of damaged β -cells in diabetic *Gymnema sylvestre* treated rats, when compared to diabetic control ones. these results indicate that *Gymnema sylvestre* extract, possessed hypoglycemic and hypolipidemic activity in long-term treatment and is also capable of regenerating β - cells and hence it could be used as a drug for treating diabetes mellitus. Because it has regenerating ability of β -cells, at least the people in

the earliest stages of the disease could be treated to delay or prevent full-blown clinical diabetes.^[34]

Hibiscus rosa (Sinensis)

Hibiscus Rosa is commonly known as *Sinensis* belongs to the family Malvaceae. It is native to East Asia. Mamun A *et al.* investigated the effect of ethanolic extract of *Hibiscus Rosa Sinensis* (EHBS) leaves on alloxan-induced diabetes with dyslipidemia in rats. Treatment of alloxan-induced diabetes with the most effective observed dose (2.0 mg/kg body weight) of EHBS for 1 week significantly reduced glucose level, TC, TG, and LDL-C, with the increase of HDL-C and weight of kidney, pancreas, and liver when compared with diabetic rats. The observation was also made for consecutive 4 weeks to confirm the results obtained in one week model. The results indicated that the EHBS leaves, in comparison with metformin, had profound hypoglycemic and hypolipidemic activities. The hypolipidemic effect of EHBS was due to the synergistic action of its different constituents, including soluble fiber, sterols, flavonoids and high content of polyunsaturated fatty acids. The exact mechanism of hypolipidemic action is not clear. However, it had been hypothesized that EHBS produced anti-hyperlipidemic effect by decreasing cholesterol synthesis, and more importantly by having antioxidant properties.^[35]

Hyptis suaveolens L(Bushmint)

Hyptis suaveolens is commonly known as Bushmint belongs to the family Lamiaceae. *Hyptis suaveolens* is native to Asia. Mishra SB *et al.* evaluated the antihyperglycemic activity of leaves of *Hyptis suaveolens* using the streptozotocin model. The coarsely powdered material was exhaustively extracted thrice with 50% aqueous ethanol, and the yield of *Hyptis suaveolens* extract (HSE) was 9.5% (w/w). A significant reduction in blood glucose was observed in diabetic animals treated with leaves of *Hyptis suaveolens* at different doses when compared with diabetic rats. Levels of triglyceride, total cholesterol, low-density lipoprotein, very low-density lipoprotein were decreased while administering *Hyptis suaveolens* extract at different doses, compared with their control values in diabetic animals.^[36]

Inula Racemosa (Puskarmool)

Inula Racemosa is commonly known as Puskarmool belongs to the family Asteraceae. *Inula racemosa* is an Asian plant in the daisy family native to the temperate and alpine western Himalayas of Xinjiang, Afghanistan, Kashmir, Nepal, Pakistan. Ajani HB *et al.* evaluated the antidiabetic effect of methanolic extract of *Inula racemosa* root in rats. The effect of the chronic treatment of (28day) methanolic extract of *Inula racemosa* (300 mg/ kg, p.o.) roots on alloxan-induced hyperglycaemia was investigated in Wistar albino rat. Fasting blood glucose levels of diabetic rats were significantly higher than those in normal rats. A significant decrease in blood glucose levels was observed in the diabetic group treated

with glibenclamide group from an initial level of 341.25 ± 17.70 to 249.58 ± 13.68 mg/dl and with methanolic extract from 341.10 ± 22.50 to 256.16 ± 21.69 mg/dl. The hyperglycemic effect of *I. racemosa* could be because of increased utilization of glucose by peripheral tissues without affecting insulin secretion. Additionally because of B- blocking activity of *I. racemosa*, it might be sensitizing insulin receptor in the periphery. On the basis of these findings, it can be assumed that the methanolic extract of roots of *Inula racemosa* possess significant hypoglycaemic and antioxidant property in alloxan induced hyperglycaemia modal in rats.^[37]

Juglans Regia(English walnut)

Juglans Regia is commonly known as English walnut belongs to the family Juglandaceae. It is native to Central Asia. Teimori M Investigated the mechanism of hypoglycemic action of *Juglans regia* Leaves Methanolic Extract in Alloxan-induced diabetic rats.

Postprandial blood glucose we display that *Juglans regia* Leaves Methanolic Extract (JRLME) decreases the PBG levels in both short-term and long-term models. The administration of JRLME attenuates Postprandial blood glucose level. The plant extract significantly inhibited α -glucosidase activity in vitro for both maltase and sucrase enzymes. *Juglans regia* leaves were effective for glucose control of diabetic rats.^[38]

Kalanchoe Pinnata(Cathedral Bells)

Kalanchoe Pinnata is commonly known as Cathedral Bells belongs to the family Crassulaceae. It is native to Madagascar. Anti-diabetic activity of *Kalanchoe Pinnata* leaf extracts was investigated by Sunayana N *et al.* in alloxan-induced diabetic Swiss albino mice. They reported that ethanol extract of *K. pinnata* (500 mg/kg body wt. Shows reduction in both postprandial and streptozocin-induced diabetes blood glucose levels, triglyceride levels. The result indicates that the active principle in *K. pinnata* leaf extract has similar to insulin treatment.^[39]

Lavandula stoechas L(Spanish Lavender)

