Method Development and Validation of an Aerosol Sampling Technique for the Analysis of Nicotine in Electronic Cigarettes

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BACKGROUND

E-cigarettes are a **popular alternative to smoking** and a tool for **smoking cessation**.[1] The **fast-growing nature of the market**, regulation and risk assessments doesn't always keep up with changes on the market. The **Tobacco Products Directive (2014/40/EU)** mandates the disclosure of all ingredients in e-liquid and forthcoming emissions.[2] There are currently **no standardized methods defined** for analyzing constituents in **e-cigarette aerosols**.

METHOD DEVELOPMENT

A variety of **parameters** were evaluated in order to develop a method for the quantitative analysis of nicotine in e-cigarette aerosols.

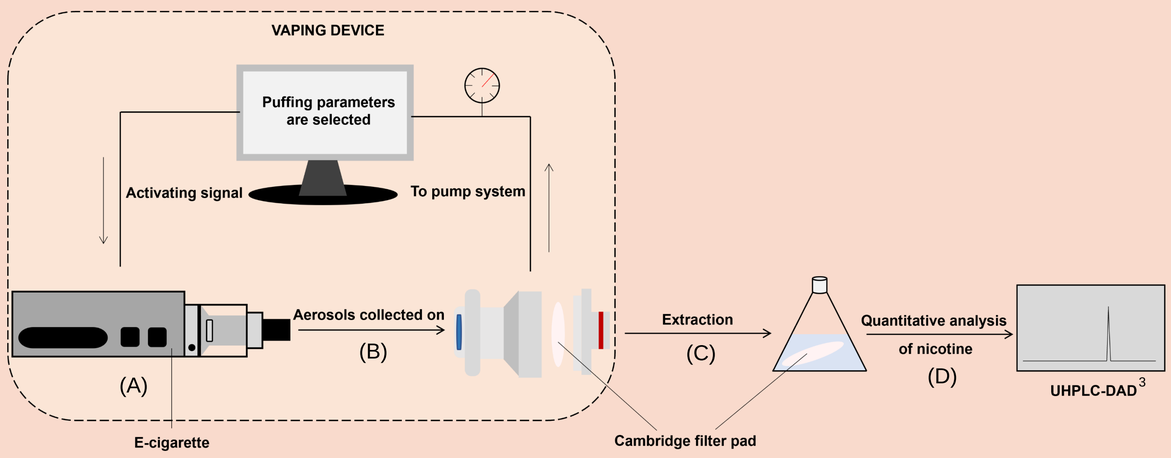
MATERIALS

Commercial vaping device

A "**mod**" or **third-generation device** was utilized as reference e-cigarette

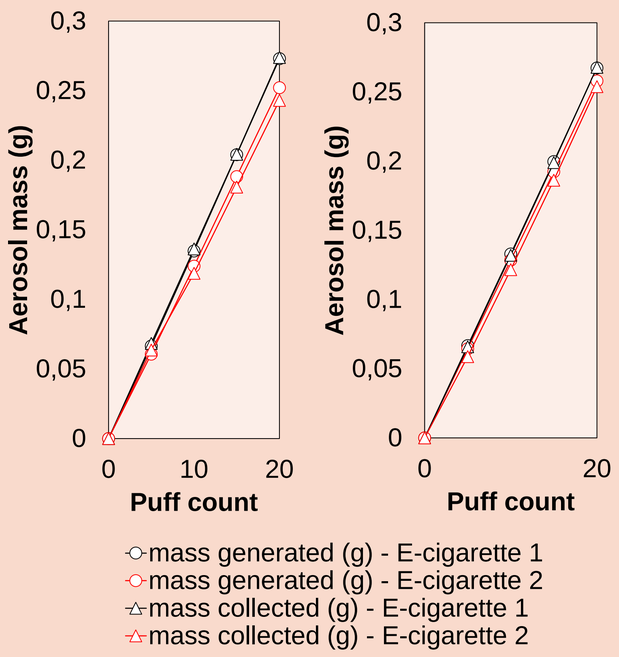
METHODS

For each crucial part of the **standard workflow**, several tests were performed to develop a method utilizing a commercial vaping robot.

