(Review Article)

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TREATMENT OF DIABETES MELLITUS WITH INDIAN HERBAL DRUGS

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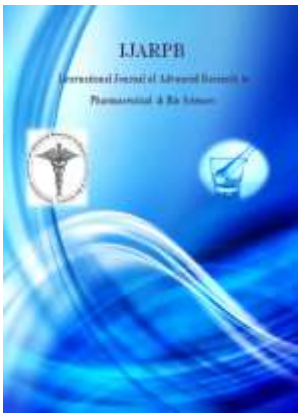

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ABSTRACT

The present article gives a general idea of diabetic mellitus, its treatment by using insulin, oral hypoglycaemic drugs and herbal drugs. Despite considerable progress in the treatment of diabetes by oral hypoglycaemic agents, search for newer drugs continues because the existing synthetic drugs have several limitations .The herbal drugs with antidiabetic activity are yet to be commercially formulated as modern medicines, even though they have been acclaimed for their therapeutic properties in the traditional systems of medicine.

KEY WORDS: Anti-diabetic activity, Herbal Drugs, Oral hypoglycaemic agents, Active chemical constituents.

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INTRODUCTION

Diabetesmellitus is a clinical syndrome characterized by inappropriate hyperglycemia caused by a relative or absolute deficiency of insulin or by a resistance to the action of insulin at the cellular level. It is themost common endocrine disorder, affecting 16 million individuals in the United States and as many as 200 millionworldwide.Diabetes has been a clinicalmodel for general medicine. The primary defect in fuel metabolism results in widespread, multi-organ complications that ultimately encompass virtuallyevery system of the body and every specialty of medicine. It has been said that to know diabetes is to know medicine and health care. Although from a clinical standpoint thismay be true, our increasing knowledge of the pathophysiology of the syndrome, togetherwith the mechanisms of long- term complications, has placed diabetes research at the frontier of immunology andmolecular biology[1].

Diabetes mellitus has been known since ages and the sweetness of diabetic urine has been mentioned in Ayurveda by Sushruta. Its pharmacotherapy however is over 80 years old. The word diabetes was coined by the Greek physicianAeretaeus in the first centuryA.D. In the 17th century, Willis observed that the urine of diabetics aswonderfully sweet as if imbuedwith honey or sugar.The presence of sugar in the urine of diabetics was demonstrated by Dobson in 1755[2].

Diabetes is a chronic disease affecting around 2-3% of the populationworldwide.Unfortunately, after the introduction of sulfonylurea andmetformin about 50 years back no major lead has been obtained in this direction of finding a proper drug for diabetes. Plant materialswhich are being used as traditionalmedicine for the treatment of diabetes are considered one of the good sources for a new drug or a lead to make a new drug. Plant extract or different folk plant preparations are being prescribed by the traditional practioners and also accepted by the users for diabetes like for any other diseases inmany countries especially in third world countries.Now-a daysmore than 400 plants are being used in different forms for hypoglycaemic effects all the claims practitioners or users are neither baseless nor absolutely. Therefore, a proper scientific evaluation a screening of plant by pharmacological tests followed by chemical investigations is necessary[3].

Table 1: Some plants having hypoglycemic activity as studied by Nahar

Plant	Plant Part	Type of Test Sample
Trigonella foenum-gracecum	seed	Alcohol ,water extract
Nephoelepsis tuberose	bulb	juice
Costus specious	rhizome	juice
Plantago ovata	husk	Powder
Allium sativum	bulb	juice
Hemidesmus indicus	root	alcoholic extract
Allium cepa	bulb	juice

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Diabetes mellitus is wide spread disorder, which has long been in the history ofmedicine .Before the advent of insulin and oral hypoglycaemic drugs themajor form of treatment involved the use of the plants. But now fromthe last two decades there has been a new trend in the preparation and marketing of herbal drugs. Further it has been estimated that in the U.S. 25% of all prescription dispensed fromcommunity pharmacies contain plant extracts4. On the basis of etiology two main categories of diabetes are recognized, viz[4].

Primary diabetes

Secondary diabetes

Primary diabetes

It is divided into two types.

Juvenile onset diabetes which is also referred as Type 1 or Insulin dependent diabetes mellitus (IDDM).

In Juvenile onset diabetes there is a profound decrease in the number of b cells in the islet of Langer hans and thus there is absolute deficiency of insulin. The main treatment for this type is insulin. Maturity onset diabetes which is also referred as Type II /Non-insulin dependent diabetes mellitus (NIDDM).

The patients are usually obese and the treatment is usually dietary, though supplementary oral hypoglycaemic drugs. It is diagnosed by blood or urinary glucose measurement. Insulin resistances as well as loss of insulin secretion contribute to the onset of disease.

Secondary Diabetes

The symptoms result from the following

Pancreatic dysfunction (pancreatitis, pancreatectomy).

Hormonal imbalance (eg: Acromegaly, pheochromacytoma, Cushing's syndrome, glucagonoma).

Drugs or chemical induced reactions (eg: glucocorticoids, anticancer agents, streptozotocin or diazoxide, thiazide, some psychoactive agents).