Lavandula Stoechas is commonly known as Spanish Lavender belongs to the family Lamiaceae. It occurs natively in several Mediterranean countries, including France, Spain, Portugal, Italy, and Greece. Sebai H *et al.* studied the phytochemical profile of *Lavandula stoechas* essential oils, collected in the area of Ain-Draham (North-West of Tunisia), as well as their protective effects against alloxan-induced diabetes and oxidative stress in rat. The principal compounds detected are: D-Fenchone (29.28%), α -pinene (23.18%), Camphor (15.97%), Camphene (7.83%), Eucapur (3.29%), Limonene, (2.71%) Linalool, (2.01%) Endobornyl Acetate (1.03%). The essential oils also contained smaller percentages of Tricyclene, Cymene, Delta-Cadinene, Selina-3,7(11)-diene. Furthermore they found that *Lavandula stoechas* essential oils significantly protected against the increase of blood glucose as well as

the decrease of antioxidant enzyme activities induced by alloxan treatment. *L. stoechas* oils may exert their antihyperglycaemic effect by potentiating plasma insulin action, secretion, or its release from bound form. Treatment of the alloxan-diabetic rats with *L. stoechas* essential oils restored the transaminase activities. *L. stoechas* supplementation, protected against an alloxan-induced decrease of plasma uric acid concentration as one of the major endogenous water-soluble antioxidants as well as tissue malondialdehyde increase, as a marker of lipid peroxidation. Subacute essential oils treatment induced a decrease in lipoperoxidation as well as an increase in antioxidant enzyme activities.^[40]

***Lee Indica*(Bandicoot Berry)**

Lee Indica is commonly known as Bandicoot Berry belongs to the family Vitaceae. It is native to India, Sri Lanka, Nepal, Bangladesh, Andaman and Nicobar Islands, Thailand, Indochina. Dalu D *et al.* evaluated antihyperglycemic and hypolipidemic activity of *Leea Indica* leaves in alloxan (150 mg/kg) induced diabetic rats. Results reveal that *Leea indica* has a beneficial effect in reducing blood glucose and lipid levels indicating its efficient antihyperglycemic and hypolipidemic activity. They suggested that the antihyperglycemic and hypolipidemic properties of *Leea indica* could be mainly due to the presence of its major compounds like ursolic acid (an effective insulin-mimetic), gallic acid (insulin secretagogue).^[41]

***Leonotis leonurus* (Lion's Tail)**

Leonotis Leonurus is commonly known as Lion's Tail belongs to the family Lamiaceae. The plant is a broad leaf evergreen large shrub native to South Africa and southern Africa. Oyedem SO *et al.* studied antidiabetic properties of aqueous leaves extract of *Leonotis leonurus* in streptozotocin-induced diabetic rats. The present findings reveal that oral administration of aqueous extract of *L. Leonurus* leaf has reduced the blood glucose levels as well as lipids. This study also showed that the plant extract improves the polydipsia, polyuria, and body weight loss of diabetic rats. Photochemical investigation showed the presence of flavonoids, tannins, phenolics, and saponins which have been reported to enhance insulin secretion and scavenge free radicals that are generated during a diabetic state. Flavonoids are well known to regenerate the damaged beta cells in diabetic rats while phenolics are found to be effective antihyperglycemic agents.^[42]

***Marrubium Vulgare* (Horehound)**

Marrubium Vulgare is commonly known as Horehound belongs to the family Lamiaceae. It is native to Europe, northern Africa, and southwestern and central Asia. Elberry AA *et al.* studied the antidiabetic and antidyslipidemic effects of the methanolic extract of the aerial part of *M. vulgare* in streptozotocin-induced diabetic rats. *M. vulgare* significantly reduced the blood glucose level starting in the second week. The extract of *vulgare* showed a significant increase in plasma insulin

and tissue glycogen contents. The antidyslipidemic effect was demonstrated by a significant reduction in plasma total cholesterol (TC), triglycerides (TG), and low-density lipoprotein-cholesterol (LDL-C), while the cardio-protective lipid, high-density lipoprotein-cholesterol (HDL-C), was increased. The results of the present study showed an increase in skeletal muscle and liver glycogen content in diabetic rats after the oral administration of *M. vulgare* which may be due to the stimulation of insulin release from beta cells.^[43]

***Momordica charantia* (Bitter Gourd)**

Momordica Charantia is commonly known as Bitter Melon belongs to the family Cucurbitaceae. It is Native to tropical and subtropical Africa and Asia. Meles DK *et al.* studied the fruit extract of bitter melon (*Momordica charantia* L.) towards blood sugar levels in alloxan induced rats. Bitter melon (*Momordica charantia* L.) extract had antidiabetic effects that can lower blood glucose level, improved pancreatic beta cell damage, and increased the Leydig cells number in a dosage of 50 mg/1 ml/day on the 21st days after treatment. The extract of bitter melon fruit (*Momordica charantia* L.) at a dosage of 50 mg/kg/1ml/day can lower blood glucose levels and increased the number of Langerhans islets and Leydig cell of hyperglycemia mice.^[44]

***Morus alba* L (Mulberry)**

Morus alba L is commonly known as Mulberry belongs to the family Moraceae. It is native to India, temperate Asia and North America. Ahn E *et al.* Studied antidiabetic effect of *Morus alba* ethanol (EtOH) extracts at a dose once a day for 22 days in streptozotocin-induced diabetic ICR mouse. Results showed that significant reduction in fasting blood and plasma glucose level in a dose-dependent manner compared to those of the diabetic control. Administration of oxyresveratrol [ORT, 0.6 g/kg BW], a major compound of MB EtOH extracts, to diabetic ICR mice also significantly reduced fasting plasma glucose levels. ORT increased hepatic glucose transporter 2 transcription and glycogen content. Plasma insulin concentration and intestinal disaccharidase activity were not different between diabetic control and ORT groups. This suggests that ORT reduced plasma glucose by stimulating hepatic glucose uptake and glycogen storage.^[45]

