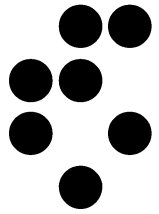


Peptidomics and Proteomics of *Conus consors* Cone Snail Venom

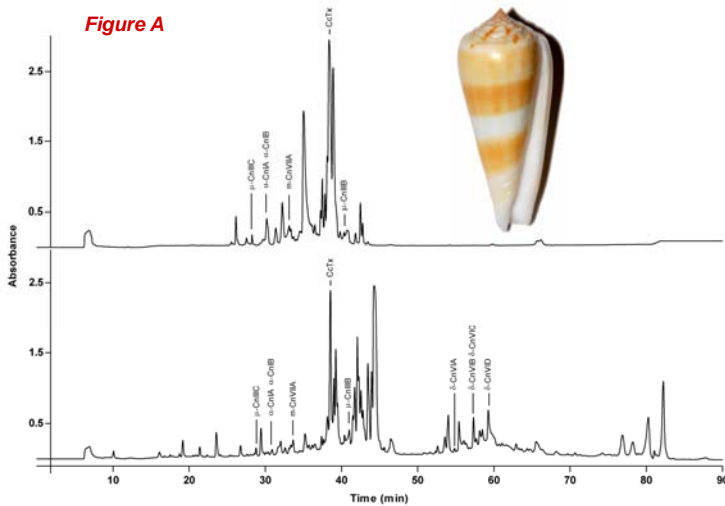
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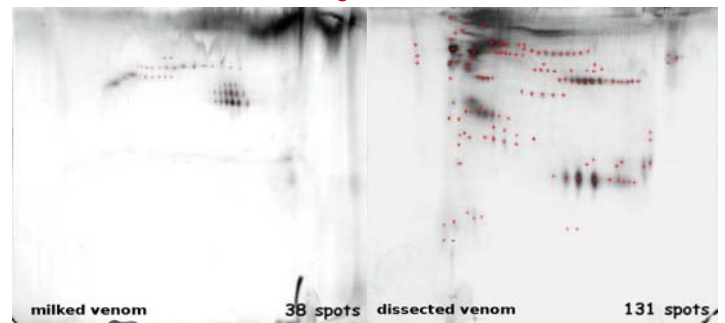
Comparison between dissected venom and milked venom

- UV chromatograms of the milked and dissected venoms of *Conus consors* show very distinct profiles:
 - much less components in the milked venom (Figure A, top) compared to the dissected venom (Figure A, bottom), particularly evident in the most hydrophobic part of the chromatogram.
- Previously described *Conus consors* peptide sequences isolated from the dissected venom duct based on bioassays were matched to the masses found in both dissected and milked venoms:
 - reduced complexity of the milked venom does not necessarily translate by less interesting material.
- Comparison of the ESI-MS mass lists of the milked and dissected venoms:
 - 150 components in the milked venom, poor in comparison to 1078 compounds in the dissected venom.
 - an overlap of only ~50%, some components could come from the salivary glands!
- Comparison of the 2D gel electrophoreses of components above 10kDa of the milked and dissected venoms:
 - 131 components in the dissected venom (Figure B, right) and “only” 38 in the milked venom (Figure B, left).
- ❖ Structure-driven and biocomputing-assisted discovery process and milkings avoid sacrificing the animals.

Introduction

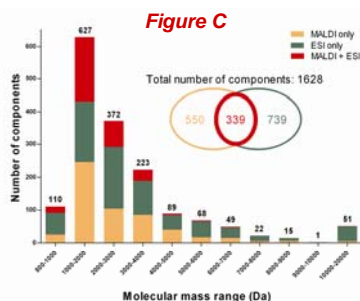
Animal venoms are highly complex mixtures of biologically active compounds. Through evolution, these have naturally and gradually been modified to match a multitude of specific targets, that enabled the development of new research tools and therapeutic drugs. Unfortunately, despite the large number of venomous animals and the complexity of their venom, only a tiny portion (estimated to represent less than 0.1%) of venom components have been identified and characterized. Through a structure-guided process and with the aim at identifying and characterizing all detectable peptides and proteins from a cone snail venom, an extensive study was performed using a combination of sampling and analytical techniques. Marine cone snails are venomous gastropods, members of the *Conidae* family which counts approximately 700 species. Here, the venom of several specimens of the piscivorous cone snail *Conus consors* (Figure A, insert) was obtained, either by milking or by dissection. After appropriate sample preparation and separation processes, the venom was analysed using different mass spectrometry techniques.

Figure B



Proteomic analysis of dissected venom

- A total of 1628 measured masses:
 - 550 compounds are detected only by MALDI-MS, 739 only by ESI-MS and 339 are common to both techniques.
 - overlap between the two techniques represents only about 20% of all the masses (Figure C, insert)!
- A left asymmetrical overall distribution is visible with about 60% of the components in the 1000 to 3000 mass range (Figure C):
 - this asymmetrical mass range distribution found in *Conus consors* venom seems specific to this particular venom.
 - masses in common represent about half of the masses detected per single technique in the 1000-2000 mass range, exponentially reducing in higher mass ranges.
- Although MALDI-MS is more sensitive than ESI-MS in terms of detection level
 - more masses were detected using ESI-MS than with MALDI-MS.
 - highly dependant on sample preparation.
- ❖ Low mass detection overlap between MALDI-MS and ESI-MS is demonstrated in several other studies:
 - both techniques are complementary and necessary to establish the broadest possible proteome mapping.



Conclusions

- More than 1700 components were detected in the dissected venom, representing more than ten times the number of venom components usually cited and demonstrating that cone snail venom complexity appears largely underestimated.
- Very low overlap between the different MS techniques, showing the importance of maximizing the valuable information that one can obtain from a single sample by using several types of MS techniques and sample preparations.
- Structure-driven and biocomputing-assisted discovery processes generate an abundance of valuable data not only in a very short time, but most importantly using much smaller sample amounts.

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European Community Integrated Project CONCO LSHB-CT-2007-037592, Contract Number 037592 (<http://www.conco.eu>) and a grant P1-0207 from the Slovenian Research Agency. We are grateful to the government of New Caledonia, to the French Navy and to the French Institut de Recherche pour le Développement (IRD) for their support.

Reference

Daniel Biass, Sébastien Dutertre, Alain Gerbault, Jean-Louis Menou, Robin Offord, Philippe Favreau, Reto Stöcklin. Comparative proteomic study of the venom of the piscivorous cone snail *Conus consors*. *Journal of Proteomics*, Volume 72, Issue 2, 6 March 2009, Pages 210-218.