

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

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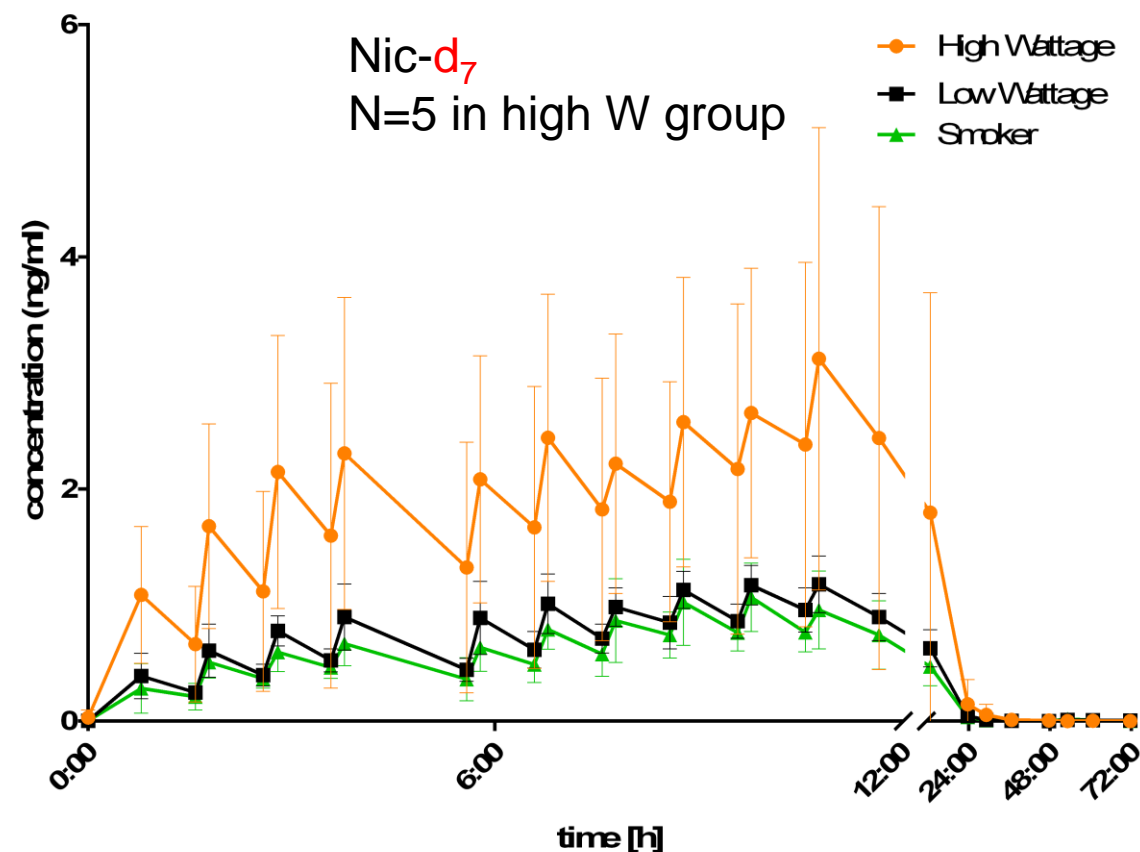
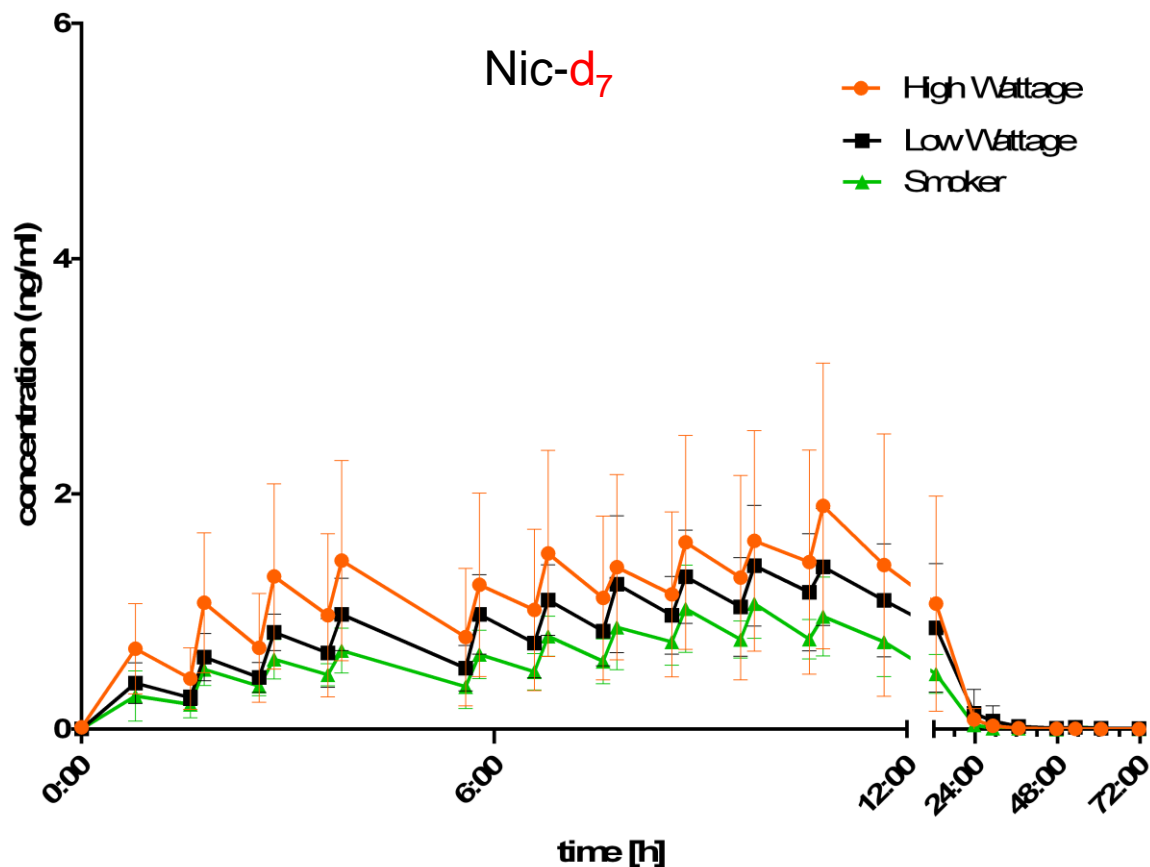
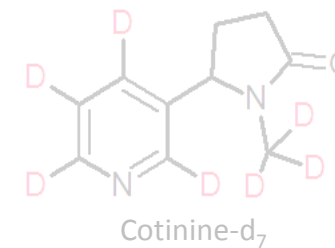
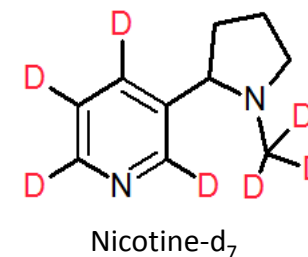
October – 08-12
ST24



Analysis of labelled Nic / Cot: Plasma

LLOQ: 0.1 ng/ml

Low wattage: 10 W
High wattage: 18 W

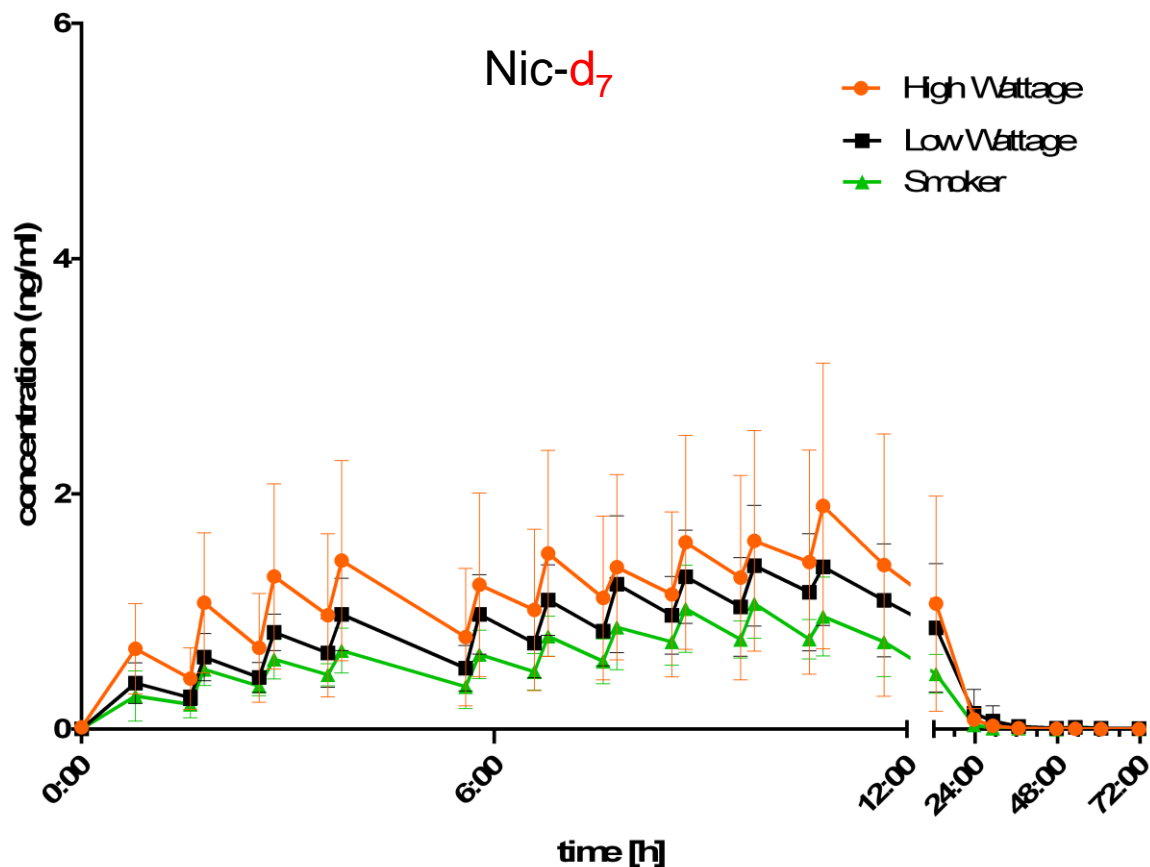
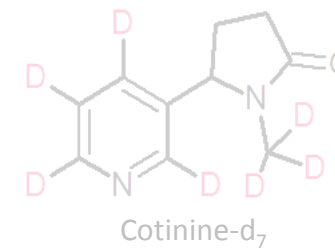
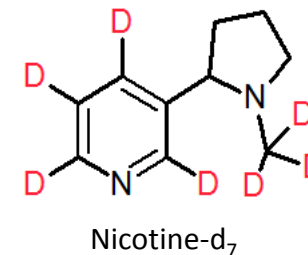


