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Interleukin (IL)-5 appears to be one of the main proinflammatory mediators among a growing number of cytokines and chemokines that induce eosinophilic inflammation. Sophoricoside and their analogs isolated from Sophora japonica show relatively potent inhibitory activity of interleukin (IL)-5 as a small molecule. To identify structural requirements of this isoflavonone for its inhibitory activity against IL-5, isoflavonones, isoflavanones, and their glycosides were prepared and tested their inhibitory activity against IL-5. Among them, 5-benzyloxy-3-(4-hydroxyphenyl)chromen-4-one (87.9 % inhibition at 50 μM, IC50 = 15.3 μM) shows the most potent activity, which is compatible activity with that of sophoricoside. The important structural requirements of these isoflavonone analogs exhibiting the inhibitory activity against IL-5 were recognized as 1) planarity of chromen-4-one ring, 2) existence of phenolic hydroxyl at 4-position of B ring, and 3) introduction of benzyloxy at 5 position, which may act as a bulky group for hydrophobic pocket in putative binding site. However glucopyranosyl moiety of sophoricoside would not be critical for the activity.

[PD1-45] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

Design, Synthesis and Biological Activities of Novel Vanilloid Receptor (VR) Agonists and Antagonists

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Recently, we have reported that several lipoxygenases products directly activate the capsaicin-activated channel as intracellular messengers in neuron. In particular, 12-(*S*)-hydroperoxyeicosatetraenoic acid turned out to be the most potent endogenous VR activator. This finding prompted us to search for a novel non-vanilloid VR agonists and antagonists. We have designed and synthesized a series of non-vanilloid VR binding ligands based on the structural similarity between 12-HPETE and capsaicin, the natural VR agonist. Our recent studies on the development of selective vanilloid receptor agonists and antagonists will be presented.

[PD1-46] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

Synthetic Approaches to Benzophenanthridines

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Benzo[c]phenanthridine alkaloids occurring in the Fumariaceae, Papaveraceae, and Rutaceae, posses numerous pharmacological activities, such as antitumor, antimicrobal and antifungal activities. Thus, they have attracted much interests of chemists and as the result, several total syntheses of these heterocycle structure were accomplished. Among that, procedures which involve 3-arylisoquinoline intermediates are useful methods and these synthons could be also applied to the preparation of other alkaloids. We have recently reported the convenient synthesis of benzophenanthridine skeleton via cyclization of 3-arylisoquinoline intermediate. In continuing research, the synthetic approaches to natural benzophenanthridines and its derivatization were carried out.

[PD1-47] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

EFFECTS OF ISOTHIAZOLE AND ISOXAZOLE DERIVATIVES AS SELECTIVE CYCLOOXYGENASE-2 INHIBITORS

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