UDCA and HS-1030 increased sub-G1 population. HS-1199 and HS-1200 also increased G1 phase population. In DNA fragmentation assay, the cells were harvested at 24 and 48 hr after the synthetic of bile acids. As results, UDCA, CDCA, HS-1030, HS-1183 and HS-1199 shows DNA ladders but not HS-1200. Western blotting performed using poly(ADP-ribose) polymerase, Bax, p53, p27, caspase-3, and cyclin E, cyclin B and -actin. In Western blots, UDCA, CDCA, HS-1030, HS-1183 lead to apoptosis. And HS-1200 shows G1 cell cycle arrest manners, interestingly only HS-1200 increased Bax level.

Effect of Synthetic Bile Acid Derivatives on the Cell Cycle Modulation of HT-29 Human Colon Cancer Cells

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We studied the effects of ursodeoxycholic acid (UDCA) and its synthetic derivatives, HS-1030 and HS-1183, and chenodeoxycholic acid (CDCA) and its synthetic derivatives, HS-1199 and HS-1200, on the human colon adenocarcinoma cell line, HT-29 (p53 mutant type). The effects on cell viability and growth were assessed by MTT assay and cell growth study. While UDCA and CDCA exhibited no significant effect, their novel derivatives inhibited the proliferation of HT-29 cell line in a concentration- and time-dependent manners. Especially, HS-1199 and HS-1200 showed the most significant anti-proliferative effects on HT-29 cell line. According to propidium iodide staining and flow cytometry analysis, this effect may be a result from S cell cycle arrest. Furthermore, we observed the level of cyclin-dependent kinase inhibitor p21 was increased after the treatment of HS-1183, HS-1199, and HS-1200. The findings suggest that these cytotoxic effects of novel bile acid derivatives on human colon adenocarcinoma cells were mediated via apoptosis through a p53-independent pathway.

Effects of cationic polyamines under 10 kD range of molecular weight on basic and induced mucin release from airway goblet cells

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In this study, we tried to investigate whether polymerized basic amino acid e.g. poly-L-lysine(PLL) which has the molecular weight under 10 kD significantly affects the physiological and stimulated mucin release from cultured hamster tracheal surface epithelial cells. Confluent primary hamster tracheal surface epithelial(HTSE) cells were metabolically radiolabeled with 3H-glucosamine for 24 hr and chased for 30 min in the presence of either PLLs or adenosine triphosphate(ATP) and PLL to assess the effects on basic or ATP-stimulated 3H-mucin release. Possible cytotoxicities of PLLs were assessed by measuring lactate dehydrogenase(LDH) release from HTSE cells during treatment. The results were as follows : (1) PLLs significantly inhibited basic mucin release from cultured HTSE cells in a dose-dependent manner from the range of 46mer(M.W. 9,600) to 14mer. (2) PLL 46mer significantly inhibited the stimulated mucin release by ATP from cultured HTSE cells. (3) there was no significant release of LDH from cultured HTSE cells during treatment. We conclude that PLLs inhibit