SUMMARY

1. Streptozotocin induced diabetic rats were used as model to study the role of dopamine and its receptors in insulin secretion.

2. The dopamine content increased in the striatum of rats injected with different doses of STZ with a decrease in the HVA and HVA/DA ratio. Dopamine content began to increase 12hrs after the injection of STZ in the striatum showing significant increase when the rats became diabetic. HVA content began decreasing 3hrs after the injection of STZ and remained low when the rats turned diabetic.

3. The dopamine content increased in the corpus striatum, cerebral cortex and decreased in the brain stem and hypothalamus of diabetic rats showing an overall decrease in the metabolism of DA.

4. The homovanillic acid content was decreased in the striatum, brain stem and hypothalamus of diabetic rats as the turnover from DA to HVA decreased proportionally.

5. The dopamine receptors in the corpus striatum decreased with no change in affinity while it increased in the cerebral cortex with a decrease in affinity. In the hypothalamus there was a decrease in affinity. Thus, the alterations in the dopamine receptors in the different brain regions had a differential effect during diabetes.

6. The B\textsubscript{max} of dopamine D\textsubscript{2} receptors in the corpus striatum and cerebral cortex increased during diabetes with no change in affinity. In the hypothalamus there was a decrease in B\textsubscript{max} with an increase in affinity while in the brain stem both B\textsubscript{max} and affinity decreased during diabetes.

7. During diabetes the expression of dopamine D\textsubscript{2} receptor mRNA was found to be increased in the striatum and cerebral cortex. In the hypothalamus and the brain stem dopamine D\textsubscript{2} receptor mRNA expression decreased during diabetes.

8. The differential alteration of dopamine DA and dopamine D\textsubscript{2} receptors in the brain could lead to the increased sympathetic activity that decreases insulin secretion in the pancreatic islets.

9. Plasma and adrenal dopamine and homovanillic acid content decreased while there was an increase in NE and EPI content during diabetes.
10. Pancreatic DA and HVA content decreased in diabetic rats. The dopamine receptors in the pancreatic islets increased with a decrease in affinity while the dopamine D2 receptors decreased in number with an increase in affinity.

11. *In vitro* studies using [3H] DA in the pancreatic islets showed an increased uptake of DA at high concentrations in the presence of glucose.

12. High concentrations of norepinephrine blocked the uptake of [3H] DA into the pancreatic islets.

13. Dopamine in high concentration (10^-4 M) inhibited the glucose induced pancreatic insulin in the pancreatic islets.

14. Dopamine in low concentration (10^-8 M) in the presence of 20mM glucose concentration stimulated significantly insulin secretion in the pancreatic islets.

15. Norepinephrine at high concentrations inhibited the stimulatory role of DA in glucose induced insulin secretions in presence of 20mM glucose concentration.

16. Bromocriptine a potent dopamine D2 receptor agonist at low concentrations stimulated glucose-induced insulin secretion while 7-OH DPAT an agonist of dopamine D2-like receptors inhibited insulin secretion.

17. Dopamine in the pancreas mediated its action through its receptors and dopamine D2 receptors are involved in the stimulation of insulin secretion.