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Peer Review

Review of: "Synthesis, ADME, Toxicity, and In Silico Molecular Docking Study of Novel β-Carboline Derivatives as Potential Inhibitor Anticancer Agents"

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The manuscript by Gaikwad and co-workers reports the synthesis of β-carboline tethered 1,3,4-oxadiazole derivatives, which are of pharmaceutical interest. The authors discuss the ADME, toxicity, and in silico molecular docking studies of the synthesized compounds. While the manuscript is generally well-written and prepared, several aspects require improvement for a higher-quality publication. Specifically, the synthesis of 1,3,4-oxadiazole derivatives has already been reported in the literature, and the authors should cite the following references:

- https://doi.org/10.1039/C8NJ04294B
- https://doi.org/10.1021/jo502518c

Additionally, the authors synthesized only two compounds with relatively low yields (40%). Since these compounds are already reported, the authors should include an optimization table to demonstrate efforts to improve yields. Furthermore, synthesizing and testing additional compounds (4-5 more) would strengthen the validity of the experiment.

Below are detailed comments for specific sections of the manuscript:

Abstract:

- Rephrase the abstract for clarity. Use general terms instead of full IUPAC names, such as "β-carboline tethered 1,3,4-oxadiazole."
- In the third line, replace with: “Additionally, in silico molecular docking studies were conducted on these…”

doi.org/10.32388/LCWAHI

- The last line of the abstract should be clarified, as it seems incomplete. For example: "β-carboline derivatives are present in commercially available and widely used drugs."

Results and Discussion:

- In Scheme 1, the structure of the starting material L-tryptophan methyl ester is missing and is incorrectly numbered as (1). The numbering and structures in Scheme 1 should be corrected accordingly, and the structures of compounds 4A and 4B should be clearly indicated in the scheme.

Molecular Docking section:

- (page 4), the IUPAC name for compound 4A is incorrectly written as "(9-benzyl-1-methyl-9H-pyrido[3,4-b] indol-3-yl)-1,3,4-oxadiazol-2-amine." Please correct this.
- On page 4, two binding energies for compound 4A are mentioned: 10.9975 kcal/mol in the third line and 11.8675 kcal/mol in the sixth line. The authors should clarify this discrepancy and discuss the docking studies of compounds 4A and 4B in proper detail, indicating which corresponds to which compound, to aid reader understanding.
- In the last line of the Molecular Docking section, the authors should clarify which compound (4A or 4B) the results refer to: "These results indicate that this compound could be useful for further research."

Molecular Prediction, ADME Parameters, and Swiss Target Prediction:

- It appears that the structures of compounds 4A and 4B are swapped in the ADME boiled egg diagram. Please check and correct this.
- In Table 1 (Pharmacokinetics Properties), clearly indicate which results correspond to which compound (4A or 4B).

Experimental Section:

- The authors should use IUPAC names and provide full details of the quantities, equivalents, and yield percentages without abbreviations.

Provide the experimental data for both synthesized compounds, including experimental yield, color, melting point, and spectroscopic data (IR, 1H-NMR, 13C-NMR). The spectra for both compounds

should be attached as supplementary material.

Declarations

Potential competing interests: No potential competing interests to declare.