

The Antibacterial Efficacy and Drug Safety Profile of *Trans*-cinnamaldehyde against *Acinetobacter baumannii*: Bioinformatics and Cheminformatics Approach

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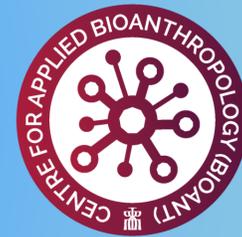
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INTRODUCTION

The discovery of antibiotics saves millions of lives worldwide, but in recent years bacterial antibiotic resistance has become a growing global problem as bacteria have become increasingly able to adapt to all known antibiotics. Projections have shown that in 2019, more than 4.9 million people worldwide died directly or indirectly as a result of antibiotic resistance (Murray et al., 2022). Therefore, it is crucial to discover new antibacterial agents that have therapeutic potential and are non-toxic and drug-safe so that humanity can successfully fight antibiotic resistance.

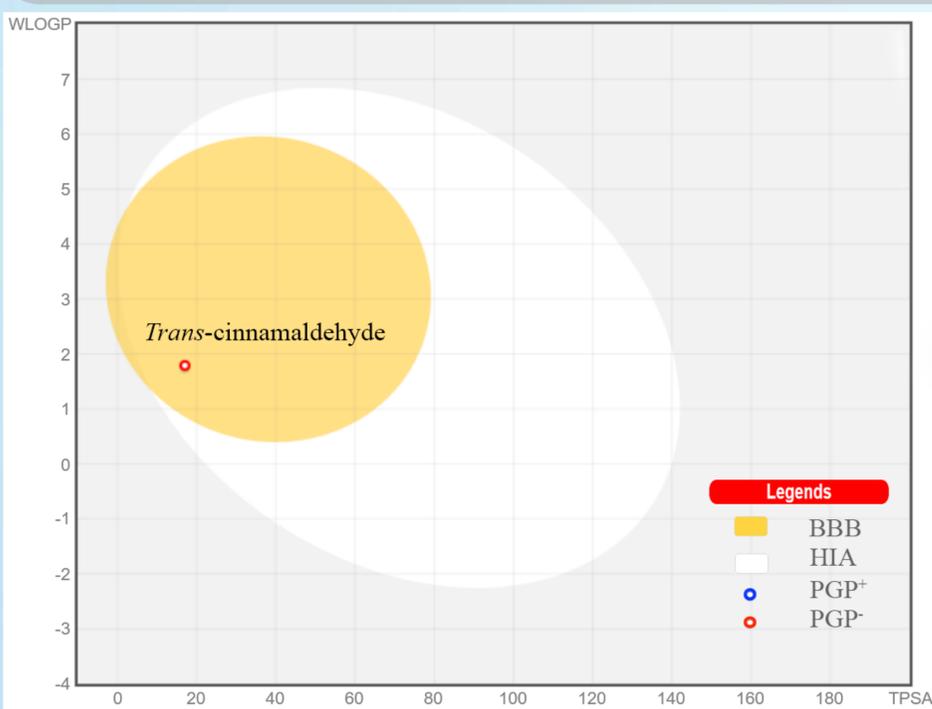


Figure 1: The Predicted Basic Pharmacokinetic Properties of *Trans*-cinnamaldehyde in the WLOGP-versus-TPSA with BOILED-egg. BBB – blood-brain barrier; HIA – human intestinal absorption; PGP+ – active efflux by P-glycoprotein (P-gp); PGP- – non-substrate of P-glycoprotein.

RESULTS

Trans-cinnamaldehyde fulfils the requirements for the number of rotatable bonds and proton acceptors, which should be readily absorbed in the gut and can cross the blood–brain barrier, but is not a substrate for P-gp, which contributes to its therapeutic potential as it is not immediately excreted from the body (Figure 1). Theoretically, it should not be hepatotoxic as it has no inhibitory effect on liver cytochromes. It meets all five of Lipinski's rules and, according to these criteria, is a molecule that could have therapeutic effects. The most promising potential targets in *Acinetobacter baumannii* are the proteins AbOmpA and bap, where *trans*-cinnamaldehyde could destabilise membrane integrity and disrupt biofilm formation (Nie et al., 2020). Molecular docking was used to create nine successful models for the possible binding of *trans*-cinnamaldehyde to the AbOmpA protein (Figure 2).

CONCLUSION

Bioinformatics and cheminformatics tools can help obtain resources for developing new antibiotics. In vitro tests need to be performed to confirm the efficacy of *trans*-cinnamaldehyde as a potential therapeutic agent against *Acinetobacter baumannii*.

AIM

The aim is to explore the antibacterial efficacy and drug safety profile of *trans*-cinnamaldehyde against *Acinetobacter baumannii* using a bioinformatics and cheminformatics approach.

METHODS

SwissADME software was used to assess *trans*-cinnamaldehyde's pharmacokinetics, drug-likeness, and medicinal chemistry friendliness, while potential therapeutic targets in *Acinetobacter baumannii* were assessed using the RCSB Protein Data Bank online platform tools and evaluated with a comprehensive review of the existing literature. AutoDock Vina v1.2.5 was used to perform all analytical docking analyses (Trott et al., 2010).

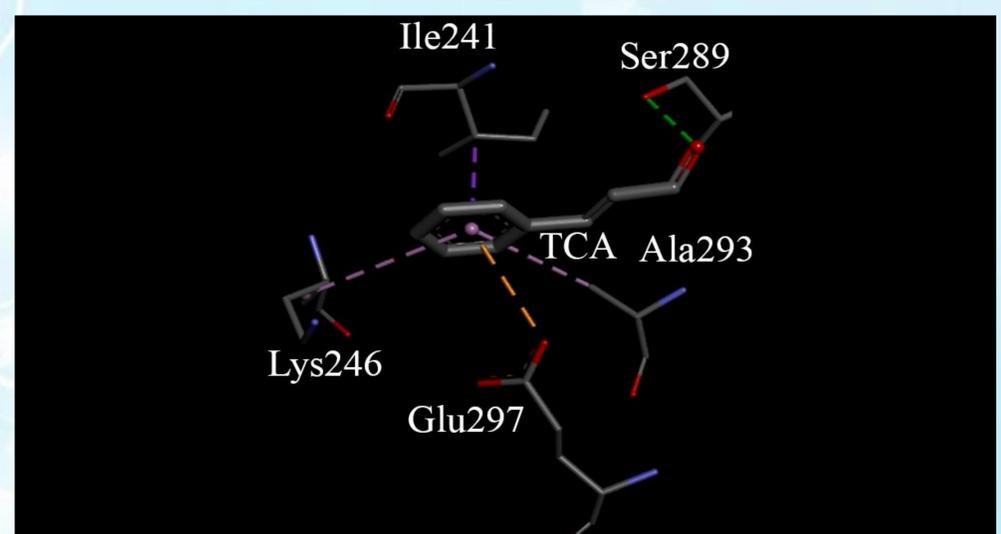


Figure 2: The Computational Prediction of the Binding Site of *Trans*-cinnamaldehyde and Amino Acids of the C-chain of AbOmpA. Binding energy = -4.0 kcal/mol, RMSD lb = 20.019 ± 0.0531 Å. Å – ångström; AbOmpA – outer membrane protein A; Ala – alanine; C – carbon; Glu – glutamate; Ile – isoleucine; kcal – kilocalories; LB – lower bound; Lys – lysine; RMSD – root mean square deviation; Ser – serine; TCA – *trans*-cinnamaldehyde.

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