Cuphiin D1, the macrocyclic hydrolyzable tannin induced apoptosis in HL-60 cell line

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Abstract

Cantharidin is isolated from Mylabris phalerata Pallas and is a potent inhibitor of hepatocellular carcinoma cells (Hep 3B cells). In the present study, the IC(50) values of cantharidin on Hep 3B cells and normal Chang liver cells were found to be 2.2 and 30.2 microM for 36 h, respectively. Furthermore, cantharidin-treated Hep 3B cells induced cell death within 1 h (IC(50)=52.8 microM), suggesting that cantharidin is an acute cytotoxic agent. We found that although cantharidin could induce cell death, it could not directly inhibit the activity of nucleic acid biosynthesis by the cellular incorporation of 3H-thymidine, 3H-uridine or 3H-leucine. Cantharidin-treated Hep 3B cells showed no evidence of major alterations in the cell cycle distribution within 1 h. However, examination of cells after treatment for 36 h showed that cantharidin regulated the cell cycle at the G(2)/M phase. Moreover, the treated Hep 3B cells had a rounded and shrunken appearance. The microvilli of treated Hep 3B cells were reduced in number and replaced by numerous blebs. Other ultrastructural changes following cantharidin treatment included the presence of lipid droplets, swelling of the mitochondria and accumulation of glycogen particles. The findings of damaged mitochondria in the cantharidin treated Hep 3B cells in this study suggest that cantharidin can induce acute and lethal toxic effects on Hep 3B cells by inhibiting the mitochondria energy system. In conclusion, this study had demonstrated that cantharidin could inhibit progression of all phases of the Hep 3B cell cycle.