Research for components with antiviral action against ZIKAV in animal venoms

Kalynka Ribeiro Cordeiro, Karla de Castro Figueiredo Bordon, Líria Hiromi Okuda, Norival Alves dos Santos Filho, Louise Oliveira Fiametti, Eliane Candiani Arantes

Abstract:
Animal venoms are rich sources of molecules that show diverse biological activities and high specificity for their targets. They have great structural and functional diversity and are able to modulate biological mechanisms involved in diseases of the nervous, cardiovascular and immune systems, in addition to diseases caused by microorganisms, including virus. Despite the large variety of molecules with potential biotechnological application, there is still an enormous difficulty in bioprospecting them, due to the small amount of starting material, low yield and the high cost of traditional purification strategies. This explains the small number of candidate molecules of animal origin currently used as biopharmaceuticals. Therefore, this work aims to carry out the purification and characterization of components from the venoms of the scorpion *Tityus serrulatus* and the snake *Crotalus durissus terrificus* with antiviral activities. The identification and characterization of potential candidate molecules will contribute to develop new biopharmaceuticals for the treatment of viruses. Firstly, the *cdt* venom was fractionated by fast protein liquid chromatography (FPLC), in a semipreparative C-18 reverse phase column. Then, the fractions were submitted to *in vitro* characterization tests to evaluate their cytotoxic activity using the MTT technique and antiviral activity. The peptides were synthesized, due to the difficulty in obtaining venom from the scorpion Tityus serrulatus, low recovery and extensive chromatogram presented. Fractions that showed low cytotoxicity and antiviral activity were submitted to Tris-Tricine-SDS-PAGE electrophoresis to assess their degree of purity. The antiviral action of isolated components were characterized by *in vitro* assays. The most promising molecules were evaluated in the presence of different strains of the ZIKV. Among them, phospholipase A2 (all of them compounds tested at concentrations ranging from 200 to 12.5 µg) proved to be the most effective. It exhibited low cytotoxicity and inhibited the viral activity of Zika virus. The fraction crotoxin has shown similar cytotoxicity, but lower antiviral protection. TsAp-1 did not show promising results against the viruses, despite his low cytotoxicity, but, TsAp-2 has shown high cytotoxicity in the higher concentrations, and did not show promising antiviral activity against the tested viruses.

Keywords: *Tityus serrulatus*, *Crotalus durissus terrificus*, antiviral, ZIKAV.