Insulin receptor abnormalities.

Certain genetic syndromes (Hyperlipidemea and muscular dystrophy).

Malnutrition

Diagnosis of early Diabetes Mellitus In moderately severe early diabetes, following features are present.

Hyperglycemia.

Glycosuria.

Loss of weight due to increased breakdown of fat and tissue protein.

Increased production of ketone bodies by liver and their incomplete utilization by the tissue leading to their accumulation in blood (Ketosis) and elimination in urine (Ketonuria).

Lowering of PH of blood due to circulating keto acids (acidosis).

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Dehydration due to elimination of large amounts of water with glucose in urine.

Increased levels of lipid, fatty acids and cholesterol in blood (lipemia).

Increased tendency to develop cataract in the eye and atheromatous and artherosclerotic lesions of blood vessels [5, 6].

Glucose- tolerance test

Currently the presence of abnormally high glucose levels in the blood is the only criterion on which diagnosis of diabetes mellitus is based.

A sensitive diagnostic criterion is provided by glucose tolerance test. After a night without food, the patient drinks a test dose of 100g of glucose dissolved in a glass of water. The blood glucose concentration is measured before the test dose and at 30min. intervals for several hours thereafter. A normal individual assimilates glucose readily, the blood glucose rising to no more than about 9 or 10mM; little or no glucose appears in urine. Diabetic individuals assimilate the test dose of glucose poorly; their glucose level far exceeds the kidney threshold (about 10mM) causing glucose to appear in their urine[6]. The results of glucose analysis are plotted as a graph against time[7].

Table 2: The main features of GIT curve in normal persons, prediabetic persons, mild diabetic, and severe diabetes are as follows

		Normal Person	Prediabetic persons	Mild diabetes	Severe diabetes
1.	**Fasting blood sugar**	80-120 mg/100ml	105-110 mg/100ml	115-125 mg/100ml	150-160 mg/100ml
2.	**Blood sugar reaches its peak to in 1 hr**	130 mg/100ml	150-160 mg/100ml	190-200 mg/100ml	320-350 mg/100ml
3.	**Returns to the fasting level**	At the end of 2-21/2 hr.	At the end of 3 hrs.	-	At the end of 4hrs
4.	**urine**	No glucose	No glucose	1- 2 % glucose	More than 2%

Treatment of DiabetesMellitus

Insulin

Oral hypoglycaemic Drugs

Herbal Drugs.

Insulin

Insulin is hormone secreted by the â cells of the islets of langerhans in the pancreas. The diabetic mellitus has been well known as a wasting disease due to insulin deficiency in human beings. The pancrease secrete

insulin.Carbohydratemetabolismis primarily under the control of insulin. Insulin deficiency occurs in a 4person due to the functional disorder of the pancreas.

OralHypoglycaemicDrugs

These drugs lower blood glucose level and are effective orally. The chief drawback of insulin is it must be given by injection. Hence, the search for orally active drugs was demanded.

CLASSIFICATION

(1) Sulfonylureas:

First generation

Tolbutamide

Chlorpropamide

Acetohexamide

Tolazamide

Second generation

Glibenclamide

Glipizide

Gliclazide

(2) Biguanides

Phenformin

Metformin

(3)Miscellaneous

(I) Acarbose

(II) Guar gum

Sulfonylureas: (Mode of Action)

Sulphonylureas activate receptors on the â islet cells of the pancrease to release more stored insulin in response to glucose. They do not increase insulin formation. They are ineffective in totally insulin deficient patients and for successful therapy probably requires about 30%of normal â cells function subjects as well as diabetes[8,9].

Biguanides: (Mode ofAction)

They do not cause insulin release but presence of some insulin is essential for their action. Suppress hepatic gluconeogenesis and glucose output fromliver, probably themajor action Enhance binding of insulin to its receptors and stimulate insulinmediated glucose disposal. Interfere with mitochondrial respiratory chainpromote peripheral glucose utilization by enhancing anaerobic glycolysis. Inhibit intestinal absorption of glucose, other hexose, amino acids and vit.B12[10].

Miscellaneous

Acarbose

It is complex oligosaccharide which reversibly inhibits á- glucosidases, the final enzymes in the digestion of carbohydrates in the brush border of small intestinalmucosa. It is mild hypoglycaemic; may be used as an adjuvant to diet in obese diabetics. Their main side effect is flatulence.

Guar gum

It is dietary fiber (polysaccharide), from Indian cluster beans (Guar) which forms a viscous gel on contact with water. Administered just before ormixed with food, it slows gastric emptying, intestinal transit and carbohydrate absorption.

Guar gum can be used to supplement diet and to lower sulfonylurea dose and as a hypocholesterolemic.

Precautionswith oral hypoglycaemic agent:

Hypoglycemia occurswith sulphonylurea compounds but occurrences are much fewer than with insulin therapy.

A biguanide should not be used in patient with renal diseases.

