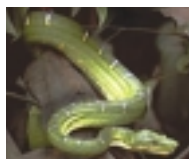


Death, where is thy sting?

Jane Bradbury, BMN News



Getting close to venomous animals is not everyone's idea of a job with a future. But deadly venoms

are proving a gold mine for molecules with interesting pharmacological properties, and the potential to treat an array of medical disorders.

Its all in the venom

Venoms are complex cocktails of molecules produced by animals for defense and for catching prey. A single snake venom might contain several hundred neurotoxic, cardiotoxic and cytotoxic proteins and peptides.

Then there are scorpions, spiders, even snails – the list of venomous creatures is long. 'There are about 1500 species of scorpions worldwide with some 100+ novel molecules in each venom,' said Paul Alewood, Professor of Chemical and Structural Biology at the University of Queensland in Brisbane (<http://www.uq.edu.au>). 'So there is the potential to discover tens of thousands of interesting molecules and their accompanying activities in scorpions alone.'

From these molecules, isolated by high performance liquid chromatography (HPLC) and mass spectrometry (MS), state-of-the-art chemistry can be used to understand their structure–function relationships and select lead molecules for development. And yet, said Alewood, 'this exciting field of research is somewhat under investigated.'

Natural products: the safety of plants

Most people who are interested in natural products look in plants, he says. 'They have the benefit that they stand

still and don't bite you,' he said. Between 25–50% of the current pharmacopoeia, estimates Alewood, comes from plant-derived materials. By contrast, few drugs have been derived from venoms.

The prime exception, says Alewood, is angiotensin converting enzyme (ACE) inhibitors, which are used worldwide to treat high blood pressure. ACE inhibitors were developed from molecules identified in the venom of a South American viper, he explains, after it was noticed that blood pressure plummeted in people bitten by this snake.

Among the researchers who are mining venoms for their pharmacological treasures is Ponnampalam Gopalakrishnakone, a Professor in the Faculty of Medicine at the National University of Singapore (<http://www.nus.edu.sg>). Speaking in Singapore at the Biomedical Research Applications in Drug Discovery Technology Asia-Pacific meeting, 3–5 November 2003 (<http://www.drugdisc.com/asiapacific>), Gopalakrishnakone explained that although natural toxins have often been used in traditional remedies, it is only in the past 10 years that the search for new drug leads in venoms has intensified.

23 new toxins

Among the 23 new toxins that his group has discovered are: hannalgesin,

a strong analgesic isolated from king cobra venom; an acidic phospholipase A₂ toxin with anticlotting activity also from king cobra venom; and anti-inflammatory peptides derived from python venom that might be useful in the treatment of rheumatoid arthritis and some forms of brain damage. His team has also isolated lead molecules from scorpion, spider and coneshell venoms.

This last group of venoms – the conotoxins – is of particular interest to Roger Drinkwater, Head of Research at biopharmaceutical firm Xenome in Brisbane, Queensland (<http://www.xenome.com>). The peptides isolated from predatory sea snails called coneshells have 'an exceptionally broad range of pharmacological activities,' said Drinkwater, 'and are highly potent and very specific, ideal attributes for new drug leads.'

Xenome, which was founded to discover and develop venom peptide drugs, is currently optimizing candidate peptides for use in chronic lung disorders, urological disorders and depressive/cognitive disorders of the CNS. The company's noradrenaline transport inhibitor Xen2174 is in late-stage preclinical trials for the treatment of acute and chronic pain. Other conotoxins for pain relief, which are being developed by independent biopharmaceutical companies, are already in clinical trials.

Conference reports

Conference participants who wish to cover a particular meeting should contact:

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