

Unleashing the power of CE to characterize snake venoms

Rob HASELBERG*

Vrije Universiteit Amsterdam

Gold statement

The information obtained with a combined CGE, CIEF, and CZE-ESI-MS approach for an extended cohort of snake venoms provides a unique insight in their compositional protein diversity.

Introduction

Snake venom is a complex mixture of bioactive compounds. Venom proteins and polypeptides are potential toxins which can attack various physiological systems of living species with devastating results. Understanding the compositional variation of snake venoms from different species is essential when designing novel approaches for the treatment of snake envenoming. Although CE seems particularly well-suited for characterization of venom constituents, so far it hardly has been exploited in this field. Here we study the combined strength of CGE, CIEF, and CZE-ESI-MS for the in-depth exploration of the biomolecular content of a variety snake venoms.

Body

The present work demonstrates the usefulness of capillary electrophoresis (CGE, CIEF, and CZE) for the profiling of snake venoms. In total, 12 different snake venoms were studied from the 3 most important subclasses. CGE was performed under both reduced and non-reduced conditions, yielding information on the molecular weight ranges of the biomolecules present. All snake families contained venom protein constituents in the range 10-20 kDa, whereas for the vipers also larger components (>20 kDa) were also found. CIEF was used to determine the charge heterogeneity of the proteinaceous components in the samples. A large variety in pI profiles was found for the tested species, covering the whole accessible pI range from 3 to 10. The combined information from CIEF and CGE was used to develop a CZE-ESI-MS method that enabled more detailed characterization of the biomolecular components. A non-covalent positively charged coating of a triple layer of polybrene-dextran sulfate-polybrene in combination with a low-pH BGE was used to prevent protein adsorption and obtain efficient separations. The use of high-resolution MS enabled acquisition of mass profiles of all venoms. Preliminary results show that within the elapid and viper venoms several three-finger toxins and phospholipases (ranging from 5.2 to 17.5 kDa) are present. In colubrids only low-molecular weight proteins (<8 kDa) were found, which could not be directly correlated yet with known protein families in this venom.

Conclusion

CE in all its facets is a excellent platform to characterize the biomolecular content of snake venoms. CGE and CIEF provide details on molecular weight and charge heterogeneity of the components, respectively, whereas CZE generates overall compositional profiles. The hyphenation with high-resolution mass spectrometry allows in-depth characterization of the individual components. To conclude, this combined CE approach provides a unique insight in the compositional diversity of an extended cohort of snake venoms.