Summary

1) Pilocarpine induced Temporal lobe epileptic rats were used as a model to study the alterations of muscarinic, muscarinic M1, glutamate receptors and their functional regulation by *Bacopa monnieri* and Bacoside A.

2) Antiepileptic activity of whole plant extract of *Bacopa monnieri* and Bacoside A were evaluated by seizure frequency over 72 hours video recording period, magnitude of drug effect in post-treatment and seizure onset latency and seizure duration in pre-treatment.

3) Acetylcholine esterase activity has been used as a marker for cholinergic activity. Acetylcholine esterase activity was measured in the brain regions. In epileptic rats the acetylcholine esterase activity was increased in the hippocampus and brainstem. In epileptic rats treated with Carbamazepine, *Bacopa monnieri* and Bacoside A, the activity of the enzyme reversed to near control.

4) Muscarinic receptor functional status was analyzed by Scatchard and displacement analysis using specific ligands [3H] QNB- general muscarinic antagonist, atropine-non radioactive general muscarinic antagonist. In epileptic rats, total muscarinic receptors were up-regulated in the hippocampus whereas it was down regulated in cerebellum and brainstem during post-treatment with Carbamazepine, *Bacopa monnieri* and Bacoside A.
5) Muscarinic M1 receptor functional status was analyzed by scatchard and displacement analysis using specific ligands [³H] QNB- general muscarinic antagonist and pirenzepine-non radioactive muscarinic M1 antagonist. During epilepsy muscarinic M1 receptors were up regulated in the hippocampus whereas it was down regulated in cerebellum and brainstem. Post-treatment with Carbamazepine, Bacopa monnieri and Bacoside A reversed the receptor changes to near control level. Muscarinic M1 receptors were down regulated in the hippocampus during the initial phase whereas it was up regulated in cerebellum. Pre-treatment with Carbamazepine, Bacopa monnieri and Bacoside A reversed the receptor changes to near control.

6) Receptor binding parametres were confirmed by studying the mRNA status of the corresponding receptor using Real Time-PCR. In hippocampus, the muscarinic receptors were up regulated in epilepsy and it was down regulated during the initial phase. In Carbamazepine, Bacopa monnieri and Bacoside A pre- and post- treated epileptic rats, the receptor activity reversed to near control.

7) Real Time-PCR studies in the cerebellum and brainstem showed that the muscarinic receptors are down regulated in epileptic rats. In Carbamazepine, Bacopa monnieri and Bacoside A post-treated epileptic rats, the receptor activity reversed to near control.

8) Glutamate dehydrogenase activity in the hippocampus, cerebellum and brainstem showed a significant increase in epileptic rats. In Bacopa monnieri
post-treated epileptic rats, glutamate dehydrogenase activity reversed to near control.

9) Glutamate receptor binding parameters in the hippocampus, cerebellum and brainstem showed a significant decrease in the binding in epileptic rats. In *Bacopa monnieri* post-treated epileptic rats, glutamate receptor binding parameters reversed to near control.

10) Real Time-PCR studies of NMDA R1 in the hippocampus, cerebellum and brainstem showed that the NMDA R1 receptors were down regulated in the epileptic rats. In *Bacopa monnieri* post-treated epileptic rats, the receptor activity reversed to near control.

11) Real Time-PCR studies of metabotropic glutamate 8 receptor in the cerebellum and brainstem showed down regulation in the epileptic rats. In *Bacopa monnieri* post-treated epileptic rats, the receptor activity reversed to near control.

12) Neo-Timm staining in the hippocampus of epileptic rats showed a dense staining in the CA1 region when compared to control which confirms mossy fibre sprouting. Post-treatment with Carbamazepine and *Bacopa monnieri* did not show reversal to the control.

13) A prominent brain activity difference was observed in epileptic rats compared to control by EEG analysis. In Carbamazepine, *Bacopa monnieri* and
Bacoside A pre- and post-treated epileptic rats, the brain activity reversed to near control.

14) Spatial learning ability of the rats were studied by Morris Water Maze experiment. In epileptic rats the learning ability of rats were impaired compared to control. *Bacopa monnieri* post-treatment reversed the learning ability to near control.

Thus from our results, we conclude that Central muscarinic, muscarinic M1 and glutamate receptor subtypes functional balance play an important role in the pathophysiology of pilocarpine induced Temporal lobe epilepsy in rats. *Bacopa monnieri* and Bacoside A extracts have a regulatory effect on epilepsy through Muscarinic, Muscarinic M1 and glutamate receptors. This has immense clinical significance in the therapeutic management of epilepsy.
Conclusion

We conclude from our studies that cholinergic system through muscarinic, muscarinic M1 and glutamate receptors play an important role in the pathophysiology of pilocarpine induced temporal lobe epilepsy in rats. Cholinergic activity indicated by acetylcholine esterase as a marker for cholinergic system increased in brain regions - hippocampus and brainstem in epilepsy. Treatment of epileptic rats with Carbamazepine, *Bacopa monnieri* and Bacoside A reversed the enzyme status to near control. The functional changes in muscarinic receptors studied in the brain regions showed that total muscarinic and muscarinic M1 receptors were up regulated in the hippocampus and were down regulated in the cerebellum and brainstem in the epileptic state. Post-treatment with Carbamazepine, *Bacopa monnieri* and Bacoside A, reversed the receptor changes to near control. Glutamate receptors were down regulated in the hippocampus, cerebellum and brainstem in epileptic rats and post-treatment with *Bacopa monnieri* reversed the receptor changes to near control. Pre-treatment with Carbamazepine, *Bacopa monnieri* and Bacoside A significantly reduced the occurrence of seizures mediated through muscarinic receptors. Electrophysiological studies confirmed the reversal observed with enzyme and receptor studies. Morris water maze experiment also showed the impairment in the spatial learning task during epilepsy and the treatment with *Bacopa monnieri* reversed the effect to near control. Thus our studies suggest that central muscarinic, muscarinic M1 and glutamate receptor subtype functional balance play an important role in pilocarpine induced temporal lobe epilepsy in rats. *Bacopa monnieri* and Bacoside A extracts have regulatory role in epilepsy through muscarinic and glutamate receptors. This has therapeutic application in the management of epilepsy.