Summary

1. Insulin induced neonatal hypoglycemic rats were used as model to study the expression patterns of dopamine receptor subtypes DA D1 and DA D2, status of second messengers- cAMP and IP3, transcription factor - CREB, second messenger enzyme phospholipase- C, GLUT 3, neuronal survival factors - NFκB, GDNF and BDNF, antioxidant enzymes- GPx and SOD and apoptotic factors - Akt-1, TNF- α, Bax and caspase-8. Experiments were designed to study the neuroprotective role of *Bacopa monnieri* and Bacoside A in neonatal hypoglycemia management.

2. Antihypoglycemic activity of *Bacopa monnieri* and Bacoside A were evaluated by the measurement of blood glucose in experimental rats. Neonatal hypoglycemic rats showed decreased blood glucose level. Glucose, *Bacopa monnieri* and Bacoside A treatments to neonatal hypoglycemic rats significantly reversed the blood glucose level.

3. Dopamine D1 and D2 receptor binding studies were done in cerebral cortex, corpus striatum, cerebellum and brain stem of control and experimental rats.

4. Dopamine D1 and D2 receptor subtypes showed differential expression pattern. Dopamine D1 receptors were decreased in cerebral cortex, corpus striatum, cerebellum and brain stem in neonatal hypoglycemic rats and hypoglycemic rats treated with glucose. The gene expression studies of dopamine D1 receptor showed a significant down regulation in cerebral cortex, corpus striatum, cerebellum and brain stem. *Bacopa monnieri* and
Bacoside A treatment reversed the altered expression of dopamine D1 receptor number and gene expression.

5. Dopamine D2 receptors were increased in cerebral cortex, corpus striatum, cerebellum and brain stem of neonatal hypoglycemic rats and hypoglycemic rats treated with glucose. The gene expression studies of dopamine D2 receptors showed a significant up regulation in cerebral cortex, corpus striatum, cerebellum and brain stem of neonatal hypoglycemic rats and hypoglycemic rats treated with glucose. *Bacopa monnieri* and Bacoside A treatment reversed the altered expression of dopamine D2 receptor number and gene expression.

6. cAMP contents were significantly decreased in cerebral cortex, corpus striatum, cerebellum and brain stem of neonatal hypoglycemic rats and hypoglycemic rats treated with glucose. *Bacopa monnieri* and Bacoside A treatment reversed cAMP contents in neonatal hypoglycemic rats.

7. IP3 contents showed differential expression pattern. IP3 content were significantly increased in brain regions- corpus striatum and brain stem, whereas IP3 content were significantly decreased in cerebral cortex and cerebellum of neonatal hypoglycemic rats and hypoglycemic rats treated with glucose. *Bacopa monnieri* and Bacoside A treatment reversed the IP3 content in cerebral cortex, corpus striatum, cerebellum and brain stem.

8. Second messenger enzyme - phospholipase C showed an increased expression in hypoglycemic brain regions - cerebral cortex, corpus striatum, cerebellum and brain stem. Treatment groups, *Bacopa monnieri* and Bacoside A showed significant reversal when compared with hypoglycemic group.
Summary

9. Gene expressions of CREB showed differential expression pattern. CREB expression was up regulated in cerebral cortex, corpus striatum and brain stem, whereas in cerebellum, CREB mRNA showed decreased expression in neonatal hypoglycemic rats and hypoglycemic rats treated with glucose. *Bacopa monnieri* and Bacoside A treatment to neonatal hypoglycemic rats significantly reversed the differential expression pattern.

10. GLUT 3 mRNA expressions were studied in cerebral cortex, corpus striatum, cerebellum and brain stem. GLUT 3 mRNA showed differential expression pattern. GLUT 3 was up regulated in brain regions- corpus striatum and cerebellum, and down regulated in the cerebral cortex and brain stem of neonatal hypoglycemic rats compared to control. Glucose, *Bacopa monnieri* and Bacoside A treatment reversed the disrupted GLUT 3 gene expression in brain regions.

11. Akt-1 showed differential expression patterns in cerebral cortex, corpus striatum, cerebellum and brain stem. Akt-1 gene expression was up regulated in cerebral cortex and corpus striatum, whereas in cerebellum and brain stem it was seen to be down regulated in neonatal hypoglycemic rats and hypoglycemic rats treated with glucose. *Bacopa monnieri* and Bacoside A treatment to neonatal hypoglycemic rats showed significant reversal in brain regions.

12. TNF-α mRNA showed differential expression patterns in cerebral cortex, corpus striatum, cerebellum and brain stem. TNF-α mRNA was decreased in cerebral cortex, corpus striatum and brain stem, whereas cerebellum showed
increased expression of TNF-α in neonatal hypoglycemic rats and hypoglycemic rats treated with glucose. *Bacopa monnieri* and Bacoside A treatment to neonatal hypoglycemic rats showed significant reversal in brain regions.

13. Gene expression of neuronal survival factors - GDNF, BDNF and NFκB was down regulated in cerebral cortex, corpus striatum, cerebellum and brain stem of neonatal hypoglycemic rats and hypoglycemic rats treated with glucose. Treatment groups *Bacopa monnieri* and Bacoside A showed significant reversal in GDNF, BDNF and NFκB expression.

14. Anti oxidant enzymes - GPx and SOD showed differential expression pattern in cerebral cortex, corpus striatum, cerebellum and brain stem of neonatal hypoglycemic rats and hypoglycemic rats treated with glucose. GPx gene expression was down regulated whereas SOD gene expression was up regulated in neonatal hypoglycemic group. Treatment groups, *Bacopa monnieri* and Bacoside A showed significant reversal in GPx and SOD gene expressions.

15. Apoptotic marker- Bax, gene expression in cerebral cortex, corpus striatum, cerebellum and brain stem was up regulated in hypoglycemic condition and hypoglycemic rats treated with glucose compared to control. *Bacopa monnieri* and Bacoside A treatment to neonatal hypoglycemic rats showed significant reversal in Bax gene expression.

16. Caspase 8 showed differential expression pattern in cerebral cortex, corpus striatum, cerebellum and brain stem. Caspase 8 gene expression in cerebral
cortex, corpus striatum and brain stem was up regulated, whereas in the cerebellum it was down regulated in hypoglycemic condition and hypoglycemic rats treated with glucose compared to control. *Bacopa monnieri* and Bacoside A treatment to neonatal hypoglycemic rats showed significant reversal in caspase 8 gene expression.

In the present study, we summarize, that dopaminergic receptor subtypes showed differential expression pattern in brain regions and it has significant role in glucose metabolism. Glucose transporter- GLUT 3 was altered in hypoglycemic condition. Transcription factor- CREB, Phospholipase- C, second messengers, antioxidant enzymes and apoptotic factors alterations were seen in neonatal hypoglycemic rats. *Bacopa monnieri* and Bacoside A treatment decreased the expression of apoptotic factors and increased the expression of neuronal survival factors in neonatal hypoglycemic rats. The adverse effects of glucose infusion alone as a resuscitation method were also evident from the present study. Our results showed that glucose administration along with *Bacopa monnieri* and Bacoside A treatment as a resuscitation method will be of tremendous advantage in neonatal care. Thus the results suggest the therapeutic role of *Bacopa monnieri* and Bacoside A in ameliorating CNS dysfunctions, to overcome neonatal hypoglycemia and for a better intellect in the later stages of life.