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

Mukhtar Idris

Potential competing interests: No potential competing interests to declare.

Reviewers Comments

The manuscript discusses the search for an Alzheimer's cure, targeting BACE-1 with compounds derived from flavonoids. Docking studies identify promising derivatives of Baicalein, Myricetin, and Quercetin, indicating potential breakthroughs in Alzheimer's research and emphasizing the importance of natural products in developing treatments for the neurodegenerative disorder. I would recommend this paper for publication if the authors can work on these major comments.

1. The authors need to work more on the introductory part; it's not easy to read and understand. Different points were made without any connections. I will also suggest the whole article should be improved by working on the grammar.
2. The authors developed an interesting workflow for the study. The authors should describe in detail the molecular docking procedure.
3. The protein-ligand interaction in figures 17 and 18 is not visible. The authors should put it to scale.
4. The authors made a statement "…The information obtained from the docking suggests the docking score, free energy, and stability of complexes…." The docking scores cannot give information about the protein stability. Perhaps a reference can be provided for the claim.
5. The authors in section 5.2. Docking Results and Interactions of Derivatives of Donepezil used the "docking score". I will suggest the authors use the word "binding energy" instead.
6. Also, the so-called docking score should be negative.
7. Figures 20 and 21 look compressed; the authors should make them to scale.
8. I will suggest the authors do at least a 100ns molecular dynamics simulation to further check the protein-ligand complex dynamics and stability.
9. However, the post-docking analysis discussion didn't detail the nature of the amino acids involved in the binding of the compounds explicitly. The authors can try to describe the amino acids involved in the hydrogen bonding with the donor-acceptor bond distances. What kind of interaction is driving the ligand binding?
10. I will suggest the authors improve the discussion part of this manuscript; a good paper does not only provide answers to questions but also makes a comparison with previous work that has been done in addressing the same question. This study in this manuscript is carefully done; I will suggest the authors discuss how these studies complement or provide new insights into existing approaches.