The associated disadvantages with insulin and oral hypoglycemic agents have lead to stimulation in the research for locating natural resources showing anti diabetic activity. Many studies have been carried out in search of a suitable plant drug that would be effective in Diabetes mellitus. Herbal remedies for diabetes have been recorded in ancient medical literature. Plants hold definite promises in the management of diabetes mellitus.

Despite considerable progress in the treatment of diabetes by oral hypoglycemic agents, search for newer drugs continues because the existing synthetic drugs have several limitations. In recent times there has been renewed interest in the plant remedies[9]. In the Ayurvedic treatment, medicines consists of plant products, either single drug or in combination with others which are considered to be less toxic and free from side effects compared to synthetic drugs[10].

In traditional systems, a number of plant extracts have been used for their hypoglycaemic activity like Karela (*Momordica charantia*), Jambul (*Syzigium cumini*), fenugreek (*Trigonella foenum-*gracecum), Gudmar (*Gymnema sylvestre*). Gymnemic acids 1 – 4, guarmarin in *Gymnema sylvestre* shows antidiabetic activity[11].

Herbal drugs

Since ancient times a number of herbal medicines have been used in the treatment of this disease. There is increasing demand by patients to use the natural products with antidiabetic activity.

Herbal medicines for diabetes can be classified into four categories according to their mode of action:

Drugs acting like insulin.

Drugs acting on insulin secreting beta cells.

Drugs acting bymodifying glucose utilization.

Drugs acting by miscellaneous mechanisms.

Herbal drugs acting like insulin:

Momordica charantia:

Fruits of Momordica charantia have been successfully used by diabetic patients and their crude extract has been shown to possess hypoglycaemic activity. Khanna and jain isolated a hypoglycaemic peptide (polypeptide-P) from

seeds and other tissues of Momordica charantia. They reported that polypeptidep is a very effective hypoglycaemic agent when administered subcutaneously to langurs and humans. Singh et al. have reported hypoglycaemic effect of acetone extract of whole fruit powder of Momordica charantia.

Drugs acting on insulin secreting betacells

Allium cepa

Allium cepa (onion) was investigated for its hypoglycaemic activity by Collip and Janet, Laurin Brahmachari andAugusti reported that the petroleum ether extract of dried onion has hypoglycaemic activity and suggested that it can be a useful substitute for tolbutamide in controlling alloxan diabetes in rats.

Pterocarpus marsupium

Rajasekharan and Tuli carried out clinical trials and found that Pterocarpus marsupium bark is effective inType 1 diabetesmellitus. Later Charkravarthy et.al. reported epicatechin to be the active hypoglycaemic constituent.

Aloes

Ghannam et al. carried out their study on 5 patients with NIDDM and also on alloxan treated diabetic mice.They reported that oral administration of aloes lowers the fasting serumglucose levels in normal and diabetic subjects.

Plant drugs acting bymodifying glucose utilisation

Zingiber officinale (ginger), *Cyamospsis tetragonolobus* (Gowar plant) and *Grewia asiatica* (phalsa) are reported to produce hypoglycaemia by modifying glucose utilisation.

Sharma and Shukla reported that ginger juice has glucose lowering effect in normal fasting animals and in alloxan diabetic animals.

Jenkins et al. reported that the hypoglycaemic effect of Cyamospsis tetragonolobus in diabetic and normal subjects.

Gowar plant and the seeds at a dose of 40g/kg showed hypoglycaemic activity similar to that of tolbutamide. Themechanismof action of gowar is probably related to its ability to increase the viscosity of gastrointestinal contents, slowgastric empting and also act as a barrier to diffusion. The workers concluded that gowar produces its hypoglycaemic action by acting at an extrapancreatic site.

The aqueous extract of Grewia asitica was tested in diabetic cats and rabbits of both sexes by Pakrashi and Mukherjee. These workers reported that the fasting blood sugar levels come down to normal after the treatment and remain as such after discontinuation of treatment for another 15 days.

Drugs acting by miscellaneous mechanisms:

Leguminous plants

Hypoglycemic activity of some leguminous plants was studied by Singh et al. and reported that legumes in diet could reduce glucose levels in

normal rats than could a normal diet. Chopra (1955) reported that leguminous plants in diet could reduce blood sugar levels and cholesterol levels because of their dietary fiber content.

Euphorbia prostrate & Fumaria parvia parviflora

Aktar et.al. reported extracts from these plants reduce blood sugar levels in normal rabbits but not in diabetic rabbits. Afew other plants with hypoglycaemic activity: Panax ginseng, Dioscorea dumatorum, Cuminum nigrum, Ocimumsanctum,Curcuma longa,Phyllanthus embelica[12, 13].

CONCLUSION

All the drugs discussed in this review have exhibited significant clinical & pharmacological activity. The potency of herbal drugs is significant & they have negligible side effects than the synthetic antidiabetic drugs. There is increasing demand by patients to use the natural productswith antidiabetic activity. In recent times there has been renewed interest in the plant remedies. Plants hold definite promises in the management of Diabetes mellitus.

Isolation & identification of active constituents from these plants, preparation of standardized dose & dosage regimen can play a significant role in improving the hypoglycaemic action.

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