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Discovery of Druggable Biologics from *Alternanthera paronychiodes*

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Introduction

Over the years, the chemical profiles of numerous herbs have been characterized, the majority of which are non-peptide compounds. This could be due to the novelty of the idea of peptides being a biologically active compound, and hence are not actively being screened for. Recently, it was found that *Viola Yedoensis* (Violaceae), 紫花地丁, a Chinese medicinal herb, contains biologically active cyclotides (Wang, Colgrave et al. 2007).

What is this about

Cyclotides belong to a class of cysteine-rich proteins, and have a circular backbone, with 6 conserved cysteine residues forming 3 disulphide bonds in a characteristic cyclic cysteine knot (CCK) motif (Fig 1.) (Trabi and Craik 2002).

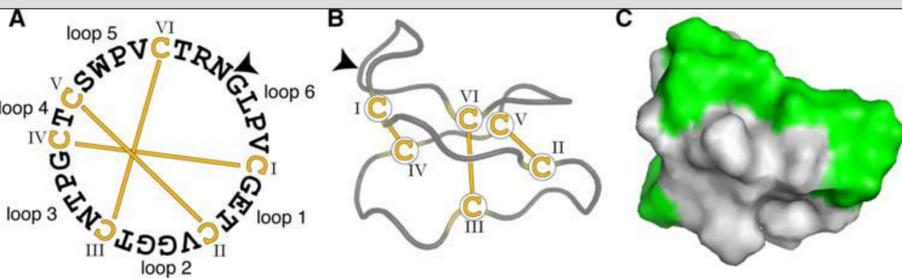


Fig 1. Schematic overview of the prototypic cyclotide kalata B1 and two precursor proteins (Craik, Mylne et al. 2009)

The circular backbone of the CCK motif confers great stability to the peptide, rendering it resistant to enzymatic hydrolysis and thermal denaturation. This stability, together with their wide range of biological activities and plasticity for modification (Clark 2006), makes them great candidates for pharmaceutical applications (Fig 2.).

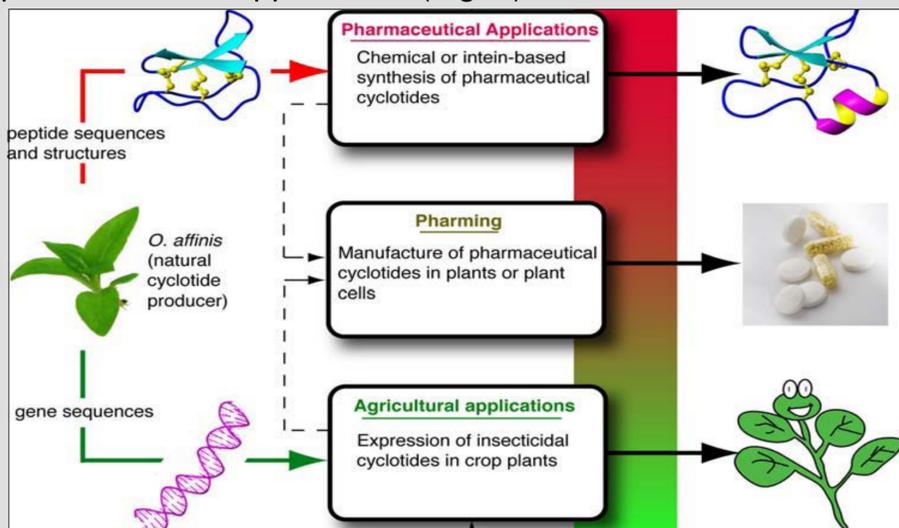
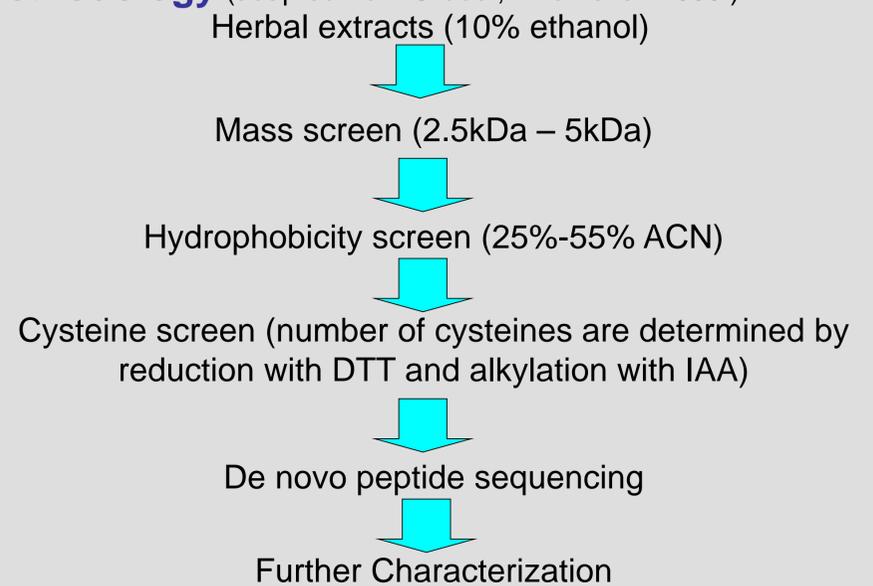


Fig 2. Overview of the potential applications of cyclotides (Craik, Mylne et al. 2009)

My Project Proposal

I aim to discover novel biologically active cysteine-rich proteins from medicinal plants.

Methodology (adapted from Gruber, Elliott et al. 2008.)



Preliminary Results

A 3686 kDa cysteine-rich peptide, Altertide P1, containing 8 cysteine residues is identified from *Alternanthera paronychioides* (Amaranthaceae), 绿苋草. Its amino acid sequence is:

CGRPGVTCGFNSNPSTVCCPPCVCDFTFDADVCFGSC

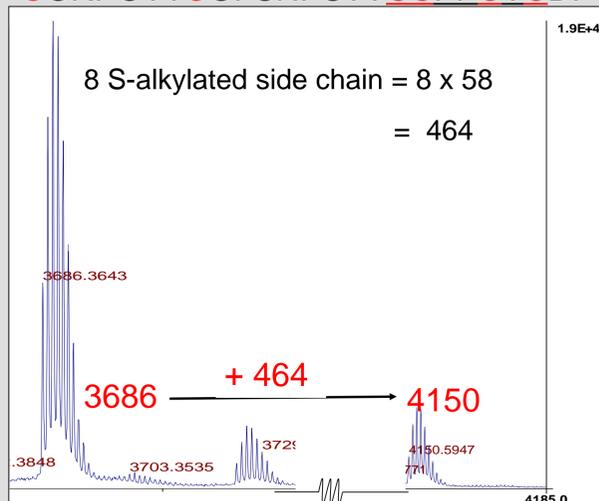


Fig 3. Incomplete alkylation of peptide 3686, demonstrating 8 cysteine

Unlike the cyclotide structure, Altertide P1 has a cysteine at both its N and C terminal, resulting in a pseudo-cyclic structure. To my understanding, the CCXXCXC pattern is also a novel motif.

The 3-dimensional structure of this peptide remains to be identified.

However, given the amino acid sequence, it is postulated that it will be highly compact and flexible, allowing for longer sequence grafting as a scaffold for drug engineering.

The function of this peptide remains to be determined.