Microplasma-Based Flowing Atmospheric-Pressure Afterglow (FAPA) Source for Ambient Desorption-Ionization Mass Spectrometry

Offer M. Zeiri^{a,b}, Andrew P. Storey^a, Steven J. Ray^{*a,c}, Gary M. Hieftje^a

Abstract. A new direct-current microplasma-based flowing atmospheric pressure afterglow (FAPA) source was developed for use in ambient desorption-ionization mass spectrometry. The annular-shaped microplasma is formed in helium between two concentric stainless-steel capillaries that are separated by an alumina tube. Current-voltage characterization of the source shows that this version of the FAPA operates in the normal glow-discharge regime. A glass surface placed in the path of the helium afterglow reaches temperatures of up to approximately 400°C; the temperature varies with distance from the source and helium flow rate through the source. Solid, liquid, and vapor samples were examined by means of a time-of-flight mass spectrometer. Results suggest that ionization occurs mainly through protonation, with only a small amount of fragmentation and adduct formation. The mass range of the source was shown to extend up to at least m/z 2722 for singly charged species. Limits of detection for several small organic molecules were in the sub-picomole range. Examination of competitive ionization revealed that signal suppression occurs only at high (mM) concentrations of competing substances.

Keywords

Ambient desorption-ionization; mass spectrometry; microplasma; ion source

1. Introduction

Since the introduction of desorption electrospray ionization (DESI) [1] and direct analysis in real time (DART) [2], ambient desorption/ionization mass spectrometry (ADIMS) has grown rapidly [3, 4]. The technique generally requires no sample preparation, and involves desorbing and ionizing analyte species directly from samples placed next to an MS atmospheric-sampling inlet. Many sources for ADIMS are plasma-based and differ from each other with respect to discharge conditions and geometries. Examples of the types of plasmas being used include corona discharges (e.g., DART, atmospheric-pressure solid analysis probe [5]), dielectric-barrier discharges (e.g., low-temperature plasma probe [6], dielectric barrier discharge ionization [7]) and glow discharges (e.g., flowing atmospheric-pressure afterglow (FAPA) [8] plasma-assisted desorption/ionization [9]), to name a few. Plasma-based sources for ADIMS have found application in many fields, including security [10, 11], consumables [12], pharmaceuticals [2, 13], and biomedical analysis [14, 15].

The FAPA source utilizes the effluent (afterglow) from a DC helium glow discharge to thermally desorb and ionize samples. Originating from the atmospheric-pressure glow discharge (APGD) [16], the FAPA has been introduced in several forms, including a pin-to-plate [8] configuration, a pin-to-capillary [17] geometry, and a concentric-electrode arrangement [18]. Applications of FAPA-MS include detection of illicit drugs [19] and drug metabolites [20], imaging [19], and polymer fingerprinting [21], among others.

Microplasmas are discharges confined to a size below 1 mm in at least one dimension [22], and are used in a variety of applications including detectors [23, 24], biomedical devices [25], and lab-on-a-chip technology [26]. Microplasmas possess several properties that make them of interest for ADIMS. Scaling laws show that under ambient conditions microplasma sizes bring them close to the minimum potential in the Paschen curve for most gases, making microplasmas very stable against arcing. Microplasmas also often possess high electron and power densities, which can result in high reagent-ion yields and high gas-plume temperatures, both of which promote sensitivity and robustness for ADIMS. Despite these attractive properties, there have been only a few literature examples of microplasmas used as sources for ADIMS [27-29]. These earlier studies took advantage of the microplasmas' controllable gas temperature and low power consumption, by operating with either a pulsed power supply or low operating currents.

