

## Abstract

Parkinson's disease (PD) is the second most commonly occurring neurodegenerative disease after Alzheimer's disease, which affects 1-3% of the population above 65 years of age. The objective of this study was to evaluate the neuroprotective effect of methanolic *Mentha piperita* (MP) leaves and roots extract in the rotenone induced mouse model of PD as well as on motor dysfunctions. The current study was conducted to determine behavioral and histological changes in rotenone induced mice after treating with methanolic MP extracts. Methanolic Leaf (LEMP) and Root (REMP) extracts of MP were prepared. Mice were randomly divided into 5 groups; (1) Control group, (2) Rotenone treated group, (3) Sinemet+Rotenone, (4) Methanolic MP Leaf+Rotenone (LEMP+Rotenone) and (5) Methanolic MP Root+Rotenone (REMP+Rotenone). Subcutaneous administration of 2.5mg/kg rotenone in sunflower containing 2% DMSO was made for 21 consecutive days (1mg/ml) in order to induce PD symptoms. Control group received same volume of vehicle (2.5 % DMSO in sunflower oil) for 21 days, Sinemet+Rotenone group received sinemet dissolved in water at a dose of 20 mg/kg orally for 28 days (7 days before rotenone administration and for 21 days with rotenone administration) and rotenone at a dose of 2.5 mg/kg s.c. for 21 days, LEMP+Rotenone group received methanolic MP leaves extract at the dose of 200 mg/kg and REMP+Rotenone group received methanolic MP roots extract at the dose of 200 mg/kg. Behavioral tests such as beam walk, pole test, stepping test, open field test, tail suspension test and stride length tests were conducted after completion of rotenone administration (21 days) in order to observe PD features and restoration of locomotor activities. Following behavioral assessment, the mice were terminally euthanized and brains were procured for histological assessment. Motor functional deficits estimation revealed bradykinesia, increased immobility time, shorter stride length and compromised coordination in rotenone-administered mice. While the treatment groups i.e LEMP+Rotenone, REMP+Rotenone and Sinemet+Rotenone showed neuroprotection in rotenone induced motor deficits. The histological study showed that in rotenone group, there was cytoplasmic shrinkage and increased vacuolation around multipolar cells in substantia nigra region, while Sinemet+Rotenone, LEMP+Rotenone and REMP+Rotenone groups showed less Department of Zoology, GCU Lahore vacuolation and less neurodegeneration. This study of behavioral and histopathological indication proves that roots and leaves extract of *Mentha piperita* could be considered to develop therapeutic strategies for clinical applications.

**Keywords:** Substantia nigra, Motor deficits, *Mentha piperita*.