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Prevalence of Diabetes mellitus and herbal medication

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Abstract:

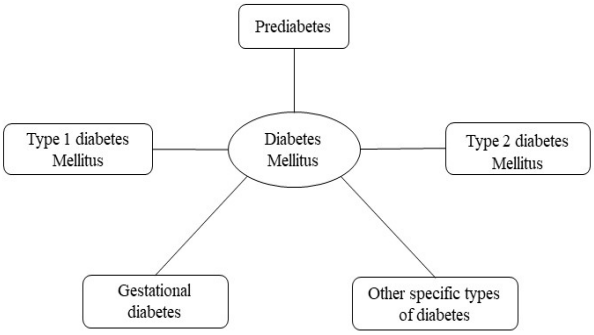
Diabetes Mellitus is a chronic metabolic disorder and a major health issues in globally which characterized by hyperglycemia with increasing prevalence. Type 2 Diabetes Mellitus is comparatively more prevalent than Type 1 Diabetes Mellitus, even though type 1 Diabetes Mellitus is not increasing with same proportion as type 2 Diabetes Mellitus, but still it increases 3-5% per year globally. Type 1 Diabetes Mellitus is due autoimmune or idiopathic attack, mostly seen in children aged 0-14 years. Type 2 Diabetes Mellitus is due to Genetic, obesity, physical inactivity, high/low birth weight and metabolic syndrome which can predominantly found in adults. There is no proper treatment to cure diabetes completely which are just controlling diabetes mellitus. This review suggests herbal medicines as better remedies than allopathic medicine because of its minimal side effects, cost-effective and availability but allopathic medicine pose adverse side effects which affects the other parts of body.

Keywords: Diabetes mellitus, epidemiology, herbal medicines

1. INTRODUCTION

Diabetes Mellitus is a chronic metabolic disorder characterized by impairment in metabolism of carbohydrates, lipids, protein and high blood glucose level. It is caused due to defect in insulin secretion by pancreas or due to ineffective response of cell to the insulin production. Insulin is secreted by β cells of Ilets of Langerhans which is important in controlling blood glucose concentration by facilitating uptake of glucose and peripheral tissues metabolism. The defect in insulin state may also lead to overproduction of hormones that are antagonist to insulin("Oral Delivery of Insulin - 1st Edition," n.d.). Common symptoms of Type 1 & 2 diabetes are fatigue, polyuria, polydipsia, polyphagia, infections, weight loss, paresthesias, blurred vision, weight loss, rapid heart rate, reduced blood pressure, body temperature and slow healing of wound or sores(Baynest, 2015). Long term consequences of diabetes mellitus include major risk factors such as microvascular and macrovascular complications (neuropathy, nephropathy, retinopathy and vascular diseases)("Autophagy and Cardiometabolic Diseases - 1st Edition," n.d.)(Xu et al., 2018). In the untreated state, both types of diabetes were characterized by increased hepatic glucose output, decreased glucose uptake in the muscles and adipose tissue. In type 1 diabetes mellitus the risk of severe lipolysis leads to diabetic ketoacidosis. The insulin activity in type 2 diabetes mellitus normally inhibits lipolysis and ketone production. The patients with type 2 diabetes mellitus are hard to develop ketoacidosis and develop a hyperosmolar which is a non-ketotic state. There are many remedies to control the diabetes mellitus but still there is no proper treatment to cure it so, still the researches are going on to find the permanent cure for diabetes mellitus(Ahmed, 2002). The current treatments used to control and cure diabetes are allopathy, homeopathy, Ayurveda and other natural remedies. In allopathy treatment which controls the problem immediately compared to other treatments but it has side effects such as kidney, heart and other complications(Wang et al., 2013). Homeopathy, Ayurveda and other natural treatments are mostly based on herbs and other natural products with less or no side effects compared to allopathy which is used traditionally to cure the problems (Abo-Youssef and Messiha, 2013). There are many benefits in choosing natural remedies over allopathy/synthetic medicines because it doesn't block the body's self-healing abilities; allopathy treatments show fast and temporary solution for certain disease such as jaundice, piles, arthritis and etc. with no permanent solutions. Ayurvedic medicines relatively take time but it gives permanent solution for the problem because it mainly focuses on the root cause of the problem to cure the affected area and related system of our body but allopathy focuses mainly on symptoms; it is highly effective in curing chronic illness; Ayurvedic medicines are cost effective as they are naturally available and as herbal medications has certain vital instructions such as diet and physical exercise for that treatment, this is due to the patients from their modern lifestyle habits to healthy lifestyle and proper dietary (Bhagour et al., n.d.). Physical exercises entail many physiological and psychological benefits for the diabetic patient. It plays an important role in physical & mental development; improving insulin sensitivity and plasma glucose control (Baynest, 2015). So, it enhances the potency of the medications by responding to the treatment with more effectively and desirably. In this review paper we are discussing some most important herbal medicines used in treatment of diabetes mellitus (Kumari et al., 2016). The classification of diabetes mellitus is represented in figure 1.

Figure 1: Classification of Diabetes Mellitus



2. TYPES AND EPIDEMIOLOGY OF DIABETES MELLITUS:

As per the World Health Organisation (WHO) estimation 422 million people were affected with diabetes mellitus in 2014 and it will be 7th leading cause of death by 2030 (Pozzilli et al., 2010). The International Diabetes Federation estimated that 382 million people had diabetes mellitus in 2013 and it is expected to increase to 592 million by 2035 (Guariguata et al., 2014).

