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Review Article

DIABETES AND INDIAN TRADITIONAL MEDICINES AN OVERVIEW

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ABSTRACT

Diabetes mellitus is a group of metabolic diseases characterised by hyperglycaemia,hypertriglyceridaemia and hypercholesterolemia resulting from defects in insulin secretion or action or both.There are lots of chemical agents available to treat diabetic but total recovery from diabetes has not been reported till date.Alternative to these synthetic agents,plant provides a potential sourceof hypoglycaemic drugs which are widely used in several traditional systems of medicines to prevent diabetes.This review mainly deals with diabetes, plants used as antidiabetics in various traditional systems of medicines and few examples of traditional herbal antidiabetic formulations available in the present market.

Keywords: Diabetes, Antidiabetics, Herbal medicines, Marketed products

INTRODUCTION

Diabetes is a chronic disorder of metabolism of carbohydrates proteins and fat[1]due to absolute or relative deficiency of insulin secretion and with varying degree of insulin resistance which can be characterized by hyperglycaemia, glycosuria, hyperlipidaemia and negative nitrogen balance[2]. It has now become an epidemic with worldwide incidence of 5% in the general population. The number of people suffering from diabetes is increasing every year and the disease now kills more people than AIDS. Till date 40.8 million patients were diagnosed with diabetes in India versus40 million HIV patients all over the world. Up to 171 million people around the globe have diabetes with this figure likely to more than double by 2030. Close to 3.2 million deaths occurring each year are believed to be attributed to problems of diabetes, 6 deaths every minute [3,4]. The 10 top countries in numbers of people suffering from diabetes are India, USA, China, Japan, Indonesia, Pakistan, Brazil, Russia, Italy and Bangladesh.

WHAT IS DIABETES?

Though Diabetes indicates two types of diseases associated with two different gland systems, it is mainly used for Diabetes mellitus. However Diabetes is mainly of two types:[5]

1. **Diabetesmellitus**
2. **Diabetesinsipidus**

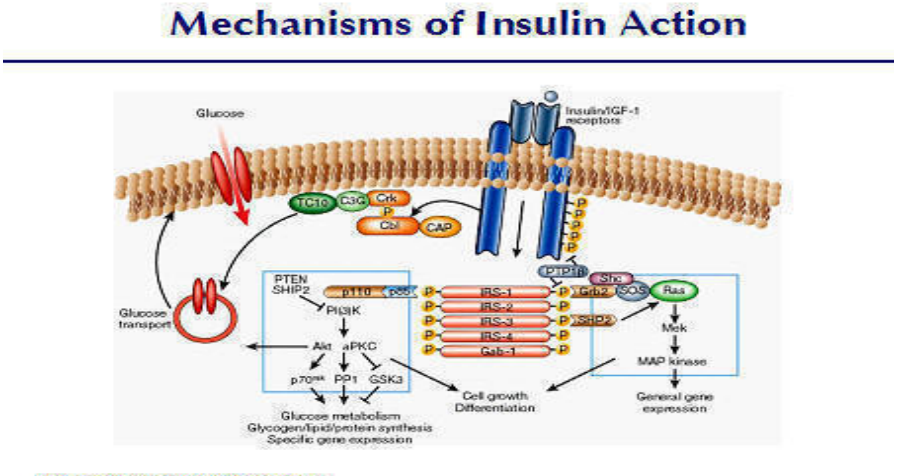
The second classification is Diabetes insipidus. This has to do with the amount of fluid or water which is retained in the system and overall is very rare. This type of diabetes is associated with Adrenal or supra renal gland and occurs due to insufficiency of Adrenal diuretic hormone[6].

Diabetes mellitus is a metabolic disorder where in human body does not produce or properly uses insulin, a hormone that is required to convert sugar, starches, and other food into energy. DM is characterized by constant high levels of blood glucose (sugar). Diabetes mellitus is caused by two reasons[7]:

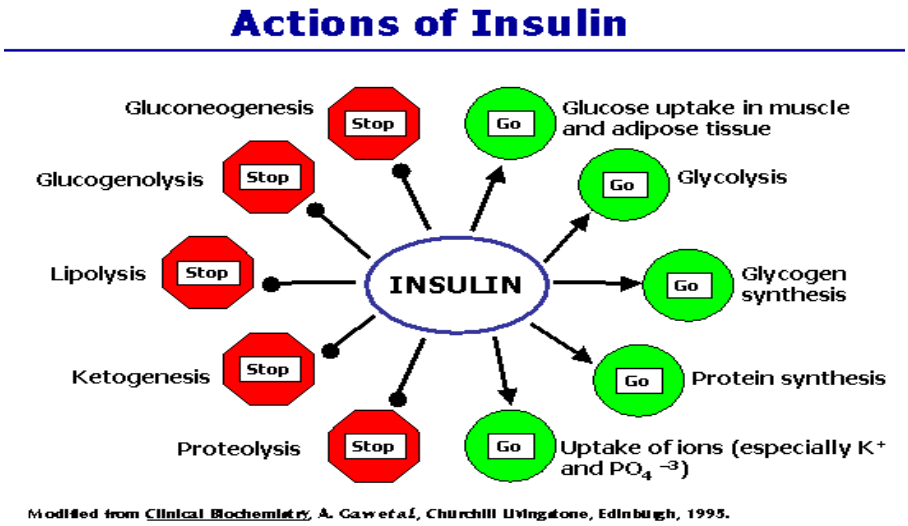
- Insufficient or no production of insulin (Insulin dependent DM).
- Improper utilisation of insulin or insulin resistance (Non-insulin dependent DM or NIDDM).