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4 In the present paper we describe and evaluate the micro-FAPA (μ -FAPA), a new design
5 that utilizes concentric electrodes to create a direct-current, annular-shaped
6 microplasma as the afterglow source. This new system is characterized by current-
7 voltage behavior, gas-plume temperature under different operating conditions, and mass
8 spectrometry data. Solid, liquid, and vapor-phase samples were analyzed to illustrate
9 the source operating principles, accessible mass range, and to evaluate limits of
10 detection for several substances. Finally, the effect of competitive ionization was
11 examined to assess the robustness of the source and its susceptibility to matrix
12 interferences.
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19 **2. Materials and methods**

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22 **2.1 FAPA design.** The μ -FAPA is based on the previously described halo-FAPA (h-
23 FAPA) design [18], but miniaturized in order to take advantage of microplasma
24 properties. A photograph and schematic diagram of the μ -FAPA source are shown in
25 Figure 1. A polyether ether ketone (PEEK) tee, drilled to allow helium introduction, was
26 used for the body of the source. The anode, a stainless-steel capillary (6.5 cm length,
27 I.D. 0.254 mm, O.D. 0.457 mm, McMaster-Carr, Elmhurst, IL), was inserted into an
28 alumina-tube insulator (5 cm length, I.D. 0.508 mm, O.D. 1.27 mm, Scientific Instrument
29 Services, Ringoes, NJ), with 2 mm of the anode exposed beyond the alumina tube. The
30 tubes were then inserted into the tee and held in place with an Upchurch LiteTouch™
31 liquid chromatography fitting. Teflon tape was used to seal the fitting to prevent gas flow
32 from the back of the source, and to hold the anode firmly in place. The cathode, a wider
33 stainless-steel capillary (2.5 cm length, I.D. 1.37 mm, O.D. 1.83 mm, McMaster-Carr,
34 Elmhurst, IL) was placed inside a second LiteTouch™ fitting, and connected to the tee,
35 so the outer cathode extended 3 mm beyond the anode. Swagelok™ connectors were
36 used to attach the side arm of the tee to the helium supply line. Because the anode was
37 so small, direct connection was difficult, so alligator clips and nichrome wire were used
38 to join the electrodes to the power supply. The μ -FAPA discharge is formed between the
39 two concentric stainless-steel capillaries, isolated over most of their length by the
40 alumina tube. The inner capillary (anode) extends two millimeters beyond the alumina
41 sleeve, resulting in a region where the μ -FAPA discharge can form. The radial distance
42 between the exposed part of the inner capillary and the outer capillary (cathode) is 0.46
43 mm. This outer capillary extends five millimeters beyond the insulator, separating the
44 discharge from the ambient atmosphere, and directing the afterglow to the sample. In
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the present experiments, helium flow typically originates from the annular channel between the outer stainless-steel capillary and the alumina tube. It is possible also to have gas flowing through the inner capillary in addition to the primary gas flow, but this mode was not employed in this preliminary study.

2.2 Gas Flow. All gas flow rates (0.5-1.5 L/min) were regulated with a mass-flow controller (Model 1179A53CS1BV, MKS Instruments, Andover, MA).

2.3 Current–Voltage Characterization. A high-voltage dc power supply (Kepco, BHK 2000-0.1 MG, Seoul) was operated in the current-limited mode. Currents ranging from 3 to 75 mA were supplied while the discharge voltage and current were monitored; each experiment was repeated five times.

2.4 Mass-Spectral Characterization. Mass spectra were obtained with a time-of-flight mass spectrometer (Unique[®], LECO Corporation, St. Joseph, MI) that has minor modifications for improved handling of the helium load; modification details have been described elsewhere [8]. An offset potential of ca. 90 V was applied to the cathode of the source by means of a DC power supply (Model E3621, Agilent Corporation, Santa Clara, CA) in order to limit the bias with respect to the voltage on the front plate (87 V) of the mass spectrometer.

