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IN VITRO SCHISTOSOMICIDAL ACTIVITY AND MOLECULAR MODELING OF QUERCITRIN AND AFZELIN ISOLATED FROM COPAIFERA OBLONGIFOLIA LEAVES

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Schistosomiasis, a neglected tropical disease, has affected millions of people globally. Treatment depends mostly on praziquantel (PZQ), but the emergence of resistance justifies the search for new therapeutic alternatives. The enzyme Thioredoxin Glutathione Reductase (TGR) from *Schistosoma mansoni* is a validated target for the development of new drugs. Species of *the genus Copaifera* are recognized in traditional medicine for their pharmacological properties, making them promising sources for the discovery of bioactive compounds. This study investigated the in *vitro* and *in silico schistosomicidal potential* of compounds isolated from the leaves of *Copaifera oblongifolia*. The hydroalcoholic extract of *C. oblongifolia leaves* was partitioned and fractionated by chromatographic techniques, resulting in the isolation of the compounds quercitrin (1) and afzelin (2), identified by spectroscopic techniques (NMR ^{1}H, NMR ^{13}C and ESI-MS). In vitro schistosomicidal activity was evaluated against adult *worms of S. mansoni* (LE strain) recovered from infected BALB/c mice. The parasites were incubated with the compounds (12.5–200 µM) and the crude extract (50 and 100 µg/mL) for 72 h. Mortality and reduction in motor activity were monitored every 24 h. Praziquantel (12.5 µg/mL) and culture medium were used as positive and negative controls, respectively. Molecular *docking* studies were performed with the GOLD *software* to evaluate the binding mode of the compounds to the active site of the TGR enzyme (PDB: 2V6O), using PZQ as a reference. The crude extract at the concentrations tested did not show significant activity. However, compounds 1 and 2 alone demonstrated potent schistosomicidal activity *in vitro*. Quercitrin (1) induced 100% mortality at the 50 µM concentration after 72 hours. Afzelin (2) was slightly less potent but still caused 100% mortality at the 200 µM concentration after 72 hours. The molecular *docking* results revealed that both compounds interact strongly with amino acid residues from the FAD binding site on the TGR enzyme, with binding energies (dG = -23.44 and -28.90 kcal mol^{-1}, respectively) comparable or even more favorable than that of PZQ (dG = -22.03 kcal mol^{-1}). This interaction, mediated by multiple hydrogen bonds and hydrophobic interactions, suggests a potential mechanism of action via inhibition of TGR, an enzyme crucial for parasite survival. The flavonoids quercitrin and afzelin, isolated from *Copaifera oblongifolia*, exhibited significant schistosomicidal activity *in vitro* and showed, by molecular modeling, a strong potential to inhibit the TGR enzyme of *S. mansoni*. These results highlight these compounds as promising candidates for future studies of drug development against schistosomiasis.

Keywords: *Schistosomiasis; Copaifera oblongifolia; Quercitrin; Afzelina; Molecular Docking; TGR.*