

## Review Form 1.6

Journal Name:	<a href="#">Journal of Pharmaceutical Research International</a>
Manuscript Number:	Ms_JPRI_82437
Title of the Manuscript:	The potency of major Teucrium polium active ingredients as the Main Protease (Mpro) of COVID-19
Type of the Article	

### **General guideline for Peer Review process:**

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound. To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

<https://www.journaljpri.com/index.php/JPRI/editorial-policy>

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### PART 1: Review Comments

	Reviewer's comment	Author's comment (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>Compulsory</b> REVISION comments	<ol style="list-style-type: none"> <li>1. Authors should remove repetition</li> <li>2. Quality of the all the figures needs to be improved with readable labelling.</li> <li>3. Authors should justify the use of control compounds.</li> <li>4. Authors should justify either with arguments, potency of proposed compounds against other serotypes of corona virus as well.</li> </ol>	
<b>Minor</b> REVISION comments	<ol style="list-style-type: none"> <li>1. Authors needs to proofread and polish the writeup to convey their message clearly.</li> <li>2. In the first line of abstract, author could write "The" before "active coronaviral protein".</li> <li>3. Authors need to write abstract in more clear and understandable form. For example, abstract line 2 "This coronaviral protein was tested using a methanol extract made from <i>T. polium</i> leaves." It doesn't mention how tested. As a suggestion, Author could mention the virtual screening/docking is applied on 8 compounds found in the methanol extract against corona virus protease enzyme.</li> <li>4. Clearly mention what is M<sup>pro</sup> and 3CL<sup>pro</sup></li> <li>5. In abstract, author could mention LBE scores of potential compounds and control compounds with its unit, i.e., kcal/mol. It could give the abstract the sense of completion.</li> <li>6. In abstract line 13, authors could rewrite the sentence "As a result, these potential compounds may be modern coronavirus inhibitors." To make it clear. As a suggestion, author could write "These compounds could be proved as potential corona viral inhibitors."</li> <li>7. In Introduction section, 2<sup>nd</sup> paragraph, author mentioned "The ongoing industrialization causes uprooting, low yield, less cultivation, and destruction". They could mention "The ongoing industrialization causes uprooting, low yield, less cultivation, and destruction" "of <i>T. polium</i>".</li> <li>8. Author should remove usage of "As a result" repeatedly and unnecessarily. There are so many instances in the paper. For example, Introduction section, 2<sup>nd</sup> paragraph, sentence 3<sup>rd</sup> and 4<sup>th</sup> have the "as a result" repeatedly mentioned without necessity. In the last paragraph there is unnecessary repetition of "furthermore" as well.</li> <li>9. Authors needs to clarify what does he/she positive attitude means in the sentence "This study demonstrates a GC-MS-based phytochemical constituents and identifies a significant bioactive mechanism involved for the <i>T. polium</i>'s positive attitude."</li> <li>10. I will suggest the authors to add references at the end of a sentence instead in the middle. For example, material and method section, paragraph 1, 2<sup>nd</sup> sentence "Al-Eisawi [14] explained a method for obtaining such leaves.". such reference placement breaks the flow of reader's attention. Kindly correct all such instances.</li> <li>11. In material and method section, Molecular docking process, author is suggested to add references for all the software used.</li> <li>12. Material and method's, extraction process, in the line "One gram of Jordanian <i>T. polium</i> leaves was restored with 10 mL of methanol as well as stirred at room temperature for five days.", there should be 'leaves were' instead of 'leaves was'.</li> <li>13. Quality of "Figure 1 should be improved, and results should be readable on looking at it". Moreover, there should be provided some details regarding Figure in the caption.</li> <li>14. Results section, Molecular docking heading, there are repeated sentences that might left there unintentionally. for example, "<i>T. polium</i> includes numerous natural phytochemical compounds.". it's mentioned in the start of the paragraph as well. Moreover, the further sentences "<i>T. polium</i> includes numerous natural phytochemical compounds. The alleged anti-corona actions of these natural phytochemical compounds were investigated using an in-silico methodology. The AutoDock algorithm can help to describe binding associations of the eight major known chemical components in the <i>T. polium</i> methanolic extract. Docking simulation makes</li> </ol>	

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	<p>use of a grid-based energy evaluation technique in which pre-calculated pleasant relationship are used as lookup tables to allow for faster assessment of ligand-protein connections.” Are also the repeated with slight change of words. Author is suggested to delete that.</p> <ol style="list-style-type: none"><li>15. In Results, Molecular docking section, 2<sup>nd</sup> paragraph is incomprehensible. Author is suggested to rewrite the sentences convey the message clearly.</li><li>16. Authors needs to mention strong reason with references to justify their use of HIV inhibitors as control in coronavirus study.</li><li>17. Authors needs to bring uniformity in terms of language. Either they can use Arabic numerals (1, 2 3, 4...) to mention number of compounds or English (one, two, three, four...). For example, at some places they have used “8” and at some parts of the paper it is mentioned as “eight”.</li><li>18. Authors are suggested to proofread and re-write discussion section. There should be careful use of English words and synonyms. One example is, “Interestingly, as shown in Table 3, 3-Hydroxytetradecanoic acid, 3-Dodecenedioic acid, D-Glucuronic, 3-Hydroxysebacic acid, and Dodecen-3-ol exceed the other phytoconstituent compounds as well as the optimistic controls by forming a strong association with destination enzyme's protease as confirmed by the LBE and Ki values.”, Authors could use “control compounds” instead of “optimistic controls and ” “target protease enzyme “instead of “destination enzyme's protease”. Similarly, “interaction” could be used instead of word “association”.</li><li>19. Authors are suggested to justify their claims made in discussion with latest references.</li><li>20. Authors are suggested to write discussion in more clear form. Most of the sentences are not clear enough to understand. The docking section of the discussion should be comprehensive.</li><li>21. What is area percent in the sentence “Table 3 shows the results of five potential inhibitor that have area percent more than 2% and LBE and Ki results better than FDA approved HIV inhibitors as a potential inhibitor.”. authors are suggested to clarify it.</li><li>22. It's not clear what authors are trying to convey in the sentence “The phytoconstituent compounds have different scores when compared to the enclosed amino acids.”. what different scores and what are enclosed amino acids here?</li><li>23. Authors are suggested to mention binding pocket residues of coronaviral protease enzyme.</li><li>24. There are other serotypes of coronavirus as well. What is author's take on that? To publish such study, authors need to justify their suggested potential compound's activity against other serotypes as well.</li><li>25. Last paragraph of the discussion section is repeated version of previous paragraph. Authors are suggested to remove the repetitions.</li><li>26. Table 3, all the images need to be revised with readable labelling. It is suggested to mention only the atoms required to show better interactions.</li><li>27. Authors are suggested to remove repetitive sentences. For example, “Docking results indicate that 3-Hydroxytetradecanoic acid, 3-Dodecenedioic acid, D-Glucuronic, 3-Hydroxysebacic acid, Dodecen-3-ol have lowest LBE scores and Ki values for 3CLpro than supportive control drugs.” Means same as “Besides that, the study of such compounds' interactions with the amino acids in 3CL<sup>pro</sup> indicated that 3-Hydroxytetradecanoic seems to have the best LBE score and Ki value compared to approved drugs and all the other studied compounds, attributed to its ability to create tight hydrogen bonds with protease.”</li></ol>	
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<b>Optional/General</b> comments		
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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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