

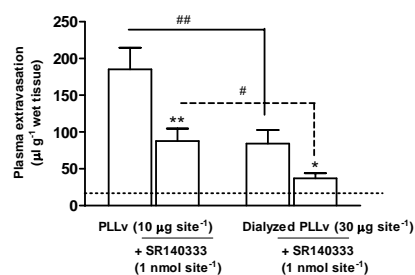
THE PLASMA PROTEIN EXTRAVASATION INDUCED BY POLISTES LANIO LANIO WASP VENOM IN THE MICE SKIN: INVOLVEMENT OF SENSORY-C FIBERS.

¹L.M. Yshii, ^{2,3}G.H.M.F. Souza, ²S. Hyslop, ³M.N. Eberlin, ⁴M.T.P. Ribela, ¹M.A. Barreto, ¹S.K.P. Costa. ¹Pharmacology Department (ICB), University of São Paulo; ²Pharmacology Department and ³Chemistry Institute, University of Campinas, ⁴IPEN/CNEN, São Paulo, Brazil.

Stings by *Polistes* sp wasps, found in Brazil, are of clinical interest as they can cause life-threatening allergic reactions, pain and inflammation (Castro *et al.*, 1994). However, little is known about the biological activity and composition of the venom. This study was undertaken to investigate the effects evoked by *Polistes lanio lanio* venom (PLLv) in the cutaneous microvasculature and to identify active inflammatory peptides.

Both male and female C57BL/6 mice (25-30 g) and Wistar rats (200 g) anesthetised with urethane (25% w/v, 100 μ l 10 g⁻¹) were used. ¹²⁵I-albumin (0.03 MBq/0.1 ml) was injected into the tail vein. Intradermal injection (i.d.; 0.05-0.10 ml) of test agents was made into the shaved dorsal skin. Following 30 min period accumulation, animals were killed and skin oedema was assessed via extravascular accumulation of ¹²⁵I-albumin (Costa *et al.*, 2003). The venom was collected by compressing the venom sac and then was lyophilized and sometimes dialyzed (MW cutoff 2000). The nano-electrospray ionization analysis of venom-containing peptides was carried out via Q-TOF mass spectrometer (Micromass, U.K.) coupled to a CapLC chromatographic system. The MS/MS spectra was processed using MaxEnt3 and sequenced via PepSeq software. PLLv (0.3-30 μ g site⁻¹) caused a potent and dose-dependent oedema formation into the dorsal skin of mice (not shown; n=3-8). The venom EC₅₀ (7 μ g) induced oedema was unaffected by the bradykinin B₂ receptor antagonist HOE 140 (0.8 nmol kg⁻¹; i.v.) but partly reduced by the B₁ receptor antagonist Des-Arg⁹-[Leu⁸]-BK (3 μ mol kg⁻¹, i.v.; 269 \pm 28 and 94.5 \pm 35* μ l site⁻¹, control and treated, n=3-4). Dialysis of PLLv reduced the oedema by 50% (Fig. 1). The substance P NK₁ receptor antagonist SR140333, but not NK₂ (SR48968), markedly reduced PLLv-evoked oedema (Fig. 1). Capsaicin treatment to deplete neuropeptides inhibited PLLv-induced response in rats (not shown; n=4). Analysis by mass spectrometry (Q-TOF/CapLC) shows that PLLv contains peptides (MW 1173 – 3581) that share C-terminal sequences with mammalian tachykinins.

Fig. 1 Effect of raw and dialyzed PLLv in the absence and presence of SR140333 (1 nmol site⁻¹; n=7-8) in the mice skin. **P*<0.05 and ***P*<0.01 vs PLLv without SR140333. #*P*<0.05 and ##*P*<0.01 dialyzed PLLv vs raw venom.



These findings provide new evidence that PLLv-induced inflammatory effect in the skin of rodents is largely mediated by the action of tachykinin-like peptides, in a manner similar to the endogenous neuropeptide Substance P. The venom-induced oedema may also involve activation of BK B₁ receptor in the cutaneous microvasculature.

Castro, F.F.M. *et al.* (1994). *J. Investig. Allergol. Clin. Immunol.*, **4**, 37-41.

Costa, S.K.P. *et al.* (2003). *Br. J. Pharmacol.*, **139**, 59-64.

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