medical sciences forum

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Abstract

4′4 Bromophenyl 4′Piperidinol Derivatives as a Multifactorial Anti-Alzheimer Agent: Synthesis, In-Vitro, and In-Silico Based Studies †

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† Presented at the 8th International Electronic Conference on Medicinal Chemistry, 1–30 November 2022; Available online: https://ecmc2022.sciforum.net/.

Abstract: 4′4 bromophenyl 4′piperidinol derivatives were synthesized, and evaluated as multifactorial agents for the treatment of Alzheimer's disease (AD). Among all the analogues, AB11 and AB14 showed the best activity against acetylcholinesterase (AChE) with IC_{50} = 0.029 µM and 0.038 µM, respectively. Both compounds also acted as a good antioxidant agent (IC_{50} = 26.38 µM for AB11 and 23.99 µM for AB14), while AB11 is the only molecule that displayed moderate inhibition of amyloid beta (Aβ) (43.25% at 500 µM). AB11 and AB14 were found selective against monoamine oxidase-B (MAO-B) with IC_{50} values of 866 µM and 763 µM, respectively. AB10, AB17, and AB70 exhibited activity against both MAO-A and MAO-B and showed inhibitory potential against acetylcholinesterase; moreover, all analogues are capable of disassembling the well-structured Aβ fibril. Molecular modeling of selected compounds displayed interactions with the active site of human MAO-B and AChE enzyme. The results suggested that AB11 is a promising multi-target hit that can be optimized further as a successful drug molecule for the treatment of AD.

Keywords: 4′4 bromophenyl 4′piperidinol; Alzheimer's disease (AD); acetylcholinesterase; molecular modeling; monoamine oxidase (MAO); antioxidant; Aβ aggregation and disaggregation

Citation: Rizvi, S.A.; Mushtaq, N.; Ahmad, A.; Anwer, L.; Asghar, S.; Arefa, M.; Zehra, A.; Arif, M.; Batool, F. 4′4 Bromophenyl 4′Piperidinol Derivatives as a Multifactorial Anti-Alzheimer Agent: Synthesis, In-Vitro, and In-Silico Based Studies. *Med. Sci. Forum* **2022**, *14*, 80. https://doi.org/10.3390/ECMC2022-13265

Academic Editor: Alfredo Berzal-Herranz

Published: 1 November 2022

Supplementary Materials: Conference poster. The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/ECMC2022-13265/s1.

Author Contributions: N.M. and A.A.; methodology, N.M. and A.A.; software, S.A.R. and A.A.; validation, S.A.R. and A.A.; formal analysis, S.A.R., L.A., S.A., M.A. (Mariam Arefa), A.Z., M.A. (Madiha Arif) and F.B.; investigation, N.M. and A.A.; resources, N.M. and A.A.; data curation, S.A.R.; writing—original draft preparation, S.A.R.; writing—review and editing, N.M. and A.A.; visualization, S.A.R.; supervision, N.M. and A.A.; funding acquisition, Higher Education Commission of Pakistan. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by Higher Education Commission of Pakistan, through HEC Indigenous PhD Fellowships for 5000 Scholars, HEC (Phase-II) grant number 520-160572-2MD6-16 (50093132).

Institutional Review Board Statement: The study was approved by the Hamdard University -Ethical Review Board (HU-ERB) Reference Number: ERB-2021-9-2.

Informed Consent Statement: Not applicable.

Data Availability Statement: All related data available.

Conflicts of Interest: The authors declare no conflict of interest.