

N,N-dialkyl-4-(2-ethylindan-2-yl)-1*H*-imidazole-1-carboxamides and related compounds for treatment of neurodegenerative diseases

Field of use

Medical sciences

Current state of technology

Preclinical studies

Intellectual property

Patent application filed

Developed by

University of Ljubljana,
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Reference

821-20/2022

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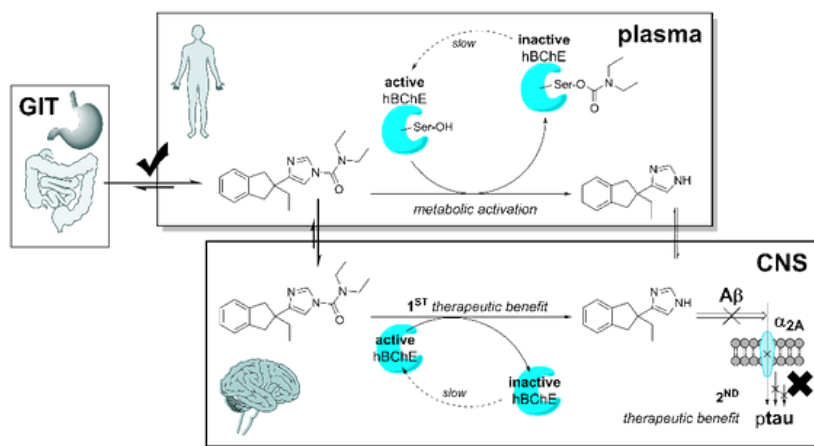
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Background

The most common type of dementia, Alzheimer's disease, is a neurodegenerative disease characterized by a progressive decline of memory and other cognitive functions due to a plethora of pathological changes in the central nervous system. By some estimates, over 50 million people are currently beset by Alzheimer's disease, with many more to follow due to the aging of the world's population. Therefore, new and efficient therapies are urgently needed to alleviate the disease's toll on the patients, their loved ones, and healthcare systems.

Description of invention

The invention relates to imidazole-1-carboxamides that have a dual mode of action – i.e., act as α_2 adrenoreceptor antagonists and cholinesterase inhibitors, as disease-modifying treatment for Alzheimer's disease and other neurodegenerative diseases. The present invention is currently being tested in animal models of neurodegenerative diseases, and our goal is to further develop it for human application.



Main advantages

The compounds presented act as pleiotropic prodrugs, which undergo metabolic activation with butyrylcholinesterase (pseudo-irreversibly inactivating the enzyme in the process, thus achieving the first therapeutic effect) to liberate the adrenergic antagonist atipamezole. The latter binds to α_2 adrenoreceptors in the brain, blocking their activation by amyloid β oligomers, and so prevents tau hyperphosphorylation further down the signalling cascade (second therapeutic effect).

Thus, our drug candidates act through different and innovative mechanisms that are expected to have a disease-modifying effect in addition to the transient improvement of the patients' cognitive status.