Review of: "Expansion of the antifungal activities through in silico docking study of compounds from Albizia lebbeck fruits"

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Potential competing interests: No potential competing interests to declare.

Bosco et al. present the article "Expansion of the antifungal activities through in silico docking study of compounds from Albizia lebbeck fruits," with a methodology based on molecular docking to explain the results previously obtained by Leutcha et al. 2022. In addition to the need to address the presentation of results, I find some serious issues in the presented work:

- The authors emphasize that "This is the first docking study using natural compounds as ligands with the 5TZ1 and 5FSA proteins," which appears to be inaccurate. A simple Google search reveals at least three studies where other compounds have been tested on either of these two proteins.

- It is unclear whether the molecular docking was performed at the active site of both proteins or if it was done with the ligand already bound to the protein. The authors mention, "Compounds (1-14) were docked for their antifungal potencies against the sterol 14-alpha demethylase (CYP51) from Candida albicans in complex with the tetrazole-based antifungal drug candidate VT1161 (VT1) (PDB Id: 5TZ1) and sterol 14-alpha demethylase (CYP51) from the pathogenic yeast Candida albicans in complex with the antifungal drug posaconazole (PDB Id: 5FSA)," which seems to indicate docking with the crystallographic protein/ligand complex. If so, what is the justification for this? To address this, the authors can provide the coordinates of the search box center and its size.

- The authors should use a reference point to ensure the correctness of the docking. This can be done by using crystallographic ligands and checking whether the proposed protocol can reproduce the conformation of the crystallographic ligand using RMSD of the found solutions and the initial conformation. This exercise allows the authors to validate their experiment and compare the results with an affinity energy.

- Similar to in vitro or in vivo experiments, in silico experiments require the reporting of repetitions. Repetitions enable the authors to ensure the consistency of their experiment, regardless of how many times it is performed. This also allows the reporting of average affinity energies with corresponding standard deviations.

- The authors report the molecular docking of 14 compounds, but in both Table 1 and 2a and 2b, it is unclear why the results of all compounds are not presented.

- There are affinity energy values in Table 1 that state "..less than -2." Does this mean values more negative than -2, or does it imply values close to 0? If the latter is true, it would suggest that the compounds did not bind well to the binding sites.

- Experimental data is available for only two tested compounds, making the authors' conclusion that the 14 compounds are "in agreement with experimental results" vague or nonsensical.

I highly recommend that the work be reconsidered for publication and dissemination to the general public.