Biomarkers of exposure specific to e-vapor products based on stable-isotope labelled ingredients - results

Landmesser A.[1,2], Scherer M. [1], Scherer G. [1], Sarkar M. [3], Edmiston J. [3], Pluym N. [1]

[1] ABF, Analytisch-Biologisches Forschungslabor GmbH, München, Germany
[2] Technical University Munich, Institute of Hydrochemistry and Chemical Balneology
[3] Altria Client Services LLC. Center for Research and Technology, Richmond, Virginia, USA

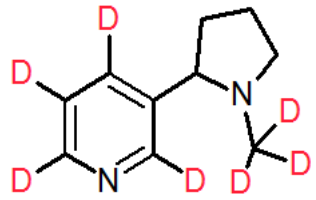
2017 CORESTA SSPT
Kitzbühel, Austria

October – 08-12
ST24

Analysis of labelled Nic / Cot: Plasma

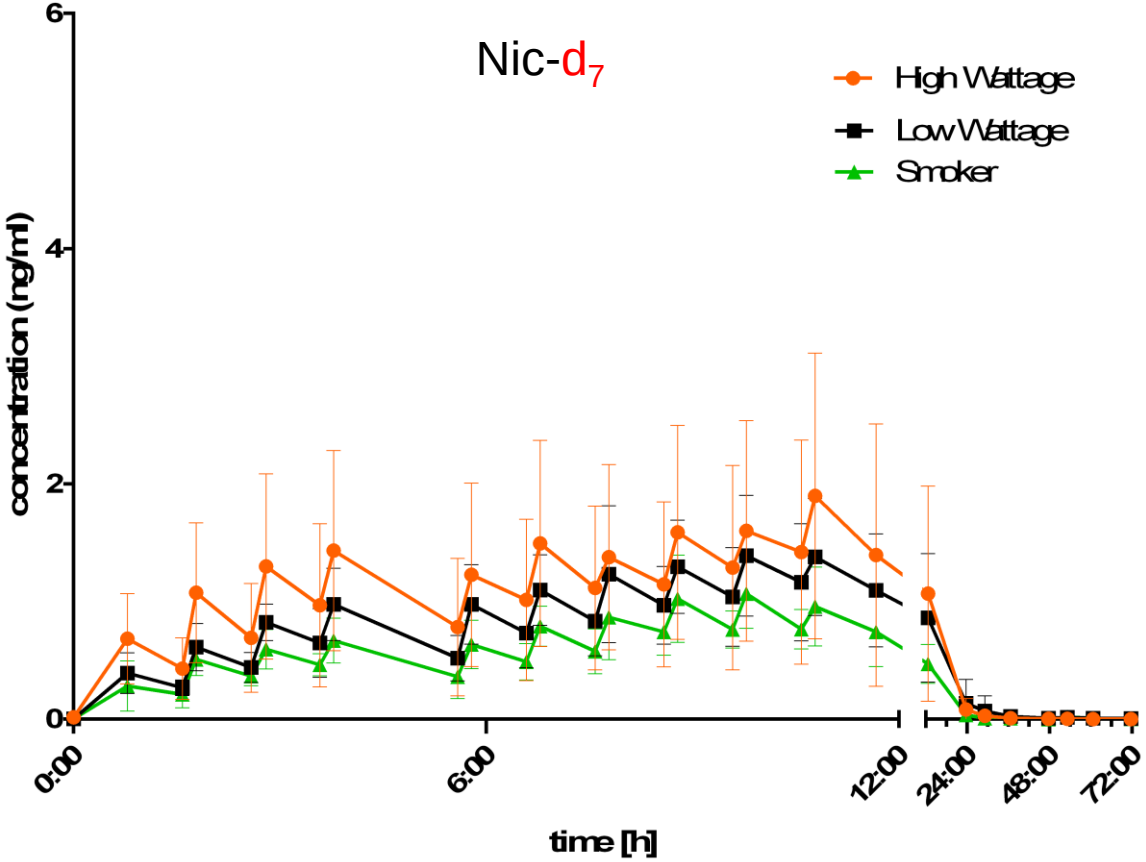
LLOQ: 0.1 ng/ml

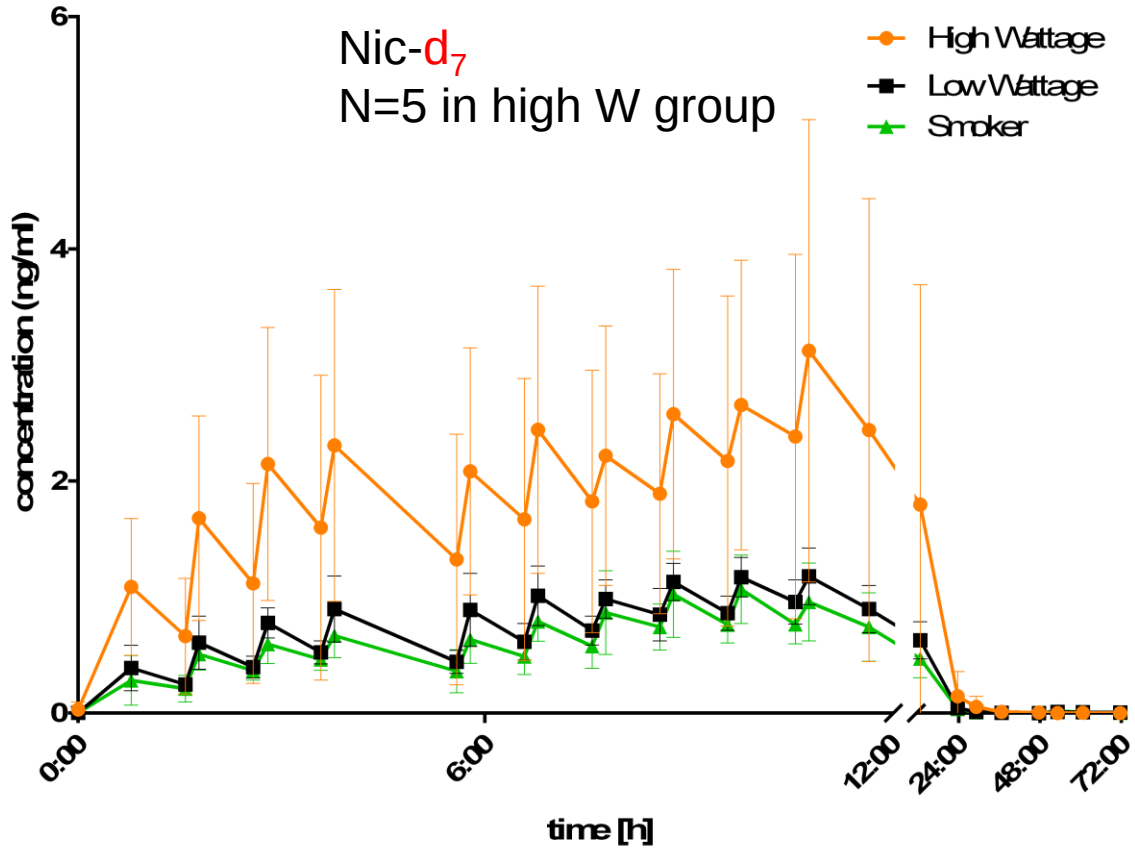
Low wattage: 10 W
High wattage: 18 W



Nicotine-d_7

Cotinine-d_7



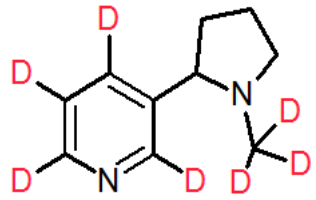


* For technical reasons spike in cigarettes does not exactly match the amounts of labelled PG, G, N in e-vapor products

Analysis of labelled Nic / Cot: Plasma

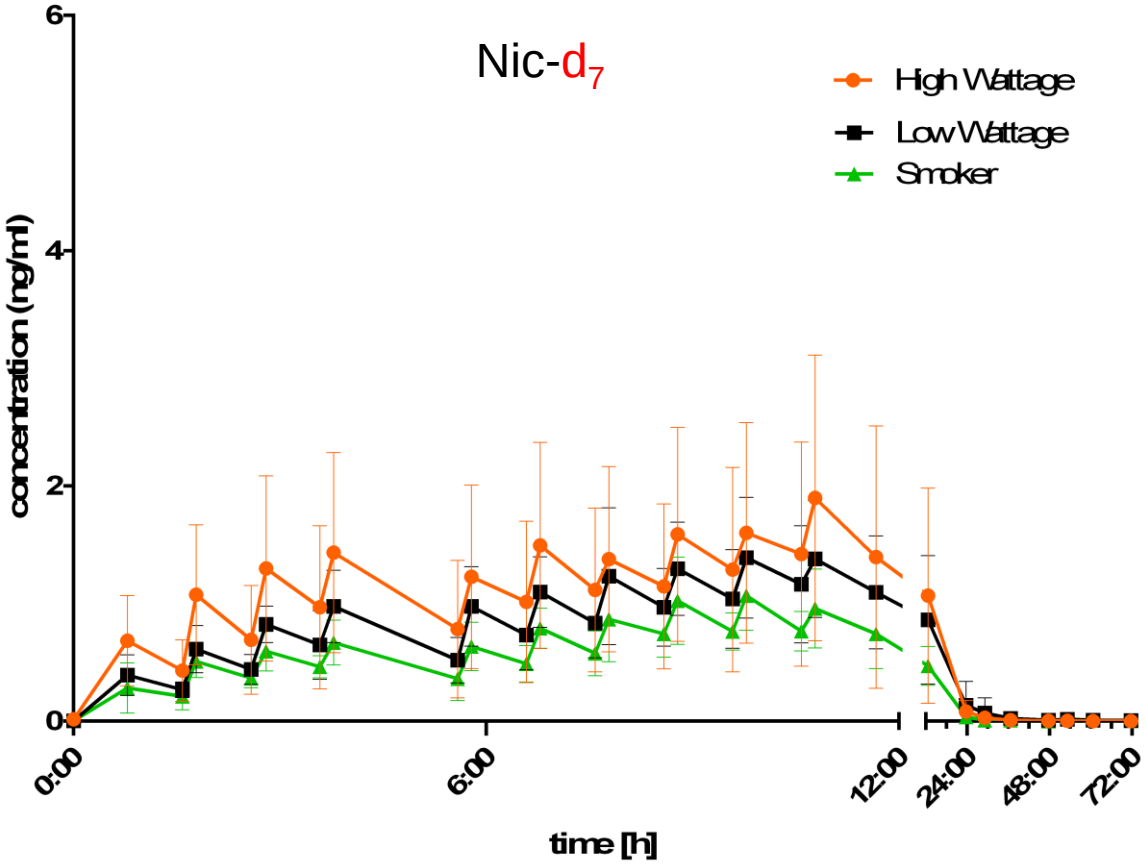
LLOQ: 0.1 ng/ml

Low wattage: 10 W
High wattage: 18 W



Nicotine-d_7

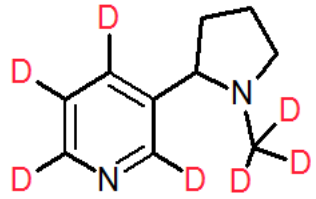
Cotinine-d_7



- Non-significant difference between vaping groups
- 5 subjects in high W group reported problems with proper consumption of the product
- Difference between both groups becomes more obvious excluding those subjects

