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# Herbs for the Management of Glucose Metabolism Disorder

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**ABSTRACT:** Diabetes has become a leading killer disease in recent years and its prevalence is a basic health indicator for member states of the WHO. The preponderance of type 2 diabetes is attributed to an increase on obesity and lack of physical activity in populations with enhanced standard of living. The management through weight loss, diet control, physical activity, mind/body medicine, biofeedback, and behaviour modification are some ways regarding improving insulin sensitivity, decreasing insulin resistivity and neglecting acidosis and ketosis and thus following normal glucose metabolism pathway. Current advances in medical and scientific research show the use of Ayurvedic herbs like salacia spp. *Tinosporacordifolia*, *Ocimum sanctum*, *Trigonella foenum graecum*, *Momordicacharantia*, *Gymnema sylvestre* etc. in diabetes management through certain active principles as hypoglycaemic agent like GS4, 4-Hydroxyleucine, stilbene, catechin, SRE, Curcuminoids etc.

Recently gene therapy used to alter glucose metabolism by regulating enzymes in glycolytic pathway – furin protease under control of glucose stimulated TGF – alpha promoter.

**KEYWORDS:** Diabetes, biofeedback, SRE, GS4, Genetherapy, resistance.

### I. INTRODUCTION

Diabetes prevents our body from turning our food into energy. Instead glucose stays in our bloodstream and left untreated can result in a range of complications.

Diabetes mellitus is caused either by lack of the hormone insulin (type 1) or the body's inability to use insulin (type 2). Type 2 diabetes is often triggered by obesity, stress and a sedentary lifestyle.

Muscle does not convert glycogen directly to glucose.

Lactic acid from muscles gets converted into pyruvate (glycolysis) which is used to produce ATP.

Pyruvate later converted into glucose and glycogen in liver.

Glucose can be synthesized from non-carbohydrate sources. This is called GLUCONEOGENESIS.

HYPOGLYCEMIA stimulates the hypothalamus to release CRF which in turn release ACTH.

Cortical hormones stimulate the release of amino acids, glycerol and fatty acids for conversion into glucose.

Disorder in glucose metabolism leads to the preponderance of disease called DIABETES MELLITUS.

The plant extracts lowers blood glucose.

The activity of pancreatic  $\beta$  cells synthesis, release, cell regeneration enhance or the increase in the inhibitory effect against insulinase & the increase of insulin sensitivity or the insulin like activity of plant extracts.

Mechanism involve glucose homeostasis, increase of synthesis of hepatic glycogen & decrease of glycogenolysis, inhibition of intestinal glucose absorption, reduction of glycaemic index of carbohydrates, reduction of the effect of glutathione.

All of these actions are responsible for reduction of diabetic complications.

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## II. RELATED WORK

Previous researches reveal that moderate weight loss and increased physical activity can prevent or delay the development of type 2 diabetes in high risk groups such as those with impaired glucose tolerance. Data from the diabetes prevention program demonstrated that weight loss and increased physical activity reduced the four year incidence of type 2 diabetes by 58% in men and women with impaired glucose tolerance. There is role of drugs like METFORMIN and ACARBOSE in prevention of diabetes. Lifestyle changes nearly twice as effective as METFORMIN THERAPY in preventing type 2 diabetes. Sedentary lifestyle and uncontrolled unbalanced diet should be avoided. Exercise, yoga, balanced diet manage the glucose level. The work in this paper emphasises on the importance of various Phytoconstituents in the management of glucose metabolism disorder. So the paper headed under two main sections: 1) CARBOHYDRATE METABOLISM & 2) ANTIDIABETIC HERBS. Under carbohydrate Metabolism section following sub-sections are discussed: a. Aerobic Respiration, b. Lactic acid from anaerobic respiration, c. Gluconeogenesis & d. Carbohydrate metabolism disorder and related complications. Antidiabetic Herbs cover 9 important plants having hypoglycaemic potential. Finally the text is concluded by the fact that the plant extracts lowers blood glucose level by rejuvenating pancreatic beta cells, decreasing insulinase activity & enhancing insulin sensitivity.

## III. OBJECTIVE OF THE STUDY

To acquire knowledge about the psychosomatic disorder caused by the abnormality in carbohydrate metabolism pathway, the disease & its types, causes associated with disease. The role of various herbs in acting as hypoglycaemic agents and mechanism involved in controlling blood glucose level & various complications associated with DIABETES MELLITUS.

## IV. RESEARCH DESIGN

Firstly existing available research in the related field is searched out & related literature gathered. After collection & analysis of data, the main text of the report is logically sequenced and broken into readily identifiable sections including results of the findings at the end.