* For technical reasons spike in cigarettes does not exactly match the amounts of labelled PG, G, N in e-vapor products

Analysis of labelled Nic / Cot: Plasma

LLOQ: 0.1 ng/ml

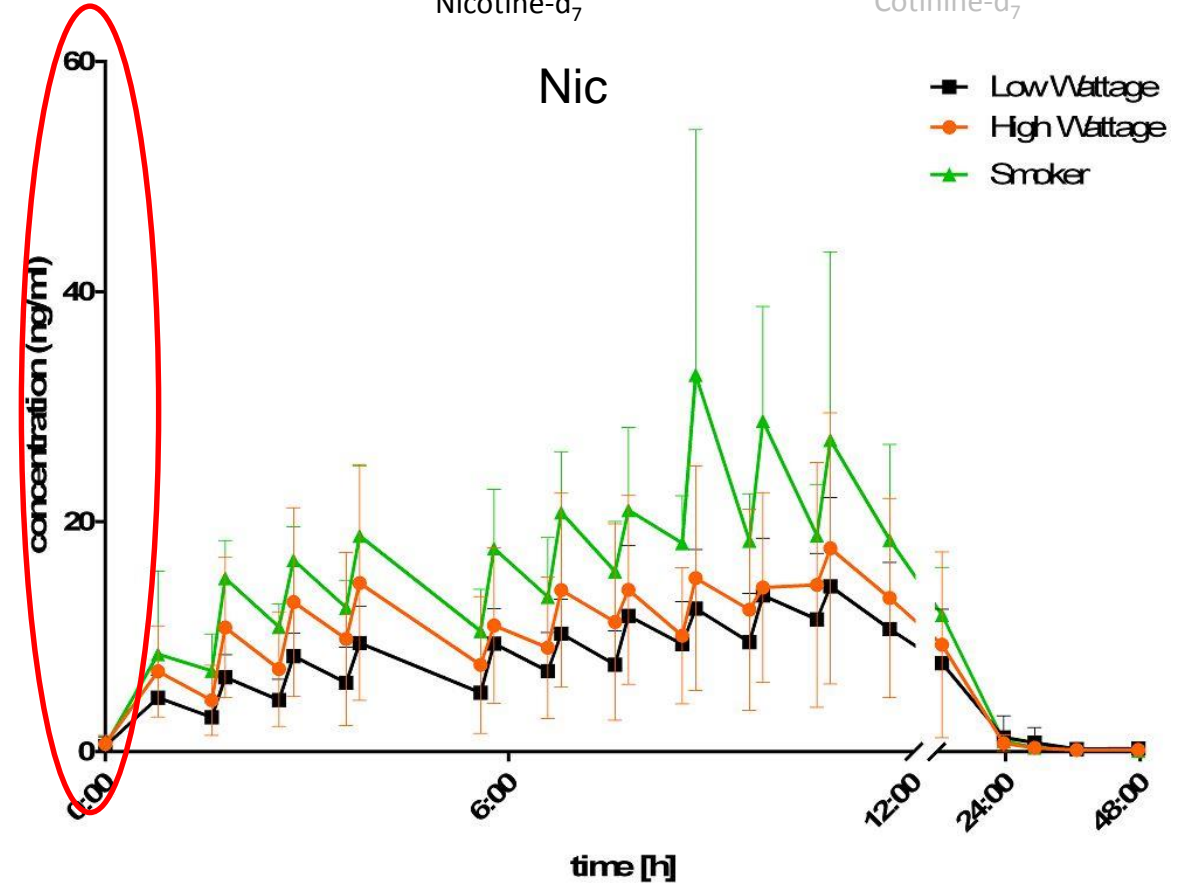
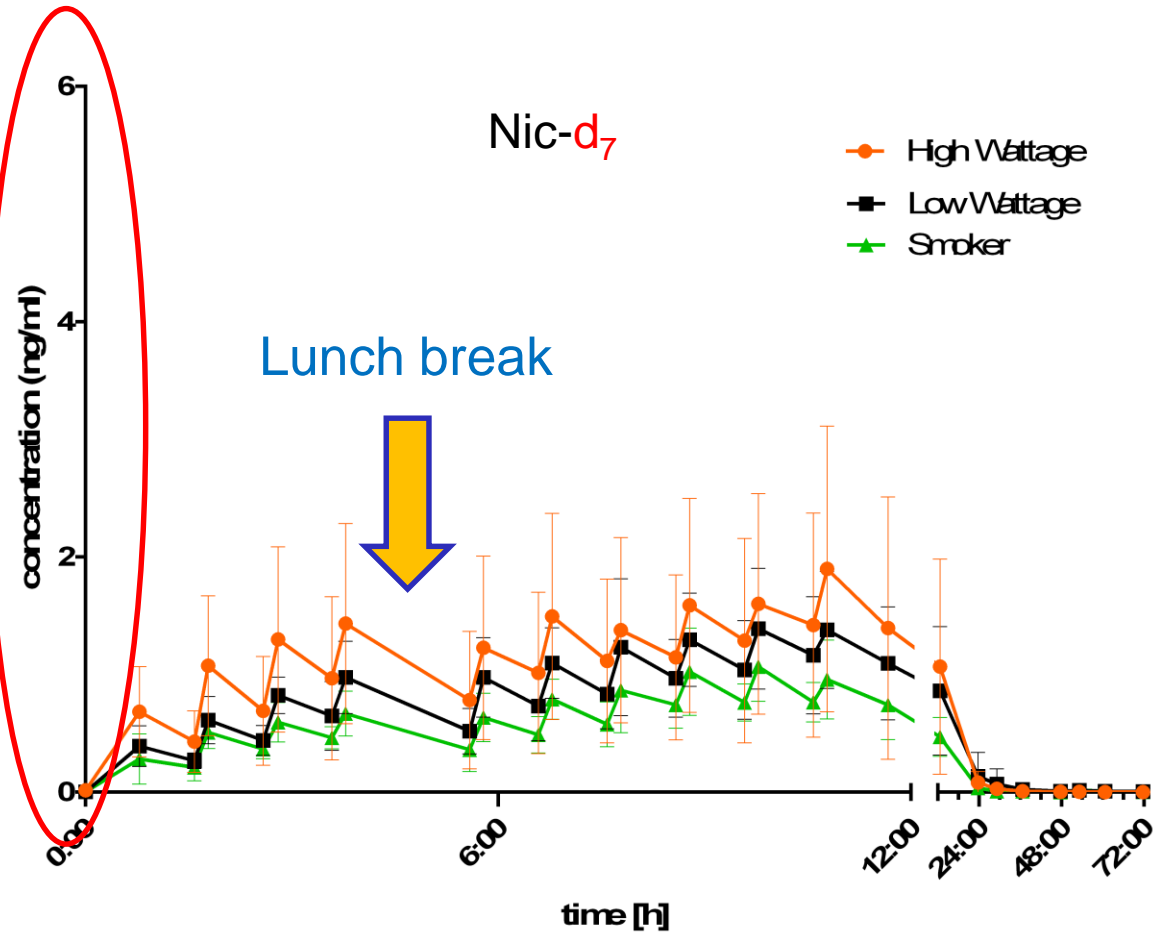
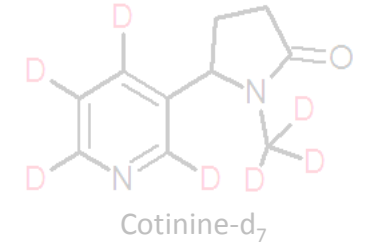
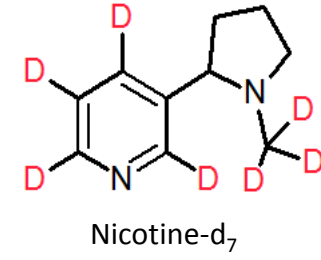
Low wattage: 10 W
High wattage: 18 W