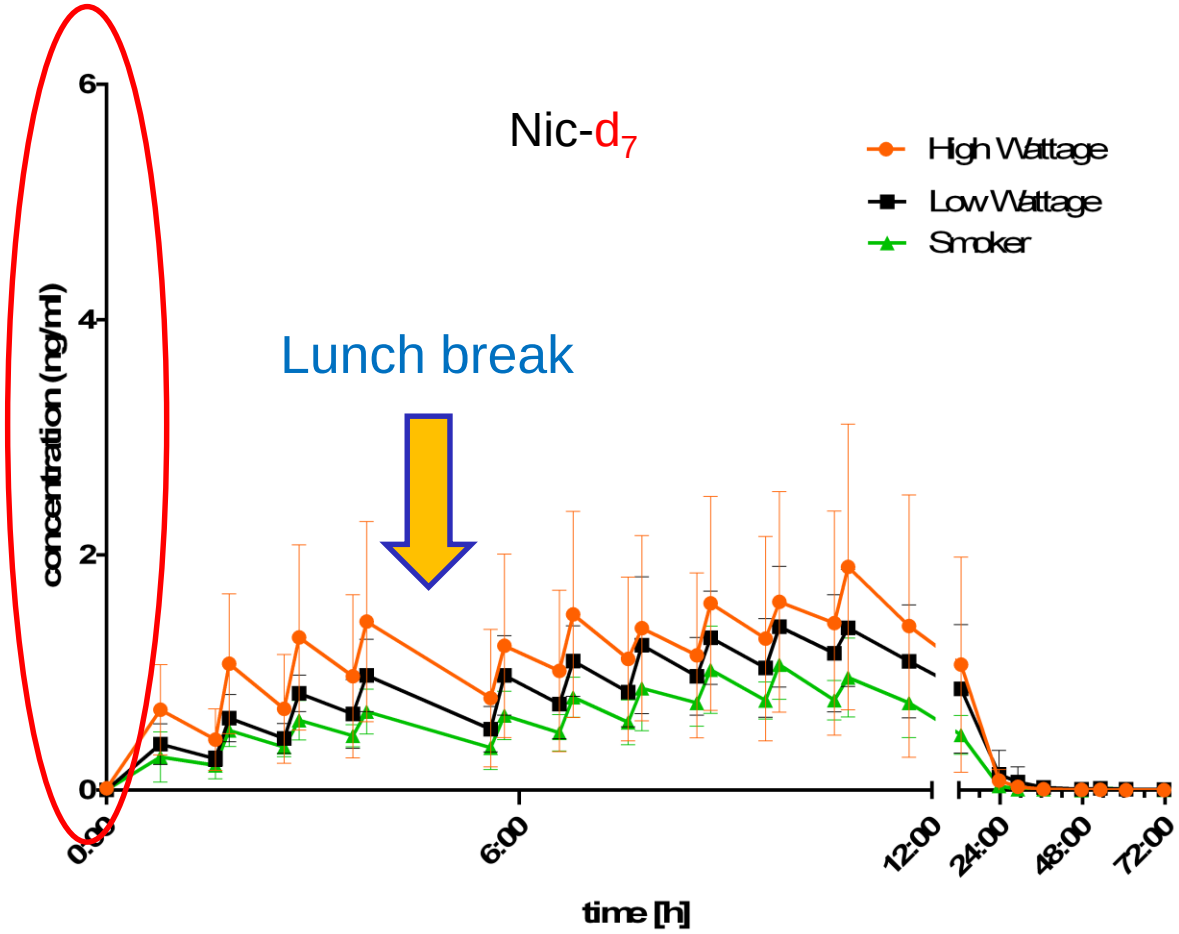
! All further evaluations compare complete data sets for all groups

