In vitro evaluation of the anthelmintic activity of BnSP-6 snake venom using bioconjugated CdSe/CdSe Magic Sized Quantum Dots tracking against *Strongyloides venezuelensis*

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Strongyloidiasis is a neglected parasitic disease caused by helminths of the genus *Strongyloides*. Currently, ivermectin is the drug of choice for its treatment, however, cases of therapeutic failure in immunosuppressed patients have been reported. The search for new drugs from natural resources is one important topic of biomedical research. In this context toxins from snake venoms have been investigated for the treatment of strongyloidiasis. Phospholipases A2 (PLA2) are enzymes that have been used in several studies due to its pharmacological potential against tumors and bacteria, among others. In the present study, we showed the action of a BnSP-6 a PLA2 homologous to the venom of *Bothrops pauloensis* against *Strongyloides venezuelensis*. Human intestinal cells (Caco-2), infective larvae and parthenogenetic females of *S. venezuelensis* were cultured and treated with different concentrations of BnSP-6 (1-100μg/ml) during 72 hours. Ivermectin was used at the standard dose (316μg/ml) as death control of the parasite. All tests were performed in triplicate. After the treatment cytotoxicity was evaluated by the quantitative colorimetric method using 3- (4,5-dimethylthiazol-2yl) -2,5-diphenyl tetrazoline bromide (MTT). Posteriorly, autophagy and apoptosis were evaluated by fluorescence lable with Monodansiylcadaverine (MDC) and Propiodium Iodide (PI) respectively and was analyzed by fluorescence microscopy (EVOS Fl). To verify the BnSP-6 site of action, bioconjugation of CdSe/CdSe magic-sized quantum dots (MSQDs), proved biocompatible, with the toxin was performed. The infective larva was treated for 24 hours with the bioconjugate and then the luminescence was monitored by fluorescence microscopy using the DAPI filter (EVOS Fl). The MTT assay did not show cytotoxicity in BnSP-6-treated intestinal control cells (Caco-2). However, in the experiments with *S. venezuelensis*, it was observed that BnSP-6 showed similar cytotoxicity in a concentration of 12x less than ivermectin. In the fluorescence assay, autophagic vacuole and cellular apoptosis were verified in both evolutionary forms of the parasite. The images of fluorescence microscopy indicated that the bioconjugate was localized at larval intestine after 24 hours, suggesting its action via intestinal absorption. Summary, in this study, we demonstrated that BnSP-6 is cytotoxic only for the parasite, it is absorbed by the intestine, causes autophagy, death by cellular apoptosis and has the most effective action against *S. venezuelensis* when compared to ivermectin, suggesting its potential for strongyloidiasis treatment.

Key words: *Strongyloides venezuelensis*, BnSP-6, snake venom, CdSe/CdSe MSQDs

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