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Review Article

Herbal Antidiabetics: A Review

Akhilesh K. Tripathi [1], Pravin K. Bhoyar [1]*, Jagdish R. Baheti[2], Dinesh M. Biyani[3], M. Khalique[4], Mayuresh S. Kothmire[2], Yogesh M. Amgaonkar[3], Anand B. Bhanarkar[3]

[1]Department of Pharmaceutics, GRKIST collge of pharmacy, Dist: Jabalpur, Madhyapradesh, India
[2]S.S.D.J. College of Pharmacy, Neminagar Chandwad, Dist: Nashik, Maharashtra, India.
[3]Department of Pharmaceutics, S.K.B. College of Pharmacy, New Kamptee, Dist: Nagpur, Maharashtra, India
[4]Shree Sainath college of pharmacy Dist, Amaravati road: Nagpur, Maharashtra, India

ABSTRACT

Diabetes mellitus (DM) is the commonest endocrine disorder that affects more than 100 million people worldwide (6% of the population)(WHO/Acadia, 1992). 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. It is found to damage many of the body systems, particularly the blood vessels and nerves. Many herbal plants with hypoglycemic properties are known from across the world. In India, diabetes has been known for a long time, but its incidence is not of the same magnitude across the subcontinent. The wide range of structures of the plant constituents, which appear to be the active hypoglycemic principles, suggests different sites of action within the body. Whether these plants truly possess hypoglycemic properties needs to be investigated for those plants that are commonly used in the management of diabetes. Researches conducted in the last few decades on plants, mentioned in ancient literature or used traditionally for diabetes, have shown antidiabetic property. Among them, 30 plants and their products (active natural principles and crude extracts) that have been mentioned used in the Indian traditional system of medicine have shown experimental or clinical antidiabetic activity. Trigonella foenumgraecum, Momordica charantia, Tinospora cordifolia, Enicostema littorae, Gymnema sylvestre, Azadirachta indica, Syzigium cumini are some of the most effective and the most commonly studied Indian plants in relation to diabetes. Based on possible mechanism of action, antidiabetic plants have been classified and described in this article.

Keywords: diabetes mellitus; hypoglycaemic; antidiabetic plants; Active chemical constituents; pharmacognosy.

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 health care. 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 (Debra-Haire-Joshu, 1991). 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 Aeretaeus in the first century A.D. In the 17th century, Willis observed that the urine of diabetics as wonderfully sweet as if imbued with honey or sugar. The presence of sugar in the urine of diabetics was demonstrated by Dobson in 1755 (Satoskar, 1999).

Diabetes mellitus is now recognized as a serious global health problem (King, 1993). Westernized cultures and populations experiencing rapid acculturation are showing a sharp rise in non-insulin-dependent diabetes mellitus (Bennett, 1980 and Zimmer, 1980).The prevalence of NIDDM is increasing exponentially (Harris, 2000). It is estimated that more than 300 million people in the world will have diabetes by the year 2025. Only in U.S.A., there are 8 million diagnosed diabetic patients, another 8-12 million undiagnosed diabetic individuals and still an additional 23 million Americans with prediabetes or impaired glucose tolerance (IGT). Various epidemiological studies in India have shown that the prevalence and manifestations of diabetes are very high (Verma, 1986, Ramchandran, 1992 and Ramaiya,

* Corresponding Author
Email: pravinbhoyarpharmacist@gmail.com
Contact: +91-9096905508
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1990).At present, approximately 18-20 million people are diabetic in India, and it is projected that by 2025, there will be 20-60 million diabetics in India, and it will have the second largest number of diabetics in the world.

There are different approaches to the treatment of diabetes, like insulin treatment in type 1 diabetes: Sulphonylureas, which release insulin from pancreas by blocking the ATP-sensitive potassium channels (Aslam, 2002); Biguanides, which decrease the insulin resistance; Thizaolidinediones, which increase the insulin sensitivity; alpha-glucodase inhibitors like acarbose, which decrease glucose absorption from intestine, thereby decreasing postprandial hyperglycemia; metiglinides like repaglimide and nateglamide, which are insulin secretogogues.

