

SNAKE VENOMICS AND ANTIVENOMICS OF *BOTHROPS COLOMBIENSIS*, A MEDICALLY IMPORTANT PITVIPER OF THE *BOTHROPS ATROX-ASPER* COMPLEX ENDEMIC TO VENEZUELA: CONTRIBUTING TO ITS TAXONOMY AND SNAKEBITE MANAGEMENT

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The taxonomic status of the medically important pitviper of the *Bothrops atrox-asper* complex endemic to Venezuela, classified as *Bothrops colombiensis*, remains *incertae sedis*. To help resolving this question, the venom proteome of *B. colombiensis* was characterized by RP-HPLC followed by analysis of each chromatographic fraction by SDS-PAGE, N-terminal sequencing, MALDI-TOF mass fingerprinting, and CID-MS/MS of tryptic peptides. The venom contained 8 types of proteins. PI Zn²⁺-metalloproteinases and K49 PLA₂ molecules comprise over 65% of the venom proteins. Other venom protein families comprised PIII Zn²⁺-metalloproteinases (11.3%), D49 PLA₂s (10.2%), L-amino acid oxidase (5.7%), medium-sized disintegrin (5.6%), serine proteinases (1%), bradykinin-potentiating peptides (0.8%), a DC-fragment (0.5%), and a CRISP protein (0.1%). Comparison of the venom proteomes of *B. colombiensis* and *B. atrox* did not support the suggested synonymy of *B. colombiensis* and *B. atrox*. The closest homologues to *B. colombiensis* appeared to be *B. asper*. A rough estimation of the similarity between their venoms indicated that these species share approximately 65-70% of their venom proteomes. The close kinship of *B. colombiensis* and *B. asper* points at the ancestor of *B. colombiensis* as the founding Central American *B. asper* ancestor. This finding may be relevant for reconstructing the natural history of Bothrops. Further, the indistinguishable immunological crossreactivity of a Venezuelan antivenom (against a mixture of *B. colombiensis* and *Crotalus durissus cumanensis* venoms) and the Costa Rican polyvalent antivenom (against a mixture of *B. asper*, *Crotalus simus*, and *Lachesis stenophrys* venoms) towards the venoms of *B. colombiensis* and *B. asper*, supports this view and suggests the possibility of indistinctly using these antivenoms for the management of snakebites by any of these Bothrops species. However, our analyses also evidenced the limited recognition capability of these antivenoms towards a number of *B. colombiensis* and *B. asper* toxins, notably medium-size disintegrins, bradykinin-potentiating peptides, PLA₂s, and PI-SVMPs.