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TRADITIONAL HERBAL DRUGS: AN EMERGING ALTERNATIVE DRUG FOR DIABETES

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ABSTRACT

This dreadful disease is found in all parts of the world and is becoming a serious threat to mankind health. It is caused by the deficiency or ineffective production of insulin by pancreas which results in increase or decrease in concentrations of glucose in the blood. There are lots of chemical agents available to control and to treat diabetic patients, but total recovery from diabetes has not been reported up to this date. Alternative to these synthetic agents, many herbal plants with hypoglycaemic properties are known from across the world. The World Health Organization (WHO) has listed 21,000 plants, which are used for medicinal purposes around the world. A list of medicinal plants with proven antidiabetic and related beneficial effects and of herbal drugs used in treatment of diabetes is compiled.

KEYWORDS: Plant, Glucose, Diabetes, Herbal, Insulin, Blood.

INTRODUCTION

Diabetes mellitus is a systemic metabolic disease characterized by hyperglycemia, hyperlipedemia, hyperaminoacidemia, and hypoinsulinaemia it leads to decrease in insulin, secretion and insulin action. Currentlyavailable therapies for diabetes include insulin and various oral antidiabetic agents such as sulfonylureas, biguanides, αglucosidase inhibitors and glinides. In developing countries products are expensive and noteasily accessible. 1 Diabetes is a heterogeneous metabolic disorder characterized by altered carbohydrate, lipid, and protein metabolism which causes hyperglycemia resulting from insufficient insulin secretion, insulin action or both. 2 It is one of the refractory diseases identified by Indian Council of Medical Research for which an alternative medicine is a need for the treatment. Diabetes mellitus has become a growing problem in the contemporary world. India has today become the diabetic capital of the world with over 20 million diabetes and this number is likely to increase to 57 million by 2025 .3 A number of medicinal plants, traditionally used for over 1000 years named Rasayana are present in herbal preparations of Indian traditional health care systems. The current review focuses on herbal drug preparations and plants used in the treatment of diabetes mellitus, a major crippling disease in the world leading to huge economic losses.[4]

Pathophysiology of Diabetes mellitus-A widespread pathological change is thickening of matrix and cellular proliferation resulting in vascular complications like, lumen narrowing, • early atherosclerosis, • sclerosis of glomerular capillaries, • retinopathy, • neuropathy • peripheral vascular insufficiency.• Enhanced glycosylation of tissue proteins due to persistent exposure to high glucose concentrations and the accumulation of larger quantities of sorbitol (a reduced product of glucose) in tissues are believed to be causative in the pathological changes of

Some of the signs and symptoms of type 1 diabetes and type 2 diabetes are

Increased thirst

- Frequent urination
- Extreme hunger
- Unexplained weight loss
- Presence of ketones in the urine (ketones are a byproduct of the breakdown of muscle and fat that happens when there's not enough available insulin)
- Fatigue
- Irritability
- Blurred vision
- Slow-healing sores
- Frequent infections, such as gums or skin infections and vaginal infections

Type 1 diabetes can develop at any age, though it often appears during childhood or adolescence. Type 2 diabetes, the more common type, can develop at any age, though it's more common in people older than 40.[1]

Type 1 diabetes mellitus [T1DM]- It is also known as insulin-dependent diabetes mellitus (IDDM), childhood diabetes or juvenile diabetes (because it mainly affect children), is characterized by the loss of insulin producing β cells of the islets of Langerhans of the pancreas leading to a deficiency in insulin production. It should be noted that there is no known preventative measure that can be taken against type 1 diabetes. Most people affected by type 1 diabetes are otherwise healthy and of a healthy weight when onset occurs. The main cause of β cell loss leading to type 1 diabetes is a T-cell mediated autoimmune attack.3 Deficiency of insulin results in altered carbohydrate and lipid metabolism which leads to ketosis and diabetic ketoacidosis, coma or death. Currently, type 1 diabetes can be treated only with insulin, with careful monitoring of blood glucose levels using blood testing monitors. Treatment of Type 1 diabetes mellitus must be continued throughout life.[5]