***Morus Nigra* (Blackberry)**

Morus Nigra is commonly known as Blackberry. It belongs to the family Moraceae. It is native to India. Hoseini HF *et al.* Studied the effect of *Morus nigra* hydroalcoholic extract on the blood glucose level in rats. After inducing diabetes via streptozotocin injection, the animals were orally received various concentrations of *M. nigra* extract. Results showed that hydroalcoholic extract at the dose of 400 mg/kg (in a short period) and 600 mg/kg (in a long period) caused a significant decrease in the blood glucose levels in the treated rats compared to control. They stated that result of this study

is due to its antioxidant activity and its inhibitory effect on hemoglobin glycosylation.^[46]

Mucuna pruriens (velvet bean)

Mucuna pruriens is commonly known as **velvet bean**. belongs to the family Fabaceae. The origin of *M. pruriens* is uncertain, but it is likely native to tropical Asia. Majekodunmi SO et.al. studied antidiabetic properties of *M. pruriens* alloxan induced diabetes in Wistar rats. Different doses of the extract were administered to diabetic rats and results were compared with normal and untreated diabetic rats. Results showed that the administration of 5, 10, 20, 30, 40, 50, and 100 mg/kg of the crude ethanolic extract of *M. pruriens* seeds to alloxan-induced diabetic rats (plasma glucose > 450 mg/dL) resulted in 18.6%, 24.9%, 30.8%, 41.4%, 49.7%, 53.1% and 55.4% reduction, respectively in blood glucose level of the diabetic rats after 8h of treatment while the administration of glibenclamide (5 mg/kg/day) resulted in 59.7% reduction. Chronic administration of the extract resulted in a significant dose-dependent reduction in the blood glucose level ($P < 0.001$). It also showed that the antidiabetic activity of *M. pruriens* seeds resides in the methanolic and ethanolic fractions of the extract. Oral administration of *M. pruriens* seed extract also significantly reduced the weight loss associated with diabetes. The study indicates that the ethanolic seed extract of *M. pruriens* possess antidiabetic activities comparable with the standard drug, glibenclamide.^[47]

Ocimum Basilicum (sweet basil)

Ocimum Basilicum is commonly known as sweet basil belongs to the family Lamiaceae. It is native to Africa and Asia. Balasubramanian A et.al. studied the Antihyperglycemic effect of the extract on α -amylase and α -glucosidase in vitro, while antidiabetic properties were studied in alloxan-induced diabetic rats treated for 28 days with extract and compared to those treated with oral metformin. The treatment with 100 and 200 mg/kg extract significantly ($P < 0.05$) reduced fasting blood glucose concentration and slightly increased mean body weight in treated groups. Oral glucose tolerance was also significantly ($P < 0.05, 0.001$) improved in 100 and 400 mg/kg extract-treated groups. The reduction of fasting blood glucose level by the extract implies that the extract may have exerted this effect through one or more of these mechanisms like peripheral utilization of glucose, increased synthesis of hepatic, glycogen by enhancement of glycogen regulatory enzyme expression in the liver, inhibition of carbohydrate metabolizing enzymes, stimulation of pancreatic insulin release, and inhibition of hepatic glucose production. The extract also enhanced glucose tolerance by suppressing a postprandial rise in glucose level, likely through enhanced insulin sensitivity and/or increased glucose uptake by skeletal muscle and adipose tissue.^[48]

Ocimum sanctum (Holy Basil)

Ocimum Sanctum is commonly known as Holy Basil belongs to the family Lamiaceae. It is native to the

Indian subcontinent and widespread as a cultivated plant throughout the Southeast Asian tropics. Nelson I et.al. studied the antidiabetic activity of ethanolic extract of leaves of plant *Ocimum sanctum* in alloxan-induced diabetes in rats. The results indicate that the ethanolic extract of *Ocimum sanctum* has significant and sustained oral hypoglycaemic activity, comparable with the hypoglycaemic effect of glibenclamide, a sulfonylurea. Extract of *Ocimum sanctum* increases intracellular calcium of beta islet cells of the pancreas and causes insulin secretion.^[49]

Picrorhiza kurroa (katuka)

Picrorhiza Kurroa is commonly known as kanuka belongs to the family Plantaginaceae. It is native to Himalayan ranges of India, Pakistan, and Nepal. Husain GM et.al. studied the mechanism of antidiabetic activity of standardized aqueous extract of *Picrorhiza kurroa* on streptozotocin-induced diabetic rats. Aqueous extract of *Picrorhiza kurroa* was orally administered to streptozotocin-induced diabetic rats, for 14 consecutive days. Plasma insulin level of diabetic rats was significantly reduced compared to normal control rats. Aqueous extract of *Picrorhiza kurroa* increased GLUT-4 content in the total membrane fractions of skeletal muscle of STZ-induced diabetic rats, which could be due to increased insulin-mediated translocation of GLUT-4 from the cytosol to the membrane.^[50]

Phyllanthus amarus (Gale Of The Wind)

Phyllanthus Amarus is commonly known as Gale Of The Wind belongs to the family Phyllanthaceae. It is native to India (where it occurs in parts of the Western Ghats in the Karnataka-Kerala region and the forests of Central India), Nepal, and Sri Lanka. Mbagwu HOC et.al. studied the hypoglycemic potential of aqueous extract of *Phyllanthus amarus* Schum was in alloxan-induced diabetic albino rats. Results revealed that highly significant ($P < 0.001$) decrease in blood glucose level of 38% and 30% (day 14) at doses of 130 and 260 mg/kg respectively. On the administration of 390 mg/kg dose of extract, significant reduction ($P < 0.001$) in blood glucose level of 41% on day 7 and 16% on day 14 were observed. These results may be due to enhanced peripheral utilization of glucose.^[51]