Traditional herbal mineral plays an important part in the treatment of diabetes. If we were able to even identify some 5-6 herbal drugs that can reduce dose of insulin by increasing resistance sensitivity, reducing insulin resistance, then we would have positively contributed in the treatment of diabetes.

Herbal medicines are often used as therapeutic remedies in combination with allopathic drugs (Ramesh, 2003). Most of the doctors did not report any complication, but nausea, vomiting, gastric problems were the common adverse effects reported with PHFs (Polyherbal formulations). Usually ayurvedic drugs are being used due to their minimum toxicity (Babara, 1993). The basis prescription of ayurvedic drugs was mainly found to be past experience of the patients. Practicing physicians expected that controlled clinical trials of the herbal antidiabetic should be conducted in humans at different hospitals to substantiate the efficacy claim. Ginger, jamun, karela, methi are being used as home remedies in diabetes mellitus due to their proved antihyperglycemic activity. Many of the pharmacists are interested in providing counseling to all their customers (patients) regarding herbal products (Ponnusankar, 2003). Herbal medicines can be relevant today only if they are applied and tested within the framework of modern sciences and subjected to the rigorous criteria for quality, safety and efficacy. Only then, herbal prod-

Table 1: Some plants having hypoglycemic activities

Sn.	Common name	Botanical name and family	Parts used	Therapeutic action
1	Asiatic ginseng	Panax ginseng (Araliaceae)	Roots	Lowers blood glucose by decreasing the rate of carbohydrate absorption, increasing glucose transport and modulation of insulin secretion
2	Ashvagandha, winter cherry	Withania somnifera (Solanaceae)	Roots	Decrease in blood glucose Level
3	Asiatic sweet-leaf	Symplocos Paniculata (Symplocaceae)	Leaves Stems	Inhibits protein tyrosine phosphatase 1B (PTP1B) 1 and 2
4	Banana	Musa sapientum Kuntz(Musaceae)	Fruits/Flower	Decreases blood glucose and glycosylated haemoglobin level
5	Banyan tree	Ficus bengalensis (Moraceae)	Bark	Inhibits insulinase activity from liver and kidney, stimulates insulin secretion
6	Barbados	Aloe barbadensis Mill. (Liliaceae)	Leaves	Stimulates synthesis and/or release of insulin from β-cells
7	Betel, Betel vine	Piper betle (Piperaceae)	Leaf	Antihyperglycemic, glucose metabolism
8	Bilwa, bael fruit	Aegle marmelos (Rutaceae)	Leaf extract	Decreases blood urea & cholesterol
9	Bitter-kola, false kola	Garcinia kola (Clusiaceae)	Seed	Hypoglycaemic and Hypolipidemic
10	Black tea	Camellia sinensis L.(Theaceae)	Leaves	Decreases blood glucose level
11	Common fig	Ficus carica L. (Moraceae)	Leaves	Decreases hyper-glycaemia and level of total cholesterol
12	Custard apple, sugar apple	Annona squamosa (Annonaceae)	Fruit pulp	Decreased urine sugar, urine protein and glyco-haemoglobin
13	Desert Indian wheat,Ispghul	Plantago ovata (Plantaginaceae)	Husks extrac	Inhibits intestinal glucose absorption, enhancement of mobility
14	Prickly chaff flower	Achyranthes aspera (Amaranthaceae	Whole plant	Provides necessary elements like Ca, Zn, Mg, Mn, and Cu to the β-cells

ucts can be comparable with modern medicines and can bring necessary confidence in prescribing doctors.

In present investigation attempts have been made to study the indigenous plants which show inhibitory effect of glucose utilization and are in use as antidiabetic agents in traditional system of medicine. Hence, the present study was performed with the aim of producing an inventory of the plants used to treat diabeties, simultaneously also included those plants which are scientifically justified as antidiabetic agents.