DIABETES MELLITUS AND INSULIN[8]

The carbohydrates we take as food is simplified to glucose molecules by various metabolic functions. This molecule serves as the source for energy or ATP production in the body required for vital functions. Insulin is a natural hormone secreted from the β- cells of pancreas which helps the cells to uptake glucose molecules from the blood stream. Hence deficiency of insulin results in the failure of glucose utilization by the cells and leading to its increased concentration in blood stream. This condition is known as diabetes.



Insulin affects the metabolism of carbohydrate, fat, proteins and ion flux by attaching to the specific insulin receptor on the cell surface. This hormone interaction is irreversible and the insulin molecule remains chemically unaltered during this contact. The hormone receptor complex is then taken inside the cell by an endocytic mechanism and metabolised to free the insulin molecule to the membrane for re-use .The glucose molecules are then oxidised to produce ATP or energy molecules. Insulin resistance is caused by the cell membrane. The excess of sugar or glucose in blood is excreted by kidney in urine [9].



COMPLICATIONSIN DIABETES

Diabetes is supposed to be the world's main killer in next 25 years in India mainly. The complications of diabetes are many and can be very dire. The main reason for this is because diabetes causes problems with the nerves as well as problems with the flow of blood through the blood vessels that supply energy for every organ. These two problems affect every organ in the human body. So, when the blood glucose levels are not maintained because of ineffective or poor self-care, this can trigger the problems with blood vessels and nerves. This in turn causes the many complications of diabetes.

These complications can be with the eyes, the heart, the kidneys, the feet and many other areas of the body. Because of the restricted blood flow when there is a problem or complication, the body is extremely slow to heal. Even if a little carelessness may lead to serious health conditions or death[10].

Diabetes is associated with many complications like micro vascular (retinopathy, neuropathy and nephropathy), macro vascular (stokes, peripheral vascular diseases and coronary heart disease)[11] and other large blood vessel diseases like atherosclerosis. The severity of these complications can be ceased having a good control on blood sugar level. Acute complications involve keto acidosis, non ketotic hyper-osmolar coma which may lead to diabetic coma. Chronic complications include the chronic increase in blood sugar level leading to the damage of blood vessels and macro vascular diseases.

CAUSES

Many scientists believe that the overall cause of the rise in diabetes is basically a change in urban cultures around the world. Medical professionals and scientists around the world believe that this is setting up the epidemic of diabetes since the two major causes of diabetes seem to be diet and exercise[12].

Decreased physical activity, increasing obesity, stress and changes in the food consumption have been proved to be the root cause of increasing diabetes in last 20 years.

Many also believe that our worldwide economic crisis is having an impact on diabetes not only in treatment but also in cause. But then again, it could be just a matter of genetics as some ethic groups seem more prone to developing diabetes than others[13].The major concerns are that the majority of this increase will occur in developing countries, due to population growth, unhealthy diets, obesity, ageing, and sedentary lifestyles.

Hence the discussion on causes can be summarized with the fact that today the main reasons leading to the growth of diabetics are

- Improper life style mainly in diet (irregular timing in taking food and use of preserved foods), exercise and sleeping habits[14].
- Extra work tension and mental stress.
- Genetics.
- Over medication and use of some allergic medicines[15].

SYMPTOMS OF DIABETES[16]

Increased fatigue	Polydipsia.
Polyuria	Polyphegia
Weight fluctuation	Blurry vision
Irritability	Infections
Poor wound healing	

DIAGNOSISOF DISEASE[17]

The blood glucose levels of a healthy man are 80mg/dl on fasting and upto 160mg/dl in the post prandial state. Diabetes mellitus is characterized by recurrent or persistent hyperglycaemia and can be diagnosed by any one of the following tests: -

- A **fasting plasma glucose (FPG) test** measures blood glucose in a person who has not eaten anything for at least 8 hours. **(>162 mg/dL).**
- An **oral glucose tolerance test (OGTT)** measures blood glucose after a person fasts at least 8 hours and 2 hours after the person takes 75g oral glucose load**(>200mg/dL)**.
- A **random plasma glucose test**, also called a casual plasma glucose test, measures blood glucose without regard to when the person being tested last ate**(200>mg/dL)**.