2.1 Prediabetes

It is an in-between stage and is characterized by increase in blood glucose level than normal level but that level not enough for the diagnosis of diabetes. According to WHO, patients with impaired fasting tolerance (IFG) at concentration of ≥6·1 (fasting plasma glucose (FPG)) and impaired glucose tolerance (IGT) at concentration of <7·0 mmol/L (fasting plasma glucose (FPG)), ≥7·8 and <11·1 mmol/L (oral glucose tolerance test (OGTT)) and 5·7–6·4% glycated haemoglobin A_{1c} (HbA_{1c}) are now referred as having "pre-diabetes (Tabák et al., 2012). Prediabetes has increased risk of developing Diabetes Mellitus 2 and other complications (Bansal, 2015).

2.2 Type 1 diabetes mellitus:

It is a juvenile diabetes, also known as Insulin Dependent Diabetes Mellitus and is characterized by destruction of beta cells by T cell mediated autoimmune attack. In this case, pancreas no longer can produce insulin due to loss of insulin secretion which leads to abnormal function of α cells and excessive secretion of glucagon. In that condition blood glucose seems to be increased and it cannot be delivered to where it is needed(Najafikhah et al., 2018). Type 1 diabetes mellitus are further classified into Type1a which is characterized by autoimmunity in the form of autoantibodies against insulin, islet cells, IA2 (protein tyrosine phosphatase), 65-KD (65-kD form of glutamate decarboxylase), ZnT8 (zinc transporter 8); this case is almost 85% to 95%. Type 1b or idiopathic is a phenotypic Type 1 diabetes mellitus and is caused by Genetic predisposition, improper β cells in pancreas and viral infections. Approximately 5% to 10% of Diabetes Mellitus are Type 1(Concannon et al., 2009). The epidemiology of type 1 diabetes was studied based on Diabetes Mondiale (DIAMOND) Project worldwide. Historically, Type 1 diabetes was more prevalent in european population but it is constantly increasing in Finland, Sweden, Colarado, India, and Germany. In Europe, juvenile diabetes was mainly found in Scandinavia and north-west Europe. There has been an increase from an incidence rate of almost 10/100,000 to 60/100,000 children in Finland and around 32/100,000 children in India (17.93 cases/100,000 children in Karnataka, 3.2 cases/100,000 children in Chennai, and 10.2 cases/100,000 children in Karnal (Haryana)). Annually, around 78,000 children aged 0-14 years were estimated to develop Type 1 diabetes worldwide (Das, 2015)(Maahs et al., 2010).

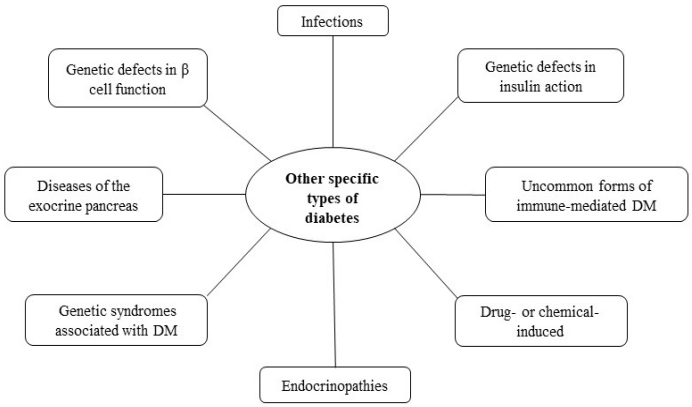
2.3 Type 2 diabetes mellitus:

It is also known as Non-Insulin Dependent Diabetes and adult onset diabetes but also seen in young people now a days. It is characterized by impaired insulin secretion by pancreatic beta cell dysfunction and insulin resistance (mainly peripheral insulin resistance) when body cells unable to react efficiently to insulin and the cells resist the effect of insulin resulting in hyperglycemic condition where glucose level in blood increases. Type 2 Diabetes Mellitus is caused by obesity, oxidative stress, overloading of glucose and lipids, inflammation, adipokines, autophagy and etc(Simu et al., 2017). Diagnosis of type 2 diabetes mellitus can be screened by Fasting plasma glucose (FPG) test; A1C test; Oral Glucose Tolerance Test (OGTT); Glucose Challenge test; Random Plasma Glucose test. Approximately 80% to 90% diabetes are Type 2 and its prevalence is higher than type 1 diabetes. It can be treated by physical exercises, proper diet, natural hypoglycemic and other naturally acquired products instead of taking allopathy medicines because of its severe side-effects (Xu et al., 2018). Incidence rate among children and adults are increasing 100,000 person/year and greatly differs based on ethnicity (Huseini et al., 2009). The recently reported incidence rate of type 2 diabetes in different countries are 49.4% in Native Americans, 22.7% in Asian/Pacific Islanders, 19.4% in African Americans, 17% in Hispanics, and 5.6% in non-Hispanic whites(Forouhi and Wareham, 2014). In March 2000, two-sided t-tests and chi-square tests were done to analyze the base differences between type 1 and 2 groups by an independent statistician. The cumulative incidence of diabetes was evaluated by calculating survival curves and the incidence of diabetes was evaluated by the two-sided log-rank test for finding difference between the type 1 and 2 groups. The result shows that overall incidence was reduced 58%. All analyses were done to know the basic factor that causes type 2 and its treatment where type 2 diabetes is mostly caused by lifestyle and lifestyle changes can prevent high risk of type 2 diabetes (Tuomilehto et al., 2001).

