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Peer Review

Review of: "In Silico Toxicity Assessment of Organophosphates: A DFT and Molecular Docking Study on Their Interaction with Human Serum Albumin (HSA)"

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The authors have performed DFT, docking, and dynamic simulations to assess the in silico toxicity of organophosphates targeting human serum albumin. There are several flaws that need to be checked and verified before performing the calculations; the issue is not having a control to indicate which areas or regions of ligands are susceptible to toxicity.

Major concerns:

1. There are numerous HBA-ligand structures available in the PDB. The authors should have analyzed the PDB ligand similarity, chosen diverse PDB complexes, and performed DFT to have this control.

2. The authors have just optimized the drawn ligands obtained from a chemical drawing program and docked them into the receptor. Do the authors confirm whether the calculated atomic charges are being supplied to perform docking using Autodock and how Autodock handles their set of ligands? Do the docking poses differ significantly from partial atomic charges, which are calculated very quickly using force fields?

3. The authors may have performed MM/QM calculations by treating the whole protein as the MM component and the ligand binding site as the QM component with the already optimized DFT ligands.

4. Please include a HOMO-LUMO and other DFT descriptors calculated for the set of organophosphates with diverse PDB HSA ligands to assess the similarity of how HSA ligands accommodate diversity and indicate toxicity.

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5. Did the authors identify sub-structures of organophosphates that cause toxicity or associate the known toxic sub-structures with the HSA receptor interactions?

Declarations

Potential competing interests: No potential competing interests to declare.