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Highlights of Analytical Chemistry in Switzerland

Spider Venom: A Rich Source of Highly Active Molecules

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Venoms of toxic animals contain a plethora of pharmacologically active molecules. Although only few of these molecules have been identified, several of the already well-characterised toxins are meanwhile being used in wide areas of cell biology as 'chemical scalpels' to dissect molecular mechanisms.

The Central American spider *Cupiennius salei* rapidly anaesthetises its prey by injecting venom which acts through complex and synergistic interactions of its components. Besides several proteins and low molecular mass compounds, more than fifty different polypeptides have been identified. These polypeptides are the main focus of our research, which to date has revealed interesting structural and functional information as well as indications for potential applications: Cupiennins (2–4 kDa) are cationic linear peptides adopting an amphipathic α-helical structure in membrane environments. In submicromolar concentrations they act bactericidally as well as cytolytically by permeating membranes in a non receptor-mediated manner. In the light of the rapid increase of multidrug resistant bacteria, the cupiennins may help as tools to analyse the general cytolytic membrane action as well as the molecular prerequisites for high antimicrobial selectivity.

CSTX-1 (the ***C**upiennius **s**alei* **t**ox**i**n-1, 8 kDa), the main toxic acting peptide in the venom of *C. salei*, contains the cystine-knot motif, a structural characteristic of several ion channel blockers. Indeed, functional studies have revealed that CSTX-1 inhibits insect calcium channels. Thus the paralysis of prey animals by *C. salei* venom appears to be largely due to an inhibition of Ca^{2+} influx into nerve and/or muscle cells. Interestingly, due to its special structure, this peptide enables a high affinity interaction with a subtype of L-type calcium channels expressed in mammalian neurons. Up to now, subtypes of L-type calcium channels have been clearly identified by molecular biology techniques but it has not yet been possible to isolate them by pharmacological means. **With CSTX-1, a new pharmacological tool is now available that may aid in dissecting the structure and function of L-type calcium channel subtypes.**

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An adult female *Cupiennius salei* sits in the axilla of a plant, holding its cocoon, which can contain up to 1500 eggs. In the upper part of the illustration the amino acid sequence of cupiennin 1a is given and structurally important lysines are highlighted with a coloured box. The amino acid sequence as well as the disulfide bridge arrangement (cysteines are highlighted with a coloured box) of CSTX-1 is presented at the bottom of the illustration.

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