2.4 Gestational diabetes mellitus:

It is a pathophysiologic condition mostly develops in women during gestation period. The elevation of blood glucose level during pregnancy is due to hormone released by placenta known as human placental lactogen (HPL) or human chorionic somatomammotropin (HCS). This helps in growth of the baby but modifies the maternal metabolism which raises the blood glucose level and makes mother body less sensitive to the insulin. Gestational diabetes patients have a risk of developing type 2 diabetes mellitus (Kampmann et al., 2015). The main risk factor for developing Gestational diabetes mellitus are hyper pre- pregnant BMI which is mostly seen in obese women and increased insulin resistance at 28th week was correlated with the BMI at 28th week reported by Hyperglycemia and Adverse Pregnancy Outcome (HAPO). Gestational diabetes mellitus can cause some complication in newborns like macrosomia, hypoglycemic, respiratory distress syndrome and develop type 2 diabetes mellitus in later stages (Yogev et al., 2010).Classification of other specific types of diabetes mellitus are represented in figure 2.

Figure 2: Classification of other specific types of Diabetes Mellitus



3. HERBAL MEDICATIONS:

Herbalism is use of various types of medicinal plants to cure the diseases. Plants have been used for medicinal purposes long before the prehistoric period(Abo-Youssef and Messiha, 2013). Unani manuscripts, Egyptian papyrus, Chinese writing were the evidence for the use of herbs to treat diseases Traditional medicinal system such as Unani, Ayurveda and Chinese medicine uses herbal therapies systematically(Kumari et al., 2016). Medicinal plants are rich in secondary metabolisms and potential source for drugs with no or less side effects. About 80% of the people worldwide rely on the herbal medicines for their primary health care. Many medicinal plants serve as anti-diabetic drugs to treat Diabetes Mellitus (Sabu and Kuttan, 2002)(Anderson et al., 2016).

3.1 Mmordica charantia:

Momordica charantia belongs to Cucurbitaceae family and commonly known as bitter melon and it is an edible fruit-pod of tendril-bearing vine native to India. It plays an important role in herbal medicines as alternatives with low or no side effects. Bitter melon is a highly nutrient dense plant, which has many important beneficial compounds such as vitamins, minerals, antioxidants, antimutagens and bioactive elements. Mainly polypeptide-p in bitter melon is used to control diabetes naturally by lowering the blood glucose level. It is mainly used to treat Diabetes mellitus particularly in hypoglycemic effects due to its main compounds isolated from bitter melon contain hypoglycemic agents such as charantin, polypeptide-p and vicine. The hypoglycemic actions of bitter melon are represented in figure 3(Uebanso et al., 2007). Animal studies have shown anti-diabetic properties of the seed, fruit pulp, leaves and whole plants of *M. charantia* repeatedly in normal animals (Joseph and Jini, 2013). *M. charantia* extracts such as aqueous extract, methanol fraction, methanol insoluble fraction administration in rats suppressed postprandial hyperglycemia by inhibiting α -glucosidase activity (Uebanso et al., 2007). The acetone extract of whole fruit powder of *M. charantia* in different doses (0.25, 0.50 and 0.75 mg/kg body weight) had lowered the blood glucose from 50.0% to 13.3% over 8^{th} to 30^{th}-day in alloxan-induced diabetic albino rats, *M. charantia* reduces overweight, serum insulin, normalizes the glucose tolerance and improves insulin sensitivity in rats fed high fat diet (Chen et al., 2003)(Chen and Li, 2005).

3.2 Aframomum melegueta

Aframomum melegueta belongs to Zingiberaceae family and commonly known guinea and alligator pepper. This plant has more medicinal and nutritive properties, hence the name 'Grains of Paradise' and it is one of the important traditional medicine (Mohammed et al., 2016). *A. melegueta* were abundantly found in central and western parts of Africa. *A. melegueta* is used as herbal medicine for many problems such as diarrhea, cough, measles, toothache, rheumatism, cardiovascular diseases, fertility issues, anemia, smallpox, chickenpox, malaria, snakebites and wounds. The anti-diabetic actions of *A. melegueta* are represented in figure 4(Mohammed et al., 2017)(Ilic et al., 2010). Animal studies, the hypoglycemic effect of *A. melegueta* has been proved by administration of *A. melegueta* leaf extract to alloxan-induced diabetes in male albino rats. The experiment is done by oral administration of alloxan at different dosage to induce diabetes and it was treated by oral administration of *A. melegueta* leaf extract at different dosage. As a result, shows decreased blood glucose level by increasing *A. melegueta* leaf extract dose when compare to their controls (Mojekwu et al., 2011). The seeds of *A. melegueta* is used in folkloric medicine and it proved that by modulating Angiotensin 1converting activity (for blood pressure regulation), lipid profile and oxidative imbalances, hypercholesterolemia, hyperlipidemia and hypertension could be managed (Adefegha et al., 2016). The study of anti-diabetic activity of ethanolic seed extract of *A. melegueta* in alloxan-induced diabetic rats were correlated by histopathology of liver and pancreatic cells. The administration of ethanolic seed extract of *A. melegueta* in diabetic rats resulted in reversed liver damaged cells and regenerated pancreatic β-cells and reduction of blood glucose level compared to control diabetic rats. This concludes that ethanolic seed extract of *A. melegueta* contains anti-diabetic effects, antioxidant effects and tissue protective properties for management of Diabetes mellitus (Nosiri et al., 2016).