Type 2 diabetes mellitus [T2DM]- Synonymously called adult-onset diabetes, maturity-onset diabetes in young (MODY), or non-insulindependent diabetes mellitus (NIDDM); is due to a combination of defective insulin secretion and insulin resistance or reduced insulin sensitivity (defective responsiveness of tissues to insulin), which almost certainly involves the insulin receptor in cell membranes. Type 2 diabetes mellitus is one of the most chronic metabolic disorder associated with co-morbidities such as obesity, hypertension, hyperlipidemia and cardiovascular disease, which, taken together, comprise the 'metabolic syndrome'. Type 2 diabetes mellitus is characterized by postprandial hyperglycemia that results from defects in both insulin action and secretion. Its chronic complications include vision damage due to retinopathy, renal failure due to nephropathy, loss of sensation or pain due to neuropathy, and accelerated atherosclerosis, which results in blindness, end-stage renal disease, amputations, and premature cardiovascular mortality. Obesity is found in approximately 55% of patients diagnosed with type 2 diabetes.[6]

Pathogenesis of type 2 diabetes- β-cell dysfunction and insulin resistance type 2 diabetes is usually the product of two distinct abnormalities viz. abnormal β-cell function and decreased insulin sensitivity. It appears that type 2 diabetes is primarily a genetic disease, based on its strong familial association and high concordance rates in identical twins7. However, no single gene has been identified that is common to a general population of type 2 diabetic patients, leading to the conclusion that this must be a polygenic disease.[8-10] Most of the type 2 diabetic patients are obese, who generally have resistance to the actions of insulin on liver, muscle and fat tissues (the major targets for the beneficial effects of insulin). An environmental influence also plays a major role by enhancing the phenotypic expression of genes that place individuals at risk for diabetes. This is becoming increasingly apparent as witnessed by the recent epidemic proportions of new-onset type 2 diabetes in cultures such as American Indian, African American, Latino, and Alaskan American. The obesity, insufficient physical activity, and excessive carbohydrate intake is an immense reason for diabetes. These clinical essentials point to the conclusion that the preliminary lesion in type 2 diabetes almost certainly involves hereditarily gritty reduction of intrinsic β-cell function, which is thus unable to passably meet the challenge of states of insulin resistance, such as obesity. As a result, the β-cell is frequently called upon to generate insulin because of uncertain hyperglycemia, and this stress progressively causes β-cell descent and accelerated apoptosis.[11] Both β-cell dysfunction and insulin confrontation works in concert to cause further descent of insulin secretion and increase insulin resistance. Nonetheless, it is interesting to consider that not all lean type 2 diabetic patients are insulin resistant, and that patients with cystic fibrosis and type 2 diabetes are characteristically insulin sensitive.[2]

Glucolipotoxicity in the β-cell and oxidative Stress- The general findings of prominent glucose and lipid levels in the blood of diabetic patients led to glucose toxicity13 and lipotoxicity.14 Relatively more information has been published about biochemical pathways through which elevated glucose concentrations can generate excessive levels of reactive oxygen species (ROS).15 These include glycolysis and oxidative phosphorylation; methylglyoxal formation and glycation; enediol and α-ketoaldehyde formation (glucoxidation); diacylglycerol formation and protein kinase C activation; glucosamine formation and hexosamine metablolism; and sorbitol metabolism. Conceptually, as β-cells are exposed to high glucose concentrations for increasingly prolonged periods of time, glucose saturates the normal route of glycolysis and increasingly is shunted to alternate pathways, such that reactive oxygen species are generated from distinct metabolic processes within and outside the mitochondria. The results also indicate that extreme levels of palmitate are allied with anomalous islet function, which leads to extreme lipid esterification that can produce ceramide, thereby escalating oxidative stress.14-16 It seems unlikely that circulating lipid level of triglyceride or cholesterol, would be accountable for destructive islet tissue and excessive circulating glucose levels lead to accelerated de novo synthesis of islet lipid. Its ability to drive synthesis of malonyl CoA, glucose contributes to lipotoxicity which inhibits β-oxidation of free fatty acids. This in turn shunts free fatty acids towards esterification pathways, thereby forming triglyceride, ceramide and other esterification products[7, 8] Lipotoxicity requires concomitant hyperglycemia to damage islet function, whereas glucose toxicity can exert harmful effects on the islet in the absence of elevated circulating triglyceride.19 The chronic hyperglycemia can cause aggravation β-cell function during decreased

protein expression of two important transcription factors: Pdx-1 (Pancreatic and duodenal homeobox-1) and MafA (Mammalian homologue of avian).15 Both proteins are critical for normal insulin gene expression, as their absence or mutation of their DNA binding sites on the insulin promoter leads to decreased mRNA levels, content and secretion of insulin

