Proceedings International
Platinum Open Access Journal (ISSN 2668-6384)

Proceedings, Abstract
Volume 4, Issue 2, 2022, 23
https://doi.org/10.33263/Proceedings42.023

Rational Design and Synthesis of Modified Natural Peptides from *Boana cordobae* and Evaluation as Multitarget Agents against Alzheimer's Disease †

Luisina Avataneo [1], Roque Spinelli [1,2], Iván Sanchis [1,2], Álvaro Rietmann [1,] Nicolás Aschemacher [1], Álvaro Siano [1,2*]

[1] Laboratorio de Péptidos Bioactivos, Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral, Edificio FBCB – Ciudad Universitaria UNL, Ruta Nacional Nº 168, km 472, CC 242. CPA S3000ZAA. Santa Fe, Argentina; avataneoluisina@gmail.com (L.A.), asiano@fbcb.unl.edu.ar (A.S.)
[2] CONICET (National Council for Scientific and Technical Research)
* Correspondence:; asiano@fbcb.unl.edu.ar (A.S.)

† Presented at The Sixth International Meeting of Pharmaceutical Sciences (RICiFa), November 10-12, 2021, Córdoba, Argentina

Received: 26.04.2022; Revised: 4.05.2022; Accepted: 6.05.2022; Published: 8.05.2022

Abstract: Alzheimer's disease (AD) is a complex neurological disorder associated with different pathways, including cholinesterase enzymes (AChE and BChE), oxidative stress, and biometals dyshomeostasis, among others. Because of this, simultaneous modulation is needed. Previously, we have reported the natural peptides *BcI-1202* and *BcI-1190*, isolated from *Boana cordobae*'s skin, with inhibitory activity against both cholinesterases. The aim of this work was the in-silico design and chemical synthesis of substitution analogs of *BcI-1202* and *BcI-1190*. For this, specific residues were changed for a tryptophan residue to achieve the formation of π-π stacking interactions with catalytic residues of cholinesterases. The results showed that the substituted analogs increase the inhibitory activities against both cholinesterases, being the analogs with two tryptophan insertions the most active. In this regard, for BChE, *BcI-1202* (A3/A6 // W3/W6) showed a 30-fold decrement in IC50 values (200µM to 6,50µM), while for *BcI-1190* (S1/A4 // W1/W4) the decrease for IC50 was 66-fold (400µM to 6,30µM). Concerning AChE, both modifications conferred potent inhibitory activity. On the other hand, the substitutions have given antioxidant and chelating capabilities. The tryptophan modifications allowed us to obtain multitarget peptides against the therapeutic pathways of AD. We propose this strategy as an innovative tool to increase bioactivity.

Keywords: peptides; inhibitors; cholinesterases; Alzheimer's disease.

Funding

This research was funded by PICT-2017-0035, PIP 2017-2019 GI. 112 201701 00462 CO.

Acknowledgments

This research has no acknowledgment.

Conflicts of Interest

The authors declare no conflict of interest.