

EVALUATION OF ANTI-DIABETIC ACTIVITY OF GLYCYRRHIZA GLABRA

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ABSTRACT

Diabetes mellitus is a chronic metabolic disorder characterized by high blood glucose concentration (hyperglycemia) caused by insulin deficiency often combined with insulin resistance. Diabetes mellitus refers to the group of diseases that leads to high blood glucose level due to defect in either insulin secretion or insulin action in the body. Hyperglycemia occurs because of uncontrolled hepatic glucose output and reduced uptake of glucose by skeletal muscle with reduced glycogen synthesis. When the renal threshold for glucose reabsorption is exceeded, glucose spills over into the urine (Glycosuria) and causes an osmotic diuresis (polyuria), which in turn results in dehydration,

thirst and increased drinking of water (polydipsia). The characteristic symptoms of diabetes mellitus are polyuria, polydipsia, polyphagia (increased hunger), blurred vision, these symptoms may be absent if the blood sugar is only mildly elevated. Diabetes mellitus is a major public health problem in the developed as well as developing countries. It is ranked seventh among the leading causes of death and third when all its fatal complications are taken into accounts.

KEYWORDS: insulin, chronic, hyperglycemia, glycosuria, polyuria, polydipsia, dehydration.

INTRODUCTION

In 2000, according to the World Health Organization, at least 171 million people worldwide suffer from diabetes i.e. 2.8% of the population (Wild. S *et al*, 2004). Its incidence is increasing rapidly, and it is estimated that by the year 2030, this number will almost double. Diabetes mellitus occurs throughout the world, but is more common (especially type 2) in the

more developed countries. The greatest increase in prevalence is, however, expected to occur in Asia and Africa, where most patients will probably be found by 2030 (Wild. S *et al*, 2004). The increase in incidence of diabetes in developing countries follows the trend of urbanization and lifestyle changes, perhaps most importantly a "Western-style" diet. This has suggested an environmental (i.e., dietary) effect, but there is little understanding of the mechanism(s) at present, though there is much speculation, some of it most compellingly presented. In 2004 Williams and Pick up said majority (90%) of patients with type-II diabetes is diagnosed before the age of 30.

TYPES OF DIABETES MELLITUS: (Senthil vasan *et al*, 2008)

1. Type I diabetes mellitus
2. Type II diabetes mellitus
3. Gestational diabetes mellitus
4. Other specific types.
 - a. Pancreatic diseases
 - Fibrocalcific pancreatitis
 - Pancreatectomy
 - Cystic fibrosis
 - b. Endocrinopathies
 - Acromegaly
 - Cushing's syndrome
 - Pheochromocytoma
 - Hyperthyroidism
 - c. Infections
 - Mumps
 - Cytomegalo virus
 - Congenital Rubella
 - d. Drug induced
 - Glucocorticoids
 - Thyroid hormones
 - Thiazides

IMPORTANT TYPES OF DIABETES MELLITUS

A. TYPE I DIABETES MELLITUS

Type I diabetes mellitus is characterized by loss of the insulin producing beta cells of the islets of Langerhans in the pancreas leading to insulin deficiency. Type I diabetes can be further classified as immune mediated or idiopathic. Type I diabetes is majorly of the immune mediated variety, where beta cell loss is a T-cell mediated auto immune attack (Rother, 2007). Type I diabetes is also called as juvenile diabetes (childhood) or insulin dependent diabetes mellitus (IDDM). There is no preventive measure that can be taken against this type I diabetes. Diet and exercise cannot reverse or prevent type I diabetes. Sensitivity and responsiveness to insulin are usually normal especially in early stages.

B. TYPE II DIABETES MELLITUS

Type II diabetes mellitus is characterized differently and it is due to insulin resistance or reduced insulin sensitivity and it may be absolutely due to reduced insulin secretion in some of the cases. Insulin receptor sensitivity decreases on insulin receptors.