2.5 Infrared Thermal Imaging. Thermal images were obtained with a Fluke Ti40 FlexCam (Fluke Corporation, Everett, WA) infrared camera. Images were analyzed with Fluke Smartview thermography software, including corrections for glass emissivity (0.92) and background temperature (22 °C). Glass microscope slides were positioned in the helium path, at a ~10° angle relative to the μ -FAPA effluent stream, at selected distances. Images were acquired for discharge currents between 3 and 75 mA, and at three helium flow rates (0.5, 1.0, and 1.5 L/min). Temperatures were allowed to equilibrate for seven minutes before three successive images were taken and averaged. Glass samples of different mass included an intact microscopic slide, an intact microscope cover slip, and a slide and cover slip broken approximately in half (masses were 4.616, 2.220, 0.282, and 0.107 g).

2.6 FAPA Images. Photographs were taken with a Canon EOS Rebel T4i camera.

2.7 Sample Introduction. For gaseous and solution samples the μ -FAPA source was placed in line with the MS inlet, at an angle of 180°. Liquid samples were analyzed by using a glass melting-point capillary. For qualitative results the capillary was merely

dipped into the target sample solution and positioned in the FAPA effluent stream. For quantitative experiments, 2 μL of the sample solution were deposited onto the open end of the capillary. The capillary was then inserted between the $\mu\text{-FAPA}$ and the MS inlet with a homemade sample holder (a delrin wand drilled at several positions to hold capillaries), which minimized differences in position between samples. Mass spectra of solids were obtained by placing each sample 7 mm from the MS inlet while the $\mu\text{-FAPA}$ was aligned at a 45° angle with respect to both the sample and MS inlet, at a distance of ca. 1-1.5 cm from the sample.

Vapor from organic solvents was generated by adding 4-10 μL of each solvent to a heated glass vial (8.5 mL), sealed with a septum. The vial was maintained at approximately 85°C with heating tape driven by a variable autotransformer (Staco, Dayton, OH). After a few minutes (to ensure complete solvent evaporation), 1-10 μL of the diluted solvent vapor were extracted from the vial by a glass syringe, and injected into a heated copper line. The line (ca. 15 cm length, O.D. 3.2 mm, I.D. 1.6 mm, and connected to a small metal tube, O.D. 1.56, I.D. 1.05 mm, at its end) was held at approximately 90°C by means of heating tape, with a He flow of 1.5 L/min. The helium and organic vapor exited the line into the space (ca. 10 mm) between the $\mu\text{-FAPA}$ and the MS inlet. The glass syringe used in the injections was washed with ethanol four times after each injection to avoid sample carryover.

2.8 Materials. All chemicals were of analytical reagent grade. The ESI tuning mix was purchased from Agilent (P/N: G2431A, Santa Clara, California). The samples used are detailed in Table 1.

2.9 Safety. Experiments described here involved direct-current high voltages (up to ca. 200 V) and currents (up to 75 mA). Such potentially dangerous currents should be employed with appropriate caution.

3. Results and discussion

3.1 FAPA design. Although the new $\mu\text{-FAPA}$ appears to be just a smaller version of the earlier h-FAPA, there are important differences. The $\mu\text{-FAPA}$ has an outer capillary area half that of the h-FAPA. As a result, though the outer electrode serves as the anode in the h-FAPA, it is the cathode in the $\mu\text{-FAPA}$ since it has a larger thermal mass and is heated the most [16]. Also, while both systems are constructed with two millimeters of

the central electrode exposed, the electrode-area ratio (outer to inner electrode) for the μ -FAPA is nearly double that of the h-FAPA (3 vs. 1.7). Therefore, the μ -FAPA discharge is dimensionally similar to a pin-to-plate configuration [16] (cathode larger than anode), whereas the h-FAPA discharge behaves more as a plate-to-plate configuration (cathode and anode areas comparable). These differences in size and electrode area lead to a much higher power density in the μ -FAPA discharge.

3.2 Current-voltage characteristics. Current-voltage curves for the μ -FAPA are presented in Figure 2, along with images of the discharge taken at particular current settings. For all currents (3-75 mA) one can observe the anode (inner) and cathode (outer) glows of the discharge. The positive column is not clearly visible, which is expected due to the closeness of the electrodes [29].

