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Toxicology of ENDS

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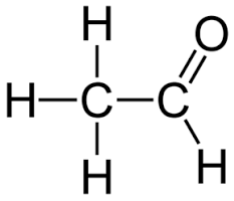
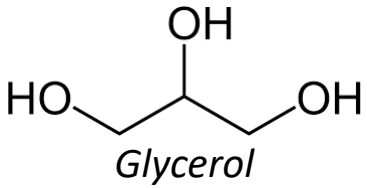
Outline

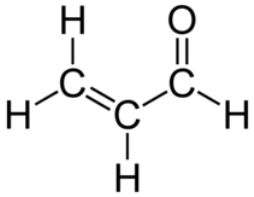
- Introduction
- ENDS characteristics and use
- The aerosol composition
- Nicotine absorption
- Conclusion



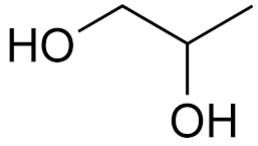
Acetaldehyde



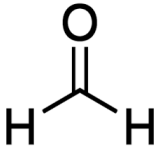
Glycerol



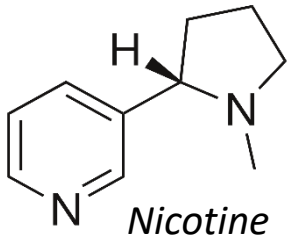
Acrolein



Propylene glycol



Formaldehyde



Nicotine

Introduction

An overview on scientific information regarding ENDS toxicology

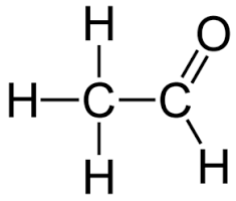
- ENDS were developed to deliver nicotine without other harmful constituents
- ENDS aerosol is far **less toxic** than tobacco cigarette smoke exposure (no combustion process)
- Evidence confirms that the **heating** of refill solutions may generate some **new components** with a certain level of toxicity such as carbonyls and metals
- Data on ENDS **toxicity is very limited**, with very few thorough risk assessment analyses

Inconsistency in results and lack of data

- Results are inconsistent on compounds released in aerosol due to **differences** in **exposure methods** and **models** among studies

- ENDS aerosol is **water soluble**: aerosol is likely be deposited in the conducting zone of the airways, and a small amount can reach the alveolar region

- Evidence of **long-term effects** is **lacking**



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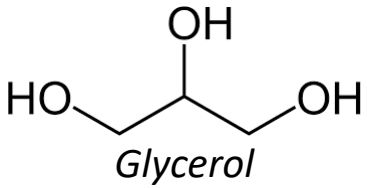

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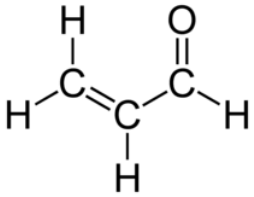

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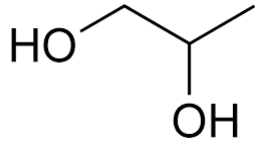

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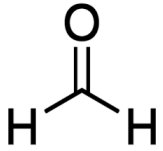

