

Review of: "Design and Molecular Screening of Various Compounds by Molecular Docking as BACE-1 Inhibitors"

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Potential competing interests: No potential competing interests to declare.

The authors have conducted a noteworthy study utilizing molecular docking analysis to identify hit compounds with flavonoid scaffolds. To enhance the quality of the research, I recommend the following revisions:

The authors have not adequately identified a specific research gap in the introduction section. While Alzheimer's disease is worthy of study, an explanation of various therapeutic interventions and progress made so far is necessary to substantiate the need for this current study. Additionally, the authors should articulate why the compounds predicted here would offer additional benefits compared to currently available options.

Docking validation should be performed to validate the analysis.

Molecular dynamics simulation should be conducted, as molecular docking analysis has been shown to be less reproducible in living systems.

MMGBSA post-docking analysis should be carried out to further assess the stability of compounds with high docking scores.

One major issue with synthetic compounds is PAINS alert and ease of synthesis. The authors should include PAINS alert and ease of synthesis in the ADME analysis to further support the efficacy of the compounds.

Minor revision:

Several sentences were not well-written and should be revised. A few examples are listed below:

- "The pathophysiology of this disease is related to the injury and death of neurons starting from the hippocampus that ultimately extends to the entire region of the brain."
- "Further, the refinements of lead compounds are accomplished by the laboratory techniques which have a tropism towards drug action with fewer side effects."

Additionally, some words were written in bold letters which should be corrected.

The authors also included a literature review section and aims and objectives. I am uncertain if this aligns with the guidelines set by the journal. The authors need to establish if the manuscript is an original article or a combination of a review and an original article. If it is the latter, the authors need to ensure this is reflected in the abstract and title.

