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Abstract

In this work, the combined use of desorption by a continuous wave near infrared diode laser and ionization by a dielectric barrier discharge-based probe (*laser desorption dielectric barrier discharge ionization mass spectrometry (LD-DBDI-MS))* is presented as an ambient ionization method for the mass spectrometric detection of non-volatile chemicals on surfaces. A separation of desorption and ionization processes could be verified. The use of the diode laser is motivated by its low cost, the ease of use and the small size. To achieve an efficient desorption the glass substrates are coated at the back side with a black point (target point, where the sample is deposited) in order to absorb the energy offered by the diode laser radiation. Subsequent ionization is accomplished by a helium plasmajet generated in the dielectric barrier discharge source. Examples on the application of this approach are shown in both positive and negative ionization modes. A wide variety of multiclass species with low vapor pressure were tested including pesticides, pharmaceuticals and explosives (reserpine, roxithromycin, propazine, prochloraz, spinosad, ampicillin, dicloxacillin, enrofloxacin, tetracycline, oxytetracycline, erythromycin, spinosad, HMX and RDX). A comparative evaluation revealed that the use of the laser is advantageous compared to just heating the substrate surface.

Keywords: ambient mass spectrometry; dielectric barrier discharge; explosive detection; surface analysis.

Introduction

Mass spectrometry (MS) has several advantages in sensitivity, speed and selectivity over other methods of chemical analysis. However, the application of MS is limited in part by the requirements for sample preparation. Often the sample must be placed in vacuum for analysis (e.g. matrix-assisted laser desorption/ionization (MALDI)[1] or dissolved or extracted in a solvent and sprayed in atmosphere (e.g. electrospray ionization mass spectrometry (ESI-MS)[2]. Therefore, a new concept of transferring ions into the mass spectrometer without any sample-manipulation or sample-preparation steps is demonstrated by a rapid introduction of at least 15 new methods in the last few years.[3-8]

These so-called ambient MS techniques can be separated into three different groups: a) desorption and ionization in one step, b) separation of ionization source and analyte source, and c) ionization followed by desorption.

In the first group "desorption and ionization in one step" ionization techniques like ESI, corona discharge and different other discharges are applied as desorption combined with ionization technique and are named: Desorption electrospray ionization (DESI)[9], desorption APCI (DAPCI)[10], desorption sonic spray ionization (DeSSI)[11], atmospheric pressure thermal desorption ionization (APTDI)[12], direct analysis in real time (DART)[13], plasma-assisted desorption/ionization (PADI)[14], low temperature plasma (LTP)[15], and dielectric barrier discharge ionization (DBDI)[16].

The second group "extractive electrospray ionization (EESI)"[17] is only described by one single experiment which shows indirectly that the desorption source could be separated from the ionization source. In this case a reagent spray and a sample spray were applied as two separate sprayers, one to nebulize the sample solution and the other to produce charged microdroplets of solvent.

The third group "desorption followed by ionization" covers measurements, where the desorption-process is separated from the ionization process. Disregarding atmospheric-pressure solids analysis probe (ASAP)[18] all other mentioned techniques like electrospray-assisted laser desorption/ionization (ELDI)[19], laser ablation electrospray ionization (LAESI)[20] and thin layer chromatography diode laser desorption atmospheric pressure chemical ionization (TLC-DLD-APCI)[21,22] apply a laser for the desorption process.

The use of a spatially well-defined energy source, such as a laser, can be used for desorption and ionization. However, in the absence of matrix, laser desorption is limited to the analysis of

low molecular weight compounds[23]. Although in MALDI an intact protein ion signal is obtained, introduction of the matrix into the solid sample without changing the surface structure remains a challenge for MALDI imaging.

It is widely recognized that the number of neutrals desorbed by the laser beam far exceeds the number of ions[24]. However, in the absence of matrix, the technique is still limited to the study of relatively low molecular weight compounds, and attempts to analyze proteins have largely failed. ESI has seldom been used as a post-ionization method. Yet, the principle of ionizing proteins by mixing the material with an ESI plume has been successfully applied[25]. The upper mass limit of laser desorption has been overcome by using ESI to post-ionize neutral protein molecules generated by laser desorption. Moreover, by using a laser for analyte desorption and electrospray for its ionization, the process of desorption is separated from the ionization process.

