Coumarin-Rasagiline Hybrids as Potent and Selective hMAO-B Inhibitors, Antioxidants, and Neuroprotective Agents

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The frequency, complexity and morbidity of neurodegenerative diseases make them a great challenge for nowadays medicine. Most of the treatments currently used for Parkinson's disease ? the second most prevalent ? are only symptomatic. Therefore, it is urgent to develop drugs that are able to act simultaneously on different targets, being able to stop neuronal death and promote the recovery of neuronal populations already affected. In this work, we studied the activity of a series of hybrid molecules, which combine the structure of both coumarin and an alkynylamine group inspired on rasagiline, as MAO inhibitors, antioxidants and neuroprotective agents. Half of the studied hybrids turned out to be selective monoamine oxidase B (hMAO-B) inhibitors in the low micro/nanomolar range, demonstrating that positions 3 (compounds 1?3) and 7 (compounds 8 and 10) of the coumarin scaffold are the most suitable for the incorporation of the alkynylamine chain. All the studied compounds proved to be capable of neutralizing free radicals (DPPH). Finally, the 4-(but-2-yn-1-ylamino)coumarin (5) showed neuroprotective effects on glial cells and the 4-methyl-7-(pent-2-yn-1-ylamino)coumarin (8) inhibited intraneuronal ROS production as well.

Antioxidants

Coumarin-rasagiline hybrids

hMAO-B inhibitors

Neuroprotectors

Parkinson's disease

4 (but 2 yn 1 ylamino)coumarin

amine oxidase (flavin containing) isoenzyme B

antioxidant

coumarin

monoamine oxidase inhibitor

neuroprotective agent

rasagiline

unclassified drug

animal experiment

antioxidant activity

Article

DPPH radical scavenging assay

embryo

enzyme inhibition

neuroprotection

nonhuman

priority journal

rat