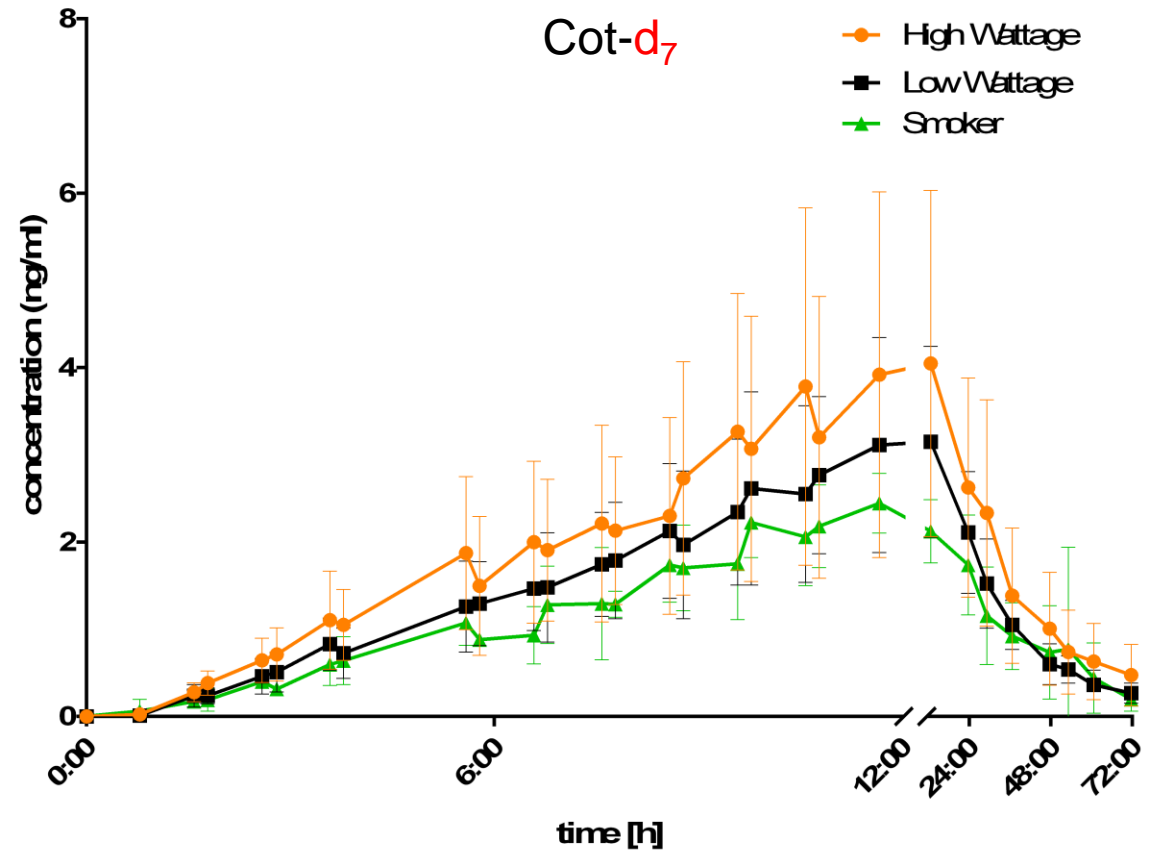
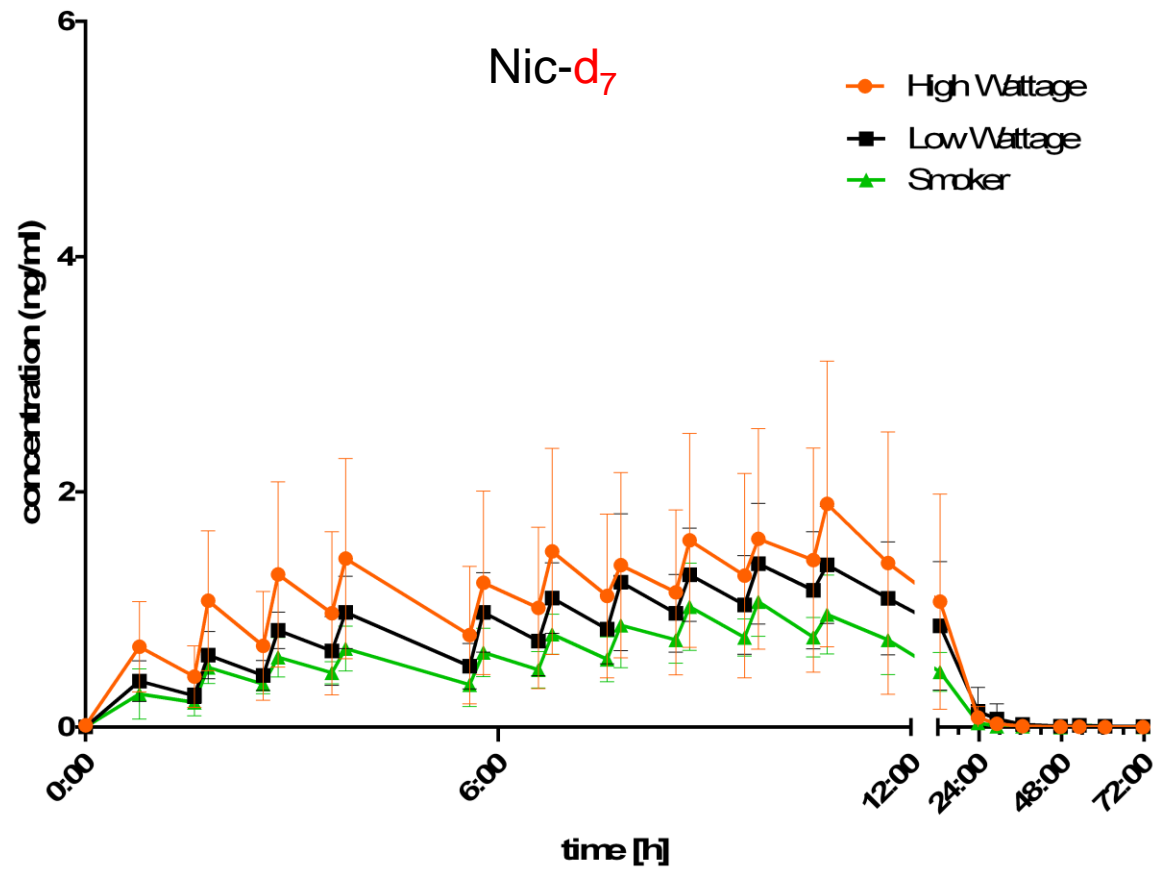
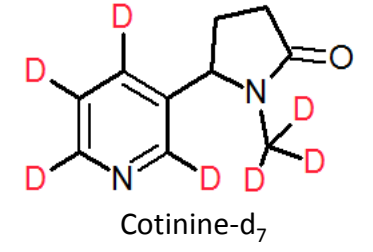
- Non-significant difference between vaping groups
- 5 subjects in high W group reported problems with proper consumption of the product
- Difference between both groups becomes more obvious excluding those subjects

