Proteomic characterization and lethality of the venom of the Black Judean scorpion, Hottentotta judaicus (Buthidae): expanded toxin diversity and revisited toxicological significance

Adolfo Borges, Bruno Lomonte, Antonieta Rojas de Arias & Julián Fernández

Abstract

The scorpion *Hottentotta judaicus* inhabits the Levant region of the Middle East, including Lebanon, Jordan, Palestine, and Israel. While previous research focused on its insecticidal properties and sodium-channel-targeting toxins, its venom remains largely unexplored using modern proteomic approaches. We analyzed the venom composition of *H. judaicus* from Lebanese specimens using nESI-MS/MS, MALDI-TOF MS, SDS-PAGE, and RP-HPLC. Venom lethality in mice was assessed (LD_{50} = 11.87 [6.59–17.16] mg/kg, i.p.), confirming moderate toxicity to vertebrates. RP-HPLC on C_{18} resolved 37 peaks, with 25 eluting between 20–40% acetonitrile. Reducing SDS-PAGE revealed predominant components < 10 kDa and minor bands at 31, 46, and 77 kDa. MaLDI-TOF MS detected 20 components from 1,000–12,000 m/z. A bottom-up shotgun nLC-MS/MS approach, following in-gel tryptic digestion of venom, identified 55 components across 15 protein families. Ion channel-active toxins [K^+ (7), Na^+ (16), Cl^- (1), ryanodine receptor (1)] and enzyme components (17) were predominant. This study provides proteomic evidence of *H. judaicus* venom components previously only identified at the transcriptomic level and reveals a richer venom profile than anticipated. Novel identified components include alternative β-subunits of lipolysis-activating proteins, as well as homologs of *Olivierus martensii* antimicrobial peptide inhibitor HAP-1, *Leiurus hebraeus* Lqhβ1, *Parabuthus transvaalicus* Birtoxin, and peptide Hj2a from *Hottentotta jayakari* exhibiting dual α/β-toxin activity on Nav1.1 channels. This expanding repertoire of potential bioactive components prompts a reevaluation of the pathophysiological consequences of *H. judaicus* envenomation in humans and further exploration of their potential biomedical applications.