



Anti-apoptotic effect of phloretin on cisplatin-induced apoptosis in HEI-OC1 auditory cells

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Abstract:

Cisplatin is a highly effective chemotherapeutic agent, but it has significant ototoxic side effects. Apoptosis is an important mechanism of cochlear hair cell loss following exposure to cisplatin. The present study examined the effects of phloretin, a natural polyphenolic compound found in apples and pears, on cisplatin-induced apoptosis. We found that phloretin induced the expression of heme oxygenase-1 (HO-1) protein in a concentration- and time-dependent manner. Phloretin induced nuclear factor-E2-related factor 2 (Nrf2) nuclear translocation, and dominant-negative Nrf2 attenuated phloretin-induced expression of HO-1. Phloretin activated the JNK, ERK and p38 mitogen-activated protein kinase (MAPK) pathways, and the JNK pathway played an important role in phloretin-induced HO-1 expression. Phloretin protected the cells against cisplatin-induced apoptosis. The protective effect of phloretin was abrogated by zinc protoporphyrin IX (ZnPP IX), a HO inhibitor. Furthermore, phloretin pretreatment inhibited mitochondrial dysfunction and the activation of caspases. These results demonstrate that the expression of HO-1 induced by phloretin is mediated by both the JNK pathway and Nrf2; the expression inhibits cisplatin-induced apoptosis in HEI-OC1 cells.

Key words:

phloretin, cisplatin, heme oxygenase-1, JNK, caspase
