High Tech Highs
Nicotine and THC delivery in the 21st century

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Cigarettes, I won't do cigarettes, nicotine will kill ya.

— Tommy Chong —
I'd rather have my kid smoking pot than drinking.

― Tommy Chong ―
Nicotine binds to receptors in the brain and other:
- Central nervous system
- Cardiovascular system
- Exocrine glands
- Gastrointestinal system
- Adrenal medulla
- Peripheral nervous system
- Other:
  - Neuromuscular junction
  - Sensory receptors
  - Other organs
Central nervous system
– Pleasure
– Arousal, enhanced vigilance
– Improved task performance
– Anxiety relief

Cardiovascular system
– ↑ Heart rate
– ↑ Cardiac output
– ↑ Blood pressure
– Coronary vasoconstriction
– Cutaneous vasoconstriction

Other
– Appetite suppression
– Increased metabolic rate
– Skeletal muscle relaxation
### Increased

<table>
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<tr>
<th>Neurotransmitter</th>
<th>Function</th>
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<tbody>
<tr>
<td>Dopamine</td>
<td>Pleasure, appetite suppression</td>
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<tr>
<td>Norepinephrine</td>
<td>Arousal, appetite suppression</td>
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<tr>
<td>Acetylcholine</td>
<td>Arousal, cognitive enhancement</td>
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<td>Glutamate</td>
<td>Learning, memory enhancement</td>
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<td>Serotonin</td>
<td>Mood modulation, appetite suppression</td>
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<td>β-Endorphin</td>
<td>Reduction of anxiety and tension</td>
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<tr>
<td>GABA</td>
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Nicotine stimulates dopamine release

Pleasurable feelings

Repeat administration

Tolerance develops

• Tobacco has been used by humans for more than 2000 years
  – Plant is native to North America

• Was an early export to Europe after explorers documented its use among natives of North America and Cuba
• In 1571 Nicolas Monardes, a Spanish physician, published a text which claimed that tobacco could cure 36 health problems.
• Public use and acceptance of tobacco grew over the next 250 years, with the primary means of imbibing being the use of cigars and snuff.
• Use of tobacco really took off in the 1880s, after the invention of Bonsack’s cigarette rolling machine.
• This was roughly 60 years after nicotine was discovered, as well as identified as toxic and insecticidal.
• Smoking has remained the most popular method of using tobacco since.
• **Cannabis**
  - Components
    - THC (Delta-9-tetrahydrocannabinol)
    - Cannabinol
    - Cannabidiol
    - Cannabiolic acid

Delta-9-tetrahydrocannabinol
Cannabinoid pharmacology

The Human Endocannabinoid System
THC and CBN are known to "fit" like lock and key into network of existing receptors. The Endocannabinoid System exists to receive cannabinoids produced inside the body called "Anandamide" and "2-Arachidonyletylglycerol". Stimulating the ECS with plant-based cannabinoids restores balance and helps maintain symptoms.

CB1 receptors are concentrated in the brain and central nervous system but also sparsely populate other parts of the human body.

Receptors are found on cell surfaces

www.the-human-solution.org
• CB1 receptor discovered in 1980 by Pfizer is the major binding site for $\Delta^9$-THC (partial agonist)
• Anti-obesity agent rimonabant CB1 receptor antagonist (taken off market in 2008- depression and suicidality)
• Responsible for psychoactive effects of marijuana
CB2 receptor identified in 1993

Cannabidiol (CBD) has low affinity for CB1 or CB2 receptors and has been shown to antagonize the actions of synthetic cannabinoid (CB) ligands at CB1 and CB2 receptors.
Marijuana

• Used for millennia as a recreational psychoactive drug and as a therapeutic agent

• 1960s - systematic study of cannabinoids

• 1980′- isolation, synthesis, metabolism, pharmacology and physiology effects of cannabinoids studied
• **1990s**- identification and cloning of cannabinoid receptors and identification of location

• **Late 1990s**- development of synthetic agonists and antagonists

• **2010s**- emergence of synthetic cannabinoids as drugs of abuse
Why smoking as a route of delivery?

