Supplementary Information (SI) for Green Chemistry.

Integrating in-vial thin film microextraction using polysiloxane-based adhesive tapes with low-temperature plasma ionization mass spectrometry: A solvent-free approach for determining cocaine and methamphetamine in saliva samples

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1. Description of the microextraction devices

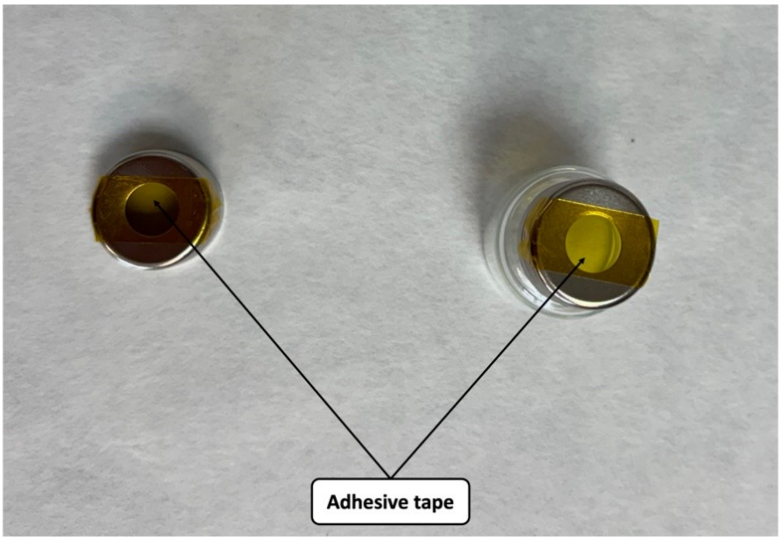


Figure S1. The cap covered with the temperature-resistant tape is shown in the left side of the picture while the right side of the pictures presents a vial closed with the modified cap. The adhesive allows to attach the tape to the cap, also exposing the polysiloxane glue to the sample

2. Interface for the integration of the thermal desorption of the analytes with the mass spectrometric analysis using the SICRIT ionization source.

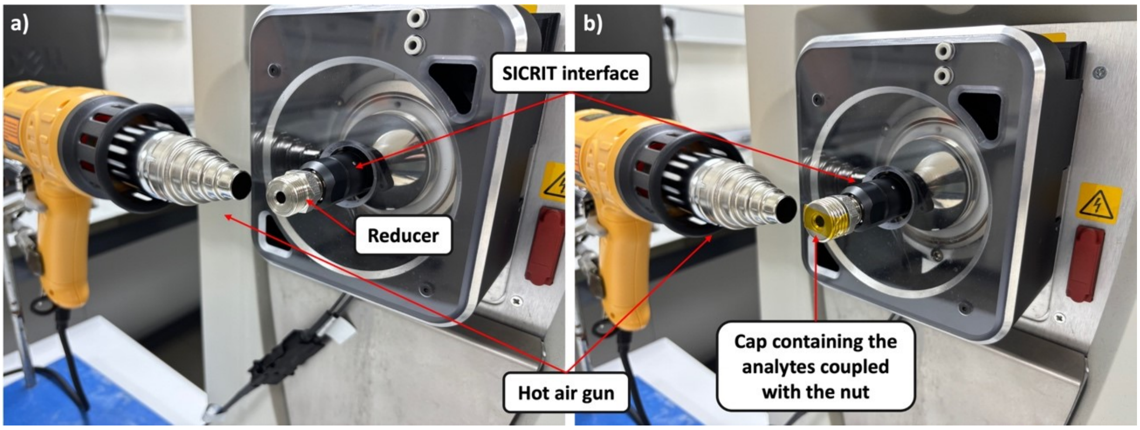


Figure S2. Interface used for the thermal desorption of the modified caps in front of the SICRIT interface. The figure shows the interface (a) between measurements and (b) during the analysis of a modified cap.

