Molecular Ionization Desorption Analysis Source (MIDAS) for Mass Spectrometry

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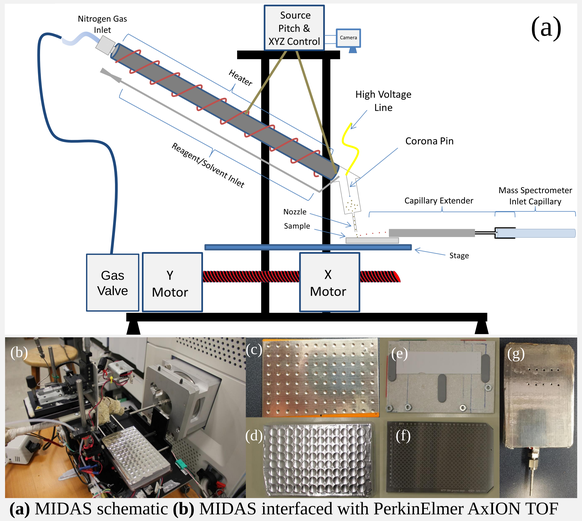
1 Introduction

The Molecular Ionization Desorption Analysis Source (MIDAS) is a Desorption Atmospheric Pressure Chemical Ionization (DAPCI) type ionization and sampling platform. MIDAS is an easy to use, versatile platform for the analysis of a variety of samples from different surfaces. MIDAS is computer controlled which allows for automated high throughput sample screening using interchangeable sample plates. MIDAS is controlled completely independently of the mass spectrometer and as a result can be used on a variety of mass spectrometers with atmospheric pressure inlets.

2 MIDAS Construction

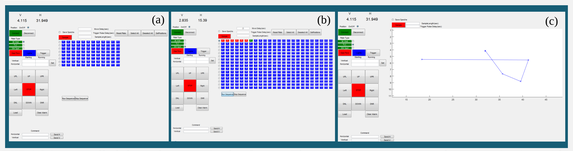


(a) MIDAS schematic **(b)** MIDAS interfaced with PerkinElmer AxION TOF Interchangeable sampling plates **(c)** small 96 well **(d)** large 96 well **(e)** TLC **(f)** 384 spot **(g)** vacuum plate to hold irregular samples

3 Instrumentation

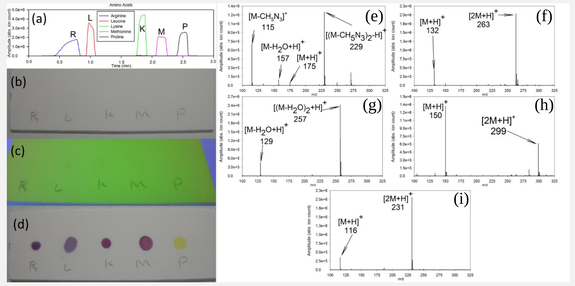
All of the flowing experiments were performed using a PerkinElmer AxION TOF mass spectrometer. No curtain gas was used at any time. No voltage was applied to the cylinder, endplate or capillary entrance at any time. Additional positive mode instrument parameters include capillary exit, skimmer, radio frequency (RF) and offset voltages of 175 V, 18 V, 470 V and 12 V, respectively. Additional negative mode instrument parameters include capillary exit, skimmer, RF and offset voltages of -100 V, -20 V, -450 V and -10.3 V, respectively. The MIDAS heater was set to supply nitrogen gas at a temperature of 180˚ C. Inlet nitrogen gas pressure was set at 40 PSI resulting in a linear velocity of 3.0 $m \cdot s^{-1}$ exiting the nozzle. Incident nozzle angle was set at 50˚ , nozzle to sample distance was 2.0 mm and source to inlet distance was 5.0 mm. In positive mode the corona electrode was operated at +3.0 kV and 6.0 µA, in negative mode -2.5 kV and 12 µA.