Figure 3: Hypoglycemic actions of bitter melon

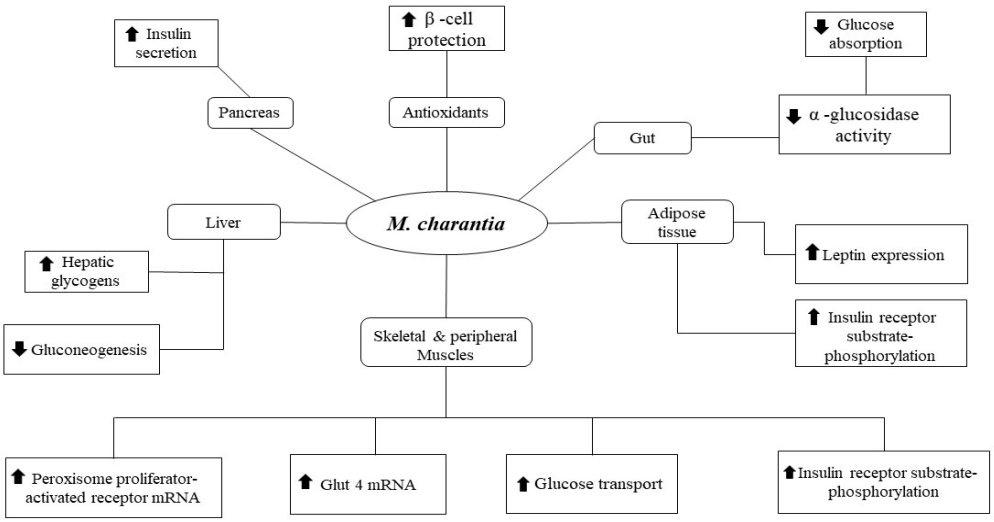
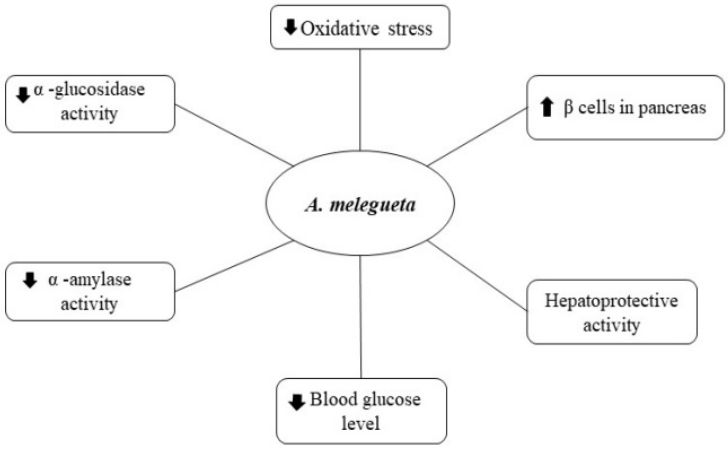


Figure 4: Anti-diabetic actions of *A. melegueta*



3.3 Withania coagulans:

Withania coagulans Dunal belongs to the family Solanaceae. Mostly found in Northern India and other drier parts of India and it is rigid, grey under shrubs with 60-120 cm which is commonly known as Indian cheese maker or punir. The dry fruit of *W. coagulans* is used by Northern India traditional healers for the treatment of diabetes (Maurya et al., 2008). Similar plant from same family,*Withania somnifera* Dunal also has similar medicinal properties as *Withania coagulans*(Kanungo et al., 2013). The alcoholic, ethanolic and aqueous extracts of *W. coagulans* has antibacterial, anthelmintic and cardiovascular effects. Mainly hot aqueous extract of *W. coagulans* has hepatoprotective, anti-inflammatory, antidiabetic effect and increases the glucose utilization in hemidiaphragm cells (Jaiswal et al., 2009). Phytochemical screening of aqueous extract of *W. coagulans* showed the presence of numerous bioactive components such as carbohydrates, glycosides, steroidal compounds, saponins, phenols, tannins, alkaloids, terpenoids, and flavanoids. The antihyperglycemic and antihyperlipidemic actions of *W. coagulans* are represented in figure 5(Shukla et al., 2012). Animal studies, the antihyperglycemic and antihyperlipidemic activity of *W. coagulans* was done by taking the aqueous and chloroform extract of *W. coagulans.* The streptozotocin-induced diabetic rats orally administered with aqueous extract showed highly significant hypoglycemic and antihyperglycemic effect; the oral administration of chloroform extract of *W. coagulans* showed non-significant glucose lowering effect and administration of both aqueous and chloroform extract combination showed better antihyperglycemic activity compared to metformin and aqueous extract alone; decease in the blood glucose, triglyceride, total cholesterol, LDL and VLDL level and significant increase in HDL level it also have anti-stress, antioxidant and immunomodulatory effects (Hoda et al., 2010). The streptozotocin-induced diabetic male albino rats intraperitoneally administered with aqueous extract of *W. coagulans* showed decreased blood glucose level, serum cholesterol and LPO at the dose of 1g kg^{-1}. *W. coagulans* aqueous extract showed free radical scavenging activity in an in vitro system via DPPH (Hemalatha et al., 2004).