Pterocarpus Marsupium (Indian kino tree)

Pterocarpus Marsupium is commonly known as the Indian kino tree belongs to the family Fabaceae. It is native to India. Mishra A et.al. studied effects of *Pterocarpus Marsupium* ethanolic extract in streptozotocin (STZ)-induced diabetic rats. ethanolic extract of *P. marsupium* heart wood showed significant improvement on oral glucose tolerance post sucrose load on normal as well as STZ-induced diabetic rats at the selected dose. Except the aqueous and chloroform fractions of ethanolic extract, all the samples also showed significant decline in blood glucose levels of STZ-induced diabetic rats. On comparison, none of the samples of *P. marsupium* showed better effect than the

standard drug metformin. The results clearly indicate that ethanolic extract cause decline in the serum levels of TC, TG and LDL-C and increase. Effect of phenolic-C-glycosides of *P. marsupium* heart wood on glucose uptake by mouse skeletal muscle cells. Further pharmacological and biochemical investigations are underway to elucidate the exact mechanism of action of phenolic glycosides present in heart wood of *P. marsupium*. Results of the present study demonstrated that four out of the five phenolic-C-glycosides stimulates the glucose utilization process in mouse skeletal muscle cells i.e. C2C12.^[52]

***Ricinus communis* (castor oil plant,)**

Ricinus communis is commonly known as castor oil plant. Castor is indigenous to the India. It belongs to family Euphorbiaceae. Gad-Elkareem studied the antidiabetic effect of ethanolic and aqueous-ethanolic extracts of wild *Ricinus communis* (*R. communis*) leaves in streptozotocin (STZ) induced diabetic rats. The administration of ethanol and ethanol-water extracts of *R. communis* leaves in STZ-induced diabetes in albino rats at 300 mg/kg/BW significantly ($P < 0.05$) reduced the blood glucose level in the treated rats. The oral administration of ethanol and aqueous-ethanol extracts of *R. communis* leaves decrease the blood glucose level in STZ-induced diabetic albino rats. This finding suggests that both extracts exhibited a potent antihyperglycemic activity in diabetic rats and may be due to the richness of the used extract in hypoglycemic alkaloids, flavonoids and saponins which could act synergistically and/or independently as a stimulant for the release of insulin following the repair of pancreatic β -cells by the extract or by inhibition of the intestinal absorption glucose.^[53]

***Smallantus sonchifolius* (Yacon)**

Smallantus sonchifolius is commonly known as Yacon belongs to the family Asteraceae. Yacon (*Smallanthus sonchifolius*) is a plant originating in the Andes in South America, from Venezuela to Northwest Argentina. Aybar MJ et.al. examined hypoglycemic effect of the water extract of the leaves of *Smallantus sonchifolius* (Yacon) in normal, transiently hyperglycemic and streptozotocin (STZ)-induced diabetic rats they showed that a single intraperitoneal injection or gastric tube administration of the yacon decoction caused a decrease in plasma glucose levels in normal rats, while the gastric tube administration of 2% yacon tea failed to produce such a decrease. Our results suggest that yacon water extract produces an increase in plasma insulin concentration.^[54]

***Swertia Chirata* (Kirata tikta)**

Swertia Chirata is commonly known as Kirata tikta belongs to the family Gentianaceae. *Swertia chirata* is a popular medicinal plant native to temperate Himalaya. Kavitha KN et.al. studied the antidiabetic activity of *Swertia chirata* (aqueous extract) on the blood glucose level of streptozotocin-induced diabetic rat models. had shown that aqueous extract of *Swertia chirata* has

antidiabetic activity and is probably due to the active principle mangiferin, present in the stem of the plant. Mangiferin has several modes of action viz Direct stimulation of β cells to release insulin. May be due to reduced intestinal absorption of glucose. Enhances glycolytic enzymes which stimulates glycogenesis in the liver and thereby contributes to reduction of blood glucose. Inhibiting α -glucosidase & other enzymes as maltase, sucrase, isomaltase & aldose reductase. Enhances peripheral utilization of glucose. Increases hepatic and muscle glycogen content, promotes β cell repair and regeneration. Exerts insulin like action by reducing the glycated haemoglobin levels. Also inhibits dipeptidyl peptidase IV mediated degradation of glucagon like peptide-1 (GLP-1) & increases GLP-1. *Swertia chirata* extract – aqueous extract at a dose of 200 mg/kg body weight, has exhibited antidiabetic activity in streptozotocin induced diabetes in rats. These extracts exhibited less marked antidiabetic activity when compared to standard drug glibenclamide in streptozotocin induced diabetes in rats.^[55]