4 Software

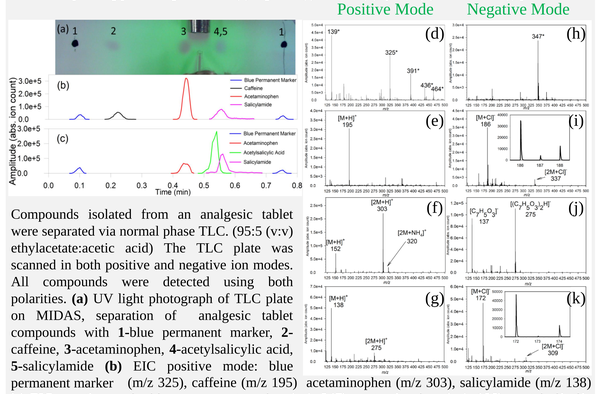


MIDAS is controlled through customized software. There are features to control communication with the computer, tray speed and position and gas valve operation. There are also options for selecting plate type **(a)** 96 well **(b)** 384 spot **(c)** TLC, which bring up additional options. Automated sequence analysis of the 96 well and 384 spot plates is possible with customizable timing options.

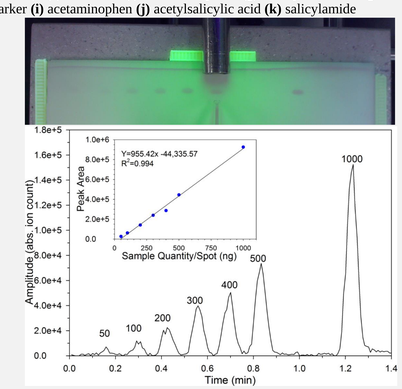
5 Applications



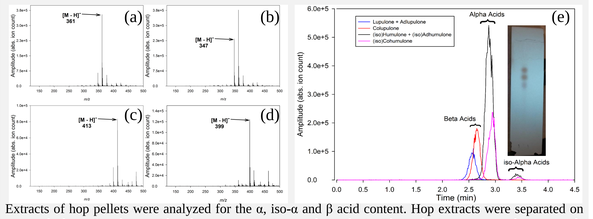
Five amino acids were spotted onto a silica gel TLC plate and analyzed directly create a representative chromatogram. This experiment illustrates the detection of compounds without the need to be able to visualize them prior to analysis. **(a)** Extracted ion chromatogram produced by directly scanning the TLC plate with the five amino acids **(b)** TLC plate under white light **(c)** TLC plate under 254 nm UV light **(d)** visualized amino acids after staining with ninhydrin. Representative mass spectra for each amino acid with corresponding peak assignment for **(e)** arginine **(f)** leucine **(h)** lysine **(h)** methionine **(i)** proline



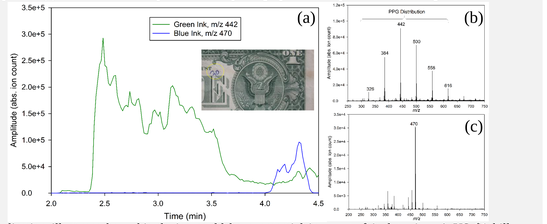
Compounds isolated from an analgesic tablet were separated via normal phase TLC. (95:5 (v:v) ethylacetate:acetic acid) The TLC plate was scanned in both positive and negative ion modes. All compounds were detected using both polarities. **(a)** UV light photograph of TLC plate on MIDAS, separation of analgesic tablet compounds with **1**-blue permanent marker, **2**-caffeine, **3**-acetaminophen, **4**-acetylsalicylic acid, **5**-salicylamide **(b)** EIC positive mode: blue permanent marker (m/z 325), caffeine (m/z 195) acetaminophen (m/z 303), salicylamide (m/z 138) **(c)** EIC negative mode: blue permanent marker (m/z 347), acetaminophen (m/z 186), acetylsalicylic acid (m/z 275), salicylamide (m/z 172). Mass Spectra of compounds obtained directly from the surface of the TLC plate. Positive Mode: **(d)** blue permanent marker (*species not identified, unique to permanent marker) **(e)** caffeine **(f)** acetaminophen **(g)** salicylamide. Negative Mode: **(h)** blue permanent marker **(i)** acetaminophen **(j)** acetylsalicylic acid **(k)** salicylamide