3. Mass spectrometry parameters for the TD-SICRIT-MS/MS analysis

The desorbed analytes were ionized in the SICRIT ionization source (frequency of 15000 Hz and an amplitude of 1400 V), and the ions analyzed in a Thermo LTQ mass spectrometer (Thermo Fisher Scientific, San Francisco, CA, USA) using the Ion Trap analyzer. The capillary voltage and the tube lens were fixed at 35 V and 110 V, respectively. The capillary temperature was fixed at 275 º C. The MS/MS isolation width was 1 amu. MS transitions are shown in Table S1. Tandem mass spectrometry (MS/MS) experiments were carried out by collision-induced dissociation (CID) using He as the collision gas. Data collection and analysis were performed with Xcalibur 2.1.0 software (Thermo Fisher Scientific).

Table S1. MRM parameters for the analysis of semivolatile compounds by TD-SICRIT-MS/MS

Compound	**MS^2 Settings**			**Scan Ranges**	
	Precursor ion (m/z)	**Normalized collision energy**	**Act. Time (ms)**	**First mass (m/z)**	**Last mass (m/z)**
Cocaine	304.1	30.0	30.000	181.10	183.10
Cocaine-d$_3$	307.1	25.0	30.000	184.00	186.00
Methamphetamine	150.2	30.0	30.000	118.00	120.00
Methamphetamine-d5	155.1	25.0	30.000	120.00	122.00

4. DI-MS/MS analysis

An Agilent 1260 Infinity liquid chromatography (LC) system (Agilent, Palo Alto, CA, USA) equipped with an Agilent 6420 Triple Quadrupole MS with an electrospray source was used for analytes optimization. A guard column (0.2 µm filter, 2.1 mm) protected the MS source from potential particles. The samples (5 µL of injection volume) were directly injected in the carrier phase (Milli-Q water and methanol in a 10:90 v/v ratio containing 26.5 mM of formic acid and 5 mM of ammonium formate), which was pumped at 0.2 mL·min^{-1}. The following ionization source parameters were optimized: gas temperature

(350 ° C), gas flow (9 L·min^{-1}), nebulizer (30 psi) and positive/negative capillary voltage (3000 V).

Table S2. MRM parameters of analytes for the analysis by DI-MS/MS

Compound	Precursor Ion (m/z)	Fragmentor Voltage (V)	Product Ion (m/z)	Collision Energy (eV)	Quantification Transition
Cocaine	304.1	125	182.1 82.1	20 32	304.1→182.1
Cocaine-d3	307.1	140	185 85.2	18 34	307.1→185
Methamphetamine	150.2	80	119.1 91.2	8 20	150.2→91.2
Methamphetamine-d5	155.1	100	92.1 91.6	18 18	155.1→92.1