At a constant helium flow rate of 1.0 L/min and at low currents, the discharge does not fill the entire inner surface of the cathode (cf. Figure 2, top). As the current is increased, so does the coverage of the cathode surface by the discharge, which grows along the cathode circumference. The rise in surface coverage of the cathode leads to a linear increase in voltage with current, until a current of ca. 32 mA is reached and the discharge covers the cathode circumference completely. These findings are consistent with previous work with the h-FAPA [18]; raising the current further causes only small changes in voltage once the entire center capillary is covered. However, the establishment of the voltage plateau occurs at higher currents in the μ -FAPA. As was the case for the h-FAPA, this delay in covering the entire inner surface of the cathode is likely the result of misalignment of the concentric electrodes. However, the less substantial inner electrode of the μ -FAPA made this behavior more pronounced.

The steady voltage at currents above 30 mA fits the behavior characteristic of a normal glow discharge and is possibly the result of continued discharge growth along the (hidden) length of the cathode, transitioning from a toroid to a cylinder. Though voltage remains relatively constant, the increasing current leads to more reagent-ion production, brighter emission (see Figure 2 images), and higher gas temperatures (discussed in detail later). The source remained within the normal-glow domain through the entire range of currents (>25 mA) used for measurements described below.

At currents of 55 and 65 mA the stainless-steel cathode glows red and yellow, respectively (cf. photo in Figure 1). This incandescence is a result of heat transferred from the discharge, and indicates the stainless steel tube reaches temperatures of

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4 approximately 525-1200°C [30]. This behavior occurred at lower currents and after
5 shorter periods of time when lower helium flow rates were employed, suggesting that the
6 flowing stream of helium cools the electrodes somewhat. This cooling and the high
7 linear flow rate that develops within the small area between the electrodes is adequate
8 to cool the source and prevent the plastic connector from melting at all flow rates
9 examined. Additionally, if the current exceeds 70 mA, the afterglow extending from the
10 source becomes visible for about 1 mm beyond the outer tube (see Figure 1A).

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17 The discharge behavior was examined also at other gas flow rates. Even at the
18 highest tested He flow rate (1.5 L/min), the stainless-steel cathode began to glow red at
19 currents above 25 mA, though the glowing was delayed by more efficient gas cooling.
20 At this higher flow rate and at currents below about 25 mA, the discharge became less
21 stable. However, at higher currents and at a helium flow rate of 1 L/min, the source
22 could be operated stably for extended periods.

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29 **3.3 Thermal imaging.** Since thermal volatilization is believed to play a major role in the
30 desorption mechanism of plasma-based ADIMS sources [3], gas temperatures of the
31 new source were mapped with an IR camera as previously done by Shelley and
32 coworkers [17]. In particular, graybody emission was measured from a glass
33 microscope slide placed at a small angle in the path of the gas stream exiting the
34 source. Temperature maps, shown in Figure 3, ranged from approximately 100° C to
35 over 366°C, the highest temperature measureable by the IR camera.

