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The Evaluation of the Antibacterial Efficacy and Drug Safety of Thymoquinone against *Acinetobacter baumannii*: Utilising Bioinformatics and Cheminformatics Methods in Microbiology

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INTRODUCTION

The discovery of antibiotics is considered one of the most important discoveries in the history of humanity. Bacterial antibiotic resistance has long been a growing global problem, and today, bacteria are becoming able to adapt to all known antibiotics. Projections have shown that in 2019, there were 1.27 million deaths due to antibiotic resistance. It is necessary to discover new antibacterial agents that have therapeutic potential and are drug-safe so that humanity can successfully overcome antibiotic resistance (1). Applying bioinformatics and chemoinformatics in microbiology can be useful to rapidly evaluate the efficacy and drug safety of potential antibacterial agents, thus avoiding the loss of resources due to unsuccessful trials.

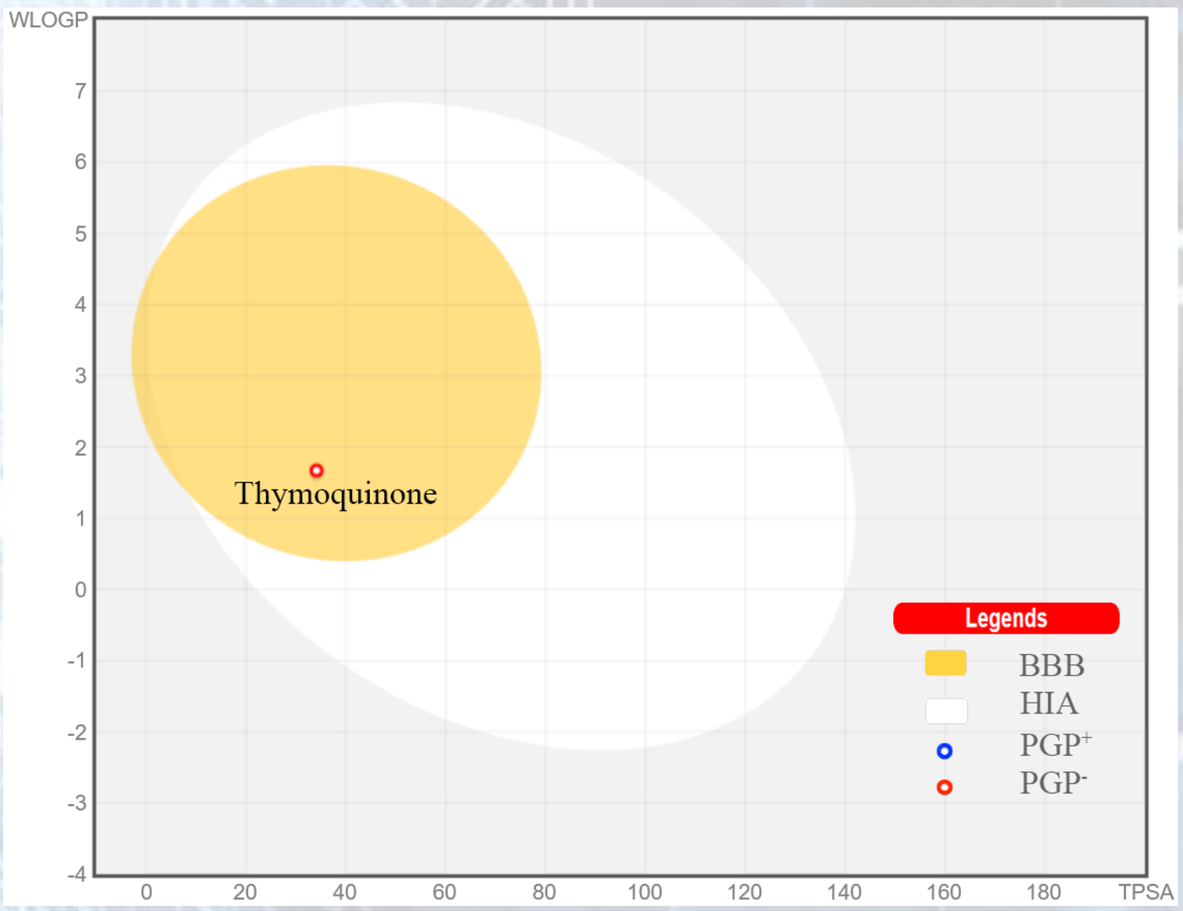

Figure 1: The Predicted Basic Pharmacokinetic Properties of thymoquinone in the WLOGP-versus-TPSA with BOILED-egg. BBB – blood-brain barrier; HIA – human intestinal absorption; PGP^+ – active efflux by P-glycoprotein (P-gp); PGP^- – non-substrate of P-glycoprotein.