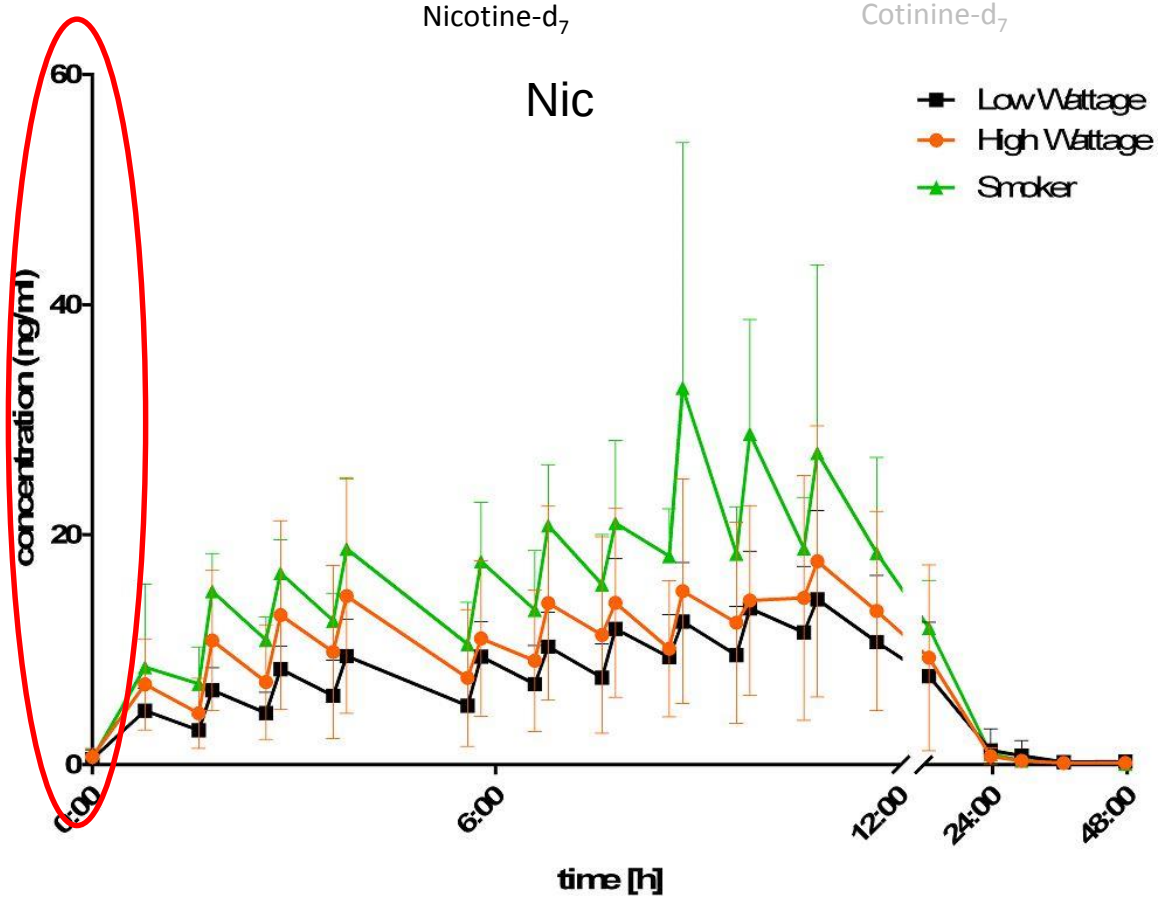
Analysis of labelled Nic / Cot: Plasma



Nicotine-d_7

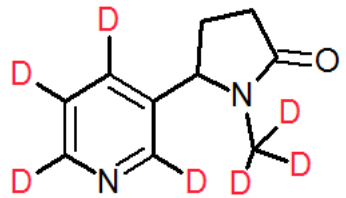
Cotinine-d_7



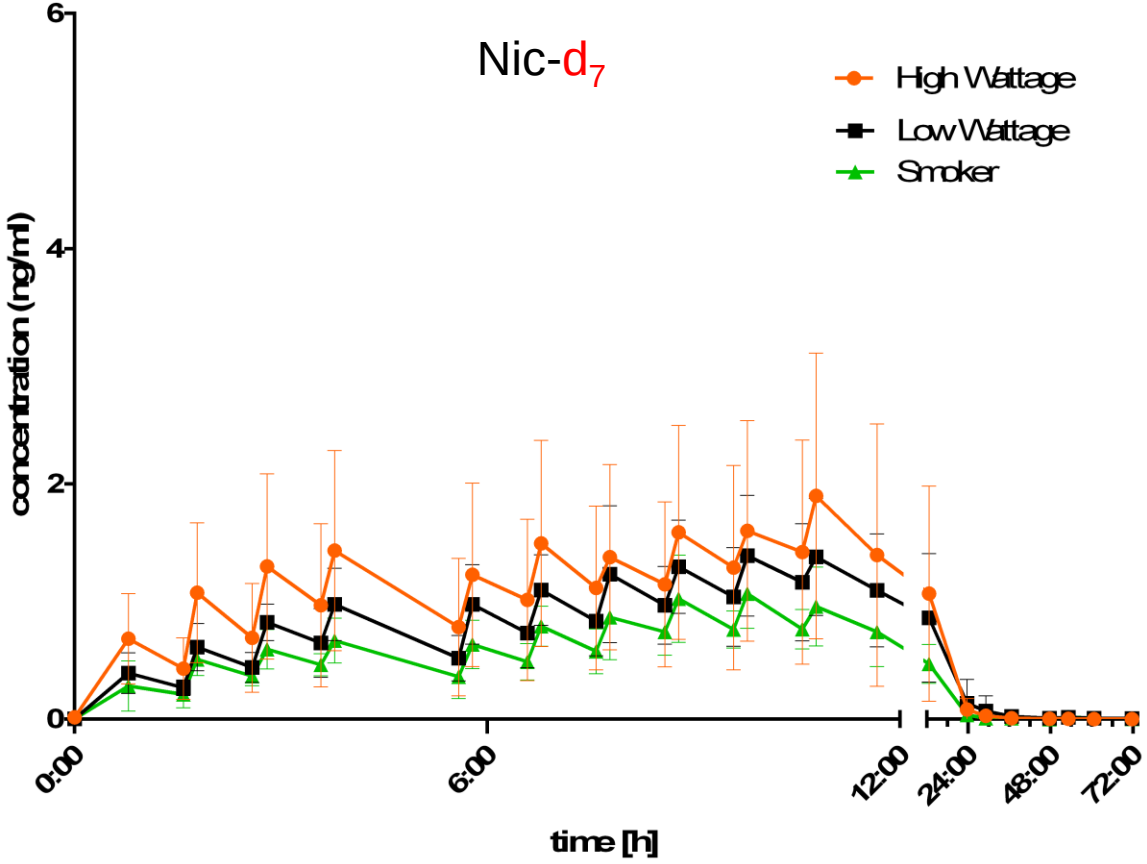


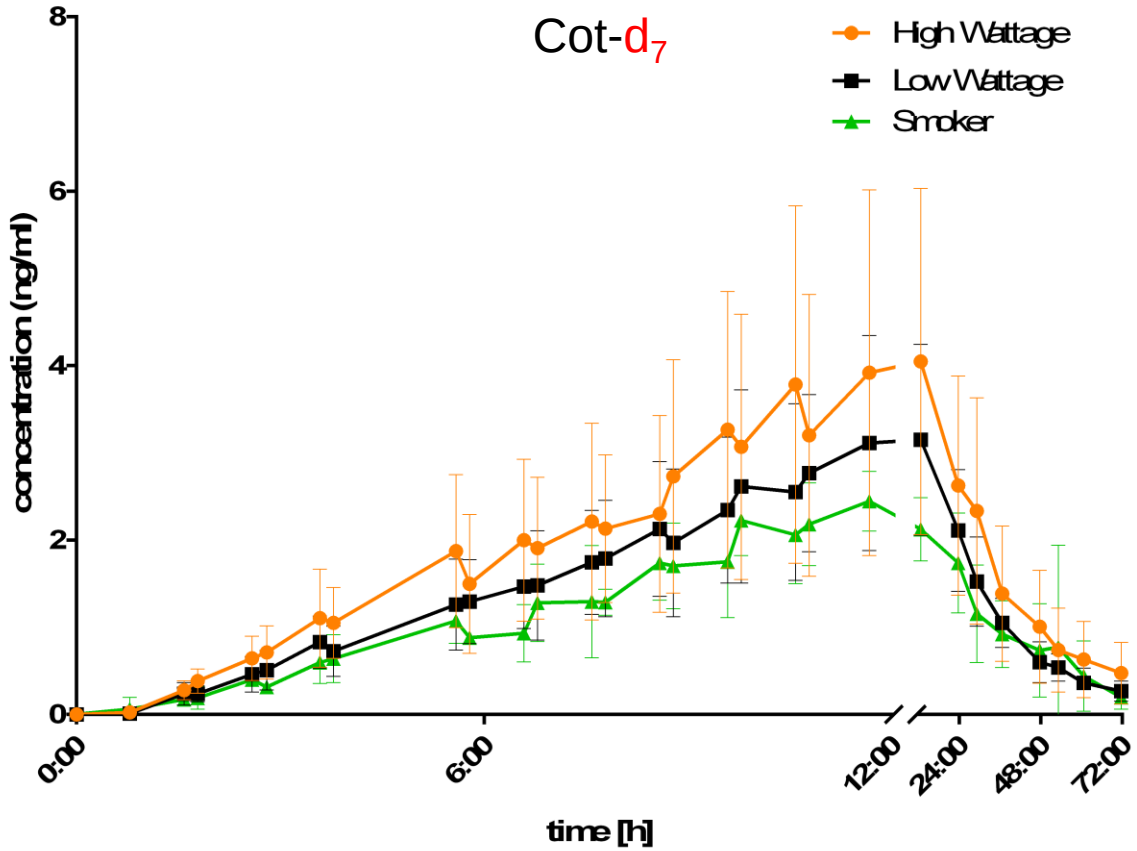
Analysis of labelled Nic / Cot: Plasma

Nicotine-d_7



Cotinine-d_7

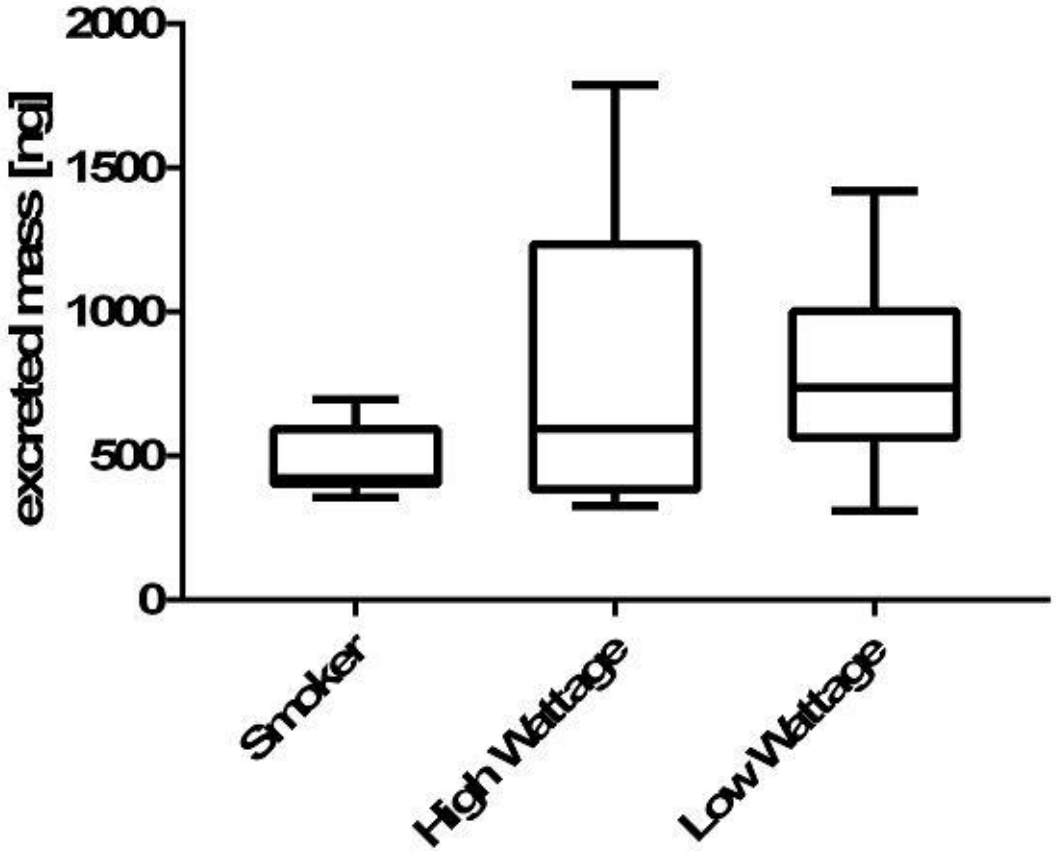




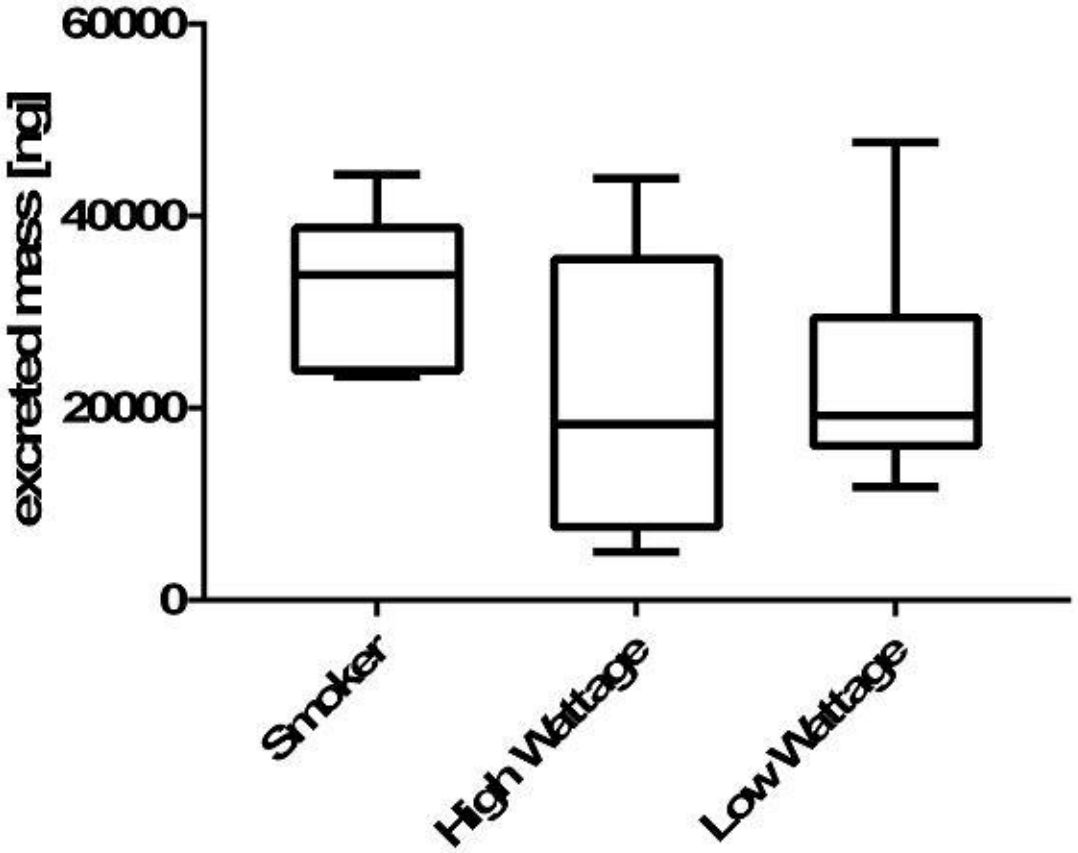
Analysis of labelled Nic + 10: Urine

Excreted mass after 72 hours

TNE labelled

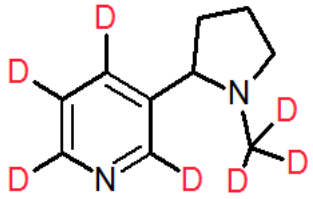


TNE unlabelled

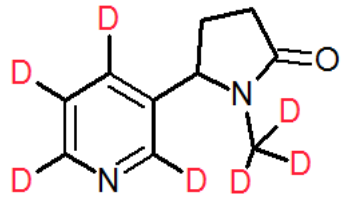


TNE: Total Nicotine Equivalents

Analysis of labelled Nic / Cot: Summary

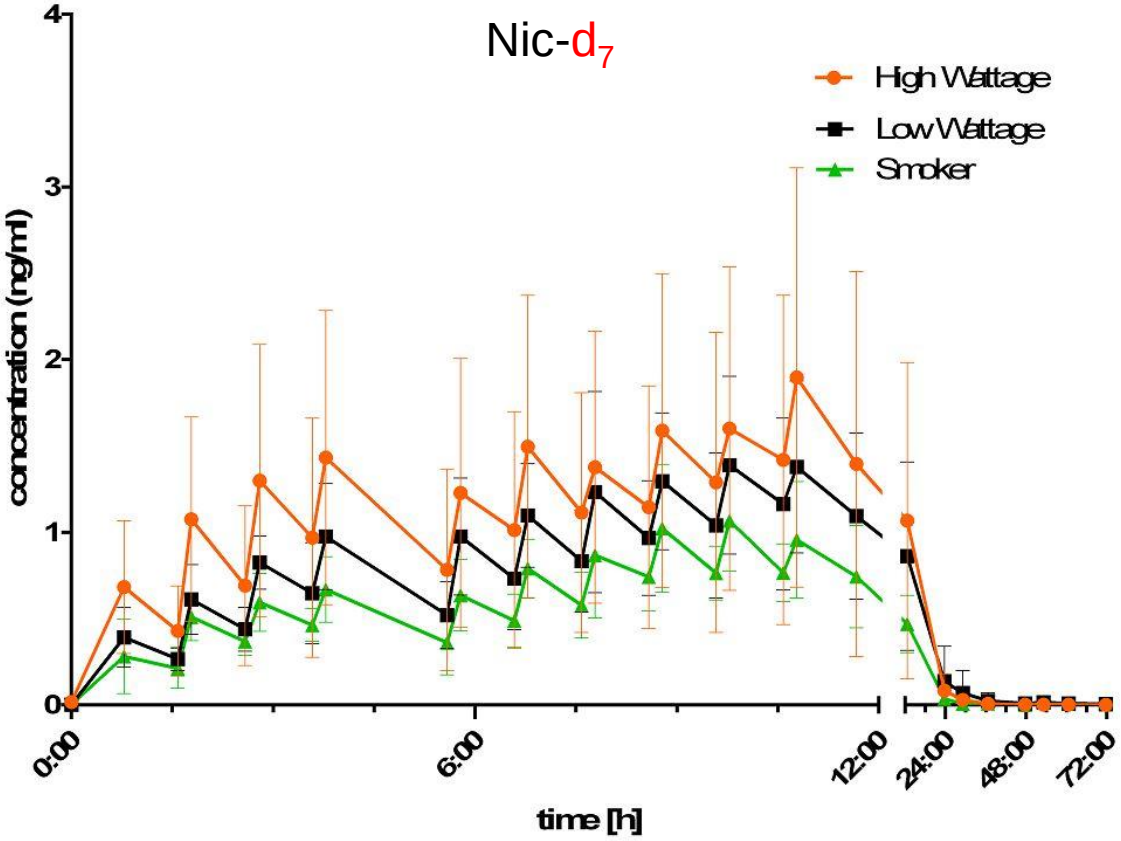


Nicotine-d_7



Cotinine-d_7

Nic-d_7

