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Unveiling the neuroprotective potential of new xanthene derivatives in Parkinson's disease

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Abstract

Background: Parkinson's disease (PD) is a neurodegenerative condition marked by the premature loss of dopaminergic neurons in the substantia nigra pars compacta. Additionally, PD is linked to several neuropathological processes, such as the formation of Lewy bodies, neuroinflammation, mitochondrial dysfunction, ferroptosis and oxidative stress [1-4]. Despite the notable progress in PD research, the development of an effective, long-term disease-modifying treatment remains elusive. For that reason, xanthene derivatives have been intensely studied and demonstrated diverse biological activities [5]. **Objective:** The main objective of this work was to evaluate, in vitro, the potential neuroprotective effects of new xanthene derivatives against MPP+, a neurotoxin widely used in vitro to mimic PD by interfering with electron transport chain, impacting ATP production and leading to reactive oxygen species (ROS) generation [6]. **Methods:** Differentiated SH-SY5Y cells were used as in vitro model and compounds (0–25 μM) cytotoxicity evaluated, 24 h after exposure, by the neutral red uptake and resazurin reduction assays, to select non-cytotoxic concentrations. To evaluate the compounds' neuroprotective effects, MPP+ was used (500 and 1000 μM). The cytotoxicity of the chemical aggressor was evaluated by the NR uptake assay 24 h after exposure to the chemical insult in the presence and absence of the xanthene derivatives (10 and 25 μM, non-cytotoxic concentrations). **Results:** All the tested compounds demonstrated to be non-cytotoxic for concentrations up to 25 μM. Some xanthene derivatives significantly reduced MPP+-induced cell death. **Conclusions:** Given the neuroprotective effects of these innovative compounds against MPP+, further studies are needed to deeper elucidate the mechanism(s) underlying the observed neuroprotection, and to explore their potential against other pathological hallmarks of PD.

Keywords: neurodegenerative disease; neuroprotection; MPP+; disease-modifying drugs

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