Pentacyclic triterpenoid compounds have various biological effects, such as anti-inflammatory, anti-hyperlipidemia, wound healing and anti-tumor activities. In this study we investigated cytotoxic effects of asiatic acid (AA), a triterpene acid, on human liver cells. AA decreased viability of HepG2 human hepatoma cells in a time- and concentration-dependent manner. Treatment with 40 M AA markedly induced apoptosis in the cells, measured by DNA ladder formation and flow cytometric analysis of hypodiploid DNA stained with propidium iodide and loss of phospholipid asymmetry detected by annexin-V binding. AA also increased intracellular Ca^{2+} level, which was blocked by TMB-8 and dantrolene, intracellular Ca^{2+} release blockers, but not by EGTA, an extracellular Ca^{2+} chelator. Moreover, AA-induced apoptosis was significantly blocked by the co-treatment with TMB-8 and dantrolene, suggesting that intracellular Ca^{2+} release plays an important role in AA-induced apoptosis in HepG2 cells.

[OB-2] [04/20/2001 (Fri) 13:45 - 14:00 / Room 2]

Urushiol Induced Apoptosis and Cell Cycle Arrest in Human Gastric Cancer Cells

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Urushiols are mixtures of olefinic catechols with a n-C15 or n-C17 alkyl side chain which is isolated from the sap of Korean lacquer tree (Rhus vernicifera Stokes). In the previous study, we evaluated the cytotoxic effect of urushiol on MKN-45 and MKN-28 cell lines. Urushiol mediated DNA fragmentation and nuclear condensation only on MKN-45 cells. In the present study we investigated the modulation of the expression of the apoptosis-related proteins after treatment of urushiol on both MKN-45 and MKN-28 cells. In MKN-45 cells the expression levels of Fas and Fas-ligand proteins were increased after treatment of urushiol. The Bcl-2 protein level was not changed but the Bax protein level was slightly upregulated on MKN-45 cells by the treatment of urushiol. In addition, caspase-3 was activated and PARP protein was cleaved on MKN-45 cells by urushiol treatment. In MKN-28 cells Bcl-2 and Bax protein level were not changed by urushiol treatment. Nevertheless, the cyclin-dependent kinase inhibitors, p21WAF1/CIP1 and p27KIP1 proteins, were upregulated on MKN-28 cell by urushiol. And cyclin-dependent kinase 2 and 4 proteins were decreased. The cyclin-dependent kinase inhibitor protein, a key regulatory protein of the cell cycle, may have contributed to cell cycle arrest in the urushiol-treated MKN-28 cells. These data suggested that urushiol induced apoptosis on MKN-45 cells and mediated cell cycle arrest on MKN-28 cells.

Oral Presentations - Field C

[C1. Biochemistry] [C2. Microbiology] [C3. Cell Biology]

[OC-1] [04/20/2001 (Fri) 14:00 - 14:15 / Room 2]

MODULATION OF HUMAN CYTOCHROME P450 3A4 EXPRESSION BY CERAMIDE, A LIPID SECOND MESSENGER