Synthesis and cyclooxygenase-2 inhibitory activity of tetrahydroaminoacridine and their analogues

Shin HS°, Kang JY, Park MS, Kwon SK

College of Pharmacy, Duksung Women's University

A series of tetrahydroaminoacridine and their analogues were synthesized. Tetrahydroaminoacridine(tacrine) is an anticholinesterase agent used in the treatment of Alzheimer's disease. Introduction of piperidine group at the para position enhanced anti-inflamatory activity for Alzheimer's disease. We investigated their ability to inhibit cyclooxygenase-1 and 2 isoforms. This series has shown potent in vitro inhibition of the enzyme cyclooxygenase-2 with % inhibition = 70.3~23.6 at 10 μg/ml. Compound 3b was the most potential inhibitor with an IC_{50}s = 15.6 μg/ml. Compound 3a and 3c displayed weak in vitro inhibition of cyclooxygenase-2 with IC_{50}s 20.2~29.2 μg/ml. The most potent analogues in this series was compound 3b with a cyclooxygenase inhibitory activity of 1/2 in excess of 5 times. These data indicate that compound 3b is an cyclooxygenase-2 inhibitor with good selectivity profile when compared with tetrahydroaminoacridine.

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The Role of Korea Chemical Bank in "Hit to Lead" process of Drug Discovery

kim sunwoo°, Kim Dongwook, Kim Sunho, Choi Yeon-joo, Kim Jooyoung, Han Mijung, Kim Okekil, Kil Kyong-ok, Kim Sungsoo

Korea Research Institute of Chemical Technology

The Korea Chemical Bank (KCB) has more than 80.000 compound collections, provided from many companies, academies and institutes. KCB has supported high-throughput screening (HTS) against 80 biological targets and identified a number of hits over 20 targets. These hits were first validated by confirming the purity and novelty of anticipated compound. We also determined their physiochemical properties. Information about structure/activity relationship (SAR), ADME, and 3D-QSAR in each compound was precisely examined and collected from molecular databases. Furthermore, we searched recent research trends for all biological targets screened. All of accumulated information were then provided to the drug development programs, which were organized in industries or institutes. Many screening hits are nonspecific (false positive). This is a serious problem in drug discovery. We recently found that many nonspecific hits from drug discovery screening projects have certain chemical structures and that they are often appeared as hits in every screening target. These data were also informed to research groups for successful lead generation. This post includes several success cases for "hit to lead" as well as a role of KCB in this process.

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3-D QSAR Studies on Thiazole and Triazole Antifungal Agents by CoMFA and CoMSIA

Thai Khac Minh°[1], Tran Thanh Dao[2], Park Hyun-Ju[1]

[1]College of Pharmacy, Sungkyunkwan University, Suwon 440-746, Korea; [2]College of Pharmacy, Kangwon National University, Chunchon 200-701, Korea