The Primary and Secondary Structure Determination of Bioactive Amphibian Peptides

A thesis submitted for the Degree of Doctor of Philosophy

by

Craig Steven Brinkworth B. Sc. (Hons)

from the

The Department of Chemistry
The University of Adelaide

THE UNIVERSITY OF ADELAIDE
AUSTRALIA

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Abstract

Amphibians secrete a mixture of biologically active compounds from within glands under the skin in response to attack by predators. One of the major class of compounds secreted in this biological arsenal are bioactive polypeptides. These peptides possess many biological functions including acting as antibiotics, anti-cancer agents and inhibiting the formation of NO by nNOS. These functions make them interesting from a therapeutic viewpoint as potential drugs.

Negative ion mass spectrometry of peptides contains significant sequencing information differing from that obtained in the positive ion mode. Information unique to negative ion mass spectrometry of peptides includes fragmentations (i) identifying the presence of a specific amino acid in the sequence (Ser, Thr, Asp, Asn, Gln, Glu) and (ii) identifying the position of specific amino acids within the peptide sequence (Phe, Ser, Thr, Asp, Asn, Gln, Glu).

The skin secretion of the _Litoria eucnemis_ contains four novel peptides belonging to two peptide families – the caerin 1s and maculatins and is the first Australian frog investigated to demonstrate this property. Three of the peptides exhibit antibacterial and anticancer activities. However, the three peptides are some of the least active, among their respective families.

Primary and secondary structural properties are important factors in determining the biological activity of polypeptides. The solution structures of three peptides Ala4Lys14-citopin 1.1 (amphipathic α-helix), Gly15Gly19-caerin 1.1 (a less-defined α-helix) and frenatin 3.1 (amphipathic α-helix with a flexible C-terminal end) are presented in a discussion about this structure/activity relationship.