TYPESOF DIABETES (DM) [18]

There are three main types of diabetes: -

- **Type 1 diabetes** (insulin-dependent diabetes mellitus, IDDM or immune-mediated or juvenile-onset diabetes). It is caused by an

auto-immune reaction where the body's defence system destroys the insulin-producing β-cells. People with type 1 diabetes produce very little or no insulin. The disease usually occurs in children or young adults. Patients completely depend on the exogenous insulin to control the levels of glucose in their blood. Genetic factors are believed to be the main reason of it.

- **Type 2 diabetes** (non-insulin dependent diabetes mellitus, NIDDM or adult-onset diabetes). It accounts for at least 90% of all cases of diabetes. It is characterised by insulin resistance and relative insulin deficiency. This occurs mainly due to loss of functional β-cells. Type 2 diabetes is associated with very serious life ceasing complications.
- **Gestational diabetes (GDM)** is a form of diabetes consisting of high blood glucose levels during pregnancy. It develops in 2-4% of pregnancies generally in 2nd or 3rd trimester. GDM usually disappears after pregnancy but women with GDM and their offspring are at an increased risk of developing Type 2 diabetes later in life.
- **Pre-diabetes**- this is body's warning sign to make some health changes. Pre-diabetes is diagnosed when the level of glucose in the blood is higher than the normal limits but not quite high enough to diagnose as Type-2 diabetes. It is the symbol of impaired glucose tolerance.

DIABETESCARE ANDMEDICATIONS

As diabetes is not completely curable it needs a life time commitment to do what is necessary to control diabetes. With proper management it can be controlled to a greater extent. All of these factors are interconnected. And in the case of Type-2 diabetes, it can be totally controlled in some cases with diet and exercise[19].

Daily monitoring of blood glucose level with a glucometer.

- Insulin injections and other medications to be taken as directed.
- Managing of diet and weight control.
- Managing a daily exercise plan.
- Daily monitoring and managing of skin and foot care.
- Daily oral hygiene.
- Regular visits to the eye doctor as well as the dentist.
- Regular checkup for blood pressure etc.

Diabetes can be managed with various types of medications

- Exogenous insulin[20].
- Oral hypoglycaemic agents[20].
- Alternative medicines like herbal treatments, Yoga, Unani medicines etc.

NEED ANDSCOPEOFALTERNATIVE REMEDY

The disease diabetes mellitus (all types) can be managed by controlling the blood glucose level with medication (oral hypoglycemic agents or insulin from external source), adopting to various exercise or yoga therapy or dietary plan. Due to modernization of life style NIDDM is growing as the major health problem in the developing countries. In India every 4th man is susceptible to develop diabetes. According to Diabetes Atlas published by the IDF, there were an estimated 40 million victims in India in 2007 and this number is predicted to rise to almost 70 million people by 2025[21]. It is estimated that every fifth person with diabetes will be an Indian& INDIA is known as the "DIABETES CAPITAL" of the world[22].

However insulin works directly in the body by utilizing the glucose molecules but the Oral hypoglycemic agents act by:

- Stimulation of β-cells
- Decreasing the absorption of glucose to blood stream from GI tract
- Increasing the sensitivity of insulin receptor on cell surface

Most of the hypoglycaemic agents and hypolipidaemics used in allopathic practice to treat diabetes mellitus and hyperlipidaemia are reported to have side effects in long term use. All treatments of DM are accompanied by specific drawbacks[23] like:

- Restriction in use of oral hypoglycemic agents by their pharmacokinetic profile.
- Secondary failure rates.
- Accompanying side effects[24].
- Development of resistance.
- Pain and difficulties associated with daily injection of insulin.
- Cost.

EXAMPLES

- Sulfonyl urea (chlorproamide causes cholestatic jaundice and sensitises kidney to ADH secretion) [25].
- Thiazolidine diones may lead to liver toxicity[25].

On the other side it has been proved that a large percentage of patients with DM develop different diseases related heart ,kidney, eyes(retina) even if having a good control on Blood sugar level throughout.

As the victims of DM are increasing in the normal population day by day there is a strong need of development natural remedies free of the problems associated with allopathic treatments and also which are able to fight against all the complications associated with DM. Hence World health committee recommends on the further investigation of traditional methods for treatment of diabetes[26].

As per the literature from Ayurveda more than 500 plants are available in the nature with anti-diabetic property and still some wealth is to be discovered. Since the age of birth of human, these plants have served human society as the answer to all diseases and alignments. Plant based products have been growing as a better choice of treating diseases due to less associated side effects and also fighting against the complications arising due to the main disease (like increased blood pressure in DM). In DM, some herbs are used which normalizes blood sugar and also acts as an antioxidant and lower cholesterol level in blood. However the hypoglycaemic activity of some extracts has been confirmed by pharmaceutical science as a source of a conventional drug like *Galega officinalis* is the source of metformin (a less toxic biguanide).

