Comparison of biomarkers of exposure in users of various tobacco / nicotine products

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Introduction

In the last two decades, various types of tobacco and nicotine products have been developed and marketed, which avoided combustion of tobacco and thus released much lower amounts of toxicants. These toxicants are almost exclusively combustion products, including polycyclic aromatic hydrocarbons (PAHs), aldehydes, volatile organic compounds (VOCs), nitrosamines, aromatic amines, and many others. The products include electronic cigarettes (ECs), heated tobacco products (HTPs), and oral tobacco (OT) such as snus and nicotine pouches. Although still controversially discussed in the public health and tobacco control communities, these products might potentially serve as tobacco harm reduction (THR) products.

The **OBJECTIVE** of this study was the identification of biomarkers and biomarker patterns in body fluids, to distinguish between combustibles, heated tobacco products, electronic cigarettes, oral tobacco and oral/dermal nicotine products used for nicotine replacement therapy (NRT), as well as a control group of non-users.

Therefore, a controlled, single-center clinical study was conducted with 60 healthy subjects, divided into 6 groups based on their sole use of the products of choice. The collected biofluids include urine, blood, saliva, exhaled breath and exhaled breath condensate. This poster presents the results for mercapturic acids, OH-PAHs, aromatic amines, nicotine and metabolites, propylene glycol and tobacco specific nitrosamines (TSNAs) across the 6 different study groups, determined in urine and plasma samples by targeted bioanalytical methods.

Experimental Design

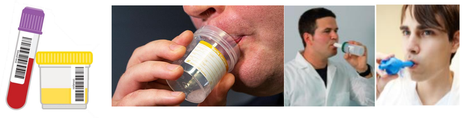
Controlled Clinical Study

10 subjects per group
3 days of confinement
5 nicotine product user groups

Day 1 → Day 2 → Day 3

Conventional Cigarettes (CC)
Heated Tobacco products (HTPs)
Electronic Cigarettes (ECs)
Oral Tobacco (OT)
Nicotine Replacement Therapy (NRT)

Biospecimen Collection



Urine, Blood (Plasma, Erythrocytes), Saliva, Exhaled Breath, Exhaled Breath Condensate

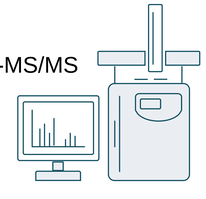
Sample Analysis



GC-MS/MS

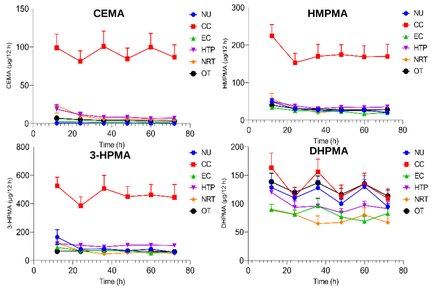


LC-MS/MS



Results and Conclusion

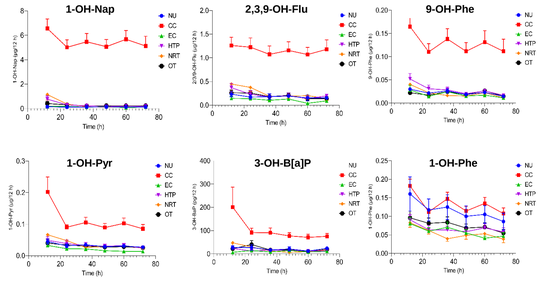
Mercapturic acids



- Smokers compared to all other groups excreted consistently and significantly elevated urinary levels of mercapturic acids (MAs)
- HTP users showed slightly elevated levels of 3-HPMA (acrolein), AAMA/GAMA (acrylamide), CEMA (acrylonitrile) and HMPMA (crotonaldehyde) compared to non-CC groups
- Vaping seems to be only a minor source for glycidol exposure (no elevation in DHPMA)

Ref: Scherer G, Pluym N, Scherer M: Drug Test Anal 2022; DOI: 10.1002/dta.3372

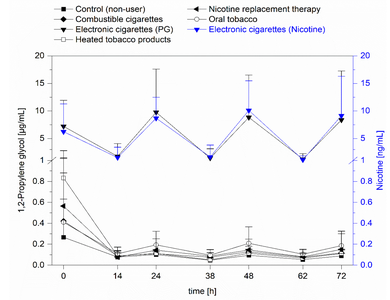
Phenolic polycyclic aromatic hydrocarbons



