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Nereistoxin

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Nereistoxin

The toxic principle of the marine annelid was first studied in 1922 by Nitta, who was fascinated by the observation that a patient who handled the worms complained of respiratory abnormality, headache, and vomiting. Nitta isolated a crystalline toxin named nereistoxin in 1934.

Nereistoxin is an unusual amine having a 1,2 dithiolane ring that is rare in natural products. Its chemical formula is $C_5H_{11}NS_2$. Qualitatively, the toxin gave reactions similar to those of thioctic acid.

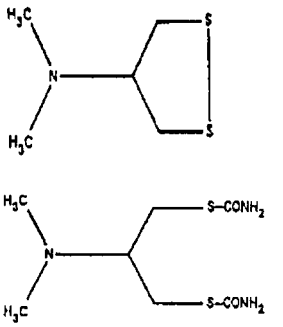
Pharmacology

Nitta tested the effects of nereistoxin in animals including mammals, birds, reptiles, and fish. He concluded that nereistoxin primarily affects the nervous system. The lethal dose that could kill 50% of a given mice population (LD_{50}) is about 30 mg/kg intraveneously, 1,000 mg/kg subcutaneously, and 118 mg/kg orally. Nereistoxin is apparently not potent. It does not affect killifish and goldfish although its toxicity is enhanced by alkaline water pH. Then it can cause paralysis and eventually death. At water pH below 5.6, nereistoxin is not toxic.

In extensive electrophysiological studies, it was discovered that nereistoxin blocks synaptic transmission in the central nervous system. But its inhibitory action on cholinesterases (a type of enzyme) is not enough to kill insects. In cockroaches, nereistoxin suppresses excitation of the abdominal nerve bundle or of the postsynaptic potential, but not all of the tail hair nerve. Since nereistoxin competes with added acetylcholine (an excitatory transmitter substance) in contraction of the frog skeletal muscle, the toxin probably blocks the synaptic transmission by competing with acetylcholine at a postsynaptic membrane receptor site of the central nervous system (CNS).

When an insect is intoxicated by nereistoxin, stimulation from inside or outside the body is not adequately transmitted to the CNS. Thus, disturbance of a CNS-mediated function results in softening of the body, loss of response, among others. The effect is complete relaxation and anesthetization of the insect.

Application in agriculture



Nereistoxin (top) was isolated in the worm *Lumbriconereis heteropoda*, and has been used as a model for the synthesis of **Padan** (bottom), which is employed as an insecticide in Japan.

Nereistoxin possesses potent insecticidal activity, particularly to the larvae of the rice stem-borer. Researchers synthesized a number of compounds with a structure similar to nereistoxin. The most effective -- 1,3-bis-(carbomolicio)-2-N, N-dimethylamine propane -- was patented and used in agriculture since 1967. Application had been extended to the rice plant skipper, the white tip rice nematode, the cabbage worm, the tea leaf roller, the green elongated leafhopper, the citrus leaf miner, the persimmon fruit moth, and others.

References: (1) Yoshiro Hashimoto. 1979. **Marine toxins and other bioactive marine metabolites.** Japan Scientific Societies Press, Tokyo. pp. 302-309. (2) Luigi Minale. 1985. *Medicine from the sea.* In: SG Richardson (ed). **Managing the Ocean; Resources, Research, Law.** Lomond Publications Inc. Maryland 1985.