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.

Thank you very much for giving me the chance to cooperate with your respected journal in reviewing this interesting work. The manuscript deals with the "**Synthesis of 1, 2-Disubstituted Benzimidazoles at Ambient Temperature Catalyzed by 1-MethylimidazoliumTetraflouroborate ([Hmim] BF_4) and Investigating TheirAnti-ovarian Cancer Properties Through Molecular Docking Studies and Calculations**". The synthesis of 1,2-disubstituted benzimidazoles catalyzed by [Hmim]BF4 and the investigation of their anti-ovarian cancer properties hold promise for advancing synthetic chemistry, catalyst development, drug discovery, and cancer research, with potential implications for the development of novel therapeutics for ovarian cancer.

There are several potential impacts of this study.

The study on the synthesis of 1,2-disubstituted benzimidazoles at ambient temperature catalyzed by 1-methylimidazolium tetrafluoroborate ([Hmim]BF4) and its investigation of their anti-ovarian cancer properties through molecular docking studies and calculations holds several potential impacts:

1. Synthetic Chemistry Advancements: The synthesis of 1,2-disubstituted benzimidazoles at ambient temperature represents a significant advancement in synthetic chemistry. This environmentally friendly and efficient method could offer a novel approach to accessing benzimidazole derivatives, which are valuable structural motifs in medicinal chemistry.
2. Catalyst Development: The use of 1-methylimidazolium tetrafluoroborate ([Hmim]BF4) as a catalyst showcases the potential of ionic liquids in catalysis. Understanding the catalytic activity of [Hmim]BF4 in benzimidazole synthesis could inspire further research into the development of novel catalysts for various organic transformations.
3. Drug Discovery Potential: The investigation of the anti-ovarian cancer properties of synthesized benzimidazoles through molecular docking studies provides valuable insights into their potential as anticancer agents. If the computational predictions are validated experimentally, these benzimidazole derivatives could serve as promising leads for the development of new ovarian cancer therapeutics.
4. Structure-Activity Relationship (SAR) Studies: By conducting molecular docking studies and calculations, the study

elucidates the interactions between the synthesized benzimidazoles and their target proteins implicated in ovarian cancer. This information contributes to SAR studies, enabling the design and optimization of more potent and selective anticancer agents.

5. Contribution to Cancer Research: Ovarian cancer remains a significant health concern, and the search for effective treatment options is ongoing. The identification of benzimidazole derivatives with potential anti-ovarian cancer properties adds to the arsenal of compounds being investigated for cancer therapy, potentially offering new avenues for treatment.
6. Interdisciplinary Collaboration: The study bridges the fields of synthetic chemistry, computational chemistry, and cancer biology, fostering interdisciplinary collaboration. Such collaborations are essential for tackling complex scientific challenges and translating basic research findings into clinically relevant applications.

The weak points of this paper.

While the paper presents some promising findings, there are several weak points that should be addressed:

1. Lack of Mechanistic Insights:

- The paper lacks detailed mechanistic insights into the reaction mechanism underlying the synthesis of 1,2-disubstituted benzimidazoles.
- Providing a deeper understanding of the reaction pathway could enhance the scientific rigor and credibility of the study.

1. Limited Characterization Techniques:

- Although the products were identified using melting point determination and NMR techniques, the absence of additional characterization techniques such as mass spectrometry or X-ray crystallography limits the thoroughness of compound characterization.
- Including more comprehensive analytical techniques would strengthen the validity of the synthesized compounds.

1. Sole Reliance on Computational Chemistry:

- While computational chemistry and drug design methods offer valuable insights into the potential anti-ovarian cancer properties of the synthesized compounds, relying solely on computational predictions without experimental validation may introduce uncertainties.
- Experimental assays or in vivo studies are necessary to confirm the anticancer activity of the compounds.

1. Ambiguous Language:

- The statement that "these compounds have the potential to become an oral anti-cancer drug" is overly optimistic and lacks substantiation.
- Such claims should be supported by robust experimental data, clinical trials, and regulatory approval processes, which are typically extensive and time-consuming.

1. Limited Scope of Biological Studies:

- The paper focuses primarily on the computational assessment of anti-ovarian cancer properties without providing experimental validation through biological assays or animal studies.
- Experimental evidence of anticancer activity is crucial for establishing the therapeutic potential of the synthesized compounds.

1. Generalization of Findings:

- The paper claims that all synthesized compounds bind to an agonist at the active site of the 6LAD protein, leading to inactivation and potential therapeutic effects in ovarian cancer treatment.
- However, the generalization of findings without individual compound-specific data or detailed binding interactions could be misleading.

Addressing these weak points by incorporating additional experimental data, providing mechanistic insights, and tempering speculative claims would strengthen the scientific rigor and credibility of the study.

My final decision was accepted after a major revision.