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Protective effects of rosmarinic acid against iron-induced neurotoxicity in SK-N-SH cells

Huamin Xu

Qingdao University, China

Rosmarinic Acid (RA) is a naturally occurring polyphenolic compound and is composed of caffeic acid and danshensu. Our previous studies have confirmed RA could protect against 6-hydroxydopamine (6-OHDA) and 1-methyl-4-phenyl pyridine cation (MPP+) induced cell injury. Improving evidence showed iron-induced α -synuclein aggregation played important roles in the etiology of Parkinson's Disease (PD). However, whether RA could protect dopaminergic neurons through inhibiting the aggregation of α -synuclein in PD is unclear and the regulation mechanisms underlying this inhibition were not elucidated. Therefore, the experiment proposed to explore the effects of rosmarinic acid against iron-induced α -synuclein aggregation in dopaminergic cells and elucidate the possible mechanisms in the SK-N-SH cells. Results showed that iron could reduce the mitochondrial transmembrane potential (Ψ_m) and induce α -synuclein aggregation in the SK-N-SH cells. In accordance with iron responsive element/iron regulatory protein (IRE/IRP) system, iron could increase the mRNA levels of α -synuclein. Results also showed that RA pre-treatment could restore the $\Delta\Psi_m$ reduction induced by iron and alleviate iron induced α -synuclein aggregation. Further, results showed RA pre-treatment could inhibit iron induced α -synuclein aggregation by up-regulating hemeoxygenase-1 (HO-1). In addition, RA pre-treatment could decrease the mRNA levels of α -synuclein via decreasing the protein levels of IRP1. These results provide new findings and new strategies for the prevention and treatment of PD.

huamin102@163.com

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