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Astaxanthin upregulates heme oxygenase-1 expression through ERK1/2 pathway and its protective effect against beta-amyloid-induced cytotoxicity in SH-SY5Y cells.

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Abstract

Astaxanthin (ATX), the most abundant flavonoids in propolis, has been proven to exert neuroprotective property against glutamate-induced neurotoxicity and ischemia-reperfusion-induced apoptosis. Previous study have revealed that ATX can rescue PC12 cells from Aβ(25-35)-induced apoptotic death. However, the mechanisms by which ATX mediates its therapeutic effects in vitro are unclear. In the present study, we explored the underlying mechanisms involved in the protective effects of ATX on the Aβ(25-35)-induced cytotoxicity in SH-SY5Y cells. Pre-treatment with ATX for 4h significantly reduced the Aβ(25-35)-induced viability loss, apoptotic rate and attenuated Aβ-mediated ROS production. In addition, ATX inhibited Aβ(25-35)-induced lowered membrane potential, decreased Bcl-2/Bax ratio. We also demonstrated that ATX could prevent the activation of p38MAPK kinase pathways induced by Aβ. Moreover, we for the first time have revealed the ATX increased antioxidant enzyme heme oxygenase-1 (HO-1) expression in concentration-dependent and time-dependent manners, which were correlated with its protective effect against Aβ(25-35)-induced injury. Because the inhibitor of HO-1 activity, ZnPP reversed the protective effect of ATX against Aβ(25-35)-induced cell death. We also demonstrated that the specific ERK inhibitor, PD98059, concentration-dependently blocked on ATX-induced HO-1 expression, and meanwhile PD98059 reversed the protective effect of ATX against Aβ25-35-induced cell death. Taken together, these findings suggest that astaxanthin can induce HO-1 expression through activation of ERK signal pathways, thereby protecting the SH-SY5Y cells from Aβ(25-35)-induced oxidative cell death.

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