Introduction
Diabetes mellitus (DM) is a well known chronic metabolic disorder, in which the body is unable to utilize glucose effectively in spite of excess of blood sugar due to insulin deficiency or impaired release of insulin by the pancreatic β cells. It may also be due to inadequate or defective insulin receptors and the production of inactive insulin or due to destruction of insulin before it can carry out its action (Guven et al., 2002).

The constellation of abnormalities, with one common manifestation—hyperglycemia, from defects in insulin secretion, insulin action or both is called diabetes mellitus. The term diabetes is derived from a Greek word, meaning "going through" or "siphon" and mellitus from the Latin word for 'honey' or sweet.

**Diabetes mellitus - An ancient history**

DM is an ancient disease, whose symptoms were described over 3500 years ago in a compendium of medical diseases acquired in Luxor by the Egyptologist George Ebers in 1872 and given the name the *Papyrus Ebers* (Schneider, 1972). The Roman physician Celsus in 10 AD first described DM as a disease of excess urination and wasting (Herrington, 1995). For more than two thousand years, DM was believed to be a disease of the kidneys and bladder. This view was supported and extended by the studies of Matthew Dobson, who in 1776 evaporated the urine from a diabetic patient and found that the residue contained sugar (Dobson, 1776).
Reports of the disorder can be traced back to the first century AD, when Aretaeus, the Cappadocian described the disorder as a chronic affection characterized by intense thirst and voluminous honey-sweet urine: “the melting down of the flesh and limbs in to urine” (Francis, 1856).

In India, DM has been known for centuries. Ayurveda physician Sushruta has accurately described diabetes around 1000 BC. Ancient records show that physicians like Charak have described diabetes in those days as ‘madhumeha’ or ‘honey urine’ due to the phenomenon of attracting ants near the urine of diabetic patients (Jachak, 2002).

DM is undoubtedly one of the familiar diseases with high morbidity rate and increasing prevalence. It is a disease which was recognized in antiquity and it’s history has been characterized by numerous cycles of discovery, neglect and rediscovery.

**Insulin deficiency – cause of diabetes**

Human insulin is a peptide hormone (molecular weight 5808) secreted from pancreatic β cells and is the key player in regulation of metabolism. It increases the uptake and utilization of glucose in different peripheral tissues by increasing the activity of glucose transporter (GLUT 4) and decreases the release of glucose in to the circulation by increasing the storage of glucose as glycogen in the liver and skeletal muscle. So absence or impaired functions of insulin as seen in diabetes lead to a condition in which there is an excess of extra cellular glucose and intracellular glucose deficiency, a situation that has been called “starvation in
the midst of plenty” (Ganong, 2001). Along with hyperglycemia, abnormalities in serum lipids (Taskinen, 1999) are also seen in DM.

Diabetes is a disorder of carbohydrate, protein, and fat metabolism resulting from an imbalance between insulin availability and insulin need. This is well manifested with many signs and symptoms. The excess blood glucose leads to glycosuria, which in turn results in polyuria. Excessive urine output leads to polydipsia. Weight loss occurs in spite of polyphagia. Ketoacidosis occurs in uncontrolled diabetes. Retinopathy, neuropathy and nephropathy are the long term complications associated with diabetes. Diabetes is also associated with micro vascular and macro vascular complications, which are the major causes of morbidity and mortality in diabetic patients (Carswell et al., 2002; Baynes, 1991).

DM affects people of all age groups and from all walks of life. There are estimated 150 million people world wide suffering from diabetes (Marx, 2002; King et al., 1998), almost five times more than the estimated number ten years ago. Reports from the World Health Organization (WHO reports, 1980) indicate that DM is one of the major killers of the present time and people in South-east Asia and Western Pacific are at most risk. In India, presently there are an estimated 19.4 million people affected by DM and these numbers are expected to increase to 57.2 million by year 2025 (Mohan and Pradeepa, 2002) i.e. one-sixth of the world total.

The possible etiology of diabetes based on the research, reveal that most of the prevalent ideas can be classified under one of the following categories:
heredity, endocrine imbalance, dietary indiscretion, obesity, infections, severe and continued stress (Udawat et al., 2001). Western interference lead to loss in physical activity and changes in food pattern from traditional unprocessed natural ingredients to highly refined, energy dense fatty and sugary fast foods. These two core factors are responsible for the high incidence of diabetes in recent years.

Management of Diabetes

1. Diet and exercise

Dietary therapy and exercise are useful, both in preventing to certain extent and managing DM. Insulin-sensitive tissues contain a population of GLUT 4 vesicles that move in to the cell membrane in response to exercise and are independent of the action of insulin (Ganong, 2001). Results of the Diabetes Prevention Program Research Group indicate that the changes in lifestyle (7% weight loss and 150 minutes of physical activity per week) could reduce the incidence of diabetes by 58% (Knowler et al., 2002).