Type II diabetes is also called as adult onset diabetes mellitus, maturity onset diabetes mellitus or non insulin dependent diabetes mellitus (NIDDM) Type II diabetes mellitus is characterized by insulin resistance, impaired glucose induced insulin secretion and inappropriately regulated glucagon secretion which in combination eventually results in hyperglycemia and in the longer term micro vascular and macro vascular diabetic complications. There are numerous theories as to the exact cause and mechanism in type II diabetes. Central obesity (fat concentrated around the waist in relation to abdominal organs, but not subcutaneous fat) is known to predispose individuals to insulin resistance. Abdominal fat is especially active hormonally, secreting a group of hormones called adipokines that may possibly impair glucose tolerance. Obesity was found to be the reason in approximately 55% of patients diagnosed with type II diabetes.

C. GESTATIONAL DIABETES MELLITUS

Gestational diabetes develops during pregnancy and it may persists or disappear after delivery. Gestational diabetes may damage the health of foetus or mother, and about 20%-50% of women with gestational diabetes develop type II diabetes later in life. Gestational diabetes mellitus (GDM) occurs in about 2%-5% of all pregnancies, including high birth weight (Macrosomia), fetal malformation and congenital heart disease. It requires careful medical supervision during the pregnancy (Lawrence *et al.*, 2008).

CAUSES OF DIABETES MELLITUS: (Arlal Rosen bloom *et al.*, 2003)

- Shortage or defective imperfect insulin produced by the body.
- Stress, fear and tension
- Hereditary either parent suffering from diabetes
- Frequent administration of steroids
- Insomnia
- Alcoholic habituation
- Addiction to sweets
- Swollen pancreas
- Smoking
- Malnutrition

COMPLICATIONS OF DIABETES MELLITUS

- Kidney (Diabetic nephropathy)
- Nerves (Diabetic neuropathy)
- Retina (Diabetic retinopathy)
- Testes (Infertility in males)
- Coronary thrombosis
- Cerebral thrombosis
- Hemorrhage

DIAGNOSIS OF DIABETES MELLITUS

The following tests performed when the patient complaint symptoms suggesting diabetes.

- Urine test for glucose and ketones
- Measurement of random blood glucose, plasma electrolytes
- Measurement of fasting blood glucose levels
- Glucose tolerance test(GTT)
- Glycosylated heamoglobin test (HbA1c)

DRUGS USED IN DIABETES MELLITUS: (KD. Tripathi, 2008)**In type I diabetes mellitus or IDDM**

- Short and rapid acting insulin
 - a) Insulin, onset 0.5 to 1 hour, duration of action 6-8 hours.
 - b) Prompt insulin zinc suspension, onset 1 hour, duration of action 12-16 hours.

- Intermediate acting
 - a) Insulin zinc suspension, onset 1-2 hour, duration 20-24 hours.
- Long acting
 - a) Extended insulin zinc suspension, onset 4-6 hour, duration 24-36 hours.

In type II diabetes mellitus or NIDDM

Oral anti diabetic drugs

- a) Sulfonyl ureas

First generation

Tolbutamide

Chlorpropamide

Second generation

Glibenclamide

Glipizide, Gliclazide, Glimepamide

- b) Biguanides

Eg: Metformin

- c) Meglitinide analogues

Eg: Nateglinide, Repaglinide

- d) α – glucosidase inhibitors

Eg: acarbose, miglitol

- e) Thiazolidine diones

Eg: Rosiglitazone, Pioglitazon

Alternative therapies for Diabetes

Diabetes and Homeopathy

Homeopathic treatment is entirely based on similarity. Homeopathic thought dictates that substances that are poisonous in large dosages or quantities can be beneficial to the body in small dosages.

Small, well-diluted dosages of appropriate substances should be placed under the tongue. Every patient is individually analysed and a treatment plan is prescribed depending exactly upon their condition. Homeopathic remedies should have no side effects.

As far as diabetes goes, substances such as Phosphorous (to lower blood sugar), Codenium and Syzygium may all be useful.

