

**BPI Review Form 070520**

Book Name:	<b>Advanced Concepts in Pharmaceutical Research</b>
Manuscript Number:	<b>Ms_BP_12271F</b>
Title of the Manuscript:	<b>SYNTHESIS AND MOLECULAR DOCKING STUDIES OF ETHYL 1-BENZENESULFONYL -2-[(E)-2-(2 METHYLPHENYL) ETHENYL] INDOLE -3-CARBOXYLATE WITH HUMAN RENIN COMPLEXED WITH INHIBITOR</b>
Type of the Article	<b>Book Chapter</b>

**PART 1: Review Comments**

	<b>Reviewer's comment</b>	<b>Author's comment</b> <i>(If agreed with the reviewer, correct the manuscript and highlight that part in the manuscript. Authors must write his/her feedback here)</i>
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<p>Is the manuscript important for the scientific community? Please write a few sentences explaining your answer</p>	<ul style="list-style-type: none"><li>• This manuscript presents novel indole compounds evaluated for their potential antihypertensive activity through inhibition of renin, a key enzyme in the production of angiotensin II.</li><li>• The molecular docking studies provide valuable insights into the mechanisms underlying their activity, further enhancing our understanding of their potential efficacy.</li><li>• This work contributes to the scientific community by expanding the potential of compounds that could be explored for the treatment of hypertension, addressing a critical need for more effective therapeutic options in cardiovascular medicine.</li></ul>	
<p>Is the title of the article suitable? Do you have any alternative Title in your mind?</p>	<p>I would suggest strongly to authors to change the title to "Synthesis guided by in-silico approaches of ... "</p>	
<p>Is the abstract of the article comprehensive? If your answer is No, please provide suggestions</p>	<p>Yes, the title looks comprehensive but can be extended more to include other analysis in complement to the molecular docking.</p>	
<p>Do you think the English quality of the article is suitable for scholarly communications? If your answer is No, please provide suggestions</p>	<ol style="list-style-type: none"><li>1. Some sentence need to be active and concise for eg. <i>"Docking studies using Molegro Virtual Docker (MVD) on the human Renin complexed with inhibitor (PDB ID: 2IKO) demonstrate its role in the molecule's antihypertensive activity."</i></li><li>2. Ensure parallel structure in phrases or lists. For example, <i>"ReRanking score and binding poses of the molecule"</i> need be revised to <i>"ReRanking <b>scores</b> and binding poses of the molecule"</i> for consistency.</li><li>3. Ensure consistent use of tense and formatting throughout the introduction paragraph. For eg, <i>"Currently the hypertension attracts the kidney diseases"</i> need to be revised to <i>"Currently, hypertension is associated with kidney diseases."</i></li><li>4. (ESRD) End stage renal disease: Acronym should be after.</li><li>5. Avoidance of repetition: Avoid repeating similar information or ideas, such as the mention of hypertension attracting kidney diseases, unless necessary for emphasis or clarity. same for the sentences here <i>"Compounds having indole groups are biologically important compounds. Indole along with their several derivatives finds a prominent place in synthetic organic chemistry"</i></li><li>6. Missing verbs at lots of places <i>"using Molegro Virtual Docker software <b>was</b> done to understand the basic mechanism of inhibition."</i></li></ol> <p>Authors need to review their manuscript carefully to correct these mistakes</p>	



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<p>Please provide your comments regarding the appropriateness of different sections of the manuscript.</p>	<ol style="list-style-type: none"><li>1. Abstract needs to be comprehensive; for eg. after first sentence need to provide details if there has been any success with drug discovery and why its challenging against modulating hypertension</li><li>2. Also, improve the transition of sentences from renin inhibitors to "indole"</li><li>3. In Introduction: Authors also need to provide more statistical data of hypertension around the world to make the study more visible. They should extend the numbers beyond India to worldwide.</li><li>4. Authors need to combine "Importance of indole" section with introduction.</li><li>5. Remove multiple and excessive use of "Molegro Virtual Docker" in abstract and introduction. <b>Explain it only in methods section or use MVD where its absolutely necessary.</b></li><li>6. <i>"Docking is frequently used to predict the binding orientation of small drug candidate to their protein targets"</i> there are lots of papers which criticize docking. So correct this sentence to say that <i>"Docking combined with other computational methods is used to predict the binding orientation and affinity...."</i></li><li>7. Explain more "Preparation of Ligand Structure": whether hydrogen added and which charges were added.</li><li>8. Define the process what changes were made to protein in "Preparation of Protein structure"</li><li>9. In the section Active site identification: provide the residue information in binding pocket and cite references where this structure was used in docking before.</li></ol> <p>More validation analysis required:</p> <ol style="list-style-type: none"><li>1. "One pose per run was retained based.." Instead carry out the same analysis on more than one poses which are in RMSD range of 1-2 Angstrom and then take the average. As ligand is dynamic and MD simulations were not performed; this analysis will provide better scores.</li><li>2. Use multiple conformations of binding site or protein or perform loop modeling of protein if there is a loop in the binding pocket and then provide results on how molecule scores on different loops. Use these two references to implement loop modeling.</li></ol> <p>For method: López-Blanco, José Ramón, et al. "RCD+: Fast loop modeling server." <i>Nucleic acids research</i> 44.W1 (2016): W395-W400. APA</p> <p>For using it: Gupta, Aayush, and Huan-Xiang Zhou. "Machine learning-enabled pipeline for large-scale virtual drug screening." <i>Journal of chemical information and modeling</i> 61.9 (2021): 4236-4244.</p> <ol style="list-style-type: none"><li>3. Perform consensus docking with other tools like VINA etc and compare the results with MVD. Authors can't rely on single docking as it provides artifacts.</li></ol>	
<p>Do you think that the references in the manuscript are proper, recent and sufficient? If you have any suggestions, please write here.</p>	<p>Yes need to provide more references based on above comments in introduction and methods. The manuscript needs a major revision.</p>	

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**PART 2:**

	<b>Reviewer's comment</b>	<b>Author's comment</b> (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
<b>Are there ethical issues in this manuscript?</b>	<i>(If yes, Kindly please write down the ethical issues here in details)</i>	

**Reviewer Details:**

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