5. Chemical characterization of the thermal resistant adhesive tape

5.1 Infrared spectroscopy

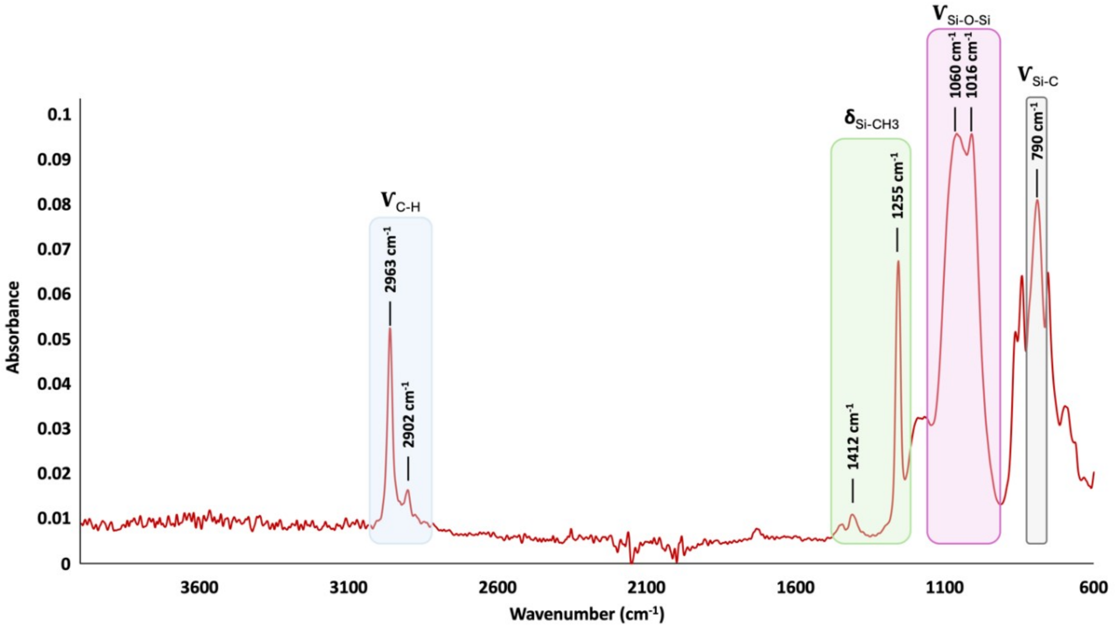


Figure S3. ATR-IR spectrum of the adhesive present in TRT.

