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INTRODUCTION
Diabetes Mellitus is a major health problem; approximately 5% of the world’s population suffers from diabetes. Surveys have suggested that the global prevalence of the disease will increase from 150 m in 2000 to 220 m in 2010 and to 300 m by 2025 (Chakrabarti and Ramanujam, 2002). Diabetes is currently the fourth leading fatal disease in the United States. Diabetes mellitus is a disorder resulting in high blood sugar levels during fasting and soon after a meal (post prandial). The symptoms are excessive urination, urine containing sugar, hunger, thirst, fatigue and weight loss. The disorder is caused due to the resistance to the effects of insulin or an insufficient production of insulin to transport glucose from blood to cells. The disease leads to chronic complications like nephropathy, neuropathy, vascular diseases (cardiac, cerebral and peripheral) and retinopathy. Diabetes affects nearly every body organ, kills more people annually than AIDS and breast cancer combined, and is staggering in terms of both human suffering and financial cost (Shapiro, 2002). The seriousness of the disease, its spread and economic burden has led to celebrating World Diabetes Day every year on 14 November, which is incidentally the birthday of Frederick Banting, who together with Charles Best discovered insulin in 1921.

1. History

Diabetes has been recognized as a disease nearly 2000 years ago. Indian physicians Sushruta and Charaka mentioned the symptoms and treatment as early as the 6th Century BC. Sushruta and Ayurveda treatise called the disease ‘madhumeha’, one of the groups of 20 conditions called pramehas in which the quality of urine is altered. In Chinese medicine, diabetes is characterized by excessive sweet urine and described in terms of ‘chi’. The Ebers Papyrus (1500 BC) contains an antidiabetic prescription of wheat germ and okra suggestive of the use of medicinal plants for treatment. However, the word diabetes was coined by Aretaeus the Cappadocian, 81-138 AD. In Greek, this means to “run through” or to “siphon”. The term Mellitus, which means “honey-like” was included by London Physician Willis in 1675AD. (Raghu Deepa, 2003). The Indian word for diabetes is Madhumeha, “Madhu” meaning sweet/sweetness and “Meha” excessive urination. It has been described in Atharveda and Caraka Samhita. It has been treated for years using Ayurveda.
2. Classification of Diabetes mellitus

WHO classifies the Syndrome of Diabetes as follows:

**Insulin dependent Diabetes Mellitus (IDDM):** This form of diabetes usually, though not always, occurs before the age of 30. It has an abrupt onset with severe symptoms and the patient is dependent on exogenous insulin throughout life. Prevalence of this type of diabetes is less than 10%.

**Non-insulin dependent Diabetes Mellitus (NIDDM):** This form of diabetes is seen in more than 90 per cent of persons with diabetes. It occurs in the adults over the age of 30 and can present no symptoms for several years. Insulin production may be normal or even high.

**Malnutrition-related Diabetes Mellitus (MRDM):** It is a major form of diabetes in an undernourished population with distinctive metabolic features that are similar to those of malnutrition.

**Gestational Diabetes Mellitus (GDM):** This happens during pregnancy. Glucose intolerance disappears after delivery. However, even persons with GDM have an increased risk of diabetes at a later stage.

**Impaired Glucose Tolerance (IGD):** Some people have an intermediate glycemic response after administration of 75 g of oral glucose load. This is an index of higher risk of diabetes especially in obese and those with Diabetic lineage (Raghu Deepa, 2003).

**Secondary Diabetes:** A form of diabetes that is secondary to certain conditions and syndromes such as pancreatic disorders, hormone disturbances, drugs and malnutrition.

Of the above-classified types of Diabetes mellitus, the more prevalent ones include IDDM or Type 1 Diabetes and NIDDM or Type 2 diabetes. Type 1 is prevalent in 10 – 15% of diabetes patients including children, adolescents and young adults. There is loss of insulin-producing islet cells in the pancreas, due to the destruction
by the body’s own immune system. Thus, it has also been classified as an autoimmune disease of the pancreas, leading to decreased insulin secretion. People with Type I diabetes must take insulin injections to control their blood sugar, as the complete absence of circulating insulin in this condition gives rise in a very short period to life threatening diabetic ketoacidosis (Chakrabarti, 2002).

