R&D Center of Pharmaceuticals, Institute of Science & Technology, CJ Corporation, 522-1, Dokpyong-ri, Majang-myon, Ichon-si, Kyonggi-do 467-810

Prostaglandins are synthesized by the enzyme cyclooxygenase (COX). Both constitutive (COX-1) and inducible (COX-2) isoforms have been identified. COX-2 expression is stimulated by inflammatory mediators such as growth factors and cytokines. Most non-steroidal anti-inflammatory drugs (NSAIDS) inhibit both isoforms of COX. Recent evidence suggests that selective inhibitors of COX-2 may possess diminished side effects relative to common NSAIDS. Novel isothiazoles and isoxazoles were identified as selective inhibitors of cyclooxygenase-2 (COX-2).
We synthesized those compounds in general and flexible methods. And we report here the results of SAR (Structure & Activity Relationships) study of both isothiazole and isoxazole derivatives.

[PD1-48] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

Synthesis of Novel Dimethylcyclopropyl Nucleosides as Potential Antiviral Agents

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The carbocyclic nucleosides have extensively studied as a promising antiviral agents having chemical and metabolical stability. In our research program for discovery of antiviral drugs, some novel dimethylcyclopropyl nucleosides possessing additional methyl spacer between purine bases and the ring was synthesized. The important intermediate, dimethylcyclopropyl alcohol was synthesized from ethyl chrysanthemate via its ozonolysis, isomerization, reduction, its protection using TBDPSCl and reduction of the ethyl ester by DIBAL-H gave the silylated cyclopropyl alcohol in good yield, which was condensed with purine bases by Mizunov reaction to give some cyclopropyl nucleosides after deprotection.

[PD1-49] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

CoMFA of 1-phenyl-2-substituted thioureas for their cytotoxicity

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The structure of 1-phenyl-2-substituted thiourea derivatives have been studied and optimized for their cytotoxic activity. The three dimensional quantitative structure activity relationship (3D-QSAR) was investigated using comparative molecular field analysis (CoMFA). The result suggested that electrostatic and steric factors of 2-alkylureido-1-phenyl propanol derivatives were correlated well with cytotoxic activity.

[PD1-50] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

Molecular Dynamics Simulation of Enantioselectivity in Metoprolol in complex

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Metoprolol (MT) is one kinds of adrenergic beta-blockers. Its (S)-enantiomer is known to be more active than the (R). Recently, the x-ray structure of beta-blocker, (S)-propranolol (a-naphthyl analogue), complexed in a mould fungal cellulase, Cel7A, was reported and the (R)-form did not build any complex. And in our previous study the conformation and stability of MT in carboxymethylated beta-cyclodextrin (BCD) complex was determined by NMR, HPLC, UV and electrophoresis measurement. Optically active BCD is often used as a chiral selector for the separation of drug enantiomers. From this study (R)-MT complex was found to be more stable than the (S)-MT