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. No

Decision: Rejection

Comments

1. **Abstract**

- In the phrase (All the synthesized compounds bind to an agonist at the active site of the 6LAD protein, which leads to the inactivation of this protein and produces beneficial effects during ovarian cancer treatment.) where are your proofs for these conclusions, and even the protein code is incorrect

1. **Introduction**

-It is very poor due to

i. No introduction about green chemistry
ii. NO background about other catalysts and methods for the synthesis of benzimidazole; instead, the authors gave unimportant information about organic and heterocyclic compounds
iii. No references to support the certain given information

e.g.1 page 3/20 lines 6-8 **(**Benzimidazole and its derivatives are considered a heterocyclic motif that is used in a wide range of medicinal applications, including antihypertensive, antifungal, anticancer, antiviral, anti-HIV, antidiabetic, anticonvulsant, anti-neoplastic, and anti-trichinosis properties. Benzimidazole and its derivatives are considered a heterocyclic motif that is used in a wide range of medicinal applications, including antihypertensive, antifungal, anticancer, antiviral, anti-HIV, antidiabetic, anticonvulsant, anti-neoplastic, and anti-trichinosis properties)

e.g.2 page 3/20 (The risk of ovarian cancer is higher in those who ovulate more, so it can be concluded that those who have never had children are at a higher risk.)

i. There are no examples of imidazole and benzimidazole as anticancer agents

ii. There are typing errors, for example;

- page 4/20, line 5 (antiblastic)
- page 3/20 o-phenylenediamine (o letter must be italic)
- iii. In Scheme 1, there are compounds 3(a-l) and 4 (a-l), but in the whole manuscript, there is no mention of how compounds 4 (a-l) were prepared or references for their spectroscopic data

2- Experimental

(i) General procedure for the preparation of 1, 2-disubstituted benzimidazole derivatives (3a-l) is a wrong title, as it describes the preparation of compound 3a only

(ii) No preparation procedures for the preparation of compounds 4a-l nor their spectroscopic data

(iii) No mention of the protein preparation for docking simulations nor a description of the docking procedures. Also, the protein code is incorrect

(iv) In section General procedure for the preparation of 1, 2-disubstituted benzimidazole derivatives (3a-l)(DMSO-d6), number 6 must be subscript

3. Results and discussion

(i) The discussion is poor because there is no discussion of the mechanism of how compounds 3 (a-l) were formed, as well as compounds 4a-l

(ii) Page 7/20, Table 1, Synthesis of 1,2-disubstituted benzimidazole derivatives, why did you draw compounds 4 (a-l)

(iii) There are typing mistakes, page 8/20; Lee Pinsky's,

(iv) It is incorrect to designate the Lipinski rule as the rule of medication; it is the rule of five

(V) Tables 3-5 show the predictions for the physicochemical and pharmacokinetic properties of compounds 3 (a-l), as well as docking energies and scores, so the title has to be corrected

(vi) Table 2, entry 9, m.p. 186-186 ??

(vii) Titles of tables 4 and 5 (Results of molecular docking calculations of synthesized compounds (4a-4l)) and Table 5. Results of molecular docking calculations of synthesized compounds (4a-4l) , these titles are wrong as the compound numbers are wrong; also, these data represent PK properties

i. Page 10/20 Table 5. Results of molecular docking calculations of synthesized compounds (4a-4l) wrong as the data refer to compounds 3a-l
ii. What is the software server used for prediction of PK properties, and what are the cutoff values for each parameter?
iii. Page 10/20 (CD-125 protein is the most common ovarian cancer marker protein and, is named 6LAD PDB in the protein database) The protein data bank code is wrong, which indicates the inaccuracy of the docking

iv. Figure 2, page 11/20, it is not a 3D graph, it is 2D

v. Figures 3 and 4, pages 12-13/20, do not give any information

vi. The docking procedures are inaccurate as the incorrect protein was used and no validation was performed

vii. There are a lot of typing mistakes

4- Supplementary material

-Compound 3a [5.59 (s, 1H, CH2)] incorrect; it has to be two protons of the methylene group

-Compound 3e (p) should be italic