In this paper, a combination of desorption by a continuous wave near infrared diode laser and ionization by a dielectric barrier discharge as ionization source is presented. This technique can be used in order to detect non-volatile chemicals. The use of the diode laser is motivated by its low cost, the ease of use and the small size. To achieve an efficient desorption the glass substrates are coated at the back side with black ink in order to absorb the energy offered by the diode laser radiation.

Several publications about ambient ionization mass spectrometry have been published for example for the screening of agrochemicals in foodstuffs using LTP[26] or electrospray[27] ionization or the detection of explosives and related compounds[28] by LTP ambient ionization mass spectrometry. The latter technique is most useful for analyzing compounds with relatively high vapor pressure. By supplemental heating the detection limits could be further improved by at least an order of magnitude for twelve of the fourteen drugs of abuse investigated[29]. Despite these compelling characteristics of LTP technique, some pharmaceuticals cannot be detected at any condition with LTP probe[30]. The thermal assistance was applied directly to the substrate surface and was limited to temperatures of ca. 120 ºC. Therefore, the potential of using a continuous wave near infrared diode laser for desorption was investigated and detailed in this study. Ionization was carried out by a dielectric barrier discharge-based probe. A set of non-volatile chemicals exhibiting low vapor pressure, and thus a priori difficult to desorb from surfaces, was selected to evaluate the performance of the presented method.

Experimental section

Chemicals. A set of different chemicals (pesticides, explosives and drugs) with varying molecular weights and low vapor pressures have been selected for this study. HPLC-grade acetonitrile and methanol for the preparation of standard stock solutions were obtained from Merck (Darmstadt, Germany). Analytical grade standards for individual compounds were purchased from Sigma-Aldrich (Madrid, Spain), Dr. Ehrenstorfer GmbH (Augsburg, Germany) or Riedel-de-Haën (Seelze, Germany). Individual standard stock solution (*ca.* 500 mg L^{-1}) were prepared in methanol and stored at -20ºC. HMX and RDX, standards were purchased as 10 mg L^{-1} solutions in methanol/acetonitrile (1:1) from AccuStandard Inc. (New Haven, CT). Then, working standards solutions were prepared by serial dilutions with methanol.

Mass spectrometry. An LCQ Classic ion trap mass spectrometer (Thermo Finnigan, USA, year of manufacturing: 1999) was used in both positive and negative ionization modes as required and full-scan acquisition over the range *m/z* 100 to 1000 depending on each individual experiment. Data were acquired and processed via the Xcalibur software (Thermo Finnigan, USA). The capillary voltage of the mass spectrometer was set to 41.5 V, the tube lens offset voltage to 43 V, and the capillary temperature was maintained at 200 ºC. The ion injection was set to AGC (automatic gain control) mode for a maximum number of charges of 5×10^7 and a maximum ion trap injection time of 50 ms with 3 microscans per spectrum. The electrospray ionization source of the instrument was used for calibration and tuning with the available reserpine and calibration mix solutions recommended for this purpose.

Dielectric Barrier Discharge Ionization Probe. Ionization was carried out by a DBD microplasma probe described elsewhere as an ionization source for LC/MS[31-35]. The plasma was operated with a helium (99.999% purity) flow of 200 mL/min. The DBD consisted of a 3-cm long glass capillary with an inner diameter of 500 μm and an outer diameter of 1.2 mm (*ca.* 5 μL of gas capacity). Rings with an inner diameter of 500 μm are located around the capillary, forming electrodes with a separation distance of 12 mm. The distance of the electrode to the end of the capillary is 2 mm. A periodic voltage pulse (4.5 kV with a frequency of 20 kHz and a

pulse width of 2 µs) is applied. The plasma electrodes are enclosed in a Teflon tube not only for safety precautions but also to prevent a discharge between the electrodes outside the capillary. This Teflon tube containing the DBD is called "plasmajet" which is directed axially towards the MS inlet.

Laser assisted thermal desorption dielectric barrier discharge ionization mass spectrometry.

