hydroxyl radicals. Whereas adenosine 5'-monophosphate as substrate exhibited a modest protection against the glutathione/Fe^{2+} action, a remarkable protection was expressed by divalent metal ions such as Zn^{2+} or Mn^{2+}. Structure-activity study with a variety of thiols indicates that the inactivating action of thiols in combination with Fe^{2+} resides in the free sulfhydyl group and amino group of thiols. Overall, thiols, expressing more inhibitory effect on the activity of 5'-nucleotidase, were found to be more effective in potentiating the Fe^{2+}-mediated inactivation. These results suggest that ecto-5'-nucleotidase from brain membrane is one of proteins susceptible to thiols/Fe^{2+}-catalyzed oxidation. The work was partly supported by Korea Research Foundation (1998-001-F00772).

[PC1-13] [10/20/2000 (Fri) 15:30 - 16:30 / [Hall B]]

Chemopreventive effect of capsaicin in SK-Hep-1 hepatocellular carcinoma cell line

Chung MY, Kang HJ, and Moon A

College of Pharmacy, Duksung Women's University, Seoul 132-714, Korea

Hepatocellular carcinoma is one of the most lethal malignancies and there is no effective preventive measure in this highly malignant disease to date. In the present study, we investigated the chemopreventive potential of capsaicin (8-methyl-N- vanillyl-6-nonenamide), the principal pungent ingredient found in hot red pepper, in SK-Hep-1 hepatocellular carcinoma cells. Treatment of capsaicin inhibited growth of SK-Hep-1 cells in a concentration-dependent manner, with an IC_{50} value of 119 uM. Methoxy-capsaicin was less potent (IC_{50} of 264 uM), indicating that the hydroxyl group of capsaicin is important in growth-inhibitory property of capsaicin. This study reveals that the inhibitory effect of capsaicin on SK-Hep-1 cell growth is mainly due to the induction of apoptosis as evidenced by DNA fragmentation and nuclear condensation. In order to investigate the molecular mechanisms of capsaicin-induced apoptosis, we examined the effect of capsaicin on anti-apoptotic Bcl-2 and pro-apoptotic Bax levels. We show that capsaicin prominently reduced the ratio of Bcl-2 to Bax which may trigger apoptosis in SK-Hep-1 cells. We also show that caspase-3 activity may be involved in capsaicin-induced apoptosis. These results demonstrate that capsaicin efficiently induced apoptosis in SK-Hep-1 cells, suggesting an effective strategy for hepatocellular carcinoma chemoprevention.

[PC1-14] [10/20/2000 (Fri) 15:30 - 16:30 / [Hall B]]

Induction of apoptosis by 3,4'-dimethoxy-5-hydroxystilbene in human myeloid leukemic HL-60 cells

Young Jin Chun°, Sung Hee Lee, Shi Yong Ryu†, Han Bok Kim‡, and Mie Young Kim

College of Pharmacy, Chungang University, Seoul 156-756; †Korea Research Institute of Chemica Technology (KRICT), Taejon 305-600; ‡Department of Life Science, Hoseo University, Asan, Chungnam 336-795.

3, 4···-Dimethoxy-5-hydroxystilbene (DMHS) is a hydroxystilbene compound obtained by methylation and acid hydrolysis of piceid (resveratrol-3-O-glucoside) from *Polygonum cuspidatum*. Herein, we report that DMHS induces programmed cell death or apoptosis in human promyelocytic leukemic HL-60 cells. We found that treatment of HL-60 cells with DMHS suppressed the cell growth in a concentration-dependent manner with IC_{50} value of 25 uM. DMHS increased the apoptosis characterized by internucleosomal DNA fragmentation and nuclear condensation. The cell death by DMHS was partially prevented by the caspase inhibitor, zVAD-fmk. DMHS caused activation of caspases such as caspase-3, -8, and -9. Immunoblot experiments revealed that DMHS-induced apoptosis was associated with the