

62. Nicotine

CHEMICAL NAME = 3-[(2S)-1-methylpyrrolidin-2-yl]pyridine

CAS NUMBER = 54-11-5

MOLECULAR FORMULA = $C_{10}N_{14}H_2$

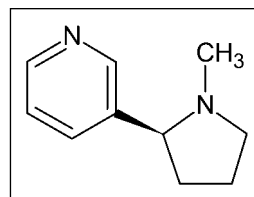
MOLAR MASS = 162.2 g/mol

COMPOSITION = C(74.0%) H(8.7%) N(17.3%)

MELTING POINT = -79.0°C

BOILING POINT = 247°C

DENSITY = 1.01 g/cm^3



Nicotine is a colorless oily liquid alkaloid. Nicotine and its derivatives are found in all green plants, but it is most closely associated with tobacco. Tobacco leaves have particularly high concentrations of nicotine, with the leaves containing between 2% and 4% by weight; common plants such as potatoes, tomatoes, celery, and eggplant contain nicotine, but the amount is too small to have an effect as a stimulant. Tobacco is native to the subtropical and tropical Americas (there are a few species indigenous to selected areas of Africa). Columbus observed Native Americans smoking, chewing, and snorting tobacco during his voyages to the Americas. Although Columbus viewed tobacco use as a heathen practice unworthy of Europeans, subsequent explorers and their crews adopted its use, which quickly spread throughout the world. As tobacco use was adopted by different cultures, some governing bodies unsuccessfully attempted to ban its use. It was widely used to treat common ailments and diseases. Early colonists in North America recognized tobacco as a cash crop for trading with Europeans and it was widely cultivated in suitable regions.

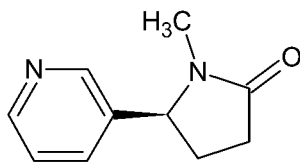
Tobacco is a member of the nightshade (Solanaceae) family and its scientific name is *Nicotiana tabacum*. The name nicotine comes from *Nicotiana* after the French ambassador Jean Nicot (1530–1600). Nicot became familiar with tobacco when he was serving as ambassador to Portugal. Impressed with its use as a medicinal herb, Nicot sent seeds and cuttings back to the French Queen Catherine de Medici (1519–1589) in 1560, noting its therapeutic properties. Tobacco was called *nicotiana* and this was used for the scientific name.

Nicotine is the second most widely used recreational drug after caffeine. At low doses, nicotine acts as a stimulant to the central nervous system by activating acetylcholine receptors, specifically called nicotinic acetylcholine receptors, in the postsynaptic neurons during nerve transmission. Nicotine from smoking is distributed throughout the body in a few minutes and crosses the blood-brain barrier in less than 10 seconds. Physiological effects include an increase in pulse, constriction of arteries that produce elevated blood pressure, an increase in breathing rate, and loss of appetite. At higher doses nicotine acts as a depressant. Nicotine is highly addictive; it is believed that it stimulates dopamine production that activates pleasure-and-reward areas in the brain. Because nicotine produces a quick ephemeral response in the brain, the continual use of tobacco is necessary to produce the physiological reward from smoking. This makes it difficult for tobacco users to quit. Classical withdrawal symptoms are associated with people trying to “kick the habit.” These include anxiety, irritability, nervousness, fatigue, and headaches.

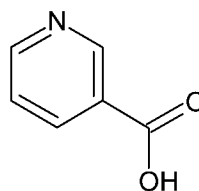
High intake of nicotine is toxic. The lethal dose of nicotine is approximately 50 mg. The average nicotine content of a cigarette is about 8 mg, and that of a cigar is typically between 100 and 200 mg, but it may be as high as 400 mg. The toxic effect of nicotine is mitigated in smokers by its oxidation to other products when tobacco is burned. The actual delivery of nicotine to the body is only about 10% of the total nicotine content of the product. Therefore a typical cigarette will deliver about 1 mg of nicotine. The average nicotine dose from the use of a smokeless tobacco product (chewing tobacco or stuff) is about two to three times the amount from a cigarette.

The nicotine molecule consists of a pyrrolidine ring attached to a pyridine ring by a bond between carbon atoms in the two-ring systems. Nicotine was isolated in impure form from tobacco in 1809 by Louis Nicholas-Vauquelin (1763–1829). Vauquelin called the substance nicotianine. In 1826, Wilhelm Posselt (1806–1877) and Karl Ludwig Reimann (1804–1872), medical students at Heidelberg University, isolated pure nicotine and published dissertations on its pharmacology in 1828. Louis Henri Melsens (1814–1886) determined nicotine’s empirical formula. Amé Pictet (1857–1937) and P. Crépieux reported the synthesis of nicotine in 1903.

Nicotine forms a number of metabolites in the body, mainly in the liver. Approximate 75% of nicotine is oxidized to cotinine, which is the primary nicotine metabolite. Cotinine can be measured in the blood, urine, and saliva and this is used as a measure of nicotine exposure in tobacco users and in those exposed to secondhand smoke. The oxidation of nicotine also produces nicotinic acid. Nicotinic acid is vitamin B₃ and has the common name niacin. Niacin deficiency results in a disease called pellagra, which is found in certain malnourished populations. Pellagra’s symptoms include dermatitis, diarrhea, sensitivity to light, and dementia.



cotinine



nicotinic acid or niacin

Nicotine in tobacco has always been used for medicinal purposes. Nicotine solutions made from soaking tobacco leaves in water have been used as pesticides for several hundred years. In modern times, numerous pharmaceutical companies have explored nicotine's use for treating diseases. Nicotine's most prevalent medicinal use is for smoking cessation in the form of alternate delivery systems such as gums and dermal patches. Nicotine is used medically for numerous conditions and its use is being explored in additional areas including pain relievers, attention deficit disorder medications and medications associated with Alzheimer's disease, Parkinson disease, colitis, herpes, and tuberculosis. Because of nicotine's potential therapeutic use, several large tobacco companies have developed pharmaceutical divisions.