Chemosensors of Highly Toxic Marine Poison Discovered

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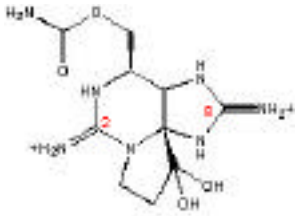
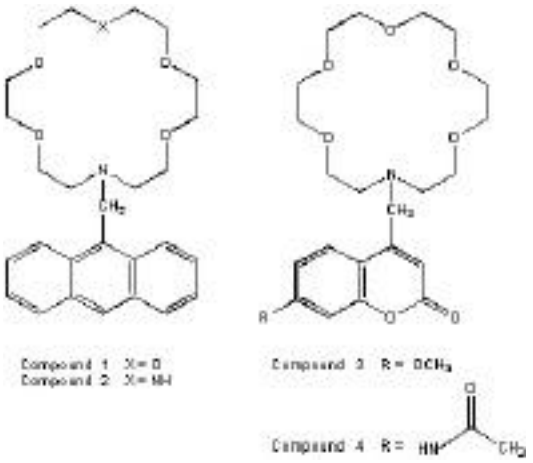
Saxitoxin, one of the most toxic substances known has caused many human deaths and much illness as a result of eating contaminated shellfish or puffer fish. It is 1000 times more toxic than the nerve gas sarin. A single dose of 0.2 milligram is fatal to humans [1].



Saxitoxin

Valuable in medical research, saxitoxin reversibly binds to the voltage-gated sodium channels of nerve cells, blocking nerve signal transmission. Produced by marine algae (the same algae responsible for 'red tides'), its natural origin means it is potentially available to terrorists. Therefore it would be most valuable to have a sensitive and rapid means of saxitoxin detection. Currently governments monitor shellfish beds for the presence of saxitoxin, usually by using mouse bioassay — a lengthy and expensive procedure. A more rapid means of detecting saxitoxin is needed, ideally one that avoids animal testing.

Now chemists at the University of Miami and Eckerd College headed by Robert Gawley and Roger Leblanc have discovered certain substituted aza-crown ethers are sensitive chemosensors for saxitoxin [2]. These have the general structures:



The anthracyl group in Compounds 1 and 2 served as a fluorescent probe. Fluorescence enhancement data suggest a 1:1 complex with saxitoxin in aqueous 80% ethanol. In the presence of water, these aza-crown ethers do not bind to sodium, potassium or calcium ions. Compared to Compound 1, Compound 2, containing two aza-nitrogen atoms gave a slight increase in saxitoxin binding.

Nine additional aza-crown ethers were synthesised from Compound 2 using combinatorial methods [2]. These additional compounds provided no increase in saxitoxin binding relative to Compound 1.

The guanidinium structures at C-2 and C-8 of the saxitoxin structure are the

binding sites with Compound 1. In similar tests with arginine and guadininium hydrochloride (both containing guanidinium ions) and adenosine (a biomolecule with a purine ring system similar to that of saxitoxin), no fluorescent enhancement was observed indicating selective saxitoxin complexation in the presence of these other compounds.

Compounds 1 and 2 are sensitive to saxitoxin concentrations as low as 5×10^{-6} molar while the mouse bioassay can detect about 10^{-6} molar saxitoxin. Coumaryl-aza crown ethers (Compounds 3 and 4) provided binding constants similar to Compound 1 [3].

References

1. Neil Edwards, **Saxitoxin…from food poisoning to chemical warfare…**

2. Robert E. Gawley, Sandra Pinet, Claudia M. Cardona, Probal K. Datta, Tong Ren, Wayne C. Guida, Jason Nydick & Roger M. Leblanc, **Chemosensors for the Marine Toxin Saxitoxin.** *J Am Chem Soc* , ASAP Article 10.1021/ja027507p.

3. Peter Kele, Jhony Orbulescu, Tiffany L. Calhoun, Robert E. Gawley & Roger M. Leblanc: **Coumaryl crown ether based chemosensors: selective detection of saxitoxin in the presence of sodium and potassium ions.** *Tetrahedron Lett* , **43**:4313–4316 (2002).

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