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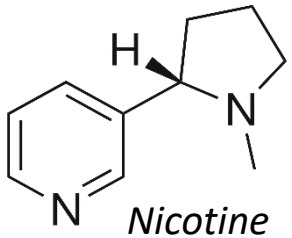
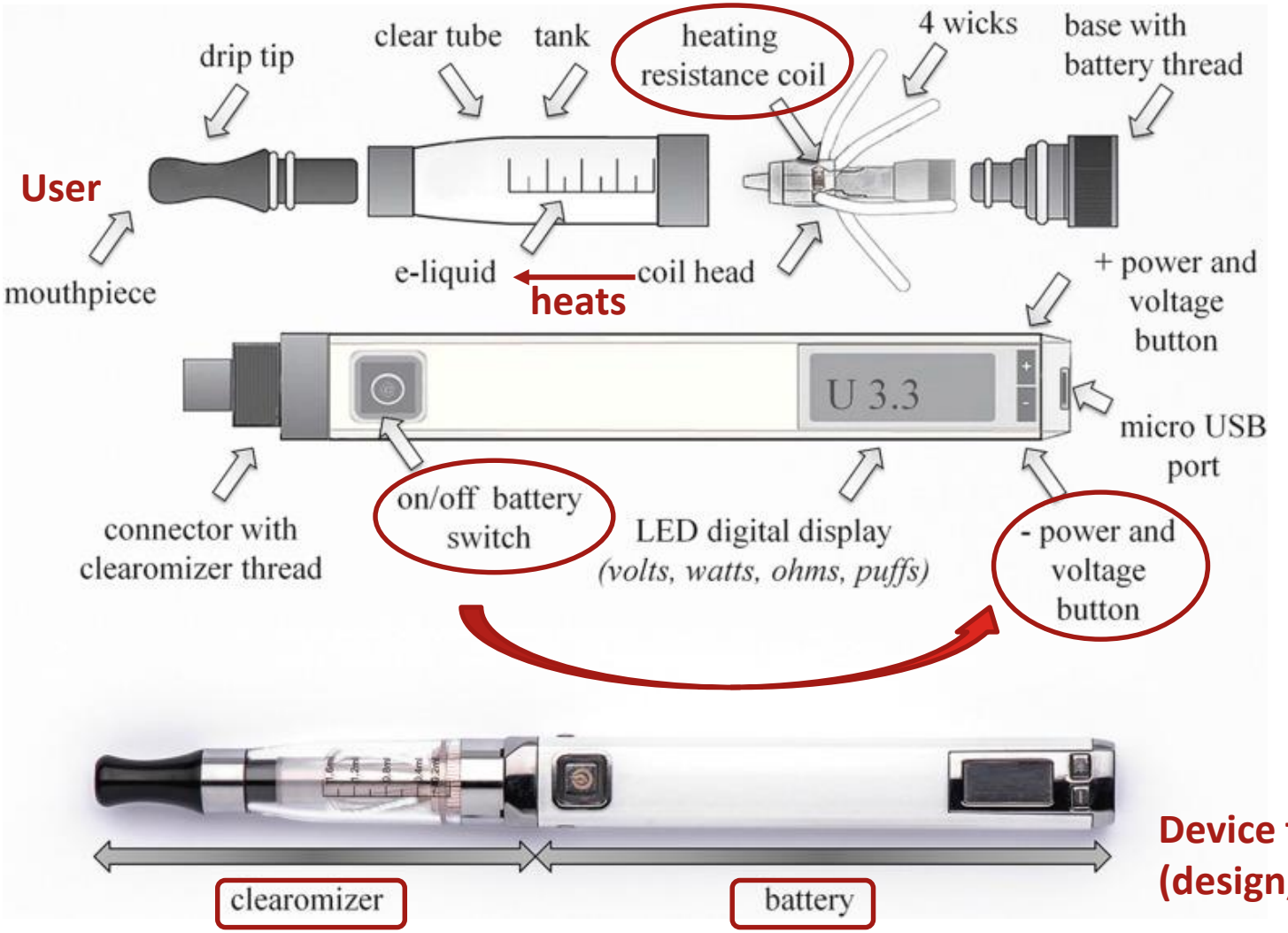


Nicotine

ENDS: characteristics and use

ENDS characteristics and parameters influencing chemical composition in aerosol



E-liquid composition

Device type (design, brands)

Giroud et al. (2015) *E-Cigarettes: A Review of New Trends in Cannabis Use*

Main components of e-liquids

Humectants/solvents

Propylene glycol

Glycerol
(or vegetable glycerin)

- Main immersing solvents
- *Form the base of e-liquid*
- *Prevent the e-liquid to dry out*
- *Dilute nicotine*
- *Allow the consistency to easily vaporized the e-liquid*
- *The ratio affects: nicotine delivery + the "cloud formation" from user (PG: carries flavours + better "throat hit" while VG: thickness of the cloud + much smoother)*

Nicotine
(≤ 20 mg/mL)

Flavoring agents

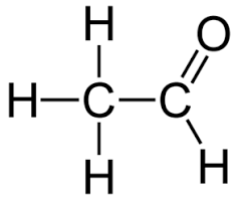
- *> 7000 flavoring agents*
- *Consist of synthetic chemicals in the liquid form*
- *Emit aromas upon heating*
- *Approved for ingestion, not tested for inhalation*

Water

Ethanol

Puffing profile

- Style of puffing **affects the concentration** of toxicants released
- The parameters of puffing are diverse and include important variables to consider to measure the compounds released:
  - The number of puffs
  - Puffing duration (time interval at which e-liquid is heated up)
  - Puff intervals (break time between puffs)
  - Puffing intensity (combination of the puff volume, puff frequency, and heating voltage)
  - Total puff volume (combination of the puff velocity and puff number)
- Varies significantly with brands and users