Glucolipotoxicity in non-β cells, insulin resistance and oxidative stress: Insulin resistance convoy the progress of pregnancy, obesity, excess growth hormone and glucocorticoid levels, and lack of exercise. Oxidative Stress play a significant role in insulin resistance and in the cellular damage of tissues that leads to the late complications of diabetes. Abnormal levels of free fatty acids, tumour necrosis factor-α, leptin and resistin are frequently found in obese individuals and are prominently mentioned as potential mediators of insulin resistance. Free fatty acids have been reported to impair insulin action through oxidative stress induced activation of nuclear factor-kβ. Secondary complications of diabetes involve microvascular and macrovascular changes that lead to retinopathy, nephropathy, neuropathy and damage to critical blood vessels, such as the coronary arteries. Stress-activated signaling pathways that might play a role in these phenomena are those involving protein kinase C, nuclear factor-kβ, p38 mitogen-activated protein kinase, advanced glycosylation end-products and their receptors and amino-terminal JUN kinases.21 Antioxidant agents that have been reported to diminish insulin resistance, are lipoic acid, NAC, aminoguanidine, vitamin C, vitamin E, resveratrol, silymarin and curcumin.[9]

Allopathic Treatment- Approaches to Drug therapy in Diabetes

Insulin

Insulin was discovered in 1921 by Banting and Best who demonstrated the hypoglycaemic action of an extract of pancreas.

Uses of insulin

Diabetes mellitus • Insulin is effective in all forms of diabetes mellitus and is a must for type 1 cases, and gestational diabetes. • Many type 2 cases can be controlled by diet, reduction in body weight and appropriate exercise supplemented, if required, by oral hypoglycaemics.[1]

A.Drugs which enhance insulin secretion

1. Sulfonylureas [KATP Channel blockers]

•Mechanism of action: Sulfonylureas provoke a brisk release of insulin from pancreas**. Indications:** Particularly suitable for patients who are not overweight, do not consume alcohol, and adhere to a consistent dietary routine.

Clinical characteristics:● Glycemic efficacy: lowers HbA1c by 1.2% over 3 months.● Long-term experience.● Low-cost**.**

Important side effects: ● Life-threatening hypoglycemia.● Increased risk in patients with renal failure.● Weight gain.● Hematological changes: granulocytopenia, hemolytic anemia.● Allergic skin reactions.● Alcohol intolerance.● Compared to metformin, sulfonylureas are associated with more cardiovascular

Contraindications: ● Severe cardiovascular comorbidity.● Obesity.● Sulfonamide allergy (particularly long-acting substances).● Severe liver failure.● Severe kidney failure[2]

2. Meglitinide analogues [KATP Channel blockers]

MOA: release of insulin from pancreas.

Drugs: Repaglinide, Nateglinide. • They induce rapid onset short lasting insulin release.Administered before each major meal to control post prandial hyperglycemia. Indications: particularly suitable for patients with postprandial peaks in blood glucose levels

Clinical characteristics: ● Glycemic efficacy: lowers HbA1c by 0.75% over 3 months.● More expensive than sulfonylureas.

Important side effects: ● Life-threatening hypoglycemia (less risky than sulfonylureas).● Increased risk in patients with renal failure.● Weight gain.● Hepatotoxicity (rare).

Contraindications: ● Severe liver failure.● Severe renal failure.

Interactions: Sulfonylureas.[2]

3. Glucagon-like peptide-1 [GLP-1] receptor agonist

• GLP-1 is an important incretin released from the gut in response to ingested glucose. • It induces insulin release from pancreatic β cells, inhibits glucagon release from α cells, slows gastric emptying and suppresses appetite.

Drugs available: Exenatide, Liraglutide(Victoza)

Clinical characteristics: ● Glycemic efficacy: lowers HbA1c by 0.5–1.5% over 3 months● Subcutaneous injection● Weight loss● No risk of hypoglycaemia

Side effects:● Gastrointestinal complaints (particularly impaired gastric emptying!)● Increased risk of pancreatitis and potentially pancreatic cancer

Contraindications: ● Preexisting symptomatic gastrointestinal motility disorders● Chronic pancreatitis or a family history of pancreatic tumors

4. Dipeptidyl peptidase-4 [DPP-4] inhibitors

• DPP-4 in rapid degradation of endogenous GLP-1, orally active inhibitors of DPP-4 have been developed as indirectly acting insulin secretagogues. • Sitagliptin,

Vildagliptin, Saxagliptin

Clinical characteristics: ● Glycemic efficacy: lowers HbA1c by 0.5–0.75% over 3 months.No risk ofhypoglycemia unless insulin and/or insulinotropic drugs are used simultaneously.

