# Investigating the mechanisms of neuroprotection by luteolin using the human neuroblastoma SH-SY5Y cell model

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## Outline

1. Introduction
2. Suppressing Cdk5 activity by luteolin inhibits $MPP^+$-induced apoptotic of neuroblastoma through Erk/Drp1 and Fak/Akt/GSK3β pathways
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4. Conclusion

## Abstract

Parkinson's disease (PD) is a progressive neurodegenerative disease characterized by the abnormal aggregation of α-synuclein protein and death of dopaminergic neurons. Luteolin is a common flavonoid found in celery, green pepper and other herbs, which has anti-oxidant and anti-apoptosis properties. As the potential mechanism of luteolin in the treatment of PD is still unclear, this study aims to investigate the different mechanisms of neuroprotection by luteolin using SH-SY5Y cell model. In regulating oxidative stress and mitochondrial dysfunction, luteolin significantly increased cell viability and reduced apoptosis in 1-methyl-4-phenylpyridinium iodide ($MPP^+$)-treated cells. Besides, luteolin not only improved lipid peroxidation, superoxide anion and mitochondrial membrane potential disruption, but also attenuated $MPP^+$-induced neurite damage *via* growth associated protein 43 (GAP43) and synapsin-1. Furthermore, overactivation of exerts neuroprotective effects *via* cyclin-dependent kinase-5 (Cdk5) in $MPP^+$-exposed cells inhibits the phosphorylation of signal-regulated kinases 1/2 (Erk1/2), dynamin-related protein 1 (Drp1), focal adhesion kinase (Fak), protein kinase B (Akt), and glycogen synthesis kinase 3β (GSK3β), while increasing the activity of cleaved caspase-3, thereby promoting apoptosis. However, pre-treatment with luteolin could reverse the expression of these proteins. In short, luteolin exerts neuroprotective effects *via* Cdk5 -mediated Erk1/2/Drp1 and Fak/Akt/GSK3β pathways. In response to endoplasmic reticulum stress, luteolin significantly enhanced cell viability, 3-hydroxy-3-methylglutaryl-coenzyme A reductase degradation 1 (HRD1) and suppressor/enhancer lin-12-like (SEL1L) mRNA levels and protein expressions. However, luteolin did not repress 6-hydroxydopamine (6-OHDA)-induced cell death when expression of HRD1 or SEL1L was suppressed by RNA interference. Hence, luteolin suppressed 6-OHDA-induced neuronal cell death *via* an upregulation of the expression of HRD1 and SEL1L. In conclusion, luteolin shows different mechanisms of neuroprotection, which could be a potential preventive agent for PD and other neurodegenerative disorders.

# Reference

**Nishiguchi, H., Omura, T., Sato, A., Kitahiro, Y., Yamamoto, K., Kunimasa J., & Yano, I.** (2024). Luteolin protects against 6-hydoroxydopamine-induced cell death *via* an upregulation of HRD1 and SEL1L. *Neurochemical Research*, *49*, 117-128.

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