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.

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

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This is a timely topic for a paper, and it is an interesting exercise. The target BACE in AD is relevant and has future potential in the search for novel therapeutics for this disease. The authors provided a good and relevant introduction to BACE, which included relevant figures. However, all the figures could be improved. If figures 1-3 are originals, the authors must mention the software used to make those figures. If the figures were adapted/modified from previous work, these MUST be referenced. For the chemical structures in figures 4-7, they must be consistent with each other (in fact, this applies to all chemical structures used in this paper). I assume the software ChemDraw was applied to draw those structures. Ball-and-stick structures of flavonoids in figures 6 and 7 are not necessary; normal structures will suffice. Furthermore, the rest of the article will require improvement as highlighted below to achieve publication standard.

Make sure all figure legends throughout this paper are detailed enough. For example, in figure 9, authors must say what sites 1-3 are!

‘Thus, ancient knowledge of **Donepezil (Standard)**, **Quercetin**, **Myricetin**, **Baicalein**, and **Ferulic acid** was chosen as probable scaffolds which are in study against Alzheimer’s disease.’ The authors should justify and provide relevant evidence with relevant references to support why those compounds were selected as scaffolds.

Does the table below Figure 9 (no table number present!) relate to the structure in Figure 9? Then where is R6? Very confusing!

‘…….ethoxy group substitution in Ring-A (phenyl ring)……..’ Where is Ring A?

Figure 14 is poorly constructed and very difficult for readers to appreciate.

The authors, while discussing the various modifications of each of the lead compounds, mentioned bioactivity all the time. The type of bioactivity must always be highlighted in the discussion.

‘4.2.2. Determination of bioactivity of the prepared ligand’ What were the results of the study using the Lipinski rule (refer to the relevant table in the discussion)?

All the figures showing molecular interactions are poor, lacking clarity; higher resolution required!

As mentioned above, this is an interesting study; however, it would have been complete if the authors could include the synthesis of the most active compounds in this study. If this was carried out, perhaps the results from *in vitro* binding analysis of BACE inhibition would complete the story.