**First Pass Metabolism**

**Nasal:** Drug absorbs directly into the veins

**Venous system:** Transports blood from nose directly to the heart – no liver metabolism

**Heart:** Pumps blood out to the entire body – no delay

**Liver:** 90% of oral dose is metabolized and destroyed by the liver before it gets to the heart

**Oral medications:** May stay in the stomach for 30-45 minutes

**Portal circulation:** All blood from the intestines is taken to the liver for detoxification
• Smoking delivers the drug directly to the lung, and from there to the brain.
• Smoking delivers drug to the brain more rapidly than any other delivery system, followed by snorting then intravenous injection.

• Rapid delivery and pharmacologic effect lead to stimulus and reward.
Vaping as a drug delivery system
E-cigarettes (vapes)

LED lights up when the smoker draws on the cigarette

Sensor detects when smoker takes a drag

Heater vaporises nicotine

BATTERY controls heater and light

CARTRIDGE holds nicotine dissolved in propylene glycol
Vaping devices
Vaping liquid (e-juice)
Cannabis oil
"Herbal" e-liquid
Elapsed time: 3 hours
What’s in e-juice?

• Nicotine (probably)
• Flavoring
• Base
  – Propylene glycol
  – Vegetable glycerin
• Additional chemicals found through product testing:
  – Diethylene glycol
  – TSNAs (low levels)
  – Formaldehyde
  – Acetaldehyde
  – Acrolein

} Carcinogens
Propylene glycol

• The Dow Chemical Company, a major manufacturer of propylene glycol, states in its product safety materials that the “inhalation exposure to [propylene glycol] mists should be avoided” (Dow Chemical Company, 2013)

• The American Chemistry Council warns against its use in theater fogs due to its potential to cause eye and respiratory irritation
“With a view to determining the safety of employing the vapors of propylene glycol and triethylene glycol in atmospheres inhabited by human beings, monkeys and rats were exposed continuously to high concentrations of these vapors for periods of 12 to 18 months.”
• “Examination at autopsy likewise failed to reveal any differences between the animals kept in glycolized air and those living in the ordinary room atmosphere.”

Tests for the chronic toxicity of propylene glycol and triethylene glycol on monkeys and rats by vapor inhalation and oral administration, *J Pharmacol Exp Ther*, Sept 1947, 91(1) 52-76.
Now

• “Our results clearly demonstrate that the tested e-cigarette vapor had toxicological effects on primary NHBE cells when exposed directly at the air-liquid interface. Interestingly, the presence of nicotine had no effect on the cell viability and only the cells of one donor showed higher oxidative stress levels after the exposure to vapor of an e-cigarette liquid containing 2.4% nicotine compared to nicotine-free liquid.”
• “We could also show, that the pure carrier substances propylene glycol and glycerol exhibited toxicological effects.”

So what’s the bottom line?

• Not smoking tobacco, so effects from tar and other combustion products aren’t going to occur.

• Likely to see lower incidence of smoking-related cancers.

• Many experts argue that long-term vaping is significantly less dangerous than continuing smoking.
• There is little research on direct health effects
• One study shows short-term pulmonary effects
• There is evidence of cytotoxicity in animals and humans
• No safety standards for e-cigarette components
• A few of the additional substances in vapor:
  – Ethylbenzene, Benzene, Toluene, Acetaldehyde, Naphthalene, Styrene, Acrolein, Nickel, Chromium, Cadmium, Selenium, Arsenic, Lead, Cobalt, Chlorobenzene, Crotonaldehyde, Chrysene, Retene

  *FDA 2012, Harmful and Potentially Harmful Substances – Established List*
FACE THE FACTS!
When tempted to over-indulge
“Reach for a Lucky instead”

He's one of the loudest men in town. With his direct manner, he's actually called 24 hours a day.
The doctor is no saint, he's honest, and he always sympathizes with his patients.

According to a recent nationwide survey:
MORE DOCTORS SMOKE CAMELS THAN ANY OTHER CIGARETTE

Reach for a LUCKY instead of a sweet

Lucky Strike, the finest cigarette you ever smoked, made of the finest tobacco.

Lucky Strike is number one in sales, number two in advertising, and number three in price.

CAMELS Cigarettes

OklahomaPoison.org