CONCLUSION

We conclude from our studies that dopaminergic system can regulate insulin secretion from pancreatic islets. Diabetes caused a marked increase in blood glucose levels and decreased the body weight. Histological studies revealed destruction in the pancreas as a result of diabetes. During diabetes a decrease in insulin secretion resulted in the accumulation of glycogen granules in the brain regions of corpus striatum, cerebral cortex and hypothalamus which were reversed by insulin therapy. The changes in dopamine and DA D2 receptor function in the corpus striatum, cerebral cortex, hypothalamus, brain stem and pancreas during diabetes causes an alteration in dopamine mediated functions. Though stimulation of sympathetic nervous system during diabetes is suggested to be an important factor in decreasing the insulin secretion, neurotransmitters their receptors and their regulatory functions have not been emphasized. We have observed an increase in the DA content in corpus striatum, cerebral cortex and decrease in hypothalamus and brain stem during diabetes. The functional significance of these changes was further explored by studying the DA and DA D2 receptors in the brain. In the corpus striatum total dopamine receptors decreased during diabetes while the dopamine D2 receptors increased. In the hypothalamus the dopamine DA receptor showed a decrease in affinity while the dopamine D2 receptor number decreased with an increase in affinity. The receptor functional changes in the cerebral cortex showed that the DA receptors increased with a decrease in affinity while the dopamine D2 receptors also increased with no change in affinity. In the brain stem the dopamine D2 receptors there was a decrease in the receptor number with a decrease in affinity during diabetes. The expression pattern of dopamine D2 receptors in the brain regions were in concordance with the receptor alterations. These alterations in the brain dopaminergic system result in an increased sympathetic stimulation during diabetes which inhibits insulin secretion. An increased sympathetic activity as a result of increased NE and EPI content directly inhibits the pancreatic insulin secretion. In the pancreatic islets an increased uptake of high concentrations of DA inhibits while a low concentration stimulates the glucose induced insulin secretion. During diabetes
the content of DA in the pancreas decreased with an increase in dopamine DA receptors. The dopamine D2 receptors decreased in the islets with an increase in its affinity. Pancreatic islets dopamine receptors are involved in the regulation of insulin secretion and impairment during diabetes affects its functional nature. Dopamine in the secretory granules of the pancreatic islets could be one of the possible elements that operate at physiological glucose concentrations controlling insulin secretion. Dopamine concentrations remain low in the pancreatic islets when there is high glucose inducing insulin secretion and this ceases as glucose concentration decreases.

Thus, we conclude that dopaminergic system is impaired during diabetes. The dopamine D2 receptors increased in the corpus striatum and cerebral cortex but decreased in the hypothalamus and brain stem indicating their involvement in regulating insulin secretion. Dopamine D2 receptor which has a stimulatory effect on insulin secretion decreased in the pancreatic islets during diabetes. Our in vitro studies confirmed the stimulatory role of dopamine D2 receptors in stimulation of glucose induced insulin secretion. A detailed study at the molecular level on the mechanisms involved in the role of dopamine in insulin secretion, its functional modification could lead to therapeutic interventions that will have immense clinical importance.