! All further evaluations compare complete data sets for all groups

Analysis of labelled Nic / Cot: Plasma



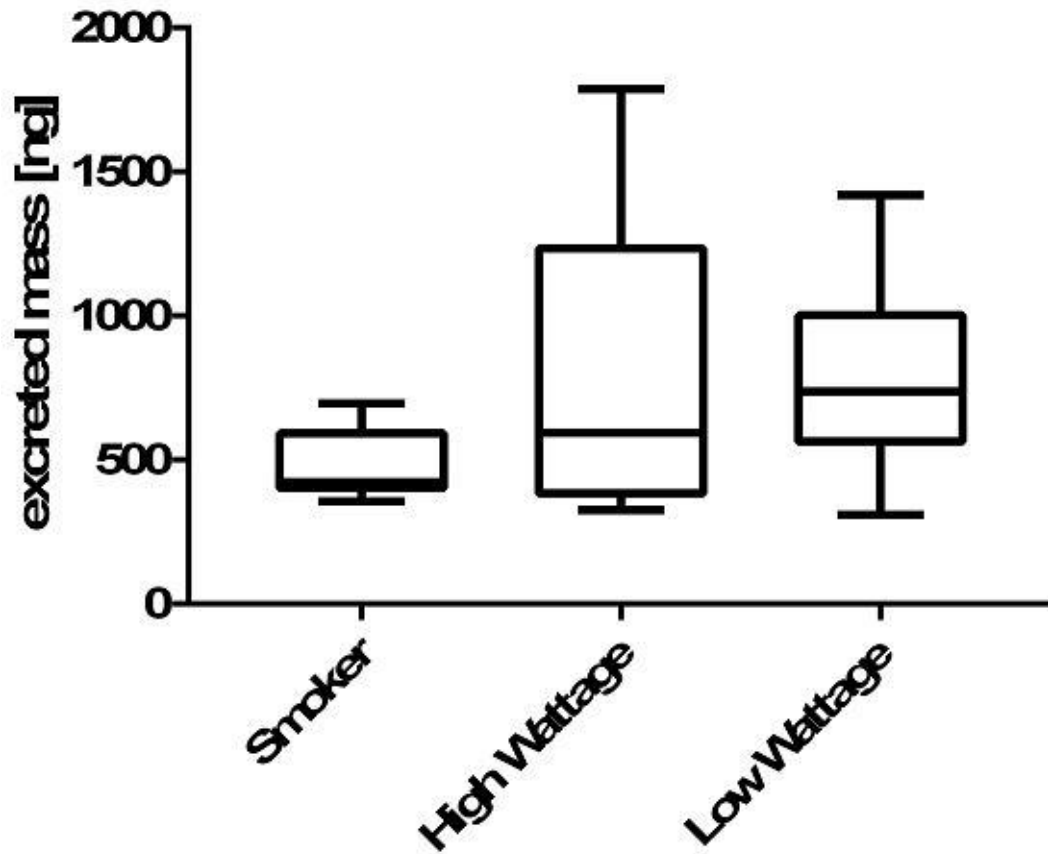
Analysis of labelled Nic / Cot: Plasma



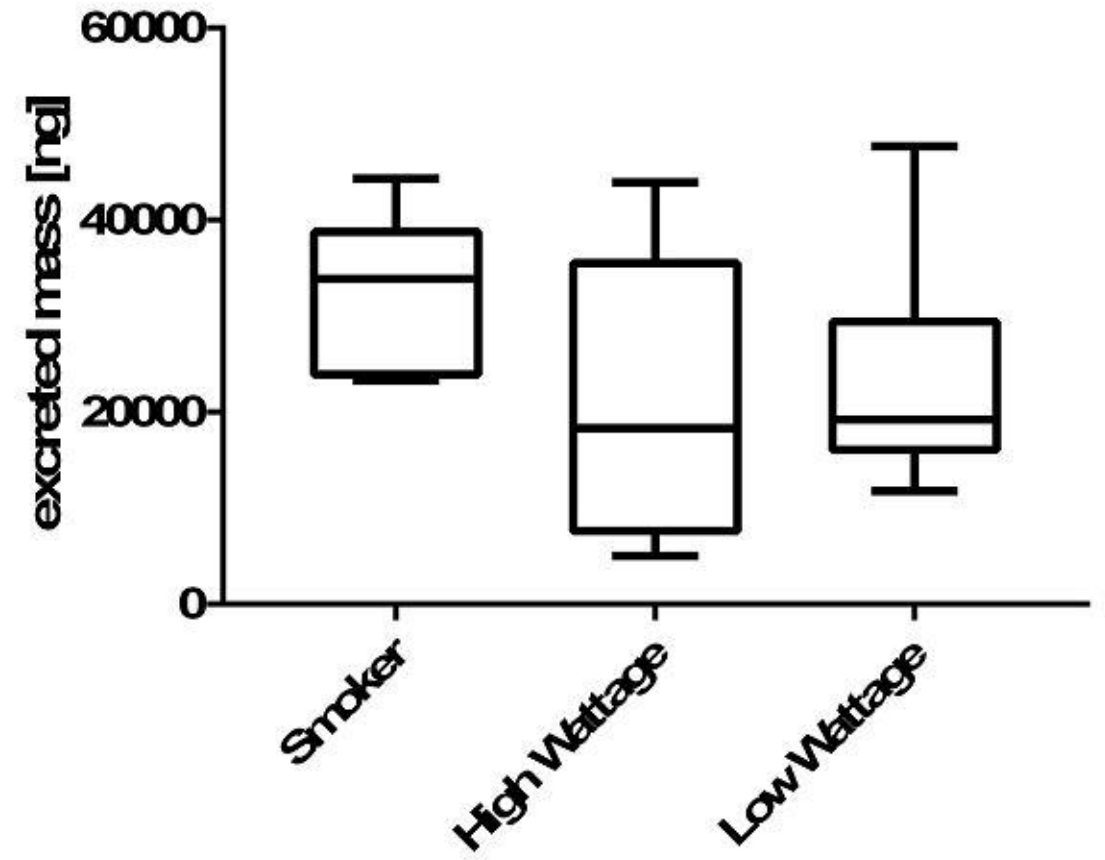
Analysis of labelled Nic + 10: Urine

Excreted mass after 72 hours

TNE labelled

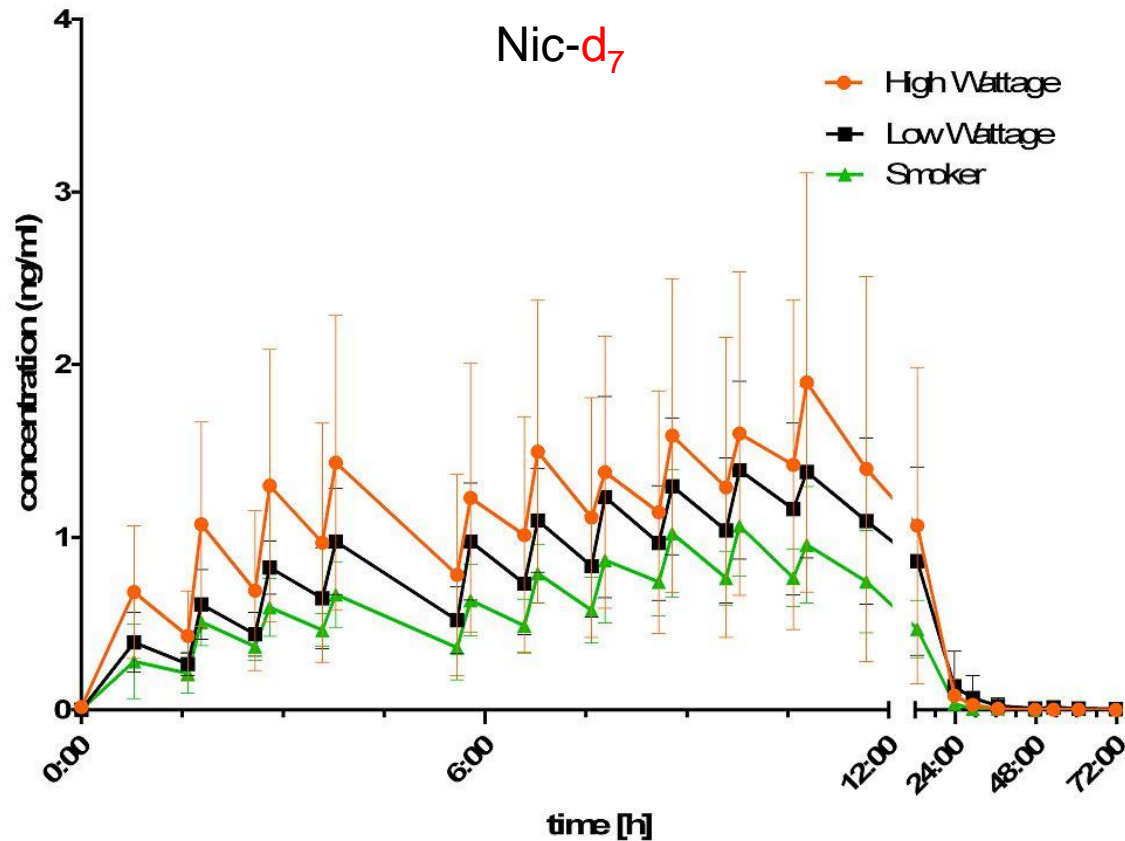
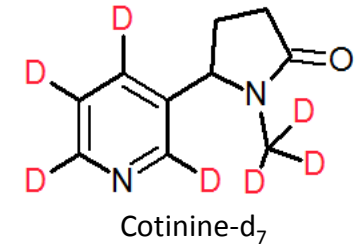
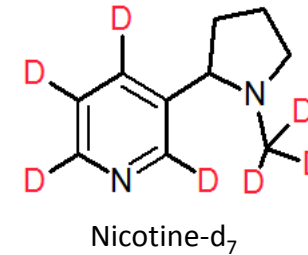


TNE unlabelled



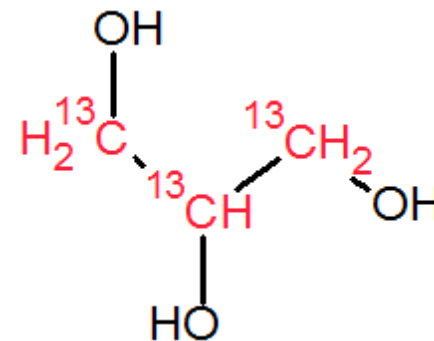
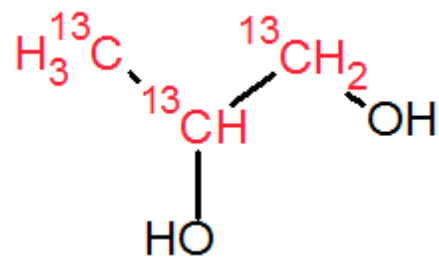
TNE: Total Nicotine Equivalents

Analysis of labelled Nic / Cot: Summary



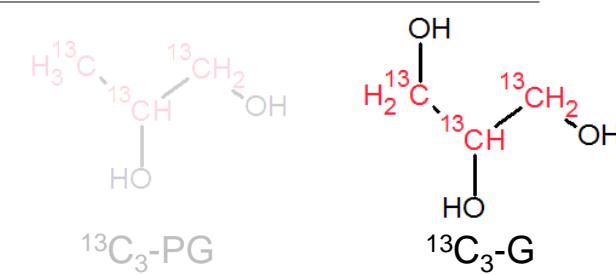
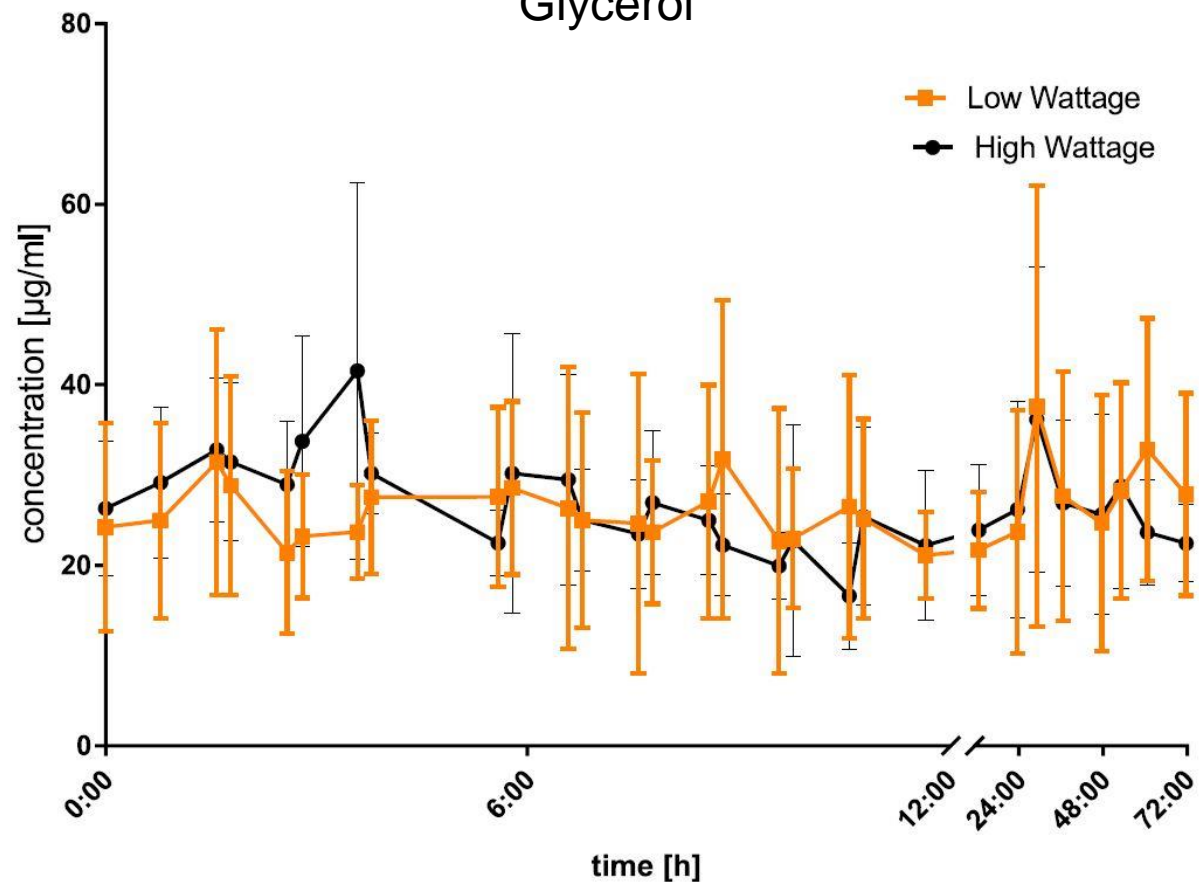
- 10% replacement with stable-isotope labelled Nic-d₇ resembled in plasma concentrations
- Dose-dependence of Nic/Cot levels in all groups
- Higher levels of Nic/Cot in high wattage group compared to low wattage group
- Uptake correlates with wattage
- Spike of Nic in conventional cigarettes resembles uptake of Nic in vapers