ANTIDIABETIC PLANTS

Ayurveda and other Indian literature advocate the use of medicinal plants in treatment of various human diseases. India has about 45,000 plant species and among them, several thousands have been claimed to possess medicinal properties. Researches conducted in the last few decades on plants, mentioned in ancient literature or used traditionally for diabetes, have shown antidiabetic property. Among them, 30 plants and their products (active natural principles and crude extracts) that have been mentioned used in the Indian traditional system of medicine have shown experimental or clinical antidiabetic activity. Trigonella foenumgraecum, Momordica charantia, Tinospora cordifolia, Enicostema littorae, Gymnema sylvestre, Azadirachta indica, Syzigium cumini are some of the most effective and the most commonly studied Indian plants in relation to diabetes. Some plants having hypoglycemic activity have been shown in Table 1.

CLASSIFICATION OF HERBAL ANTIDIABETICS

The wide range of structures of the plant constituents, which appear to be the active hypoglycemic principles, suggests different sites of action within the body. Certain plants having active antidiabetic principles isolated have been shown in Table 2. Based on the possible mechanism of action, reported plant antidiabetics may be classified as follows.

1. Drugs acting like insulin

The purified protein extract of the fruits, seeds and callus of Momordica charantia (bitter gourd) is reported to be homologous to animal insulin, and it produced consistent hypoglycemic effect when tested on rats, gerbils, langurs and human beings.

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.

Panax ginseng

Ginseng polypeptide, isolated from the root of Panax ginseng, was demonstrated to decrease the level of blood sugar and liver glycogen when injected intravenously to rats. Mice were injected subcutaneous daily dose of 50 and 100 mg/kg for 7 successive days. GPP was also found to decrease blood glucose and liver glycogen and various experimental hyperglycemia induced by injection of adrenaline glucose and alloxan. The aqueous extract of root of panax ginseng showed a remarkable hypoglycemic activity on administration to mice. The hypoglycemic effect of pongamia pinnata flowers, in normal persons and outdoor patients suffering from non-insulin dependent diabetes mellitus (NIDDM).

Thus the flowers of P. pinnata, causing a consistent hypoglycemic effect both in normal subjects and patients with NIDDM, have been attributed to direct insulin-like action.

2. Drugs increasing insulin secretion from beta cells of pancreas

The alcoholic extract of the roots of Panax ginseng lowered the blood glucose level by stimulating insulin release, especially glucose-induced insulin release from pancreatic islets. The hypoglycemic action of the seeds of the Acacia species was reported to be due to in-

Table 2: Active antidiabetic principles isolated from certain plants

Plant	Part Used	Active Principles
Acontium carmichaeii	Root	Aconitan A, B, C and D
Anemarans	Rhizomes	Anemarans A, B, C and D
Atractylodes japonica	Rhizomes	Glycans A, B, C and D
Coptis chinensis	Aerial part	Bernerine
Capsicum annum	Fruit	Capsaicin
Dioscorea japonica	Rhizome	Glycans A, B, C, D, E, F
Galega officinalis	Seed	Galegin
Gandoderma lucidium	Fruit	GlycansA,B
Lathyrus japonica	Seed	Lathyrines
Oriza sativum	Root	Glycans A, B, C, D
Tinospora cardifolia	Plant	1,2 Substituted Pyrolidines

creased secretion of insulin from β 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.

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.

Azadirachta indica

Effect of Azadirachta indica leaf extract on serotonin inhibition in glucose-mediated insulin release in rat pancreas was reported to elucidate the possible mechanism of antihyperglycemic effect. A. indica leaf extract blocks significantly the inhibitory effect of serotonin on insulin secretion mediated by glucose. Hypoglycemic effect observed with Azadirachta indica when given as leaf extract and seed oil was comparable to that of glibenclamide. A. indica could be of benefit in diabetes mellitus for controlling the blood sugar or may also be helpful in preventing or delaying the onset of the disease.

Syzigium cumini

Hot water extract of dried fruits and seeds of Syzigium cumini is taken orally for diabetes. Hot water extract of dried seeds taken orally is prescribed in Ayurvedic medicine for diabetes. The tea prepared from leaves of Syzygium cumini and skeels of S. jambos has been reported to be used frequently by diabetic patients in Brazil.

Eugenia jambolana

Herbal extracts of Momordica charantia and Eugenia jambolana have been shown to reduce hyperglycemia in diabetic animal models and human patients. However, no work has been done so far to assess their effect on insulin resistance. The oral administration of the extract resulted in enhancement in serum insulin levels in normoglycemic and diabetic condition. Extracts of this plant stimulated insulin secretion. These extracts inhibited insulinase activity from liver and kidney.

