Coated Blade Spray – High Resolution Mass Spectrometry: a versatile tool for sample profiling and screening of controlled substances in complex matrices

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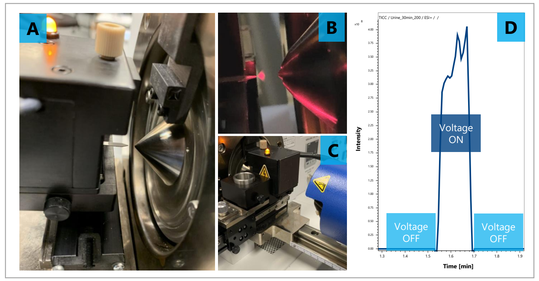
Introduction

Coated Blade Spray (CBS) is a technology that allows for analyte collection and direct-to-MS interface from a single device [1-4]. Essentially, CBS is a coated stainless steel sheet with the shape of a small sword which, thanks to its ultra-thin coating, permits rapid enrichment of small molecules present in complex samples. Further, it allows for ionization via ESI mechanism once the coated area is wetted with a small amount of solvent (<15µL) and a high-potential is applied to the non-coated area of the device[5-7] . Herein, we demonstrate how CBS coupled to High Resolution Mass Spectrometry (HRMS) enables rapid profiling of aqueous and solid matrices. Unlike other ambient-ionization technologies, CBS allows sampling to be performed remotely, cleaning-up the sample and retaining relevant chemical information that facilitates its classification via chemometric tools. Furthermore, we explore CBS-HRMS as a tool for screening and quantitation of controlled substances in biological matrices such as urine.

Experimental

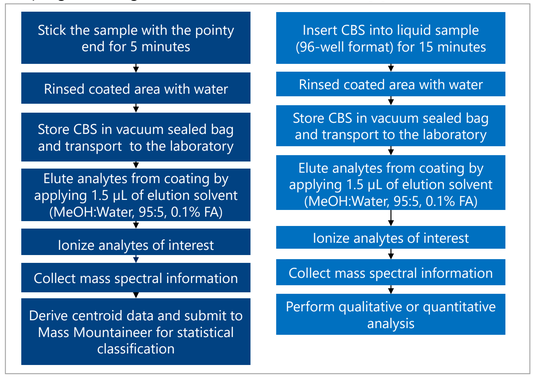
Coated Blade Spray devices with a coating length of 10 mm and coating thickness of 10 µm were used for all the experiments herein described. The coating consisted of 5 µm Hydrophobic-Lipophilic Balance (HLB) particles immobilized with polyacrylonitrile. Data collection was conducted on an AccuTOF™ Time-of-Flight MS (JEOL, Peabody, MA) within the range of 50-1000 m/z. CBS devices were adapted to fit into the JEOL PaperSpray™ interface and electrospray was generated by adding 1.5 µL on the coated area and applying a positive voltage of 3.75 kV. Spray time was approximately 10 seconds per blade and the data was processed using msAxel LP. Chemometric analyses were performed with Mass Mountaineer™ software for mass spectra collected over the m/z range 80-1000.

Figure 1 Coated Blade Spray installed on an AccuTOF Time-of-Flight MS via commercially available JEOL PaperSpray interface; hence, facilitating rapid transition between diverse ambient ionization technologies (A-C). Insert D presents an example of an ion chronogram collected with CBS in urine sample, while insert B displays Taylor cone generated from CBS device with a voltage of 3.75 kV and a distance of approximately 4 mm from the MS inlet.



Experimental (cont.)

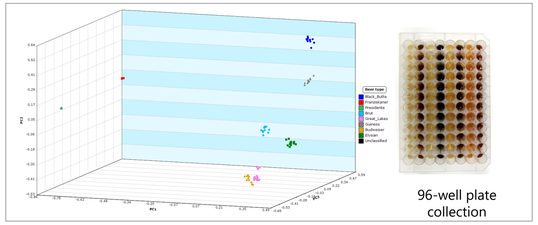
Diagram 1 Experimental workflow followed for analysis of solid samples (left, meat and fish tissue) and liquid samples (right, beer and urine). In the case of liquid samples, the devices were preconditioned, prior to the sampling, following conditions described elsewhere [4].



Results

Sample profiling via mass spectrometry requires taking either the sample to the lab or the MS to the sample [8, 9]. Herein, we show how CBS can be used to collect and store chemical information from liquid and solid samples. In combination with a HRMS and appropriate statistical tools, chemicals stored on the coating can be used for sample discrimination. As can be seen in Figure 2, the discriminant analysis of principal components (DAPC) in combination with Kernel Principal Component Analysis (KPCA) allowed for adequate classification of each of the beer brands under evaluation. Further, when using 60 principal components (PC), the leave-one-out cross validation (LOOCV) and the Support Vector Machine (SVM) unequivocally identified each of the samples.

