

# Cyclic Conotoxins

## Market overview

Conotoxins, with their exquisite specificity and potency for receptors and ion channels, have created much excitement as drug leads. They offer a vast untapped resource of potentially therapeutic agents (> 50,000 compounds) of which less than 0.1% have been studied. However, like most peptides, their beneficial activities may potentially be undermined by their susceptibility to proteases (lack of stability) and poor bioavailability.

By cyclising the conotoxin peptides we have been able to engineer peptides with preserved bio-activity and greatly improved resistance to proteolytic degradation.

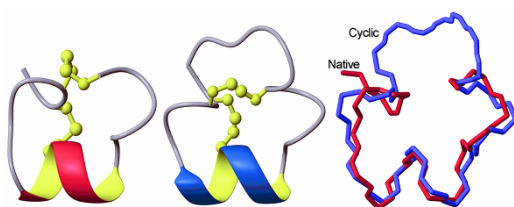
## Development status

This platform technology is aimed at making conotoxin peptides more stable and bio-available while retaining bioactivity of the molecule. The method involves synthesising the cyclic conotoxin peptides by joining the N and C termini of the molecule with a peptide linker.

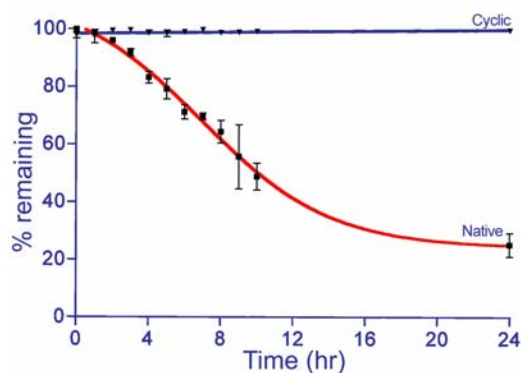
The method of cyclisation has been shown to be successful in stabilising the peptide against biological degradation including proteolytic attack as well as blood plasma stability. The resulting cyclic conotoxins have also been shown to maintain structural integrity and biological activity, making them potentially exciting new drug leads. The technology has been demonstrated successfully for a range of conotoxin peptides across a number of classes.

Conotoxins have been linked to a number of indications to date including pain, neuromuscular disorders, and neurological disorders, such as epilepsy, Alzheimer's disease and Parkinson's disease.

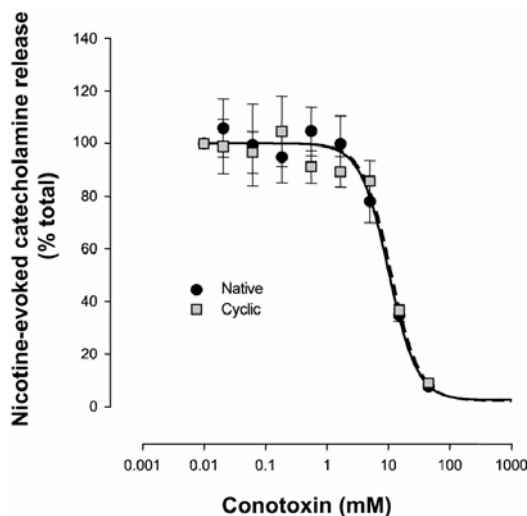
Recent developments have given rise to exciting new results that have further validated this technology.



Ribbon representation of a native conotoxin (left), ribbon representation of the cyclic conotoxin (centre) and superimposition of the backbone residues of native and the cyclic peptides (right).



The stability of a native peptide and its cyclic analogue against proteolytic attack by EndoGluC.



Retained biological activity for the cyclic analogue. Concentration-response curves for inhibition of nicotine (5mM)-evoked catecholamine release from isolated bovine chromaffin cells by increasing concentrations of native conotoxin and cyclised conotoxin.

## Intellectual property

Patent protection in relation to this technology has been sought in Australia, Europe and the United States. The United States patent has proceeded to grant. The patent application has been accepted in Australia and is under prosecution in Europe.

## Business opportunity

We are currently seeking collaborative or licensing partners with validated peptide leads to further develop into stable and optimised compounds through the use of our technology.

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