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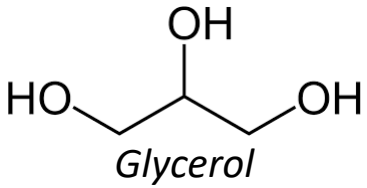

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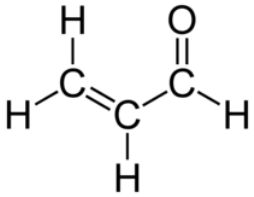
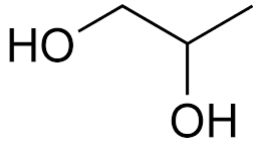


Acrolein



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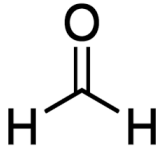
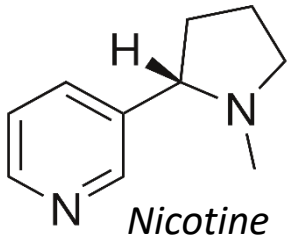


Formaldehyde



Nicotine

What is the composition of the aerosols?

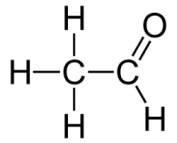
The potential toxicants in aerosols

- Approximately **250 chemical** substances may be detected in the aerosols including nicotine, flavorings, alkaloids, volatile organic compounds (VOCs), pyridine, and carbonyl compounds
- A high **correlation** with several compounds and the operating power of ENDS
- This implies that **e-liquid ingredients** might be **chemically altered** during the **vaporization** process

PG and VG: potential health effects

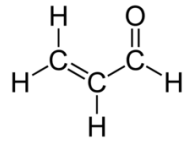
- The **most common symptom** reported is a **dry mouth and throat**, which is considered to originate from the water-absorbing property of PG and glycerol
- No study on long-term exposure to PG and glycerol

Primary concerns: carbonyls



Acetaldehyde

- Traces measured in e-liquids
- Dominant components in aerosols:
  - Acetaldehyde
  - Formaldehyde
  - Acrolein (not in e-liquid)



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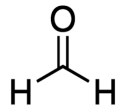