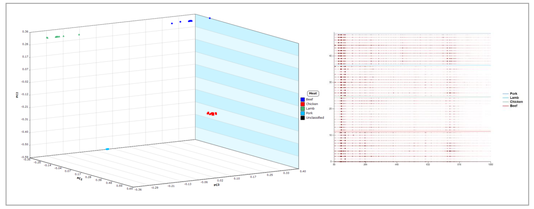
Figure 2 DAPC-KPCA plot classification of diverse beer brands (left). Photo of the 96-well plate with 12-samples of each beer kind. Sampling was performed using a 96-CBS arrangement (right).



Results (cont.)

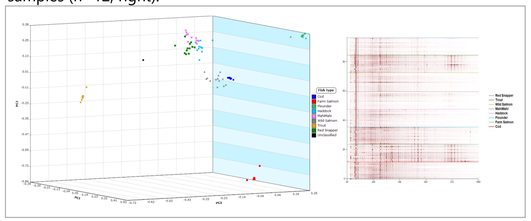
Likewise, CBS was capable of differentiating different types of meat samples. As can be seen in Figure 4, the DAPC-KPCA plot showed clear distinction of each meat. By using 60 PC, the LOOCV and SVM lead to a predictability of 94 and 96%, respectively.

Figure 4 DAPC-KPCA plot classification of miscellaneous fish types (left). Heat map representing mass spectra attained for each of the meat samples (n=12; right).



In a third experiment, CBS was used to differentiate diverse fish samples. As can be seen in Figure 4, the DAPC-KPCA plot showed clear distinction of each species. Similar to the meat samples, by using 60 PC, the LOOCV and SVM lead to a predictability of 94 and 96%, respectively. Certainly, further improvements are expected by controlling the spatial location where the blade is inserted onto the fish for analyte collection. Besides, our work is also focused on studying a much larger cohort for each of the samples and the exploration of other elution/ionization solvents, so to increase the coverage of analytes under scrutiny (i.e. balance coverage).

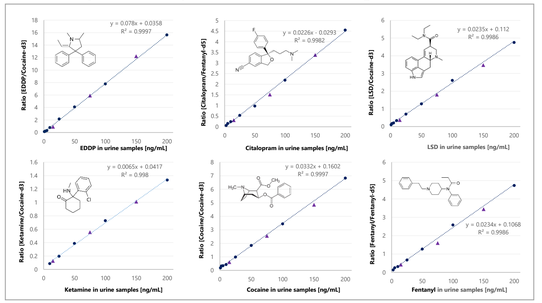
Figure 5 DAPC-KPCA plot classification of miscellaneous fish types (left). Heat map representing mass spectra attained for each of the fish samples (n=12; right).



Finally, we evaluated the coupling of CBS to the JEOL TOF towards the semi-quantitative analysis of several drugs of different classes in human urine samples. Extraction time was set to 15 minutes and data collection was 5 seconds per blade. Potential inter-blade errors were corrected using two isotopic labelled internal standards. As can be seen in Figure 6, limits of quantitation in the low ng/mL range were attained for the drugs under evaluation. Though the performance can not be compared to that previously attained on a triple quadrupole (QqQ) MS, LOD (1-10 ng/mL) were acceptable for most of the targeted analytes. In addition, accuracy for the validation points range between 75-112% at the three levels under investigation.

Results (cont.)

Figure 6 Calibration curves for EDDP, Citalopram, LSD, Ketamine, Cocaine and Fentanyl. Validation points at 15, 75 and 150 ng/mL.



Summary

1. CBS was used, as a proof-of-concept for profiling of beer, meat and fish samples. In the case of aqueous matrices, 96 samples can be scrutinized at the same time, allowing for total analysis time under 1 minute per sample.
2. Unlike other methods, were the mass spectrometer must be transported to the place of sampling, sample collection with CBS was performed in one location (Bellefonte, PA) and analyzed at a different location (Peabody, MA) without major hassle as the "sample" (sample information) was safely transported on a airplane.
3. Although, the limits of quantitation attained via CBS-TOF fall behind those previously attained with QqQ instruments [4], the results showed the potential towards rapid screening with TOF systems.
4. Since the chemical information of the sample is stored in the coated material, it is invisible to the bare eye and encrypted to the trained eye; thus, making CBS an ideal tool, not only for profiling, but also from a chain of custody perspective [9].

References

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