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41 As shown in the plots at the bottom of Figure 3, the maximum measured
42 temperature was found to climb linearly with discharge current, and higher helium flow
43 rates resulted in lower surface temperatures. The qualitative reasons for this
44 observation are clear: greater source power leads to higher plume (and surface)
45 temperatures, while increased gas flows enhance the rate of heat transfer from the
46 sample and reduce local temperatures. Though the linear dependence of temperature
47 on current affords some degree of control over desorption of analytes, the specific
48 values should not be over-interpreted. Measured surface temperatures vary based on
49 the relative sampling location with respect to the source plume, and measured surface
50 temperatures are lower than the true temperature of the effluent from the source
51 because of the thermal mass of the microscope slide and heat loss to the surrounding
52 atmosphere. Under the same conditions (1 L/min He, 25 mA), the spatial-temperature
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4 gradient of the afterglow in the μ -FAPA was about 25% lower than it was for the pin-to-
5 plate source [31]. The plume visibly extended between 4 and 5 cm beyond the capillary
6 outlet when the source was operated at a current of 25 mA.
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10 Further, surface temperatures measured in these experiments are dependent on
11 factors such as target material, mass, shape, and its distance from the μ -FAPA source.
12 Thus, surface desorption temperatures might vary significantly for different sample
13 surfaces or substrates even under the same source conditions. For example, in
14 exploratory experiments the surface temperature of glass samples was found to be a
15 function of both sample mass, area, and sampling distance (see supplemental Figure
16 S1). As a consequence, direct comparisons of desorption temperatures achieved by
17 different sources, plumes, and substrates are questionable, and should be made only if
18 the experimental setup is identical.
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22 **3.4 Mass spectrometry results.** The μ -FAPA was evaluated as a desorption-ionization
23 source for mass spectrometric analysis of solid, liquid and vapor samples, with no
24 sample preparation. Figure 4 shows representative mass spectra from the analysis of
25 methamphetamine and lidocaine samples. In addition, a list of samples analyzed, along
26 with the base peak, fragments, and adducts are provided in Table 1. Over twenty
27 samples were examined, both in pure forms and as common mixtures, with examples
28 that include pharmaceuticals, small organic molecules, steroids, illicit substances, and
29 common solvents. For solid samples (see Figure S2 for representative spectra), the
30 maximum signal was attained in less than ten seconds from the time the μ -FAPA was lit.
31 The source exhibited no difficulty analyzing complex sample types (pharmaceutical
32 tablets, hydrocodone, aspirin and acetaminophen).
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36 Several conclusions can be drawn from these results. In general, mass spectra
37 show only minor fragmentation or adduct formation and the base peaks are
38 predominantly the protonated molecular ion. Most vapor samples listed in Table 1
39 produced only protonated molecular ions; the sole exception is acetonitrile. When
40 molecular fragmentation does occur for condensed-phase substances, it is often easily
41 interpreted to provide structural or confirmatory information. For example, the only major
42 fragment of methamphetamine in Figure 4A is from the loss of a methylamine group
43 ($MH^+-NH_2CH_3$). Similarly, many of the compounds listed in Table 1 show the loss of
44 common leaving groups (e.g. $M-OH$, $M-H_2O$), just as with other ionization sources.
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Mass spectra from the μ -FAPA exhibit fragmentation and adduct formation that are common in plasma-based ADI-MS systems, and in APCI sources in general. In contrast to ionization sources such as electrospray ionization (ESI), which employs proton transfer as the basis of almost all ionization, the FAPA discharge plume also contains radical reagent-ion species (e.g. NO^+) that promote charge-transfer ionization. Molecules with low proton-exchange reactivity often then form radical ions; for example, the mass spectrum of anthracene (cf. Table 1) shows an M^+ peak with a magnitude approximately equal to that of the protonated ion. Many other molecules show similar behavior, and the formation of $\text{M}-1$ and $\text{M}-2$ fragment ions is also found in Table 1; such fragmentation is common in electron-impact ionization sources.

The rich chemistry of the FAPA afterglow can also result in less conventional adduct species. For example, an adduct ion of lidocaine ($\text{M}+17^+$) is observed, which possibly results from the addition of O and H atoms, a combination that is not common in APCI and ESI spectra [32]. As with other ambient sources [33], the addition of atomic oxygen to form $\text{M}+16^+$ occurs for conjugated species (e.g. anthracene) in Table 1. Prior work has shown that formation of this adduct can be reduced simply by decreasing the influx of atmospheric species into the plume by extending the outside capillary in the pin-to-capillary version [17]. A similar design modification is underway for the μ -FAPA source.