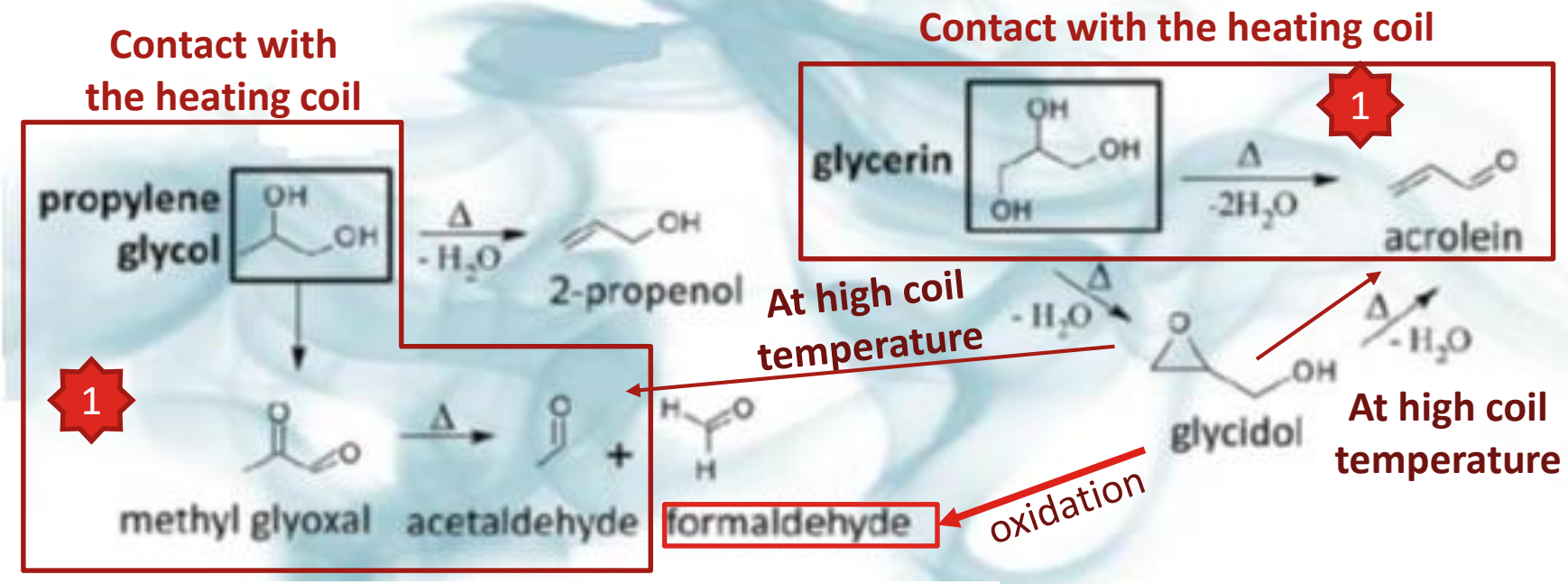
Formaldehyde

- Concentrations vary among brands and among samples of the same device
- May cause irritation to the respiratory tract and potential carcinogens

How do explain variations among carbonyl concentrations?

- Carbonyls generated when e-liquid is heated

Main sources: oxidation of PG and VG



Sleiman et al. (2016) *Emissions from Electronic Cigarettes: Key Parameters Affecting the Release of Harmful Chemicals*

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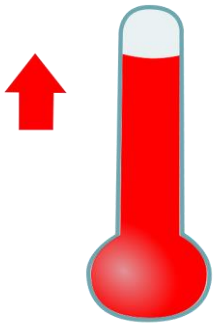
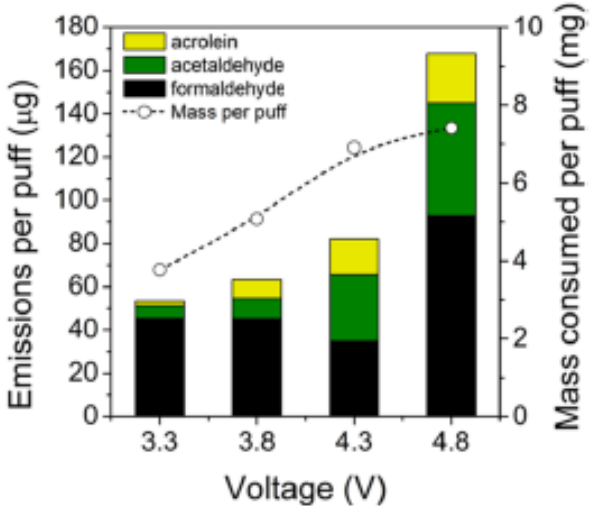


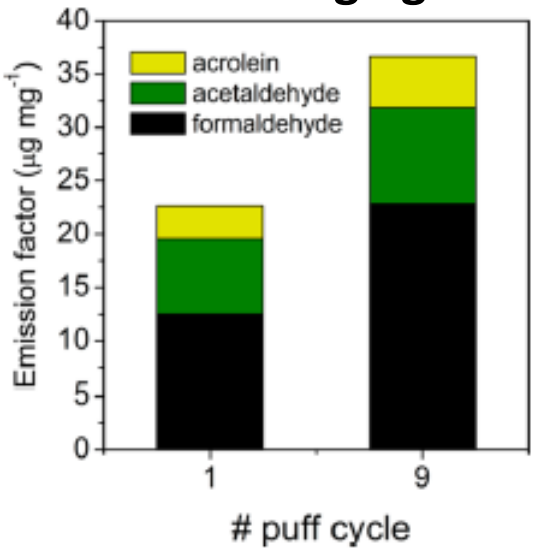
- Carbonyls generated when e-liquid is heated
- The battery output voltage significantly affects the concentration of carbonyl:
  High voltage = high concentrations
- Heating coil temperatures above 300°C
  (low concentrations below 300°C)
- Low e-liquid levels within tank due to airflow increase and overheating
- After several uses of ENDS: increase up to 60% of carbonyl emission due to degradation of polymerization by-products upon heating
- Flavoring compounds may also play a role