Analysis of PG / G



Analysis of labelled PG / G: Plasma

Glycerol

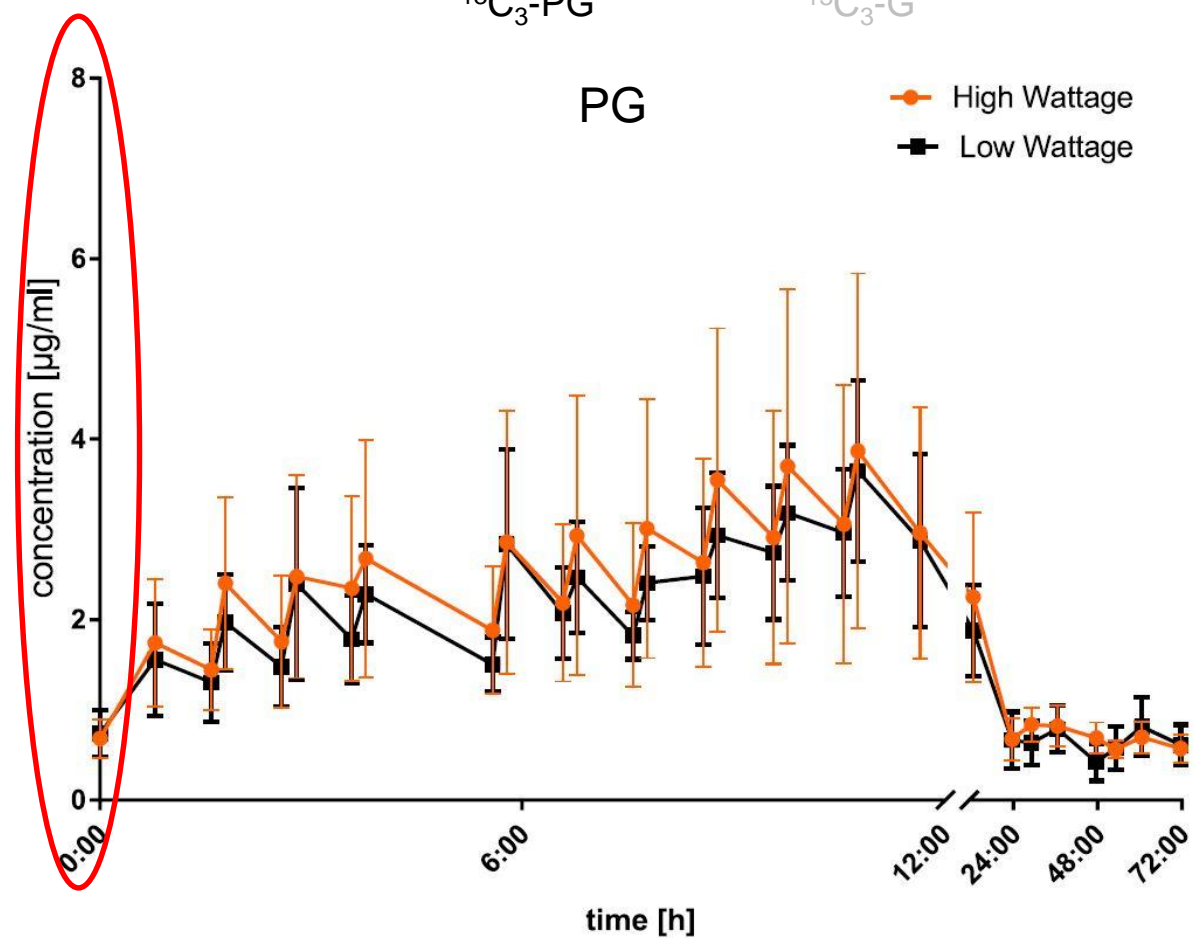
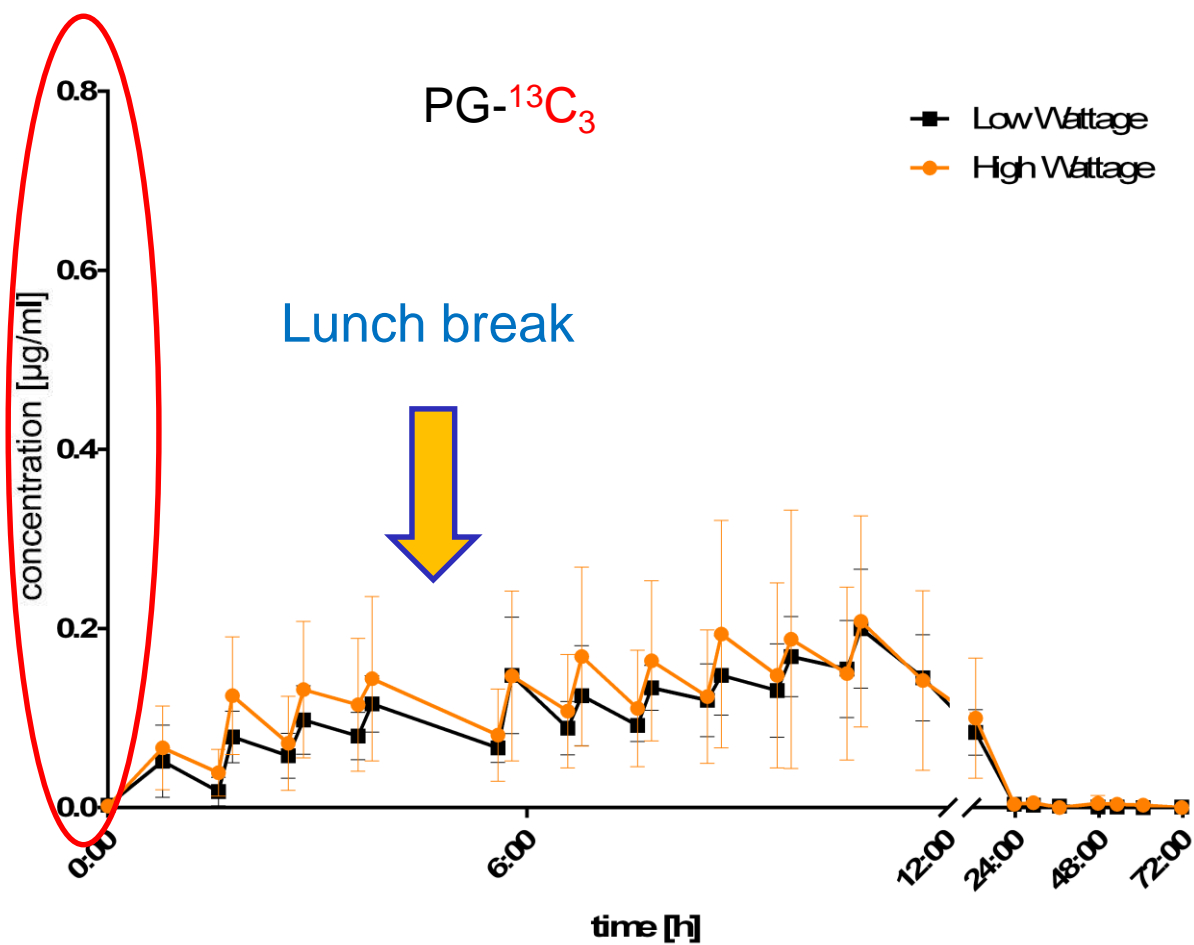
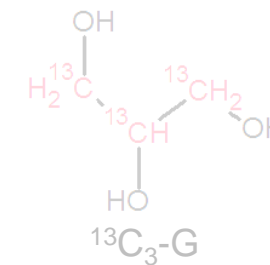
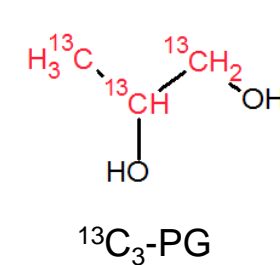


No dose-dependent alterations of G concentrations in plasma
Labelled G ($^{13}\text{C}_3\text{-G}$) not detectable in plasma after vaping

LLOQ: 0.05 µg/ml

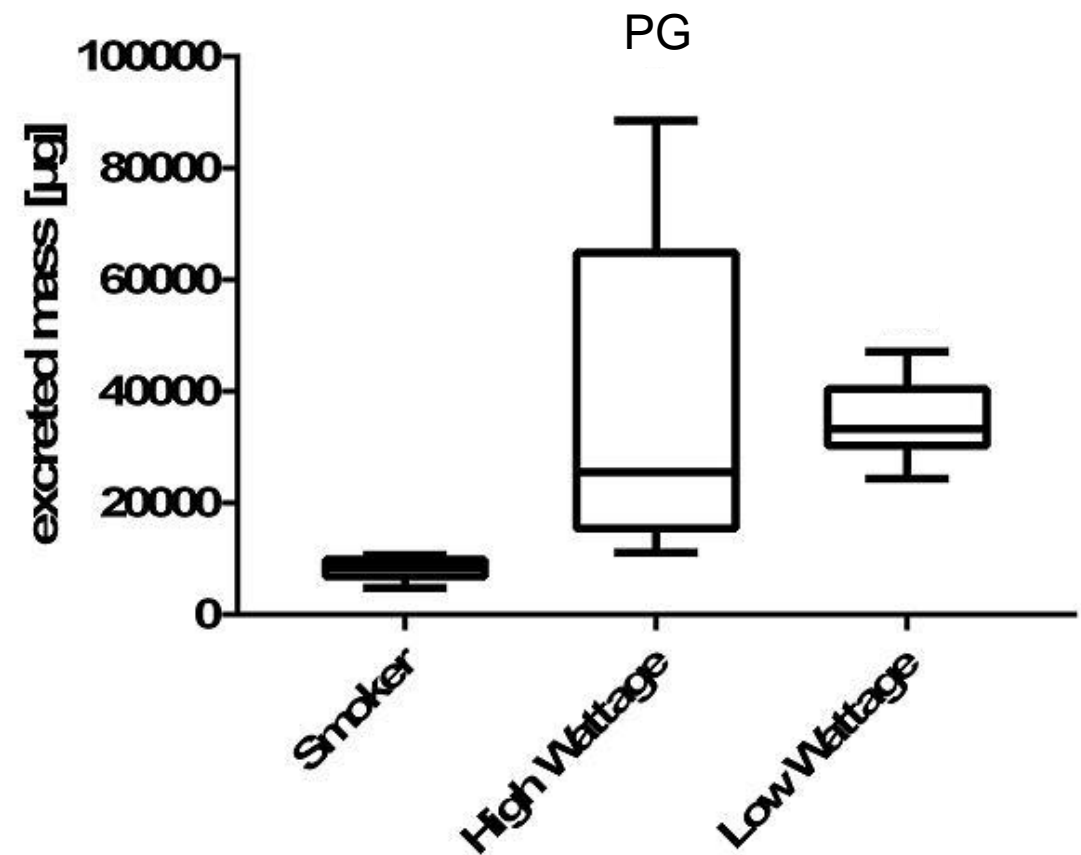
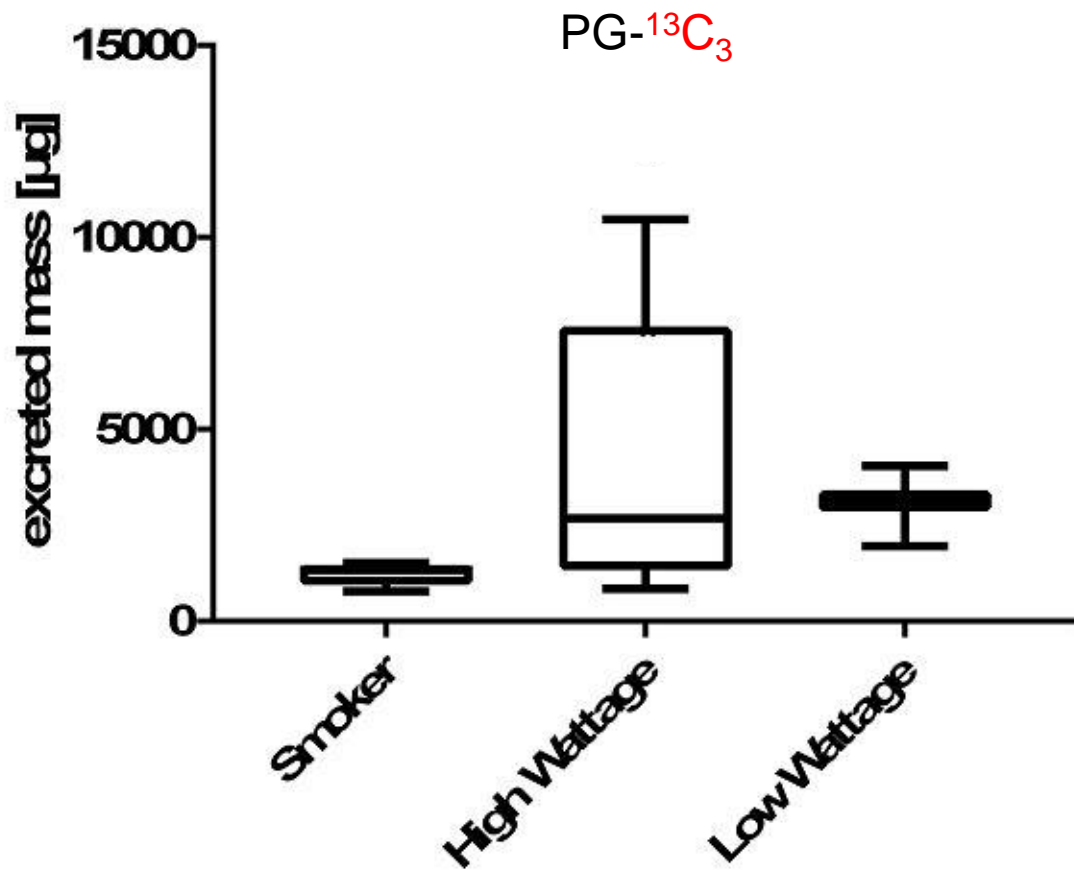
Analysis of labelled PG / G: Plasma

