



FACT SHEET

SAXITOXIN (mytilotoxin; shellfish toxins; STX, PSP)

1. Background [1,2,5,6]

Saxitoxins are neurotoxic poisons produced naturally by certain types of planktonic algae (dinoflagellates). The consumption of shellfish (e.g. mussels, butter clams and oysters) that have accumulated the toxin when feeding on these organisms may cause paralytic shellfish poisoning in humans (mytilotoxism). It should be noted that the concentration of the toxin can be higher still - as much as 10 mg of saxitoxin per 100 g of mussel flesh – when algal blooms occur. Another source of PSP toxins are freshwater cyanobacteria (e.g. *Aphanizomenon flos-aquae*).

The first complete chemical analysis and synthesis of saxitoxin was conducted by Kishi in 1977. Given that it is extremely difficult to synthesise, saxitoxin (and its derivatives) cannot be readily procured.

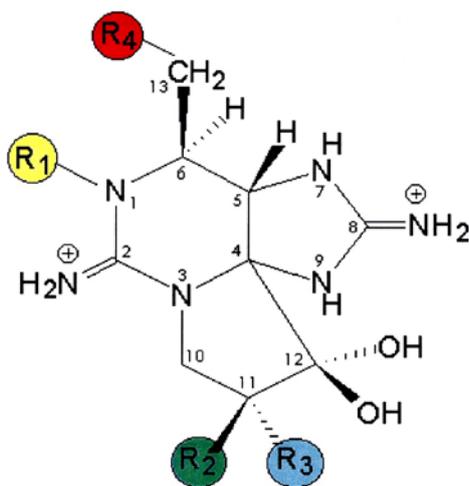
2. Saxitoxin as a bioweapon

Classified as Agent TZ (chemical weapon designation), saxitoxin is considered to have chemical weapon potential due to its high toxicity. Researchers have shown that it would be possible to spike ammunition with saxitoxin, thus ensuring the immediate death of the victim. Saxitoxin is much more poisonous than the synthetic nerve gas sarin and, like the phytotoxin ricin, is also classified as a biological weapon.

Saxitoxin is listed in the Chemical Weapons Convention (List 1). The toxin also appears in the Annex (War Weapons List) to the German War Weapons Control Act.

3. Chemical structure and properties [1]

The best known PSP toxin is saxitoxin. Further 20 PSP toxins which have been isolated to date, show a high structural similarity to saxitoxin (Fig. 1).



Toxin	R1	R2	R3	R4	Molekulargewicht [g/mol]
STX	H	H	H		301
NEO	OH	H	H		317
GTX1	OH	H	OSO ₃ ⁻	H ₂ N-COO	412
GTX2	H	H	OSO ₃ ⁻	(Carbamoyl-)	396
GTX3	H	OSO ₃ ⁻	H		396
GTX4	OH	OSO ₃ ⁻	H		412
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B1	H	H	H		380
B2	OH	H	H		396
C3	OH	H	OSO ₃ ⁻	O ₃ S-NH-COO	492
C1	H	H	OSO ₃ ⁻	(N-Sulfo-	476
C2	H	OSO ₃ ⁻	H	carbamoyl-)	476
C4	OH	OSO ₃ ⁻	H		492
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dcSTX	H	H	H		258
dcNEO	OH	H	H		274
dcGTX1	OH	H	OSO ₃ ⁻	OH	369
dcGTX2	H	H	OSO ₃ ⁻	(Decarbamoyl-)	353
dcGTX3	H	OSO ₃ ⁻	H		353
dcGTX4	OH	OSO ₃ ⁻	H		369
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doSTX	H	H	H	H	242
doGTX2	H	H	OSO ₃ ⁻	(Deoxy-	337
doGTX3	H	OSO ₃ ⁻	H	decarbamoyl-)	337

Fig. 1: Structure of saxitoxin and its derivatives

PSP toxins are soluble in water, methanol and ethanol, but not in other organic solvents. They remain stable in slightly acidic environments, but tend to oxidise when exposed to alkaline conditions.

4. Toxicity [1,7]

Saxitoxin (STX) is a powerful neurotoxin. Like tetrodotoxin, STX binds to the sodium channels in nerve cells, thereby blocking the influx of sodium ions (Fig. 2). A single STX molecule is enough to block one sodium channel. The two guanidine sub-structures present in saxitoxin must be protonated.