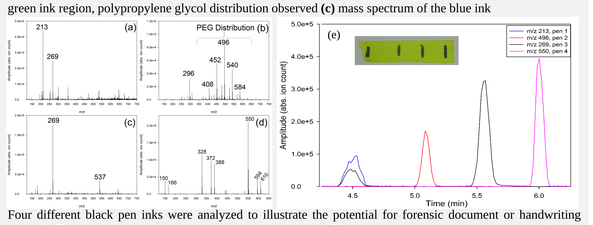
Quantitative performance of the device was illustrated using a calibration curve of caffeine spotted on a normal phase TLC plate. Sample concentration ranged from 50-1000 ng/spot. The plate was developed along the short axis to improve local sample concentration and improve response.



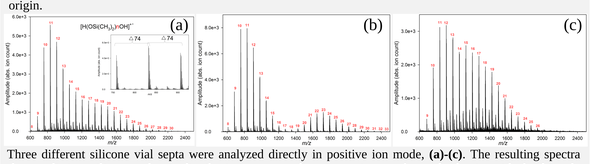
Extracts of hop pellets were analyzed for the α, iso-α and β acid content. Hop extracts were separated on reversed phase C_{18} plates with subsequent negative mode analysis. Three distinct groups of compounds were detected. All acids were detected as deprotonated species. Representative mass spectra for three groups of acids **(a)** (iso)humulone and (iso)adhumulone **(b)** iso(cohumulone) **(c)** lupulone and adlupulone **(d)** colupulone **(e)** EIC of the acid separation with photograph of TLC plate under UV light.



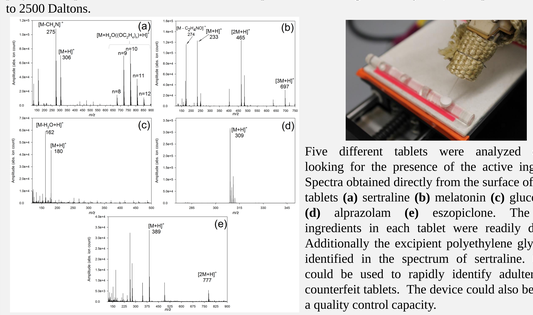
This application illustrates how this device could have potential in counterfeit detection. A US $1 bill was scanned directly using MIDAS in positive mode. This note had the number '30' written on it which could easily be distinguished **(a)** Extracted ion chromatogram of the two different ink regions **(b)** mass spectrum of the green ink region, polypropylene glycol distribution observed **(c)** mass spectrum of the blue ink



Four different black pen inks were analyzed to illustrate the potential for forensic document or handwriting analysis. Each pen produced a distinct mass spectrum, **(a)**-**(d)**. The identity of each of the observed species was not investigated further. The EIC, **(e)** also indicates that pens 1 and 3 share a common compound. These pens were from the same brand but different model. These experiments indicate that not only mass spectral fingerprints for specific pens can be obtained, but potentially more general information about manufacturing origin.

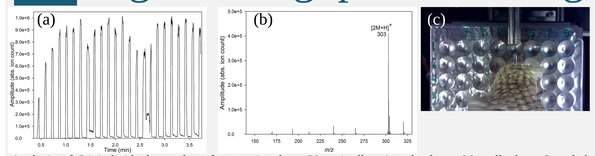


Three different silicone vial septa were analyzed directly in positive ion mode, **(a)-(c)**. The resulting spectra show a distinct silicone polymer distribution corresponding to varying numbers of subunits with the formula $[H(OSi(CH_3)_2)_nOH]^{+\bullet}$. Despite all being silicone, each can easily be distinguished based on the different polymer composition. Also illustrated here is the potential mass range for the system, with species observed up to 2500 Daltons.

