An LC-MS/MS Approach for the Detection of Alcohol Biomarkers (PEth Homologues) and Recreative Drugs in Blood

Maria, Marisa[a*] ; Neng, Nuno[a,b], Berg, Thomas[c]

[a] Centro de Química Estrutural, Institute of Molecular Sciences, Departamento de Química e Bioquímica, Faculdade de Ciências, Universidade de Lisboa, Campo Grande, 1749-016 Lisboa, Portugal.
[b] Laboratório de Ciências Forenses e Psicológicas Egas Moniz, Egas Moniz Center for Interdisciplinary Research, Egas Moniz School of Health & Science, Quinta da Granja, 2829-511 Caparica, Portugal.
[c] Department of Forensic Sciences, Division of Laboratory Medicine, Section of Drug Abuse Research, Oslo University Hospital, P.O. Box 4950 Nydalen, N0424, Lovisenberggt. 6 Oslo 0456, Norway.

* E-mail: marisahm1998@gmail.com

1 Background

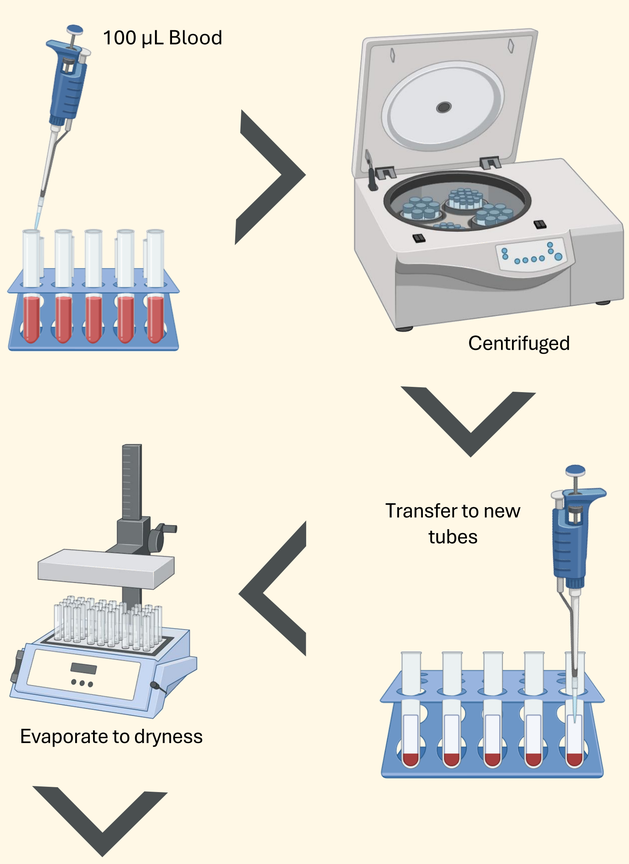
Alcohol and drug use increases the risk of addiction, health problems and dangers associated with the use of polysubstances [1, 2]. The simultaneous determination of the biomarker phosphatidylethanol (PEth, biomarker associated to alcohol consumption [3]) and other drugs allows the detection of polysubstance use, saving both time and costs compared to the use of separate methods.

2 Objective

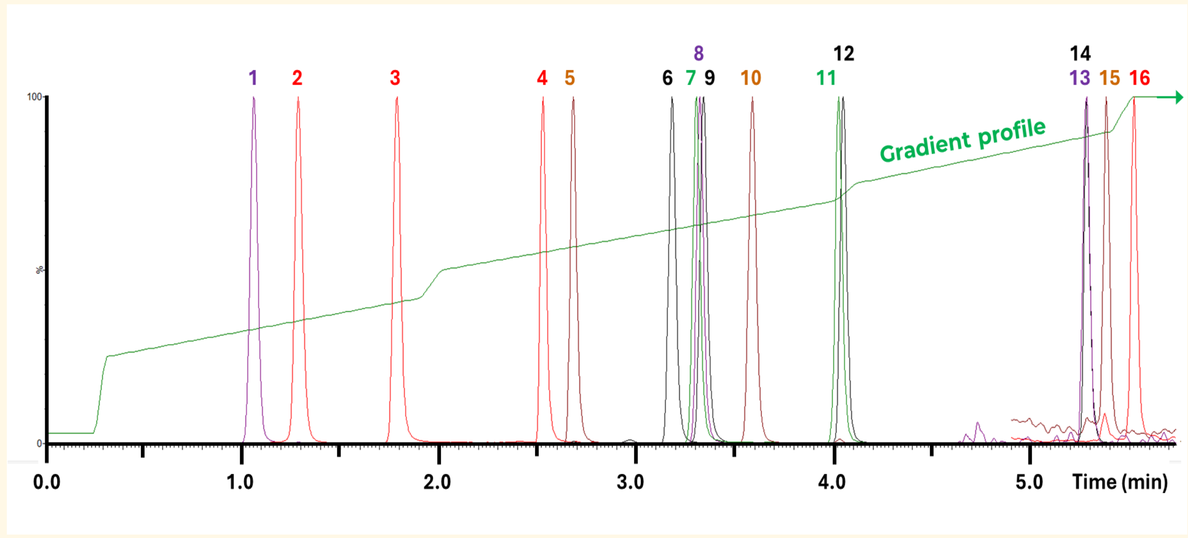
In this study, a liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS) method was developed for the determination of cocaine, benzoylecgonine, cocaethylene, crack, as well as three PEth homologues ten other drugs and metabolites.