The toxicity of saxitoxin is much greater than that of synthetic neurotoxins. Consequently, it ranks alongside other proteins, such as ricin and botulinum toxin, as one of the most poisonous chemical substances known to mankind.

LD₅₀ (Mouse): oral : 263 µg/kg
i.p. : 10 µg/kg

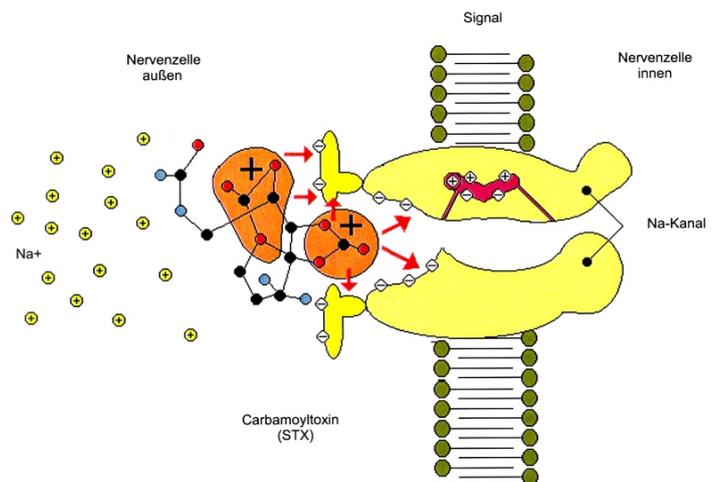


Fig. 2: Model of how PSP toxins bind to the surface of excitable nerve cell membranes

5. Analysis [3,4,5,8]

A variety of biological, biochemical and chemical procedures can be used to analyse saxitoxin. These can be divided into two groups: non-chromatographic and chromatographic. The first group includes bioassays, immunoassays and fluorimetric assays. However, these are only capable of producing a summary identification of several PSP toxins (total toxicity).

However, over the last 15 years, highly sensitive chromatographic procedures have been developed which make it possible to identify individual compounds with greater precision. Over time, the HPLC method, which uses fluorescence detection, has become the standard procedure.

The SPIEZ LABORATORY uses the following procedures to analyse saxitoxin:

- HPLC method using fluorescence detection (using pre-column derivatisation with peroxide according to DIN EN 14526)
- LC/MS
- ELISA (RIDASCREEN FAST Saxitoxin; r-biopharm)
- Immunochemistry (JELLETT; Rapid Test for PSP)

Other common analytical procedures include capillary electrophoresis and mouse bioassay. However, these are not used by the SPIEZ LABORATORY.

5. Literature/Information

- [1] E. Jaime; Analytik und Vorkommen von Paralytic Shellfish Poisoning (PSP)-Toxinen in marinen Organismen; Dissertation; Friedrich-Schiller-Universität Jena, 2003.
- [2] H. Russmann; Toxine: Biogene Gifte und potenzielle Kampfstoffe; Springer-Verlag Heidelberg; Band 46, Nummer 11; p. 989-996; 2003.
- [3] DIN EN 14526: Bestimmung von Saxitoxin und DC-Saxitoxin in Muscheln; HPLC - Verfahren mit Vorsäulenderivatisierung mit Peroxid- oder Periodatoxidation; Deutsche Fassung, 2004.

- [4] Turner et al.; Journal of AOAC International Vol. 92, No. 1, 2009.
- [5] Leigh Lehane; Paralytic Shellfish Poisoning - a review; National Office of Animal and Plant Health Agriculture, Fisheries and Forestry; Australia, Canberra, 2000.
- [6] Maria Wiese et al; Neurotoxic Alkaloids: Saxitoxin and Its Analogs; Mar. Drugs 2010, 8, 2185-2211.
- [7] Marian E. van Apeldoorn et al; Toxins of cyanobacteria; Toxins of cyanobacteria, Mol. Nutr. Food Res. 2007, 51, 7-60.
- [8] A. R. Humpage et al; Comparison of analytical tools and biological assays for detection of paralytic shellfish poisoning toxins, Analytical and Bioanalytical Chemistry Volume 397, Number 5 (2010), 1655-1671.

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