Diabetes mellitus with its devastating consequences has now assumed epidemic proportions in many countries in the world. There are 143 million people worldwide suffering from diabetes mellitus, almost five times more than the estimates of ten years ago. This number may probably double by the year 2030. As a result, human race will be under serious threat of the disease ‘Diabetes’ in this century.

Diabetes mellitus can be briefly defined as a state in which homeostasis of carbohydrate and lipid metabolism is improperly regulated by insulin. This results primarily in elevated fasting and postprandial blood glucose levels. If this imbalance in glucose homeostasis does not return to normalcy and continues for a protracted period of time, it leads to hyperglycemia which in the long run results into the syndrome named diabetes mellitus. Diabetes is becoming a pandemic disease and though there are surge of drugs/ traditional remedies to treat or prevent the conditions, its prevalence continue to soar. The work embodied in the present thesis has been carried out to meet some purposes. The internationally accepted albino rat models for diabetes mellitus and insulin resistance have been standardized by chemical treatment, manipulation in the diet and heavy alcohol administration and some new classes of antidiabetic agents have been identified by using these animal models. Some of the molecules were also found to have potential for reversing insulin resistance which emerges with the new ray of hope for better management of type 2 diabetes mellitus (NIDDM) and insulin resistance.

Armamentarium available today for the treatment of diabetes is replete with large number of potent and focused drugs. Insulin sensitizers (roziglitazones and pioglitazones), postprandial glucose regulator (repaglinide), new generation insulin secretagogues (glimepiride), α-glucosidase inhibitors (acarbose) and insulin (lispro and aspart) have enormously helped in achieving better metabolic control, albeit at a premium. However, their impact on long term outcome of diabetes related end point remains to be proven. Better understanding of cellular and molecular biology has set the stage for the development of even better molecules for the treatment of diabetes. The present study is an attempt to identify few target based antidiabetic compounds like inhibitors of glucose-6-phosphatase, glycogen phosphorylase and protein tyrosine phosphatase. The potential inhibitors of these enzymes can be developed as antidiabetic
agents. Several lead molecules have been identified during the course of the present *in vitro* study. However, these lead molecules need further study to confirm their antidiabetic potential *in vivo*.

Alcohol drinking is an accepted social practice in many societies; it is a common substance of abuse. Alcohol abuse is thought to be a risk factor for the cause of liver damage, hyperlipidemia and insulin resistance. Since the use and abuse of alcoholic beverages and the incidence of insulin resistance or NIDDM are in the increase, these issues of public health need a thread-base analysis. During the ethanol metabolism, the aldehyde degradation produces reactive metabolites, which causes toxicity to almost all the organs. An alcohol-fed rat model was developed by chronic administration of ethanol to rats which caused significant alterations in various biochemical parameters of serum and insulin sensitive and insulin insensitive tissues (liver, muscle and kidney). Hyperglycemia, hyperinsulinemia, glucose intolerance, insulin resistance and hypertriglyceridemia were also observed in these rats. The coexistence of liver toxicity, hyperlipidemia, hyperinsulinemia and insulin resistance in alcohol fed rats appears a good model for studying the effect of new classes of synthetic compounds/ natural products for their combined or individual effect, if any, on hepatoprotective, dyslipidemic, antihyperglycemic and insulin resistance reversal properties. The findings will not only help in delineating the molecular mechanism(s) caused to insulin sensitivity or resistance in alcoholism but also provide clue for the prognosis of diabetes and its management.