3 Methodology

Whole blood was prepared by liquid-liquid extraction (LLE) and then analysed by reversed phase LC-MS/MS.



4 Results and Discussion



1. Benzoylecgonine
2. Hydromorphone
3. AEME
4. LSD
5. Articaine
6. Cocaine
7. Tapentadol
8. Lidocaine
9. Tramadol
10. Cocaethylene
11. Bupivacaine
12. Fentanyl
13. Buprenorphine
14. PEth 16:0/18:2
15. PEth 16:0/18:1
16. PEth 18:0/18:1

Figure 1: MRM chromatogram of the 16 compounds of interest. Mobile phase composition was 0.025 % ammonia in Type 1 water, pH 10.7 (Solvent A) and MeOH (Solvent B)

Table 1: Precision, accuracy, recovery matrix effect (ME) and corrected matrix effect (ME Corr.)

Compounds	Precision (RSD %)	Accuracy (%)	Recovery (%)	Matrix Effect ME (%)	Matrix Effect ME Corr. (%)
PEth 16:0/18:1	5 - 22	± 9 - 13	63-76	60-78	100-101
PEth 16:0/18:2	7 - 31	± 1 - 10	60-82	52-56	97-101
PEth 18:0/18:1	5 - 10	± 0 - 8	65-76	74-97	97-102
LSD	4 - 22	± 1 - 18	62-70	144-158	98-103
Cocaine	2 - 6	± 2 - 13	66-71	102-105	98-99
Cocaethylene	3 - 9	± 1 - 10	67-74	95-99	94

Compounds	Precision (RSD %)	Accuracy (%)	Recovery (%)	Matrix Effect ME (%)	Matrix Effect ME Corr. (%)
Benzolecognine	2 - 6	± 0 - 9	10-12	105-107	98-99
AEME	5 - 16	± 3 - 11	48-65	99-105	96-98
Licocaine	4 - 7	± 4 - 22	67-79	94-105	91-98
Articaine	4 - 7	± 1 - 23	65-81	102-104	95-96
Bupivacaine	4 - 10	± 3 - 43	68-83	95-104	94-100

Compounds	Precision (RSD %)	Accuracy (%)	Recovery (%)	Matrix Effect ME (%)	Matrix Effect ME Corr. (%)
Buprenorphine	5 - 32	± 1 - 5	30-59	171-178	100-107
Fentanyl	3 - 6	± 0 - 13	65-74	104-105	95-99
Hydromorphone	3 - 6	± 1 - 8	51-57	123-125	97-101
Tramadol	3 - 10	± 1 - 9	66-73	111-115	97
Tapentadol	6 - 13	± 0 - 7	58-79	142-165	123-138

5 Conclusion

An LC-MS/MS sensitive, precise and accurate method was fully developed and validated for the quantification of sixteen compounds. The method determined simultaneously cocaine and its metabolites, three PEth homologues and ten additional drugs and metabolites.

The inclusion of multiple PEths in this study allows for a more comprehensive assessment of alcohol consumption and its interaction with other substances, making it valuable for clinical and forensic analysis of polydrug use.

6 References

1. Compton, W. M., & Volkow, N. D. (2006). *Drug and alcohol dependence*, *83 Suppl 1*, S4–S7; 2. Bonfiglio, N. S., Portoghese, I., Renati, R., Mascia, M. L., & Penna, M. P. (2022). *International Journal of Environmental Research and Public Health*, *19*(24), 16759; 3. Hahn, J. A., Anton, R. F., & Javors, M. A. (2016). *Alcoholism, clinical and experimental research*, *40*(11), 2292–2295.

Acknowledgments

Centro de Química Estrutural is a Research Unit funded by Fundação para a Ciência e a Tecnologia through projects UIDB/00100/2020 (https://doi.org/10.54499/UIDB/00100/2020) and UIDP/00100/2020 (https://doi.org/10.54499/UIDP/00100/2020). Institute of Molecular Sciences is an Associate Laboratory funded by Fundação para a Ciência e a Tecnologia through project LA/P/0056/2020 (https://doi.org/10.54499/LA/P/0056/2020). CiiEM has provided support through Project 10.54499/UIDB/04585/2020, funded by FCT. Marisa Henriques Maria is grateful to acknowledge her PhD grant no. 2022.10965.BDANA awarded by Fundação para a Ciência e a Tecnologia.