On the other hand, Type 2 diabetes is prevalent in 85 – 90 percent of the total diabetic patients, where insulin resistance and abnormal carbohydrate metabolism are considered to be the causative factors of the disease. Insulin is needed to get blood glucose into the body cells to metabolize glucose within the cells to produce energy and to store a glucose reserve in the liver and the muscle cells. A decrease in the action of insulin on the target organs -- the liver and muscle -- is called insulin resistance. Obesity is a major risk factor for persons with diabetes provoking or maintaining the state of insulin resistance. Even children are no longer immune to Type 2 diabetes. Analysts predict that a major increase in the incidence of the disease will be driven by type 2 diabetes. NIDDM is neither an immune mediated condition nor is it prone to ketoacidosis unlike IDDM (Kathleen, 2002). For NIDDM, diet control is a treatment in itself.

3. Diabetes in India

India has the highest number of persons with diabetes in the world with about 19 million clinically diagnosed people. The disease has hit the urban population hard with no discrimination in age, gender or status. The disease has assumed epidemic proportions as the disease hits 2.4 percent people in rural, 5.9 percent in semi-urban and 12 percent people in urban areas. According to WHO, the figure will reach an alarming 57 million by 2025 AD. To add to the woes, many Indians do not realize that they are victims of the disease and have no awareness, access or sometimes the affordability to have a regular health check up (WHO report, 2001).

Patients discover they have the disease usually accidentally and in advanced stages when they go to a clinic to cure a manifestation or symptom of the disease. The treatment is a life long process, which just about helps in controlling the disease
but not curing it. This puts a huge economic burden on the individual and the nation at large.

Lifestyle, faulty dietary habits, lack of exercise, inheritance and environment are the main contributory factors to diabetes. Of all these, diet and lifestyle have a direct bearing on the onset of disease. Diet management, supported by suitable lifestyles changes, plays a pivotal role in the prevention and control of diabetes. (Raghu Deepa, 2003)

4. Causes of Diabetes
The causes of diabetes mellitus are unclear, however, they seem to have both hereditary and environment factors involved.

i) Genetic Considerations: Research has shown that people who develop diabetes have common genetic markers. IDDM and NIDDM are genetically substantially different, with the former showing more hereditary links. In Type 1 diabetes, the immune system is believed to be triggered by a virus or another microorganism to destroy the cells in the pancreas that produce insulin (Edgren, 2002). HLA-B8 individuals are more susceptible to autoimmune factors (Pizzorno, 1995).

ii) Environmental Factors: These are important in induction of genes responsible for onset of both types of diabetes. Age, obesity, family history, diet, lifestyle and other disorders may be factors for cause of diabetes, especially Type 2 (Edgren, 2002). Stressful life tends to self-indulgence and pampering oneself with tasty foods, hampering health.

5. Symptoms of Diabetes
Symptoms of diabetes can develop suddenly (over days or weeks) or can develop gradually (over several years). Ketoacidosis, a condition due to starvation or uncontrolled diabetes, is common in Type 1 diabetes. Ketones are acid compounds, which form in the blood when the body breaks down fats and proteins. Symptoms include abdominal vomiting, rapid breathing, extreme tiredness and drowsiness. Patients with ketoacidosis also have a sweet breath odour. Left untreated, this condition can lead to coma and death. With Type 2 diabetes, the condition may not
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been for a long time. Early signs are tiredness, extreme thirst and urination. Other symptoms of Type 2 diabetes may include sudden weight loss, slow wound healing, chronic infections of the gums and urinary tract, blurred vision, numbness in the feet and legs (Diabetes, http://www.en.wikipedia.org).

6. Diagnosis of Diabetes

The National Diabetes Data Group of the National Institute of Health, USA recommends the following criteria in diagnosing diabetes:

1. Fasting (overnight): Venous plasma glucose concentration greater than or equal to 140 mg/dl on at least two separate occasions.
2. Following ingestion of 75g of glucose: Venous plasma glucose concentration greater than or equal to 200mg/dl at two hours post injection and at least one other sample during the two hour test. (Pizzorno, 1995)

7. Conventional Medical Treatments

IDDM or Type 1 Diabetes requires insulin. Insulin preparations have been used in the treatment of diabetes since 1922. Since insulin is not absorbed orally, it must be injected. Conventional insulin therapy involves administering crystalline insulin, usually a mixture of rapid-and intermediate-acting insulin, once or twice daily. This method is being replaced by intensified insulin therapy where the insulin is given in increasingly sophisticated and complex regimes. Intensified insulin therapy is implemented through either multiple daily injections or the use of the “insulin pump” to administer a continuous supply of insulin (Amiel, 1993). It is designed to mimic as closely the possible continuous variations in plasma insulin levels produced by healthy pancreas, thereby reducing the chronic complications of diabetes.

