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TITLE

EVALUATION OF THE POTENTIAL OF CHALCONES AGAINST SCHISTOSOMA MANSONI

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ABSTRACT

Schistosomiasis is a neglected disease that affects populations in tropical and subtropical regions. The disease is caused by trematodes of the genus Schistosoma, with Schistosoma mansoni being the only species present in Brazil. Currently, praziquantel (PZQ) is the only drug available for the treatment of this parasitic disease. After decades of mass administration, the number of treatment failures has been increasing, raising concerns about the emergence of tolerant or resistant strains, and highlighting the need for new therapeutic alternatives. Chalcones are plant-derived metabolites have demonstrated broad antiparasitic activity, suggesting that compounds of this class could be promising candidates for drug development. In this study, we evaluated the schistosomicidal potential of six chalcones in vitro at different concentrations: 5 µg/mL, 2.5 µg/mL, 1.25 µg/mL, and 0.675 µg/mL over 72 hours. We then, selected the two chalcones with notable in vitro activity for in vivo testing at a concentration of 100 mg/kg in mice infected with 70 cercariae. In the in vitro assays, male and female S. mansoni were evaluated on a scale of 0 to 3, where scores of 1 to 3 indicated varying levels of viability: At score 3, the worms were viable, showing no tegumental damage or contractions; at score 1, the worms were non-viable, with significant tegumental damage and intense contractions; A score of 0, indicated that the worms were dead, showing no movement. At the concentration of 5 µg/mL, chalcones 3, 4, and 6 killed 100% of males and females within 24 hours. By 48 hours, males and females exposed to chalcone 2 and females exposed to chalcone 5 showed 100% mortality. Males exposed to chalcone 5 and males and females exposed to chalcone 1 showed over 50% mortality and significantly reduced viability (<1) by the end of the experiment. At the lower concentrations (2.5 µg/mL, 1.25 µg/mL, and 0.625 µg/mL), none of the compounds killed 100% of the whitin 72 hours. However, all groups showed a statistically significant reduction in viability compared to the untreated control and yielded results comparable to PZQ. Chalcone 3 stood out for maintaining activity at all concentrations tested, while compound 5 was particularly effective at lower concentrations, suggesting better solubilization. Consequently, these two chalcones were selected for in vivo assays. In the in vivo schistosomicidal assays, chalcone 3 significantly reduced the number of females recovered during perfusion compared to the control group. Additionally, both chalcone 3 and chalcone 5 effectively reduced the number of eggs per gram of feces, as well as the number of immature, mature, and total eggs found in the oogram. These results indicate that the tested compounds hold potential for the treatment of schistosomiasis.

KEYWORDS

Schistosomiasis; Chalcones; In Vitro Assay; In Vivo Assay

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