Figure 5: antihyperglycemic and antihyperlipidemic actions of *W. coagulans*

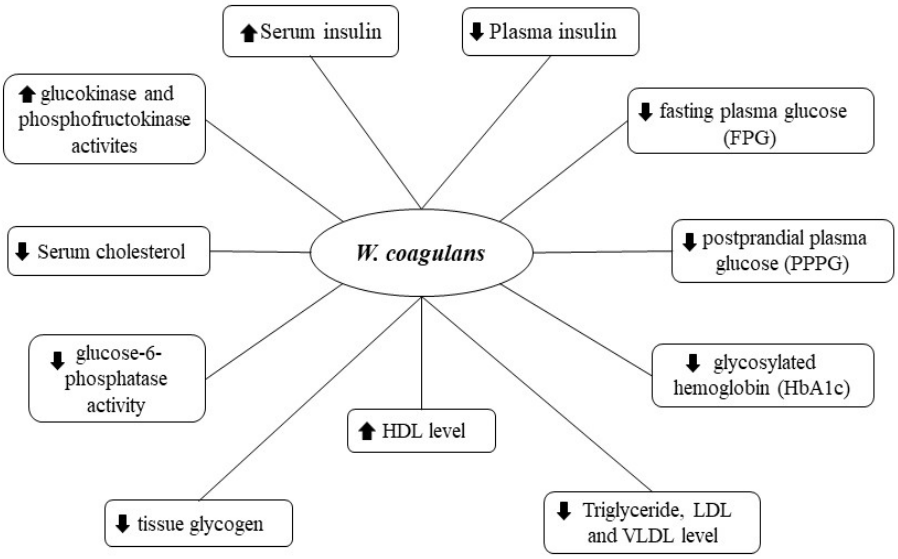


Figure 6: antihyperglycemic and antihyperlipidemic actions of *W. coagulans*

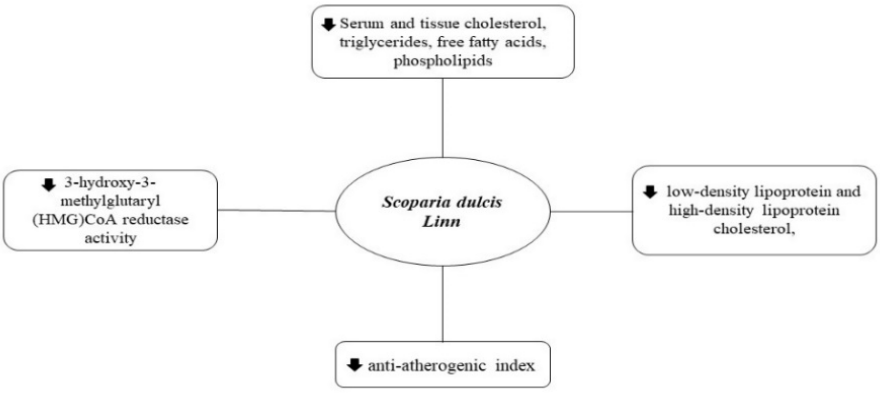


Figure 7: Anti-diabetic actions of *G. sylvestre*

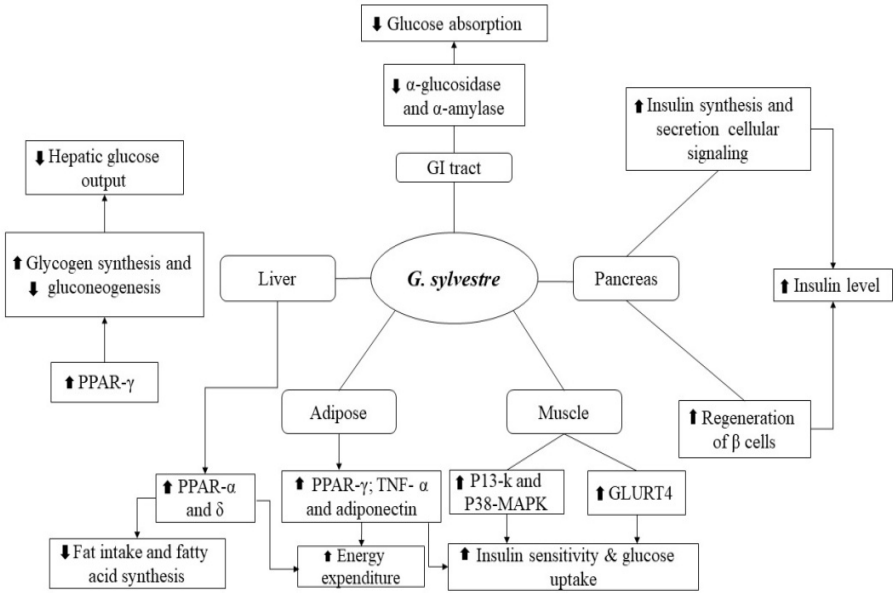
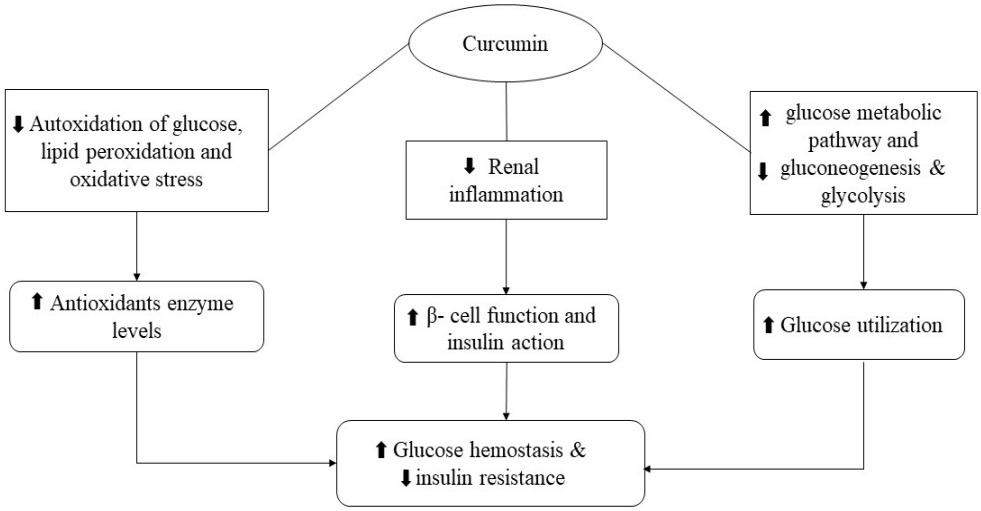


