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Adenylyl Cyclase Inhibitors for Neuropathic and Inflammatory Pain Treatment

A novel series of adenylyl cyclase type 1 (AC1) inhibitors, producible through efficient synthesis, offers a potential first-in-class therapeutic option for neuropathic and inflammatory chronic pain with minimized side effects.

Chronic pain, such as neuropathic pain, is common in multiple diseases and is a major health concern. Due the multifaceted nature of pain, its basic mechanism is poorly understood; therefore, current therapies are do not meet the needs of many patients. Researchers have identified adenylyl cyclase type 1 (AC1) as a potential target for pain therapy. This enzyme is present in neurons, but not in heart, liver, or kidney cells, which would minimize side effects of AC1 inhibitors to non-neuronal tissues. Currently, only one inhibitor against AC1, called NB001, has been identified. There is a need to identify new therapeutics that target AC1.

Researchers at Purdue University have developed a series of compounds that inhibit AC1 in cell culture with IC50 values in the low micromolar range. In addition, these new AC1 inhibitors can be produced via mild and efficient reaction chemistry with high regioselectivity, stereoselectivity, and excellent yield. This new technology will not only facilitate chronic pain therapy but provides an effective synthetic route to optimize these lead compounds.

Advantages:

-Potential first in class therapeutic for neuropathic and inflammatory pain

-Fewer predicted side effects

Potential Applications:

-Chronic pain therapy

-Pharmaceutical industry

Related Publication:

Technology ID

2015-DAI-67035

Category

Pharmaceuticals/Small Molecule Therapeutics

Pharmaceuticals/Pharmaceutical Manufacturing & Methods

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Zhishi Ye et al., Palladium-Catalyzed Regio- and Stereoselective Î³-Arylation of Tertiary Allylic Amines: Identification of Potent Adenylyl Cyclase Inhibitors

Org. Lett., 2015, 17 (4), pp 892â€“895

TRL: 3

Intellectual Property:

Provisional-Patent, 2015-02-16, United States | Utility Patent, 2016-02-16, United States | CON-Patent, 2018-03-14, United States

Keywords: Chronic pain therapy, neuropathic pain, adenylyl cyclase type 1, AC1 inhibitors, pharmaceutical industry, lead compounds optimization, inflammatory pain, AC1 antagonist, efficient synthetic route, cell culture inhibitors