SUMMARY

1. Pancreatic regeneration after partial pancreatectomy was used as a model system to study pancreatic β-cell proliferation in rats.

2. Primary cultures of pancreatic islets were used as the *in vitro* system to study pancreatic islet cell proliferation and insulin secretion.

3. 

4. GABA content was analysed using displacement method. It decreased in the brain regions during active islet cell proliferation.

5. GABA receptor functional status was analysed by Scatchard and displacement analysis using \([^3]H\) ligands. Receptor kinetic parameters data were confirmed by studying the mRNA status of the corresponding receptor using Real Time-PCR. GABA_A receptors were down regulated and GABA_B receptors were up regulated in brain regions during active islet cell proliferation.

6. Pancreatic islet GABA content was decreased in 72 hrs pancreatectomised rats. Pancreatic islet GABA_A receptor down regulation was observed during islet DNA synthesis. GABA_B receptor up regulation was found during pancreatic regeneration.

7. *In vitro* insulin secretion study during 1 hour showed that GABA has inhibited the insulin secretion in a dose dependent manner in normal and hyperglycaemic conditions. Bicuculline did not antagonize this effect. GABA_A agonist, muscimol inhibited glucose stimulated insulin secretion from pancreatic islets except in the lowest concentration of \(10^{-9}\)M in presence of 4mM glucose and at \(10^{-7}\) and \(10^{-4}\)M muscimol in presence of 20mM glucose. GABA_B agonist. Baclofen also inhibited glucose induced insulin secretion. Baclofen enhanced
glucose induced insulin secretion at the concentrations of $10^{-5}$M at 4mM glucose and at $10^{-9}$M in presence of 20mM glucose.

8. During 24 hours *in vitro* insulin secretion study it was observed that all concentrations of GABA has inhibited glucose stimulated insulin secretion from pancreatic islets. Muscimol, the GABA$_A$ agonist, inhibited the insulin secretion but, gave an enhanced secretion of insulin in presence of 4mM glucose at $10^{-7}$, $10^{-5}$ and $10^{-4}$M muscimol at 4mM glucose concentration. But in presence of 20mM glucose, muscimol significantly inhibited the insulin secretion. GABA$_B$ agonist, baclofen also inhibited glucose induced insulin secretion in presence of both 4mM and 20mM glucose.

9. *In vitro* DNA synthesis studies showed that activation of GABA$_A$ receptor by adding muscimol, a specific agonist, inhibited islet DNA synthesis. Also, the addition of baclofen, a specific -agonist of GABA$_B$ receptor resulted in the stimulation of DNA synthesis.

Thus, the regulation of GABA$_A$ and GABA$_B$ receptors in the brain and pancreatic islets plays an important role in insulin secretion and islet cell proliferation during pancreatic regeneration.