## V. CARBOHYDRATE METABOLISM

### a. AEROBIC RESPIRATION

Sugars such as glucose enter the liver from the gut by the hepatic portal vein. Liver maintains the blood glucose level at approximately 90 mg glucose per 100 cubic cm blood. All hexoses including galactose and fructose are converted to glucose by the liver and stored as the insoluble polysaccharides glycogen. Up to 100 gm. stored here but rest in muscle. The conversion of glucose to glycogen is known as GLYCOGENESIS & is stimulated by the presence of INSULIN.

Glycogen is broken down to glucose to prevent the blood glucose level falling below 60 mg per 100 cu.cm blood. This process is called GLYCOGENOLYSIS & involves the activation of a phosphorylase enzyme by the hormone glucagon, is made in the pancreas & in danger, stress or cold this activity is also stimulated by adrenaline, released by the adrenal medulla & nor-adrenaline released by the adrenal medulla and the endings of the sympathetic neurons.

### b. LACTIC ACID FROM ANAEROBIC RESPIRATION

Muscle does not convert glycogen directly to glucose because it does not release glucose into the blood for rest of the body, unlike the liver. Muscle only breaks down glycogen if it needs glucose for its own respiration, in which case the glycogen is converted to glucose phosphate but is then converted to pyruvate (glycolysis) which is used to produce ATP during aerobic or anaerobic respiration in skeletal muscle can be converted later into glucose in the liver.

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## c. GLUCONEOGENESIS

When the demand for glucose has exhausted the glycogen store in the liver, glucose can be synthesized from non-carbohydrate sources. This is called GLUCONEOGENESIS. Low blood glucose levels (hypoglycaemia) stimulate the process which helps satisfy immediate demand. Low blood glucose levels also stimulate the hypothalamus to release CRF which in turn release adrenocorticotrophic hormone (ACTH) from the anterior pituitary gland. This leads to synthesis and release of increasing amounts of the glucocorticoid hormones, particularly cortisol. These stimulates the release of amino acids, glycerol and fatty acids, present in the tissues, into the blood and increase the rate of synthesis of enzymes, in the liver which convert amino acids and glycerol into glucose. Fatty acids are converted into acetyl coenzyme and used directly in the Krebs cycle. Carbohydrate in the body which cannot be used or stored as glycogen is converted into fats and stored.

## D. CARBOHYDRATE METABOLISM DISORDER AND RELATED COMPLICATIONS

In a person suffering from type 1 diabetes there is an insufficient or no supply of insulin. In type 2 diabetes, insulin may be present in sufficient quantities but is unable to unlock the doors of the cells. In the normal case, insulin fits on to specific sites called insulin receptors located on the surface of the cell (the key holes) & unlocks the doors to let glucose enter. If the insulin cannot fit in properly due to lack of insulin receptors on the cell surface, the doors remain locked causing a condition called insulin resistance. If the doors of the cells remain unopened, due to lack of insulin or difficulty in utilizing insulin, glucose cannot enter the cells and remains in the blood. This causes increase in blood sugar levels even if no food is eaten. The body begins to use alternative food sources (body fat & protein) for energy. The patient therefore loses weight, lives easily and has an increased appetite (POLYPHAGIA).

Excess glucose in the blood is harmful too. Sugar accumulation in the blood results in increased workload on kidneys and increased sugar levels in the urine. The sugar enters the urine in solution form, draining water from the urination (POLYURIA) and induces thirst (POLYDIPSIA) in the patient. High blood sugar levels over protracted periods of time causes glycation of the key body proteins inducing secondary symptoms such as RETINOPATHY which may lead to blindness, NEUROPATHY (nerve degeneration) which may lead to gangrene & NEPHROPATHY which may lead to kidney malfunctions.

Diabetics space meals adequately over the day to avoid glucose overload and low blood sugar. Whole grains and vegetables have a low glycaemic index.

## VI. ANTIDIABETIC PLANTS

Ayurvedic physicians have treated diabetics for thousands of years using a combination of regulated lifestyle and herbal formulations. Some of the important herbs for lowering glucose levels are:

### 1. GYMNEMASYLVESTRE (Australian cow plant)

Gymnema extracts could induce the pancreas to secrete insulin.

Contain triterpenoids having pharmacological properties.

The constituent saponins have the effect of suppressing the taste of sweetness.

Block the taste of sweetness and help to regulate blood sugar by blocking the absorption of sugar in the intestine and stimulating insulin release from the pancreas.

Acts as laxative and diuretic.

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### 2. MOMORDICA CHARANTIA (Bitter gourd)

It is a proven hypoglycemic agent in NIDDM.