- Smokers exhibited the highest urinary OH-PAH levels with a clear dose dependency based on cigarettes per day
- Urinary excretion of 1-/2-OH-Nap, 2-/3-/9-OH-Flu, 4-/9-OH-Phe, 1-OH-Pyr and 3-OH-B[a]P showed a clear distinction, this was not the case for 1-/2-/3-OH-Phe
- Variations in the ratios of the OH-PAH excretions between smokers and the other groups. The mean ratios for Day 3 ranged from 2.1 (1-OH-Phe) to 35.8 (1-OH-Nap)

Ref: Scherer G, Scherer M, Rogner N, Pluym N: Arch Toxicol 2022; DOI: 10.1007/s00204-022-03349-4

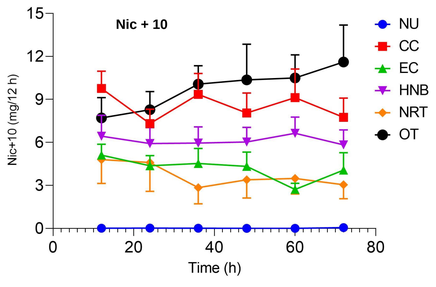
1,2-Propylene glycol (PG)



- Significant differences in PG excretion of e-cigarette users compared to other nicotine product user groups and non-users
- Strong correlation between intake (e-liquid consumption) as well as Nicotine and PG in 24h urine
- PG in urine (plasma) as specific biomarker for e-cigarette consumption

Ref: Burkhardt T, Pluym N, Scherer G, Scherer M. Separations 2021; DOI: 10.3390/separations8100171

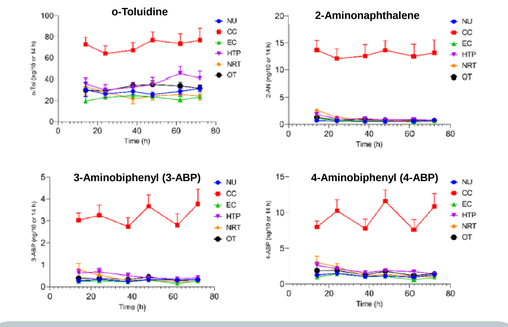
Nicotine equivalents



- Nicotine uptake doses from various products show a large overlap between each other
- Relatively stable levels over time achieved for urinary nicotine equivalents
- CC and OT groups exhibited consistently the highest levels

Ref: Scherer G, Mutze J, Pluym N, Scherer M: Assessment of nicotine delivery and uptake in users of various tobacco/nicotine products. Curr Res Toxicol 2022; DOI: 10.1016/j.crtox.2022.100067

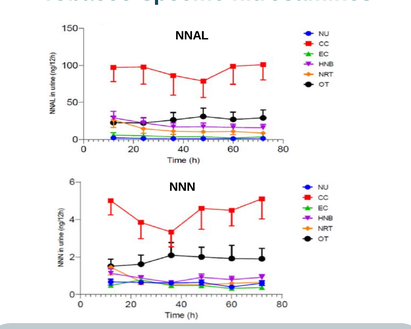
Aromatic amines



- Highest mean levels for all four aromatic amines at all time points for smokers
- Slight elevation was observed for the HTP group compared to non-CC users for o-toluidine, 3-ABP and 4-ABP
- 3-/4-ABP showed a notably different excretion pattern in smokers compared to other biomarkers, with lower values in the urine fractions collected over night

Ref: Scherer G, Riedel K, Pluym N, Scherer M: Assessment of the Exposure to Aromatic Amines in Users of Various Tobacco/Nicotine Products. ACS omega 2022; DOI: 10.1021/acsomega.2c06130

Tobacco-specific nitrosamines



- Smokers followed by OT and HTP users exhibited the highest mean levels for NNAL and NNN in urine
- The time excretion followed a typical circadian rhythm with the lowest concentrations in the morning and the highest in the late afternoon

Ref: Scherer G, Scherer M, Mutze J, Hauke T, Pluym N: Assessment of the Exposure to Tobacco-Specific Nitrosamines and Minor Tobacco Alkaloids in Users of Various Tobacco/Nicotine Products. Chem Res Toxicol 2022; DOI: 10.1021/acs.chemrestox.2c00020



CONCLUSION

First study to assess a comprehensive number of relevant THR product classes

EXPOSURE → RISK EVALUATION

SPECIFICITY → COMPLIANCE

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