***Syzygium Cumini* (Malabar plum)**

Syzygium Cumini is commonly known as Malabar plum belongs to Family Myrtaceae. It is native to Bangladesh, India, Nepal, Pakistan, Sri Lanka, Malaysia, the Philippines, and Indonesia. Bhuyan ZA et.al. studied the effects of powder and ethanol extract of *Syzygium cumini* seeds (1.25/ kg bw) treatment for 21 days on glucose homeostasis, serum insulin, serum lipids and liver glycogen content in streptozotocin (STZ) induced type 2 diabetic rats. The ethanol extract of *S. cumini* seed coat was evaluated recently for its potent antioxidant potential against DPPH \cdot , OH \cdot , O $_2^{\cdot-}$ and lipid peroxidation and high degree of phenolic and anthocyanins content, it significantly decreased free radical damage and hepatic lipid peroxidation. Therefore, the antidiabetic effect of *S. cumini* seed powder and ethanol extract in present studies, which was found after 21 days of consecutive feeding, may be due to increased insulin sensitivity. Insulin sensitivity can be increased by affecting these mechanisms. The extracts may also improve insulin sensitivity by reducing glucotoxicity which is one of the causes of insulin resistance in type 2 rats. In the present study, anti-hyperlipidemic efficacy of *S. cumini* seed powder and ethanol extract was evaluated and the efficacy was compared with glibenclamide. The results showed that seed powder and extract after 21 days of chronic feeding significantly increased serum HDL-cholesterol and decreased LDL-cholesterol. Thus, *S. cumini* seed powder and ethanol extract have potential antihyperlipidemic effect in type 2 diabetic model rats.^[56]

Kumar A et.al. studied the anti-diabetic effect of ethyl acetate and methanolic extracts of SC seed and isolated compound mycaminose, against streptozotocin-induced diabetic rats. A compound, mycaminose was isolated from SC seed extract. The results of this experimental study indicate that isolated compound 'Mycaminose', ethyl acetate and methanol extracts possess anti-diabetic

effects against STZ-induced diabetic rats. The possible mechanism by which seed brings about a decrease in blood sugar level may be by potentiation of the insulin effect of plasma by increasing either the pancreatic secretion of insulin from beta-cells of the islets of Langerhans or its release from the bound form. A number of other plants have been reported to exert hypoglycemic activity through insulin release-stimulatory effects.^[57]

***Terminalia Arjuna* (Arjun Tree)**

Terminalia Arjuna is commonly known as Arjun Tree belongs to the family Combretaceae. The arjuna is seen across the Indian Subcontinent and is usually found growing on river banks or near dry river beds in Uttar Pradesh, Bihar, Maharashtra, Madhya Pradesh. Alam Morshed M et. al. studied antidiabetic and antilipidemic property of *Terminalia arjuna* in streptozotocin-induced type 2 diabetic model rats. The results of the experimental study suggest that *T. arjuna* possesses hypoglycemic and hypolipidemic effects and can be served as a source of potent antidiabetic agent. Results indicate that *T. arjuna* may interfere with the intestinal glucose absorption in the gut. It may also act by modifying the peripheral uptake of glucose and probably increasing the sensitivity of insulin. The obtained results also indicate that in the case of Type 2 diabetic rats both the first well as second phases of insulin response to glucose is impaired, whereas, *T. arjuna* increases the activities of glycolytic enzymes (hexokinase, phosphoglucosomerase) and decreases aldolase enzyme activities in the liver and kidney. It was, maybe, and due to restoration delayed insulin response. The extract also reduces the gluconeogenic enzymes (glucose-6-phosphatase and fructose-1, 6-biphosphatase) to a normal level whenever it becomes high.^[58]

***Trigonella foenum-graecum* (Fenugreek)**

Trigonella foenum-graecum is commonly known as Fenugreek belongs to the family Fabaceae. It is native to India, China, and North Africa. Mawla A et.al. studied the effects of ethanol extract of *Trigonella foenum-graecum* (Fenugreek) seeds on the blood glucose levels in alloxan-induced diabetic rats at different doses (2g/kg, 1g/kg, 0.5g/kg and 0.1g/kg). The hypoglycemic effect of extract was compared with that of the standard antidiabetic drug (glibenpiride, 4mg/kg) single dose. The extract showed significant activity against the diabetic state induced by alloxan but the intensity of hypoglycemic effect varied from dose to dose. The most effective dose recognized was 1g/kg but that is still lower than the standard antidiabetic drug. No acute toxicity was observed for ethanol extract of *T. foenum-graecum* seed when it was administered orally at high dose level (3 g/kg body weight), which is higher than effective antihyperglycemic dose, and closely observed for 24 hrs for any mortality and next 10 days for any delayed toxic effects on gross behavioral activities. Phytochemical group tests were also accomplished and presence of alkaloids, steroids and carbohydrates were recognized in

the extract.^[59]

***Vitex negundo* (Chinese Chaste Tree)**

Vitex Negundo is commonly known as the Chinese Chaste Tree belongs to the family Verbenaceae. It is originated in India and the Philippines. Aqueous and ethanol leaf extract of *Vitex negundo* was studied by Prasanna Raja P et.al. for its antidiabetic activity using the alloxan-induced diabetic model in rats. Aqueous extract showed ($P < 0.01$) significant activity than the ethanol extract at the tested dose level, which was comparable to glibenclamide, a standard antidiabetic drug. The aqueous and ethanol extract of *Vitex negundo* leaf was found to exhibit a signifying hypoglycemic activity in alloxan-induced diabetic rats. When compare both extract activity, aqueous extract, has shown a significant effect than ethanol extract. Further Studies are needed to isolate and characterize the bioactivity compounds of antidiabetic from *Vitex negundo* leaf medicinal plant.^[60]