LLOQ: 0.10 µg/ml



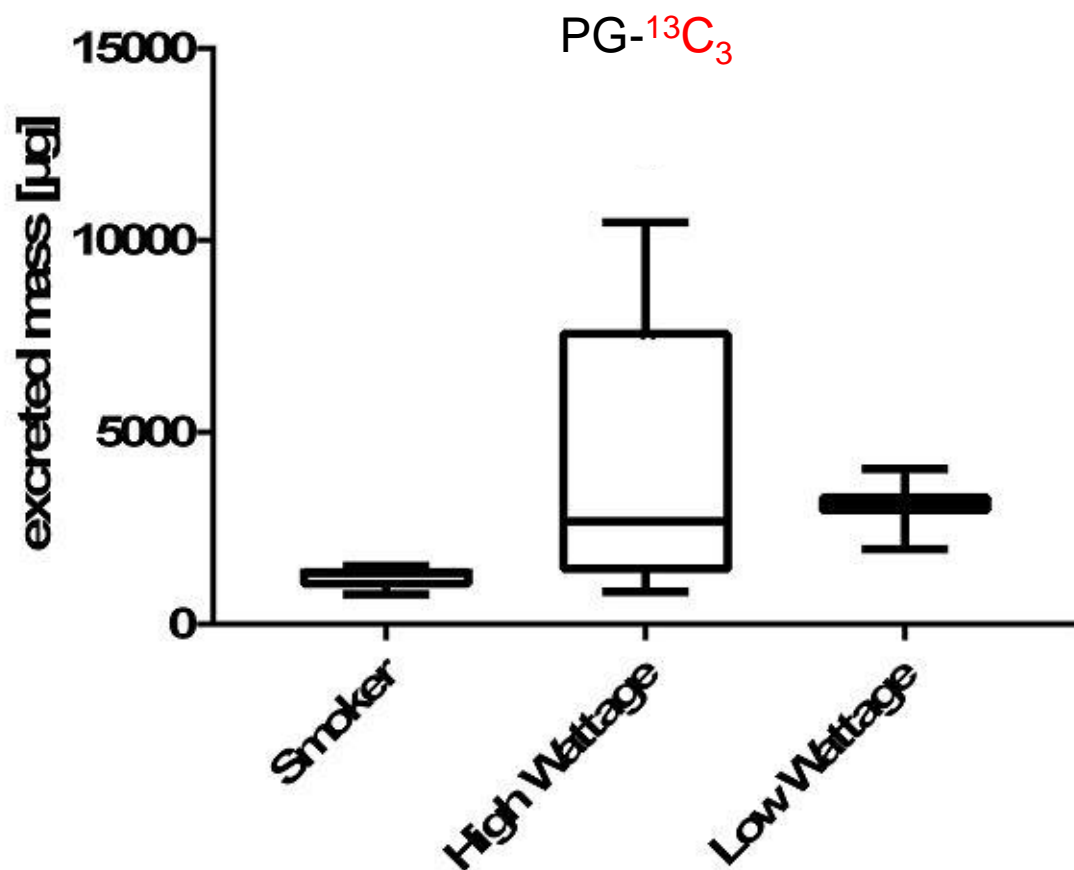
Analysis of labelled PG / G: Urine

Excreted mass after 72 hours



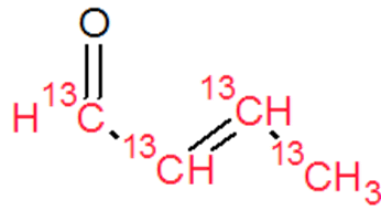
Analysis of labelled PG / G: Summary

Excreted mass after 72 hours

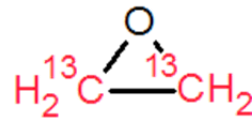


- 10% replacement with stable-isotope labelled PG resembled in plasma concentrations
- Dose-dependence proven for PG
- PG levels in smokers significantly lower compared to both vaper groups
- Indication for “losses” of PG (and G?) during pyrolysis due to decomposition

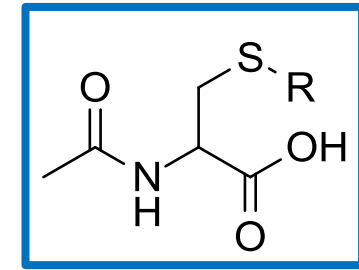
Thermal degradation (pyrolysis) of PG / G



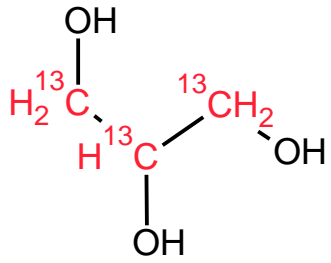
¹³C₄-Crotonaldehyde
(¹³C₄-HMPMA)



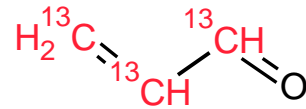
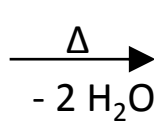
¹³C₂-Ethylene oxide
(¹³C₂-HEMA)



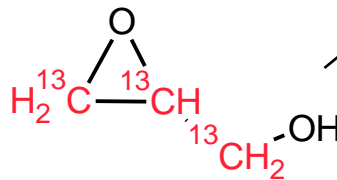
Mercapturic acids



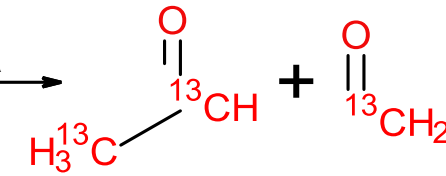
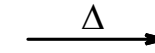
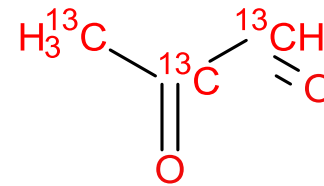
¹³C₃-Glycerol



¹³C₃-Acrolein
(¹³C₃-3-HPMA)

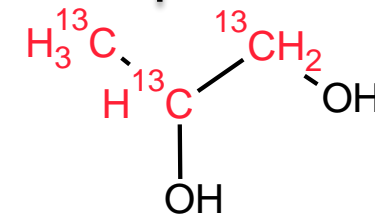


¹³C₃-Glycidol
(¹³C₃-DHPMA)

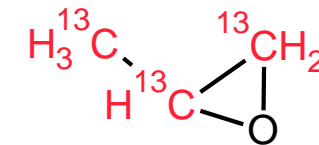
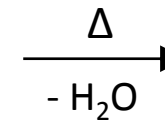


¹³C₂-Acetaldehyde

¹³C-Formaldehyde



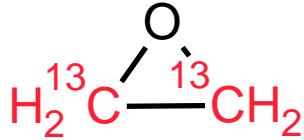
¹³C₃-Propylene glycol



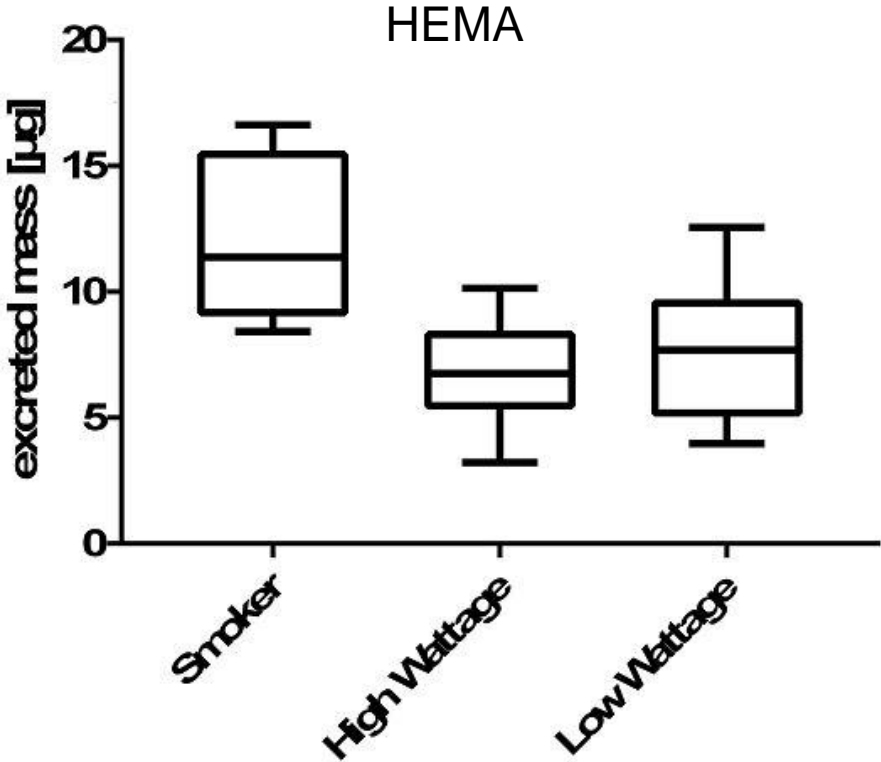
¹³C₃-Propylene oxide
(¹³C₃-2-HPMA)

Mercapturic acid for ethylene oxide (HEMA)