Figure 1 shows a scheme and a photo of the experimental assembly consisting of a diode laser, glass target where the sample is deposited, a DBD-plasmajet and a LCQ Classic ion trap mass spectrometer from which the inlet is presented. The distance from the laser spot on the glass target to the front of the heated capillary inlet (transfer capillary) of the LCQ Classic ion trap mass spectrometer was 2.5 mm and the target is 1 mm below the axis of the transfer capillary. The DBD-jet was positioned on axis of the transfer capillary with the jet tip 25 mm far away from the inlet and therefore 1 mm above the glass target. Both, the target as well as the DBDI source could be moved by xy-stages in order to optimize the geometrical conditions. A laser beam from a diode laser (OTF 30P-40 from OPTOTOOLS) with a wavelength of 808.8 nm guided by an optical fiber is aligned on the sample spot of the target and desorbs analytes from the surface of the sample substrate (glass slide). The laser beam with a maximum power of 16.8 W is focused on the surface with a calculated spot diameter of 50 µm resulting in a maximum power density of 8.6×10^5 W/cm^2. In the following experiments a power of 2.6 W corresponding to a power density of 1.3×10^5 W/cm^2 was applied. Since the laser wavelength is 808.8 nm, most of the analytes have no absorption in this wavelength range. Therefore, the analytes can sustain this power density (fluence) without being damaged. Fluences of used pulsed lasers are three orders of magnitude higher.

The desorbed molecules are transferred to the plasmajet, where they are ionized and subsequently transported into the inlet of the mass spectrometer. 1W focused on the same spot diameter of 50 µm is presumably near to the 'threshold' for desorption by a continuous wave near infrared diode laser when a black surface is the target of the analytes. Spectra with similar intensities can be obtained at 2W, whereas at 4W a marginal improvement in signal intensity can be expected, which can often be cancelled by poor sample-to-sample reproducibility and resulted

in notable increase of background noise[21]. To achieve efficient desorption, glass substrates were used which were coated at the back side with printed black dots of 3 mm diameter.

< **Figure 1**>

Thermal desorption dielectric barrier discharge ionization mass spectrometry. An aliquot of 1 µL of sample solution was deposited on a glass slide. The temperature was controlled by means of an electrically heated copper-block (see **Figure 1**). In this experiment, laser is turned off so that desorption is only prompted by heating the surface where the sample is deposited.

Safety Hazard Note. The employed continuous-wave diode laser is of laser safety class 4. Safety precautions have to be taken when working with free beams of such lasers by wearing protective goggles.

Results and discussion

Preliminary studies and general considerations

Based on the extended use of plasma-based ambient ionization sources such as LTP, DART, PADI and other related techniques[13-15], we hypothesized the eventual use of DBDI plasmajet, primary designed as ionization source for LC/MS[31-32] as a plasma-based ambient ionization method.

Different preliminary experiments were performed with the plasmajet oriented towards the sample or at positions/angles in which both desorption, ionization and ion transportation were successfully accomplished. Positive results were obtained when testing relatively volatile species such as acetaminophen even in condensate form such as tablets.

Compared to other ambient methods, the direct DBDI is much more sensitive on the position of the sample in front of the mass spectrometer, the angle of the laser beam in respect to the sample as well as to the mass spectrometer inlet axis.

Interestingly, these observations regarding geometrical dependence contrast with other similar (based on the same DBD principle) ambient ionization sources described in the literature, particularly in the case of low temperature plasma (LTP) probe[15], characterized by a low

dependence on the angle/geometry between the LTP probe and the MS inlet[28]. This feature enables different experiments involving desorption and ionization steps if the probe is close enough to both, the target sample and the MS inlet. For instance direct interrogation of liquid surfaces was described by Harper *et al*.[15]. Both the carrier gas (helium) flow rate used and the relative position of the inner pin electrode also exerted an impact on the optimized distances between probe, sample and MS inlet.