***Zingiber officinale* (Ginger)**

Zingiber officinale is commonly known as Ginger belongs to Zingiberaceae. It is native to India. The genus *Zingiber* is native to Southeast Asia especially in Thailand, China, the Indian Subcontinent, and New Guinea. Bolanle I et.al studied the hypoglycaemic effect of aqueous extracts of raw *Zingiber officinale* in alloxan-induced diabetic and insulin-resistant diabetic rats. The experimental rats exhibited hyperglycemia accompanied by weight loss to confirm their diabetic state. Ginger effectively reduced fasting blood glucose and malondialdehyde levels in alloxan-induced diabetic and insulin-resistant diabetic rats compared to control and ginger-only treated rats. Furthermore, ginger increased serum insulin level and also enhanced insulin sensitivity in alloxan-induced diabetic and insulin-resistant diabetic rats compared to control and ginger-only treated rats. The results of the study clearly show that dietary ginger has a hypoglycaemic effect, enhances insulin synthesis in male rats, and has high antioxidant activity. One of the likely mechanisms is the action of malondialdehyde, which acts as a scavenger of oxygen radicals.^[61]

REFERENCES

1. Baynest HW. Classification, Pathophysiology, Diagnosis and Management of Diabetes Mellitus. *J Diabetes Metab*, 2015; 06(05).
2. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes Res Clin Pract*, 2019; 157: 107843.
3. Bhavani R. Antidiabetic activity medicinal plant *Aegle marmelos* (linn .) on alloxan induced diabetic rats. *Int Res J Pharm Biosci*, 2014; 1(1): 36–44.
4. Eidi A, Eidi M, Esmaeili E. Antidiabetic effect of garlic (*Allium sativum* L.) in normal and

- streptozotocin-induced diabetic rats. *Phytomedicine*, 2006; 13(9–10): 624–9.
5. Sangala R, Kodati D, Burra S, Gopu J, Dubasi A. Evaluation of Antidiabetic Activity of *Annona Squamosa* Linn Seed in Alloxan – Induced Diabetic Rats. *Int J Preclin Res*, 2011; 2(2): 100–6.
 6. Value SJRI, Shahin N, Alam S, Ali M. Pharmacognostical Standardisation and Antidiabetic activity of *Artocarpus Heterophyllus* Leaves Lam . *Int J Drug Dev Res*, 2012; 4(1): 346–52.
 7. EC DIABETES AND METABOLIC RESEARCH Research Protocol Therapeutic Efficacy of, 2020; 2: 1–4.
 8. Senthilkumar MK, Sivakumar P, Changanakkattil F, Rajesh V, Perumal P. Evaluation of anti-diabetic activity of *Bambusa vulgaris* leaves in streptozotocin induced diabetic rats. *Int J Pharm Sci Drug*, 2011; 3(3): 208–10.
 9. Nirmala a, Saroja S. Hypoglycemic effect of *Basella rubra* in streptozotocin–induced diabetic albino rats. *J Pharmacogn Phyther*, 2009; 1(2): 25–30.
 10. Kumar S, Shachi K, Dubey U. Anti-Diabetic and Haematinic Effects of Beet Root Juice (*Beta vulgaris* L.) in Alloxan Induced Type-1 Diabetic Albino Rats. *J Diabetes Res Ther*, 2020; 9–11.
 11. Chitravel R, Kaliyaperumal S. Antidiabetic potential of *Biophytum sensitivum* whole plant extracts in STZ induced diabetic rats. *Int J Sci Eng Res*, 2018; 9(6): 72–7.
 12. Nalamolu RK, Boini KM, Nammi S. Effect of chronic administration of *Boerhaavia diffusa* Linn. leaf extract on experimental diabetes in rats. *Trop J Pharm Res*, 2007; 3(1).
 13. Nalamolu RK, Boini KM, Nammi S. Effect of chronic administration of *Boerhaavia diffusa* Linn. leaf extract on experimental diabetes in rats. *Trop J Pharm Res*, 2007; 3(1): 305–9.
 14. Anand P, Murali YK, Tandon V, Murthy PS, Chandra R. Insulinotropic effect of aqueous extract of *Brassica nigra* improves glucose homeostasis in streptozotocin induced diabetic rats. *Exp Clin Endocrinol Diabetes*, 2009; 117(6): 251–6.
