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Abstract

(2-Imidazolin-4-yl)phosphonates: Green Chemistry and Biology Walk Together †

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2-Imidazoline-containing compounds constitute a valuable class of agents that modulate α_2-adrenergic receptors and often show a high affinity for imidazoline I_2-receptors (I_2-IR). Moreover, 2-imidazolines are an important class of heterocyclic scaffolds found in natural product chemistry, coordination chemistry, and homogeneous catalysis. To meet the demand for 2-imidazoline-containing compounds, different synthetic approximations were developed. In this work, we describe an efficient and user-friendly synthetic process involving the combination of isocyanide-based multicomponent reaction and microwave heating without the need of anhydrous atmosphere or additional solvents that generates unprecedented (2-imidazolin-4-yl)phosphonates [1].

We assessed the pharmacological profile and selectivity of the prepared compounds upon I_2-IR. Owing to the outstanding high I_2-IR affinity of one of the prepared compounds and high selectivity devoid to the α_2-adrenoceptor of other compounds, markedly better than any described I_2-IR ligand to date, (2-imidazolin-4-yl)phosphonates might be considered as a suitable scaffold for designing novel I_2-IR ligands [2]. In addition, we demonstrated the effectiveness of two of the new I_2-IR ligands in an in vivo female model for cognitive decline (SAMP8), and we analyzed the pathological biomarkers for neurodegeneration. This study is the first experimental evidence that demonstrates the possibility of using this receptor as a target for cognitive impairment [3].

Note, theoretical studies were carried out for designing compounds with enhanced activity and selectivity upon I_2-IR based on created 3D-QSAR model.

In this work, green chemistry to access an unprecedented scaffold and promising pharmacological results in the neurodegeneration field walked together.

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