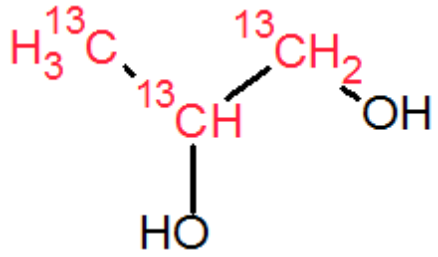


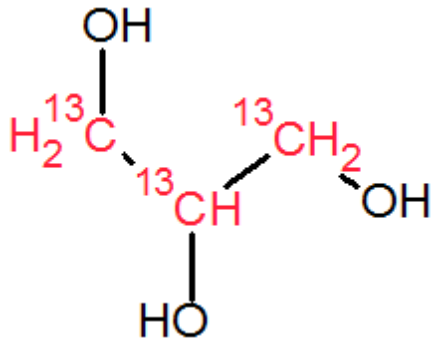
- 10% replacement with stable-isotope labelled Nic-d_7 resembled in plasma concentrations
- Dose-dependence of Nic/Cot levels in all groups
- Higher levels of Nic/Cot in high wattage group compared to low wattage group

➢ Uptake correlates with wattage

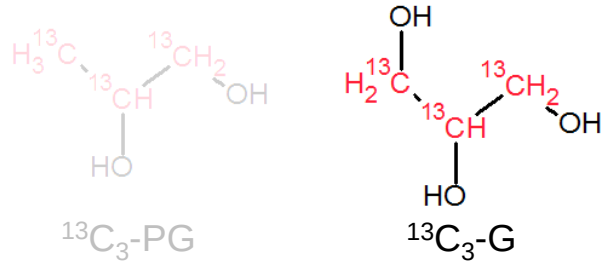
➢ Spike of Nic in conventional cigarettes resembles uptake of Nic in vapers

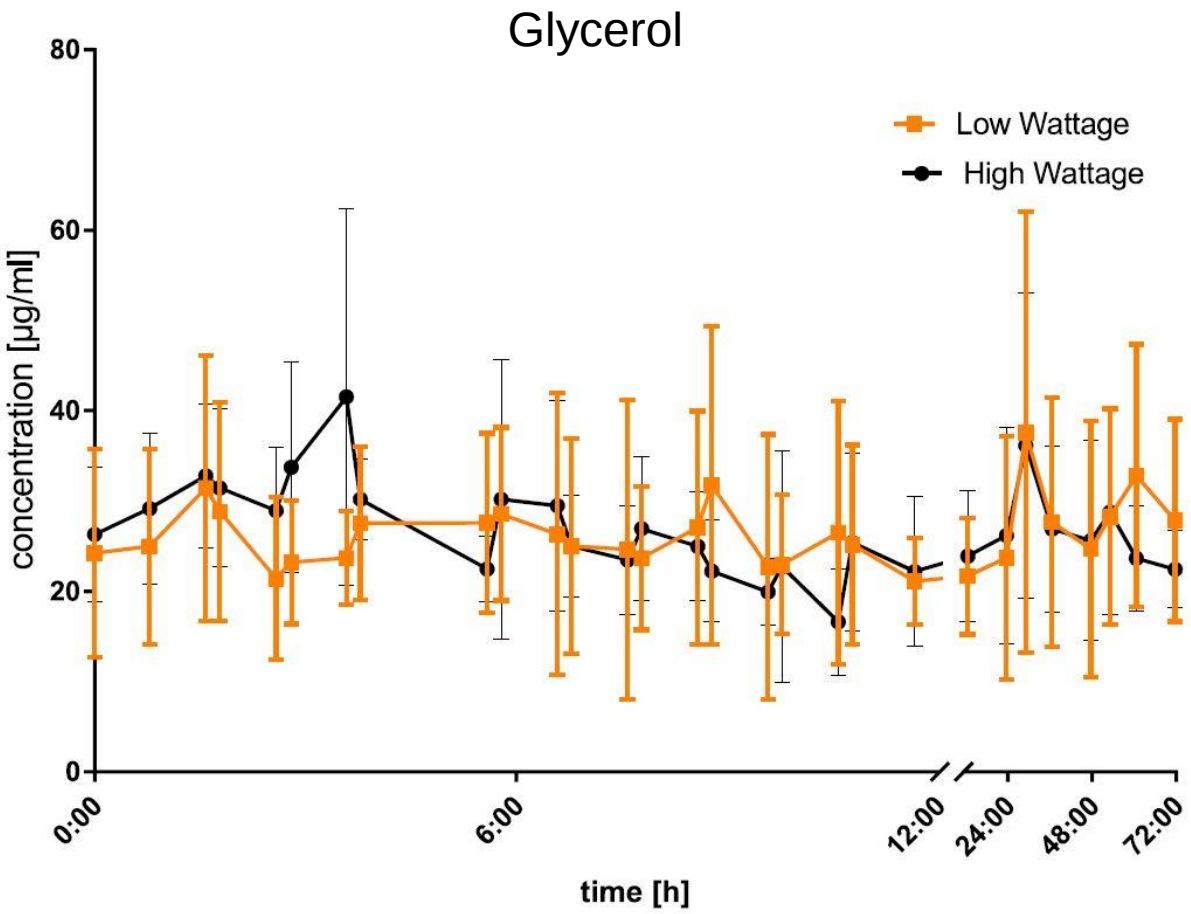
Analysis of PG / G





Analysis of labelled PG / G: Plasma



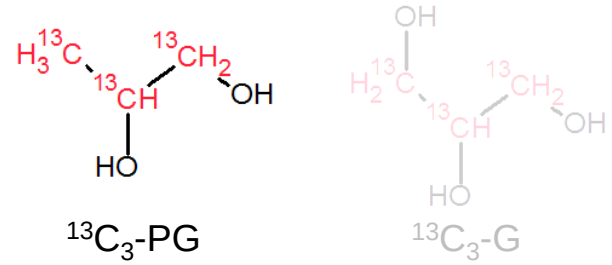


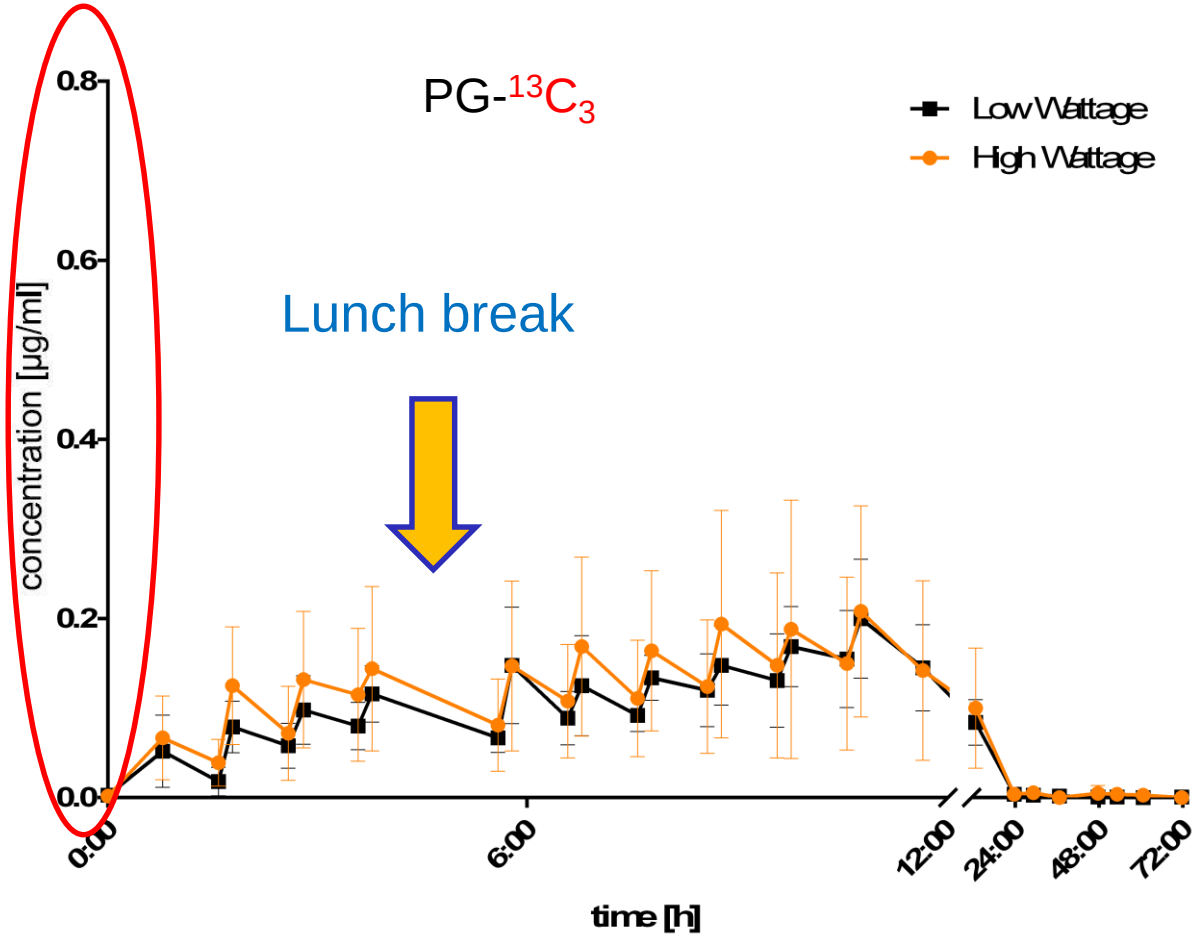
No dose-dependent alterations of G concentrations in plasma
Labelled G ($^{13}C_3$-G) not detectable in plasma after vaping

