

Strychnine

CAS: 57-24-9

MF: C₂₁H₂₂N₂O₂

MW: 334.4

logKow=1.68

Solubility: poorly soluble in water (0.014 g/100 ml); low solubility in all organic solvents [1].

Major uses

Strychnine is a basic alkaloid obtained primarily from the seeds of the *Strychnos nux-vomica* tree, which inhabits India, Sri Lanka, and northern Australia. It was introduced to Europe in the 16th century as a rodent poison. Later, it was accepted as a circulatory and respiratory stimulant, and was formerly used as a common component of tonics, aphrodisiacs, and some medical preparations. At present, strychnine containing medications are no longer used. However, strychnine is still used in veterinary medications, in rodenticides, and avicides [2].

Human toxicity

Strychnine is a highly toxic poison. In spite of this fact, strychnine poisoning is relatively rare; the majority of poisoning cases result from the accidental or intentional ingestion of strychnine-containing rodenticides. Most typical early symptoms of poisoning are muscle spasms and seizures which can occur within 5-15 min, and are reported to be extremely painful. Patients with strychnine poisoning remain awake during seizures, unless they develop *anoxia* (oxygen depletion) or severe acidosis.

Prognosis is good if the patient can be supported over the first 6 to 12 h. Seizures generally subside within 12 to 24 h after ingestion. Seizures may result in hyperthermia, metabolic and respiratory acidosis, rhabdomyolysis (the breakdown of muscle fibers resulting in the release of muscle fiber contents into the circulation), and renal failure. Loss of consciousness (coma) may follow severe or prolonged seizures and appears to result from the central nervous system (CNS) acidosis and hypoxia (reviewed in [3]).

Early deaths result from respiratory failure and subsequent cardiac arrest. The reason of death can be *asphyxia* – a condition of severely deficient supply of oxygen to the body, which can lead to unconsciousness and brain damage.

The minimum lethal oral doses in adults reported in the literature range from 30 to 120 mg per 70 kg person [3].

Strychnine blood levels have ranged from 0.5 to 90 mg/l (1.5 μM - 269.0 μM) in fatal poisonings [4, 5]. Post-mortem blood concentrations ranged from 0.2 to 40 mg/l (0.6 μM - 119.6 μM) in 34 cases described in the literature [6].

Occupational exposure limit: 0.15 mg/m³ [1].

Carcinogenicity: there is no evidence of carcinogenicity (IARC, 2004) [3].

Kinetic data

Absorption: strychnine is rapidly absorbed from the gastrointestinal tract following ingestion, sniffing, or intravenous use. The half-life of absorption is about 15 min [7].

Kinetics: first-order.

Volume of distribution: 13 l/kg (at overdose) [7].

Distribution: half of a dose is distributed in 5 min to all tissues of the body [2]. Equal distribution between plasma and erythrocytes was reported. Symptoms of poisoning may occur after 5-60 min and averaging 15-20 min [2].

Accumulation: in the liver and kidney.

Passage of blood-brain barrier: free.

Time to peak blood concentration: 15-60 min [2].

Plasma protein binding: slight (data unknown).

Elimination half-life: 10-11 h [7]. Elimination via hepatic metabolism (see below)..

Metabolism and excretion

Strychnine undergoes oxidative biotransformation in the liver via microsomal enzymes. *In vitro* studies in the supernatant fractions from rat and rabbit livers indicate that strychnine-N-oxide is the major metabolite (15%) and the other metabolites accounted for less than 1%. The major enzyme responsible for metabolism was the cytochrome P450 mono-oxygenase [8].

Excretion: strychnine is excreted in the urine and can be detected there 24 h or more following ingestion [3]. Only 20% or less is excreted unchanged in the urine (reviewed in [8]).

Toxicological mechanisms

Strychnine antagonizes the effect of glycine. Glycine, the major postsynaptic inhibitory neurotransmitter in mammalian spinal cord and brain stem, is thought to produce a postsynaptic inhibitory potential (hyperpolarization) via an increase in chloride conduction [9]. Glycine is normally released from presynaptic inhibitory interneurons during motor neuron depolarization. It then binds to receptors on the motor neuron, which inhibits further motor neuron depolarization. The inhibitory postsynaptic potential appears to result from an increase in chloride conductance. Strychnine prevents the uptake of glycine at inhibitory synapses, especially in the ventral horns of the spinal cord. This results in excessive motor neuron activity and, consequently, in muscle contractions (convulsions) in poisoned patients [3].

Target organs: CNS, heart, liver, kidney.

References

1. International Chemical Safety Cards; via Internet.
2. Ellenhorn M, Schonwald S, Ordog G, Wasserberger J (1997) *Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning*. 2nd ed., pp. 1660-1663. Williams & Wilkins.
3. Poisindex, Thomson Micromedex (2006).

4. Baselt, R.C. (2000) *Disposition of Toxic Drugs and Chemicals in Man*. 5th ed. Chemical Toxicology Institute, Foster City, CA.
5. Winek, C.L., Wahba, W.W., Esposito, F.M. (1986) Fatal strychnine ingestion. *J Analyt Toxicol* 10, 120-121.
6. Ekwall, B., Ekwall, Ba., Clemedson, C. (2001) *Strychnine*. The MEIC Monograph. <http://www.cctoxconsulting.a.se>
7. Heiser, J.M., Daya, M.R., Magnussen, A.R. (1992) Massive strychnine intoxication: serial blood levels in a fatal case. *Clin Toxicol* 30(2), 269-283.
8. Mishima, M., Tanimoto, Y., Oguri, Z., Yoshimura, H. (1985) Metabolism of strychnine in vitro. *Drug Metab Dispos* 13(6), 716-721.
9. Haddad, L.M. & Winchester, J.F. (1990) *Clinical Management of Poisoning and Drug Overdose*. 2nd ed., pp. 1119-1123. W.B. Saunders Company.

***Written by Ada Kolman, February 2006; revised March 2007
ada.kolman@telia.com***