 15. Valavala VK, Vangipurapu RK, Banam VR, Pulukurthi UMR, Turlapati NR. Effect of mustard (*brassica juncea*) leaf extract on streptozotocin-induced diabetic cataract in wistar rats. *J Food Biochem*, 2011; 35(1): 109–24.
 16. Kumar JSP, Tharaheswari M, Rani SS, Sudha S. *Cassia auriculata* Flower Extract Articulate its Antidiabetic Effects by Regulating Antioxidant Levels in Plasma, Liver and Pancreas in T2DM Rats. *Am J Phytomedicine Clin Ther*, 2016; 2(6): 705–22.
 17. Chakrabarti S, Biswas TK, Rokeya B, Ali L, Mosihuzzaman M, Nahar N, et al. Advanced studies on the hypoglycemic effect of *Caesalpinia bonducella* F. in type 1 and 2 diabetes in Long Evans rats. *J Ethnopharmacol*, 2003; 84(1): 41–6.
 18. Solikhah TI, Setiawan B, Ismukada DR. Antidiabetic activity of papaya leaf extract (*Carica Papaya* L.) isolated with maceration method in alloxan-induced diabetic mice. *Syst Rev Pharm*, 2020; 11(9): 774–8.
 19. Leena M. *Catharanthus roseus* Leaves as an Anti-diabetic and Hypolipidemic Agents in Alloxan - Induced Diabetic Rats. *Am J Phytomedicine Clin Ther*, 2014; 2(12): 1393–6.
 20. Chakraborty U, Das H. Antidiabetic and Antioxidant Activities of *Cinnamomum tamala* Leaf Extracts in STZ-Treated Diabetic Rats. *Glob J Biotechnol Biochem*, 2010; 5(1): 12–8.
 21. Islam A, Tasnin MN, Bari MW, Hossain MI, Islam MA. In Vitro Antioxidant and In Vivo Antidiabetic Properties of *Citrus Maxima* Leaf Extracts in Alloxan-Induced Swiss Albino Diabetic Mice. *Asian Food Sci J*, 2021; (March): 66–79.
 22. Victor Emojevwe EJ. ANTI DIABETIC EFFECTS OF THE *COCOS NUCIFERA* (COCONUT) HUSK EXTRACT. *J Med Appl Biosci*, 2012; 4(September): 16–8.
 23. Aligita W, Susilawati E, Septiani H, Atsil R. Antidiabetic activity of coriander (*Coriandrum Sativum* L) leaves' ethanolic extract. *Int J Pharm Phytopharm Res*, 2018; 8(2): 59–63.
 24. Olatunde A, E.B. J, H., Tijjani OSM and, C.D. L. Anti-diabetic Activity of Aqueous Extract of *Curcuma longa* (Linn) Rhizome in Normal and Alloxan-Induced Diabetic Rats. *Researcher*, 2014; 6(7): 58–65.
 25. Niranjana S. Antidiabetic activity of ethanolic extract of *Dalbergia sissoo* L. leaves in alloxan-induced diabetic rats. *Int J Curr Pharm Res*, 2010; 2(2): 24–7.
 26. Manickam D, Periyasamy L. Antidiabetic effect of methanolic extract of *Decalepis hamiltonii* root (wight and Arn) in normal and alloxan induced diabetic rats. *J Pharm Res*. 2013; 6(1): 166–72.
 27. Kumar S, Kumar V, Prakash O. Antidiabetic and antihyperlipidemic effects of *Dillenia indica* (L.) leaves extract. *Brazilian J Pharm Sci*, 2011; 47(2): 373–8.
 28. Muthukumaran P, Hazeena Begumand V, Kalaiarasan P. Anti-diabetic activity of *Dodonaea viscosa* (L) leaf extracts. *Int J PharmTech Res*, 2011; 3(1): 136–9.
 29. Maroo J, Ghosh A, Mathur R, Vasu VT, Gupta S. Antidiabetic efficacy of *Enicostemma littorale* methanol extract in alloxan-induced diabetic rats. *Pharm Biol*, 2003; 41(5): 388–91.
 30. Ahmad ZM, Ali M, Mir SR. Anti-diabetic activity of *Ficus carica* L . stem barks and isolation of two new flavonol esters from the plant by using spectroscopical techniques. *Asian J Biomed Pharm Sci*, 2013; 3(18): 22–8.
 31. Sailaja Rao P, Krishna Mohan G, Srinivas P. Evaluation of anti-diabetic activity of *Hydnocarpus laurifolia* in streptozotocin induced diabetic rats. *Asian J Pharm Clin Res*, 2014; 7(5): 62–4.
 32. Akah PA, Uzodinma SU, Okolo CE. Antidiabetic activity of aqueous and methanol extract and