Important side effects: ● Gastrointestinal complaints: diarrhea, constipation (milder thanin GLP-1 agonist exposure).● Nasopharyngitis and upper respiratory tract infection.● Arthralgia.● Headaches, dizziness.● Urinary infections (mild).● Increased risk of pancreatitis.● Acute renal failure.

Contraindications:● Hypersensitivity.● Liver failure.[2]

B. Drugs which overcome insulin resistance

1. Biguanide

• Phenformin higher risk of lactic acidosis banned in India since 2003. • Metformin: Enhances insulin-mediated glucose uptake and disposal in skeletal muscle and fat.

Indications: drug of choice in all patients with type 2 diabetes.

Clinical characteristics:● Glycemic efficacy: lowers HbA1c by 1.2–2% over 3 months.● Weight loss or weight stabilization.● No risk of hypoglycemia.● Beneficial effect on dyslipidemia.● Studies show metformin reduces the risk of macroangiopathic complications in diabetic patients.● Cost-effective.

Important side effects: ● Metformin-associated lactic acidosis.● Incidence: ~ 8 cases/100,000 patient years.● Clinical features: frequently nonspecific.● Gastrointestinal prodromal symptoms: nausea, vomiting, diarrhea, abdominal pain.● Severe symptoms: muscle cramps, hyperventilation, apathy, disorientation, coma.

High-risk groups: ● Elderly individuals.● Patients with cardiac or renal insufficiency.● Diagnostics.● Arterial blood gas (ABG): metabolic acidosis and anion gap.● ↑ Serum lactate.● Treatment: discontinue metformin and treat acidosis.● Gastrointestinal complaints are common: nausea, diarrhea, flatulence.● Vitamin B12 deficiency.● Metallic taste in the mouth [dysgeusia].

Contraindications: ● Renal failure (if creatinine clearance < 30 mL/min).● Severe liver failure.● Intravenous iodinated contrast medium.● Pause metformin prior to surgery.● Chronic pancreatitis, starvation ketosis, ketoacidosis, sepsis.● Heart failure (NYHA III and IV), respiratory failure, shock, sepsis.● Alcoholism.

Important interactions: sulfonylureas[2]

2. Thiazolidinedione (PPARγ agonist) Pioglitazone • MOA: Glitazones tend to reverse insulin resistance by enhancing GLUT4 expression and translocation. • Entry of glucose into muscle and fat is improved. (**Rosiglitazone,** is banned in India due to unacceptable increase in risk of myocardial infarction, CHF, stroke and death.[2]

Miscellaneous

1.α Glucosidase inhibitors

• **Acarbose:** inhibits α-glucosidases, the final enzymes for the digestion of carbohydrates in the brush border of small intestine mucosa. •Flatulence, abdominal discomfort and loose stool are produced in about 50% patients due to fermentation of unabsorbed carbohydrates.

Mechanism of action: ● Inhibits alpha-glucosidase.● Decreased intestinal glucose absorption.● The drug is particularly effective in controlling postprandial blood glucose levels.● The undigested carbohydrates reach the colon, where they are degraded byintestinal bacteria, resulting in the production of intestinal gas.

Clinical characteristics: ● Glycemic efficacy: lowers HbA1c by 0.8% over 3 months.● No risk of hypoglycemia.

Important side effects: gastrointestinal complaints (flatulence, abdominaldiscomfort, diarrhea).

Contraindications● Inflammatory bowel disease.● Conditions associated with malabsorption.● Severe renal failure.[2]

2. Sodium-glucose co-transport-2 [SGLT2] inhibitor

•Practically all the glucose filtered at the glomerulus is reabsorbed in the proximal tubules. • The major transporter which accomplishes this is SGLT-2, • Inhibition of SGLT-2 induces glucosuria and lowers blood glucose in type 2 DM, as well as causes weight loss.[2]

Common contraindications of antidiabetic agents

● **Pregnancy and breastfeeding [gestational diabetes]** All antidiabetic agents contraindicate**d.** Antidiabetic drugs should be substituted with human insulin as early as possible (ideally prior to the pregnancy).

