Qeios

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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I offer some comments to enrich this computational study, and the overall quality of work is good. After some improvements, I suggest this for publication.

1. Introduction

Strengths:

- The introduction effectively highlights the significance of organophosphates (OPs) and their toxic effects on humans, plants, and the environment.

- The background on Human Serum Albumin (HSA) and its role in toxicity is well integrated.

Suggestions for Improvement:

- Simplify complex sentences to improve readability for a broader audience.

For example, break down the mechanisms of AChE inhibition into smaller, easier-to-follow steps.

- Include recent statistics or studies that quantify the global impact of OP toxicity to establish urgency.

- Add a clearer statement of the study's objective earlier in the introduction. Currently, the main research aim is embedded mid-section, which can dilute its impact.

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2. Methodology

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Strengths:

- The computational tools (DFT, molecular docking with AutoDock, Swiss-ADME, ProTox-3.0) are well-justified and appropriately selected for this study.

- The step-by-step detailing of ligand and receptor preparation ensures replicability.

- Parameters like the Genetic Algorithm (GA) configuration and binding affinity selection criteria (RMSD values) are clearly defined.

Suggestions for Improvement:

- Include a flowchart summarizing the entire methodology, from ligand modeling to docking and toxicity analysis. This would make the methods more visually comprehensible.

- Provide more context about the choice of the 6-311G(d,p) basis set in DFT calculations for readers unfamiliar with computational chemistry.

- Explain why specific OP compounds were selected—e.g., Azinphos-methyl, Malathion, etc.—based on their prevalence or previous toxicity reports.

- Discuss any potential limitations of the tools used, such as the docking software assuming rigid receptors.

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3. Results

Strengths:

- Comprehensive reporting of docking scores and interactions between OP compounds and HSA.

- Effective use of visuals like tables and graphs to summarize key findings (e.g., Table 1: docking scores, Figure 2: binding affinity plot).

- Azinphos-methyl is highlighted as the most potent compound, with supporting evidence from multiple analyses.

Suggestions for Improvement:

- Annotate graphs (e.g., Figure 2) more thoroughly. Include descriptions of key trends or outliers directly in the figure captions.

- Provide more detailed comparisons of binding modes for compounds with high versus low binding affinities. For instance, why does Azinphos-methyl bind more strongly than Malathion?

- Link findings more explicitly to biological implications. For example, explain how specific interactions (e.g., pi-sulfur bonds) might interfere with HSA's transport functions.

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4. Discussion and Conclusion

Strengths:

- The discussion effectively synthesizes results and reiterates the significance of computational approaches in toxicity predictions.

- The conclusion outlines potential applications, such as drug development and environmental policy interventions.

Suggestions for Improvement:

- Expand on how in silico findings can bridge gaps to in vivo and in vitro studies. Discuss any challenges in translating these computational results to experimental systems.

- Highlight broader implications for pesticide regulation and sustainable agriculture, particularly in regions heavily reliant on OPs.

- The conclusion could end with a stronger call to action or specific recommendations for future research directions.

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5. Figures and Tables

Strengths:

- Tables like the ADMET analysis and docking scores are clear and well-structured.

- Visualizations of docking interactions (e.g., Figure 3) are detailed and enhance understanding of ligand-receptor binding.

Suggestions for Improvement:

- Add legends or color coding to make tables easier to interpret at a glance. For example, highlight compounds with high toxicity classes or strong binding affinities in bold or specific colors.

- Ensure all figures (e.g., Figure 1: Azinphos-methyl structure) have detailed captions that explain their relevance to the study.

- Include more comparative visuals to showcase differences between strong and weak binders (e.g., overlaying docking poses of Azinphos-methyl and Malathion).

Declarations

Potential competing interests: No potential competing interests to declare.