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

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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

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A dimeric Cinchona alkaloid ammonium salt, a,a'-bis[O(9)-allylcinchonidinium]-m-xylene dibromide, has been developed as a new efficient phase transfer catalyst; the catalytic enantioselective alkylation of N-(diphenylmethylene)glycine tert-butyl ester proceed in a high enantiomeric excess (90~99% ee).

[PD1-2] [04/20/2001 (Fri) 13:30 - 14:30 / Hall 4]

Synrthesis and antiviral activity of 2'-UP-azido-2',3'-dideoxy-4'-thionucleosides

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Since the discovery of D-3'-azido-3'-deoxythymidine (AZT) as potent anti-AIDS drug, many D-2',3'-dideoxynucleosides with various substituents such as fluoro or azido group at C2 or C3 position have been synthesized and evaluated for antiviral activities. Among these compounds, D-2'-UP-azido-2',3'-dideoxynucleosides have exhibited very potent anti-HIV activity. Based on the bioisosteric rationale, we have been interested in synthesizing the corresponding D-2'-UP-azido-2',3'-dideoxy-4'-thionucleo-sides and comparing their antiviral activities. The target nucleosides were synthesized from the condensation of nucleoside bases with D-4-thiosugar acetate. Synthesis of 4-thiosugar acetate was started from L-xylose which was converted to the 4-thioarabitol derivative. The key step, azidation was completed by mesylation of the alcohol followed by treating with sodium azide. Azidation was proceeded with retention of stereochemistry unlike DAST fluorination. Finally synthesis of sugar acetate was accomplished by oxidation to the sulfoxide followed by Pummerer rearrangement. Using this sugar acetate, we have obtaineded variuous pyrimidine and purine nucleosides and evaluated them for antiviral activities. Most of the synthesized compounds were found to be slightly active but they were cytotoxic, too. So, antiviral activities were originated from inherent cytotoxicity of the synthesized compounds.

[PD1-3] [04/20/2001 (Fri) 13:30 - 14:30 / Hall 4]

Synthesis of Sweet Sesquiterpene, (+)-Hernandulcin

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(+)-Hernandulcin was isolated as a sweet bisabolane sesquiterpene constituent of an aztec herb Lippia dulcis Trev. (Verbenaceae). It has shown to be 1,000 times as sweet as sucrose and non-toxic to human. The absolute stereochemistry of (+)-hernandulcin was determined by Mori et al., in 1985 by means of synthesizing all of the four possible stereoisomers. A concise synthesis of (+)-hernandulcin from (-)-isopulegol is reported here. Selective epoxidation followed by opening of the epoxide with prenyl Grignard, which was prepared from prenyl chloride and magnesium in the presence of purified cuprous iodide, afforded the tertiary alcohol with correct stereochemistry. Oxidation of the secondary alcohol and double bond formation provided (+)-hernandulcin.

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

Synthesis and Biological Activity of FTase Inhibitors Containing Isoleucyl Surrogates