● **Renal failure**: Antidiabetic drugs that may be administered if GFR < 30mL/min include DPP-4 inhibitors, incretin mimetic drugs, meglitinides, and thiazolidinediones. ● Morbidity and surgery.

Pause antidiabetic treatment in the following cases

● Major surgery performed under general anesthesia. ● Acute conditions requiring hospitalization (infections, organ failure).● Elective procedures associated with an increased risk of hypoglycemia (periods offasting, irregular food intake).[3]

Insulinotropic agents ● Mechanism: stimulate the secretion of insulin from pancreatic β-cells.● Glucose-independent: Insulin is secreted regardless of the blood glucose level, even if blood glucose levels are low → risk of hypoglycemia.● Sulfonylurea, meglitinides.● Glucose-dependent: Insulin secretion is stimulated by elevated blood glucose levels (postprandially). These antidiabetic agents depend on residual β-cellfunction.● GLP-1 agonists, DPP-4 inhibitors.[3]

Non-insulinotropic agents ● Mechanism: These agents do not depend on residual insulin production.● Effective in patients with nonfunctional endocrine pancreatic β-cells. ● Biguanides (metformin), SGLT-2 inhibitor, thiazolidinediones, alpha-glucosidase inhibitors.[3]

Herbal Anti diabetic drugs

Introduction Treatment of Diabetes mellitus without any adverse effects is still the biggest question to medical practioners. According to world ethanobotanical 800 medicinal plants are used for the prevention of diabetes mellitus. Clinically proven that only 450 medicinal plants possess anti diabetic properties from which 109 medicinal plants have complete mode of action. In ancient time doctor and lay person used traditional medicinal plants with their active constituents and properties for the treatment of various diseases such as heart diseases, cancer and diabetes. There is a long history of traditional plants used for the control of diabetes in India and China. There are various books available such as Charaka Samhita and Susruta Samhita which explains phytopharmacology features of diabetes and its adverse effect.[6] Synthetic drugs which are used for treatment of diabetes are associated with various adverse effect such as sickness, vomiting, dysentery, alcohol flush, migraine, swelling, malignant anemia and faintness. Herbal drugs are proved to be a better choice over synthetic drugs because of less side effects and adverse effects. Herbal formulations are easily available without prescription. These herbal drugs are used for life threatening disease. These drugs are also used when chemical drugs are ineffective in treatment of disease. These are natural and safe drugs i.e. there is no toxic effects. Herbal drugs permanently cure person and treat the disease while synthetic drugs are not permanently cured the diseases. Herbal formulations contain natural herbs and fruits and vegetables extract which are beneficial in treatment of various diseases without any adverse effects. On the other hand chemical drugs are prepared synthetically and have side effect also. Herbal formulations are cheap as compared to all opathic medicines. Herbal formulations are Eco friendly. Herbal formulations are produced from natural products while all opathic medicines are produced from chemical and chemically modified natural products. Herbal formulations are available without prescription while all opathic medicines are available with prescription.[6]

How do herbs work?

For most herbs, the specific ingredient that causes a therapeutic effect is not known. Whole herbs contain many ingredients, and it is likely that they work together to produce the desired medicinal effect. The type of environment (climate, bugs, soil quality) in which a plant grew will affect its components, as will how and when it was harvested and processed.[4]

What is herbal medicine good for?

Herbalists treat many conditions such as asthma, eczema, premenstrual syndrome, rheumatoid arthritis, migraine, menopausal symptoms, chronic fatigue, and irritable bowel syndrome, among others. Herbal preparations are best taken under the guidance of a trained professional. Be sure to consult with your doctor or an herbalist before selftreating. Some common herbs and their uses are discussed below. Please see our monographs on individual herbs for detailed descriptions of uses as well as risks, side effects, and potential interactions.

Herbal Drugs with antidiabetic properties

attakaka volubilis [L.f.] Stapf. [Asclepiadaceae]

Synonyms: Perun-kurinjan

The plant is a fleshy and very large climber found throughout the plains with papery leaves. Leaf powder is taken orally along with cow's milk. Dosage: 50-75 ml of mixture is taken twice a day after food for 90 days

Figure 2: Herbal Plant Perun kurinjan Used As Antidiabetic.

