3. Need for Study

Type 2 diabetes mellitus is a multifactorial disease leading to several complications and as such demands multiple therapeutic approaches. The management of type 2 diabetes is a global problem until now and successful treatment is not yet discovered. There are many oral hypoglycemic agents developed for patients, but no one has ever been reported to have recovered totally from diabetes. Also there is some fear in the minds of many diabetic patients about the side effects of oral hypoglycaemic agents (OHAs), even though there is no scientific basis for it. Thus, there is lot of scope for alternative therapy, either from herbal formulations or indigenous plants, as add on therapy, in the long-term management of type 2 diabetes (Satyanarayana et al, 2006).

Before the advent of insulin and oral hypoglycemic agents, the major form of treatment for diabetes was plant extracts or different folk plant preparations prescribed by traditional practitioners. Nowadays, more than 400 plants are being used in different forms for their hypoglycemic effects in treating diabetes, with tall claims of efficacy by patients and practitioners (Malviya et al 2010). Despite the presence of known antidiabetic medicines in the pharmaceutical market, remedies from medicinal plants are used with varying success by a good number of diabetic patients. Further, it has been estimated that in the U.S., 25% of all prescriptions dispensed from community pharmacies contain plant extracts. Plant drugs and herbal formulations are frequently considered to be less toxic and freer of side effects. According to WHO recommendations, hypoglycemic agents of plant origin used in traditional medicine are important in the management of Diabetes (WHO, 1980).

The attributed antihyperglycemic effect of these plants is due to their ability to restore the function of pancreatic tissues and thereby increase the insulin output. The other mechanism may be by inhibiting the intestinal absorption of glucose or facilitation of metabolites in insulin-dependent pathways. These actions of herbal drugs protect the β-cells and iron out the excursions of blood glucose. Another mechanism by which plant extracts help to contain the diabetic pathology is by acting as antioxidants. Free radicals generated by the metabolic process in the body leads to an oxidative stress, damaging different proteins. The antioxidant properties of herbal drugs may be able to help contain this damage. In short, there is very little biological knowledge on the specific modes of action of these compounds, but most of the plants have been found to contain substances like glycosides, alkaloids, terpenoids and flavonoids, which are frequently quoted as having antidiabetic effects (Loew and Kaszkin, 2002).
Therefore, medicinal plants need to be explored with greater scientific enthusiasm and amalgamated in the modern medicine practice. There is also increasing demand from patients to use natural products with antidiabetic activity; hence, the modern medicine must scientifically assess and incorporate these herbal medicines in their antidiabetic drug armamentarium.

In view of multidimensional activity of plant drugs beneficial to complex disorders like Diabetes, the pharmacological investigation of TSE is designed in the study with array of biomarkers of diabetes, so that maximum aspect of antidiabetic action of TSE is elucidated. Under diabetic state, reactive oxygen species (oxidative stress) are produced, through the glycation reaction in various tissues are reported to play a key role in the development of chronic complications including gastrointestinal dysmotility (Sakurai and Tsuschia., 1988). Glucagon-like peptide (GLP-1) is a gut hormone, secreted in response to absorbed nutrients exerts a broad range of actions such as stimulating insulin release, reducing glucagon release, and plummeting gastric emptying (Willms et al., 1996; Baggio et al., 2004).

Therefore, it was important to investigate and characterize the pharmacological profile of TSE which includes study of the effects on body weight, blood glucose, plasma insulin in STZ induced diabetic rats. It is also proposed to investigate the effects on gastric emptying and small intestinal transit in streptozotocin induced diabetic rats and assesses the effects of chronic administration of TSE on glycaemic control, β-cell secretary functions, advance glycation end product (HbA1c), tumor necrosis factor-α (TNF-α), and pancreatic islet immunohistochemistry.

Adipose tissue is involved in the regulation of both glucose and lipid homeostasis, confer a gatekeeper role on adipocytes in the regulation of lipid metabolism (Guilherme et al., 2008). Type 2 diabetes which is frequently characterized by insulin resistance of peripheral tissues such as liver, muscle, and fat with low adiponectin serum levels might provide a link of this pathological state (Yang et al., 2001). Postprandial hyperglycemia results from abnormal insulin secretion by β-cells in response to a meal, impaired hepatic glucose production, and defective glucose uptake by peripheral insulin-sensitive tissues, particularly the skeletal muscle. Thus, there is a need to be a new focus on suppression of postprandial hyperglycemia in treatment of not only diabetic patients but also individuals with impaired glucose tolerance (Rendell, 2004).
So, the presented work is aimed to explore the effect of TSE on α-glucosidase, serum adiponectin level and lipid profile (HDL, LDL, Cholesterol).

A rise in cytoplasmic free calcium concentration ([Ca$^{2+}$]$_i$), owing to influx through voltage-gated L-type Ca$^{2+}$ channels in the plasma membrane, is a central component of the stimulus-secretion coupling mechanism leading to insulin release by the pancreatic β-cell (Prentki and Matschinsky, 1987).

It arises a need to investigate the effect of TSE on cytoplasmic free Ca$^{2+}$ in pancreatic islet cells and whether the insulin secretagogue action of Tamarind seeds is due to alteration in cytosolic calcium concentration or else.

GLP-1 not only regulates the expression of the insulin gene but also other β-cell genes implicated in insulin secretion (Wang et al., 1997), such as those encoding glucokinase and GLUT-2. Insulin-resistant glucose utilization in peripheral tissues such as muscle and adipose tissues is a universal feature of both insulin-dependent (IDDM) and non-insulin-dependent (NIDDM) diabetes mellitus. In this process, GLUT, Sterol-regulatory-element-binding proteins-1c (SREBP-1c) along with other components plays crucial role. (Charron et al., 1989). GLUT-4 is a member of glucose transporter family that is mainly expressed in skeletal muscle, heart and adipose tissues. It plays a critical role in insulin stimulated glucose transport in these tissues, with glucose uptake occurring when insulin stimulates the translocation of GLUT-4 from the intracellular pool to the plasma membrane (Shepherd and Kahn, 1999). GLUT-2 is the primary glucose transporter isoform in the liver and is pivotal in glucose homeostasis by mediating bidirectional transport of glucose (Bell et al., 1990). SREBP-1c regulates the transcription of genes involved in cholesterol and fatty acid metabolism (Ayala et al., 2009). SREBP-1c expression and nuclear abundance were low in the liver of STZ-induced diabetic rats, and markedly increased after insulin treatment (Shimomura et al., 1999).

Therefore, the present study was designed to investigate the insulin mimetic impact of TSE on the molecular mechanisms of glucose uptake in STZ-rats. With these views, we have studied the effect of TSE on GLUT-2 protein and SREBP-1c mRNA expression in the liver and GLUT-4 protein and mRNA expression in skeletal muscle in STZ model of type 2 diabetes mellitus.
Moreover, it is well known that excessive apoptosis of the pancreatic β-cell is associated with diabetes. So this necessitates the importance of determination of β-cell apoptosis in pancreas.