MECHANISMOF ACTIONOFHERBAL REMEDIES[27]

- Initiate release of insulin (*Acacia arabica*) [28].
- Insulin releasing & insulin like activity (*Agrimony eupatoria*)[29].
- Stimulating the effects on glucose utilization and antioxidant enzyme (*Allium cepa*)[30].
- Stimulation of synthesis and insulin secretion (*Aloe vera*)[31].
- Inhibition of renal glucose absorption (*Artemisia pallens*Wall)[32].
- Protection of destruction and regeneration of the β- cells (*Beta vulgaris*)[33].
- Increase insulin secretion & reduction of insulin binding on the insulin receptor (*Capsicum frutescens*)[34].
- Glycogenolytic effect due to epinephrine action was blocked (*Azadirachta indica*)[35].

India having a rich heritage of traditional medicine constituting with its different components like Ayurveda, Siddhaand Unani. Standardization of herbal formulations is essential in order to assess the quality of drugs, based on the concentration of their active principles. The development of these traditional systems of medicines with the perspectives of safety, efficacy, and quality will

helps not only to preserve the traditional heritage but also to rationalize the use of natural products in healthcare [36, 37, 38]. Most of the traditional systems are found to be effective in the treatment of diabetes but they are not preferred over allopathic treatments due to lack of standardisation technique. Central Council of research in Ayurveda and Siddha has given preliminary guidelines for standardising these conventional formulations. For the uniformity of batches in production of herbal formulations it is necessary to develop method of evaluation. Hence, there is the need to search for effective and safe drugs for these ailments [39]. Pharmaceutical research across the world shows that natural products are potential sources of novel molecules for drug development[40].

In the present era, market of all commodities has become global. Health has been of utmost importance since ancient times for the mankind. Market of health-related products has been active and the products are manufactured at different parts of the world and sold all over. Standardization is necessary to make sure the availability of a uniform product in all parts of the world. Standardization assures a consistently stronger product with guaranteed constituents[41].

WHO collaborates and assists health ministries in establishing mechanisms for the introduction of traditional plant medicines into primary healthcare programs, in assessing safety and efficacy, in ensuring adequate supplies, and in the quality control of raw and processed materials. Herbal formulation in general can be standardized schematically as to formulate the medicament using raw materials collected from different localities and a comparative chemical efficacy of different batches of formulation is to be observed. A preparation with better clinical efficacy has to be selected. The routine physical, chemical, and pharmacological parameters are to be checked for all the batches to select the final finished product and to validate the whole manufacturing process[42].

ANTIDIABETIC PLANTSIN TRADITIONAL MEDICINES

The NAPRALERT database lists over 1200 species of plants representing 725 genera in 183 families extending from the marine algae and fungi with antidiabetic activity. Over half of these have been used ethnopharmacologically in traditional medicine as antidiabetics, and some 50% of these traditional remedies have been studied experimentally[43].

In India, plants like *Abroma augusta*(L.) L.f., *Abutilum indicum* (L.) Sw., *Aconitum palmatum* D. Don., *Aloe barbadensis* Mill, *Asparagus racemosus* Wild., *Berberis aristata* DC., *Calamus rotang* (L.), *Cannabis sativa* (L.), *Catharanthus roseus* (L.) G. Don., *Cinnamomum tamala* (Buch.-Ham.) Nees, *Coccinea grandis*(L.)Voigt.,*Costus speciosus* (Koening) Sm., *Ficus racemosa* (L.), *Ipomoea batatus* (L.) Lamk.,*Momordica chrantia* (L.), *Nardostachys jatamansi* DC., *Picrorhiza kurrooa* Royle ex Benth., *Quercus lanata* Sm., *Swertia chirayita* (Roxb. ex Flem.) Karst.,*Syzygium cuminii* (L.) Skeels, *Trigonella foenum-graecum* (L.), *Urtica dioica* (L.), *Zingiber officinale* Rosc., *Allium cepa* L., *Allium sativum* L., *Aloe vera* (L.) Burm.f.,*Cajanus cajan* (L.)Millsp.,*Coccinia indica* Wight & Arn., *Caesalpinia bonducella* (L.) Roxb., *Ficus bengalensis* L., *Gymnema sylvestre* R. Br., *Momordica charantia* L., *Ocimum sanctum* L., *Pterocarpus marsupium* Roxb., *Tinospora cordifolia* (Wild.) Hook.f. & Thomson, etc., are most commonly used species in traditional medicine as antidiabetic agents [44, 45].

SCIENTIFICALLY VALIDATED ANTIDIABETIC PLANTS

Among the traditional plants used for diabetes, only a small number of these have received scientific and medical evaluation as follows:

***Aegle marmelos* (L.)Correa ex Roxb. (Family: Rutaceae)**

The leaf extract of *Aegle marmelose* (L.) Corea ex Roxb.was found to be as effective as insulin in the restoration of blood glucose and body weight to normal levels. *A.marmelose* can be used as potentiel hypoglycaemic agent[46].Alloxan induced diabetic animals were given insulin injections while another group received *A. marmelose* leaf extract. The blood glucose levels in the extract treated animals were near to that of controls. Blood urea and serum cholesterol increased significantly in alloxan diabetic rats. Treatment with the leaf extract decreased the blood urea and serum cholesterol compared to controls. A similar effect was seen with insulin treatment. Consequently, the active principle of *A. marmelose* extract had similar hypoglycaemic effect to that of insulin[47].

