According to current educated guess, the global human population emerges to be in the midst of an epidemic of diabetes. In spite of the enormous steps that have been made in the perceptive and executive of diabetes, the disease and disease-related problems are increasing spontaneously. Equivalent to this, current investigations and studies in understanding the pathophysiology of the disease process have opened up numerous novel avenues to recognize and expand new therapies to fight the diabetic condition. Simultaneously, phytochemicals bioactive compounds identified from traditional medicinal plants are presenting an exhilarating prospect for the improvement of novel therapeutics. This has step up the world wide effort to exploit and collect those medicinal plants that bear considerable amount of potential phytochemicals presenting multiple beneficial effects in combating with diabetes and diabetes-related difficulties. Therefore, as the disease is progressing alarming rates, there is an urgent need of identifying indigenous natural resources in order to procure them, and study in detail, their potential on different newly identified targets in order to develop them as new therapeutics.

In these regard we have made an attempt to screen and check the potent nature of the plant (*Sapindus saponaria*) belonging to the family Sapindaceae in controlling diabetes.

**Summary of the thesis:**

The leaves of *Sapindus saponaria* (SS) were collected and phytochemical studies were made with different solvents using Petroleum ether, ethanol and chloroform, *n*-Butanol, isopropanol, methanol, acetone and water. The extracts showed different extractive values (8.2, 7.6, 6.7, 5, 6.2, 5.3, 7 and 7.8 respectively) and showed the presences of different bioactive compound (Alkaloids, Saponins, flavonoids, Terpenes, Glycosides steroids, sesquiterpene and Oligoglycosides). Based upon the literature this given us the positive signal which may induce anti-diabetic activity.

In the present study diabetes was induced in male wistar albino rats aged 4 months (body weight 180-200g) by intraperitoneal administration of Streptozotocin (STZ) (dissolved in 0.01M citrate buffer, pH 4.5) at a dose of 50mg/kg.b.w. To these
rats the aqueous leaves extract was given orally to evaluation of SS leaf extract on glucose and body weight of STZ induced diabetic rats. The SS aqueous leaf extract is able to control the glucose level almost equal to control and diabetic (SS; 100 mg/kg bw) treated rats. Similarly SS leaf extract provided promising results in change in the body weight of the treated albino rats control rats are equal to 180 gm (Rajkumar et al., 1991). The induction of diabetes brought the body weight decreased by 28gms, when compared to the control. Control rats exhibited 15.4 mg/dl Hemoglobin (Hb) content in blood sample. Diabetic induction caused the decrease of Hb content to 6.0 mg/dl. Glyoxylated Hb increase almost normal (0.62±0.03) is an indicator of diabetes and this increased is proportional to the fasting blood glucose level. Therefore this measurement gives information about the glycemic index of the diabetic animals. The glycogen levels also increased to normal (3.56±0.34). These blood glucose levels are regulated by either catalytic enzyme of anabolic enzymes. Glycogen synthase values (799.1 μmoles of UDP formed/h/mg protein) and glycogen phosphorylase values (660.3±47.3 μmoles of Pi liberated/h/mg protein) reached almost normal. The activity of hexokinase showed 60% decrease in its activity under diabetes and this activity brought to the normal levels due to the administration of SS treatment. Similarly the enzymes are related to the glucose synthesis like glucose 6 phosphotase and fructose 1, 6 bis phosphotase showed 2 fold increase in the activity under diabetic condition and activities are regulated to normal by the oral administration of SS leaf extract. The results are in agreement with Laakso et al., 1995, Gancedo and Gancedo, 1971, Bopanna et al., 1997.

In this chapter we have done the evaluation studies on lipid metabolism, lipid peroxidation and antioxidant activity of *sapindus saponaria* leaf extract in STZ induced diabetic rats. The results indicated that on 100 mg/b.w of SS oral diet there is decrease in the total cholesterol (103.65 mg/dl) , Triglyceride (18.94 mg/dl) and Free fatty acids(61.12mg/dl) to normal levels when compared with the diabetic control rats due to its anti lipidemic activity of SS aqueous extract. The tissue total liver cholesterol (7.84 mg/g wet tissue) and triglycerides (7.88 mg/g wet tissue) exhibited the same values which are very much equivalent normal. The serum HDL (60), LDL(32) and VLDL(28 mg/dl) respectively. In diabetic control rats the lipid peroxidation (TBARS and HP) levels reached (nearly 5.12 and 19.42) due to the
Summary & Conclusion

oxidative stress caused by ROS such as hydroxyl, superoxide and hydro peroxyl radicals. These levels after SS diet nearly resulted as 2.79 nmoles/ml and 8.88 X 10^{-5} mm/dl which clearly indicated the protection mechanism. To minimize the oxidative stress certain biomolecules like antioxidants namely glutathione, vitamin C, vitamin E and ceroloplasmin (plasma protein) are reported in literature. Therefore in this investigation an attempt has been made to measure the antioxidant levels in control diabetic and diabetic treated rats the levels of above antioxidants decreased by 50%. The antioxidant enzymes like SOD and CAT are considered primary enzymes, since they are involved in the direct elimination of ROS. Hence attempt has been to study the activities of above enzymes. The decrease in SOD, CAT in diabetic control rats (4.12 units/min / mg protein, 42.66 n moles/ 100 g tissue) are brought to (9.76 units/min / mg protein and 78.58 n moles/ 100 g tissue) respectively. However, in this study, we found that SS leaf extract maintains erythrocytes antioxidant enzymatic activity of GPx at near normal level. Our results indicate that the preventive effects of SS-leaf extract may be due to inhibition of lipid peroxidation and scavenging of free radicals by its antioxidant nature. The altered activities of these enzymes in diabetic rats treated with SS leaf extract indicate the protective nature on pancreatic tissue.

