6-benzthiazolesulfonyl chloride and determined the biological activities. Many benzthiazolesulfonamide inhibitors have a potent inhibitory activity with the IC50 value of nM against MMP-2/MMP-9 along with very good selectivity against MMP-1 and some inhibitor has a good pharmacokinetic profile.
In this meeting, we will discuss the design, synthesis, and activity of the highly selective inhibitors of MMP-2 and MMP-9.

[PD1-18] [04/20/2001 (Fri) 13:30 - 14:30 / Hall 4]

Design and Synthesis of the Highly Selective Inhibitors of Type IV Collagenase(MMP-2 and MMP-9) of Benzthiazolesulfonamide Derivatives I

Bae HY, Min HK, Kim KC, Ryu CH, Lee JW, Paek SH, Park YJ, Chae MY, Yoo JU

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Matrix metalloproteinases (MMPs) are a family of Zinc endopeptidase that are capable of hydrolyzing the extracelluar matrix of connective tissues and basement membranes. Although their roles in the normal and pathological turnover of these tissues are not completely understood, the elevated levels of these enzymes, particularly MMP-3 and MMP-1, found in the synovium and cartilage of rheumatoid arthritis patients have suggested a role for these enzymes in this disease process. MMP-2 and MMP-9 are particularly proficient at degrading basement membranes and are thought to play a role in tumor metastasis and angiogenesis.
We have focused on the discovery of potent, selective, and oral absorptive inhibitors of MMP-2/MMP-9. By structure-activity relationship studies and structural analysis, we have discovered that 2-alkyl, arylthio-6-benzthiazolesulfonyl moieties are very useful substituent for S1'sub-site in enzymes. Various inhibitors are synthesized by the reaction of simple amino acid with 2-alkyl, arylthio-6-benzthiazolesulfonyl chloride and determined the biological activities.
In this meeting, we will discuss the design, synthesis, and activity of the highly selective inhibitors of MMP-2 and MMP-9.

[PD1-19] [04/20/2001 (Fri) 13:30 - 14:30 / Hall 4]

Design and Synthesis of the Highly Selective Inhibitors of Type IV Collagenase(MMP-2 and MMP-9) of Biphenylbutyric Acid Derivatives

Ryu CH, Min HK, Kim KC, Bae HY, Lee JW, Paek SH, Park YJ, Chae MY, Yoo JU

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Matrix metalloproteinases (MMPs) are a family of Zinc endopeptidase that are capable of hydrolyzing the extracelluar matrix of connective tissues and basement membranes. Although their roles in the normal and pathological turnover of these tissues are not completely understood, the elevated levels of these enzymes, particularly MMP-3 and MMP-1, found in the synovium and cartilage of rheumatoid arthritis patients have suggested a role for these enzymes in this disease process. MMP-2 and MMP-9 are particularly proficient at degrading basement membranes and are thought to play a role in tumor metastasis and angiogenesis.
We have focused on the discovery of potent, selective, and oral absorptive inhibitors of MMP-2/MMP-9. By structure-activity relationship studies, we found that N-substituted-5-(biphenyl-4-yl)-5-oxo-3-carboxylvaleric amide derivatives exhibited inhibitory activity with the IC50 value of nM against MMP-2 and some inhibitor has a good pharmacokinetic profile.
In this meeting, we will discuss the design, synthesis, and activity of the highly selective inhibitors of MMP-2 and MMP-9.