CHAPTER – XI

SUMMARY

Diabetes mellitus was induced in eight-week old adult male albino rats after being approved by the Institutional Animal Ethics Committee of Annamalai University. Streptozotocin was utilized for diabetic induction. The leaves of the experimental plant, *Pimenta dioica* were collected from kumuli, kerala state. Glibenclamide, the standard antidiabetic drug was also used for the treatment of diabetes as a reference drug. The experimental animals were divided into five groups, each with eight animals.

The anti-diabetic study exhibited a drastic decline in the body weight, plasma insulin and haemoglobin content in the diabetic induced rats which upon the administration of the two doses of the methanolic leaf extracts of *P.dioica* and the drug, glibenclamide brought back the above parameters to near normal levels.

The blood glucose, glycosylated haemoglobin, urea, uric acid and creatinine levels significantly got elevated in the diabetic rats which upon treatment with the two dosages of the methanolic leaf extract of *P.dioica* as well as the drug, glibenclamide reverted back the above studied parameters.
The studies on the serum lipid profile revealed a significant increase in the levels of total cholesterol, triglycerides, LDL and VLDL in the diabetic induced rats when compared with that of the normal animals, whereas serum HDL showed a decreasing trend. After administrating the methanolic leaf extracts of *P. dioica* and the standard drug, glibenclamide, the above parameters reverted back to normal.

The status of the anti-oxidant enzymes in the liver tissues showed an increasing trend in the case of TBARS, whereas a decreasing trend in the case of SOD, CAT, GSH and GPx in the STZ induced diabetic rats. All the above studied enzymes returned back to normal values gradually, on treatment with the two dosages of *P. dioica* methanolic leaf extracts as well as the drug, glibenclamide.

A similar trend was observed with respect to all the anti-oxidant enzymes in the kidney tissues of STZ induced diabetic animals which upon treatment with the *P. dioica* leaf methanolic extracts and the drug, glibenclamide, significantly reverted back to normal levels.

The histopathological observations in the pancreas of the STZ induced diabetic rats revealed decrease in the size of the islets and a decrease in the number of β-cells. The islets cells were shrunken with cellular infiltration and fibrosis. The islet cells were also diminished and depleted. The above affected pancreas of the rats after
administering with the two dosages of the *P.dioica* leaf methanolic extracts showed a dramatic recovery and the cellular alterations were restored to normal. The standard drug, glibenclamide also revealed the reversion to normal cellular architecture.

The histopathological alterations observed in the liver tissues of the diabetic induced animals were hypertrophy of hepatocytes with dense cytoplasm, swollen nucleus, distorted cells around the central vein and peripheral fatty infiltration with focal necrosis. The administration of *P.dioica* leaf extracts at 75 and 150 mg/kg b.w in the above animals reverted back the distorted nature of the hepatocytes and the necrotic condition tended to change back progressively. The hypertrophic stature also changed to normal.

The GC-MS analysis in the methanolic leaf extract of *P.dioica* confirmed the presence of eight major phytocomponents based on the retention indices, area percentage and chemical structure. In terms of percentage occurrence, phenol, 2-methoxy – 3- 3(2- propenyl)-, hop - 22 (29) – en -3.beta. – ol and hentriacontane were found to be predominant in the plant leaf extract. This qualitative and quantitative analysis of such phytochemical constituents could contribute to the medicinal quality of the leaves of *P.dioica*. 
Molecular docking study was carried out for the compound phenol, 2-methoxy - 3 - (2 - propenyl)- isolated from p.dioica leaves. The above compound showed higher binding energy against the Dipeptidyl peptidase -1V protein. The effects of complex formation by Dipeptidyl peptidase – 1V protein may become a prospective target for the potential inhibition of diabetes. The mechanism of action could thus be formulated that phenol, 2 – methoxy – 3 – ( 2- propenyl) – inhibit the activity of Dipeptidyl peptidase -1V, that is involved in diabetes.

The biomechanical studies on the bones of diabetic and treated rats indicated marginal and authentic fluctuations. FEM was employed for the above analysis. The microhardness test and the tensile strength test also revealed substantial variations in the bone structure among the diabetic induced and P.dioica leaf extract treated rats. The standard antidiabetic drug, glibenclamide treated rats also yielded similar results resembling the restoration potential of the plant extracts.