Cytotoxic effects of cuphiin D1 on the growth of human cervical carcinoma and normal cells

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Abstract

Cuphiin D1 (CD1), macrocyclic hydrolyzable tannin isolated from Cuphea hyssopifolia, has been shown to exert an antitumor effect both in vitro and in vivo. Furthermore, CD1 significantly inhibited the growth of the human cervical carcinoma, i.e. HeLa, cells and showed less cytotoxicity to normal primary-cultured cervical fibroblasts. In this study, we explored the cytotoxic mechanism of CD1 on HeLa cells. The cytotoxic effects of CD1 showed dose-dependency at 3.15-100 micrograms/ml on HeLa for 12, 24, 48 and 72 hours and with an IC50 value at 14.2 micrograms/ml for 48 hours. However, the IC50 value of CD1 in primary-cultured normal cervical fibroblasts was 74.5 micrograms/ml. Therefore, the selectivity shown by CD1 is ascribed to differences in growth speeds between normal and tumor cells. HeLa cells treated with 50 micrograms/ml CD1 for 24 hours exhibited chromatin condensation, indicating the occurrence of apoptosis. Flow cytometric analysis demonstrated the presence of apoptotic cells with low DNA content among HeLa cells. CD1 also caused DNA fragmentation and inhibited Bcl-2, pro-caspase 3, and inactived PARP expression in HeLa cells. These results suggest that the inhibition of Bcl-2 expression in HeLa cells might account for the mechanism of CD1-induced apoptosis.