RESULTS

Thymoquinone fulfills the requirements for the number of rotatable bonds, proton donors and acceptors, should be easily absorbed in the intestine and can cross the blood–brain barrier, but is not a substrate for P-gp (Figure 1). It should not be hepatotoxic as it has no inhibitory effect on liver cytochromes. It satisfies Lipinski's rules and is, therefore, a molecule that could have therapeutic effects. The most promising potential targets in *Acinetobacter baumannii* are the proteins AbOmpA and bap. Here, thymoquinone could induce reactive oxygen species that destabilise membrane integrity and disrupt biofilm formation by damaging the secondary and tertiary structure of *Acinetobacter baumannii* proteins and possibly also affect its nucleic acids, leading to cell death (3). Molecular docking was used to create nine successful models for the possible binding of thymoquinone to the AbOmpA protein (Figure 2).

CONCLUSION

Bioinformatics and chemoinformatics tools can be helpful in microbiology. It seems promising to perform in vitro tests to assess the antibacterial efficacy of thymoquinone as an antibacterial agent against *Acinetobacter baumannii*.

AIM

The aim is to explore the potential of thymoquinone as an antibacterial agent by utilising bioinformatics and chemoinformatics tools to evaluate its efficacy, safety and potential therapeutic targets against *Acinetobacter baumannii*.

METHODS

SwissADME software was used to assess timiquinone'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 existing literature. AutoDock Vina v1.2.5 was used to perform all analytical docking analyses (2).

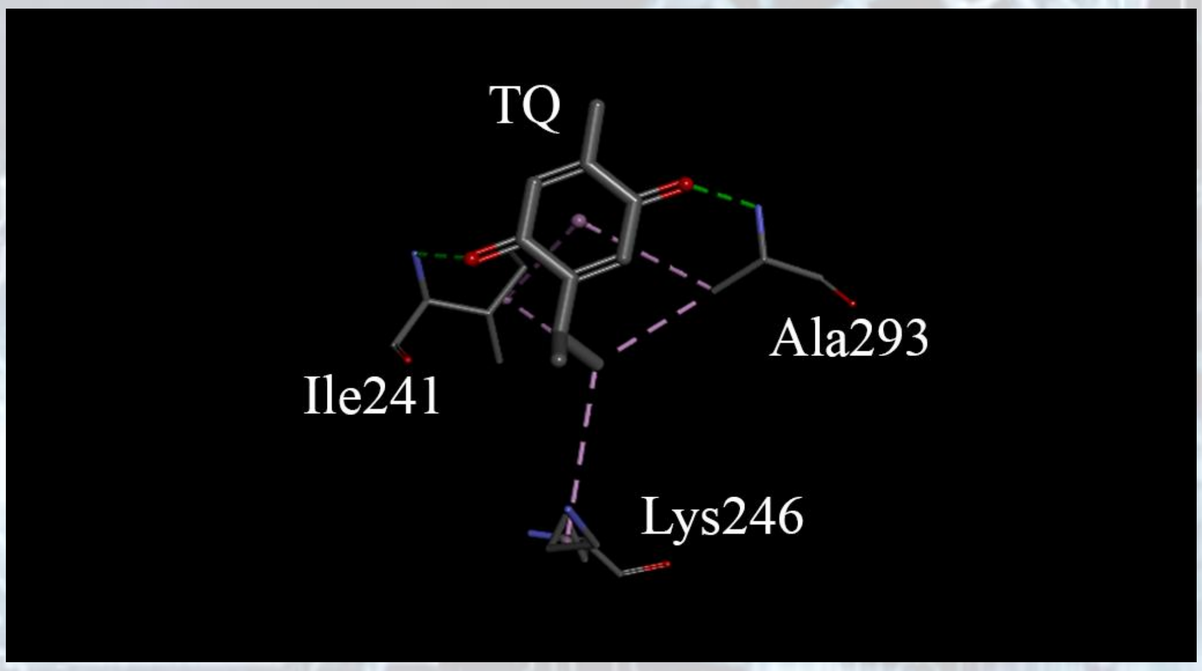

Figure 2: The Computational Prediction of the Binding Site of thymoquinone and Amino Acids of the C-chain of AbOmpA. Binding energy = -4.7 ± 0.00 kcal/mol, RMSD lb = 0.00 ± 0.00 Å, RMSD ub = 0.00 ± 0.00 Å. Å – ångström; AbOmpA – outer membrane protein A; Ala – alanine; C – carbon; Ile – isoleucine; kcal – kilocalories; LB – lower bound; Lys – lysine; mol – mole; RMSD – root mean square deviation; TQ – thymoquinone; ub – upper bound.

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