In the final accord we have evaluated the effect of the SS plant aqueous extract on liver and pancreas of diabetic rats by doing histopathological examination. Streptozotocin is well known for its selective pancreatic islet β cell cytotoxicity and in many animal species; STZ induces diabetes that resembles human hyperglycemic non-ketotic diabetes mellitus. The photomicrographs of the liver of diabetic rats treated with SS showing normal liver architecture with slight congestions in central vein, normal sinusoidal spaces and normal hepatocytes. Oral administration of SS leaf extract for 30 days effectively restored the pathological changes in STZ induced diabetic rat pancreatic tissues.

In this present investigation an attempt has been made to identify the potential plant in the control and STZ induced type II diabetes. For this study the leaves of Sapindus saponaria (SS) were collected from the local areas. After preparation of the different extracts of above selected plant, there phytochemical studies were made and the aqueous extract were fed to the STZ induced diabetic rats and the analysis has
been made regarding the control and diabete rats induced changes in carbohydrate, lipid metabolism and histopathology of pancreas and liver in albino rats. After conducting the biochemical studies the following conclusions were made.

- The phytochemical screening of the plant *Sapindus saponaria* (SS) with different solvent (Petroleum ether, ethanol, chloroform, *n*-Butanol, isopropanol, methanol and acetone) extracts contains Alkaloids, Saponins, flavonoids, Terpenes, Glycosides, steroids sesquiterpene and Oligoglycosides).

- STZ is able to induce type II diabetes in experimental wistar rats. Diabetes induction caused alterations in both carbohydrates as well as lipid metabolism. The aqueous extract SS at a dose of 60 and 100 mg/kg b.w showed the maximum antihyperglycemic activity. So the long term treatment studies were carried out with the dose of 60 and 100 mg SS / kg b.w.

- Long term treatment of diabetic rats with the SS aqueous extract at a dose of 100 mg/kg.b.w for 30 days resulted in 68% reduction in FBG levels, with significant improvement in glycemic control (HbA1c).

- Treatment with SS aqueous extract prevented the loss of body weights and enhanced the hepatic glycogen levels in diabetic rats reflecting the efficacy of SS in the maintenance of normal carbohydrate metabolism.

- The activities of carbohydrate metabolizing enzymes hexokinase, glucose-6-phosphate dehydrogenase were significantly increased where as those of gluconeogenic enzymes (glucose-6-phosphatase and fructose-1, 6-bisphosphatase) were significantly decreased in liver and kidney of diabetic rats after treatment with the SS aqueous extract. Oral administration of aqueous extract of SS is able to control the diabetes induced alterations in enzymes related to carbohydrate metabolism to significant levels.
Summary & Conclusion

- The treatment with SS produced significant antihyperlipidemic activity in diabetic rats by decreasing the elevated levels of serum TG, total, LDL, VLDL cholesterol and by increasing HDL cholesterol by exhibiting an impression of inhibitory effect on HMG-CoA reductase, the key regulatory enzyme in cholesterol biosynthesis.

- The long term treatment of diabetic rats with SS reduced the oxidative stress by lowering the levels of TBARS and CAT activity. It also increased the activities of enzymatic (SOD and GPx) and non enzymatic (GSH, vitamin C and vitamin E) antioxidant levels in plasma and tissues reflecting the antioxidant efficacy of the SS.

- Histological studies have shown the following:
  a) In diabetic untreated rat pancreas there was insulitis with lymphocytic infiltrations along with atrophy and destruction of β cells. Regenerative changes in the tissue architecture of pancreas were observed in the diabetic rats treated with SS.

  b) Diabetic untreated rats showed degenerative liver with severe congestion of central vein, hemorrhages in the sinusoidal spaces and granular appearance of the hepatocytes (degenerative change) with cloudy swelling (hazzy nucleus). Treatment with SS in diabetic rats showed normal liver architecture with slight congestions in central vein, normal sinusoidal spaces and normal hepatocytes.

From all these observations it is concluded that the aqueous extract of *Sapindus saponaria* possess significant antidiabetic activity. This antidiabetic activity could be due to its stimulatory effect on insulin secretion resulting in improvement in the expression of insulin dependent genes with associated changes in carbohydrate metabolizing enzymes, lipid metabolism, oxidative stress and antioxidant defense systems. In our present investigation we have find out that there are many bioactive
compound in the leaf aqueous extract mainly Saponins, flavonoids, Terpenes, Glycosides and steroids for pharmacological evaluations. From our Studies it is evident that these bioactive compounds in group (or) individually from *S.saponaria* extract exerted potential mechanism of action with speculating against anti hyperglycemic activity. The *Sapindus saponaria* leaf extract, possesses stimulatory effect against anti-diabetic activities in STZ diabetic rats and showed a consistent effect on the STZ induced changes in the blood sugar level and the β-cells population in the pancreas. It is conclude that the leaf extract of *S.saponaria* extract exhibited significant anti-hyperglycemic activity and can be used for the treatment of insulin dependent diabetes mellitus