5.2 Energy Dispersive X-ray spectroscopy (EDX) of the adhesive tape

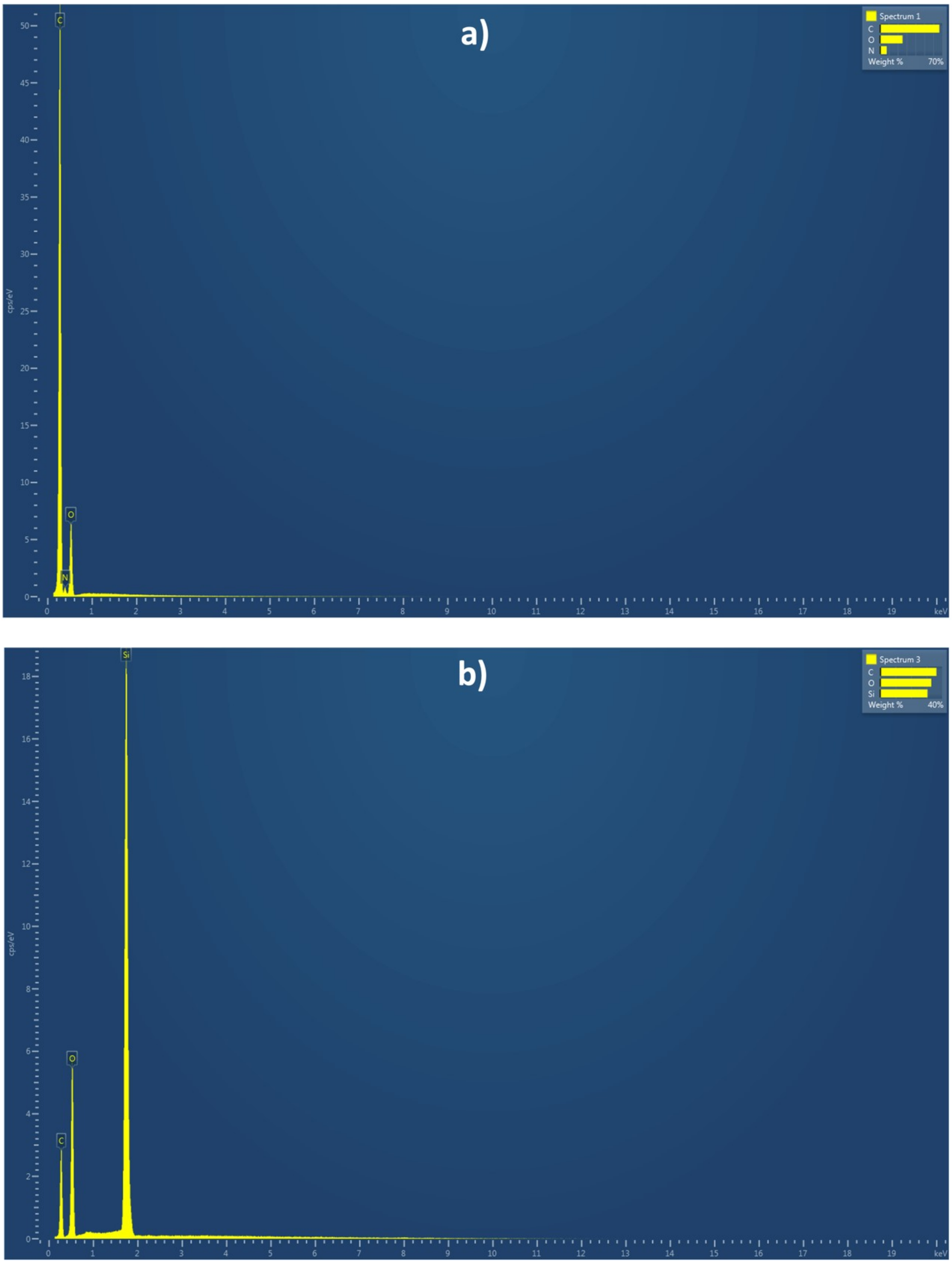


Figure S4. SEM-EDX analysis of the (a) polyimide film and the (b) polysiloxane adhesive coating.

Table S3. Distribution of Si, C, N, and O of both sides of the adhesive tape

Element	Polyimide film		Adhesive coating	
	Wt %	Atomic %	Wt %	Atomic %
Si	-	-	30.60	17.63
C	66.76	72.14	36.35	48.96
N	7.73	7.16	-	-
O	25.52	20.70	33.04	33.41

6. Characteristics of the target compounds

Table S4. Chemical characteristics of the target analytes (Source: PubChem)

Compound	Boiling Point (º C)	log P
Cocaine	187	2.3
Methamphetamine	212	2.07
Codeine	250	1.39
Methadone	No data	3.39

7. Correction of the ionic strength effect on the analytical signal using internal standards

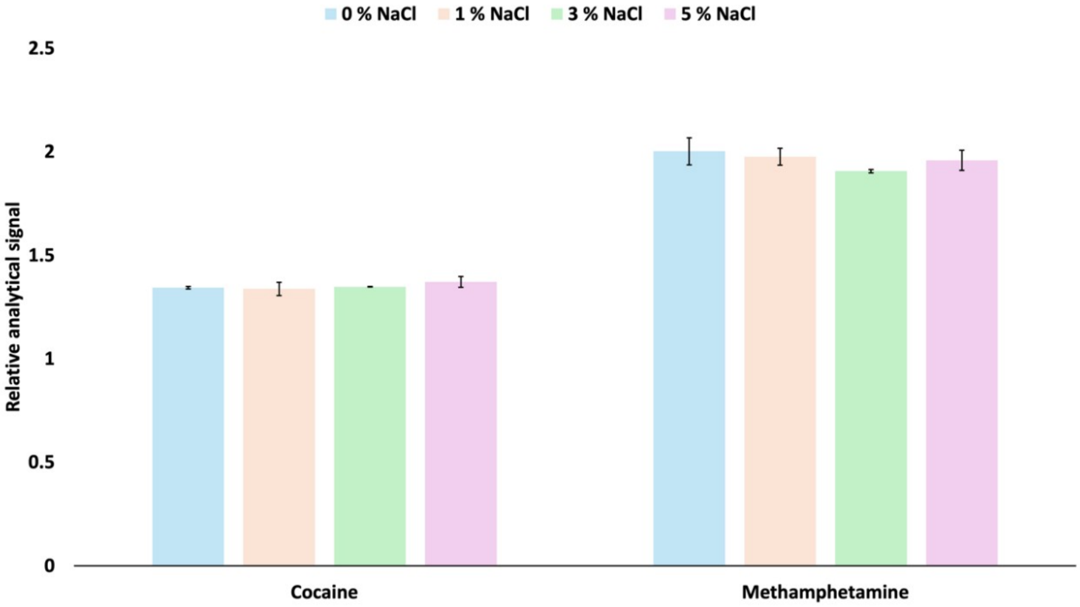


Figure S5. Relative signals obtained at different ionic strengths.

