# Nicotine

CAS: 54-11-5
MF: $C_{10}H_{14}N_2$
MW: 162.23
log Kow= 1.17
Solubility: Miscible with water below 60°C. Good solubility in alcohol, chloroform, and ether [1].

## Major use

Nicotine is an alkaloid derived from the stems and leaves of the tobacco plant and its primary usage is cigarettes. Moreover, nicotine is used in medicine; as an insecticide, and in tanning. It is also used in veterinary treatment against helminthes and some other parasites [2].

## Human toxicity

Symptoms of nicotine intoxication generally include nausea, vomiting, abdominal pain and increased salivation. Confusion, agitation, restlessness followed by lethargy, convulsions and coma may be noted following severe exposure. Hypertension, tachycardia and tachypnea may occur, followed by hypotension, bradycardia and bradypnea. The duration of symptoms is about 1 to 2 h following mild exposure, up to 18 to 24 h following severe intoxication.

Nicotine is highly toxic. About 2 to 5 mg can cause nausea. The lethal oral dose for adults has been estimated to be approximately 40 to 60 mg. Survival has, however, been reported after ingestion of 1 to 4 g. The main lethal symptoms are CNS excitation/depression (main cause of death) and cardiovascular failure [2].

According to Winek, lethal serum concentration is between 5 and 52 mg/l [3]. The mean lethal serum concentration, based on the values from several handbooks, is 22 mg/l [4].

Working place limit: TLV-TWA: 0.5 mg/$m^2$ skin [2].

## Kinetic data

*Absorption* occurs rapidly from oral mucosa (under 20%), gastrointestinal tract (except stomach), respiratory tract, and skin [2].

*Kinetic* is biphasic [4].

*Volume of distribution:*1-3 l/kg [2, 3]. Smokers appear to have a decreased volume of distribution (2 l/kg) compared to non-smokers (3 l/kg) [2].

*Accumulation in vital organs*: nicotine accumulates in lipid-rich organs, such as CNS, liver, and kidney [4].

*The plasma half-life:* 10 minutes and 2.2 hours [3]. The elimination of nicotine is biphasic [4]. The elimination half-lives of nicotine and cotinine are longer in non-smokers than in smokers.

*Time to peak*: >0.5 h [4]. 15 to 30 minutes after chewing nicotine gum [2].

*Protein binding:* high [4], according to Poisindex [2] ranging from 4.9% to 20%.

*Passage of blood-brain barrier:* free [4].

**Metabolism and excretion**
Seventy % to 75% of nicotine is metabolized in the liver. Small amounts are metabolized in lung and kidney [2].

The principle metabolites are isomethylnicotinium ion, nornicotine, cotinine, and nicotine-1'-N-oxide. Cotinine is present in serum in approximately 10 times the amount of nicotine [2].

*Metabolites more toxic than nicotine:* none [4].

*Excretion:* 10% to 20% is excreted unchanged by the kidneys. With a urinary pH under 5, 23% is excreted unchanged; with a pH above 7.0, only 2% is excreted unchanged [2].

**Toxicological mechanisms**
Nicotine causes blockade of nicotinic cholinergic receptors in the brain, autonomic ganglia, and neuromuscular junction. Thus, central nervous system, sympathetic or parasympathetic autonomic, and neuromuscular effects may be seen in varying combinations.

**Target organs***:* CNS and PNS [4].

**References**

1. HSDB, TOXNET (2005).
2. Poisindex, Thomson Micromedex (2005).
3. Winek, C.L. (1994) Drug and chemical blood level data. *Winek's Toxicological Annual*, Pittsburgh. Allegheny County Department Laboratories.
4. Ekwall, B., Clemedson, C., Crafoord, B., Ekwall, B., Hallander, S., Walum, E. & Bondesson, I. (1998) MEIC Evaluation of Acute Systemic Toxicity: Part V. Rodent and Human Toxicity Data for the 50 Reference Chemicals, ATLA 26, 571-616.



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