***Anthemis mobilis* Linn.(Family: Compositae)**

Anthemis mobilis Linn.is a 3 hydroxy-3-methylglutaric acid (HMG) containing flavonoids, glucoside hamaemeloside which has been shown to have *in vivo* hypoglycaemic activity comparable to that of free HMG[48].In humans, this plant is among twelve herbs most commonly used to treat diabetes in Saudi Arabia[50]. In alloxan-treated rabbits and mice, it has been shown that the aqueous extract of the plant produced an initial hyperglycaemia which was followed by hypoglycaemia[49].

***Artemisia pallens* Wall.ex DC. (Family: Compositae)**

Oral administration of an extract of the aerial parts of *Artemisia pallens Wall*. produced a dose-dependent reduction in glycaemia in alloxan induced diabetic rats. In fasted healthy rats, the extract caused moderate hypoglycaemia at a higher dose. Only the methanol extract was active whereas the water extract was inactive[51].

***Asteracantha longifolia* Nees (Family: Acanthaceae)**

Oral administration of the extract of *Asteracantha longifolia* Nees. (20 g/kg of starting material) can significantly improve glucose tolerance in healthy human subjects and diabetic patients[52].

***Azadirachta indica* A. Juss. (Family: Meliaceae)**

An *Azadirachta indica* leaf extract was found to have no action on peripheral utilization of glucose or on hepaticglycogen in healthy and streptozotocin-induced diabetic rabbits. The reduction in peripheral utilization of glucose and glycogenolytic effect due to epinephrine was blocked by the *A. indica* leaf extract, almost completely in diabetic rabbits and to a certain extent in healthy animals[53].More recently, it has been demonstrated that in an *in vitro* rat pancreas preparation, *A. indica* leaf extract significantly blocked the inhibitory effect of serotonin on insulin secretion mediated by glucose[54 55].

***Biophytum sensitivum* (L.) DC. (Family: Oxalidaceae)**

Sub diabetic, mildly diabetic and severely diabetic male rabbits were induced by alloxan. Assessment of the activity of the extract from *Biophytum sensitivum* DC leaves was made by measuring the fall in fasting plasma glucose level and improvement in the OGTT, following single dose and prolonged administrations. Following a single dose administration, there was fall in 1 and 2.5 h glucose values by 26 % and 27 %, respectively in the sub diabetic rabbits, and by 37 % and 38 % in the mildly diabetic rabbits. Improved OGTT response was also shown in the sub diabetic as well as in the mildly diabetic rabbits. More significant improvements occurred following one week of the above treatment. It was concluded that the plant composites had a hypoglycaemic effect probably due to pancreatic β-cell stimulating action[56].

***Bombax ceiba* L. (Family: Bombacaceae)**

In Sprague-Dawley rats, a dose of 500 mg/kg of Shamimin (a C-flavonol glucoside from *Bombax ceiba*) produced a significant reduction in glycaemia[57].

***Brassica juncea* (L.)Czern. (Family: Brassicaceae),**

This study demonstrated the effect of *Brassica juncea* Coss (Leaf Mustard) on carbohydrate metabolism in rats. It showed significant hypoglycaemic action. There was increased activity of glycogen synthetase, and a decrease in glycogenolysis and gluconeogenesis demonstrated by a decreased activity of glycogen phosphorylase and gluconeogenic enzymes[58].

***Cajanus cajan*(L.)Millsp. (Family: Fabaceae),**

Single doses of unroasted seeds of *Cajanus cajan* Millsp. *(Pigeon pea)* (60 % and 80 %) caused a significant reduction in serum glucose levels 1-3 h after oral administration to healthy and alloxan induced mice. In contrast, roasted seeds caused a significant increase in serum glucose levels during the 3 h experimental period. The

authors concluded that roasting of seeds at high temperature for 30 min resulted in the total loss of the hypoglycaemic component but not the hyperglycaemic principle present in the seeds. [59]

***Caesalpinia bonducella* (L.)Roxb.(Family: Cesalpinaceae)**

In healthy rats, both the aqueous and 50 % ethanolic extracts of *Caesalpinia bonducella* seeds exhibitedhypoglycaemic activity as early as 4 h after administration at a lower dose of 100 mg/kg. The hypoglycaemia produced by the aqueous extract was of prolonged duration as compared to the ethanolic extract. In diabetic rats, both extracts produced marked antihyperglycaemic effects from day 5 onwards[60].