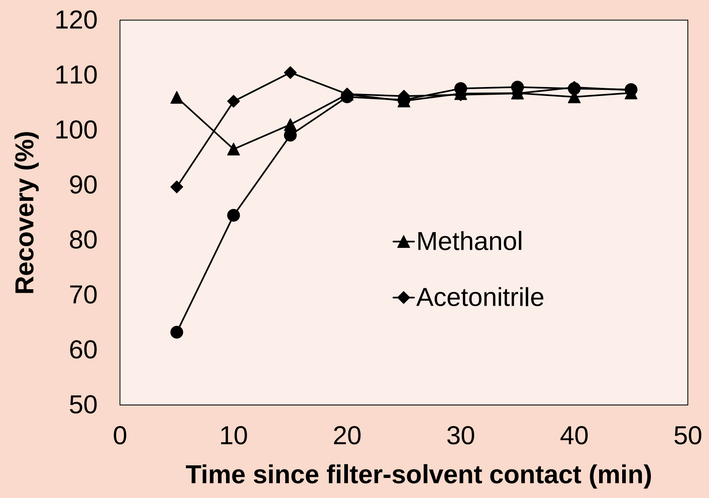


Puff number optimization[(A)]
Coil durability testing[(A)]
CFP saturation testing, within-brand differences[(A,B)]
Collection method selection[(B)]
Solvent selection[(C)]
Extraction conditions[(C)]

RESULTS

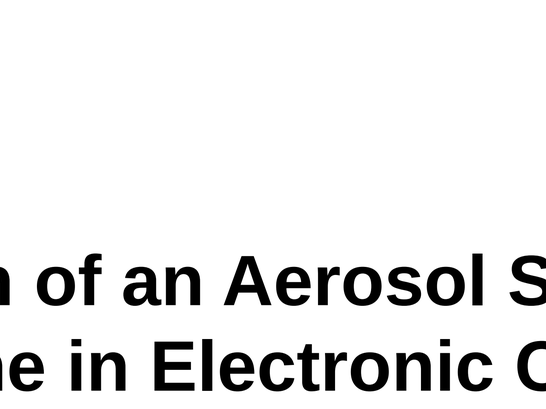


CPF saturation testing and **within-brand differences[(A,B)]** of the reference device and coil. Aerosol generation occurred in a linear fashion during collection on the filters ($R^2 \geq 0.9995$). After 20 puffs, e-cigarette 1 consistently produced 8.247% more aerosol than e-cigarette 2 (A). The difference reduced to 3.605% after switching coils (B).

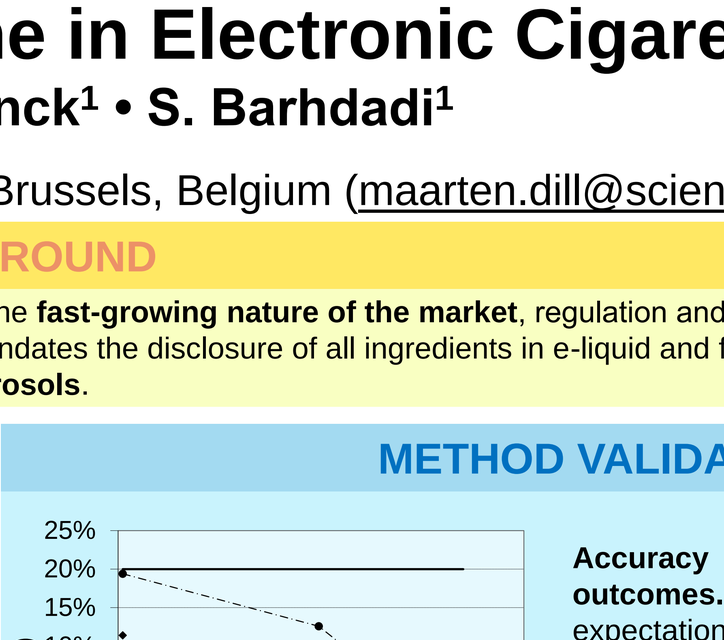


Extraction capacity of different solvents on CFP-spiked e-liquids[(C)]. The spiked filters were immersed in three different solvents: methanol, acetonitrile, and ammonium borate buffer. After 20 minutes, all three solvents showed similar extraction capacities.