Raw or juice form can be efficacious in lowering blood glucose level.

Possess hypolipidemic activity hence delays the late complications of diabetes.

Being hypoglycemic increase insulin secretion, enhance glucose uptake by adipose or muscle tissues and inhibit glucose absorption from intestine and glucose production from liver.

### 3. TRIGONELLA FOENUM GRAECUM (Fenugreek)

The protein fraction of the seeds contains the amino acid 4-hydroxyleucine which stimulates insulin production.

Lowers urinary sugar and saponins present in seeds reduces serum cholesterol level.

Prevent secondary complications of diabetes such as HYPERLIPIDEMIA.

Adjunct use of fenugreek seeds improves glycemic control and decreases insulin resistance in mild type -2 patients.

Seeds contain 50% fiber of which 20% is mucilaginous fiber similar to guar gum, known hypoglycemic agent.

### 4. COCCINIA INDICA (IVY GOURD)

Phytoconstituents reported are cephalandrol, triacontane, lupeol, b-sitosterol, cephalandrine A, cephalandrine B, stigma-7-en-3-one, taraxerone and taraxerol. These act like insulin.

Depress the gluconeogenic enzymes, enhance glucose oxidation, restores the LPL activity & correct the LDH.

### 5. SZYGIUM CUMINI (Blue berry)

The compound MYCAMINOSE, ETHYL ACETATE & methanol extracted produced significant reduction in the blood glucose level.

LUPEOL suppress the progression of Diabetes.

Ethanol extract shows competitive inhibition of  $\alpha$ amylase &  $\alpha$  glucosidase like antidiabetic drug ACARBOSE.

Mycaminose mechanism of action similar to the drug GLIBENCLAMIDE.

Stigma sterol shows antidiabetic activities.

### 6. CATHARANTHUS ROSEUS (Vinca rosea)

Alkaloids VINDOLINE, VINDOLIDINE, VINDOLICINE, and VINDOLININE induced high glucose uptake in  $\beta$  - TC6 & C2C12 Cells.

The activity of the hepatic enzymes such as hexokinase increased & glucose 6-phosphatase & fructose 1,6 - biphosphatase decreased by its leaf extract.

These alkaloids showed good antioxidant potential by alleviating hydrogen peroxide induced oxidative damage in  $\beta$  - TC6 cells.

### 7. EMBLICA OFFICINALIS (Gooseberry)

The tannoids present are potent inhibitors of Aldolase Reductase.

Tannins, polyphenols (541.3 mg gallic acid), flavonoids, vitamin C, chromium, zinc possess hypoglycaemic & hypolipidemic role and enhance hemoglobin levels.

Amla decreases LDL & increases HDL cholesterol.

### 8. PTEROCARPUS MARSUPIUM (Bastard teak)

Pterocarpus marsupium is a rich source of polyphenolic compounds. The key compounds include the diary propane derivative, propterol, the stilbene, pterostilbene, the hydrochalcone, pterosupin, the benzofuranone, marsupin; the flavonoid, liquiritigenin and the catechin, epicatechin. Pterostilbene & Epicatechin are reported to have blood sugar lowering effects. Epicatechin have an effect on the conversion of PROINSULIN-INSULIN. Pancreatic beta cell regeneration observed in alloxan-induced diabetic rats that received flavonoid fraction from the bark of Pterocarpus marsupium.

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## 9. SALACIA OBLONGA & S. RETICULATA

Constituents of a botanical extract obtained from the dried roots of *S. reticulata* (fam: Celastraceae) found to inhibit alpha-glucosidase enzymes thus lowering glucose levels. SALICINOL & KOTALANOL are the two important glucosidase inhibitor. It has an additional benefit of weight gain inhibition. It lowers serum cholesterol, triglycerides and increasing HDL cholesterol levels.

## VII. CONCLUSION

Moderate weight loss improves glycaemic control, reduces CARDIOVASCULAR DISEASE risk & can prevent the development of type 2 diabetes.

There are herbs which are hypoglycaemic as well as prevent secondary complications of diabetes such as HYPERLIPIDEMIA, ATHEROSCLEROSIS.

The most common are *Gymnema sylvestris*, *Momordica charantia*, *Trigonella* sp., *Szygium cumini*, *Coccinia indica*, *Embllica officinalis*, *Catharanthus roseus*, etc.

The safety & efficacy of these herbs validated by lab experiments & clinical trials.

Many new bioactive drugs isolated from plants having hypoglycaemic effects showed antidiabetic activity equal & more potent than oral drugs like daonil, chlorpropamide.

The toxic effects of these plants should also be elucidated.

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