Nicotine: Everything You Need to Know but Have Never Been Told

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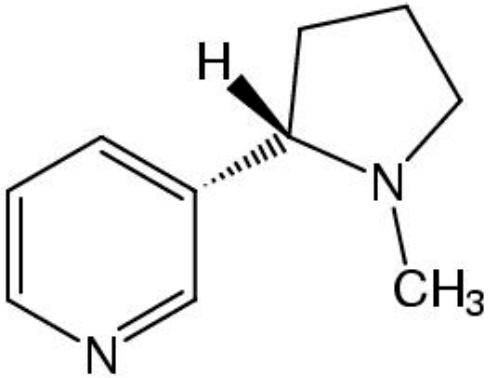
Conflict of Interests

- I have written honored expert opinions for manufacturers and retailers of vape products.
- I served as unpaid expert witness in policy decision-making on the regulation of vaping (Austria & Germany, 2014-2017).
- I served as honored expert witness in a patent case on e-liquids (USA, 2017).
- I am financially, legally and personally independent of my clients and received no funding from the tobacco or vape industry.

Nicotine



- contained (1–15 %) in the leaves of the nightshade plant family (tobacco, tomato, eggplant, chili pepper, potato and many more);
- protects plants against predatory insects;
- potent synthetic analogs (neonicotinoids) approved as pesticides;
- most commonly consumed *via* inhalation of smoke from burned tobacco ("smoking");
- perceived by the general public as highly addictive and neurotoxic lethal poison.

Nicotiana tabacum

Solanum lycopersicum

Solanum melongena

Capsicum

Tobacco Smoke

Toxic Compounds Formed by Tobacco Combustion

- >60 established cancerogens;
- nitrogen oxides (NO, NO_2, N_2O_4);
- carbon monoxide (CO);
- metal ions;
- >5,000 compounds, including reactive carbonyls;
- solid particles (tar) deposited in the lungs.

} virtually absent in vapor

Documented Health Risks of Smoking

- cancer
  (about 50% of all cancer deaths are caused by smoking; see Siegel et al., JAMA 2015);
- chronic obstructive pulmonary diseases; >80 % of COPD patients are smokers;
- cardiovascular diseases (coronary artery disease, myocardial infarction, stroke, impaired blood perfusion of tissues);
- 7.000,000 deaths per year are caused by smoking;
- smoking kills half of its users.

Established Biological Effects of Nicotine

- slight, short-term increases in blood pressure and heart rate (similar to caffeine or exercise);
- angiogenesis (growth of new blood vessels);
- moderate inhibition of inflammation associated with immune suppression;
- psychoactive (stimulant/sedative);
- activation of reward-pathways in the brain associated with pleasure (basis for dependence?);
- several other effects observed *in vitro* or in animal models (relevance for humans questionable).

Potential Risks of Nicotine Consumption

- **Pregnancy:** impaired embryonic development in rats and mice (?);
  no evidence for adverse birth outcomes in clinical studies (observation of children for up to 2 years);
- **Cardiovascular Diseases:** potential health risk for patients with severe coronary artery disease, e.g. survived myocardial infarction (controversial);
- **Cancer:** nicotine is not cancerogenic, but accelerated growth of established tumors was observed in animal studies (due to angiogenesis); no clinical data.

Potential Benefits of Nicotine Consumption

- improved cognitive performance
  (self-treatment of schizophrenic patients by smoking?);
- protection against neurodegenerative diseases (M. Alzheimer, M. Parkinson);
- protection against ulcerative colitis, a nasty inflammatory bowel disease.

Toxicity of Nicotine

Does Nicotine Act as a Neurotoxin?

- Nicotine mimics some effects of the endogenous neurotransmitter acetylcholine.
- At very high concentrations, the effects of nicotine are reversed.
  (inhibition of neuronal function = neurotoxicity)
- If applied at small amounts at a time (smoking, vaping, gums, patches), rapid metabolism and distribution of nicotine keeps plasma levels far below neurotoxic tresholds.

Risk of Nicotine Poisoning by Vaping or DIY Preparation of Liquids?

- first signs of overdosing: headache, dizziness, in severe cases vomitting;
- symptoms result in unwitting "self-titration" (documented for smokers and vapers);
- very slow resorption of nicotine through skin;
- oral bioavailability: ~20% (due to hepatic first pass effect);
- lethal oral dose for adults in the absence of vomitting: ~1 g, 50 ml with 20 mg/ml.

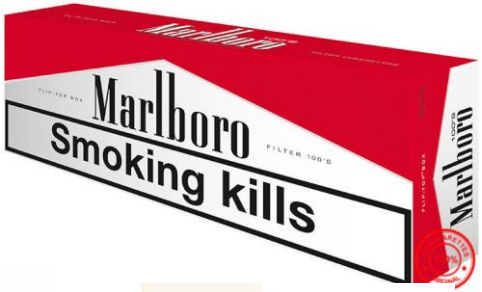
Summary of the Hard Facts (beyond dispute)

- Inhalation of nicotine (*via* smoking or vaping) is not neurotoxic.
- Unintentional swallowing of a few drops (or even a few ml) of liquid is completely harmless.
- There are no adverse effects of liquids unintentionally spilled on skin.
- Suicide attempts by drinking nicotine containing solutions are mostly unsuccessful due to vomitting.

Caveat

- Small children are at higher risk (according to lower body weight).
- Therefore, nicotine containing liquids have to be kept out of the reach of children. (like toilet cleaners, guns, medicinal products, tobacco cigarettes, alcoholic drinks, matches etc)

20 "shots" à 10 ml
(TPD2 version)



Nicotine Dependence?

Smokers don't die of their dependence but of the smoke!

- If at all, animals do not self-administer nicotine as readily as hard drugs like cocaine or heroin.
- The rewarding effects of nicotine are markedly potentiated by other constituents of tobacco smoke, in particular inhibitors of monoamine oxidases.
- The long-term efficiency of nicotine replacement for smoking cessation is close to placebo (>95 % failure after 12 months).
- Never-smokers treated for up to 6 months with nicotine patches did not become dependent.
- Based on these and other facts, Karl Fagerström renamed his famous and widely applied test for nicotine dependence to "Fagerström test for cigarette dependence".

Commentary

Determinants of Tobacco Use and Renaming the FTND to the Fagerström Test for Cigarette Dependence

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Determinants of Cigarette Dependence

(adapted from Fagerström, 2012)

- **drug-induced pleasure reward**
  (nicotine plus other constituents of tobacco smoke);
- **throat hit**
  (*via* activation of nicotinergic receptors on sensory C-fibers in the upper airways);
- **habit and conditioning**
  (smoking-associated behavior).

Electronic vaporizers provide nicotine + throat hit + behavior.