Excreted mass after 48 hours



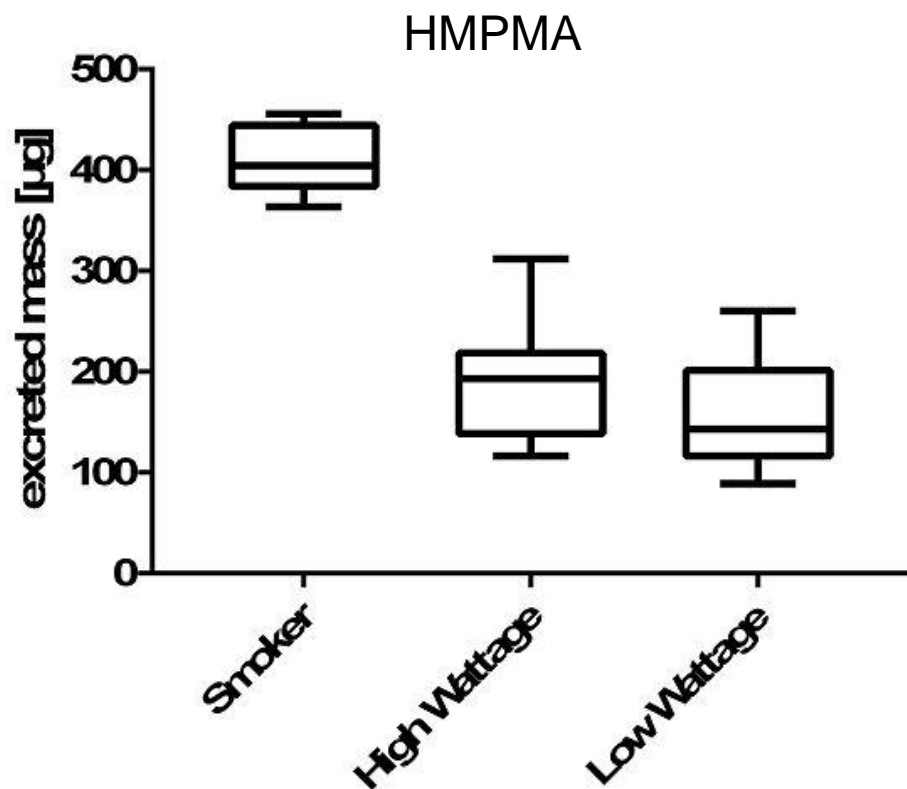
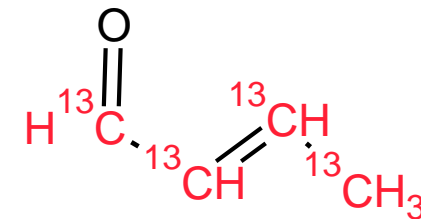
LLOQ: 0.2 ng/ml; ~ 60 ng



No labelled HEMA detected!

Mercapturic acid for crotonaldehyde (HMPMA)

Excreted mass after 48 hours



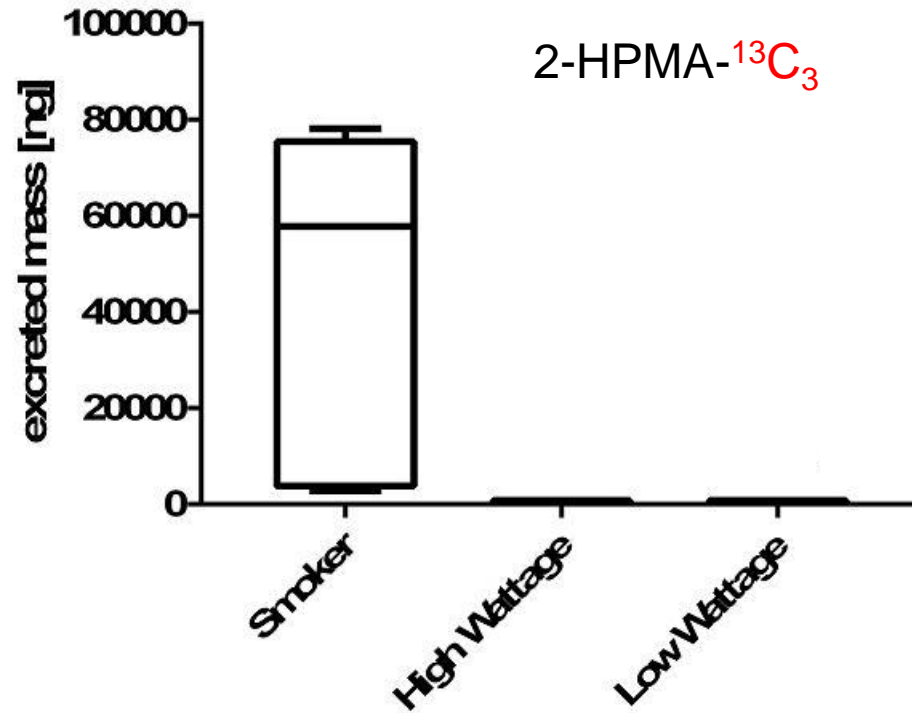
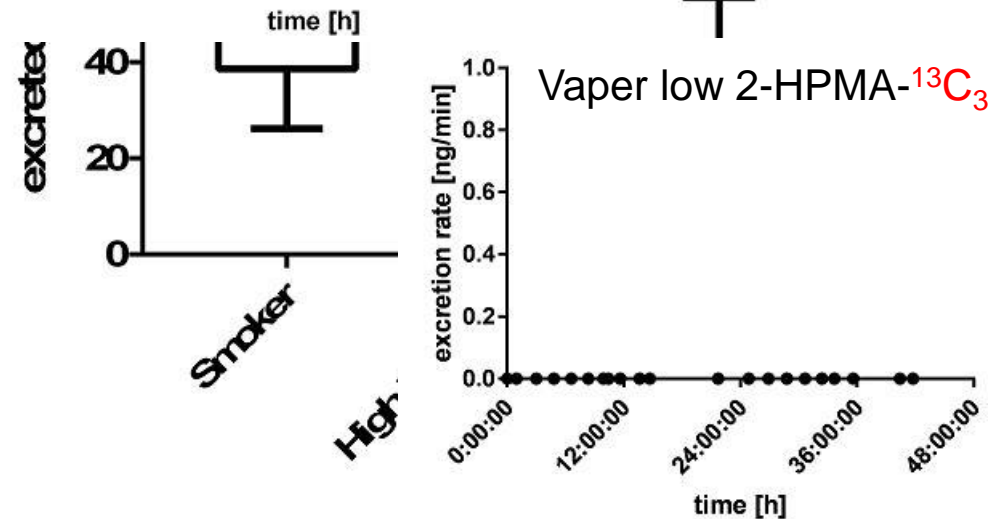
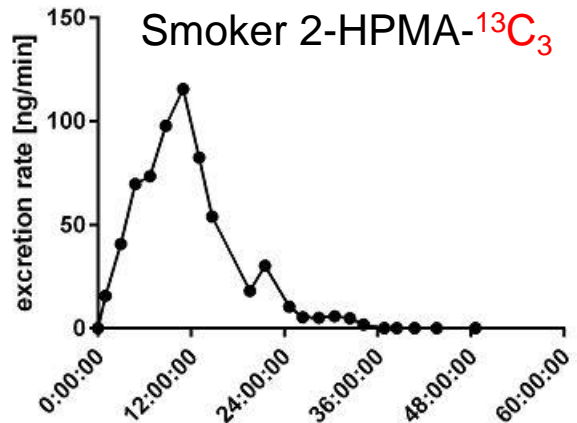
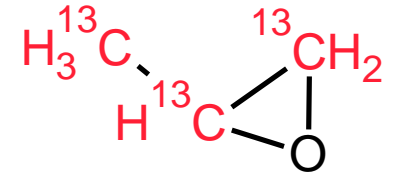
LLOQ: 5 ng/ml; ~ 1.5 µg

No labelled HMPMA detected!

Mercapturic acid for propylene oxide (2-HPMA)

LLOQ: ~1.25 ng/min; ~150 ng

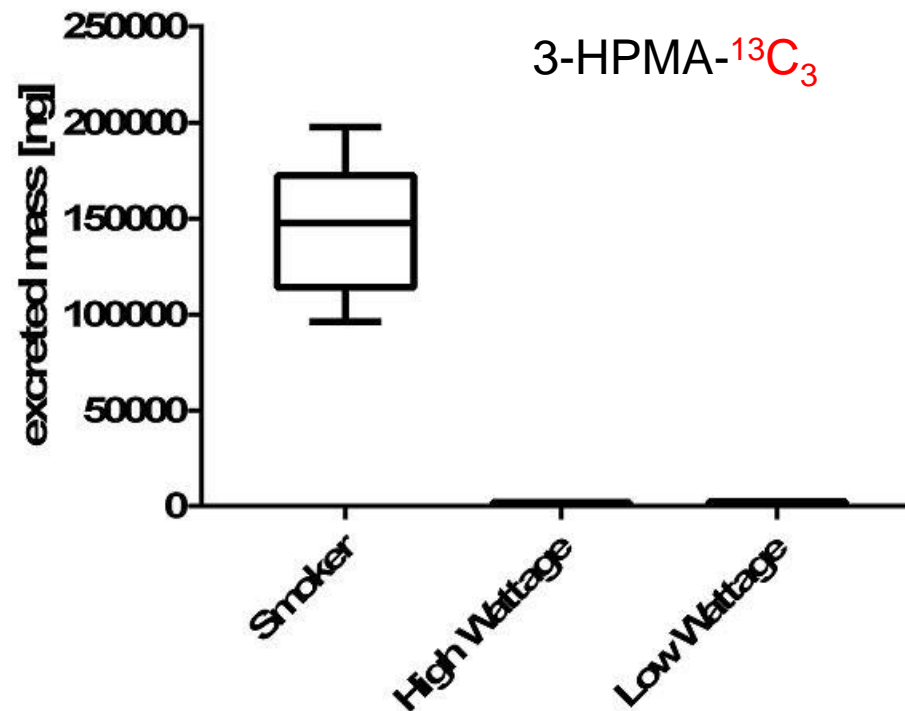
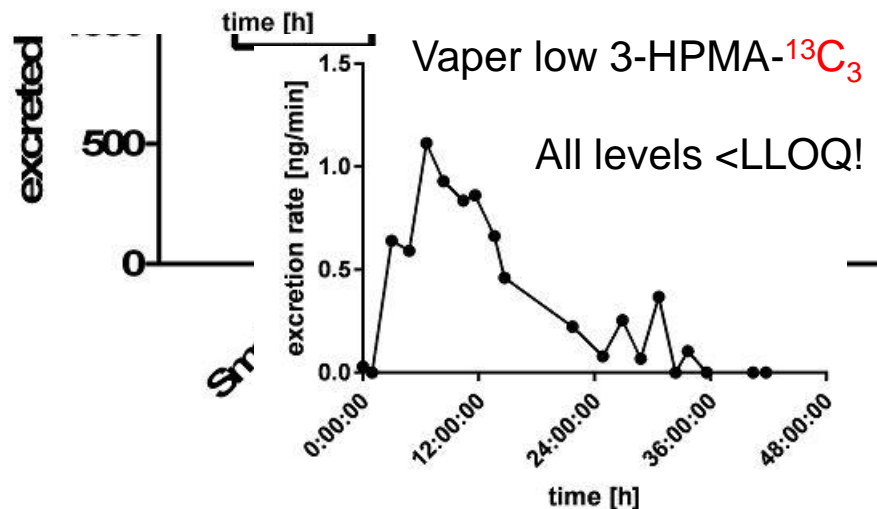
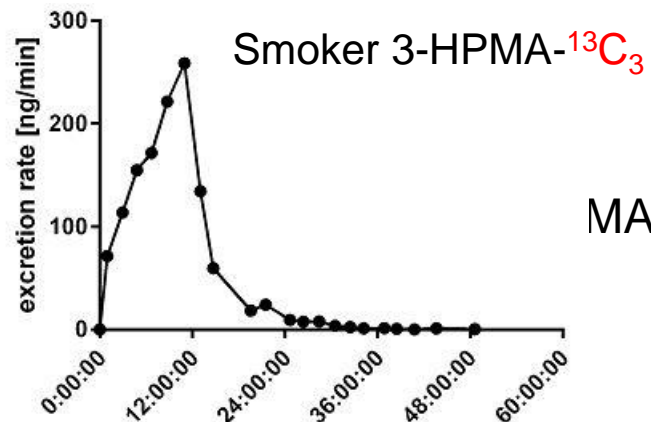
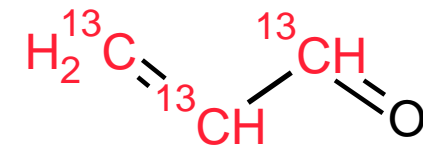
Excreted mass after 48 hours