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.

Medicago sativa

Medicago sativa L. (Lucerne, alfalfa) when supplied in the diet (6.25 % by weight) and infusion (1g/400 ml) reduced the level of hyperglycaemia in streptozotocin-induced diabetes (Swatson, 1990). An aqueous extract of the plant (1 mg/ml) stimulated 2-deoxy-glucose transport (1.8 fold), glucose oxidation (1.7 fold) and incorporation of glucose into glycogen (1.6 fold) in mouse abdominal muscle. In acute, 20 min tests, 0.25-1 mg/ml aqueous extract of Lucerne evoked a stepwise 2.5-6.3 fold stimulation of insulin secretion from the BRIN-BD11 pancreatic beta cell line.

3. Drugs acting by regeneration of γ-cells of the islets of Langerhans

The Morus bomoysis (mulberry) leaves treated with anaerobic condition were reported to decrease blood glucose level in alloxan-induced type 1 diabetic mice.

Pterocarpus marsupium

The decoction of P. marsupium was administered for diabetes mellitus patients for 30 days. Singh,AK et al. revealed that the decoction is effective in the management of diabetes mellitus. Feeding the ethyl acetate soluble fraction of an absolute ethanol extract of P. marsupium wood for 5 days to alloxan diabetic rats significantly lowered blood sugar level (Ahmad,1991). (Chakrabarti D et.al suggested that aqueous extract of P. marsupium exhibited antidiabetic activity in diabetic rats and human beings. The blood sugar lowering effect of 95% ethanolic extract of Red Sandal hyperglycemic and streptozotocin diabetic albino rats. It was found to be effective in lowering the glucose level (Nagaarjun, 1991). Epicatechin, isolated from the heartwood of Pterocarpus marsupium, showed regeneration of the b-cell population of the islets, which were earlier necrosis by alloxan.

Tinospora cordifolia

Tinospora cordifolia have insulin-like action and can significantly reduce the blood glucose but not the lipid levels in alloxan-induced rabbits. Literature supports the traditional belief that T. crispa extract effects in the treatment of diabetes by its action on the endocrine pancreas. Oral administration of the extract of Tinospora cordifolia roots for 6 weeks resulted in significant reduction in blood and urine glucose and in lipids in serum and showed its hypoglycemic action.

T. crispa

The mechanism of action of antihyperglycemic effect of T. crispa is not due to interference with intestinal glucose uptake or uptake of the sugar into the peripheral cells. The antihyperglycemic effect of T. crispa is probably due to stimulation of insulin release via modulation of â-cells. That the insulinotropic effect of T. crispa is physiological suggests that the extract contains a compound that could be purified for use in the treatment of type-2 diabetes (Jha, 2003).

Gymnema sylvestre

Gymnema sylvestre leaves cause hypoglycemia in experimental animals, which sets in soon after the administration either by mouth or by injection. The main constituent of Gymnema is gymnemic acid, which is a complex mixture of at least nine closely related acidic glycosides, the main ones being Gymnemic acid A-D. The drug acts indirectly through stimulation in insulin secretion of the pancreas, as it has no direct action on the carbohydrate metabolism. The study showed that while Gymnema significantly reduced glucose levels in the hyperglycemic rats, it had no effect on normal rats (Gupta, 1962). One study examined treatment by Gymnema for streptozotocin diabetic rats. Oral administration of Gymnema corrected the hyperglycemia in moderately diabetic rats, and the results continued for more than 2 months after Gymnema was discontinued. Gymnema did not reduce blood sugar levels in the severe and toxic groups of diabetic rats, but it did prolong their survival time (Srivastava, 1968). Srivastava, Y. et al, revealed that the lack of results in lowering blood glucose levels in the severe and toxic diabetic rats may have been due to complete destruction of the â-cells by alloxan. Gymnema has recently been tested in open clinical trials. Administration to 27 patients with insulin-dependent diabetes on insulin therapy significantly reduced insulin requirements, fasting blood glucose, and glycosylated hemoglobin and serum lipids over a 6- to 34-month period. Shanmugasundaram, ER, et.al suggested that gymnema appeared to enhance endogenous insulin, possibly by regeneration of the residual β-cells. The effectiveness of Gymnema in noninsulin- dependent diabetes was investigated in 22 patients with a history of poor blood sugar control. A significant reduction in blood glucose, glycosylated hemoglobin and conventional drug usage was observed over a period of 20 months.

