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TITLE

SCREENING OF SNAKE VENOMS FOR THE IDENTIFICATION OF POSSIBLE NOVEL THERAPEUTICAL TARGETS AND TOXINS WITH SCHISTOSOMICIDAL POTENTIAL

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ABSTRACT

Schistosomiasis is a neglected tropical disease caused by flatworms of the genus Schistosoma. Treatment of the disease relies only on a partially effective drug, praziquantel. Therefore, new therapeutic alternatives are needed. Snake venoms have lethal activity against different organisms, ranging from bacteria to higher vertebrates. Several venoms have been shown to be active against protozoa, however, data on the activity of venoms against helminths are scarce. In the search for new antischistosomal compounds, we tested here the in vitro effects of crude venoms from eight Bothrops snake species, from Crotalus d. terrificus and venom fractions against two developmental stages of Schistosoma mansoni, post-infectious larvae (schistosomula) and adults. We obtained adult S. mansoni worms by perfusion of infected hamsters. We monitored mortality, motility, pairing rates and oviposition of adult worms over 72 h of incubation with the venoms. Furthermore, we assessed the viability of adult and schistosomula worms by ATP quantification. We used scanning electron microscopy (SEM) to examine morphological changes after incubation with venom and EdU assays to measure the effect of venom against parasite stem cells proliferation. We subjected B. jararacussu venom to size-exclusion chromatography and analyzed the effects of protein fractions on parasite viability. We found that adult worms incubated with each venom at concentrations of 100 and 50 µg/mL showed a reduction in parasite viability, motility, pairing, and egg laying. Schistosomula incubated with each venom at concentrations of 3.12, 6.25, 12.5, 25, and 50 µg/mL showed a significant dose and time-dependent decrease in viability. Adult and schistosomula showed the most significant changes after exposure to B. jararacussu venom, which was therefore chosen for further assays. B. jararacussu venom at concentrations of 25 and 50 µg/mL resulted in tegumental damage of adult worms, as shown by SEM. EdU assays revealed a reduction in worm stem cells when incubated with B. jararacussu venom at 50 and 100 µg/mL. Seven fractions of B. jararacussu venom were investigated for antischistosomal activity. After incubation of schistosomula and adult worms with each fraction at 25 or 50 µg/mL, we observed that fraction 4 significantly reduced the viability of these parasites. In conclusion, the anthelmintic activity of snake venoms and their components against S. mansoni is promising, justifying further investigations.

KEYWORDS

Schistosoma mansoni; Snake vVnoms; Natural Compounds

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