

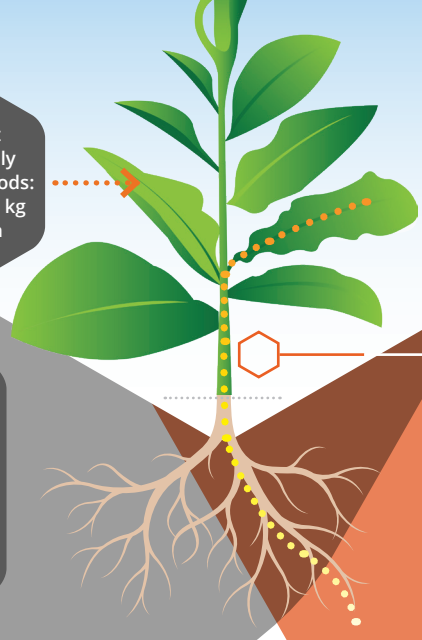
What Is Nicotine?



Nicotine is a naturally occurring compound found in the 'nightshade' family of plants which includes tobacco, aubergines, peppers, tomatoes and potatoes.

Levels in food are 2 - 7 micrograms per kg.¹

Levels in the tobacco plant are substantially higher than in foods: 8 - 50 grams per kg depending on type/origin.



Nicotine is organically produced in the roots and stored in the leaf. It is an inherent part of the plant produced to protect it from insects.

Tobacco products contain nicotine as part of tobacco. Nicotine is **NOT** separately added cigarettes and heated tobacco products.

99% PURITY pharmaceutical grade nicotine

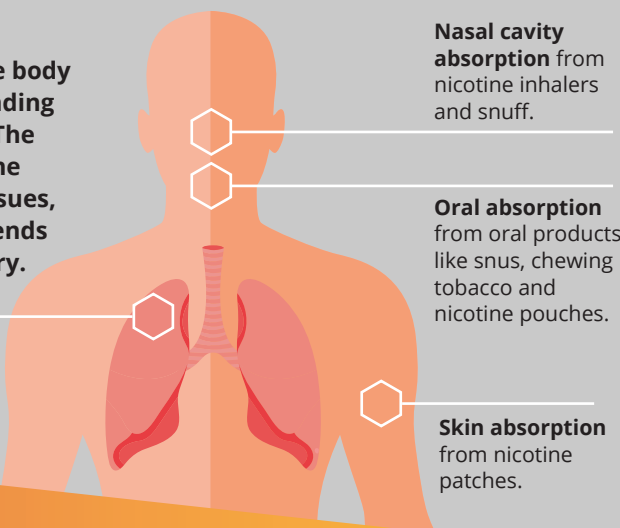
Nicotine is **added** to some Next Generation Products (NGPs) that do not contain tobacco.

The nicotine applied to NGPs is extracted from tobacco leaf as a clear liquid and is of high quality and purity.

It is the same as the nicotine used in over-the-counter pharmaceutical and medically licensed products.

What Happens When You Consume Nicotine?

Nicotine can enter the body in various ways depending on the product used. The speed at which nicotine reaches the body's tissues, organs and brain depends on the route of delivery.



Nasal cavity absorption from nicotine inhalers and snuff.

Oral absorption from oral products like snus, chewing tobacco and nicotine pouches.

Skin absorption from nicotine patches.

Lung inhalation from cigarettes, heated tobacco products and vapes.

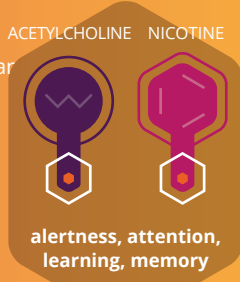


Effects of Adult Nicotine Consumption

Nicotine is considered a mild stimulant and produces a broad range of physical effects. These effects are transient and not dissimilar to those experienced when drinking coffee or watching a horror movie.

How Does Nicotine Work?

Part of nicotine looks very similar to a chemical messenger (acetylcholine) that naturally occurs in our bodies and plays an important role in alertness, attention, learning and memory.



Nicotine binds to the same receptors in our bodies as acetylcholine, mimicking its action. In adult smokers, nicotine has similar effects to acetylcholine.



Although it is a stimulant, it can have different effects: Adult nicotine users report small doses can lead to alertness, and larger doses to relaxation.²

¹Siegmund, B et al. Determination of the nicotine content of various edible nightshades (Solanaceae) and their products and estimation of the associated dietary nicotine intake. Journal of Agricultural and Food Chemistry. 1999; 46: 3113-3120.
²Mündel T. Nicotine: Sporting Friend or Foe? A Review of the Athlete Use, Performance Consequences and Other Considerations. Sports Med 2017;47 (12): 2497-2506

There are around 7,000 chemicals in tobacco smoke, of which nicotine is one.

Is Nicotine Harmful?

Nicotine is an addictive substance.

Nicotine is not considered to be risk-free. However, public health experts worldwide conclude that the toxicants generated from burning tobacco, not nicotine, are the primary cause of smoking-related diseases.³



Decoupled from tobacco smoke, nicotine's long-term safety profile has been established through years of pharmaceutical clinical trials and decades of 'over-the-counter' use.



