

Pomegranate Attenuated Levodopa-Induced Dyskinesia and Dopaminergic Degeneration in MPTP Mice Models of Parkinson's Disease

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Abstract : Parkinson's disease (PD) results primarily from the death of dopaminergic neurons in the substantia nigra. Soon after the discovery of levodopa and its beneficial effects in chronic administration, debilitating involuntary movements observed, termed levodopa-induced dyskinesia (LID) with poorly understood pathogenesis. Polyphenol-rich compounds, like pomegranate, provided neuroprotection in several animal models of brain diseases. In the present work, we investigated whether pomegranate has preventive effects following 4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced dopaminergic degenerations and the potential to diminish LID in mice. Mice model of PD was induced by MPTP (30 mg/kg daily for five consecutive days). To induce a mice model of LID, valid PD mice were treated with levodopa (50 mg/kg, i.p) for 15 days. Then the effects of chronic co-administration of pomegranate juice (20 ml/kg) with levodopa and continuing for 10 days, evaluated. Behavioural tests were performed in all groups, every other day including: Abnormal involuntary movements (AIMS), forelimb adjusting steps, cylinder, and catatonia tests. Finally, brain tissue sections were prepared to study substantia nigra changes and dopamine neuron density after treatments. With this MPTP regimen, significant movement disorders revealed in AIMS tests and there was a reduction in dopamine striatal density. Levodopa attenuates their loss caused by MPTP, however, in chronic administration, dyskinesia observed in forelimb adjusting step and cylinder tests. Besides, catatonia observed in some cases. Chronic pomegranate co-administration significantly improved LID in both tests and reduced dopaminergic loss in substantia nigra. These data indicate that pomegranate might be a good adjunct for preserving dopaminergic neurons in the substantia nigra and reducing LID in mice.

Keywords : levodopa-induced dyskinesia, MPTP, Parkinson's disease, pomegranate

Conference Title : ICSRD 2020 : International Conference on Scientific Research and Development

Conference Location : Chicago, United States

Conference Dates : December 12-13, 2020