Review of: "Synthesis of 1, 2-Disubstituted Benzimidazoles at Ambient Temperature Catalyzed by 1-Methylimidazolium Tetraflouroborate ([Hmim] BF_4) and Investigating Their Anti-ovarian Cancer Properties Through Molecular Docking Studies and Calculations"

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Potential competing interests: No potential competing interests to declare.

Review manuscript ID #: Qeios R7LIUP entitled: “Synthesis of 1, 2-Disubstituted Benzimidazoles at Ambient Temperature Catalyzed by 1-Methylimidazolium

Tetraflouroborate ([Hmim] BF_4) and Investigating Their Anti-ovarian Cancer Properties Through Molecular Docking Studies and Calculations". Authors reported an environmentally benign method for the synthesis of 1, 2-disubstituted benzimidazoles by the reaction of aromatic aldehydes and o-phenylenediamines in the presence of ([Hmim] BF4) under green conditions. The anti-ovarian cancer properties of these compounds were studied only by computational chemistry methods.

Here are some suggestions about the manuscript when significant revisions are required. To improve its quality, the following points should be clarified:

- The title conveniently represents the study, although a spelling mistake has been noticed: tetraflouroborate should be corrected to tetrafluoroborate. Please remove the underscore from the chemical formula of the catalyst.
- The chemistry part of the study is in general acceptable; however, the docking investigational study is poor, primitive, irrelevant, and should be supported by work conducted on a plausible biological target test as several mechanisms could be involved in activity. It requires major modification to solidify the design as ovarian anticancer agents that should be interpreted into activity. As the major part of the manuscript is based on theoretical studies, this should be backed with biological testing. As these benzimidazole derivatives have been previously synthesized, I wonder if they were tested for such properties. The manuscript requires extensive discussion to reach reasonable conclusions about the anti-ovarian cancer properties.
- English language should be checked all over the manuscript and corrected. There are language, typographical, spelling, and grammatical mistakes such as “Lee Pinsky”, "who ovulate more", “suffers”. Some verbs are not correct or not reported in the proper tense, and many sentences should be reconstructed. Repetition has also been observed, as, for example, “Among the heterocyclic compounds, the heterocyclic compounds…….”
- Introduction section should be more concise, avoiding unnecessary information and details, and should be revised

properly. Many chemistry pieces of information are elementary and should not be mentioned. For example, "Organic compounds have various structures, many of these structures have a ring system that consists of carbon atoms and at least one other element, which are called heterocyclic compounds", and “Benzimidazole is an aromatic heterocyclic compound consisting of two fused rings of benzene and imidazole”. References are missing in some parts of the introduction.

- Synthesized compounds have been characterized only by melting points. It would be more convenient to characterize these compounds by spectroscopic tools.
- A big mistake stands in the Lipinski rule of 5, which has been wrongly reported as Lee Pinsky or Le Pinsky. The rule of 5 is a fact and should be explained to a minimum.
- The legend of table 3 wrongly describes the content of the table. Please correct.
- The legends of tables 4 and 5 also wrongly describe the content of the tables except for the dock scores and docking energies.
- Docking scores are reported but lack units (Kcal/mol), while RMSD energy scores values are not reported at all. They should be added.
- What program was used in the docking study?
- In the docking section, please report the method for ligand preparation as well as the docking protocol. The reader should understand the protocol of the docking study, which should be reproducible.
- Provide more details on the specific amino acids and binding pockets targeted in the molecular docking studies.
- The authors should mention the distance criteria that determine the H-bond and hydrophobic interactions, since the hydrogen bonding distance ensures the adequacy of optimum hydrogen bonding.
- In the conclusion section, the word suffers has been reported. In my opinion, literally, the word suffers means a disadvantage and should be replaced by another word, such as provides.

The actual form of the work does not significantly advance the understanding or development in this field. The above-mentioned major changes should be considered before the paper can be recommended for publication.