According to some studies, the following health endpoints have been associated with nicotine:

Improvement in symptoms of neurological disorders:^{4,5,6,7,8}
 • Parkinson's • Alzheimer's
 • Tourette's • ADHD

Enhanced performance:^{9,10,11,12}
 Concentration /Memory/
 Alertness

Enhanced mood (reduced depression)¹³

To date nicotine has not been established to cause, by itself, cardiovascular disease or cancer^{14,15}

Improved fine motor skills¹⁴

Improvement in ulcerative colitis^{6,16}

Transient increases in heart rate and blood pressure

Toxic at high doses which are not reached when used as intended by adult smokers¹⁷

Exposure during adolescence may have lasting adverse consequences for brain development¹⁵

May aggravate diabetes due to potential irregularity in glucose metabolism¹⁸

FEMALE: May lead to adverse effects on fetal brain development¹⁵
 FEMALE: May increase likelihood of preterm delivery and stillbirth¹⁵

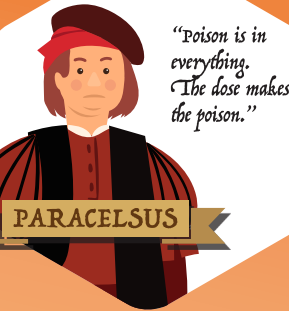
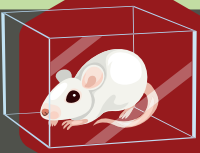
Public health bodies agree that adult mothers should consider vaping during pregnancy if they won't stop smoking.¹⁹

Some animal studies suggest nicotine could:¹⁷

- Negatively impact adolescent brain development.
- Have adverse reproductive effects.
- Aggravate insulin resistance and diabetes.

There is limited human data to support these studies with more research required.

That said, we are unequivocal that youth, pregnant women, and people with diabetes should not use nicotine products, and strongly support youth access prevention efforts.



"Poison is in everything. The dose makes the poison."

PARACELSUS

Like many substances, at high doses nicotine can be poisonous. However, it is not poisonous at the intended levels typically consumed by adult NGP users.



CYANIDE FORMALDEHYDE

Many foods naturally contain poisonous chemicals. No diet is free of them.



Coffee reportedly contains 19 cancer causing chemicals.²⁰

The presence of harmful chemicals does not always cause harm. It is the levels of chemicals consumed or ingested that is important.

Advances in innovation mean nicotine can now be completely de-coupled from harmful cigarette smoke, creating an increasing choice of less harmful alternatives for adult smokers who would otherwise have continued to smoke.

Non-combustible nicotine products present an attractive **tobacco harm reduction** alternative for adult smokers because the nicotine in these products is consumed without burning tobacco. In fact, vapes and nicotine pouches do not contain any tobacco at all.

To help build belief in the positive public health potential of tobacco harm reduction, we think it's important to continue to explore, explain and demystify nicotine's relationship with smoking, smoking-related disease and NGPs.

This will hopefully help more adult smokers make informed choices about transitioning to potentially harm-reduced nicotine products, compared to the health risks of continued cigarette use.

³Harm reduction in nicotine addiction: helping people who can't quit. A report by the Tobacco Advisory Group of the Royal College of Physicians, October 2007.

⁴<https://www.parkinsons.org.uk/get-involved/can-nicotine-stop-some-parkinsons-symptoms>

⁵<https://www.alzdiscovery.org/cognitive-vitality/ratings/nicotine>

⁶Levin ED, et al., March 1. Nicotine effects on adults with attention-deficit/hyperactivity disorder. *Psychopharmacology (Berl)*. 1996 Jan; 123(1):55-63

⁷http://www.schizophrenia.com/nicotine_benefits.html

⁸<https://www.cochranejournal.com/cdsr/doi/10.1002/14651858.CD004838.pub2/full>

⁹Gray JA, et al., Neurochemical mechanisms mediating the behavioural and cognitive effects of nicotine. *Drug Dev Res* 1994; 31: 31-17.

¹⁰Foulds Jet al. Cognitive performance effects of subcutaneous nicotine in smokers and never-smokers. *Psychopharmacology* 1996; 127: 31-8.

¹¹Heishman SJ, et al Meta-analysis of the acute effects of nicotine and smoking on human performance. *Psychopharmacology (Berl)*. 2010 Jul;210(4):453-69. doi: 10.1007/s00213-010-1848-1. Epub 2010 Apr 24.

¹²Warburton DM. The functional conception of nicotine use. In: Clarke PBS, Quik M, Adlkofer F, Thurau K, editors: *Effects of Nicotine on Biological Systems II: Advances in Pharmacological Sciences - V. Nicotine and Smoking: Current Controversies*. Basel: Birkhauser Verlag; 1995. pp.257-64.

¹³Warburton DM. The puzzle of nicotine use. In Lader M (eds) *The Psychopharmacology of Addiction* Oxford: Oxford University Press 1988 p27-49

¹⁴<https://www.rcplondon.ac.uk/projects/outputs/nicotine-without-smoke-tobacco-harm-reduction>

¹⁵https://www.cdc.gov/tobacco/data_statistics/sgr/50th-anniversary/index.html

¹⁶https://www.cochrane.org/CD004722/BD_transdermal-nicotine-for-the-treatment-of-active-ulcerative-colitis

¹⁷Mayer B (2014) How much nicotine kills a human? Tracing back the generally accepted lethal dose to dubious self-experiments in the nineteenth century *Arch. Toxicol.* 88 (1): 5-7

¹⁸<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2811111/>

¹⁹<https://www.nhs.uk/conditions/pregnancy-and-baby/smoking-pregnant/>

²⁰What is risk? Science politics and public health. Roger Bate