TREATMENT OF DIABETES MELLITUS WITH INDIAN HERBAL DRUGS

Sharma* A K, Aggarwal1 A, Singhal1 V K,
Seth G.L. Bihani S.D. College of Technical Education1, Sri Ganganagar, Rajasthan

Corresponding Author:
Ajay Kumar Sharma*
Seth G.L. Bihani S.D. College of Technical Education1, Sri Ganganagar, Rajasthan

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.
INTRODUCTION

Diabetes mellitus 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 the most common endocrine disorder, affecting 16 million individuals in the United States and as many as 200 million worldwide. Diabetes has been a clinical model for general medicine. The primary defect in fuel metabolism results in widespread, multi-organ complications that ultimately encompass virtually every system of the body and every specialty of medicine. It has been said that to know diabetes is to know medicine and healthcare. Although from a clinical standpoint this may be true, our increasing knowledge of the pathophysiology of the syndrome, together with the mechanisms of long-term complications, has placed diabetes research at the frontier of immunology and molecular biology.

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 physician Aretaeus in the first century A.D. In the 17th century, Willis observed that the urine of diabetics was wonderfully sweet as if imbued with honey or sugar. The presence of sugar in the urine of diabetics was demonstrated by Dobson in 1755.

Diabetes is a chronic disease affecting around 2-3% of the population worldwide. Unfortunately, after the introduction of sulfonylurea and metformin about 50 years back no major lead has been obtained in this direction of finding a proper drug for diabetes. Plant materials which are being used as traditional medicine 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 practitioners and also accepted by the users for diabetes like for any other diseases in many countries especially in third world countries. Now-a-days more 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.

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

<table>
<thead>
<tr>
<th>Plant</th>
<th>Plant Part</th>
<th>Type of Test Sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trigonella foenum-graecum</td>
<td>seed</td>
<td>Alcohol, water extract</td>
</tr>
<tr>
<td>Nepheleopsis tuberosa</td>
<td>bulb</td>
<td>juice</td>
</tr>
<tr>
<td>Costus specious</td>
<td>rhizome</td>
<td>juice</td>
</tr>
<tr>
<td>Plantago ovata</td>
<td>husk</td>
<td>Powder</td>
</tr>
<tr>
<td>Allium sativum</td>
<td>bulb</td>
<td>juice</td>
</tr>
<tr>
<td>Hemidesmus indicus</td>
<td>root</td>
<td>alcoholic extract</td>
</tr>
<tr>
<td>Allium cepa</td>
<td>bulb</td>
<td>juice</td>
</tr>
</tbody>
</table>
Diabetes mellitus is a widespread disorder, which has long been in the history of medicine. Before the advent of insulin and oral hypoglycaemic drugs, the major form of treatment involved the use of the plants. But now from the 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 from community pharmacies contain plant extracts. On the basis of etiology, two main categories of diabetes are recognized, viz.

**Primary diabetes**

Secondary diabetes

**Secondary Diabetes**

The symptoms result from the following:

- Pancreatic dysfunction (pancreatitis, pancreatectomy).
- Hormonal imbalance (e.g., Acromegaly, pheochromacytoma, Cushing’s syndrome, glucagonoma).
- Drugs or chemical-induced reactions (e.g., glucocorticoids, anticancer agents, streptozotocin or diazoxide, thiazide, some psychoactive agents).

**Insulin receptor abnormalities.**

- Certain genetic syndromes (Hyperlipidemia 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).
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.

**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.

The results of glucose analysis are plotted as a graph against time.

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

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

**Treatment of Diabetes Mellitus**

- **Insulin**
  - Oral hypoglycaemic Drugs
  - Herbal Drugs.
  - **Insulin**
    - Insulin is hormone secreted by the α 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 pancreas secrete
insulin. Carbohydrate metabolism is primarily under the control of insulin. Insulin deficiency occurs in a person due to the functional disorder of the pancreas.

**Oral Hypoglycaemic Drugs**

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 ß islet cells of the pancreas 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 ß cells function subjects as well as diabetes.

**Biguanides: (Mode of Action)**

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

**Miscellaneous**

**Acarbose**

It is complex oligosaccharide which reversibly inhibits α-glucosidases, the final enzymes in the digestion of carbohydrates in the brush border of small intestinal mucosa. 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 or mixed 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.

**Precautions with oral hypoglycaemic agent:**

Hypoglycemia occurs with 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. 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.

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

**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 by modifying 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 polypeptide 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 beta cells**

**Allium cepa**

*Allium cepa* (onion) was investigated for its hypoglycaemic activity by Collip and Janet, Laurin Brahmachari and Augusti 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 in Type 1 diabetes mellitus. 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 serum glucose levels in normal and diabetic subjects.

**Plant drugs acting by modifying 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. The mechanism of action of gowar is probably related to its ability to increase the viscosity of gastrointestinal contents, slow gastric emptying 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 asiatica* 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. A few other plants with hypoglycaemic activity: Panax ginseng, Dioscorea dumatorum, Cuminum nigrum, Ocimum sanctum, 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 products with 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.

**REFERENCE**
