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PROTECTIVE EFFECTS OF NANOQUERCETIN AGAINST MPTP-INDUCED PARKINSONISM IN ZEBRAFISH LARVAE

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INTRODUCTION: Parkinson's disease (PD) is the second most common degenerative disease in the world, and there is no treatment that can reverse its progression. The neurotoxin MPTP is used to mimic the effects of PD *in vivo* , such as Zebrafish (*Danio rerio*), a widely accepted experimental model of PD. Quercetin, a flavonoid with antioxidant properties, has been investigated for its cytoprotective potential. However, due to its low bioavailability, a delivery system, such as nanoemulsion, is required. **OBJECTIVE:** The present work aims to investigate the neuroprotective effects of nanoemulsified Quercetin against MPTP-induced parkinsonism in zebrafish larvae. **MATERIALS AND METHODS:** Zebrafish larvae were collected 1 hour after fertilization. At 4 days post fertilization (dpf), larvae were relocated into 96-well plates with pretreatments (Quercetin or Nanoquercetin). At 5 dpf, MPTP was added, and oxidative parameter analyses, such as Reduced Glutathione (GSH), Lipid Peroxidation Product (TBARS) and Reactive Oxygen Species (ROS), were performed at 7 dpf. Experimental protocols were approved by CEUA/FURG, license P015/2022. **RESULTS AND CONCLUSION:** For GSH analysis, the control showed the highest levels, while the MPTP group exhibited a significant reduction in the antioxidant capacity, demonstrating MPTP's efficiency in compromising antioxidant defense. Furthermore, the groups treated with Nanoquercetin still had remarkable decreases in GSH levels, highlighting that MPTP's effect could not be reverted by any treatment with Quercetin. TBARS analysis showed a considerable increase in lipid peroxidation on the MPTP group compared to the control. Interestingly the groups containing Quercetin and Nanoquercetin had a significant reduction of lipid peroxidation levels, suggesting that Quercetin provides substantial protection against MPTP-induced lipid damage. MPTP exposure increased ROS production by approximately 10% compared to the control. Both Quercetin and Nanoquercetin counteracted oxidative stress compared to their respective control groups. It is evident that MPTP successfully induced oxidative stress by reducing GSH and increasing TBARS and ROS levels. Furthermore, while neither Quercetin nor Nanoquercetin reversed the GSH deficit, both attenuated lipid peroxidation and ROS production, with Nanoquercetin demonstrating better results. Thus, quercetin nanoemulsion may be a good candidate for more studies in a search for a treatment to attenuate Parkinson's disease progression.

Keywords: Neurodegeneration, nanomedicine, flavonoids, oxidative stress.