Type 2 diabetes or NIDDM is generally controlled with diet therapy. Oral hypoglycemic agents, or where necessary, insulin is used if the control in sugar levels is not maintained by diet therapy alone. The oral hypoglycemic agents commonly used are derivatives of sulfa drugs or Sulfonylurea like Chlorpropamide, Glipizide, Glyburide, Tolazamide and Tolbutamide (Murray,
1995). These appear to stimulate the secretion of additional insulin by the pancreas as well as enhance the sensitivity of body tissues to insulin.

8. Complications of Diabetes

Hyperglycemia leads to the development of numerous complications. The complication could be acute or chronic depending on the blood sugar level control. Monitoring and controlling the degree of hyperglycemia is critical to the prevention of major diabetic complications.

8.1 Acute complications

Diabetics are susceptible to three major acute complications:

1. **Hypoglycemia**: This phenomenon is more common in Type 1 than Type 2 diabetes because of insulin injections as treatment. Daytime hypoglycemia episodes are usually recognized by sweating, tremors, tiredness and hunger. Night time hypoglycemia may manifest as night sweats, unpleasant dreams, or early morning headache.

2. **Diabetic ketoacidosis**: This complication is also more prevalent in Type 1 diabetes. Due to lack of insulin, there is a build up of ketoacids, which in turn can cause numerous metabolic problems and coma. Coma is usually preceded by a day or more of increased urination and thirst as well as marked fatigue, nausea and vomiting (Murray, 1995).

3. **Non-ketogenic Hyperosmolar Syndrome**: This is a true medical emergency with a mortality rate of more than 50 percent. It is usually the result of profound dehydration secondary to the deficient fluid intake or precipitating events such as pneumonia, burns, stroke, surgery, certain drugs such as phenytoin, glucocorticoids, diuretics and diazoxide. The onset of the syndrome may be insidious over weakness, increased urination and thirst, and progressively worse signs of dehydration (Murray, 1995).

8.2 Chronic complications

On a long-term basis, the diabetic’s health is deteriorated by repeated elevations in blood sugar levels. There are two primary mechanism behind the development of
most chronic complications of diabetes: glycosylated proteins and intracellular accumulation of sorbitol. Some of the chronic complications are:

1. **Atherosclerosis:** A non-diabetic has two to three times lower risk of dying of atherosclerosis as the increased glycosylated LDL molecules increase the LDL-cholesterol levels, which in turn increase the risk of heart attacks and strokes.

2. **Diabetic neuropathy:** Diabetic neuropathy is amongst the most frequent complications of diabetes. Loss of peripheral nerve function, tingling sensations, numbness, loss of function, pain and muscle weakness are common traits of the disease. The neuropathy can affect deeper nerves and result in impaired heart function, alternating bouts of diarrhoea and constipation, inability to empty the bladder and impotence. This condition is attributed to intracellular sorbitol accumulation.

3. **Diabetic retinopathy:** This is a serious eye disease that can result in blindness and the lesions are divided into background or simple retinopathy and proliferative or malignant retinopathy.

4. **Diabetic nephropathy:** This is a common complication and a leading cause of death in diabetes. The afferent and efferent arterioles, the renal artery, the glomerulus, peritubular regions show lesions that could lead to edema, hypertension, proteinuria, and complete renal failure.

5. **Diabetic Foot Ulcers:** Ischemia and peripheral neuropathy are the key factors in development of foot ulcers. Gangrenes, however, can be prevented by proper foot care, the avoidance of tobacco, and methods to improve local circulation (Diabetic complications, http://www.wikipedia.org).

### 9. Therapeutic Considerations

Proper and effective treatment of the diabetic patient requires the careful integration of a wide range of therapies.