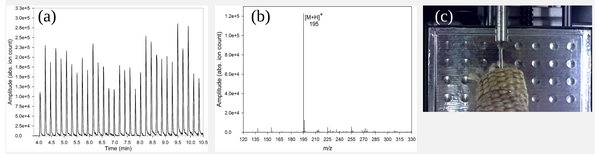


Five different tablets were analyzed directly, looking for the presence of the active ingredient. Spectra obtained directly from the surface of various tablets **(a)** sertraline **(b)** melatonin **(c)** glucosamine **(d)** alprazolam **(e)** eszopiclone. The active ingredients in each tablet were readily detected. Additionally the excipient polyethylene glycol was identified in the spectrum of sertraline. MIDAS could be used to rapidly identify adulterated or counterfeit tablets. The device could also be used in a quality control capacity.

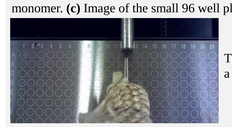
6 High Throughput Screening



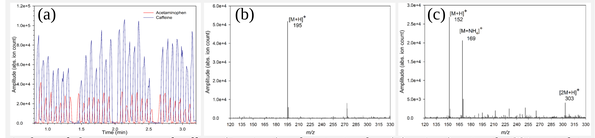
Analysis of 24 individual samples of acetaminophen, 50 ng/well, using the large 96 well plate. Sampled continuously without use of the gas valve. **(a)** Sample carryover is observed in the EIC as the tray is moved to the next row. **(b)** Acetaminophen is detected primarily as a protonated dimer. **(c)** Image of the large 96 well plate on MIDAS



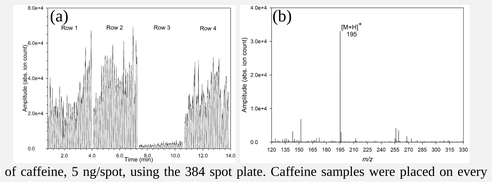
Analysis of 31 individual samples of caffeine, 2.5 ng/well, using the small 96 well plate. Sampled continuously without use of the gas valve. To avoid carryover, the tray was paused in between each sample well to allow time for the signal to return to baseline **(a)** EIC of the caffeine signal **(b)** Caffeine is detected as a protonated monomer. **(c)** Image of the small 96 well plate on MIDAS



The following experiments were preformed using a stainless steel 384 spot plate.



Analysis of alternating spots of caffeine (5 ng/spot) and acetaminophen (50 ng/spot), using the 384 spot plate. Sampled continuously without use of the gas valve. Sampling spatial resolution is approximated to be 3-4 mm and as a result signal overlap is observed **(a)** EIC of the caffeine and acetaminophen signals **(b)** Caffeine is detected as a protonated monomer. **(c)** Acetaminophen is detected as a protonated monomer and dimer as well as with an ammonium adduct.



Analysis of caffeine, 5 ng/spot, using the 384 spot plate. Caffeine samples were placed on every spot on rows 1, 2 and 4 with row 3 left as a blank. Sampled discretely using the gas valve. The gas valve is automatically closed when the tray is moved to prevent ionization, then opened when the next spot is reached for sampling. **(a)** EIC of the caffeine signal **(b)** Caffeine is detected as a protonated monomer. Using the gas valve signal carryover is eliminated.

7 Conclusion

MIDAS represents a useful tool for mass spectrometry and general analytical chemistry. The system allows for rapid analysis of a samples with automated analysis capability. The use of interchangeable sampling plates provides the ability to quickly change between different experiments. External controls allow the MIDAS to be used on a variety of instrumentation with minimal adaptation.

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