2. Oral anti-hyperglycemic drugs

Anti-hyperglycemic drugs help diabetics to use their body's insulin more effectively. These medications are effective only for type 2 diabetics, who produce some amount of insulin. Oral anti-hyperglycemic drugs like sulfonylureas exert their actions by increasing pancreatic insulin secretion. Though they have some advantages as they reduce microvascular risk and decrease fasting and post-prandial glucose levels, they do have disadvantages like risk of hypoglycemia, weight gain, and hyperinsulinemia (Inzucchi, 2002). Other drugs like meglitinides
and phenylalanines stimulate pancreatic β-cells secretion like sulfonylureas. But these drugs have a short duration of action and to be taken shortly before meals (Nancy, 2002). α -Glucosidase inhibitors like acarbose and miglitol delay the gastrointestinal absorption of glucose by inhibiting enzyme α-glucosidase, which break down ingested carbohydrates. This leads to a slower and lesser post prandial rise in blood glucose levels. There is no risk of hypoglycemia with α- glucosidase inhibitor mono therapy. However, abdominal discomfort, diarrhea, and troublesome intestinal gas often develop as a result of carbohydrate fermentation in the intestine (Chakrabarti et al., 2002; Nancy, 2002).

3. Insulin therapy

In type1 DM, where there is an absolute deficiency of insulin, insulin therapy forms a major component of treatment. In type 2 DM, insulin release from the pancreas may be altered or sometimes deficient in amount. Therefore insulin therapy also plays a part in management of type 2 DM, especially when diabetes has been present for a long time (Doyle and Egan, 2003).

Limitations of insulin therapy

Insulin is universally accepted as the most effective and desirable treatment for diabetes. However it’s use is limited for the following reasons

- First of all, insulin therapy needs to be continued in diabetic patients and diabetes is not going to be cured even after long term treatment.
• The beneficial effects of insulin do not last more than a few hours after injection and repeated injections are needed to maintain the normal glucose level in diabetic patients.

• Many patients require combination therapy with one or more insulin sensitizers (metformin or thiazolidinediones) to reduce insulin resistance and an insulin secretagogue (sulfonylureas or meglitinides) to restore acute insulin response and to control postprandial blood glucose levels (Nancy, 2002). To achieve these, use of insulin sensitizers should be continued during insulin therapy to reduce insulin resistance and reduce insulin requirements.

• Risk of hypoglycemia may occur during the over dosage of insulin therapy.

These factors are the important reasons for the recent surge in the search for alternative drugs for treatment of diabetes.

4. Role of alternative medicine

The importance of alternative medicine has increased recently and attracted the attention of many researchers all over the world (Al-Rowais, 2002). The scope of alternative medicine is enormous and includes all therapeutic procedures or practices, which lie outside the mainstream of medical practice (Ginsburg, 1990). They may be differentiated into pharmacological category (namely herbal treatments or homeopathy), physical remedies (acupuncture or chiropractics), dietary approaches (macrobiotics or vegetarianisms), or cognitive
treatment (hypnosis). Therefore alternative medicine appears to be heterogenous in treating DM (Ernst, 1994).

**Indigenous herbs**

Herbs play a significant role in modern days, as people today are more concerned about the side effects and the cost effectiveness of drugs and have began to rely more firmly upon herbs, which are comparatively less exploited for their medicinal qualities. Selection of herbs is based on the information given in the traditional texts. Pharmaceutical research conducted over the past three decades shows that natural products are potential sources of novel molecules for drug development.

Many indigenous Indian medicinal plants have been successfully used to treat diabetes and some of them have been tested. The ethnobotanical information reports that, about 800 plants may possess anti-diabetic potential (Aguilara et al., 1998). Several herbs have shown anti-diabetic activity when assessed using presently available experimental techniques (Grover et al., 2002; Ajit Kar et al., 2003; Dahanukar and Thatte, 1997). However, search for new anti-diabetic drugs still continues.

Over the past twenty years, various approaches have been undertaken with objective of restoring normal blood sugar levels with Ayurvedic preparations in diabetic patients. These are not only to control blood glucose but also to reduce the other derangements occurring in diabetes and also to protect the body from various
complications like retinopathy and neuropathy. Research is on progress to look for various herbal preparations as they are effective with minimal side effects.

Tinospora cordifolia as an anti-diabetic herbal drug

*Tinospora cordifolia* (Willd.) Miers ex Hook. F. & Thoms. (TC) belongs to the Menispermaceae family and known as Gulancha in English, Guduchi in Sanskrit, and Giloya in Hindi. It is a large, glabrous, deciduous climbing succulent shrub, commonly found in hedges. It has been known for long in Ayurvedic literature as a tonic, vitalizer and as a remedy for diabetes and other metabolic disorders (Nadkarni, 1954; Chopra et al., 1958). Previous studies showed that plant stem and roots possess anti-hyperglycemic (Gupta et al., 1967; Stanely et al., 2000) properties.

However, scientific studies on anti-diabetic activities of TC and it’s effect on glucose metabolism, other metabolic derangements and it’s mechanism of action in streptozotocin induced diabetic rats have not been reported so far. So with this objective the present study was undertaken to evaluate the anti-diabetic effect of TC in diabetic rats and it’s efficacy was compared with the standard drug insulin.