

Protective Effects of Flavonoid Rutin Against Aminochrome Neurotoxicity

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Abstract

Causes of dopaminergic neuronal loss in Parkinson's disease (PD) are subject of investigation and the common use of models of acute neurodegeneration induced by neurotoxins 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), 6-hydroxydopamine, and rotenone contributed to advances in the study of PD. However, the use of study models more similar to the pathophysiology of PD is required for advances in early diagnosis and translational pharmacology. Aminochrome (AMI), a compound derived from dopamine oxidation and a precursor of neuromelanin, is able to induce all the mechanisms associated with neurodegeneration. Previously, we showed AMI is cytotoxic in primary culture of mesencephalic cells (PCMC) and induces *in vitro* and *in vivo* neuroinflammation. On the other hand, the effect of rutin in central nervous system cells has revealed anti-inflammatory, antioxidative, and neuroprotective potential. However, there have been no data studies on the effect of rutin against aminochrome neurotoxicity. Here, we show that rutin prevents lysosomal dysfunction and aminochrome-induced cell death in SHSY-5Y cells, protects PCMC against aminochrome cytotoxicity, and prevents *in vivo* loss of dopaminergic neurons in substantia nigra pars compacta (SNPc), as well as microgliosis and astrogliosis. Additionally, we show that rutin decreases levels of interleukin-1 β (IL-1 β) mRNA and increases levels of glia-derived neurotrophic factor (GDNF) and nerve-derived neurotrophic factor (NGF) mRNA. We evidence for the first time the protective effect of rutin on PD aminochrome-induced models and suggest the potential role of the anti-inflammatory activity and upregulation of NGF and GDNF in the mechanism of rutin action against aminochrome neurotoxicity. © 2023, The Author(s), under exclusive licence to Springer Science+Business Media, LLC, part of Springer Nature.

Author keywords

Dopamine; Neuroinflammation; Neuroprotection; Parkinson's disease; Rutin