Effects of different parameters on carbonyl emission

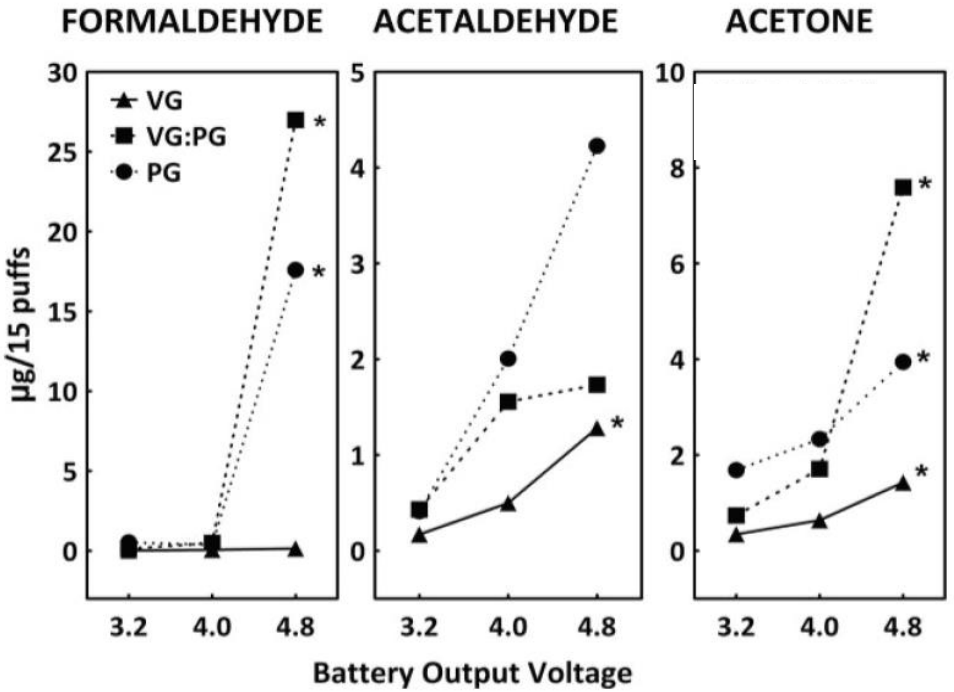
Voltage



Device aging



Solvents



Kosmider et al (2014) *Carbonyl Compounds in Electronic Cigarette Vapors: Effects of Nicotine Solvent and Battery Output Voltage*

* Indicates statistically significant increase from 3.2 Volts ($p < 0.05$)

Sleiman et al. (2016) *Emissions from Electronic Cigarettes: Key Parameters Affecting the Release of Harmful Chemicals*

