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Structure-activity relationship studies of allylamine type of antimycotics were carried out to evaluate the effect of naphthyl and methyl portion of naftifine. Compounds with 4-fluorphenyl, 2-fluorophenyl, 2,4-dichlorophenyl, 2,6-dichlorophenyl, 4-nitrophenyl, and 2,3-dihydro-benzo[1,4]dioxin-6-yl instead of naphthyl group with hydrogen, methyl, and ethyl in the place of methyl in naftifine were synthesized and tested their in vitro anti-fungal activity against five different fungi. Eight compounds showed significant antifungal activity against T. mentagrophytes. (E)-N-ethyl-(3-phenyl-2-propenyl)-4-nitro-benzenemethaneamine displayed moderate antifungal activity against all five different fungi.

[PD1-53] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Total Synthesis of New Apicidin Derivatives as Potent Antitumor Agents

hyungkyo kim°
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The antiparasitic agent apicidin, which was recently isolated from cultures of Fusarium Pallidoroseum, belongs to a rare group of cyclictetrapeptide fungal metabolites. Apicidin inhibits protozoal HDAC and is orally active against Plasmodium berghei malaria in mice. The biological activity of apicidin appears to be attributable to inhibition of apicomplexan HDAC at low nanomolar concentrations. In the present, we have worked about the synthesis of new apicidin derivatives and discovered that apicidin and some derivatives have mild antitumor activity. They caused the change of tumor cells to normal ones in morphology. As part of our program toward the development of new antitumor agents, we designed and synthesized several cyclictetrapeptide compounds, especially the side chain moiety of Apicidin. A key step in this synthesis is the coupling reaction of ethylvinyl ketone and iodide, prepared from the appropriately protected L-serine.In this presentation, we will report the total synthesis of these Apicidin analogues.

[PD1-54] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Synthesis and BK_{Ca}-channel Opening Activity of Substituted 10-H-Benzo[4-5]furo[3,2-b]indole-carboxylic acids

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Large-conductance Ca^{2+} activated potassium channels (BK_{Ca}) are widely distributed and play key roles in various cell functions. In nerve cells, BK_{Ca} channels shorten the duration of action potentials and block Ca^{2+} entry thereby repolarizing excitable cells after excitation. BK_{Ca} channel opening has been postulated to confer neuroprotection during stroke and has attracted attention as a means for therapeutic intervention in asthma, hypertension, convulsion, and traumatic brain injury. Several novel benzofuroindole derivatives are prepared and evaluated as openers of the cloned BK_{Ca} channel macroscopic and single channel level rSlo channels expressed in Xenopus laevis oocytes by utilizing electrophysiological methods. From this study a potent BK_{Ca} channel opener (LDD 108) was identified as an effective opener in heterogeneous expression system.

[PD1-55] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Synthesis of Novel 3-(H or aralkyl)-1-phenyl-5-(p-H or halo)phenyl-2-thiohydantoins as Selective COX-2 Inhibitors

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Nonsteriodal antiinflammatory drugs(NSAIDs) are widely used to treat pain, fever, and inflammatory conditions

including osteoarthritis. But chronic patients suffer from gastrointestinal disturbances such as discomfort, nausea, peptic ulcer and severe bleeding because NSAIDs inhibit not only COX-2 associated with anti-inflammatory activity, but also COX-1 accompanied with side effects in the stomach and kidney. Therefore, in this study, we designed a new 2-thiohydantoin derivatives as selective COX-2 inhibitors is that the 5-membered heterocycle ring is substituted with two aryl groups. These compounds were prepared through esterification, bromination, C-N bond formation and cyclization from commercially available (p-H or halo)phenylacetic acid. 1,5-Diaryl-2-thiohydantoin ring was synthesized through methyl α-(p-H , methoxy, sulfamyl)phenyl-(p-H or halo)phenylacetates with potassium isothiocyanate. Particularly, N-aralkylgroup could be introduced in 3-position of 2-thiohydantoin ring by one-pot reaction of methyl α-(p-H, methoxy, sulfamyl)phenyl-(p-H or halo)phenylacetates with aralkyl isothiocynate.

[PD1-56] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Structure Activity Relationships of Thiazole and Thiadiazole Derivatives as Potent and Selective Human Adenosine A_3 Receptor Antagonists

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4-(4-Methoxyphenyl)-2-aminothiazole and 3-(4-methoxyphenyl)-5-aminothiadiazole derivatives have been synthesized and evaluated as selective antagonists for human adenosine A_3 receptors. A methoxy group in the 4-position of the phenyl ring and N-acetyl or propionyl substitutions of the aminothiazole and aminothiadiazole templates displayed great increases of binding affinity and selectivity for human adenosine A_3 receptors. The most potent A_3 antagonist of the present series, N-[3-(4-methoxy-phenyl)-[1,2,4]thiadiazol-5-yl]-acetamide exhibiting a K_i value of 0.79 nM at human adenosine A_3 receptors, showed antagonistic property in a functional assay of cAMP biosynthesis involved in one of the signal transduction pathways of adenosine A_3 receptors. Molecular modeling study of conformation search and receptor docking experiments to investigate the dramatic differences of binding affinities between two regioisomers of thiadiazole analogs, N-[3-(4-Methoxyphenyl)-[1,2,4-thiadiazole-5-yl]-acetamide and N-[5-(4-Methoxyphenyl)-1,3,4-thiadiazole-2-yl]-acetamide, suggested possible binding mechanisms in the binding pockets of adenosine receptors.

[PD2-1] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

Antioxidant activity compounds from Euryale ferox

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Seeds of Euryale ferox have been used for disorder of kidney, hysterorrhea of female and a tonic. In this study, in order to investigate the efficacy of antioxidant activity, the bio-activity guided fraction and isolation of physiologically active substance were performed. Roots, stems, flowers(seeds) were extracted with MeOH and each fractions were examined antioxidant activity by DPPH method. It was revealed that flowers(seeds) frtion has significantly antioxidant activity. From flowers(seeds) frction, H_2O, 30%, 60%, 100% MeOH and acetone fractions were examined antioxidant activity by DPPH method. It was revealed that 30% MeOH frtion has significantly antioxidant activity. From 30% MeOH fraction, three phenolic compounds (methyl gallate, 1-O-galloyl-2,3-HHDP-α-D-glucose, gallic acid) were isolated. To investigate the antioxidant activities of each compounds, we were measured radical scavening activity with DPPH method and anti-lipid peroxidative efficacy on low density lipoprotein(LDL) with TBARS assay.

[PD2-2] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]