Overall, the preponderance of the protonated molecular ion as the base peak, the presence of limited fragmentation, and the formation of specific adducts indicates that the μ -FAPA is a soft ionization source similar to previous FAPA designs [8, 18]. Indeed, spectra from the μ -FAPA source and halo-FAPA are virtually identical [18], supporting the hypothesis that similar desorption and ionization pathways are at work. The behavior suggests an ionization source that produces a large number of proton donors, but that also is able to ionize molecules by other pathways such as charge-transfer reaction.

To evaluate the mass range of the source, a commercial ESI tuning mix of phosphazenes was analyzed. The mix contains six phosphazenes, which yield MH^+ peaks at m/z of 322, 622, 922, 1522, 2122, and 2722. All of these masses are present in the spectrum (SI, Figure S3).

3.5 Quantification. The quantitative capabilities of the source were investigated with dried aqueous calibration standards. As indicated above, 2- μL solution samples were

deposited atop glass capillaries, introduced into the source afterglow plume, and the base-peak signal integrated until all material was removed (a period of about 10 seconds, until the signal returned to baseline levels). Care was taken to replicate sampling conditions for these experiments. However, variations in conditions, including sampling geometry, surface interaction between the analyte and the surface substrate, and volatility of the sample can affect this desorption period dramatically. Calibration curves were then constructed for several analytes (representative plots can be found in the SI, Figure S4). All curves were linear over a range of at least four orders of magnitude (see also SI, Table S1). Limits of detection for four aqueous-solution samples (acetaminophen, benzoic acid, caffeine, and melamine) were found to be in the sub-picomole range (34, 230, 160 and 790 femtomole, respectively). Depending upon the analyte, femtomole detection limits are typically observed for small molecules with other ADIMS sources, including DART[34] and DESI[35]. The relative molar sensitivity for these analytes is correlated with both their proton affinities, and their volatilities. Of course, limits of detection are dictated also by the chemical blank of the measurement. For example, although melamine has a higher proton affinity than acetaminophen, the two yield similar detection limits because of chemical noise in the determination of melamine.

3.6 Matrix effects. Concomitant substances that are more easily ionized than an analyte of interest and that are present in high abundance can suppress the response of the analyte ion, causing a matrix-dependent error. Because ADIMS is often applied to complex samples of unknown composition, and because the foregoing MS results suggest the main ionization pathway of the new source to involve proton transfer, the robustness of the μ -FAPA against competitive ionization was examined.

Samples of fixed concentration (7.5 mM caffeine) were doped with specific competing (matrix) substances, melamine and tris(hydroxymethyl)aminomethane (tris), at micro- to millimolar concentrations. Figure 5 shows the relative caffeine response in the presence and absence of various concentrations of matrix species. Competitive-ionization signal suppression was not observed until matrix concentrations were in the mM range, comparable to that of caffeine. If molecules with much lower proton affinities were to be determined, they might yield weaker signals; however, sensitivity would depend upon whether or not those molecules depend on protonation as an ionization pathway and whether species with higher proton affinities are present. Matrix effects for

such molecules would need to be evaluated independently for each analyte.. This behavior is on a scale similar to the signal suppression by competitive ionization described by Shelley and Hieftje [36]. As the proton affinities for both matrix substances are quite high (data provided in SI table S2), the relatively mild suppression suggests that the reagent-ion concentration from the μ -FAPA is high, despite its small dimensions.