Flavoring agents contribute to carbonyl emissions

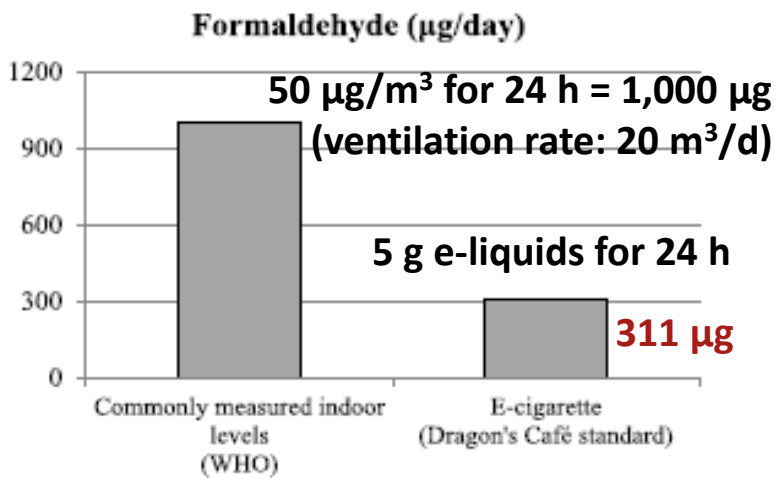
µg/g e-liquid

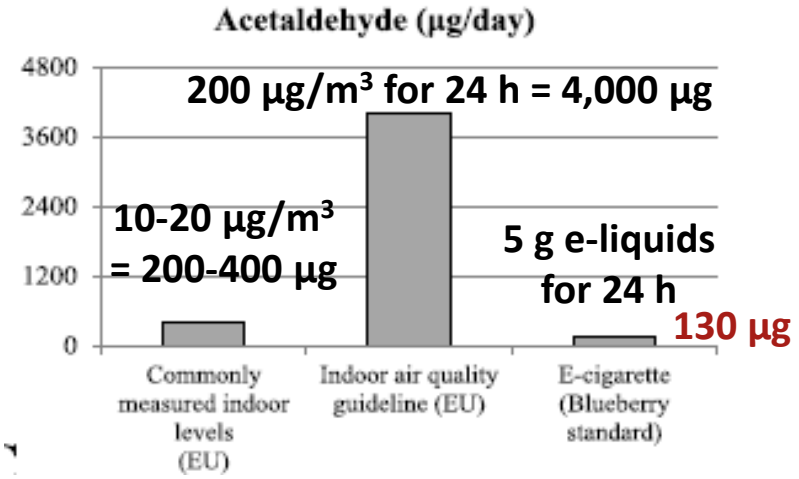
Sample	Formaldehyde	Acetaldehyde	Acrolein
Unflavoured	16.1 (2.0)	5.6 (1.2)	2.4 (1.8)
Standard versions			
ECBlend blueberry	18.0 (3.7)	26.0 (6.2)	18.3 (5.8)
ECBlend Dragon's café	62.2 (2.6)	14.3 (3.6)	10.8 (4.2)
ECBlend watermelon	10.7 (6.9)	22.0 (19.4)	13.4 (10.4)
Sweetened versions			
ECBlend blueberry	19.0 (4.7)	25.0 (7.6)	19.4 (4.4)
ECBlend Dragon's café	56.8 (0.9)	12.1 (1.3)	5.4 (1.8)
ECBlend watermelon	8.3 (2.0)	17.7 (6.2)	9.3 (4.7)

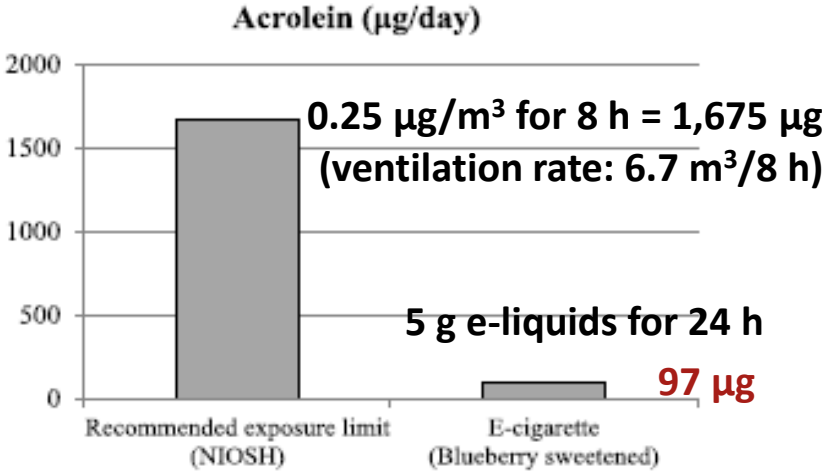
Farsalinos and Voudris (2018) *Do flavouring compounds contribute to aldehyde emissions in e-cigarettes?*

- No propionaldehyde or crotonaldehyde detected
- 60% PG and 40% VG; 1.2% nicotine
- Voltage: 4V; 1.5 Ohm; 10.7W

How to interpret these concentrations?







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Second concerns: Flavoring agents

- **Little information** available on health effect during long-term exposures by inhalation
- Some are **sensitizing**, **irritating**, or **toxic**:
  - Diacetyl and acetylpropionyl: associated with adverse respiratory health outcomes
  - Cinnamaldehyde (cinnamon-flavored, caramel, fruity): cytotoxic and genotoxic at low concentrations (in vitro studies)
- Saccharides, used to make sweet e-liquid flavors, degrade and produce aldehydes and furans (irritation to the upper respiratory tract)
- **Furan** concentration are **correlated** with **power** of the device and **sweetener concentration**, but not puff duration