8. Calibration curves of cocaine and methamphetamine by TD-SICRIT-MS/MS

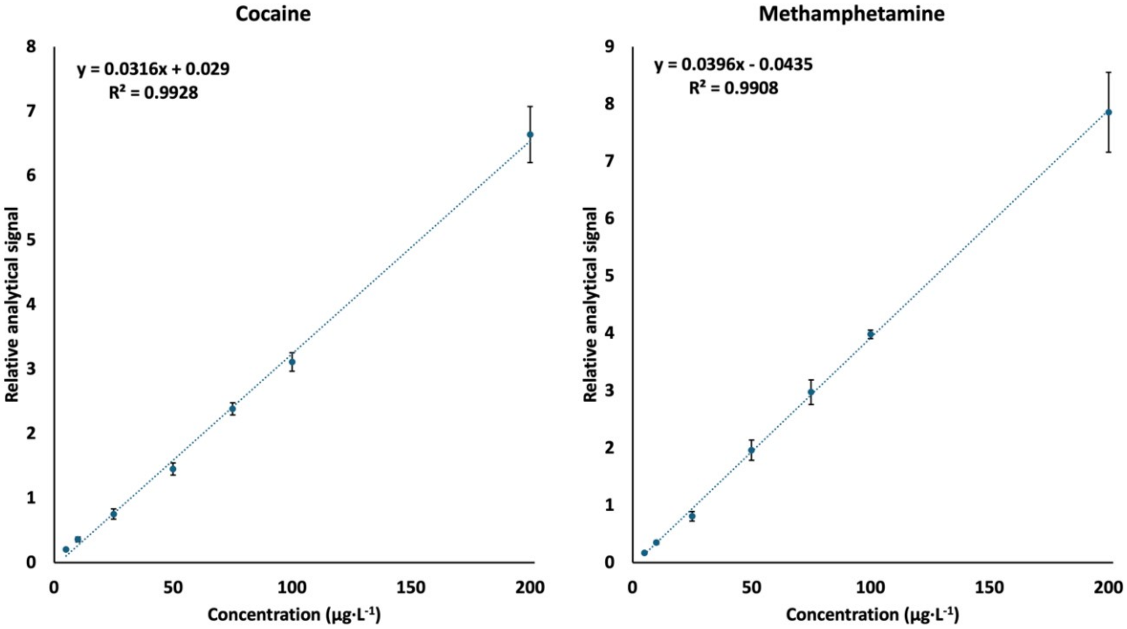


Figure S6. Calibration curves for the analysis of cocaine and methamphetamine by the TD-SICRIT-MS/MS method.

9. Evaluation of the stability of the analytes once extracted and stored in the tapes

The stability of the analytes in the tape, once extracted, was investigated at two concentrations (10 and 200 µg·L^{-1}) and two storing temperatures (room temperature and 4 º C) for two weeks. After the extraction, the caps were just covered with parafilm to avoid tape contamination. The relative analytical signals were used as analytical parameters, and their evolution was compared with those obtained on the same day of extraction (denoted as week 0). The results are shown in Figure S7, representing the average value for two replicates and the corresponding statistical range. The results demonstrated the appropriate stability of the analytes on the tapes. However, for on-site applications, more extreme conditions should be evaluated to simulate ordinary mail shipping. In this regard, the sample storage, done here simply with parafilm, should be improved.

