Selecting the Right Remote Sampling Platform for Quantitative Metabolomics: Metabolite Stability and Analytical Considerations

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Introduction

Remote sampling for health monitoring has grown in popularity due to its convenience and potential for decentralized diagnostics. The study aimed to evaluate the stability of metabolites in using Mitra® Tips with VAMS® technology. VAMS was developed to overcome challenges such as non-homogenious sample spread and hematocrit variability while providing a more precise collection of a defined blood volume and reducing hematocrit-related bias. VAMS is particularly suited for pharmacokinetic studies that require very small blood volumes [1]. Previous studies have explored VAMS for metabolomics and a comprehensive analysis of spectral features [2]. Building upon this foundational work, this study provides a more detailed assessment of the stability of over 630 metabolites in VAMS and DBS samples. The goal is to determine if these sampling methods can meet the logistical requirements for home sampling and be successfully integrated into a quantitative metabolomics workflow.

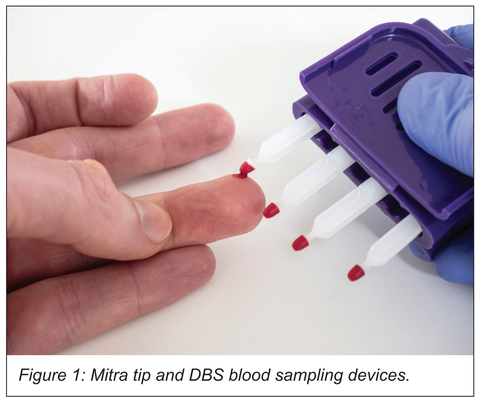

Figure 1: Mitra tip and DBS blood sampling devices.

Methods

- Sample Collection: Blood samples from 3 healthy individuals – 10µL Mitra Device – in Triplicates
- Storage: Dry at Room Temperature (RT) for 2h up to seven days.
- Metabolic Analysis: Biocrates MxP® Quant 500 kit, which assesses up to 630 metabolites
- Extraction method: Methanol-based solution
- Analytical platform: Agilent 1290 UHPLC – SCIEX QTRAP 5500 Instrument
- Acceptance criteria:
  - Metabolites Detectability set in ≥50% of all samples
  - Stability set within 85–115% between RT vs identical frozen samples
  - CVs as per kit specifications (e.g. <15% for all 7-point calibrated metabolites)

Figure 2: Biocrates MxP Quant 500 kit.

Results

- At 0 days RT: Mitra tips showed a wide range of detectable metabolites, with high numbers for amine oxides (17), nucleobase-derivatives (18), and vitamins & cofactors (24).
- 3 days RT: Maintained good overall stability. The number of detected metabolites for many classes was comparable to the day 0 samples, indicating robust stability.
  - 249 stable metabolites (40% of the kits portfolio) were found to be stable and detectable.
  - Stronger for polar small molecules - 69 for Mitra tips vs. 52 with legacy technology.

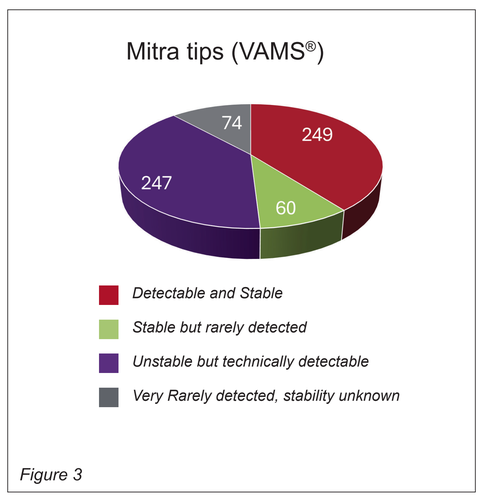

Figure 3

- 5 days RT: A slight decrease in the number of detected metabolites was observed for several classes, although the majority remained stable. (194)
- 7 days RT: Continued to show a high degree of stability for most metabolites, despite a general trend of decreasing numbers over the seven-day period. (147)

	Alkaloids	Amine Oxides	Amino Acids	Amino acid-related	Bile Acides	Biogenic amines	Carbohydrates	Carboxylicacids	Cresols	Fatty acids	Hormones	Indoles derivatives	Nucleobase-related	Vitamins & cofactors	Acylcarnitines	Ceramides	Cholesterol esters	Diacylglycerols	Dihydroceramides	Glycerophosphospholipds	Sphingolipids	Triacylglycerols
DBS, 3 days RT	1	1	14	15	8	4	1	2	1	2	1	3	1	0	5	17	11	3	2	49	19	14	99
Mitra tips, 0 days RT	1	1	20	23	12	7	1	6	1	7	3	3	2	1	19	26	16	10	5	87	34	174	174
Mitra tips, 3 days RT	1	0	17	17	12	7	0	3	1	4	2	3	1	1	18	24	4	4	5	35	28	14	48
Mitra tips, 5 days RT	1	0	17	16	12	6	0	3	1	1	2	3	1	1	14	24	3	3	3	26	27	13	17
Mitra tips, 6 days RT	1	0	10	11	12	3	0	2	1	1	1	2	1	1	14	23	2	3	3	13	24	13	6

Table 1: Comparison of detectable and stable metabolites (summarized per metabolite class) in DBS and Mitra Tips when stored over several days at room temperature.

Conclusion

- Mitra tips: Best for **small molecules** (e.g., neurotransmitters, bile acids, acylcarnitines), with reduced hematocrit bias—ideal for **4P medicine** (personalized, predictive, preventive, participatory).
- DBS: Best for **lipid-focused analyses** (e.g., triacylglycerols, TMAO) and monitoring **blood glucose**.
- Stability decreases significantly after **five days at room temperature**, highlighting the importance of prompt analysis or improved stabilization strategies.

Key take aways:

- Both methods are **viable for remote metabolomics**, but the choice depends on:
  - **Target metabolite class** (lipids vs. small molecules).
  - **Clinical application** (cardiovascular risk vs. metabolic or neurological health).
  - **Reliability and user-friendliness** of the collection procedure
- Rapid drying and sample handling significantly influence metabolite integrity.
- Incorporating stabilizers or standardizing extraction protocols could further improve robustness and comparability.

References

[1] Dodeja, P., Giannoutsos, S., Caritis, S., & Venkataramanan, R. (2023). Applications of Volumetric Absorptive Micro-sampling Technique: A Systematic Critical Review. Therapeutic Drug Monitoring, 45(4), 431-462.
[2] Volani, C., Malfertheiner, C., Caprioli, G., Fjelstrup, S., Pramstaller, P. P., Rainer, J., & Paglia, G. (2023). VAMS-Based Blood Capillary Sampling for Mass Spectrometry-Based Human Metabolomics Studies. Metabolites, 13(2), 146.

Acknowledgement

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