**J Venom Anim Toxins incl Trop Dis.**
**V.15, n.4, p.799-800, 2009.**
**Thesis.**
**ISSN 1678-9199.**

# CHARACTERIZATION OF *Bothrops jararaca* SNAKE VENOM EFFECTS ON RAT VAS DEFERENS

**Thesis:** J. M. Sciani submitted this thesis for her Masters in Pharmacology at the Federal University of São Paulo, UNIFESP, São Paulo, São Paulo State, Brazil, 2008.

**Advisor:** Professor Lúcia Lameirão Garcez-do-Carmo

**ABSTRACT:** The main compounds of *Bothrops jararaca* venom are serine peptidases, metallopeptidases and phospholipases $A_2$. These enzymes cause several symptoms, as hemorrhage, coagulation disturbances, edema and myotoxicity. However, effects on smooth muscle are not clear yet. Previous studies in our laboratory have shown that *Bothrops jararaca* crude venom (CV) provokes contractions of rat vas deferens, followed by relaxation. The aim of this study was to characterize which components of *Bothrops jararaca* venom are responsible for contraction and if this reaction is neurogenic or myogenic. Vas deferens were isolated and mounted in an appropriated chamber containing continuously aerated nutritive solution at 37°C. Organs were electrically stimulated (5 Hz, 3 ms, 90 V, in trains of 10 s) during 60 minutes. Once established, fractions from 1 up to 6 (100 µg/mL), obtained by gel filtration chromatography (Sephacryl S-100 resin) were added. Before and after samples incubation, vas deferens was stimulated with KCl (80 mM). Using the same protocol, before adding to tissue, fractions were pre-incubated with EDTA (100 µM), a metallopeptidase inhibitor, or PMSF (100 µM), a serine peptidase inhibitor. Hoe 140 (100 nM), $B_2$ receptor antagonist, also was incubated with vas deferens, before venom addition. Fractions 4, 5 and 6 did not cause significant effects on vas deferens, which excluded the phospholipase $A_2$ action. Fraction 1 caused similar effects compared to CV, an increase of neurogenic and myogenic contractions, but did not inhibit any of them. The contractile effect was

inhibited by PMSF and Hoe 140, indicating that serine peptidase and bradykinin are responsible by neurogenic and myogenic contraction, probably by bradykinin release by serine peptidases, from the vas deferens. KCl-induced contraction was not altered. On the other hand, fractions 2 and 3 inhibited contractions (neurogenic, myogenic and induced by KCl) and these effects were reverted by EDTA incubation, but not by PMSF. These data indicate that metallopeptidases are responsible for diminishing contractions, probably by damaging effects on the organ, since these enzymes are effective on the extracellular matrix, an important element to the tissue structure.

**KEY WORDS:** *Bothrops jararaca* venom, metallopeptidases, serine peptidases, bradykinin.

**CORRESPONDENCE TO:**

JULIANA MOZER SCIANI, Instituto Butantan, São Paulo, SP, 05503-900, Brasil. Phone: +55 11 3726 7222, ext. 2101. Email: jmsciani@usp.br.