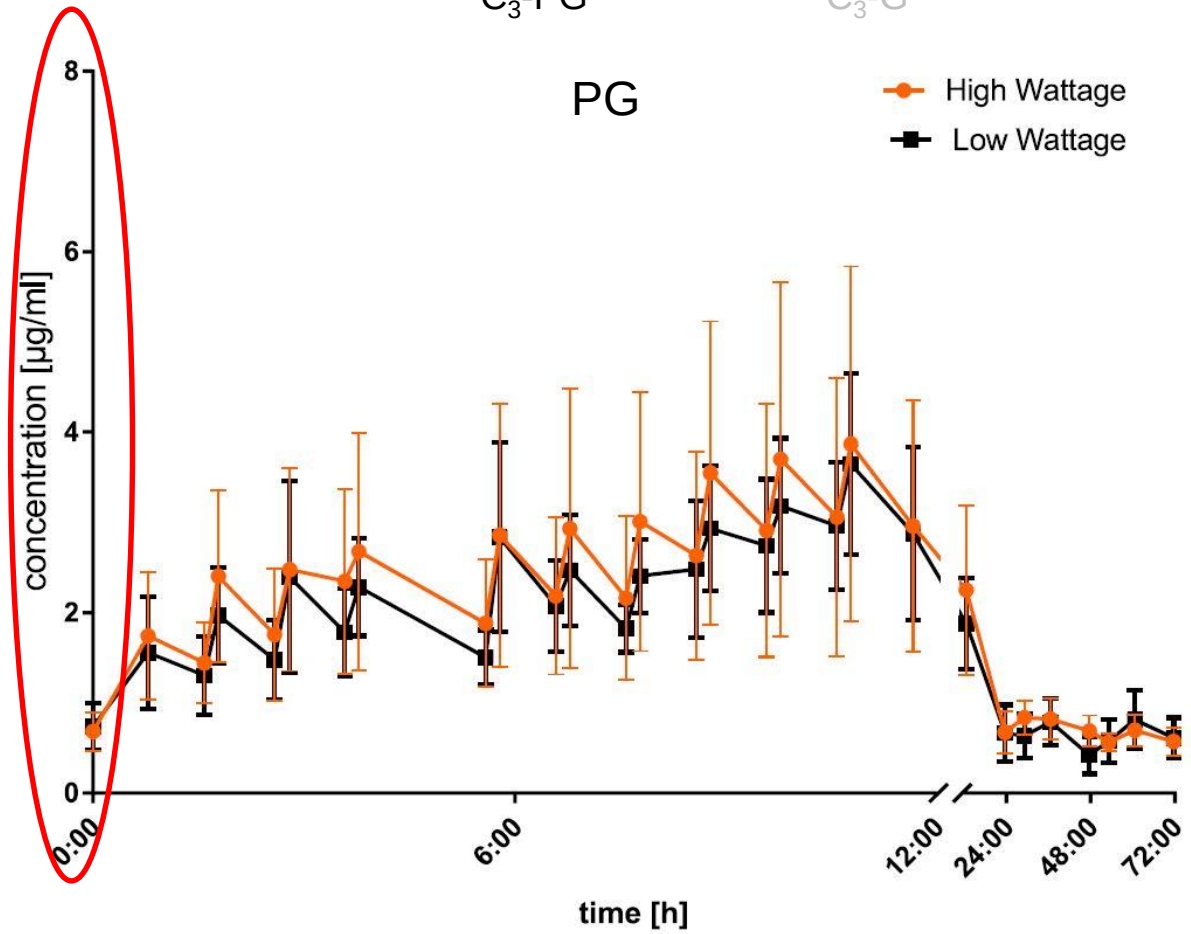
LLOQ: 0.05 µg/ml

Analysis of labelled PG / G: Plasma

LLOQ: 0.10 µg/ml



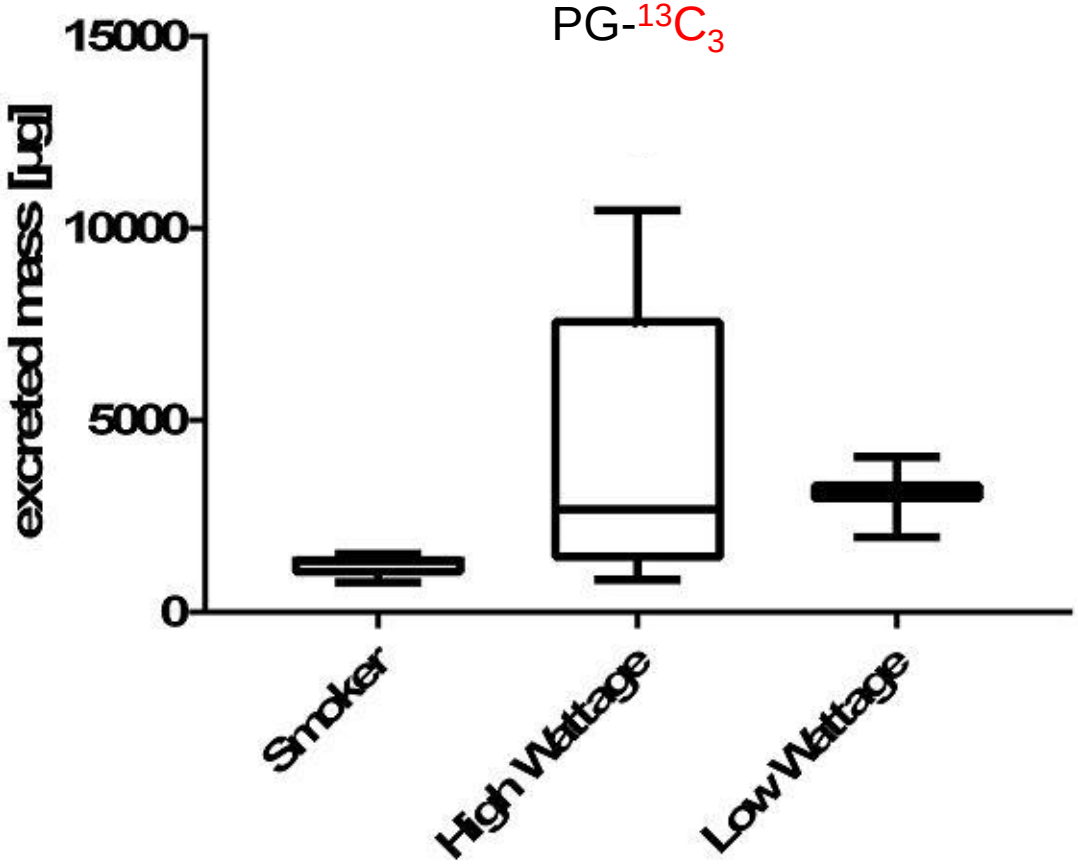




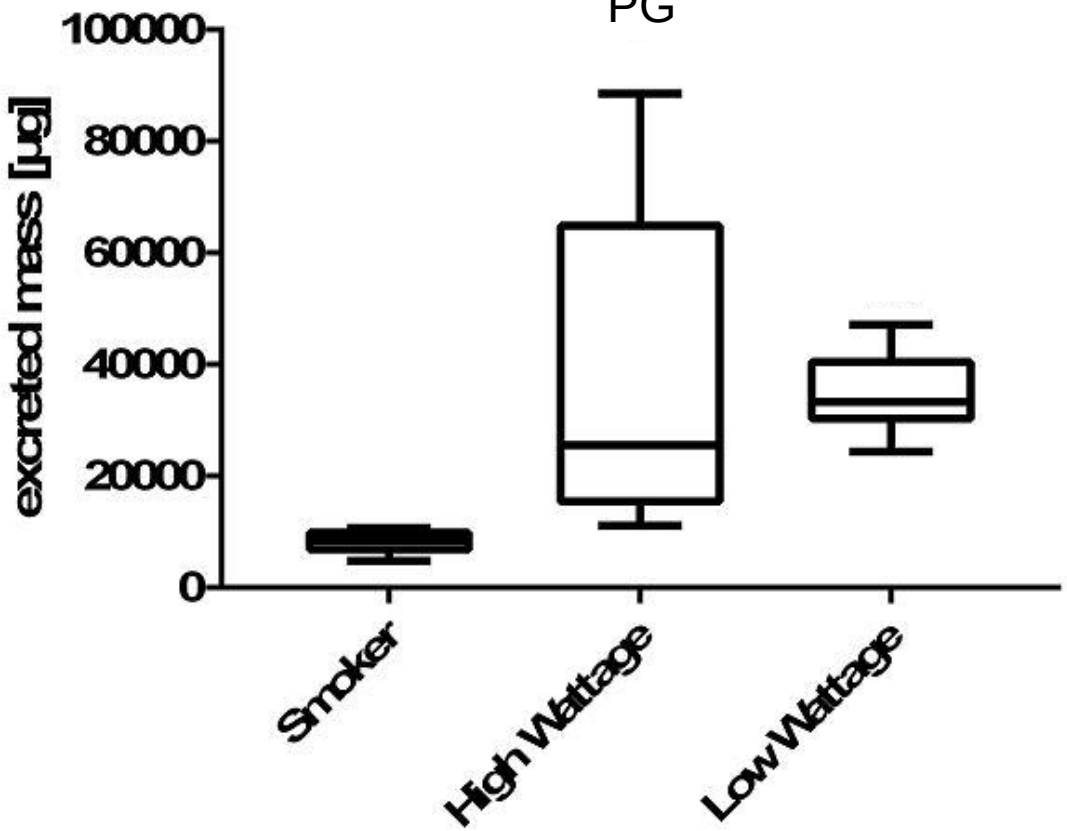
Analysis of labelled PG / G: Urine

Excreted mass after 72 hours

PG-$^{13}C_3$

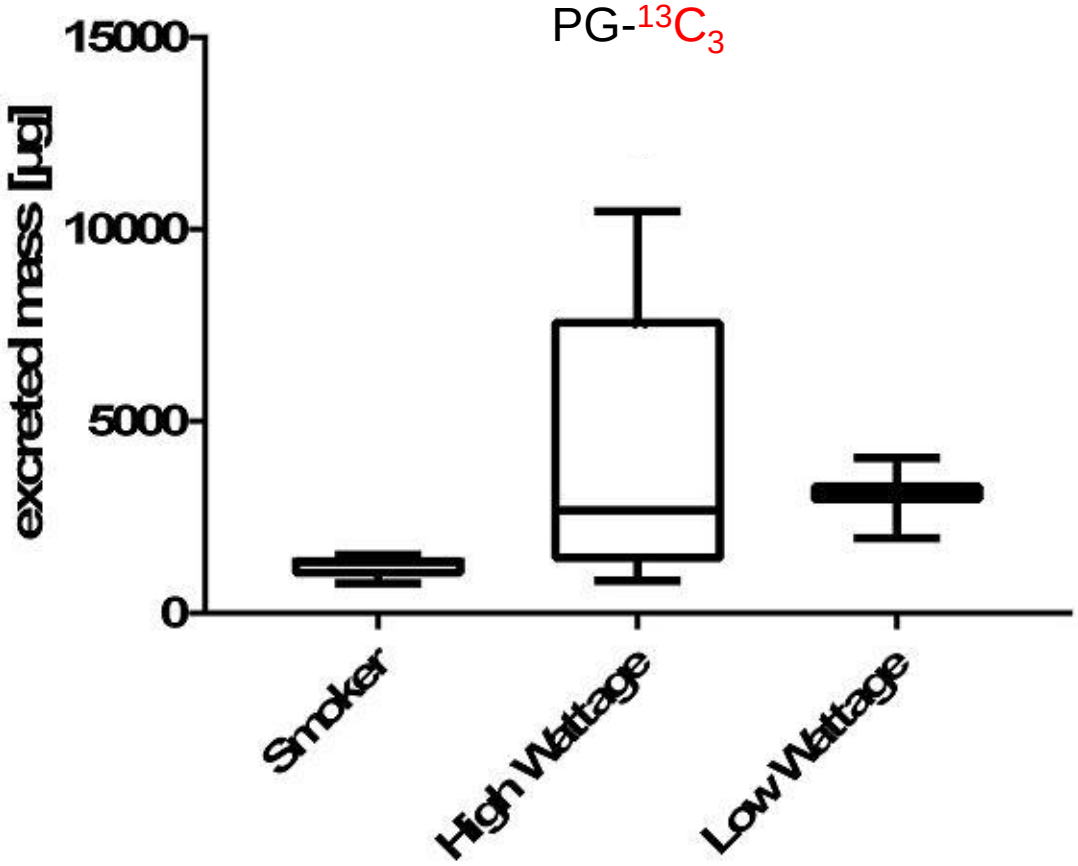


PG



Analysis of labelled PG / G: Summary

Excreted mass after 72 hours

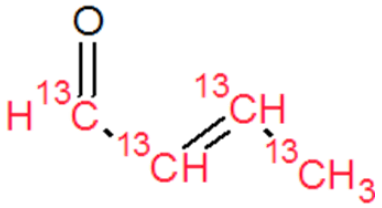


- 10% replacement with stable-isotope labelled PG resembled in plasma concentrations
- Dose-dependence proven for PG

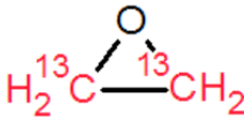
- PG levels in smokers significantly lower compared to both vaper groups

➢ Indication for “losses” of PG (and G?) during pyrolysis due to decomposition

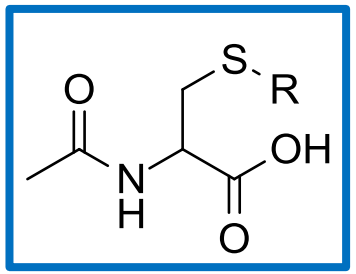