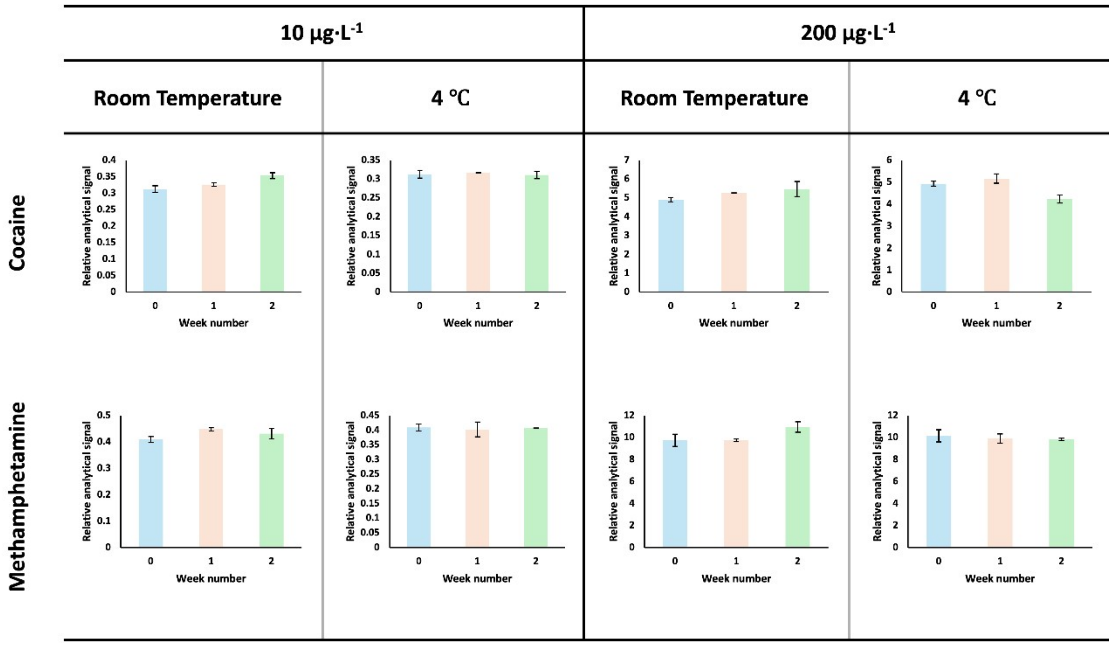
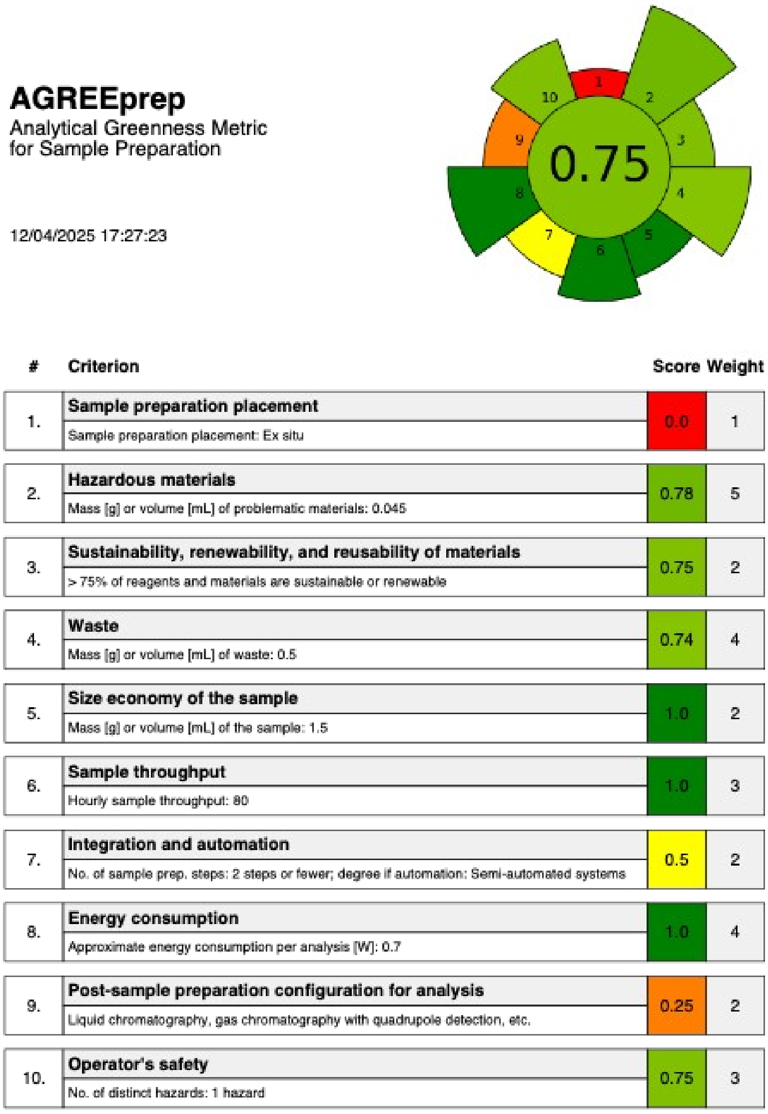


