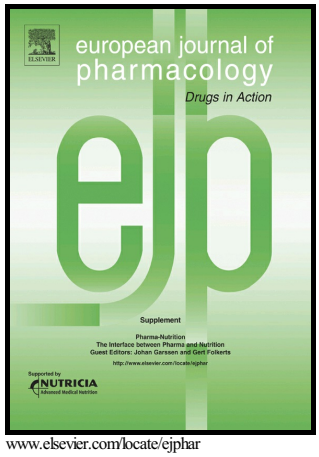

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In vivo and in vitro ADMET profiling and in vivo pharmacodynamic investigations of a selective α7 nicotinic acetylcholine receptor agonist with a spirocyclic Δ^2-isoxazoline molecular skeleton

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Abstract

(±)-3-Methoxy-1-oxa-2,7-diaza-7,10-ethanospiro[4.5]dec-2-ene sesquifumarate (±)-**1** was previously characterized as the most selective agonist at α7 neuronal nicotinic acetylcholine receptors in a series of spirocyclic quinuclidinyl-Δ^2-isoxazoline derivatives. In this study, we performed different in vitro biological assays aimed at characterizing the ADMET properties of (±)-**1**. Then, we tested the compound in vivo in behavioral studies including classical novel object recognition and inhibitory avoidance tests in the rat, and a spatial memory assay in zebrafish involving a rapid T-maze task. The results indicated an overall favorable profile for (±)-**1** in view of potential therapeutic applications targeting the central nervous system.

Keywords: α7 Nicotinic acetylcholine receptors - Agonist - eADMET - Novel object recognition test - Episodic memory passive avoidance test - Learning/memory in zebrafish

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