Synthesis and biological evaluation of potential acetylcholinesterase inhibitors based on a benzoxazine core

Méndez-Rojas, Claudio

Quiroz, Gabriel

Faúndez, Mario

Gallardo-Garrido, Carlos

Pessoa-Mahana, C. David

Chung, Hery

Gallardo-Toledo, Eduardo

Saitz-Barría, Claudio

Araya-Maturana, Ramiro

Kogan, Marcelo J.

Zúñiga-López, María C.

Iturriaga-Vásquez, Patricio

Va

 With the purpose of expanding the structural variety of chemical compounds available as pharmacological tools for the treatment of Alzheimer's disease, we synthesized and evaluated a novel series of indole-benzoxazinones (Family I) and benzoxazine-arylpiperazine derivatives (Family II) for potential human acetylcholinesterase (hAChE) inhibitory properties. The most active compounds 7a and 7d demonstrated effective inhibitory profiles with Ki values of 20.3 ± 0.9 ?M and 20.2 ± 0.9 ?M, respectively. Kinetic inhibition assays showed non-competitive inhibition of AChE by the tested compounds. According to our docking studies, the most active compounds from both series (Families I and II) showed a binding mode similar to donepezil and interact with the same residues.