# EXPLORING SCHIFF BASES AS PROMISING ALTERNATIVES TO TRADITIONAL DRUGS IN THE *IN SILICO* TREATMENT OF ANTI-LEISHMANIASIS

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Leishmanioses are complex diseases prevalent in (sub)tropical regions, caused by the protozoan *Leishmania* spp. and transmitted by phlebotomine sandflies. With visceral and cutaneous manifestations, they affect 2 million people annually, resulting in 70,000 deaths, classified by the WHO as a global cause of death from infectious diseases. Tripanothione Reductase (TR), EC 1.8.1.1, a crucial enzyme in the parasite's redox metabolism, emerges as a therapeutic target, and its inhibition can disrupt the redox balance, leading to the parasite's death. Current treatment is based on Amphotericin B, Pentamidine, and Meglumine antimony, with a limited understanding of the mechanism of action and severe side effects. In this context, the present study aims to explore Schiff base compounds, either found in nature or synthesized, as promising sources that need to be investigated. These compounds are characterized by a double bond between carbon and nitrogen atoms, which can combine with alkyl or aryl groups. Thirty-two structures from the PubChem database were selected and compared to commercial inhibitors. The emerging therapeutic evaluation was investigated using *in silico* molecular docking methods against the protein with PDB code 2JK6, employing AutoDock Vina, PLIP for interaction analysis and toxicity assessments. Virtual screening with a library of 32 Schiff base compounds showed promise, with notable compounds such as 3-Quinolinamine ($\Delta G$ = -10.5 kcal/mol), 1,3-bis[(E)-(2-amino-4-ethyl-5-hydroxy-phenyl)methyleneamino]urea ($\Delta G$ = -10.4 kcal/mol), and Naphtaldehyde disulfide Schiff base ($\Delta G$ of -9.8 kcal/mol) demonstrating significant affinities with *Leishmania* infantum TR, surpassing commercial inhibitors (Amphotericin B with $\Delta G$ = -9 kcal/mol; Pentamidine with $\Delta G$ = -8.8 kcal/mol; Meglumine antimony with $\Delta G$ = -5.9 kcal/mol). To assess the safety of the highlighted compounds, a toxicity screening was conducted, concluding the efficacy of Schiff base compounds against TR protein as alternatives to conventional treatment for leishmaniasis based on computational studies.