Luteolin attenuates MPP+-induced neurodegeneration via modulation of oxidative stress, apoptosis, and PRDX-6 expression

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Oxidative stress resulting from mitochondrial dysfunction plays a critical role in the progression of neurodegenerative diseases. Luteolin, a naturally occurring flavonoid found in many plants, has been suggested to have potential benefits in preventing and treating these conditions. However, the molecular mechanisms underlying these effects remain poorly understood. Peroxiredoxin (PRDX) enzymes, essential for cellular antioxidant defense, consist of six isoforms (PRDX 1–6). Among these, PRDX-6 is a bifunctional enzyme with antioxidant and phospholipase activities. Recent studies have identified PRDX-6 as a promising therapeutic target for neurodegenerative disorders. This study aimed to investigate the neuroprotective mechanisms of luteolin and, for the first time, examine its effects on PRDX-6 expression in an *in vitro* neurodegeneration model induced by 1-methyl-4-phenyl pyridinium (MPP^+) in human neuroblastoma (SH-SY5Y) cell line. SH-SY5Y cells were pretreated with luteolin (0.1–10 µM) 6 hrs before exposure to MPP^+ (0.5 mM). The study evaluated (i) cell viability and cytotoxicity using MTT and LDH assays, (ii) intracellular reactive oxygen species (ROS) levels using the DCFH-DA assay, and (iii) protein expression levels of PRDX-6, α-synuclein, and apoptotic markers (Bax, Bcl-2, cleaved PARP, cytochrome c) via immunoblotting. The results demonstrated that the IC_{50} value of luteolin in SH-SY5Y cells was 33.27 µM. Luteolin pretreatment significantly reduced MPP^+-induced cell death and ROS production in a dose-dependent manner ($p< 0.01$). Additionally, it notably decreased the expression of α-synuclein, Bax, cleaved PARP, and cytochrome c proteins at 5 and 10 µM concentrations while significantly increasing PRDX-6 and Bcl-2 expression compared to MPP^+-treated cells ($p< 0.05$). These findings suggest that luteolin exerts neuroprotective effects by alleviating oxidative stress, modulating apoptotic signaling pathways, and upregulating PRDX-6 expression in SH-SY5Y cells.