

Cytotoxic Activity of Coumarins from the Fruits of *Cnidium monnieri* on Leukemia Cell Lines

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Abstract

Cnidii monnieri Fructus [CmF; *Cnidium monnieri* (L.) Cusson] is used as a tonic agent in traditional Chinese medicine. In a previous Chinese herb-cytotoxicity screening test, the ethanol extract of CmF exhibited strong effects on human leukemia (HL-60), cervical carcinoma (HeLa) and colorectal carcinoma (CoLo 205) cells. Then, the CmF extract was subjected to silica gel column chromatography and recrystallization to give five coumarins: osthol, imperatorin, bergapten, isopimpinellin, and xanthotoxin. Among these compounds, osthol showed the strongest cytotoxic activity on tumor cell lines. The structure-activity relationship established from the results indicated that the prenyl group has an important role in the cytotoxic effects. However, imperatorin showed the highest sensitivity to HL-60 cells and the least cytotoxicity to normal PBMCs. Osthol and imperatorin both caused apoptotic bodies, DNA fragmentation, and enhanced PARP degradation in HL-60 cells by biochemical analysis. These results indicate that osthol and imperatorin can induce apoptosis in HL-60 cells. Therefore, osthol and imperatorin are cytotoxic marker substances in the fruits of *Cnidium monnieri*.

Key words

Cnidium monnieri - Umbelliferae - osthol - imperatorin - HL-60 cell - apoptosis