Figure 8: Anti-diabetic actions of *Curcuma longa*



3.4 Scoparia dulcis:

Scoparia dulcisLinn belongs to Scrophulariaceae family. They are commonly known as sweet broom weed and widely distributed in the tropical and subtropical regions of Asia and South America. *Scoparia dulcis Linn* is a perennial herb, traditionally used to cure stomach troubles, hypertension, inflammation, bronchitis, hemorrhoids, hepatitis, diabetes, analgesic and antipyretic. Some bioactive substances from *Scoparia dulcis* such as *scoparic* acid A, *scoparic* acid B, *scopadulcic* acid A and B, *scopadulciol*, and *scopadulin* helps in curing many diseases (Latha et al., 2004a). Nath in 1973, isolated and characterized a compound called amellin and glycoside from *Scoparia dulcis Linn* which showed effective antidiabetic properties in short period of time. The flavonoids such as quercetin, p-coumaric acid, luteolin and apigenin from *Scoparia dulcis Linn* helps glucose uptake by cells. The anti-diabetic actions of *Scoparia dulcis Linn* are represented in figure 6(Beh et al., 2013). In vivo studies, the antidiabetic activity of *Scoparia dulcis Linn* Suh as streptozotocin-induced diabetic rats (1ml/kg) were orally administered (using gavage) with aqueous extracts (100, 200 and 400 mg/kg) which shows Highly significant antihyperglycemic effect ($P < 0.001$), decreases the blood glucose level, increased blood insulin levels and increased body weight were seen on completion of 15 days in the group which was administered 200 mg/kg when compared to other groups (Latha et al., 2004a). To investigate and study the effect of *Scoparia dulcis Linn* plant extract on hepatic key metabolic enzymes of carbohydrate metabolism, the streptozotocin-induced diabetic rats were orally administered with aqueous, ethanol and chloroform extracts of *Scoparia dulcis Linn* (50, 100 and 200mg/kg/ day). Although decrease in blood sugar was seen effectively from first week, at third week ofadministered with aqueous extract (200mg/kg/day) shows completely decreased blood glucose level which was seems to be similar to the ontrol group and administration of ethanol and chloroform extract (200mg/kg/day) showed decrease of blood glucose level later (i.e., after completion of third week). Aqueous extract showed high anti-hyperglycemic effect while compared to ethanol and chloroform extract (Pari and Latha, 2005). In vitro studies, the insulin secretagogue activity of *Scoparia dulcis Linn* was studied using a rat insulinoma cell line (RINm5F). The islets were isolated, cultured and treated with streptozotocin (5mM) and *Scoparia dulcis Linn* plant extract (1,10 and 100µg/ml). The stimulatory effect on insulin secretion from islets was seen in aqueous extract of *Scoparia dulcis Linn*. Incubation of islets with 10µg/ml of aqueous extract increased the insulin secretion compared to others. The cytotoxicity assay was done to check the prevention of streptozotocin-induced cell death by *Scoparia dulcis* Plant Extract (SPEt) and resulted in increased cell viability while treating with 10µg/ml of aqueous extract. Griess nitrite assay was done to check the effect of SPEt on STZ induced nitrite formation by RIN cells which showed complete inhibition of nitrite formation at 10µg/ml of aqueous extract (Latha et al., 2004b).

3.5 Gymnema sylvestre:

Gymnemasylvestre belongs to family Asclepiadaceae which is commonly known as gurmar. *G.sylvestre* is a perennial woody climber and widely distributed in tropical areas of India, China, Africa and Australia (Pham et al., 2018). It is using in ayurvedic medicines as both single and multi-herb formulation to treat diabetes mellitus and other diseases. The extracts of leaves, roots and other parts of *G. sylvestre* has anti-hyperglycemic, anti-hyperlipidemic, anti-microbial, anti-oxidant, anti-inflammatory and anti-cancer activities (Kamble et al., 2016). Main active peek or compound of gymnemic acids was isolated from the leaves of *G. sylvestre* which is known as anti-sweet compounds which is also called in terms of gymnemagenin (GMG), a hydrolyzed product of gymnemic acids and it is reported as biomarker for pharmacokinetic studies. The anti-diabetic actions of *G. sylvestre* are represented in figure 7(Rathore et al., 2016).

In vivo studies, To study the antidiabetic, hypolipidemic and histopathological analysis of *G. sylvestre* (R.Br)

leaves, streptozotocin-induced diabetic rats (150mg/kg, intraperitoneally) were orally administered with *G. sylvestre* methanolic extract (GSME) at different concentrations (100,200 and 400mg/mL) and one group was orally administered with glibenclamide (5g/kg) showed reduced blood glucose level, serum cholesterol, triglycerides, phospholipids, LDL, VLDL and free fatty acids, whereas it increased plasma protein total hemoglobin, HDL cholesterol, serum insulin level and body weight when compared to untreated diabetic rats. GSME showed favorable effect on histopathological studies in streptozotocin-induced diabetic rats (Prabhu and Vijayakumar, 2014). To study effect *G. sylvestre* leaves extract on physiological parameters of diabetes mellitus was carried out in streptozotocin-induced diabetic male albino rats (45mg/kg) and it was administrated with *G. sylvestre* leaves extract (18mg/kg, intragastrically) which resulted in decreased plasma glucose, triglycerides, cholesterol and LDL-cholesterol, alanine aminotransaminase (ALT), aspartate aminotransaminase (AST) and malondialdehyde levels while compared to streptozotocin-induced diabetic rats and also increases in plasma insulin, HDL-cholesterol and Erythrocyte SOD levels while compared to streptozotocin-induced diabetic rats. There was no significant difference between Plasma catalase and glutathione (GSH) level while compared to streptozotocin-induced diabetic rats (El Shafey et al., 2013).