Thermal degradation (pyrolysis) of PG / G



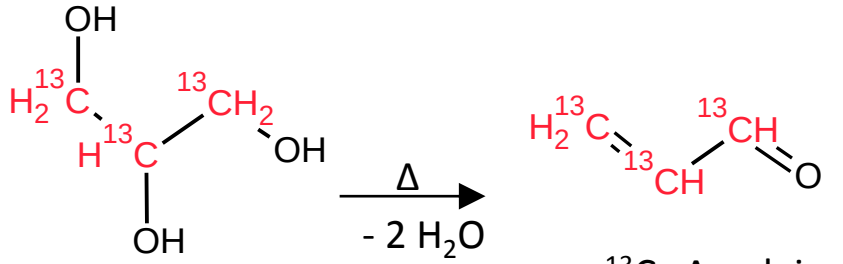
$^{13}C_4$-Crotonaldehyde
($^{13}C_4$-HMPMA)



$^{13}C_2$-Ethylene oxide
($^{13}C_2$-HEMA)

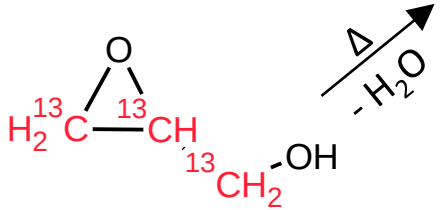


Mercapturic acids

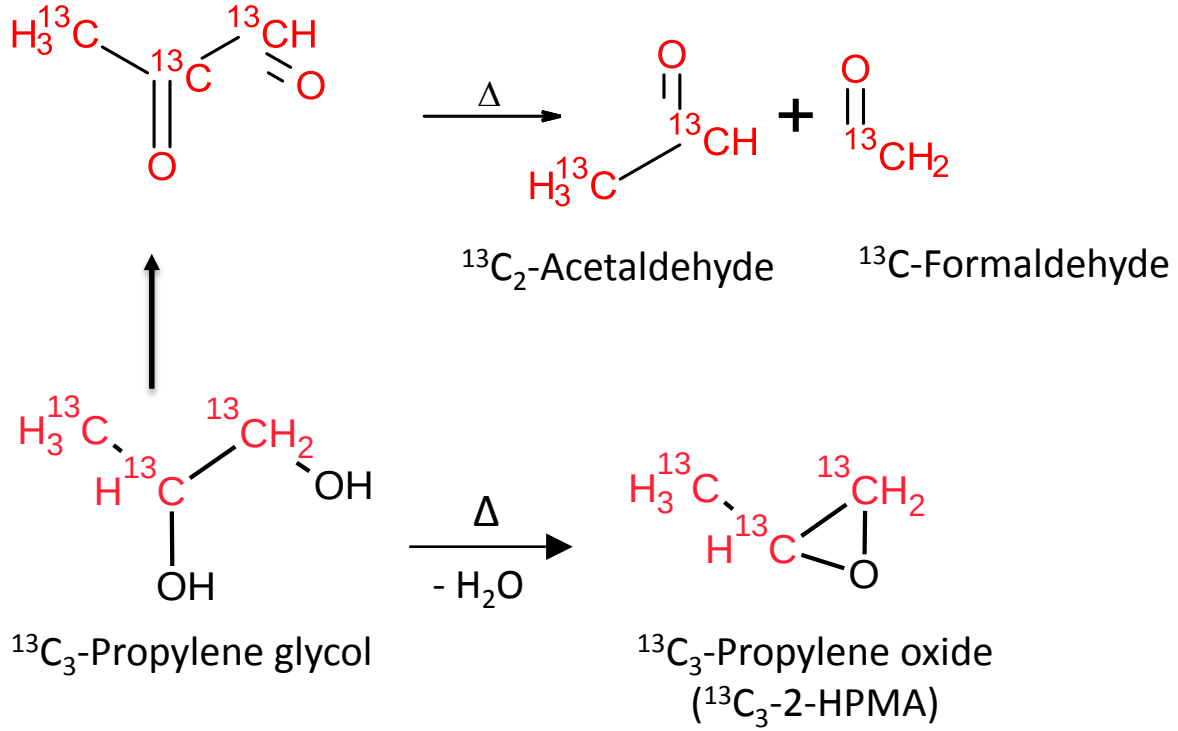


$^{13}C_3$-Glycerol

$^{13}C_3$-Acrolein
($^{13}C_3$-3-HPMA)



$^{13}C_3$-Glycidol
($^{13}C_3$-DHPMA)



$^{13}C_2$-Acetaldehyde

^{13}C-Formaldehyde

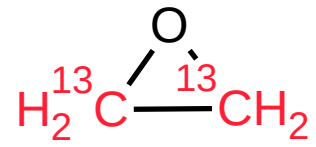
$^{13}C_3$-Propylene glycol

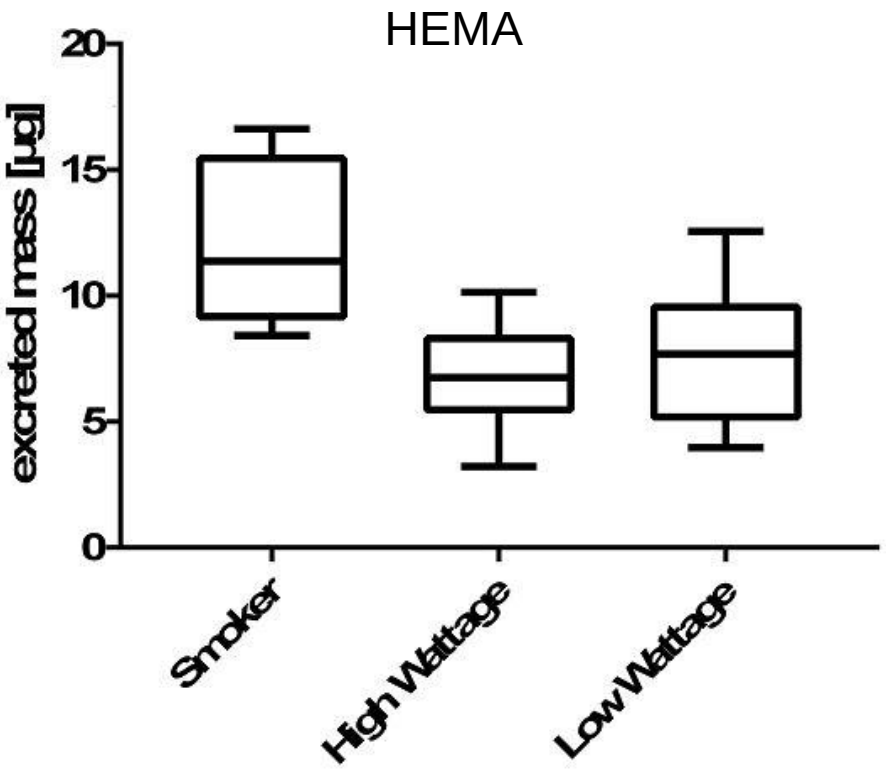
$^{13}C_3$-Propylene oxide
($^{13}C_3$-2-HPMA)

Sleiman, M., *et al.* Emissions from Electronic Cigarettes: Key Parameters Affecting the Release of Harmful Chemicals. *Environ. Sci. Technol.* **2016**

Mercapturic acid for ethylene oxide (HEMA)

