SUMMARY AND CONCLUSION

In the present study the antidiabetic principle γ- sitosterol was isolated from *L.nodiflora* whole plant using bioassay guided separation. Antihyperglycemic, antihyperlipidemic and antioxidant properties γ- sitosterol were studied in detail using normal and streptozotocin induced diabetic rats. Insulin secretion assay was conducted to know the mechanism of insulin release from pancreas. In addition histological examinations of pancreas, liver and kidney were carried out.

- Chronic treatment with γ- sitosterol to diabetic rats decreased the plasma glucose levels by increasing the plasma insulin levels.
- During dose determination 20 mg/kg /b.wt dose of γ- sitosterol showed better plasma glucose lowering effect.
- Oral administration of active principle γ- sitosterol 20 mg/kg /b.wt for 21 days decreased the fasting plasma glucose level (-44.31 %) and increased the insulin level (69.05%) in STZ induced diabetic rats.
- Decreased levels of total hemoglobin, liver, muscle glycogen content and increased levels of HbA1c, blood urea and albumin/globulin ratio in diabetic rats were restored after oral administration of γ- sitosterol.
- Serum and tissue carbohydrate metabolism enzymes were altered in diabetic rats. After continuous treatment with γ- sitosterol, serum and tissue hexokinase were increased; at the same time glucose-6-phosphatase and fructose 1, 6-bisphosphatase levels were significantly decreased.
- Oral administration of γ- sitosterol significantly increased hepatic glycogen synthase system as a result of increased insulin secretion.
In the diabetic condition lipid metabolism was altered. Serum and tissue concentrations of lipid-parameters cholesterol, triglycerides and free fatty acids were significantly restored by the administration of γ- sitosterol.

LDL, VLDL and HDL cholesterols were significantly altered in diabetic rats. Administration of γ- sitosterol to diabetic rats significantly increased the HDL cholesterol levels and at the same decreased the LDL and VLDL fraction levels.

Administration of γ- sitosterol reduced the increased oxidative stress observed in diabetic rats which increased the non-enzymatic (ascorbic acid, α-tocopherol and GSH) and enzymatic (SOD, CAT, and GPx) antioxidant levels.

In diabetic rats, alterations of the enzymes related to liver function were significantly higher than those of normal value. Oral administration of γ- sitosterol for 21 days improved the liver function by decreasing the serum ALT, AST, ALP and ACP levels in both normal as well as in diabetic rats.

The decrease in glycoproteins (hexose, hexosamine, sialic acid and fucose) content in tissues was observed in diabetic rats. Oral administration with γ- sitosterol and glibenclamide to diabetic rats significantly reversed the changes of glycoproteins levels near normal.

Studies with isolated pancreatic islets revealed that γ- sitosterol works by the principle of closing the K+ ATP channel and releases insulin from the islets of the pancreas.

Oral administration of γ- sitosterol to STZ –diabetic rats showed several insulin positive β-cells in the islets of Langerhans, which was confirmed by Immunohistochemical study.

This resulted in the preservation of β-cells mass and insulin secretory granules, which further potentiated the efficiency of γ- sitosterol. This apparently normal architecture of β-
cells, as evident through electron microscopy, may be attributed to the residual $\beta$-cell mass restored by $\gamma$-sitosterol that may secrete insulin and alleviate diabetes mediated complication.

- All the results were comparable with the reference drug glibenclamide.
- The docking studies of the ligand $\gamma$-sitosterol with four different target proteins showed that this is a good molecule which docks well at very low energy with various targets related to diabetes mellitus. Hence $\gamma$-sitosterol can be considered for developing into a potent antidiabetic drug.
- The isolated molecule $\gamma$-sitosterol produced moderate antifeedant effect against *Helicoverpa armigera*.
- $\gamma$-sitosterol didn’t produce any toxic effect in liver, kidney and heart during the acute and chronic toxicity study. $\gamma$-sitosterol was not lethal in the usual range of oral antidiabetic drug i.e. 20mg to 200mg/kg b.wt in experimental animal models.

**CONCLUSION**

The present study was aimed to isolate and identify the antidiabetic principle from *L. nodiflora*. Using bioassay guided separation we have isolated an active principle from *L. nodiflora*. The active principle was identified as $\gamma$-sitosterol using physical and spectroscopic datas (IR, $^1$H NMR, $^{13}$NMR and GC-MS). The isolated compound exhibited significant antihyperglycemic, antihyperlipidemic and antioxidant effects in STZ-diabetic rats and the results were comparable with glibenclamide. $\gamma$-sitosterol appeared to reverse the damaged endocrine tissue and there by stimulating the secretion of insulin in $\beta$-cells as revealed by insulin secretion assay. $\gamma$-sitosterol proved to be superior to many oral hypoglycemic agents, possessing both antihyperglycemic, antilipidemic and antioxidant properties without any undesirable side
effects. The docking studies of the ligand \(\gamma\)-sitosterol with four different target proteins showed that this is a good molecule which docks well with various targets related to diabetes mellitus. The results of the present findings suggest that \(\gamma\)-sitosterol may provide new therapeutic avenues to treat diabetes.