3.6 Curcuma longa

Curcuma longa belongs to family Zingiberaceae and commonly known as turmeric (Chuengsamarn et al., 2012). It is one of the important herbal plant in the Indian traditional medicine and can be mostly seen in tropical and subtropical regions turmeric contain main essential compounds mainly curcuminoids with the many biological activities such as antibacterial, anti-inflammatory, antioxidant, antiproliferative, antifibrotic (Mirnejad et al., 2014)and it is also used as therapeutic agents to treat cardiovascular diseases, renal diseases, neurodegenerative disorders and hepatic damages (Amalraj et al., 2017)(Rivera-Mancía et al., 2018). Recent researches have proved that curcumin has antihyperglycemic activity which helps in reduction of glucose in tolerance, insulin resistance, hyperglycemia, hyperlipidemia, β cells apoptosis and necrosis. A few clinical trials were done with type 2 diabetes patients. Curcumin is extensively used to treat diabetes associated complications. The anti-diabetic actions of *Curcuma longa* are represented in figure 8(Zhang et al., 2013)(Kato et al., 2017).

In vivo studies, the antihyperglycemic activity of *curcuma longa Linn* is studied in kg Tab dexamethasone- induced male rabbits (10mg/kg) by oral administration of *Curcuma longa* rhizome powder (unprocessed *Haridra* rhizome powder) and Insulin plant. Rabbits were grouped into - first group - control; second group were orally administrated with insulin plant leaf powder (250 mg/kg/day) and third group were orally administrated unprocessed *Haridra* rhizome powder (250 mg/kg/day). At the end of 21 days, the rabbits treated with insulin plant leaf powder and unprocessed *Haridra* rhizome powder showed highly significant that is p=0.0001 decrease in blood glucose level. When compared to insulin plant leaf powder, unprocessed *Haridra* rhizome powder shows significant of p=0.0109 blood sugar. So, this shows that curcuma longa has high potent antihyperglycemic activity than insulin plant (Deogade et al., 2017).

In vivo studies, the antidiabetic activity of *Curcuma longa* (turmeric) studied using ethanolic extract of Curcuma longa rhizome in alloxan-induced albino diabetic rats and compared with standard anti diabetic drug Pioglitazone. Five groups of albino rats were taken, normal control treated with 10ml/kg normal saline; diabetic control treated with 10ml/kg normal saline; Euglycemic rats treated with 300mg/kg ethanolic extract of turmeric; Diabetic rats treated with 300mg/kg ethanolic extract of turmeric; Diabetic control treated with 500mg/kg ethanolic extract of turmeric; Diabetic rats treated with 6mg/kg Pioglitazone. The drugs were orally administrated for 28 days and study was divided into acute study (1, 3, 5, 7 hours) and chronic study (7, 14, 21, 28 days) and blood glucose level was estimated. At end of 28 days chronic study showed significant ($p < 0.05$) decrease in blood glucose, whereas in acute study the is no significant reduction in blood glucose level (Santoshkumar et al., 2013). Similar study was done by oral administration of 200mg/kg aqueous extract of *Curcuma longa* rhizomeshowed significant ($p<0.05$) decrease in the level of High-Density Lipoprotein (HDL), body weight and albumin compared to untreated diabetic rats and significant ($p<0.05$) increase in the blood glucose level, total cholesterol, Low Density Lipoprotein (LDL) and triglyceride (TG). So, this shows that *Curcuma longa* can be used to treat diabetes mellitus (“(PDF) Anti-diabetic Activity of Aqueous Extract of Curcuma longa (Linn) Rhizome in Normal and Alloxan-Induced Diabetic Rats,” n.d.).

3.7 Polyherbal 1:

The prepared a polyherbal formulation containing *Glycosmis pentaphylla*, *Tridax procumbens*, and *Mangifera indica* and investigated its antidiabetic activity (Petchi et al., 2014). The stem bark of *G. pentaphylla* has shown antidiabetic activity against STZ-induced diabetes and antiarthritic activity against Freund’s complete adjuvant-induced arthritis. Similarly, ethanolic extracts of *T. procumbens* and *M. indica* has been known to possess hypoglycemic effect. Thus, the antidiabetic potential of these plants has been established but their synergistic action was to be found out (Petchi et al., 2013)(Kamble et al., 2016). For this study, ethanol extracts of the stem bark of *G. pentaphylla*, whole plant of *T. procumbens*, and leaves of *M. indica* in the ratio of 2:2:1 were utilised to prepare the formulation by wet granulation method. The formulation was standardised as per WHO guidelines to ensure consistency in quality (pH, moisture content, weight variation, heavy metal limit, microbial load, etc.). Fingerprint analysis of the formulation by HPTLC exhibited separation at 366 nm and that the active compounds were present in all the three extracts. Acute

toxicity of the polyherbal formulation in healthy wistar rats was not seen over 14 days in doses upto 2000 mg/kg. When the formulation in two doses (250 and 500 mg/kg) was administered to rats with diabetes mellitus induced by streptozotocin and nicotinamide, antidiabetic activity similar to that of glibenclamide was seen. The histopathology studies also indicated that the formulation possessed antidiabetic behaviour.