Mercapturic acid for acrolein (3-HPMA)

LLOQ: ~5 ng/min; ~600 ng

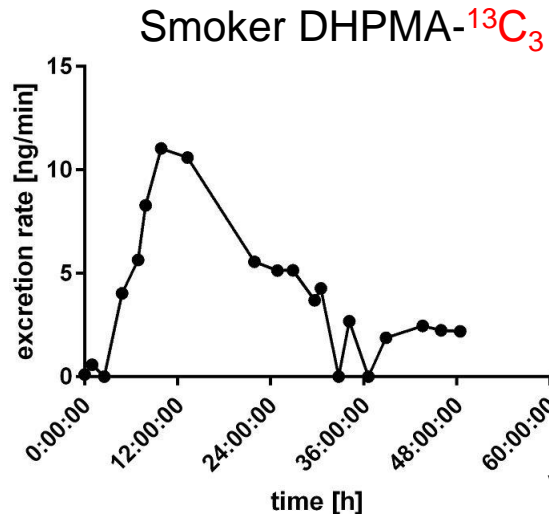
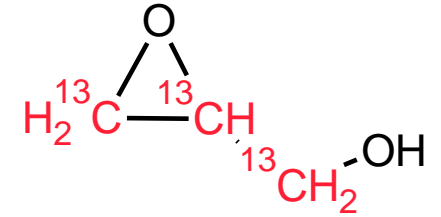
Excreted mass after 48 hours



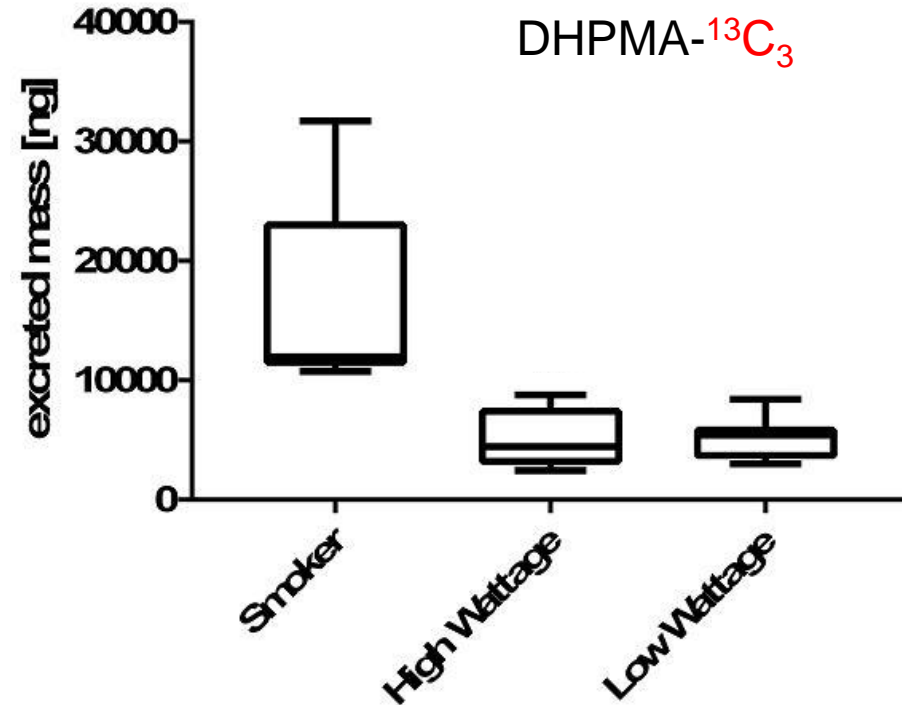
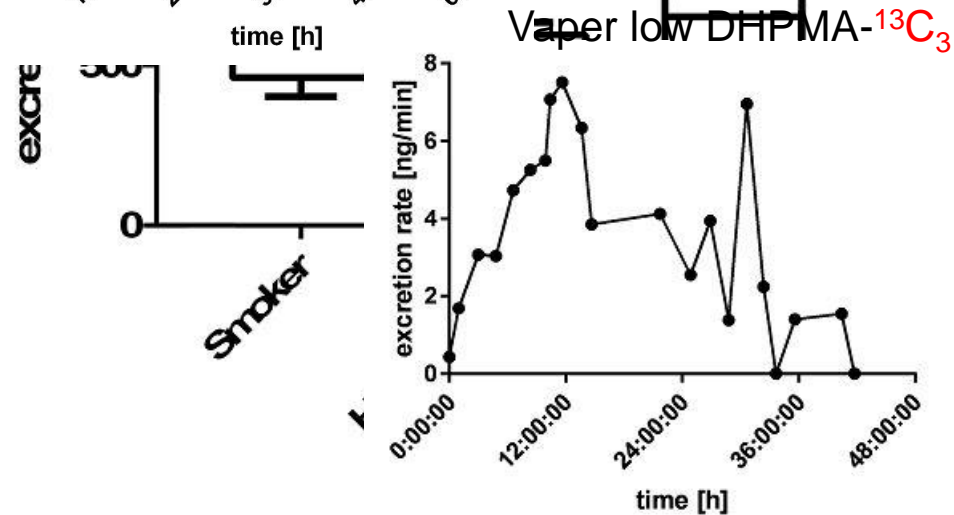
Mercapturic acid for glycidol (DHPMA)

LLOQ: ~2 ng/min; ~240 ng

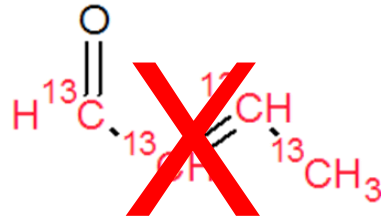
Excreted mass after 48 hours



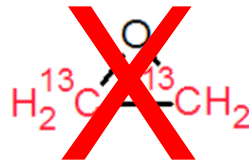
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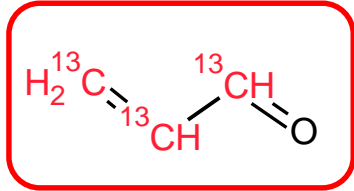
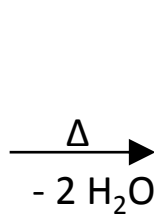
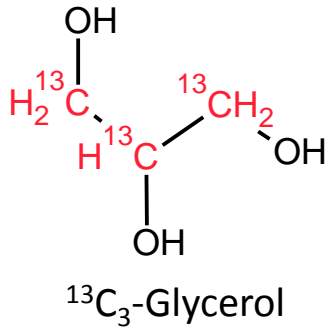
Thermal degradation (pyrolysis) of PG / G



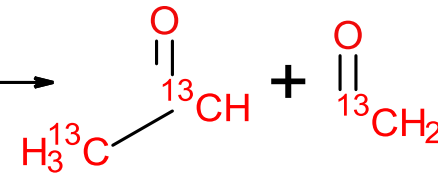
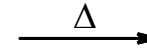
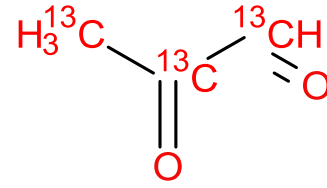
$^{13}\text{C}_4$ -Crotonaldehyde
($^{13}\text{C}_4$ -HMPMA)



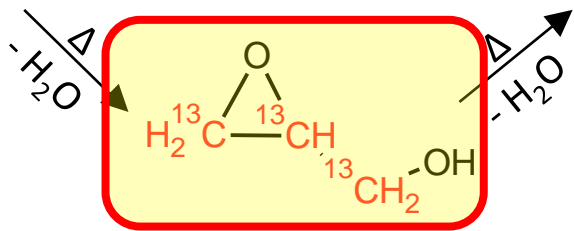
$^{13}\text{C}_2$ -Ethylene oxide
($^{13}\text{C}_2$ -HEMA)



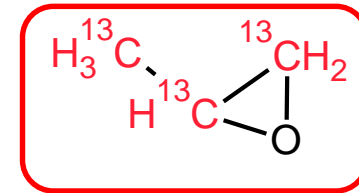
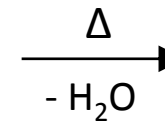
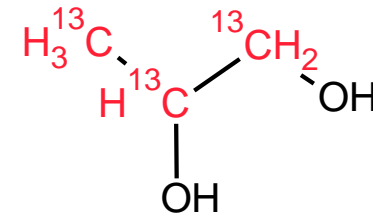
$^{13}\text{C}_3$ -Acrolein
($^{13}\text{C}_3$ -3-HPMA)



$^{13}\text{C}_2$ -Acetaldehyde ^{13}C -Formaldehyde



$^{13}\text{C}_3$ -Glycidol
($^{13}\text{C}_3$ -DHPMA)



$^{13}\text{C}_3$ -Propylene glycol $^{13}\text{C}_3$ -Propylene oxide
($^{13}\text{C}_3$ -2-HPMA)

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-d₇ / PG vs. PG-¹³C₃)
 - Conventional cigarettes spiked with Nic-d₇ / PG-¹³C₃ / G-¹³C₃ 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



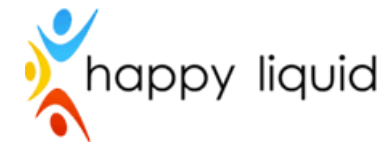
CTC North

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



Happy Liquid

Thomas Mrva



Aptochem

Francois Deschamps



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