The features of both LTP probe and DBDI plasmajet are summarized in **Table 1**. One of the main differences that could explain this effect is the size of the plasma and the subsequent volume of the afterglow responsible for desorption, ionization and transportation effects in LTP experiment. The ruggedness of geometrical issues in LTP contrasts however with the hampered ability to produce images with a reasonably high spatial resolution (*e.g.* below 250 μm). In an attempt to improve spatial resolution and imaging capabilities, Liu *et al.*[36], proposed the use of decreasing inner diameters of the LTP probe down to 100 μm in order to improve spatial resolution of LTP and successful application to artwork imaging was presented.

<Table 1>

With all these considerations, and with the previous experience on the use of the DBDI plasmajet as an effective LC/MS interface obtaining efficient ionization of different species in both positive and negative ion mode with picogram sensitivity at the level of commercially available APCI/ESI sources[31], we considered that the analytical performance of the combination of DBD-based ionization with the aid of a diode laser (to promote desorption step) should be explored.

Two experiments were envisaged: (1) the use of a continuous wave diode laser (because of ease of use and prizing) and (2) a device (copper-block electrically heated where sample substrate (glass slide) was deposited) to heat the sample target in order to prompt thermal desorption of analytes prior to ionization with the DBDI plasmajet. The use of a heated sample substrate was proposed to extend the applicability of LTP probe to low volatile or low vapor pressure species[28]. In this sense, several authors have reported on thermal desorption as the main desorption mechanism in the ambient ionization sources[4-7,9,15,17,19,37-42]. However, recent experimental data has evidenced that different mechanisms (likely involving high-speed particles/surface

collision/sputtering) to thermal desorption are responsible for desorption of selected chemicals by LTP probe[20].

Diode Laser Desorption DBDI ambient mass spectrometry: setup and optimization

The herbicide propazine was selected as the model compound to optimize the experimental set-up. This compound was sensitive to DBDI ionization in the positive ion mode (*m/z* 230)[32] and showed two characteristic fragment ions with *m/z* 188 and 146 (**Figure 2a and 2b**). **Figure 2a** depicts measurements of propazine on glass target, whereas **Figure 2b** shows results with an additional black dot under the glass plate. It is obvious that in the case of the glass substrate without the black dot the signal increases with the switch on of the laser without a pronounced maximum, whereas in the case with the black dot under the glass surface a signal of 12 s length is measured. In this case, the protonated molecule signal is more intense than the fragment ions in contrast to the case without black dot, where the fragment ion is as high as the protonated molecule.

In addition to compounds such as propazine, higher molecular weight species with extremely low vapor pressure were also tested, using as a reference a set of species interrogated with LTP-MS with inferior results[30]. As an example of the implementation of LD-DBDI-MS, **Figure 2c** shows the mass spectra obtained from roxithromycin. As can be noticed in **Figure 2a** and **Figure 2c**, when a black dot is below the glass substrate the nature of the signal is transient after turn on laser and usually lasts for 6-12 s, depending on experimental conditions. Different parameters affecting the performance of the experiment were evaluated including the spotted sample volume or laser power applied.

< **Figure 2** >

Study of sample volume, sample spot size and diode laser desorption. 3 μL were selected as sample volume in preliminary studies based on previous experiences[15,27-28]. Therefore, we decided to test a small volume, 1 μL, and check the differences in the desorbed area and intensity. Either 1 or 3 μL of a methanolic solution of propazine (410 mg L^{-1}) were brought on a glass substrate with a thickness of 100 μm and on another glass substrate of the same thickness but with a black dot at the backside. The methanol was allowed to evaporate within less than 5

min at room temperature. In the case of the glass substrate without the black dot the signal increases with the switch on of the laser without a pronounced maximum, whereas in the case with the black dot under the glass surface a signal of 6-18 s length is measured. In both experiments, a transient signal was obtained although when using the substrate with a dark surface underneath the target the laser energy was absorbed more efficiently providing an overall higher signal. Results shown throughout the text are mass spectra averaged form 3-5 seconds of maximum value of analyte signal.

