CHAPTER 3

SCOPE OF THE STUDY

PD is a progressive neurodegenerative disorder characterised by the dopaminergic degeneration in SNpc, resulting from decreased dopamine levels. Besides, glial cells such as microglia and astrocytes are the aggravating perpetrators in PD. It is clear that alleviating dopaminergic functions alone cannot be a complete therapeutic strategy, hence restoration of astrocytes functions should also be considered in PD. Various pathogenetic mechanisms were shown to be involved in PD, including mitochondrial dysfunctions, inflammatory processes, oxidative stress, trophic factor deficiency and apoptosis. These causative or triggering factors interact with one another creating a vicious cycle with complex pathogenetic mechanism in PD. Till date there is no effective therapy to stop or at least slow down the neurodegeneration in PD patients. Current therapies include dopaminergic therapy, dopamine agonists, MAO-B inhibitors, COMT inhibitors, anticholinergic drugs, surgical procedures such as pallidotomy and more specifically deep brain stimulation of the globus pallidus pars interna (GPI) or subthalamic nucleus (STN), and stem cell transplantation. Although dopamine replenishment with levodopa (L-Dopa), being a gold standard for symptomatic treatment of PD, but it is reported to have severe side effects on long term treatment in clinical situation. This shows that restoration of dopaminergic system functions or dopamine level alone will not be sufficient in the treatment of PD, it seems that simultaneous alleviation of other causative factors majorly the astrocytic functions is also necessary.

Accumulating evidences shows the crucial role of AT1R, a renin angiotensin system member, in dopaminergic degeneration. TEL, an AT1R antagonist, has been reported to exert neuroprotective effect in animal models of PD. The present study establishes the neuroprotective effect of TEL in acute and chronic MPTP model of Parkinsonism, with respect to the glial-neuronal association in PD and which also adds evidences to disease-modifying therapeutic approach using central renin-angiotensin system modulator.