***Catharanthus roseus* (L.) G. Don. (Family: Apocynaceae)**

Oral administration of the aqueous fraction of an alcoholic extract of leaves of *Catharanthus roseus* leads to marked lowering of glycaemia in normal and streptozotocin-induced diabetic rats. This effect was comparable with that of tolbutamide[61]. Three suspension cultures of *C. roseus* were obtained from three different cell lines (CWS, CW-A and CWS-G). In the production medium, the first cell line produced 0.1 % ajmalicine and the cell extract caused a 71 % decrease in glycaemia in diabetic rats. In contrast, in the growth medium, CWS produced trace amounts of alkaloids and the extract did not show any anti-diabetic activity. The CWA cell line synthesized 0.036 % ajmalicine. The extract had no hypoglycaemic effect while in the growth medium the cells produced trace amounts of alkaloids and the extract induced an 86 % decrease in blood sugar. The CWS-G cell line did not produce significant levels of alkaloids and had no hypoglycaemic effect[62].

Oral administration of the aqueous fraction of an alcoholic extract of leaves of *Vinca rosea* L. *Catharanthus roseus* leads to marked lowering of glycaemia in normal and streptozotocin-induced diabetic rats. This effect was comparable with that of tolbutamide[64].

***Citrullus colocynthis* (L.)Schrad. (Family: Cucurbitaceae)**

This study showed the insulinotropic effect of *Citrullus colocynthis* fruits. Different extracts were obtained from the seeds of this plant: RN II (crude extract), RN VI (aqueous alcoholic extract), RN X (purified extract) and RN XVII (beta-pyrazol-1-ylalanine, the major free amino acid derivative present in the seeds). All tested extracts, when perfused for 20 min at 0.1 mg/ml, immediately and significantly induced insulin secretion *in vitro* in the isolated rat pancreas and isolated rat islets in the presence of 8.3 mM glucose[63].

***Coriandrum sativum* L. (Family: Apiaceae)**

Seeds of *Coriandrum sativum* (Coriander), when supplied in the diet (6.25 % by weight) and infusion (1 g/400 ml) in place of drinking, reduced the hyperglycaemia during the development of streptozotocin-induced diabetes in mice[65].

***Cuminum cyminum* L. (Family: Apiaceae)**

The antihyperglycaemic effect *Cuminum cyminum* was studied in healthy rabbits subjected to weekly subcutaneous glucose tolerance tests after gastric administration of water, tolbutamide or a traditional preparation of the plant. The results showed that the *C. Cyminum* significantly decreased the area under glucose tolerance curve and the hyperglycaemic peak[66].

***Daucus carota* L. (Family: Apiaceae)**

Male Swiss mice were orally loaded with glucose after the extracts of *Daucus carota* L.had been given by oralloading. The extract of *Daucus carota* L.was prepared by boilingthe dried material with water or macerating it with 80 % ethanol. It was shown that the extract improved the glucose tolerance[67].

***Eugenia jambolana* L. (Family: Myrtaceae)**

The hypoglycaemic activity of the extract of jamun pulp from the fruit of *Eugenia jambolana* Lam. (Gambol) =*Syzigium cumini* Skeels (Jamum) was seen after 30 min, while the seeds of the same fruit required 24 h to produce the same effect. These results were confirmed in streptozotocin-induced diabetic animals. The oral administration of the extract resulted in the enhancement of insulinemia in normo glycaemic and diabetic rats. The incubation of isolated pancreatic islet cells of normal and diabetic animals with this plant extracts resulted in increased insulin secretion. This extract inhibited insulinase activity from liver and kidney[68].

***Ipomoea batatas* (L.) Lam. (Family: Convolvulaceae)**

Oral administration of *Ipomea batatas*produced a reduction in hyperinsulinemia in Zucker fatty rats by 23%, 26%, 60% and 50%, 3, 4, 6 and 8 weeks after treatment respectively. These results were comparable to that of troglitazone, an insulin sensitizer. After 7 weeks of treatment, increase in glycaemia after glucose load was inhibited by the administration of *I. batatas*. Moreover, it normalized lipid metabolism and produced a regranulation of pancreatic islet B-cells after 8 weeks of treatment[69].

***Lantana camara* L. (Family: Verbenaceae)**

Once daily administration of the juice of *Lantana camara* leaves given at different dose levels (60, 300, 600 and 1500 mg/kg/day) for 14 days in rats resulted in alterations in various haemato- and biochemical parameters. A strong hypoglycaemic effect was seen with 1500 mg only[70].

***Mangifera indica* L. (Family: Anacardiaceae)**

The antidiabetic activity of *Mangifera indica* was seen when an extract of the leaves of *M. indica* was given to rats 60 min before the glucose. The hypoglycaemic effect of the aqueous extract was compared with that of an oral dose of chlorpropamide (200 mg/kg). The hypoglycaemic action of this plant may be due to a reduction in the intestinal absorption of glucose[71].

***Musa sapientum* L. (Family: Musaceae)**

Musa sapientum Kuntze (Banana) significantly decreased the hyperglycaemic peak and the area under the glucose tolerance curve in hyperglycaemic rabbits.[72] Oral administration of 1.5, 0.2 and 0.25 g/kg body weight of the chloroform extract of the flowers of *M. sapientum* during a 30-day period caused a decrease in blood glucose and glycosylated haemoglobin levels and an increase in total haemoglobin. The extract showed antihyperglycaemic action and an antioxidant effect. Banana flower was more effective than glibenclamide[73].