#### 9.1 Diet

Dietary modifications and treatment is fundamental to the success of treatment of diabetes. Clinical treatments with a primitive diet high in complex carbohydrate
and dietary fibers, and low in fat have shown a superior therapeutic effect over oral hypoglycemic agents and insulin. The high carbohydrate, high plant fiber (HCF) diet has a positive effect on the metabolism, its consequence being reduced post prandial hyperglycemia, a delayed hypoglycemia, increased insulin sensitivity to insulin, reduced cholesterol and triglyceride levels with increased HDL-cholesterol levels and progressive weight reduction. Refined sugars increase hyperglycemia while the water-soluble fibers of carbohydrates, which include hemicellulose, mucilage, gum, and pectin, are capable of slowing down digestion and absorption of carbohydrates. This prevents rapid rises in blood sugar; increases the sensitivity of the tissues to insulin, thereby preventing the excessive secretion of insulin; and improving uptake of glucose by the liver and other tissues, thereby preventing a sustained elevation of blood sugar.

Indian diet is mainly cereal based, providing 70-80 percent energy from carbohydrates. Nutrient quality and density in food grains decreases with poor soil quality, over refinement, extraction, cooking methods, washing and straining resulting in loss of good nutrients like vitamins, fibers, fat and proteins. The benefit of whole grains and cereals came to light during both the World Wars, when the milling of grains were banned due to their shortage. The death rate fell by 34 percent and the incidence of cancer, diabetes, high blood pressure, heart and kidney diseases dropped considerably (Raghu Deepa, 2003).

On a diet rich in carbohydrates, in excess at a time within 5-10 minutes, flooding of blood with glucose begins. The glucose enters through the gut and the liver. This must be responded by high secretion and action of insulin. About 25 to 40 percent of this glucose goes to the liver and intestine and 20 – 25 percent is taken up by the brain and blood cells (brain uses energy derived from glucose) for which insulin aid is not required. Another 15-20 percent glucose is taken up by the skeletal muscles which is very much insulin dependent. Short-term infusion of high glucose in blood through refined carbohydrate sources, for example, refined flour (Maida) and potato, coupled with lack of physical activity, increases the burden on insulin. Both secretion and action of insulin has to increase abruptly and abnormally to maintain glucose within a narrow range. In order to maintain homeostasis, the body has to maintain glucose within a range of around 5mM to
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help itself against hypoglycemia during periods of fasting and against excessively high levels (hyperglycemia) following the ingestion of high carbohydrate diet. Rising glucose is directed to the muscles and liver and as a result blood sugar plummets or drops, sometimes going below the minimum baseline. The sudden and dramatic decline in blood sugar can lead to more hunger after consumption of a meal and can contribute to overeating and obesity. Overworking the system over a period of time disrupts the functioning of all the parts involved and the system eventually breaks down.

Normally, the body maintains blood sugar levels by sending the excess to the muscle and the liver. The muscle utilizes the energy first from the glucose and nearly half of it is oxidized for energy during muscle activity. In the liver some glucose is stored as glycogen and whenever the body is short of glucose, glycogen is reconverted to glucose to maintain the blood sugar level. The increase in glucose over and above the storage capacity of the liver translates to triglycerides. Here, the insulin plays a very pivotal role. The pancreas releases insulin to balance the sugar levels. The homeostatic system is disrupted in those suffering from diabetes either due to non-production or non-action of insulin. Further, an increase in triglycerides automatically triggers a drop in HDL, the good cholesterol. Thus, over consumption of calories without expenditure is stored as fat leading to central obesity. In obesity, even though insulin is adequately secreted, it is ineffective because the receptor site is blocked by fat on the outer surface of the cell (Raghu Deepa, 2003).

Malnourishment at the fetal stage and infancy signals the gene to adapt to these conditions. The child thus is preconditioned to grow up with less food. In the later stages of life, if and when the conditions become better, and consumption increases, the body cannot cope with the sudden change. This leads to obesity. (Thrifty Gene Hypothesis by Barker, 1986). Wealth and health studies have revealed that increase in wealth does not necessarily mean increase in health. More often than not the neo rich tend towards junk foods, soft drinks, alcohol, ice creams and the like instead of health promoting foods such as green leafy vegetables, fruits, whole grains etc.
A combination of two starch-rich foods such as Roti or Rice and Potato curry in India is nutritionally imbalanced. Eating the same with Dal or any other vegetable will be a more balanced approach.