4. Drugs inhibiting glucagon secretion from β- cells in pancreas

Ke-Tang-Ling (an oriental antidiabetic drug) decreased glucose levels in NIDDM patients, suggesting an inhibitory effect on glucagons secretion from a-cells in pancreas.

5. Drug reducing absorption of glucose from gastrointestinal tract

Cyamposis tertragonoloba

Cyamopsis tetragonolobus (gower) has been reported to reduce postprandial hyperglycemia in normal and diabetic volunteers. The petroleum extract of C. tertragonoloba when given orally reduced the hyperglycemia induced by streptozotacin in male albino rats. Clinical studies in UK revealed that the dietetic supplementation with guar gum could decrease the need of insulin and oral antidiabetics, improving the glycemic profile and the control of the metabolic state, showing progressive decrease in the amount of HbA1c. Five grams of guar granules thrice a day reduced fasting and postprandial plasma glucose levels. Cuminum nigrum reduced the blood sugar levels of normal as well as diabetic rabbits without decreasing the total lipid levels, which indicated that the drug might be acting partly by inhibiting the absorption of glucose from the gastrointestinal tract.

Ocimum sanctum

Oral administration of an alcoholic extract of leaves of Ocimum sanctum Linn. (Tulasi) reduced glycaemia in normoglycaemic, glucose-fed hyperglycaemic and streptozotocin-induced diabetic rats. Furthermore, the extract potentiated the action of exogenous insulin in healthy rats. The activity of the extract was 91% and 70 % that of tolbutamide in healthy and diabetic rats, respectively (Chattopadhyay, 1993). Reduction in fasting blood glucose was obtained after one month of treatment of healthy and diabetic rats with O. sanctum leaf powder (Rai, 1997).

The effect of the aqueous extract of Mangifera indica leaves on blood glucose level was assesed in normoglycemic glucoseinduced hyperglycemic and streptozotocin (STZ) induced diabetic rats.

6. Drugs inhibiting aldose reductase activity

Roots of Paeonia latiflora, roots and rhizomes of Glycyrrhiza glabra, rhizomes of Atractyloides lancea and bark of Cinnamomum cortex inhibited rat lens aldose reductase activities. Paeonia latiflora and Glycyrrhiza glabra significantly inhibited the accumulation of sorbitol within human red blood cells. These results suggested that the effectiveness of these kampo medicines in some of the chronic diabetic complications might be due to inhibition of aldose reductase activities. Treatment with water extract of 1:1 mixture of cortex of Phellodendron amurense and cortex of Aralia elata significantly inhibited the aldose reductase activity in the lenses of diabetic rats. Consequently, a dramatic reduction in the high sorbitol content in the lenses of diabetic rats was observed.

Aralia elata

Yoshikawa M, et.al suggested that Elatoside E, a new hypoglycemic principle isolated from the root cortex, was shown to affect the elevation of plasma glucose level by oral sugar tolerance test in rats. The hypoglycemic activity of oleanolic acid and nine oleanolic acid glycosides obtained from root cortex have also been examined and were found to exhibit hypoglycemic activity. Three saponins, named as Elatosides G, H and I, isolated from young shoot of A. elata, were also found to exhibit potent hypoglycemic activity in the oral glucose tolerance test in rats.

7. Drugs increasing glucose utilization

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 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. The hypoglycaemic effect of Salvia lavandifolia Vahl.reported previously and suggested that this hypoglycaemic effect may arise increased peripheral uptake of glucose

8. Drugs reducing lactic dehydrogenase and γ-glutamyl transpeptidase

Several extracts from the stem and the flowers of Lythrum salicaria were evaluated for their hypoglycemic activity in rats. The ether extracts of the stem and the flowers showed significant hypoglycemic activity in rats with glucose- and epinephrine-induced hyperglycemia when the animals were given oral doses equivalent to 10 g/kg of the starting material. The ether extract of the stem reduced elevated lactic dehydrogenase activity, whereas the extract of the flowers accentuated the elevated levels of aspartate aminotransferase induced by streptozotocin.

