medical sciences forum

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Abstract

Design, Synthesis, Molecular Docking Studies, and Biological Evaluation of 1, 3, 4-oxadiazol-3(2*H*)-yl] Ethan-1-one Derivatives as Antimicrobial Agents †

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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: A number of novel 1, 3, 4-oxadiazole analogues have been designed and synthesized through the condensation of substituted aldehyde/ketone with substituted benzohydrazide to form substituted *N*′-alkylidene benzohydrazide and then cyclization of *N*′-alkylidene benzohydrazide to form 1, 3, 4-oxadiazole derivatives. To investigate the antimicrobial data on a structural basis, in-silico docking studies of the synthesized compounds (**4a**–**4r**) into the crystal structure of *E. coli* DNA gyrase (Type-2 topoisomerase) using Autodock PyRx virtual screening program were performed to predict the affinity and orientation of the synthesized compounds at the activities by using 6rks Protein Data Bank (PDB). Inhibiting the ATPase activity of gyrase blocks the introduction of negative supercoils in DNA and traps the chromosome in a positively supercoiled state that may have a downstream impact on cell physiology and division. The results indicate that ketone-substituted benzohydrazide derivatives show good binding affinity (−8 kcal to −9 kcal) and electron-withdrawing group such as $–NO_2$ and –Cl present at R1 increases the affinity of scaffold and DNA gyrase receptors and binds into the specificity pocket. In this pocket, the 1, 3, 4-oxadiazole nucleus of these compounds interacts with the amino acid Alanine A: 421, Valine A: 420, Tyrosine A: 478, and Glutamine A: 381 residues of the target. Also, it is verified by in vitro antimicrobial screening, where all the compounds were active against tested bacterial strains. Among these compounds **4**(**c**), **4**(**d**), (**4e**), (**4h**), (**4i**), **4**(**m**), **4**(**n**), **4**(**o**), **4**(**p**), and (**4q**) showed good bacterial zone inhibition.

Keywords: 1, 3, 4-oxadiazole; molecular docking; in vitro antimicrobial activity

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Citation: Likhar, R.; Khan, T. Design, Synthesis, Molecular Docking Studies, and Biological Evaluation of 1, 3, 4-oxadiazol-3(2*H*)-yl] Ethan-1-one Derivatives as Antimicrobial Agents. *Med. Sci. Forum* **2022**, *14*, 143. https://doi.org/10.3390/ECMC2022-13247

Academic Editor: Alfredo Berzal-Herranz

Published: 1 November 2022

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/ECMC2022-13247/s1.

Author Contributions: Conceptualization: T.K.; Methodology: R.L. and T.K.; Writing—originaldraft preparation: R.L.; Writing—review and editing: R.L. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: This study did not require any approval from Ethical committee.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

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