9.2 Nutritional Supplements
The treatment of diabetes requires supplementation as diabetics have an increased need for many nutrients. The supplements help control blood sugar level as well as ameliorate or help prevent many of the major complications of the disease.

1. Chromium: Chromium is a key constituent of the glucose tolerance factor. It works closely with insulin in facilitating the uptake of glucose into cells. Without chromium, insulin's action is retarded and glucose levels are elevated (Mooradian, 1994). The effect of chromium in lowering fasting glucose levels and increased glucose tolerance appears to be due to the increased insulin sensitivity.

2. Vitamin C: Vitamin C is essential for proper immune function; connective tissue formation; manufacture of nerve transmitting compounds and neurohormones; absorption and utilization of various other nutritional factors. The transport of Vitamin C is facilitated into the cells by insulin and hence many diabetics lack intracellular Vitamin C (Cunningham, 1991). Vitamin C at a high dose has shown to reduce the accumulation of sorbitol in the erythrocytes of diabetics and also inhibit the glycosylation of proteins (Davie, 1992).

3. Niacin and Niacinamide: Supplementing the diet of diabetics with niacin has been shown to exert many favourable effects, the foremost being preventing the development of diabetes in experimental animals, mainly Type 1 diabetes (Pocoit, 1993). The mechanism of action appears to be inhibition of macrophage- and interleukin 1- mediated beta cell damage, inhibition of nitric oxide production, along with niacinamides anti-oxidant role (Anderson, 1994).

4. Biotin: Biotin supplementation has been shown to enhance insulin sensitivity and increase the activity of the enzyme glucokinase, which in diabetics is considerably low. It significantly reduces fasting blood sugar levels and improved blood glucose control in Type 1 diabetes (Reddi, 1988).
5. **Vitamin B6**: Vitamin B6 supplementation appears to offer significant protection against the development of diabetic neuropathy by inhibition of glycosylation of proteins (Solomon, 1989).

6. **Vitamin B12**: A Vitamin B12 deficiency, characteristic in diabetics is characterized by numbness of the feet, pins and needles sensations, or a burning feeling, which are typical symptoms of diabetic neuropathy. The supplementation corrects the deficiency (Bhatt, 1983).

7. **Vitamin E**: Intake of Vitamin E is shown to improve insulin action as well as correct many metabolic problems because of its anti-oxidant property (Paolisso, 1993).

8. **Magnesium**: A cofactor in many enzymatic reactions involved in energy metabolism and glucose transport mechanism (Raghu Deepa, 2003), its supplementation could prevent complications like retinopathy and heart diseases (White, 1993).

9. **Potassium**: Potassium has been observed to improve sensitivity, responsiveness and secretion. It also seems to enable reduce the risk of heart diseases, atherosclerosis and cancer (Kharo, 1984).

10. **Manganese**: The supplementation of manganese provides better enzymes functions of systems involved in blood sugar control, energy metabolism, and thyroid hormone function, as its amount is less in diabetics and its function as a co-factor reduced (Pizzorno, 1995).

11. **Zinc**: Zinc is involved in the synthesis, secretion and utilization of insulin. It has a protective effect against beta-cell destruction. Zinc supplementation has shown to improve insulin levels in diabetics (Mooradian, 1987).

12. **Flavonoids**: Flavonoids may be useful in diabetes as they seem to promote insulin secretion and are observed to be potent inhibitors of sorbitol accumulation. They are also known to increase intracellular Vitamin C levels, support immune system, thereby, helping the diabetics.

13. **Essential Fatty Acids**: EFA help in preventing the formation of diabetic complications like atherosclerosis and neuropathy. Diabetics have been reported to show an erratic essential fatty acid metabolism, which in turn is due to intracellular deficiencies of Vitamin C, magnesium, Vitamin B6 and Zinc. Omega-3-fatty acids supplementation plays a significant role in lowering total cholesterol, LDL-cholesterol and total triglycerides in diabetics (Axelrod, 1994).
14. **Carnitine**: A significant reduction in total serum lipid and an increase in HDL-cholesterol levels have been observed in diabetics given carnitine supplementation (Westervel, 1993).

