of them decreased TEER value and increased the permeability of heparin disaccharides in a dose-dependent and time-dependent manner. Furthermore, there was difference among these compounds with respect to absorption enhancing activity and cytotoxicity. Phytolaccoside B and E showed both drastical enhancing activity and severe cytotoxicity. In case of phytolaccoside G, it had no significant enhancing effect and cytotoxicity as compared to the control. Phytolaccoside F and I had mild enhancing effects and cytotoxicity. Phytolaccoside D_2 had an absorption enhancing effect without severe cytotoxicity. In considering the mechanisms, Phytolaccoside F and I seemed to regulate the tight junction permeability via both IP_3- and DAG-pathways. On the other hand, phytolaccoside B and D_2 showed the effects by IP_3-pathway and the absorption enhancing effect of phytolaccoside E was not affected by inhibitors except BAPTA. It may increase the intracellular Ca^{2+} level by other mechanisms in modulating the paracellular permeability. Our results indicate that a series of phytolaccosides from *Phytolacca americana* may be applied as absorption enhancers which can increase the paracellular transport of hydrophilic compounds such as glycosaminoglycans and protein/peptide drugs.

[PC3-4] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

Induction of p21WAF1/Cip1 expression via Sp1 sites by apicidin is mediated by Sp3

Ahn SH, Bae GU, Hong SY*, Lee HY#, Han JW and Lee HW

Department of Biochemistry, College of Pharmacy, *Department of Genetic Engineering, College of Life Science and Natural Resources, Sungkyunkwan University, #Department of Pharmacology, College of Medicine, Konyang University

We previously reported that apicidin, a novel histone deacetylase inhibitor, inhibits proliferation of tumor cells via induction of $p21^{WAF1/Cip1}$ and gelsolin. In this study, we tried to determine the molecular mechanisms by which apicidin induce $p21^{WAF1/Cip1}$ gene activation in HeLa cells. Apicidin treatment induced $p21^{WAF1/Cip1}$ mRNA independently of de novo protein synthesis and activated the $p21^{WAF1/Cip1}$ promoter through two Sp1 sites located at -82 and -69 relative to the transcription start site. Although, Sp1 and Sp3 have been shown to be the major factors binding to the Sp1 site of $p21^{WAF1/Cip1}$ promoter as measured by EMSA, apicidin did not alter their DNA binding activities. Moreover, Sp3, but not Sp1, mediated apicidin-mediated transcriptional activation of $p21^{WAF1/Cip1}$ gene promoter, whereas both Sp1 and Sp3 were suppressive in the absence of apicidin treatment. Taken together, these results demonstrate that Sp3 mediates the transcriptional activation of the $p21^{WAF1/Cip1}$ gene promoter by apicidin via Sp1 site in HeLa cells.

Poster Presentations - Field D1. Medicinal Chemistry

[PD1-1] [04/20/2001 (Fri) 13:30 - 14:30 / Hall 4]

Synthesis and Application of Dimeric Cinchona Alkaloid Phase-Transfer Catalysts: a,a'-Bis[O(9)-allylcinchonidinium]-o, m, or p-xylene dibromide

Sang-sup Jew,* Byeong-Seon Jeong°, Mi-Sook Yoo, Hoon Huh and Hyeung-geun Park*

College of Pharmacy, Seoul National University, Seoul 151-742, Korea