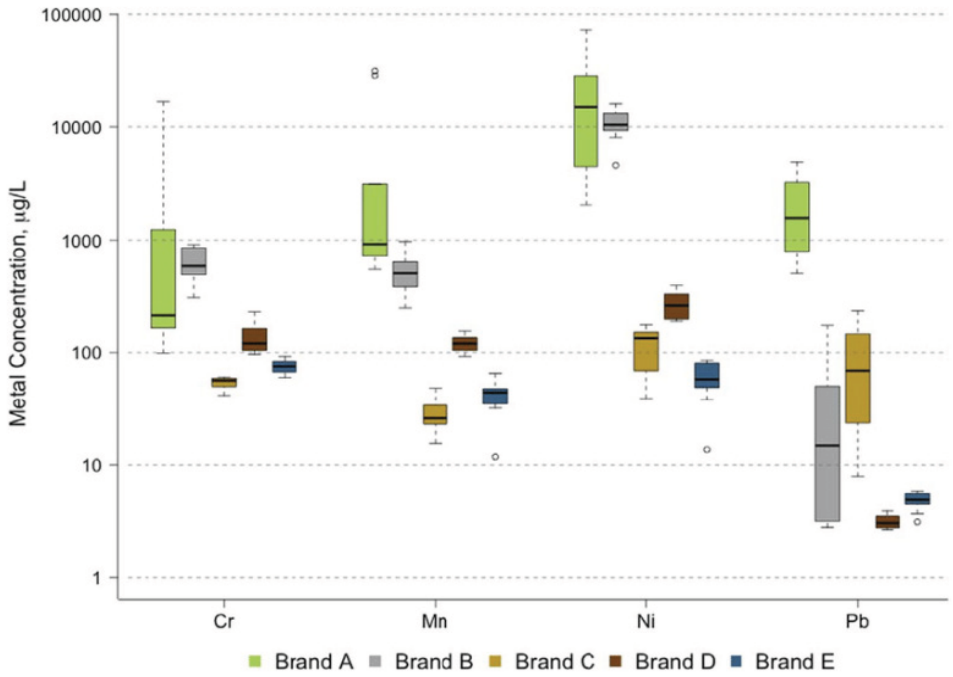
VOCs: very low concentrations

- Not present in e-liquid (unless impurities)
- Produced at **much lower concentrations** than carbonyls
- Main compounds, depending on flavors:
  - Ethanol
  - M,p-xylene
  - Styrene
  - Toluene
  - Benzene

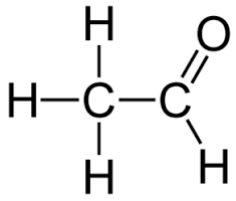
Metals: in e-liquids and emissions

- The origin of the metals could be:
  - the metallic coil used to heat the e-liquid
  - other parts of the e-cigarette device
  - e-liquids
- Some of the key metals include **chromium**, **nickel**, **lead**, **manganese**, aluminum, tin, iron

Distribution of metal concentrations within and across brands of ENDS



Hess et al. (2017) *E-cigarettes as a source of toxic and potentially carcinogenic metals*



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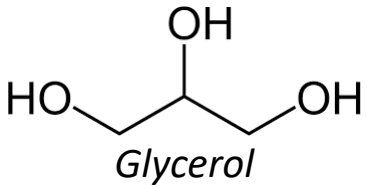

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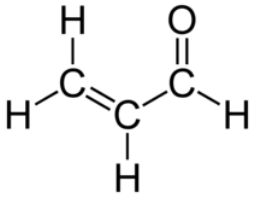

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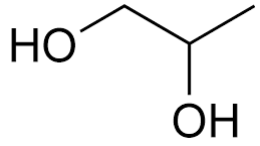

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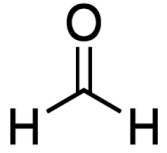

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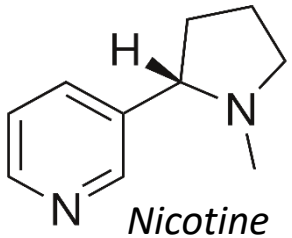


