

Parkinson's disease is the commonly occurring neurodegenerative disease that about 1 to 3% of the population was affected by it, mostly age above 65 years. This study was performed to evaluate the neuroprotective role of *Mentha piperita* (MP), *Murraya koenigii* (MK), *Morus alba* (MA) and d-carvone (CV) in the rotenone-induced PD mouse model. The phytochemical analysis of plant extract through gas chromatography-mass spectroscopy (GC-MS) was performed. Firstly, the influence of plant extracts on rotenone-challenged mice was investigated for motor dysfunctions, extent of neurodegeneration in SN neurons, brain dopamine levels, antioxidant capacities and modulation of gene expressions. Adult male Swiss albino mice were assigned to nine groups (n=9): control (2.5% DMSO), rotenone (2.5 mg/kg), MP+ROT (200mg/kg and 2.5mg/kg, respectively), MP (200 mg/kg), MK+ROT (200mg/kg and 2.5mg/kg, respectively), MK (200 mg/kg), MA+ROT (200mg/kg and 2.5mg/kg, respectively), MA (200 mg/kg) and SIN+ROT, reference treatment containing levodopa and carbidopa (20 mg/kg and rotenone 2.5mg/kg). A separate series of experiment was performed for d-carvone, an active ingredient, chosen for its possible therapeutic potential on PD mice. Adult Swiss albino male mice were assigned to five groups (n=6): control (2.5% DMSO), rotenone (2.5 mg/kg), CV+ROT (75mg/kg and 2.5mg/kg, respectively), CV (75 mg/kg) and SIN+ROT, (20 mg/kg and 2.5mg/kg). Parkinson's disease symptoms were observed, using open field, beam walk, stepping, pole climb down, tail suspension tests and stride length measurements. The antioxidant tests were performed for the levels of lipid peroxidation (LPO), reduced glutathione (GSH) and superoxide dismutase (SOD), and activities of catalase (CAT) and glutathione-S-transferase (GST), and substantia nigra was also evaluated histologically using hematoxylin and eosin stain. For the chosen genes, RT-qPCR was used for the modulated gene expression and analysis dopamine levels was done using HPLC. The treatment groups reduced the rotenone induced deficits and showed improvement in the behavioral and enhanced the antioxidant activities (LPO, CAT, GSH, GST and SOD). Plant extracts and CV prevented SN neurodegeneration and partially rescued the dopamine level in the brain. The genes expression related to dopamine production and binding, its antioxidant potential and synapse establishment were showed change in extracts and CV administered brains. Current experiment suggested therapeutic potential of MP, MK and MA extract and neuroprotective potential, and it can be due to their antioxidant activities. The comparison of neuroprotective effect of plant extracts and CV through the evaluation of their antioxidant potential against rotenone-induced neurodegeneration, indicates that bioactive ingredient exhibited potentiated effects compared to the plant extracts. Taken together, current study provides evidence-based data for potential therapeutic benefits of medicinal plants and d-carvone. Current data can be utilized with further investigations to design an effective strategy to prevent the PD progression through augmenting neuroprotective capacities of SN neurons.