Excreted mass after 48 hours



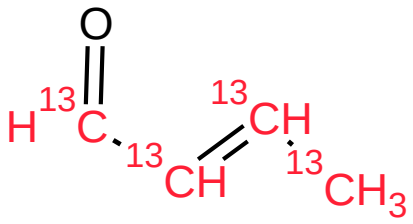


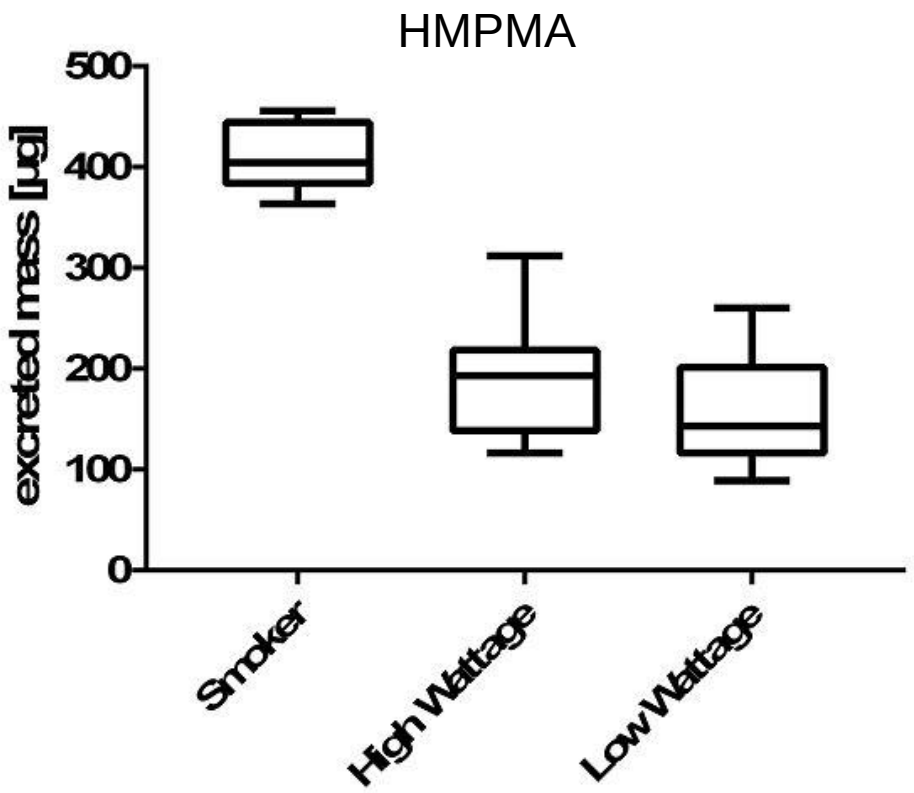
LLOQ: 0.2 ng/ml; ~ 60 ng

No labelled HEMA detected!

Mercapturic acid for crotonaldehyde (HMPMA)

Excreted mass after 48 hours





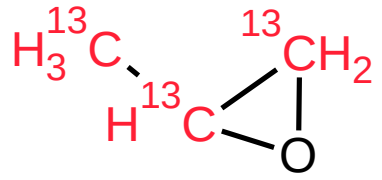
LLOQ: 5 ng/ml; ~ 1.5 µg

No labelled HMPMA detected!

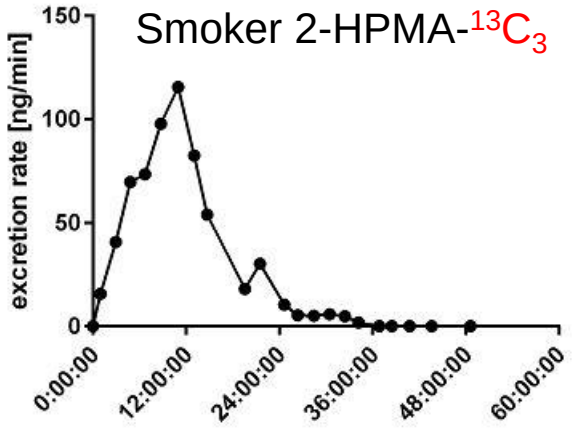
Mercapturic acid for propylene oxide (2-HPMA)

LLOQ: ~1.25 ng/min; ~150 ng

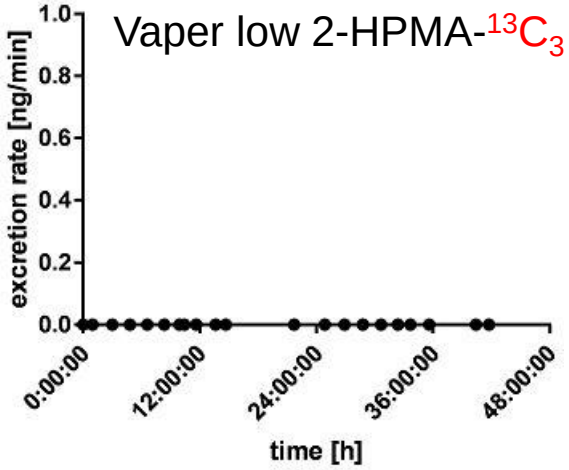
Excreted mass after 48 hours



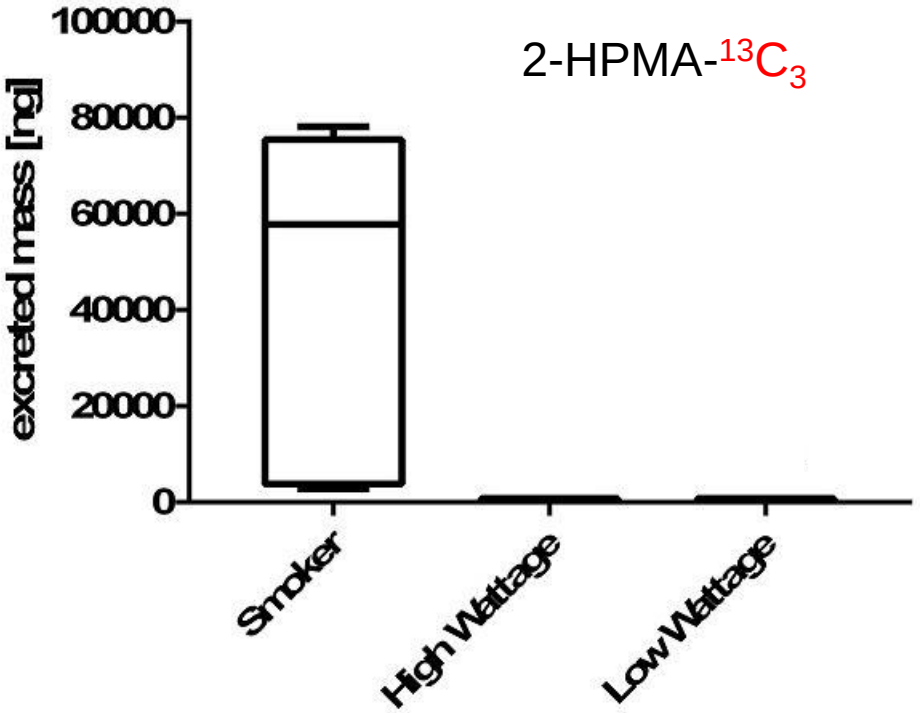
Smoker 2-HPMA-$^{13}C_3$



Vaper low 2-HPMA-$^{13}C_3$



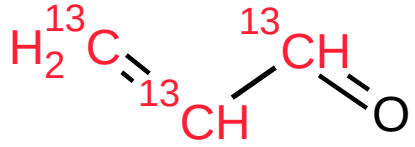
2-HPMA-$^{13}C_3$



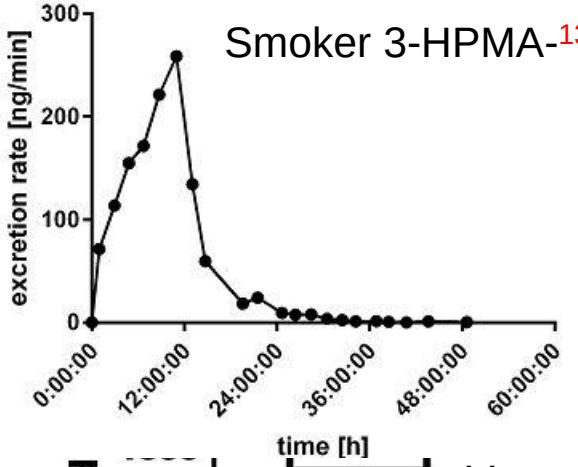
Mercapturic acid for acrolein (3-HPMA)

LLOQ: ~5 ng/min; ~600 ng

Excreted mass after 48 hours



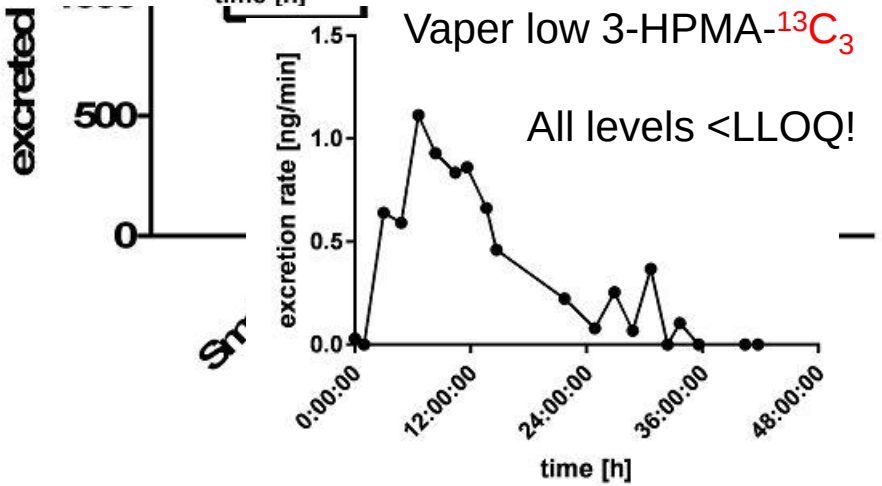
Smoker 3-HPMA-$^{13}C_3$



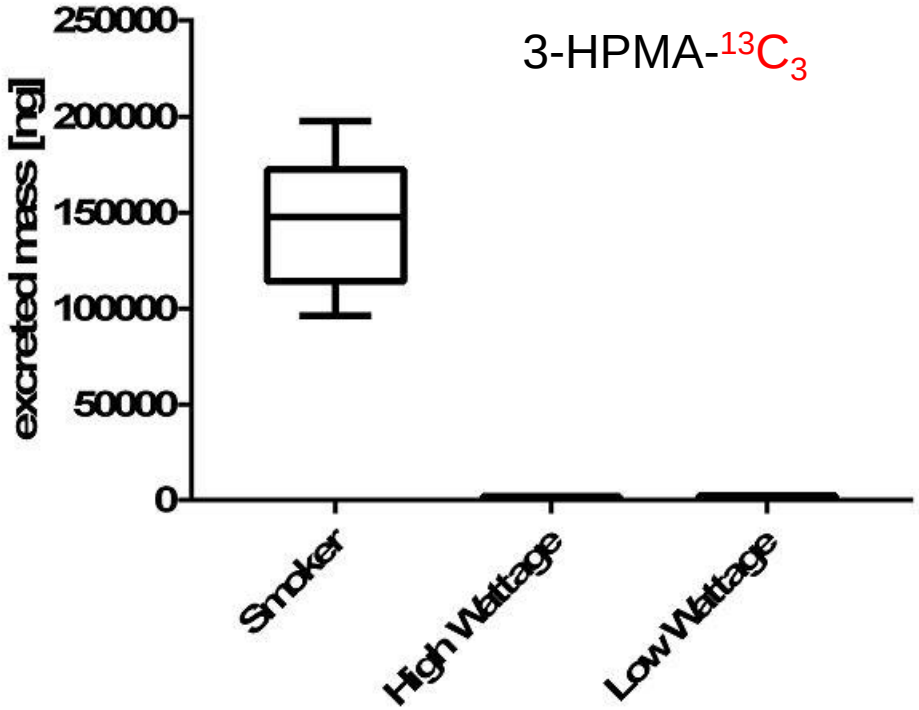
MA

Vaper low 3-HPMA-$^{13}C_3$

All levels <LLOQ!