4. Conclusions

A new source for ADIMS was developed, based on a previous h-FAPA design, but utilizing the afterglow of a direct-current microplasma. Current-voltage characteristics revealed the source to operate stably with currents up to 75 mA, and thermal imaging of graybody radiation from a glass slide inserted in the source afterglow revealed temperatures above 350°C were easily achievable at the sample surface. Samples in vapor, liquid and solid form were examined with ADIMS and revealed that the μ -FAPA source creates ions of similar type and signal magnitude as its larger counterpart. Most substances appeared to be ionized mainly by protonation, with little fragmentation or adduct addition. Adducts observed with the source were similar to those observed with conventional plasma-based ADIMS systems. The μ -FAPA source achieved sub-picomole limits of detection, with a linear dynamic range that extended over four orders of magnitude. The susceptibility of the source to competitive ionization was also examined and determined to be similar to that of prior FAPA sources, and better than most other ADIMS sources. The smaller dimensions of the μ -FAPA source, and its higher power density, seem to recommend the source for several future applications. Because the plume of the μ -FAPA is smaller than the one created by the prior h-FAPA system, this FAPA geometry (or a smaller one) might provide greater spatial resolution for rapid chemical imaging. Additionally, the smaller volume of the source results in less dilution of the analyte stream within the ionization volume, which should lead to higher S/N ratios. The use of the μ -FAPA with a separations system such as gas chromatography would seem to be advantageous for this reason. From these studies, the new μ -FAPA appears promising, and further applications are currently being pursued.

5. Acknowledgements

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Figure 1. A. Photograph of μ -FAPA (70 mA, 1.0 L/min He flow). Inset shows closeup of μ -FAPA tip and visible afterglow. B. Diagram of μ -FAPA. 1. PEEK Tee and ferrule (black) 2. Stainless-steel anode (dark gray) 3. Alumina insulator (white) 4. Stainless-steel cathode (light gray). Helium flow is in yellow, discharge afterglow in pink.

Figure 2. Top: Photographs of the μ -FAPA discharge at selected currents with a He flow rate of 1 L/min. Bottom: Current-voltage behavior of the μ -FAPA at particular He flow rates. Error bars indicate the standard deviation of five replicate measurements.

Figure 3. Top: Infrared temperature images of a glass microscope slide (25x75x1.0 mm, 4.7 g) placed in front of the μ -FAPA source, operated with discharge currents (from top to bottom) of 15, 25, 35, and 45 mA, at a helium flow rate of 1 L/min. False-color scale is on right; orientation of glass slide and source are below. Bottom: The highest glass temperature measured at several discharge currents and three He flow rates (0.5 L/min – black, 1.0 L/min – blue, 1.5 L/min - red). The near edge of the slide was located 0.8 mm from the capillary outlet of the source. Each value is the average of three measurements. Error bars are included but due to the small standard deviation, are hidden behind the data markers.

Figure 4. Representative mass spectra obtained with the μ -FAPA source for A. methamphetamine and B. lidocaine. In both spectra the dominant peak is the protonated molecular ion. The peak at m/z 119 in spectrum A is a methamphetamine fragment after the loss of two methyl groups. The peak at m/z 251 in spectrum B is lidocaine after a hydroxyl addition. Results for all collected spectra are summarized in Table 1.

Figure 5. Caffeine (7.5 mM) signal with different concentrations of A. Tris(hydroxymethyl)aminomethane (Tris), B. Melamine. Ion suppression, leading to lower signal, is observed only when additive concentration is in mM range.

Table 1. Sample material and state, base peak, fragments, and adducts for all substances examined with the μ -FAPA.

