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AI-driven virtual screening for combatting antibiotic resistance: a promising therapeutic approach

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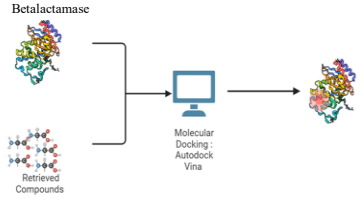
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Introduction

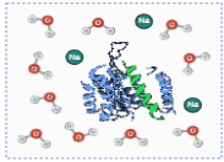
The emergence of multi-resistant and pan-resistant enterobacteria to betalactam antibiotics poses a significant threat to human health. The prevailing resistance mechanism in enterobacteria involves the production of beta-lactamases, enzymes that break down the beta-lactam cycle. Thus, compounds inhibiting these enzymes seem promising candidates for potential drugs.

Material and methods

① Virtual screening

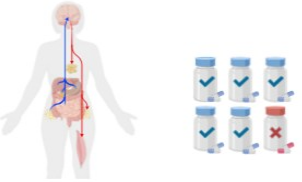


② Molecular Dynamics



Desmond Software

③ ADMET Prediction



Admet AI

Results

The results highlight the effectiveness of the compound, with a binding affinity of -11.458 kcal/mol, surpassing that of the commercial beta-lactam inhibitor clavulanic acid (-6.8 kcal/mol). The interactions between the compound and the target are shown in Figure 1. Molecular dynamics results, RMSD and RMSF plots further support the stability of the compound under simulated conditions (Figure 2). Finally, the ADMET predictions summarized in Table 1 show that the selected compound adheres to all drug-likeness rules and exhibits good pharmacokinetic properties, underscoring its potential as a promising therapeutic candidate.

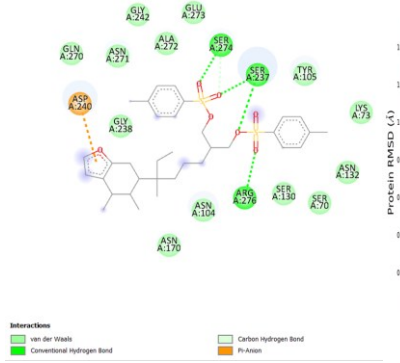


Figure 1. 2D diagram showing the interactions between the molecule and the beta-lactamase.

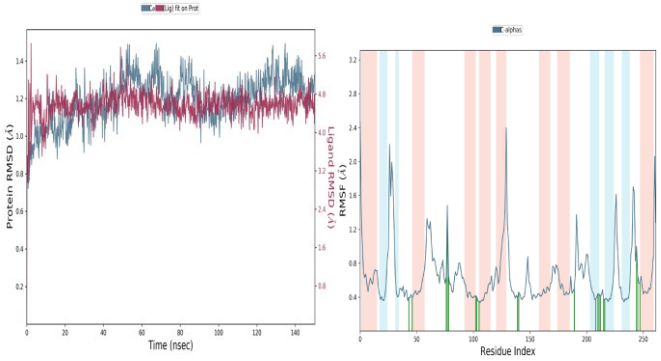


Figure 2. RMSD and RMSF plots illustrating the complex stability throughout the simulation.

Table 1. ADMET results of the molecule

Molecule	Compound
Lipinski rule	Accepted
Blood-Brain barrier	BBB-
Human Intestinal Absorption	HIA++
Caco-2 Permeability	Caco2-
P-glycoprotein Inhibitor	Non-inhibitor
Solubility	Poor
CYP450 1A2 Inhibitor	Non-inhibitor
CYP450 2C9 Inhibitor	Yes
CYP450 2D6 Inhibitor	Non-inhibitor
CYP450 2C19 Inhibitor	Non-inhibitor
CYP450 3A4 Inhibitor	Non-inhibitor
AMES Toxicity	Non-toxic

Conclusion

This study highlights the potential of virtual screening and molecular dynamics as powerful tools in the search for novel inhibitors of beta-lactamase enzymes. Further *in vitro* and *in vivo* studies are warranted to confirm these findings.

References

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- Schrödinger Release 2017-3: Desmond Molecular Dynamics System; D. E. Shaw Research: New York, NY, 2017; Maestro-Desmond Interoperability Tools, Schrödinger, New York, NY, **2017**.
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