15. **Inositol**: Inositol supplementation has helped treatment of diabetic neuropathy since it helps reestablish normal myoinositol levels in the deficient neurons, in experimental animals (Leslie, 1993).

### 9.3 Exercise

Exercise improves many parameters in both IDDM and NIDDM by enhancing insulin sensitivity with a consequent diminishing need of exogenous insulin, improved glucose tolerance, reduced total serum cholesterol and triglycerides with increased HDL levels resulting in a more anti-atherogenic state and in obese diabetics improved weight loss (Pizzorno and Murray, 1995).

### 10. Alternative medicines/ Nutraceutical Therapy

Many ethnic groups with a high prevalence of diabetes (Native Americans, Hispanics and Asians) come from cultures with a long history of traditional ethnomedicinal use. In developing countries like India, traditional medicine, which is mainly plant-based, is commonly used along with conventional medicine.

Ayurveda, which is believed to be between 3000 – 5000 years old, originated in India’s Vedic period. “Ayurveda” comes from the words Ayur meaning life and Veda meaning knowledge, which together translate into “the Science of Life”. The Indian word for diabetes is “Madhumeha”, madhu for sweetness and meha for excessive urination. Madhumeha, its complications and treatment have been described in the Siddha system, a variant of Ayurveda, originating in South India. Ethnobotanical studies of traditional herb remedies used for diabetes around the world have identified more than 1,00 species of plants with hypoglycemic activity. The Indian pharmacopoeia has a list of herbal plants used for treatment of diabetes. There are about 20 antidiabetic plants most widely used around the world of which 85 percent plants are listed in India either in Ayurvedic formulations or in Siddha system (Shanmugasundaram, 1981). Hundreds of products are marketed as “Natural” agents for lowering blood sugar and decreasing long-term complications.
(Shapiro, 2002) and these are typically combination products. These products are also known as “Botanicals” or “Botanical Medicines” (Pizzorno, 1995).

Diabetes, therefore, as cited in history, was being treated with plant medicines even before the advent of insulin. In 1980, the World Health Organization urged researchers to examine whether traditional medicines produced any beneficial clinical results. This urge stemmed a lot of productive work on various plants and some of them are now commonly used for their hypoglycemic action.

10.1 Herbs commonly used to treat diabetes
In the recent years, apart from dietary fibers and omega-3 fatty acids, a variety of plant sources with several phytochemicals are found to help in disease prevention and health promotion. About 500 such health beneficial phytochemicals have been identified. These include phenolic compounds, flavonoids, isoflavonoids, coumarins, lignans, indoles, anthocyanins, isothiocyanides, diterpenes, and phytoestrogens (Raghu Deepa, 2003).

In the treatment of diabetes and nutrition management, some plants are said to have beneficial and preventive attributes, such as:

- **Tea:** Tea contains abundant polyphenolics and antioxidant properties and hence found to be capable of inhibiting glucose transport, which aids in diabetes control.

- **Momordica charantia:** Commonly known as bitter gourd or Karela, it has been used extensively as a remedy for diabetes. The blood sugar lowering action of the fresh juice or extract of the unripe fruit has been clearly established in human clinical trials as well as experimental models (Srivastava, 1993).

- **Trigonella foenum graecum:** This is commonly known as Fenugreek or methi. Fenugreek seeds have demonstrated significant anti-diabetic effects in experimental and clinical studies. The active principle is in the defatted portion of the seed and contains the alkaloid trigonelline, nicotinic acid and coumarins (Sharma, 1990).
Gymnema sylvestre: Commonly known as Gurmar, it is known to possess antidiabetic properties. The leaves of this plant have been used for more than 2,500 years to treat diabetes. The leaves destroy the taste of sweetness when chewed and also enhance glucose control (Shanmugasundaram, 1990).

Panax ginseng: The herb, commonly known as ginseng, has been shown to potentially lower glucose levels. The principle components believed to be responsible for inducing the hypoglycemic activity are triterpenoid saponins glycosides, commonly referred to as ginsenosides and panaxosides (Konno, 1985).

Ocimum sanctum/album: This herb, commonly known as Holi Basil or Tulsi has been observed to decrease fasting and post prandial blood and urine glucose levels (Yeh, 2003).