Abrus precatorius L. [Fabaceae]
Synonyms: Kundumani
The plant is a climber commonly known as Wild Liquorice and found through the plains of India.4 Leaf of this plant is mixed with the leaves of Andrographis paniculata, Gymnema sylvestre and seeds of Syzygium cumini. The mixture is shade dried and ground into powder and taken orally along with cow's milk. Dosage: About 50 ml of mixture is taken twice a day before food for 120 days.[5]

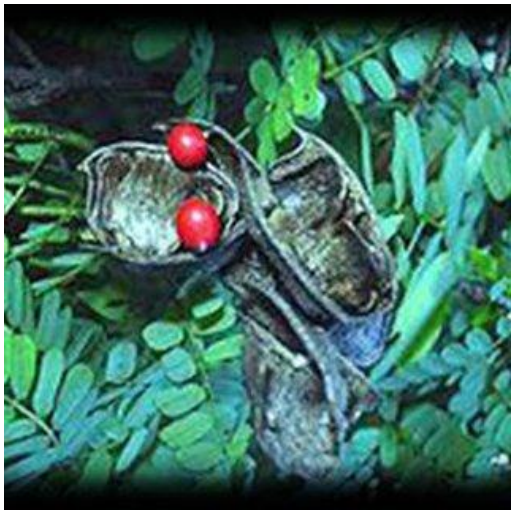

Figure 3: Kundumani Used As Antidiabetic.

Trigonella foenum graecum: [fenugreek]
It is found all over India and the fenugreek seeds are usually used as one of the major constituents of Indian spices. 4-hydroxyleucine, a novel amino acid from fenugreek seeds increased glucose stimulated insulin release by isolated islet cells in both rats and humans. Oral administration of 2 and 8 g/kg of plant extract produced dose dependent decrease in the blood glucose levels in both normal as well as diabetic rats. Administration of fenugreek seeds also improved glucose metabolism and normalized creatinine kinase activity in heart, skeletal muscle and liver of diabetic rats. It also reduced hepatic and renal glucose-6-phosphatase and fructose –1, 6-biphosphatase activity. This plant also shows antioxidant activity

Figure 4: Fenugreek Used As Antidiabetic.

Aloe vera and Aloe barbadensis
Aloe, a popular houseplant, has a long history as a multipurpose folk remedy. The plant can be separated into two basic products: gel and latex.6 Aloe vera gel is the leaf pulp or mucilage, aloe latex, commonly referred to as "aloe juice," is a bitter yellow exudate from the pericyclic tubules just beneath the outer skin of the leaves. Extracts of aloe gum effectively increases glucose tolerance in both normal and diabetic rats. Treatment of chronic but not single dose of exudates of Aloe barbadensis leaves showed hypoglycemic effect in alloxanized diabetic rats. Single as well as chronic doses of bitter principle of the same plant also showed hypoglycemic effect in diabetic rats. This action of Aloe vera and its bitter principle is through stimulation of synthesis and/or release of insulin from pancreatic beta cells. This plant also has an antiinflammatory activity in a dose dependent manner and improves wound healing in dm.

Figure 5: Herbal Plant Aloe Vera Used As Antidiabetic.

Mangifera indica: [Mango]
The leaves of this plant are used as an antidiabetic agent in Nigerian folk medicine, although when aqueous extract given orally did not alter blood glucose level in either normoglycemic or streptozotocin induced diabetic rats. However, antidiabetic activity was seen when the extract and glucose were administered simultaneously and also when the extract was given to the rats 60 min before the glucose. The results indicate that aqueous extract of Mangifera indica possess hypoglycemic activity. This may be due to an intestinal reduction of the absorption of glucose.[7]

Figure 6: Herbal plant mango used As antidiabetic.

Tinospora cordifolia: [Guduchi]
It is a large, glabrous, deciduous climbing shrub belonging to the family Menispermaceae. It is widely distributed throughout India and commonly known as Guduchi. Oral administration of the extract ofTinospora cordifolia (T. cordifolia) roots for 6 weeks resulted in a significant reduction in blood and urine glucose and in lipids in serum and tissues in alloxan diabetic rats. The extract also prevented a decrease in body weight. T. cordifolia is widely used in Indian ayurvedic medicine for treating diabetes mellitus

Figure 7: Guduchi Used As Antidiabetic.

