Review of: "Thiazole Schiff Bases as Potential Breast Cancer Drugs through Design, Synthesis, and In Silico Analysis"

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Potential competing interests: No potential competing interests to declare.

Suggestions:

To improve the quality and qualification of the manuscript, and taking into account the results of the study focused on thiazole-incorporated Schiff base derivatives in the context of their binding affinities to critical proteins involved in hormone-dependent breast cancer and inflammation, the following suggestions are proposed:

- Expand the compound library: include a broader range of thiazole derivatives with varying functional groups to assess how different substituents affect binding affinities and interactions with target proteins. Furthermore, all compounds should be fully characterized, involving HR-MS studies or elemental analysis.
- It is suggested that the study be focused on varying the electron-donating and electron-withdrawing groups on the thiazole ring. This will help to identify optimal substituents that improve binding affinities for specific receptors (4FX3, 4OAR, 3NUP, and 3ERT).
- Perform molecular dynamics simulations: After identifying the best candidates from docking studies, perform molecular dynamics (MD) simulations to assess the stability and flexibility of the ligand-receptor complexes over time. This will provide insight into the dynamics of binding and help identify potential conformational changes.

It is suggested to use MM/PBSA or MM/GBSA methods during MD simulations to calculate the binding free energies of TZ compounds with target proteins. This analysis can yield more reliable estimates of binding affinities than docking scores alone.

- Employ the most promising TZ compounds (e.g., TZ6, TZ8) for further structural optimization based on the binding interactions observed in docking studies and MD simulations. Consider modifications that improve hydrophilicity or steric fit without compromising affinity.
- A correlation between docking scores and biological activity should be established involving molecular dynamics findings and biological activities to understand which binding interactions are most crucial for efficacy.