9. Drugs inhibiting glycogen-metabolizing enzymes

Effect of trihydroxy octadecadiene acids from Bryonia alba on the activity of glycogen-metabolizing enzymes has been studied, and these phytoconstituents were found to exert a direct effect on glycogen phosphorylase, phosphoprotein phosphatase and hexokinase in the liver and muscle tissues of albino rats having alloxan-induced diabetes. Drugs acting on liver glycogen Different extracts of Aralia elata were studied to determine if they could mimic insulin actions such as activation of ERK2, PI3-kinase and glycogen synthesis in liver cells.

Allium sativum

Srivastava K, et.al suggested that the extract of A. sativum inhibits the formation of diabetic cataract due to excessive accumulation of polyols and hydration of the lenses of diabetic rats fed with galactose-, glucose- and xylose-rich diet. 5- Methyl cysteine sulphoxide, a sulphurcontaining amino acid isolated from A. cepa, showed antidiabetic effect on oral administration of the compound at dose 200 mg/kg for a period of 45 days to alloxan diabetic rats. Kumar V, et.al suggested that it controlled the blood glucose in serum and altered the activities of liver hexokinase glucose-6-phosphatase and hemoglobin coenzyme-A reductase towards normal. Administration of aqueous extract of Allium sativum (garlic) in the concentration of 10 ml/kg/day to rabbits significantly increased liver glycogen and free amino acids, which resulted in significant decrease in fasting blood sugar, triglycerides (in serum, liver and aorta) and liver serum proteins as compared to those in sucrose-fed group.

The pectin isolated from the fruits of Coccinia indica significantly reduced blood glucose levels when orally administered to normoglycemic rats. The reduction may be due to decreased absorption of glucose from the intestine, higher rate of glycolysis by the higher activity of hexokinase (one of the key enzymes of glycolysis) and enhanced rate of glycogenesis as evidenced by the higher amount of liverglycogen present in the pectin-administered groups.

10. Drugs increasing glyoxalase 1 activity in liver

In the liver of the diabetic rat, the glyoxalase 1 activity decreases. This leads to hyperglycemia and deterioration of other biochemical parameters in diabetic animals. The powdered seed of Trigonella foenumgraecum, when administered to such diabetic rats, reverses the activity of glyoxalase 1 to control values and restores the other general biochemical parameters.

Trigonella foenumgraecum

The effect of fenugreek seeds (Trigonella foenumgraecum) on blood glucose and the serum lipid profile was reported in insulin-independent (type 1) diabetes patients. Jha N, et.al suggested that the antidiabetic property of fenugreek seed is associated with the defatted seed material, which is rich in fibers, saponins and proteins. The results show that the antidiabetic properties of fenugreek seeds are contained in the testa and endosperm. This sub-fraction is rich in fibers; it is not possible to exclude the existence of one or more unknown active pharmacological compounds in this sub-fraction of the seed. Study reported that fenugreek given in a dose of 2.5 g twice daily for 3 months to healthy individuals did not affect the blood lipids and blood sugar. Fenugreek decreased significantly the blood sugar in mild NIDDM cases and slightly decreased it in severe condition. Mechanism of action of fenugreek seeds as an orally active hypoglycemic effect may be mediated through stimulating insulin synthesis and or secretion from the beta pancreatic cells of Langerhans. The effect may also be evident by increasing the sensitivity of tissues to available insulin. The hypoglycemic effect was observed to be slow but sustained, without any risk of developing severe hypoglycemia. The activities of gluconeogenic enzymes were higher in both liver and kidney during diabetes; however, the activities of the lipogenic enzymes decreased in both tissues during diabetes. The therapeutic role of Trigo-

nella seed powder in type 1 diabetes is due to change of glucose and lipid metabolizing enzyme activities to normal values, thus stabilizing glucose homeostasis in the liver and kidney.

