E-cigarettes and Vaping: Chemistry and Toxicology Considerations

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Disclosure

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What are e-cigarettes?

“Cig-a-like” (~2007)

Nicotine liquid  Heating element  Power source
Cartridge  Atomizer  Battery

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Tank system
Mod
E-cigar
E-pipe
E-hookah

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- Heating element
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How many U.S. adults are using e-cigarettes?

- 22% of all people
- 25% of all men
- 19% of all women
There are more e-cigarette users than smokers

Only some e-cigarette users are former smokers (~30% in Minnesota)
There are more e-cigarette users than smokers

Percentage of adult e-cigarette users who are also cigarette smokers

36.7% Utah

47.5% Minnesota

72.1% Missouri
There are more e-cigarette users than smokers

Percentage of adult e-cigarette users who never smoked tobacco cigarettes

Hu et al. Prev Chronic Dis 2019;16:180362
E-cigarette use among youth is on the rise

Cullen et al. MMWR Morb Mortal Wkly Rep 2018;67:1276–1277

Are there harmful consequences from e-cigarettes?
Harm from smoking is due to toxic and cancer-causing chemicals in cigarette smoke.

Over 7,000 constituents
- numerous toxicants
- more than 70 carcinogens

Nicotine
Addiction

https://www.cdc.gov/vitalsigns/tobaccouse/smoking/infographic.html
What is in e-cigarettes?

Cancers
- Head or Neck
- Lung
- Leukemia
- Stomach
- Kidney
- Pancreas
- Colon
- Bladder
- Cervix

Chronic Diseases
- Stroke
- Blindness
- Gum infection
- Aortic rupture
- Heart disease
- Pneumonia
- Hardening of the arteries
- Chronic lung disease & asthma
- Reduced fertility
- Hip fracture
Nicotine is almost always present in e-cigarettes

- Typically 6 – 24 mg/mL
- Nicotine is mostly in harsh form
- High levels of nicotine are hard to inhale

- Up to 65 mg/mL
- Nicotine is present as salt
- High levels of nicotine are easy to inhale

JUUL and some other “pods”
How nicotine works

Normal acetylcholine and receptors

Too much activity at acetylcholine receptors

Less acetylcholine and fewer receptors

Not enough acetylcholine and receptors

Reasons behind JUUL popularity among youth

- Advertising
- Flavors
- High nicotine content

Cullen et al. MMWR Morb Mortal Wkly Rep 2018;67:1276–1277
Effects of nicotine on adolescents

- Brain vulnerability to the neural remodeling from nicotine exposure
- Alterations in cognition (memory, attention, auditory processing) and behavior (impulsivity, anxiety)
- Greater susceptibility to the addictive effects of nicotine
- Potential predisposition to other substances of abuse
Some E-cigarette Users Are Having Seizures, Most Reports Involving Youth and Young Adults

The FDA has become aware that some people who use e-cigarettes have experienced seizures, with most reports involving youth or young adult users. Seizures or convulsions are known potential side effects of nicotine toxicity and have been reported in the scientific literature in relation to intentional or accidental swallowing of e-liquid. However, a recent uptick in voluntary reports of adverse experiences with tobacco products that mentioned seizures occurring with e-cigarette use (e.g., vaping) signal a potential emerging safety issue. The FDA continues to monitor all adverse experiences reported to the agency about the use of e-cigarettes and encourages the public to report cases of individuals who use e-cigarettes and have had a seizure via the online Safety Reporting Portal, as further described below.
FDA NEWS RELEASE

FDA warns JUUL Labs for marketing unauthorized modified risk tobacco products, including in outreach to youth

Agency sends additional letter requesting more information on several issues, including outreach and marketing practices, as part of ongoing investigation

The warning letter identifies several statements, including statements discussed in testimony from a July 2019 Congressional hearing on JUUL. According to that testimony, a JUUL representative speaking with students at his presentation in a school stated that:

- JUUL “was much safer than cigarettes” and that “FDA would approve it any day.”
- JUUL was “totally safe.”
- A student “…should mention JUUL to his [nicotine-addicted] friend…because that’s a safer alternative than smoking cigarettes, and it would be better for the kid to use.”
- “FDA was about to come out and say it [JUUL] was 99% safer than cigarettes…and that…would happen very soon….”
Are e-cigarettes safe?
Other chemicals in e-liquids: \textit{It is not just nicotine and water!}

- Nicotine
- Propylene glycol (PG)
- Vegetable glycerin (VG)
- Contaminants
- Flavoring chemicals

more than 7,000 unique flavors in 2014

Aerosols are more complex than liquids

Aerosols

- Nicotine
- Propylene glycol (PG)
- Vegetable glycerin (VG)
- Flavoring agents
- Contaminants

Masonic Cancer Center
University of Minnesota

Office of Academic Clinical Affairs
University of Minnesota
Driven to Discover®
E-liquids produce harmful chemicals during “vaping”

Decomposition of solvent components (propylene glycol and vegetable glycerin):

- Irritants
- Respiratory toxicants
- Carcinogens
Carcinogens Can Alter DNA

\[ GGAATTT\]
\[ AACGTTGCTTAACCTCTTTGATTTGAT \]

ADDUCT
\[ (add\ a\ duck) \]

formaldehyde
\[ H_3C=CH \]

acetaldehyde
\[ H\equiv\CH \]
Levels of harmful chemicals in e-cigarette aerosols depend on device characteristics

**Container type**
- Volume, material, refillable or disposable (accumulation of toxicants on the wick material, leaching of toxicants)

**Power settings**
- Higher voltage affects nicotine delivery and formation of toxicants

**Heating element characteristics**
- Coil resistance is associated with the temperature and also affects nicotine delivery and toxicant formation

466 brands in 2014
E-cigarette, or vaping, product use-associated lung injury (EVALI)

- As of January 21, 2020, a total of 2,711 hospitalized EVALI cases or deaths have been reported to CDC.
- Vitamin E acetate, an additive in some THC-containing e-cigarette products is the likely cause.
- Vitamin E acetate was found in lung fluid samples from 48 of 51 EVALI patients.

https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html
Formation of a cancer-causing chemical in e-cigarette users

Nitrate (diet) → Bacteria (natural oral microflora) → Nitrite (can also be present in diet) → Nornicotine → Acidic environment → Endogenous nitrosation → NNN

Can cause cancer of the mouth and esophagus

Bustamante et al. Chemical Research in Toxicology, 2018
Is there anything good about e-cigarettes?
Exposures to many harmful chemicals are lower from exclusive use of e-cigarettes than from cigarettes.

Biomarker-based studies
Exposures to many harmful chemicals are lower from exclusive use of e-cigarettes than from cigarettes.

Relative levels of biomarkers:

- Acrolein
- Crotonaldehyde
- Benzene
- NNK

Hecht et al. Nicotine & Tobacco Research 2014
Complete switching is necessary to reduce exposures!

Exposure to a tobacco-specific lung carcinogen NNK

Exposure to acrolein

E-cigarettes may help adult addicted smokers

- E-cigarettes may help non-pregnant adult smokers if used as a complete substitute for all cigarettes and other smoked tobacco products.
- E-cigarettes are not currently approved by the FDA as a quit smoking aid.

Fetal effects of nicotine

Prenatal nicotine/tobacco exposure negatively affects:

- Fetal brain and neuronal development
- Arousal and hypoxic stress response
- Stress hormone regulation
- In utero lung development (decreased pulmonary function)
- Auditory processing
- Cognitive development
What is the bottom line?
It depends who is using e-cigarettes, and where they are getting the product.

Regulation of contents is necessary!

Research is needed:
- Effects of long-term use
- Effects of dual use
- Effects in people with various health issues
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