***Morus alba*L.(Family: Moraceae)**

The hypoglycaemic effects of hot water extracts (WE) from*Morus alba*L. was tested in fasted and nonfasted streptozotocin-induced diabetic mice at a single dose of200 mg/kg (i.p.). The WE of *M. alba*exhibited the most potent hypoglycaemic effects. The most potent fractions of *M. alba*and cortex Mori Radicis were ethanol-insoluble extracts (A2). These A2 fractions produced a decrease in glycaemia of 24.6 ± 6.0 % and 60.5 ± 9.1% in nonfasted streptozotocin-mice, and 81.4 ± 7.9 % and 77.3 ± 5.8 in fasted streptozotocin-mice, respectively[74].

***Nelumbo nucifera* Gaertn. (Family:Nymphaeaceae)**

A methanol extract of *Nelumbo nucifera* Gaerth (East Indian Lotus) obtained by soxhlet extraction from finelypulverized rhizomes was used. The extract (300 mg/kg and 600 mg/kg, orally) caused a decrease in glycaemia instreptozotocin-induced diabetic rats by 53 % and 55 %, respectively at the end of 12 h[75].Oral administration of the ethanolic extract of rhizomes of *N. nucifera* markedly reduced the glycaemia of healthy, glucose-fedhyperglycaemic and streptozotocin-induced diabetic rats compared to control. The extract improved glucosetolerance and potentiated the action of exogenously injected insulin in normal rats. The extract exhibited activity of 73% and 67 % of that of tolbutamide in normal and diabetic rats, respectively[76].

***Phyllanthus amarus* Schumach. & Thonn. (Family: Euphorbiaceae)**

Ten human subjects were treated with a preparation of the whole plant, *Phyllanthus amarus* Shum. &Thon.,for ten days (9 subjects were hypertensive and four were diabetic).Glycaemia was reduced in the treated group[77].

***Pterocarpus marsupium* Roxb. (Family: Fabaceae)**

The hypoglycaemic effect was investigated after i. p. administration of marsupsin, pterosupin and pterostilbene (3 important phenolic constituents of heartwood of *Pterocarpus marsupium* . Marsupsin and pterostilbene significantly lowered the glycaemia of diabetic rats, and the effect was comparable to that of 1, 1-dimethylbiguanide (metformin)[78].

***Punica granatum* L. (Family:Punicaceae)**

Oral administration of the aqueous-ethanolic (50%, v/v) extract of the flowers of *Punica gratum* L. (Gulnarfarsi)produced a significant decrease in glycaemia in normoglycaemic, glucose-fed hyperglycaemic and alloxaninduced diabetic rats. The maximum effect was found at 400 mg/kg[79].

Psacalium peltatum* Cass.(Family: Asteraceae), *Psacalium decompositum* Cass.*(Family:Asteraceae),

Psacalium peltatum Cass. significantly decreased the area under glucose tolerance curve in healthy rabbits subjected weekly to oral glucose tolerance tests compared to control (27.9 %), or tolbutamide-treated (14.3 %) animals[80] .Moreover, traditional preparation of *P. peltatum* had a hypoglycaemic effect similar to that of tolbutamide in healthy and mildly diabetic rabbits but had no effect in severely diabetic rabbits. These results suggested that some pancreatic function or the presence of insulin is required for the hypoglycaemic activity of these plants[81].

The root decoction of *Psacalium decompositum* reduced the glycaemia of normal mice after i. p. administration and lowered the hyperglycaemic peak (17.1 %) in rabbits with temporal hyperglycaemia[82].The water extract obtained from the root of *P. decompositum* significantly lowered blood glucose in a dose-dependent manner in healthy mice after intra peritoneal administration. Moreover, the precipitate obtained from the water extract macerated with methanol produced a decrease in glycaemia in normoglycaemic mice and in mildly diabetic mice. Two polysaccharides components isolated from this precipitate have hypoglycaemic effects in healthy mice[83].

***Salacia oblonga* Wall. (Family: Celastaceae)**

From the petroleum ether extract of the root bark of *Salacia oblonga* Wall., two biologically active fractions have been isolated. The chloroform eluted fraction of the petroleum ether extract and a fluorescent compound separated from it by thin layer chromatography demonstrated about 60 % and 76 % of the hypoglycaemic potency of an equal dose of tolbutamide (250 mg/kg) in albino rats[84].

***Salacia reticulata* Wight. (Family: Celastaceae)**

Diabetic rats were given aqueous extract of *Salacia reticulata Wight* orally and the plasma glucose concentration was determined at regular intervals. An hypoglycaemic effect was obtained at all doses tested (0.5 g/kg, 1.0 g/kg and 5.0 g/kg). The maximum percentage decrease in plasma glucose was observed between 1-5 h following the administration of the extract [85]. A potent natural alpha-glucosidase inhibitor called kotalanol was isolated and found to show more potent inhibitory activity against sucrase than salacinol and acarbose[86].

