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

Thabo Makgoba[1]

1 University of the Western Cape

Potential competing interests: No potential competing interests to declare.

The manuscript titled: Design and Molecular Screening of Various Compounds by Molecular Docking as BACE-1 Inhibitors is a research article detailing the use of in silico methods to discover novel BACE1 inhibitors.

This manuscript needs a lot of work done on it. It has a lot of flaws and grammar and syntax errors should be attended to thoroughly.

Introduction: Authors must define abbreviations once, then use them through-out the document. Authors must decide to either use B-amyloid or amyloid beta.

Literature review: Fig 1 and 2 essentially explain the same enzymatic process. Fig 3 is described as the active site of BACE1, however, only the full protein is seen and no efforts of highlighting the active site are done.

Chemical structures thought-out the document should have the same size, same bond angle and length.

Figures provided in the document should be of high quality.

Fig 6 and 7 can be combined.

Construction of a chemical library: Unclear if authors are validating the use of a specific compound library or they are validating the use of their chosen standard ligands.

Authors sometimes refer to BACE1 as BACEI. This needs to be rectified.

Figure 9 is not explained.

Table above 4.2.1.2 is not defined.

Fig 11, 12, and 13, the structures of said molecules are not similar to the structures in Fig 6. Changing it to core structures can be more suitable.

Section 4.2.3: some information about BACE1 is repeated.

Section 5.1 has no content

Section 5.3, the table 2, 3,and 4 have the same description. It can causes confusion.

On page 25, experimental data or previously published data needs to be provided for the claim.

Selected pose of ligands in the document should also be visualised in 3D in the active site of BACE1.

The docking score is sometimes regarded as a positive integer. This needs to be rectified.

The study presented hit molecules predicted from an *in silico* study and it mentioned possible applications of the molecules. However, it makes me wonder about the *in vitro* and *in vivo* bio-activities of the molecules discovered. I suggest that authors present also the required studies needed to showcase the claims about the molecules' inhibitory activity towards BACE1. Or at least mention the future studies.