Nicotine

Nicotine intake using ENDS

Variability of nicotine content

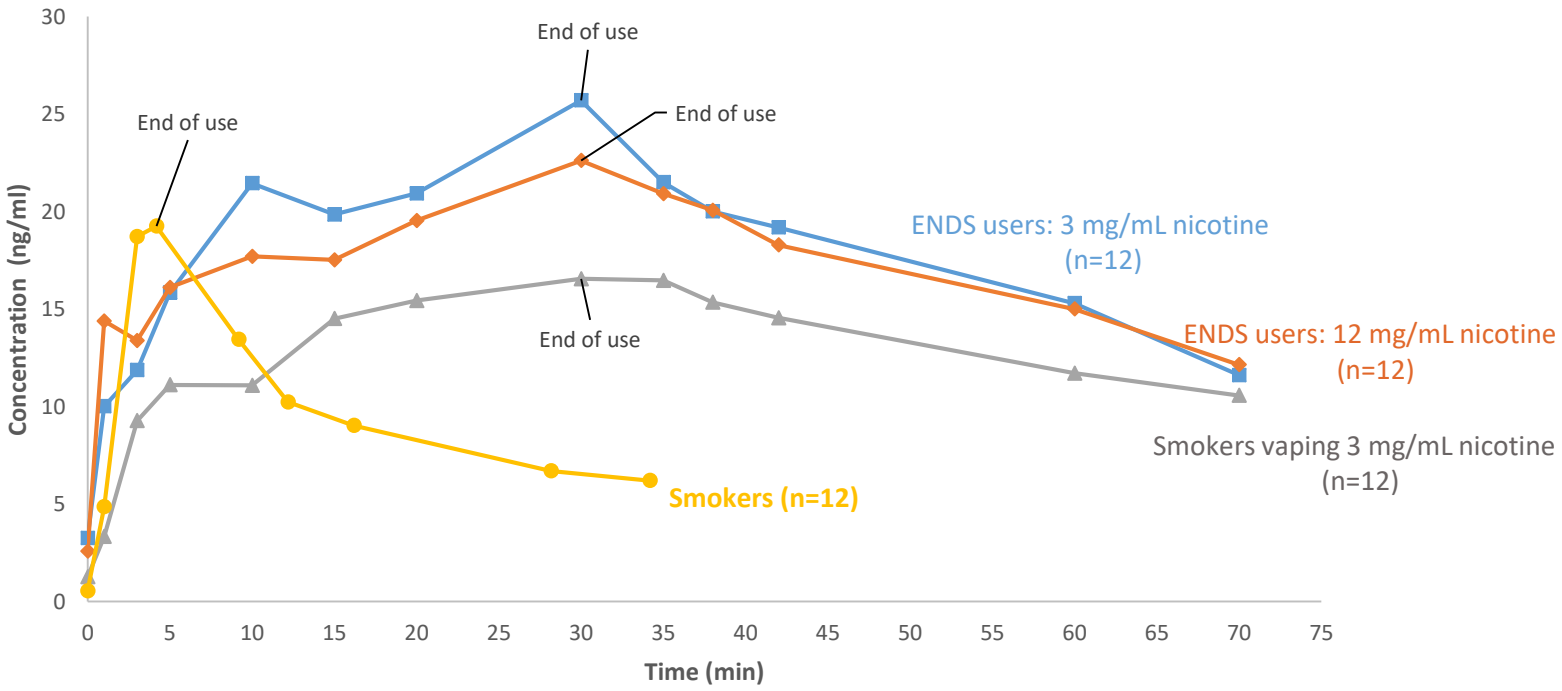
- Nicotine content is **highly variable** and depends on **product characteristics** (including device and e-liquid characteristics) and how the device is **operated**
- **Nicotine concentration** in aerosols **increases** with:
  - ENDS power (coil temperature, voltage
  - E-liquid nicotine concentration
  - Puff duration
  - Alkaline pH in e-liquid improves its bioavailability

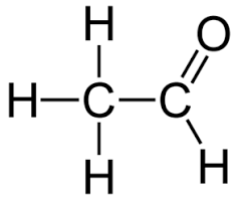
Pharmacokinetics of nicotine

- **Nicotine intake** from ENDS devices among experienced adult users can be **comparable** to that from **combustible tobacco cigarettes**

Innokin
Endura T20s

Nicotine concentration (ng/mL) in plasma:
comparison between dual users and ENDS users following two nicotine intakes





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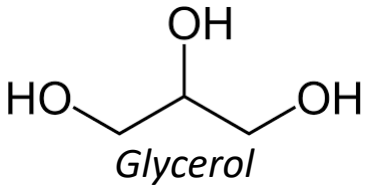
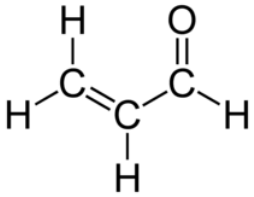


Glycerol



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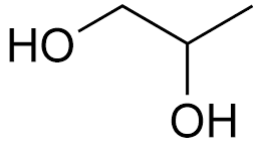

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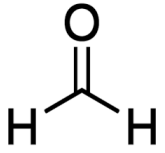

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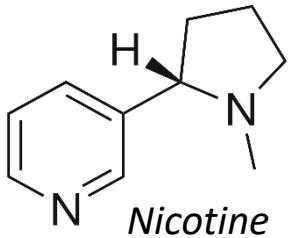

Nicotine

Conclusion

Overall conclusions

- Nicotine intake is comparable to tobacco cigarettes
- ENDS aerosol is far less toxic than tobacco cigarette smoke exposure (no combustion process)
- Potential harmful toxicants are still present in ENDS emissions and aerosols
- To limit the exposure to toxicants, it is important to accurately set-up ENDS parameters and select appropriate devices and e-liquids

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Thank you for your attention