

Approach for Phase Problems of High-Ordered Brain Function Related and Mid-sized Molecules

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Theonellapeptolide-Id (TNLP) is a cyclic tridecapeptide lactone and has been isolated from the Okinawa marine sponge *Theonella swinhoei* with the related macrocodes and peptolides.

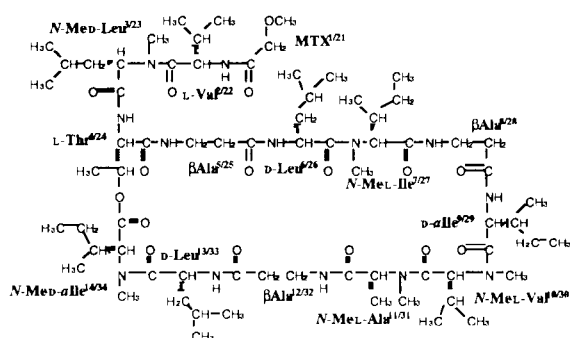


Fig.1 Chemical Structure of TNLP-Id

It includes unusual amino acids, β -alanine (β Ala) and *allo*-isoleucine (*alle*), and is cyclized by a unique ester linkage between the C-terminus and the O γ atom of Thr side chain. The N-terminus of this peptide is also capped by the methoxyacetyl group (MTX). The aliphatic side chains and the methylations on amide bonds bring the hydrophobicity, and the peptide is soluble in organic solvents. TNLPs have the strong cytotoxicities¹, which are advantageous for survivor from predation by other organs. Furthermore, the notable functions, Na⁺ and Ca²⁺ transport activities and prevention of fertilization, have been also reported. Although we wonder how the hydrophobic peptides achieve their purpose under the water, their properties are still under investigation. We have attempted the characterization of TNLP-Id by the structural approach.

In the asymmetric unit, two peptolide molecules were existed with solvent molecules, and total molecular weight were over 3000 Dalton. The crystal structure including solvent molecules was finally determined at 0.80 Å resolution by using synchrotron radiation. The conformations of two independent molecules were similar to each other and were also similar to the previously reported structure. About thirteen hydrated waters were found at disordered nineteen sites, and they were located on a certain region to avoid the contacts with aliphatic side chains of peptolide in the crystal. The spatial dispositions of solvent molecules and peptides subsequently created the amphipathic layer structure. This unique behavior was elucidated by X-ray analysis as a noteworthy characteristic of TNLP-Id.

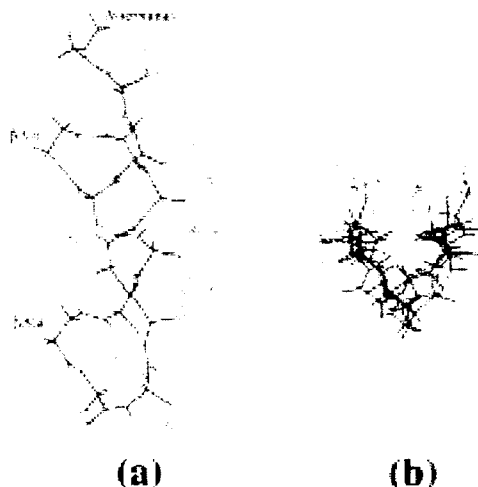


Fig.2 Solved Structure of TNLP-Id
Molecule 1 is projected to (a) the long and (b) short side of the peptide ring.