Acacia arabica: [Babhul]
It is found all over India mainly in the wild habitat. The plant extract acts as an antidiabetic agent by acting as secretagouge to release insulin. It induces hypoglycemia in control rats but not in alloxanized animals. Powdered seeds of Acacia arabica when administered (2, 3 and 4

g/kg body weight) to normal rabbits induced hypoglycemic effect by initiating release of insulin from pancreatic beta cells.[7]

Figure 8: Acacia Used As Antidiabetic.

Allium cepa: [onion]

Various ether soluble fractions as well as insoluble fractions of dried onion powder show anti-hyperglycemic activity in diabetic rabbits. Allium cepa is also known to have antioxidant and hypolipidaemic activity.[5] Administration of a sulfur containing amino acid from Allium cepa, S-methyl cysteine sulphoxide (SMCS) (200 mg/kg for 45 days) to alloxan induced diabetic rats significantly controlled blood glucose as well as lipids in serum and tissues and normalized the activities of liver hexokinase, glucose 6-phosphatase and HMG Co A reductase. When diabetic patients were given single oral dose of 50 g of onion juice, it significantly controlled post prandial glucose levels.[7]

Figure: 9 Herbal Plant Onion Used As Antidiabetic.

Allium sativum: [garlic]

This is a perennial herb cultivated throughout India. Allicin, a sulfur-containing compound is responsible for its pungent odour and it has been shown to have significant hypoglycemic activity. 6 This effect is thought to be due to increased hepatic metabolism, increased insulin release from pancreatic beta cells and/or insulin sparing effect. Aqueous homogenate of garlic (10 ml/kg/day) administered orally to sucrose fed rabbits (10 g/kg/day in water for two months) significantly increased hepatic glycogen and free amino acid content, decreased fasting blood glucose, and triglyceride levels in serum in comparison to sucrose controls.[7]

Figure 10: Garlic Used As Anidiabetic.

Ocimum sanctum: [holy basil]
It is commonly known as Tulsi. Since ancient times, this plant is known for its medicinal properties. The aqueous extract of leaves of Ocimum sanctum showed the significant reduction in blood sugar level in both normal and alloxan induced diabetic rats. Significant reduction in fasting blood glucose, uronic acid, total amino acid, total cholesterol, triglyceride and total lipid indicated the hypoglycemic and hypolipidemic effects of tulsi in diabetic rats. Oral administration of plant extract (200 mg/kg) for 30 days led to decrease in the plasma glucose level by approximately 9.06 and 26.4% on 15 and 30 days of the experiment respectively. Renal glycogen content increased 10 fold while skeletal muscle and hepatic glycogen levels decreased by 68 and 75% respectively in diabetic rats as compared to control

Figure 11: Tulsi Used As Anidiabetic.

Momordica charantia: [bitter gourd] Cucurbitaceae).
Synonym: Kaattu pagar-kai.
The plant is commonly known as Bitter guard and has many varieties Momordica charantia is commonly used as an antidiabetic and antihyperglycemic agent in India as well as other Asian countries. Extracts of fruit pulp, seed, leaves and whole plant was shown to have hypoglycemic effect in various animal models. Polypeptide p, isolated from fruit, seeds and tissues of M. charantia showed significant hypoglycemic effect when administered subcutaneously to langurs and humans. Ethanolic extracts of M. charantia (200 mg/kg) showed an antihyperglycemic and also hypoglycemic effect in normal and STZ diabetic rats. This may be because of inhibition of glucose-6-phosphatase besides fructose-1, 6-biphosphatase in the liver and stimulation of hepatic glucose-6-phosphate dehydrogenase activities.[4] The plant is climbing shrub and generally cultivatedeverywhere in India.Unripe fruits are taken orally along with food. Dosage: 2-3 fresh unripe fruits aretaken at any time per day for three months.[5]

Figure12: Herbal plant bitter gourd used as antidiabetic.

Azadirachta indica:[Neem]
Hydroalcoholic extracts of this plant showed anti hyperglycemic activity in streptozotocin treated rats and this effect is because of increase in glucose uptake and glycogen deposition in isolated rat hemidiaphragm. Apart from having anti-diabetic activity, this plant also has antibacterial, antimalarial, antifertility, hepatoprotective and antioxidant effects.

Figure 13: Neem Used As Antidiabetic.