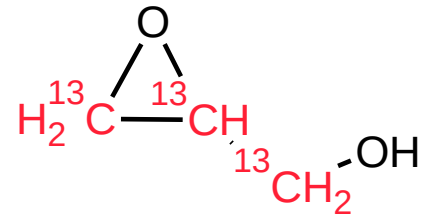
3-HPMA-$^{13}C_3$



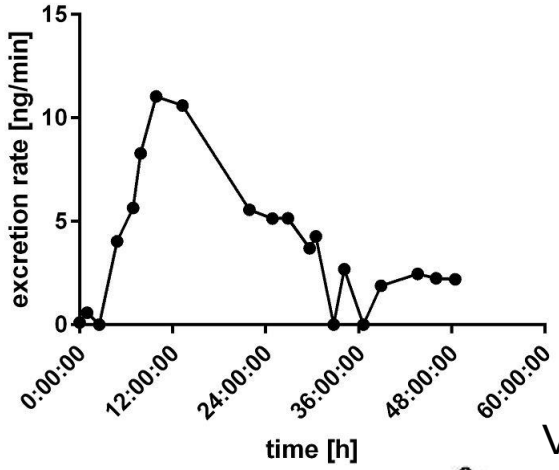
Mercapturic acid for glycidol (DHPMA)

LLOQ: ~2 ng/min; ~240 ng

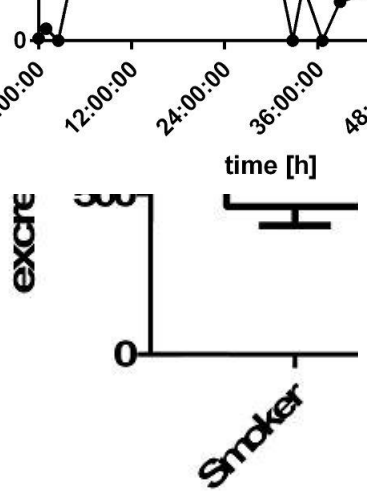
Excreted mass after 48 hours



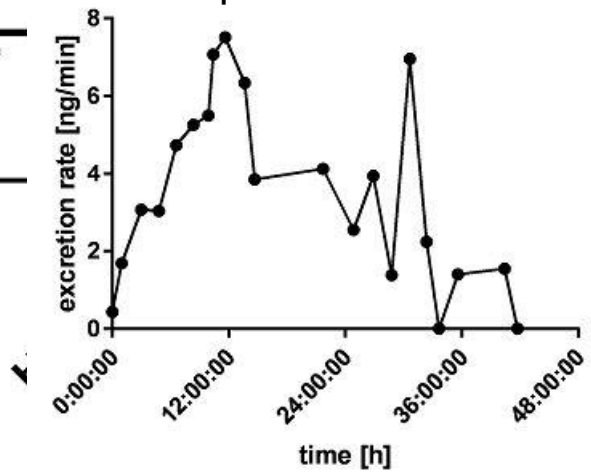
Smoker DHPMA-$^{13}C_3$



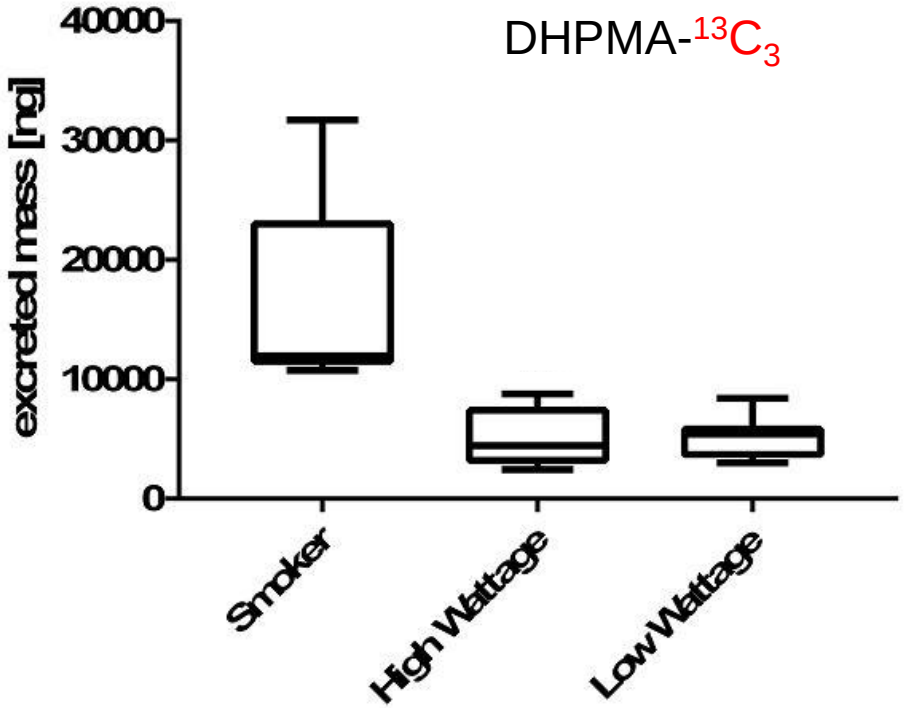
IA



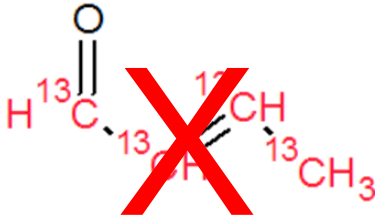
Vaper low DHPMA-$^{13}C_3$



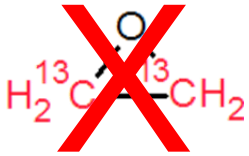
DHPMA-$^{13}C_3$



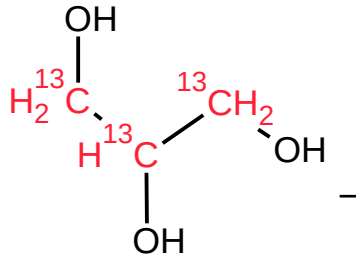
Thermal degradation (pyrolysis) of PG / G



$^{13}C_4$-Crotonaldehyde
($^{13}C_4$-HMPMA)

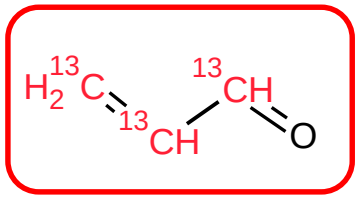


$^{13}C_2$-Ethylene oxide
($^{13}C_2$-HEMA)



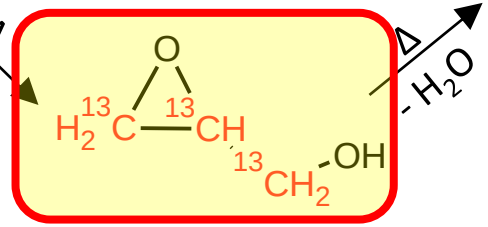
$^{13}C_3$-Glycerol

Δ
$- 2\ H_2O$



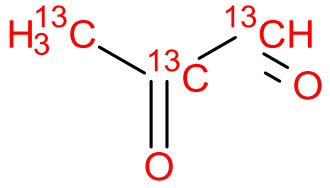
$^{13}C_3$-Acrolein
($^{13}C_3$-3-HPMA)

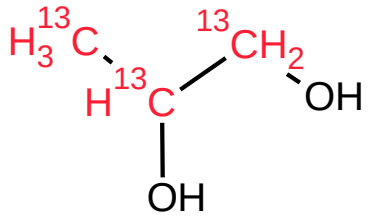
Δ
$- H_2O$



Δ
$- H_2O$

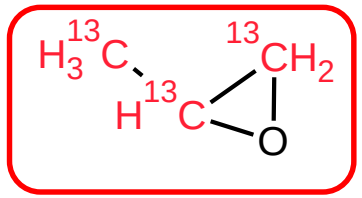
$^{13}C_3$-Glycidol
($^{13}C_3$-DHPMA)





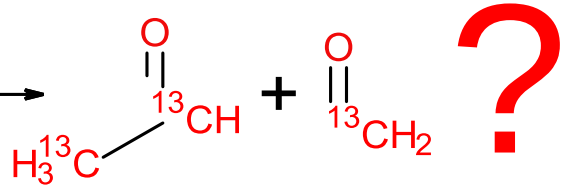
$^{13}C_3$-Propylene glycol

Δ
$- H_2O$



$^{13}C_3$-Propylene oxide
($^{13}C_3$-2-HPMA)

Δ



$^{13}C_2$-Acetaldehyde

^{13}C-Formaldehyde

Sleiman, M., *et al.* Emissions from Electronic Cigarettes: Key Parameters Affecting the Release of Harmful Chemicals. *Environ. Sci. Technol.* **2016**

Conclusion

- E-cigarette specific uptake of main ingredients nicotine, propylene glycol and glycerol investigated using stable-isotope labelling (10 % replacement)
  - Dose-dependence proven for PG / Nic
  - 10 % replacement is resembled in plasma (Nic vs. Nic-d_7 / PG vs. PG-$^{13}C_3$)

- Conventional cigarettes spiked with Nic-d_7 / PG-$^{13}C_3$ / G-$^{13}C_3$ as positive control
  - Investigation of potential thermal decomposition of PG/G
  - Proof-of-concept for bioanalytical methods to detect decomposition products

- MAs of acrolein (3-HPMA) and propylene oxide (2-HPMA) were found in their labelled form in urine of smokers
- MA of glycidol (DHPMA) already observed under vaping conditions (in both groups)

➢ Stable-isotope labelling approach suitable to investigate E-vaping specific uptake and metabolism of main ingredients and their decomposition products

Acknowledgement

TUM

Prof. Dr. Reinhard Nießner

ABF

Anne Landmesser, Michael Göttel, Dina Janket, Philip Peslalz, Lena Thurnes

CTC North

Ralf Freese, Jan Pfeiffer, Annegret Kathagen-Buhmann, Anne Meier

Happy Liquid

Thomas Mrva

Aptochem

Francois Deschamps

Funding:

Altria Client Services

Thank you for your attention

Visit www.abf-lab.com