Coccinia indica: This plant, commonly known as ivy gourd or kanduri, shows hypoglycemic activity, which is attributed to the presence of the active principles b-sitosterol, cucurbitacin, and B-glycosides (Shanmugasundaram, 1985).

Pterocarpus marsupium: Commonly known as False teak and Bijasal, this tree has tannins, flavonoids and phenolic constituents such as marsupin, pterosotiilene, and epicatechin, which have shown hypoglycemic activity in experimental rats (Chakravarty, 1980).

Gingko biloba: This plant commonly, known as Gingko, has been shown to improve the blood flow to peripheral tissues like the arms, legs, fingers and toes, which is an important effect as peripheral vascular insufficiency is very common in diabetes. The active principle is ginkoflavoglycosides (Pizzorno, 1995).

Azadirachta indica: This tree, commonly known as Neem, known to have bitter principles has shown to have hypoglycemic effects on both experimental animals and in human studies (Shapiro, 2002).

Treatments of diabetes with conventional oral hypoglycemic agents, which are derivatives of sulfonylurea, have a limited effect. There are evidences indicating the long-term harmful side effects, the major side effects being hypoglycemia, allergic skin reactions, headache, fatigue, indigestion, nausea and vomiting and
liver damage. In comparison the botanical medicines are known to have no or fewer side effects making their studies imperative for the treatment of diabetes. However, this is a misconception and studies need to verify the toxicology of the various plant extracts or materials used in the herbal drugs before its use as a therapeutic drug.

In view of the increasing inclination and acceptance of herbal drugs and products by the people as well as practitioners for the treatment of various ailments, our study involves research on various plants having hypoglycemic activity.

11. Objectives

This preliminary study has been taken up:

- To selectively study three to four plants used as an alternative medicine for treatment of diabetes with the view of ascertaining their hypoglycemic activity. A deliberate selection of one of the plants was such that its hypoglycemic activity was reported and promoted to have a comparative study.
- To check the capability of the selected plants to reduce blood sugar in experimental diabetic rat models.
- To standardize protocol for the micropropagation of the plants having significant hypoglycemic activity with the view of ascertaining means of reducing depletion of source material.
- To evaluate regenerated plants in vitro or callus culture for enhanced anti-diabetic activity.
- To initiate cell suspension studies of the plant exhibiting maximum hypoglycemic activity with the aim of setting up of possible bioreactors for commercial scale-up of the product, and
- To initiate elucidation of the bioactive principle.

12. Plan of Work

Four plants viz. Gymnema sylvestre R.Br., Catharanthus roseus L., Tabernaemontana divaricata and Ocimum basilicum var. Thai Queen were selected for study of their hypoglycemic activity. Gymnema sylvestre was
deliberated by the WHO to have hypoglycemic activity and hence was selected. *Catharanthus roseus* was also reported to be used ethnomedicinally for treatment of diabetes, while the latter two plants were thought to have anti diabetic properties by local people.

Leaves of the plants were collected. Aqueous extracts of the leaves were checked for hypoglycemic activity in alloxan induced diabetic rat models. The leaves were also dried and various extracts including petroleum ether extract, benzene extract, chloroform extract and alcohol extract were prepared from the ground powder using Soxhlet apparatus. These extracts were used for preliminary phytochemical analysis and hypoglycemic activity.

Preliminary phytochemical analysis was carried out using leaf powder of each of the plants and various tests were carried out for presence of alkaloids, flavonoids, saponins and tannins, iridoids and proanthocyanidins. Further elucidation of the extract having hypoglycemic activity for the bioactive principle was done using thin layer chromatography.

Tissue culture studies were initiated in all the plants showing hypoglycemic activity to establish standardized protocols for surface sterilization, explant establishment and regeneration. Various plant growth media and plant growth regulators including auxins and cytokinins were used to initiate cultures. Some of the cultures were checked for presence of hypoglycemic activity.

Cell suspension cultures were established for the plant showing maximum hypoglycemic activity. These cell suspensions were checked for the class of phytochemicals having the anti-diabetic property using thin layer chromatography and UV spectrophotometer. Pilot studies were carried out in a 2 L bioreactor to optimize conditions for enhanced production of the secondary metabolite. The parameters checked for enhanced production of secondary metabolites were temperature, pH, light and plant growth regulators.