Diabetes and Ayurvedic Medicine

Ayurvedic Medicine is a unique form of healthcare based on establishing and maintaining an internal balance, as opposed to singling out individual symptoms for treatment. Ayurvedic medicine adjusts its regimen for the individual. Beyond this, Ayurvedic medicine is deeply rooted in mystical and spiritual ideology that accompanies its teachings.

Several studies have linked Ayurvedic medicine and diabetes in a positive light. Ayurvedic medicine is conceptualised and practised as eight distinctive specialities, some of which have an application for the treatment of diabetes.

Ayurveda diagnoses diabetes as being a metabolic disorder that fits into the Kapha category, due to poor functioning of the Agni.

Common Ayurvedic treatment concentrates on a multidisciplinary approach to diabetes. The first will be intense modification of the diet, in which sugar is eliminated and simple carbohydrates are replaced by complex carbohydrates. Panchkarma, a cleansing program, is typically employed and will probably include massages, herbal therapy, saunas and fasting. This will possibly be followed by a herbal purge and yoga and breathing exercises. Herbs and a strict diet make up the basis of the treatment.

Yoga therapy is a part of the Ayurvedic treatment system. Yoga should, as well as stimulating the body through exercise, leave the subject feeling refreshed and relaxed.

OBJECTIVES

Diabetes mellitus is a metabolic disorder affecting carbohydrate, fat and protein metabolism. A worldwide survey reported that diabetes mellitus is affecting nearly 10% of the population every year. The treatment of diabetes mellitus in clinical practice has been confined to use oral hypoglycemic agents and insulin, the former being reported to be endowed with characteristic profiles of serious side effects. This leads to increasing demand for herbal drugs with anti-diabetic factor with little side effects. A large number of plants have been recognized to be effective in the treatment of diabetes mellitus.

Herbal drugs claimed to relieve not only the symptoms of diabetes mellitus, but also they can regenerate and repair the dysfunctional pancreas. *Glycyrrhiza glabra* plant is widely used in folk medicine for various purposes. The present study is aimed at evaluating the antidiabetic activity of a *Glycyrrhiza glabra* methanolic extract. *Glycyrrhiza glabra* is reported to have

many biological activities including antibacterial, immunostimulant, antidiarrhoeal, antioxidant, anti-inflammatory, anti HIV, antipyretic, antimalarial. Its hypoglycemic and antihyperglycemic activities are not well reported.

Hence present study is carryout with an objective to evaluate the effect of acute and chronic administration of methanolic extract of *Glycyrrhiza glabra* in STZ induced type I and II diabetic rats by measuring various biochemical parameters.

The present study is carried with the following objectives.

- To study the effect of single dose of *Glycyrrhiza glabra* methanolic extract on blood glucose level in normal rats.
- To study the effect of single dose of *Glycyrrhiza glabra* methanolic extract on blood glucose level in streptozotocin induced type I and type II diabetic rats.
- To study the effect of chronic administration of *Glycyrrhiza glabra* methanolic extract on diabetic animals for a period of 7 days. The following parameters are evaluated before and after the administration of the extract.
 - Oxidative stress
 - Lipid profile
 - Blood glucose
 - Nootropic activity
 - Immunostimulant activity
 - Liver glycogen
 - Cerebroprotective activity.

CONCLUSION

- The probable mechanism may have an insulin sensitizing effect, by attenuating the impairment of insulin stimulated glucose disposal in insulin resistant rats and also it may follow sulfonyl urea group mechanism.
- Upon the chronic administration of *Glycyrrhiza glabra* methanolic extract for a period of 7 days to normal and type II diabetic rats shown
 - ✓ Significant hypoglycaemic and antidiabetic activity.
 - ✓ Lowering of lipid profile
 - ✓ Antioxidant activity
 - ✓ Increasing the hepatic glycogen in diabetic rats but not in normal rats.

- Thus the folk use of this plant in treating diabetes is justified and also it helps in preventing diabetic complications and serves as a good adjuvant in the present armamentarium of antidiabetic drugs.
- Further investigation is in progress to find out its mechanism of action and to establish its potential in the treatment of macro vascular complications of diabetes.

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