Sample	Base peak (m/z)	Notable coincident ions with predicted adducts and fragments (percentage of base peak by height)		Sample information
Acetaminophen (solution)	152 (MH ⁺)			Sigma Aldrich, BioXra, ≥99.0% pure
Acetaminophen tablet	152 (MH ⁺)	109 (-COCH ₃) 29.5% 110 (-COCH ₂) 46.4%	151 (M ⁺) 17.5%	TopCare, 500 mg
Acetone (vapor)	59 (MH ⁺)			EMD, ACS Grade
Acetonitrile (vapor)	42 (MH ⁺)	47 (+5H) 37.1% 70 (+COH) 23.8%	80 (unknown) 34.6% 118 (unknown) 22.5%	EMD, OmniSolv, HPLC grade
Acetophenone (vapor)	121 (MH ⁺)			Mallinckrodt, ACS grade
Anthracene (solid)	179 (MH ⁺)	165 (unknown) 21.4% 167 (unknown) 38.9% 178 (M ⁺) 85.4% 193 (-H+O) 44.9%	194 (M+O) 92.9% 195 (MH+O) 95.0% 196 (MH+OH) 25.8% 211 (MH+2O) 24.3%	Fluka Chemika, >99% pure
Ascorbic acid (solution)	141 (-35) (-2H ₂ O, +H)	95 (-CO ₄ H ₆) 70.0% 97 (-CO ₄ H ₄) 18.6% 111 (-4O, -H) 25.1% 113 (-CO ₃ H ₄) 37.2% 129 (-CO ₂ H ₄) 62.9%	131 (-2O, -C, -H) 20.9% 157 (-OH, -2H) 17.0% 159 (-OH) 15.9% 175 (-H) 18.4% 177 (MH ⁺) 70.1%	Fisher Scientific, 99.8% pure

Aspirin (Bayer chewable low dose aspirin)	121 (-C ₂ O ₂ H ₃)	122 (-C ₂ O ₂ H ₂) 57.9% 139 (unknown) 15.7% 163 (-OH) 83.9%	164 (-O) 35.5% 181 (MH ⁺) 22.7% 198 (unknown) 48.4%	Bayer, chewable low dose, orange flavored, 81 mg
Benzoic acid (solution)	79 (-COO)	105 (-OH) 28.2% 123 (MH ⁺) 46.6%	129 (unknown) 29.2% 147 (-H+CN) 23.3%	Mallinckrodt, ACS grade
Bupropion hydrochloride (300 mg, Watson)	240 (M ⁺)	184 (-C ₄ H ₈) 31.9% 241 (+H) 33.7%	242 (Cl isotope) 69.5%	Watson Labs, 300 mg, Extended Release
Caffeine (solution)	195 (MH ⁺)			Sigma, ACS grade
Escitalopram oxalate tablet	325 (MH ⁺)			Lexapro, 10 mg
Ethyl acetate (vapor)	89 (MH ⁺)			Mallinckrodt, ACS grade
Hydrocodone tablet	300 (MH ⁺)	184 (unknown) 32.8% 240 (-C ₂ O ₂ H ₃) 86.8%	242 (-C ₂ O ₂ H) 30.7%	Mallinckrodt Pharma, 500 mg
Hydrocortisone (solution)	363 (MH ⁺)	303 (-C ₂ O ₃) 68.4% 304 (-C ₂ O ₃ +H) 17.1% 345 (-OH) 50.1%	349 (-O, +3H) 18.9% 361 (-H) 21.4% 409 (unknown) 45.3%	Sigma Life Science, ≥98% Pure
Ibuprofen tablet	148 (-58) (-2C,-2O,-2H)	110 (unknown) 15.7% 163 (-2O,-C, +H) 22.8%	191 (-O, +H) 21.3% 206 (M ⁺) 34.8%	Advil, 200 mg
Lidocaine (solution)	235 (MH ⁺)	251 (+OH) 23.4%		Sigma, ≥98% pure
Methyl Ethyl Ketone (vapor)	73 (MH ⁺)			Mallinckrodt, ACS Grade

Melamine (solution)	127 (MH ⁺)	129 (+3H) 19.8%	147 (+3H, +H ₂ O) 17.6%	Aldrich Chemistry, 99% pure
Methamphetamine (solution)	150 (MH ⁺)	119 (-C ₂ H ₆) 55.7%	148 (-H) 43.3%	Restek, 1000µg/mL in acetonitrile
Progesterone (solution)	315 (MH ⁺)	313 (-H) 15.3% 316 (unknown) 65.0%	317 (unknown) 19.3	Sigma Life Science, suitable for cell culture
Salicylic acid (solution)	121 (M-OH ⁺)	139 (MH ⁺) 7.5%		Mallinkrodt, ACS grade

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