***Swertia chirayita* (Roxb. ex Fleming) H. Karst. (Family:Gentianaceae)**

A xanthone was isolated from the hexane fraction *of Swertia chirayita* Bush-Ham.and identified as 1,8-dihydroxy-3,5-dimethoxyxanthone (swerchirin). It has a very significant blood sugar lowering effect in fasted, fed, glucose loaded, and tolbutamide pre-treated albino rats. The ED_{50} for 40 % glycaemia lowering in CF male albino rats is 23.1 mg/kg when orally administered[87]. The effect of swerchirin isolated from hexane fraction of *S. chirayita* on blood sugar levels of healthy and streptozotocin-treated rats was studied. Swerchirin (50 mg/kg, p.o.) suspended in gum acacia was fed through cannula to healthy and diabetic rats. Blood glucose levels measured at 0, 1, 3 and 7 h after after treatment showed a very significant glucose lowering effect of this plant in healthy and mildly diabetic rats[88].

***Sida cordifolia* L. (Family: Malvaceae)**

Sida cordifolia extracts of the aerial and root parts showed hypoglycaemic activity. Moreover, the methanol extract of root was found to possess significant hypoglycaemic activity[89].

***Tinospora cordifolia* (Willd.) Hook.f. & Thomson (Family: Menispermaceae)**

Oral administration of an aqueous extract of *Tinospora cordifolia* roots produced a significant decrease inglycaemia and brain lipids in alloxan-induced diabetic rats[90].

ANTIDIABETIC PLANTS IN CLINICAL TRIALS

Allium cepa L., *Clerodendron phlomoides* Linn.,*Cinnamomum tamala* (Buch.-Ham.) T. Nees & Eberm.,*Coccinia indica* Wight & Arn., *Enicostemma littorale*Blume, *Ficus bengalensis* L., *Momordica charantia* L., *Pterocarpus marsupium* Roxb., *Cyamopsis tetragonolobus*(L.) Taub., *Cephalandra indica* Naud.,*Casearia esculenta* Roxb., *Cannabis indica* (Lam.) E.Small & Cronq., *and Syzygium cumini* L. when subjected to clinical trials, showed promising hypoglycaemic effects [91,92]. *Cecropia obtusifolia* Bertol.And*Marrubium vulgare* L. produced beneficial effects on carbohydrate and lipid metabolisms when it was administered as an adjunct on patients with type 2 diabetes and reduced the blood glucose levels [93]. *Asteracantha longifolia* Nees was reported to improve glucose tolerance in healthy human subjects and diabetic patients.Significant reduction in glycaemia was observed when *Panax quinquefolius L* was taken 40 min before glucose load in non-diabetic subjects and the same result was seen in diabetic subjects. *Gymnema Sylvestre* R. Br.treated patients showed a significant reduction in blood glucose, glycosylated haemoglobin and glycosylated plasma proteins. Intake of *Opuntia streptacantha* Lem.by the type II group was followed by a significant reduction in serum glucose and insulin concentration reaching 40.8 mg/dL and 7.8 μU/mL less than basal values at 180 min. Acute hypoglycaemic effect of no pal was observed in patients with type II diabetes but not in healthy subjects. In 10 human subjects, when treated with a preparation of the whole plant, *Phyllanthus amarus* Shum. & Thon.for ten days, the blood glucose level was reduced. The treatment with *Withania somnifera* Dunal produced a decrease in blood glucose levels that was comparable with effects of an oral hypoglycaemic drug [93].

MARKETED POLYHERBAL PRODUCTS

In Indian market today many polyherbal formulations are available in the form of vati, churna, arka, quath etc. for the cure of diabetes. Some important formulations are given below.

- Madhuhari powder.
- Dianex.
- Madhumeha churna.
- Glucocare.
- Glucolib.
- Diasulin.
- Madhunasini vati.
- Diasulin.
- Diagon tablet.
- Diaveda capsule.
- Diamed.

CONCLUSION

Phyto therapy for diabetes has been followed all over the World successfully. Herbs are used to manage Type 1 and Type II diabetes and their complications. The plants mentioned above have been considered for their possible hypoglycemic activity. Scientific validation of several Indian plant species has proved the efficacy of the botanicals in reducing the blood sugar level. However, there are numerous other plants still await scientific inquiry, which have mentioned in the indigenous systems of medicine for health care all over the world. A large number of plants, screened for their antidiabeiic effect, have yielded certain interesting leads as

mentioned above, but till to date no plant-based drug has reached such an advanced stage of investigation or development as to substitute or reduce the need for the currently-available oral synthetic drugs. However, the interest in herbal drug research continues with an expectation that some day or the other, we would be able to bring a safer and more effective compound with all the desired parameters of a drug that could replace the synthetic medicines.

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