11. Drugs increasing glucose uptake in lipocytes

Gupta SS, et al., revealed that the hypoglycemic activity of the extract of S. Japonica was observed in streptozotacin-induced hyperglycemic rats. It was found that an aqueous ethanolic extract was more effective than a mixture of tolbutamide and buformine in lowering blood glucose level. Bellidifolin, isolated from S. japonica, was found to be a potent hypoglycemic agent in streptozotocin-induced diabetic rats by both oral and interperitoneal administration. Bellidifolin significantly lowered the loaded glucose level in normal as well as diabetic rats.[(69)] Bellidifolin, isolated from Swertia japonica, was found to be a potent hypoglycemic agent in STZ-induced diabetic rats by both oral and i.p. administration. Bellidifolin stimulated glucose uptake in Rat 1 fibroblasts expressing human insulin receptors. (Both insulin and bellidifolin significantly stimulated 2-deoxy- D-glucose uptake activity in fibroblasts.)

12. Drugs inhibiting glucose-6-phosphate system

The aqueous extract of Bauhinia megalandra leaves causes a decrease of nearly 50% in the glucose production, from lactate or fructose of rat liver slices incubated in Krebs-ringer bicarbonate buffer supplemented with oleate-saturated albumin.

13. Drugs increasing the creatine kinase levels in tissues

As compared to control rats, creatine kinase activities were found to decrease significantly in heart, skeletal muscle and liver of experimental diabetic rats. Trigonella foenumgraecum normalized this activity and restored the normoglycemia.

14. Drugs having oxygen radical scavenging activity

The fruit juice of Momordica charantia was found to be a potent scavenger of superoxide and hydroxyl radicals. Since these oxygen radicals are implicated in diabetics, the antidiabetic action of Momordica charantia has been mediated through this mechanism.

The hypoglycemic effect of the aqueous extract of the bark of Pterocarpus marsupium, alcoholic extract of seeds of Trigonella foenumgraecum and leaves of Ocium sanctum was investigated in both normal and alloxan-induced diabetic rats. In a placebo-controlled study, the effect of ginger and fenugreek was examined on blood lipids, blood sugar, platelet aggregation, fibrinogen and fibrinolytic activity. Fenugreek administration did not affect platelet aggregation, fibrinolytic activity and fibrinogen. The efficacy of Momordica charantia, Eugenia jambolana, Tinospora cordifolia and Mucuna pruriens was reported in the prevention of diabetic cataract. Momordica charantia and Eugenia jambolana were reported to have better protective effect in the development of cataract as compared to Tinospora cordifolia and Mucuna pruriens. Momordica charantia and Eugenia jambolana were reported to have a partial but significant preventive effect in renal hypertrophy as compared to Tinospora cordifolia and Mucuna pruriens (Rathi, 2002).

SOME MINERALS USED IN DIABETES MELLITUS

Some of the mineral remedies consist of Bangabhasma (calcinated tin), Jistbhasma (calcinated zinc), Abrhabhasma (mica ash), and Lohabhasma (calcinated iron). Some of the commercial preparations (e.g., Nowojar) containing above bhasmas were very effective in NIDDM; in case of IDDM, it helped in reducing dose of insulin. Some complexes with metformin and tolbutamide with zinc, cadmium, cobalt and copper have some complexes with the exception of complexes have shown good hypoglycemic effect. Zinc complexes have shown to have good blood-sugar-lowering activity. Shilajit, an organo-mineral preparation found in nature, has been used as a tonic in diabetes mellitus.

Rasayana therapy in diabetes mellitus: Rasayana is an important branch of Ayurveda. The main goal of Rasayana therapy is better quality of life with increased lifespan. Rasayana includes drug formulations, dietary regime and code of conduct. Many of the drugs used in Rasayana therapy in diabetes mellitus have excellent antioxidant properties, like Phyllanthus emblica, Azadirachta indica, Ocium sanctum and Tinospora cordifolia.

The Rasayana approach to treat diabetes consists of

- Aeara Rasayana (antistress)
- Ajasrika Rasayana (dietary control)
- Osad Rasayana (antistress)
- Kamya Rasayana (preventive)
- Naimittika Rasayana (hypoglycemic)

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.

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