Mechanism of Action of Herbal Antidiabetics
The antidiabetic activity of herbs depends upon variety of mechanisms. The mechanism of action of herbal anti diabetic could be grouped as- • Adrenomimeticism, pancreatic beta cell potassium channel blocking, cAMP (2nd messenger) stimulation Inhibition in renal glucose reabsorption • Stimulation of insulin secretion from beta cells of islets or/and inhibition of insulin degradative processes • Reduction in insulin resistance • Providing certain necessary elements like calcium, zinc, magnesium, manganese and copper for the beta-cells • Regenerating and/or repairing pancreatic beta cells • Increasing the size and number of cells in the islets of Langerhans • Stimulation of insulin secretion • Stimulation of glycogenesis and hepatic glycolysis • Protective effect on the destruction of the beta cells • Improvement in digestion along with reduction in blood sugar and urea • Prevention of pathological conversion of starch to glucose • Inhibition of β -galactocidase and α–glucocidase • Cortisol lowering activities • Inhibition of alpha-amylase[6]

Herbal drug formulation
Diabecon manufactured by 'to increase peripheral utilization of glucose, increase hepatic and muscle glucagon contents, promote B cells repair and regeneration and increase c peptide level.6 and increase c peptide level.[6]

Epinsulin Marketed by Swastik formulations, contains epicatechin, a benzopyran, as an active principle. Epicatechin increases the cAMP content of the islet, which is associated with increased insulin release. It plays a role in the conversion of proinsulin to insulin by increasing cathepsin activity. Additionally it has an insulin-mimetic effect on osmotic fragility of human erythrocytes and it inhibits Na/K ATPase activity from patient's erythrocytes. It corrects the neuropathy, retinopathy and disturbed metabolism of glucose and lipids. It maintains the integrity of all organ systems affected by the disease. It is reported to be a curative for diabetes, Non Insulin Dependent Diabetes Mellitus (NIDDM) and a good adjuvant for Insulin Dependent Diabetes Mellitus (IDDM), in order to reduce the amount

of needed insulin. It is advised along with existing oral hypoglycemic drugs and is known to prevent diabetic complications. It has gentle hypoglycemic activity and hence induces no risk of being hypoglycemic.[7]

Pancreatic Tonic

(ayurvedic herbal supplement)- Pancreas Tonic is a botanical mixture of traditional Indian Ayurvedic herbs currently available as a dietary supplement.

Bitter gourd powder marketed by garry and sun It lowers blood & urine sugar levels. It increases body‟s resistance against infections and purifies blood. Bitter Gourd has excellent medicinal virtues. It is antidotal, antipyretic tonic, appetizing, stomachic, antibilious and laxative. The bitter Gourd is also used in native medicines of Asia and Africa. The Bitter gourd is specifically used as a folk medicine for diabetes. It contains compounds like bitter glycosides, saponins, alkaloids, reducing sugars, phenolics, oils, free acids, polypeptides, sterols, 17-amino acids including methionine and a crystalline product named insulin. It is reported to have hypoglycemic activity in addition to being antihaemorrhoidal, astringent, stomachic, emmenagogue, hepatic stimulant, anthelmintic and blood purifier

Polyherbal Formulations for Diabetes

Plant formulation and combined extracts of plants are used a drug of choice rather than individual. Various herbal formulations such as diamed, coagent db, Diasulin. Polyherbal formulation of Annona squamosa and Nigella sativa on blood glucose, plasma insulin, tissue lipid profile, and lipidperoxidation in streptozotocin induced diabetic rats. Aqueous extract of Polyherbal formulation of Annona squamosa and Nigella sativa was administered orally (200 mg/kg body weight) for 30 days. The different doses of Polyherbal formulation on blood glucose and plasma insulin in diabetic rats were studied and the levels of lipid peroxides and tissue lipids were also estimated in streptozotocin induced diabetic rats. The effects were compared with tolbutamide. Treatment with Polyherbal formulation and tolbutamide resulted in a significant reduction of blood glucose and increase in plasma insulin

CONCLUSION

Herbal therapy for diabetes has been followed all over the World successfully. Herbs are used to manage Type 1 and Type II diabetes and their complications. For this, therapies developed along the principles of western medicine (allopathic) are often limited in efficacy, carry the risk of adverse effects, and are often too costly, especially for the developing world. The above-mentioned plants have been considered for their possible hypoglycemic actions and the researchers have carried out some preliminary investigations. Scientific validation of several Indian plant species has proved the efficacy of the botanicals in reducing the sugar level could be considered as of possible therapeutic value. Thus many different plants have been used individually or in formulations for treatment of diabetes.

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