METHOD VALIDATION



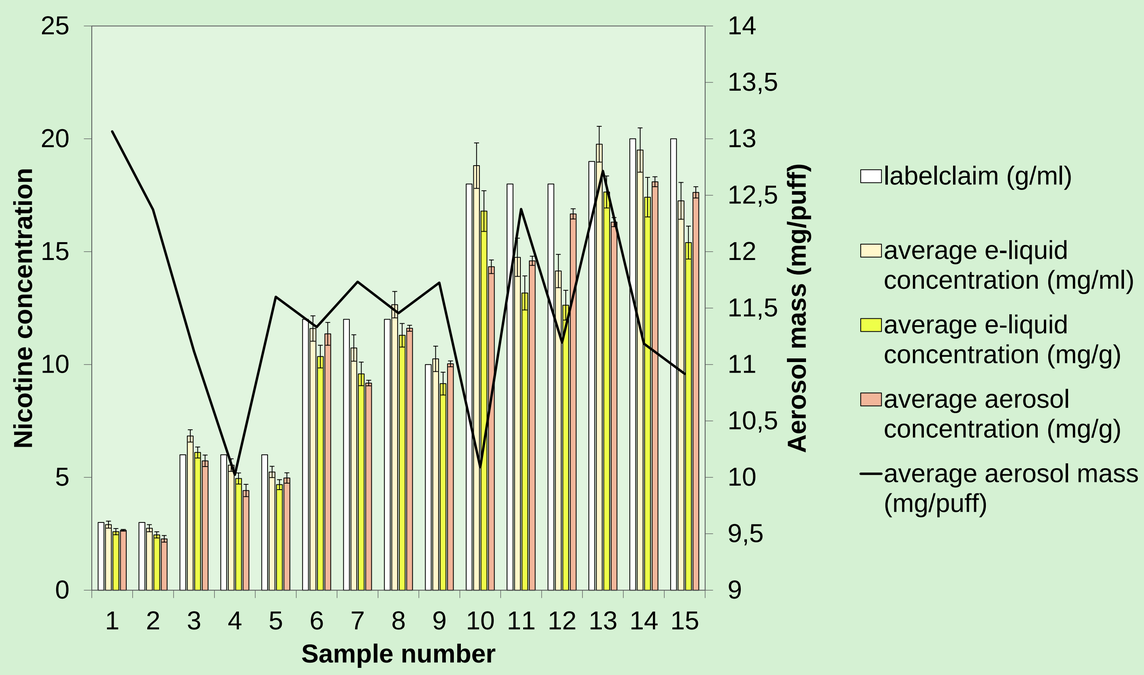
Accuracy profiles of method validation outcomes. The tolerance intervals for β-expectation did not exceed the acceptance limits of ±20%. The highest relative bias observed was -6.26% at the highest concentration level. The within-run repeatability and intermediate precision were acceptable with the highest RSD being less than 5%.



Robustness testing. The nicotine and aerosol mass transfer was investigated by altering puffing parameters (power, puff duration and puff volume), the time until extraction and the filter position. Significant changes are highlighted *.

- 15 W
- 20 W
- 2 seconds (puff duration)
- 4 seconds (puff duration)
- 50 ml (puff volume)
- 60 ml (puff volume)
- Immediate extraction
- Extraction after 24 hours
- Front side of filter
- Back side of filter

METHOD APPLICATION



Labeled nicotine concentrations compared to measured nicotine concentrations in corresponding e-liquids and aerosols. E-liquids and their respective aerosols exhibit comparable nicotine concentrations, with recoveries ranging from 92.79% to 109.72%.

CONCLUSION

In this study, aerosols were generated using a **commercial smoking machine**, collected on CFP, extracted in ammonium borate buffer, and analyzed using UPLC-DAD. It is important to note that the method has a **limitation** of requiring re-validation if there is a deviation from the validated puffing parameters. This method has **applications** in nicotine dosimetry studies, market research, and investigating aerosol transfer phenomena. It may also be utilized to develop and validate new collection methods for analyzing other constituents in e-cigarette aerosols.

[1] R. Wang, S. Bhadriraju, S.A. Glantz, E-Cigarette Use and Adult Cigarette Smoking Cessation: A Meta-Analysis, Am J Public Health. 111 (2021) 230-246. https://doi.org/10.2105/AJPH.2020.305999.
[2] European Parliament and the Council of the European Union, Directive 2014/40/EU of the European Parliament and of the Council of 3 April 2014 on the approximation of the laws, regulations and administrative provisions of the Member States concerning the manufacture, presentation and sale of tobacco and related pr, Off. J. Eur. Union (2014) no. April, 1–38. Available online: https://eur-lex.europa.eu/eli/dir/2014/40/oj (accessed on 12 February 2024).
[3] S. Barhdadi, B. Desmedt, P. Courselle, V. Rogiers, T. Vanhaecke, E. Deconinck, A simple dilute-and-shoot method for screening and simultaneous quantification of nicotine and alkaloid impurities in electronic cigarette refills (e-liquids) by UHPLC-DAD, Journal of Pharmaceutical and Biomedical Analysis 169 (2019) 225–234. https://doi.org/10.1016/j.jpba.2019.03.002.