- fractions of *Gongronema latifolium* (asclepidaceae) leaves in alloxan diabetic rats. *J Appl Pharm Sci*, 2011; 1(9): 99–102.
33. Verma N, Shakya VK, Saxena RC. Antidiabetic activity of glycoside isolated from *Gymnema sylvestre* in streptozotocin induced diabetic rats. *Asian J Chem*, 2008; 20(7): 5033–6.
 34. Karuppusamy C, Venkatesan P, Kalaiselvan R. Evaluation of antidiabetic activity of miglitol nanoparticles in streptozotocin induced diabetic rats. *Int J Res Pharm Sci*, 2017; 8(1): 103–8.
 35. Mamun A, Islam S, Alam AK, Rahman MAA, Rashid M. Effects of Ethanolic Extract of *Hibiscus rosa-sinensis* Leaves on Alloxan-Induced Diabetes with Dyslipidemia in Rats. *Bangladesh Pharm J.*, 2013; 16(1): 27–31.
 36. Mishra SB, Verma A, Mukerjee A, Vijayakumar M. Anti-hyperglycemic activity of leaves extract of *Hyptis suaveolens* L. Poit in streptozotocin induced diabetic rats. *Asian Pac J Trop Med*, 2011; 4(9): 689–93.
 37. Ajani HB, Patel HP, Shah GB, Acharya SR. Evaluation of Antidiabetic Effect of, 2009; 129: 118–29.
 38. Teimori M, Montasser Kouhsari S, Ghafarzadegan R, Hajiaghvae R. Study of hypoglycemic effect of *Juglans regia* leaves and its mechanism. *J Med Plants*, 2010; 9(SUPPL 6): 57–65.
 39. Sunayana N, Raghavendra VB, Uzma M, Girish ST. Anti-Diabetic Properties Of *Kalanchoe pinnata* (LAM.) PERS. In Alloxan Induced Diabetic Mice. *Asian J Res Biol Pharm Sci*, 2016; 4(4): 143–51.
 40. Sebai H, Selmi S, Rtibi K, Souli A, Gharbi N, Sakly M. Lavender (*Lavandula stoechas* L.) essential oils attenuate hyperglycemia and protect against oxidative stress in alloxan-induced diabetic rats. *Lipids Health Dis*, 2013; 12(1).
 41. Dalu D, Duggirala S, Akarapu S. Anti Hyperglycemic and Hypolipidemic Activity of *Lea Indica*. *Int J Bioassay*, 2014; 3(May 2014): 3155–64.
 42. Oyedem SO, Yakubu MT, Afolayan AJ. Antidiabetic activities of aqueous leaves extract of *Leonotis leonurus* in streptozotocin induced diabetic rats. *J Med Plants Res*, 2011; 5(1): 119–25.
 43. Elberry AA, Harraz FM, Ghareib SA, Gabr SA, Nagy AA, Abdel-Sattar E. Methanolic extract of *Marrubium vulgare* ameliorates hyperglycemia and dyslipidemia in streptozotocin-induced diabetic rats. *Int J Diabetes Mellit*, 2015; 3(1): 37–44.
 44. Meles DK, Wurlina, Adnyana DPA, Rinaldhi CP, Octaviani RR, Cempaka DKS. The antidiabetic effect of bitter melon (*Momordica charantia* L.) extracts towards glucose concentration, langerhans islets, and leydig cells of hyperglycemic mice (*rattus norvegicus*). *EurAsian J Biosci*, 2019; 13(2): 757–62.
 45. Ahn E, Lee J, Jeon YH, Choi SW, Kim E. Anti-diabetic effects of mulberry (*Morus alba* L.) branches and oxyresveratrol in streptozotocin-induced diabetic mice. *Food Sci Biotechnol*, 2017; 26(6): 1693–702.
 46. Hoseini HF, Saeidnia S, Gohari AR, Yazdanpanah M, Hadjiakhoondi A. Investigation of antihyperglycemic effect of *Morus nigra* on blood glucose level in streptozotocin diabetic rats. *Pharmacologyonline*, 2009; 3(May 2014): 732–6.
 47. Majekodunmi SO, Oyagbemi AA, Umukoro S, Odeku OA. Evaluation of the anti-diabetic properties of *Mucuna pruriens* seed extract. *Asian Pac J Trop Med*, 2011; 4(8): 632–6.
 48. Balasubramanian A, Ramalingam K. Hypoglycemic Activity of *Casearia esculenta* Roxb. in Normal and Diabetic Albino Rats. *Iran J Pharm Res*, 2006; 0(0): 47–51.
 49. Nelson I. Oguanobi. Effects of aqueous leaf extract of *Ocimum gratissimum* on oral glucose tolerance test in type-2 model diabetic rats. *African J Pharm Pharmacol*, 2012; 6(9): 630–5.
 50. Husain GM, Rai R, Rai G, Singh HB, Thakur AK, Kumar V. Potential mechanism of anti-diabetic activity of *Picrorhiza kurroa*. *Tang [Humanitas Med*, 2014; 4(4): 27.1-27.5.
 51. Mbagwu HOC, Jackson C, Jackson I, Ekpe G, Eyaekop U, Essien G. Evaluation of the hypoglycemic effect of aqueous extract of *Phyllanthus amarus* in alloxan-induced diabetic albino rats, 2011; 2(3): 158–60.
 52. Mishra A, Srivastava R, Srivastava SP, Gautam S, Tamrakar AK, Maurya R, et al. Antidiabetic activity of heart wood of *Pterocarpus marsupium* Roxb. and analysis of phytoconstituents. *Indian J Exp Biol*, 2013; 51(5): 363–74.
 53. Gad-Elkareem MAM, Abdelgadir EH, Badawy OM, Kadri A. Potential antidiabetic effect of ethanolic and aqueous-ethanolic extracts of *Ricinus communis* leaves on streptozotocin-induced diabetes in rats. *PeerJ*, 2019; 2019(2).
 54. Aybar MJ, Sánchez Riera AN, Grau A, Sánchez SS. Hypoglycemic effect of the water extract of *Smallantus sonchifolius* (yacon) leaves in normal and diabetic rats. *J Ethnopharmacol*, 2001; 74(2): 125–32.
 55. Kavitha KN, Dattari AN. Experimental evaluation of antidiabetic activity of *Swertia chirata* aqueous extract. *J Public health Res*, 2013; 1(2): 71–5.
 56. Bhuyan ZA, Rokeya B, Masum N, Hossain S, Mahmud I. Antidiabetic effect of *Syzygium cumini* L. Seed on type 2 diabetic rats. *Dhaka Univ J Biol Sci*, 1970; 19(2): 157–64.
 57. Kumar A, Ilavarasan R, Jayachandran T, Deecaraman M, Aravindan P, Padmanabhan N, et al. Anti-diabetic activity of *Syzygium cumini* and its isolated compound against streptozotocin-induced diabetic rats. *J Med Plants Res*, 2008; 2(9): 246–9.
 58. Alam Morshed M, Haque A, Rokeya B, Ali L. Anti-hyperglycemic and lipid lowering effect of *Terminalia arjuna* bark extract on streptozotocin induced type 2 diabetic model rats. *Int J Pharm Pharm Sci*, 2011; 3(4): 449–53.
 59. Mowla A, Alauddin M, Rahman A, Ahmed K.

Antihyperglycemic effect of trigonella foenum-graecum (fenugreek) seed extract in alloxan-induced diabetic rats and its use in diabetes mellitus: a brief qualitative phytochemical and acute toxicity test on the extract, 2009; 6(3): 255-261.

60. Prasanna Raja P, Sivakumar V, Riyazullah MS. Antidiabetic potential of aqueous and ethanol leaf extracts of *Vitex negundo*. *Int J Pharmacogn Phytochem Res*, 2012; 4(2): 38–40.
61. Bolanle I, Arikawe A. Alloxan-Induced and Insulin-Resistant Diabetic Male Rats. *Nig J Physiol Sci*, 2011; 26: 89–96.