Figure S7. Study of the stability of the analytes on the tape after extraction.

9. Evaluation of the sustainability of the in-vial microextraction using Analytical Greenness Metric for Sample Preparation metric

The application of AGREEprep metrics provided a final score of 0.75. This value, considered in isolation, does not provide a general idea of the sustainability of the method. However, this value is better than those reported for SPME-GC-MS methods,[1] which can be selected as a comparable technique due to the use of microextraction, thermal desorption, and mass spectrometry.



AGREEprep
Analytical Greenness Metric
for Sample Preparation

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#	Criterion	Score	Weight
1.	**Sample preparation placement** Sample preparation placement: Ex situ	0.0	1
2.	**Hazardous materials** Mass [g] or volume [mL] of problematic materials: 0.045	0.78	5
3.	**Sustainability, renewability, and reusability of materials** > 75% of reagents and materials are sustainable or renewable	0.75	2
4.	**Waste** Mass [g] or volume [mL] of waste: 0.5	0.74	4
5.	**Size economy of the sample** Mass [g] or volume [mL] of the sample: 1.5	1.0	2
6.	**Sample throughput** Hourly sample throughput: 80	1.0	3
7.	**Integration and automation** No. of sample prep. steps: 2 steps or fewer; degree if automation: Semi-automated systems	0.5	2
8.	**Energy consumption** Approximate energy consumption per analysis [W]: 0.7	1.0	4
9.	**Post-sample preparation configuration for analysis** Liquid chromatography, gas chromatography with quadrupole detection, etc.	0.25	2
10.	**Operator's safety** No. of distinct hazards: 1 hazard	0.75	3

Figure S8. AGREEprep evaluation of the in-vial microextraction technique where the individual score and weight for each criterion are also indicated.

10. Evaluation of the practicality of the in-vial microextraction combined with TD-SICRIT-MS/MS using Blue Applicability Grade Index metric.

The pictogram obtained after the application of the BAGI metric is presented in Figure S7. The value overpasses the cut-off level established by the metric, 60 points, thus demonstrating the applicability of the method.

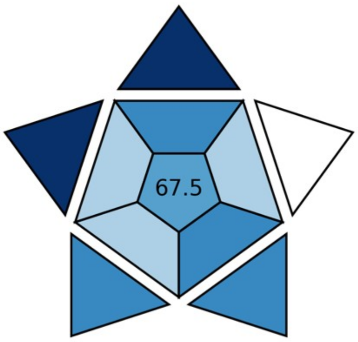

Figure S9. BAGI evaluation of the in-vial microextraction technique.

References

1 R. Rajput and S. Desai, *Green Analytical Chemistry*, 2024, **11**, 100167.