Proteomic characterization of venom of the medically important Southeast Asian Naja sumatrana (Equatorial spitting cobra)

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ABSTRACT

The proteome of Naja sumatrana (Equatorial spitting cobra) venom was investigated by shotgun analysis and a combination of on-exchange chromatography and reverse phase HPLC. Shotgun analysis revealed the presence of 39 proteins in the venom while the chromatographic approach identified 37 venom proteins. The results indicated that, like other Asian cobra venoms, N. sumatrana contains large number of three finger toxins and phospholipases A2, which together constitute 92.1% by weight of venom protein. However, only eight of the toxins can be considered as major venom toxins. These include two phospholipases A2, three neurotoxins (two long neurotoxins and a short neurotoxin) and three cardiotoxins. The eight major toxins have relative abundance of 1.6–27.2% venom proteins and together account for 89.8% (by weight) of total venom protein. Other venom proteins identified include Zn-metalloproteases, disintegrin, Thaexin, CRISP, neutralizing peptide, complement depiring factors, cobra venom factors, venom nerve growth factor and cobra serum albumin. The proteome of N. sumatrana venom is similar to proteome of other Asian cobra venoms but differs from that of African spitting cobra venom. Our results confirm that the main toxic action of N. sumatrana venom is neurotoxic but the large amount of cardiotoxins and phospholipases A2 are likely to contribute significantly to the overall pathophysiological action of the venom. The differences in toxin distribution between N. sumatrana venom and African spitting cobra venoms suggest possible differences in the pathophysiological actions of N. sumatrana venom and the African spitting cobra venom, and explain why antivenom raised against Asian cobra venom is not effective against African spitting cobra venom.

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Introduction

Snake bite remains a serious yet neglected tropical disease. The global figure of snake envenomation cases has been estimated to be more than 1.8 million annually (Kasturiratne et al., 2008). At the moment, antivenom therapy is the only effective treatment for snake envenomation. The development of effective antivenom and improvement of management of snake envenomation require a clear understanding of the pathogenesis and toxicological properties of the venom (Ménez et al., 2006; Williams et al., 2011).

Snake venoms are also known to contain novel toxins with potential therapeutic and diagnosis applications (Gomes et al., 2010; Kapoor, 2010; Koh et al., 2006; Pal et al., 2002) as snake venoms are complex mixtures containing predominantly enzymatic or non-enzymatic proteins and poly peptides that possess various pharmacological actions (Deley and Kni, 2009; MacKessy, 2009).

Recent advances in proteomics have made it possible to globally identify protein components in the venom, including those that exist only in minute amount. This detailed knowledge of the toxin composition of venoms will contribute not only to in-depth understanding on the pathogenesis of snake envenomation mechanism and development of antivenom but also could lead to discovery of novel drugs and biomedical tools (Ménez et al., 2006). To date, proteomic characterization of venom proteins of a considerable number of medically important venomous snakes have been reported (Ali et al., 2013; Calvet et al., 2007, 2009; Nawar et al., 2003; Peiras et al., 2011; Wagstaff et al., 2009).

In Malaysia, cobra bite appears to be one of the commonly causes of snake envenomation (Chew et al., 2011; Jamaiah et al., 2004, 2006) and usually treated by the Thai Neuro Polyvalent Antivenom imported from Thailand. There are two species of common cobras in Malaysia: Naja kaouthia and Naja sumatrana, both listed as one of the category 1 medically important venomous snakes of Southeast Asia (Wüster, 2010). Of these two cobras, N. sumatrana is widely distributed in the central and southern regions of Peninsula Malaysia, Borneo and Sumatra (Wüster, 1996) and is also known as the Equatorial spitting cobra (Wüster, 1996), one of the venom-spitting species in Southeast Asia that are able to cause venom ophthalmitis. Clinically, cobra bites produce systemic envenomation syndrome with the characteristic neuromuscular