3.8 Polyherbal 2:

Polyherbal concoctions of 11 different plants, numbering up to 5, in various concentrations selected randomly, were formulated (Panda et al., 2013). The plants selected had been documented for their usefulness, including their antidiabetic activity. The herbal plants used in this study were *Ferula assa-foetida, Annona squamosa, Zingiber officinale, Gymnema sylvestre, Tamarindus indica, Azadirachta indica, Trigonella foenum-graecum, Moringa oleifera, Aegle marmelos, Cajanus cajan, Cinnamomum tamala*. Many extracts from these plants have been shown to reduce blood sugar levels in STZ- or alloxan - induced diabetic rats, some help in body weight gain and decreased serum lipid levels. *Annona squamosa* has been historically claimed to have antidiabetic properties (Baskaran et al 1990); *Gymnema sylvestre seems to regenerate/repair beta cells in type II diabetes.* The acute toxicity of these preparations was then tested in albino rats and LD_{50} (600 mg/kg) dose determined. The effectiveness of these formulations (400 mg/kg body weight/day dose) were also tested in STZ-induced diabetic rats over a period of 21 days. Hypoglycaemic activity of all the formulations were found to be almost similar or more than that observed when using glibenclamide. Also, biochemical tests of liver in diabetic control group suggested that these formulations also helped to lower the enzyme levels back to normal levels (Shirwaikar et al., 2004).

3.9 Polyherbal 3:

A polyherbal formulation comprising of extracts from *Salacia roxburghii, Salacia oblonga, Garcinia indica, and Lagerstroemia parviflora* was prepared (Subhasree et al., 2015). Utilizing the patent by M/s Varanasi Bio Research Pvt Ltd. These plants were selected after an initial screening for their hypoglycemic properties from the ayurvedic literature 'Sharangdhar Samhita'. The plants belonging to the genus Salacia has been known for treating diabetes, skin diseases, inflammation among other ailments. *G. indica* has been used over the years for their antimicrobial, antioxidant and anti-obesity properties. L. speciosa has also been studied for their antidiabetic activity. Doses of the polyherbal formulation upto 2000 mg/kg did not induce any toxic effects. Adult Sprague Dawley rats were utilised for the study by given high fat diet (HFD) and injected with STZ (35 mg/kg, i.p.) to simulate characteristics of human type 2 diabetes. Oral doses of the Polyherbal formulation was administered in two dosage (200 mg/kg/day and 400 mg/kg/day) to different groups and compared to rats which were given metformin (250 mg/kg) once a day. Reduction in the blood glucose levels of the diabetic rats was observed after 28 days in the groups administered with both the doses of the formulation in line with that of the groups given metformin; also, insulin levels were elevated after treatment. The lipid profile also suggests that the PHF may help lower the serum lipid levels. The authors also suggest that the antidiabetic activity can be attributed, in part, α-glucosidase inhibitory activity of Salacia and glucose uptake activity of tannins in Lagerstroemia species (Srinivasan et al., 2005).

3.10 Polyherbal 4:

A study was carried out to assess the antidiabetic activity of 'Kathakakhadiradi Kashyam'(KKS), an ayurvedic formulation used traditionally for treating diabetes and its symptoms (Azeez et al., 2016). This herbal formulation is prepared from plants such as *Strychnos potatorum, Acacia catechu, Woodfordia fruticose, Salacia reticulate, Curcuma longa, Biophytum Senstivium, Ziziphus jujube, Cyclea Peltata, Mangifera indica, Terminalia chebula* and *Cyperus rotundus.* Phytochemical analysis of KKS shows the presence of carbohydrates, proteins, amino acids, flavanoids, saponins, phenols and tannins. The effects of the polyherbal was tested on albino rats after induction of diabetes by administering 60 mg/kg STZ. Different group of rats were treated with different dosages (0.54ml/kg, 1.08 ml/kg, 2.16 ml/kg) and compared with rats treated with glibenclamide (0.5 mg/kg). The glucose level measurements were made at regular intervals upto 4 hours after administration of the investigative drug for 28 days. The results indicated that KKS produced effects similar to the standard antidiabetic drug glibenclamide. The authors suggest that the formulation may act extensively to produce hypoglycemic effects, including but not limited to regeneration of beta cells, increase in the size and number of islets of Langerhans, stimulation of insulin secretion, reducing insulin resistance. They also assert that molecular level approaches are necessary to identify the mechanism of action of the formulation (Azeez et al., n.d.).

4. CONCLUSION:

India is dubbed as the diabetes capital of the world, accounting for the highest number of patients. Difference in prevalence rates of diabetes in Indian population are expected because of larger variation in the prevalence of macro vascular complication and other risk factors in different regions of the country. With the increasing population and lifestyle changes, this number is only expected to grow. Hence it is important to establish comprehensive treatment options that is safe, accessible and effective. Herbal medicines can, after proved by research, help supplement commercially available drugs. Still there is no proper stage of development of plant-based drug that can replace or reduce synthetic drug usage. So, with an expectation that in future, synthetic medicines would be replaced by herbal medicines will all desired parameters for effective and safer treatment to cure the diseases. There are many antidiabetic plants, certain important plants were mentioned above. So, this review is a small step towards achieving that.

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