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Characterization of two Moroccan scorpion venoms: Proteomic analysis, neurotoxicity, myotoxicity and sensitivity to neutralization by experimental polyclonal anti-venom

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Buthus occitanus and Androctonus mauretanicus are two medically important scorpions implicated in the pathogenesis of scorpion stings in Morocco. In this study, we first report on the neurotoxicity and myotoxicity of Androctonus mauretanicus (Am) and Buthus occitanus (Bo) venoms, as well as on the neutralizing capacity of experimental antivenom towards the neuromuscular and myotoxic activities of these venoms. Second, we examined the efficacy of commercially-available polyvalent antivenom regarding its ability to prevent or reduce mortality (in vivo testing in mice), myotoxicity and neurotoxicity of venoms. The protein contents of Am and Bo venoms were investigated using an original scorpion venomic approach. The pharmacological effects of Am and Bo venoms were investigated in vitro using chick biventer cervicis nerve-muscle preparations. The protective potency of commercial polyclonal anti-venom was also investigated. This anti-venom was made from serum of horse that was hyperimmunized with a mixture of three scorpion venoms: Two venoms from the most venomous species of North Africa, Bo and Androctonus australis hector (Aah) and one venom from the most venomous species living in Middle East (Leiurus quinquestriatus). The results obtained were finally compared to the values of ED50 in assays of lethal activity neutralization in mice. Our findings: 1) The sequential analysis of venom fractions revealed a highly complex venom proteome which counted a total of 80 and 140 proteins for Bo and Am venoms, respectively. In Am venom, we report a content of 21% enzymes, 43% sodium channel-specific toxins (89% are alpha-toxins and 11% are beta-toxins), 20% potassium channel-specific toxins, 4% chloride channel-specific toxins, 3% unknown peptides and 9% other activities. Among Am toxins, 17% are insect toxins whereas 83% are mammal toxins. In Bo venom, we found 18% enzymes, 58% sodium channel-specific toxins (90% are alpha-toxins and 10% are beta-toxins), 15% potassium channel-specific toxins, 5% chloride channel-specific toxins, 1% unknown peptides and 8% other activities. Among Bo toxins, 19% are insect toxins and 81% are mammal toxins. From data analyses, it appears that Am and Bo venoms contain a number of compounds sharing high sequence identities with alpha-toxins from structural and immunological groups 1 to 3. 2) It was found that Am and Bo venoms contain myotoxins and postsynaptic neurotoxins. In agreement with lethal potencies of these venoms in mice, Am venom exhibited greater neurotoxicity and myotoxicity than those observed with Bo venom.

Significance:

1. Interestingly, our results show that Am and Bo venoms are complex mixtures of molecules (especially Am venom). When Am venom is concerned, our results agreed well with previous reports highlighting a high frequency of compounds sharing a high structural identity with toxins (suggesting a particular danger of Am venom to humans
2. These findings strongly suggest that Am and Bo venoms contain distinct toxin components that are responsible for myotoxic and/or neurotoxic effects. The data also indicate it would be appropriate to add the Am venom, together with Bo and Aah venoms, to potentially produce more efficient polyvalent antivenom.

Biography

Oukkache Naoual has completed his PhD in Biochemistry. She has an expertise in the field of study of venoms and the improvement of antivenoms. She did internships on the study of venoms and antivenoms production from Butantan Institute in Brazil, The Institute of Biotechnology of Mexico and Monash University in Malaysia. She works now as Researcher at Pasteur Institute in Morocco.

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