PARTICIPATION OF SERINE PROTEASES, METALLOPROTEASES AND PHOSPHOLIPASES A\textsubscript{2} IN THE LOCAL EFFECTS INDUCED BY BOTHROPS ALTERNATUS SNAKE VENOM

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Introduction and objectives: Envenomation caused by snakes from Bothrops sp. elicits pronounced local effects, characterized by edema, hemorrhage, pain and necrosis. The pathogenesis of these effects can be associated with the direct action of different toxins from snake venoms, which induce tissue damage and inflammation. In this work, we investigate the contribution of serine proteases, metalloproteases and phospholipases A\textsubscript{2} to the inflammatory effects induced by B. alternatus venom. Materials and methods: B. alternatus venom (10 - 100 \mu g) was injected into the animals hind-paw in order to establish a dose and time-dependence of venom-induced edematogenic, hyperalgesic and myotoxic effects. The venom (1.0 mg/mL) was treated with 2 mM phenylmethanesulfonyl fluoride (PMSF, serine proteases inhibitor), 10 mM 1,10-phenanthroline (Phe, metalloproteases inhibition) or 20 mM 2,4’dibromoacetophenone (BAP, phospholipases A\textsubscript{2} inhibitor) and the progress of those effects were monitored. All experiments were carried out 3 rats or mice/group, following ethical parameters and using ANOVA to statistical analysis. Results and conclusions: B. alternatus venom was able to induce significant edema, hyperalgesia and myotoxicity in experimental animals. The maximum increased hind-paw swelling occurred at 1 hour after injection of venom, which disappears within 24 hours. While a significant decrease in pain threshold occurred between 3 and 6 hours after venom inject and still keeping at 24 hours. The venom was able induced a myotoxic effect demonstrated by the elevation on plasma creatine kinase (CK) to activity in mice. The intensity of edema was markedly reduced by venom treated with Phe and BAP. All chemical treatments inhibited the hyperalgesia, but they did not reduce of myotoxicity induced by crude venom. Finally, our findings indicate that metalloproteases and phospholipases A\textsubscript{2} play an important role in the development of edema and hyperalgesia venom-induced. However, the serinoproteases contributes specifically with hyperalgesia induced by B. alternatus venom.

Key Words: snake venom, Bothrops alternatus, inflammatory reactions.

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