Figure 3 shows photos obtained by a microscope from two glass slides with printed black ink dots of 3000 µm diameter at the backside. On the front side of one glass slide a 1 µL droplet of 410 mg L^{-1} propazine in methanol was positioned on a spot where the ink is located. On the other one a 3 µL droplet was positioned. The area covered by the dried samples can be recognized by the many small crystal like spots on the surface shown in the two pictures before laser desorption. The 1 µL dried sample covers an area on the front side which is smaller than the area of the ink dot (3000 µm), while the 3 µL dried sample is larger. Pictures taken after laser desorption show a bright area which is visible in the middle of the sample spots. This area is marked by a diameter arrow of 500 µm and shows the surface which is ablated from the black ink dot at the backside of the slide. Therefore, the light of the microscope passes this area without any absorption and is therefore brighter than the surrounding where the black ink is still at the back surface. The less bright area marked with a diameter arrow of 1600 µm around the ablated surface is the area, where the sample is desorbed from the front side of the slide. In the case of the 1 µL dried sample the dried surface of the sample was smaller than the black dot area on the backside and in the case of the 3 µL vice versa. But both dried sample surfaces exceed the size of the less bright area. Therefore, the obtained signal height measured for propazine was in both cases comparable with that shown in **Figure 2b**.

< **Figure 3** >

In both experiments, during the laser irradiation a similar sized part of the black dot with a diameter of 500 µm is ablated. The diameter of the laser focus is 50 µm. When the laser is started the surrounding of the laser spot at the backside of the glass slide is heated. The temperature threshold for ablation is reached at a radius of 250 µm and the temperature threshold

for desorption in respect to the temperature conductance through the glass slide is reached at a radius of 800 µm. Therefore, from the size of the area which is desorbed the amount of desorbed sample can be calculated. A 3 µL sample of 410 mg L^{-1} propazine in methanol gives a dried surface with a diameter of 4 mm. The desorbed area has a diameter of 1.6 mm and is therefore by a factor of $(4 / 1.6)^2 = 6.25$ smaller. With a 3-µL sample aliquot of 410 mg L^{-1} propazine, an absolute amount 1.23 µg of propazine will be distributed on the droplet surface. Therefore, the absolute amount of the desorbed solute is *ca.* 200 ng. A similar amount of sample is desorbed when a 1-µL sample aliquot is probed. Taking into account the factor corresponding to the desorbed area, optimized sensitivity could be expected when the width of the laser-focus will be increased so that the threshold intensity $I_{th,d}$ at the edge of the dried sample will be sufficient for desorption.

Influence of laser power and laser-target positioning. Diode laser power was studied between 0.4 a 4 W. Depending on the analyte vapor pressure an increased power is required. For instance, in the case of cocaine (relatively volatile) optimized signals could be obtained even with 1 W. The transient signal length can be modulated by varying the applied diode laser power. Higher laser power will be associated to shorter and steeper signals. As a default value for the experiments 2.6 W was used for all the tested analytes.

Different relative positioning geometries between laser and target were tested in order to find the most favorable position to enhance the analyte signal. When the laser was focused on the glass surface, less power was necessary to desorb the analytes, but the desorbed area was smaller. However, if the laser was not focused on the glass plate to have a wider desorption area, less sensitivity was obtained for propazine, even when increasing the laser power. A distance between laser and target of 130 mm was used which was associated to a laser spot size of ca. 50 µm.

Diode laser desorption DBDI ambient mass spectrometry: analytical performance.

Detection of selected non-volatile pesticides and pharmaceuticals. A set of non-volatile chemicals exhibiting low vapor pressure and therefore a priori difficult to desorb from surfaces was selected. Different pharmaceuticals with low vapor pressure (ampicillin, ciprofloxacin,

dicloxacillin, enrofloxacin, erythromycin, oxytetracycline, tetracycline, reserpine and roxithromycin) and some pesticides (spinosad, prochloraz, propazine) were tested with the proposed diode laser desorption DBDI ambient mass spectrometry method. Previous studies using LTP probe even with a heated substrate at 120 ºC did not produce the satisfactory desorption of these species[30]. However, the use of the proposed combination laser-DBDI yielded positive results of all the tested species. **Figure 4** shows the LD-DBDI-MS analyses of selected pharmaceuticals (tetracycline, oxytetracycline and erythromycin) and a pesticide (spinosad) using standard solutions of 3 µL acquired in the positive ionization mode with the ion trap operated in full-scan mode. Interestingly, in the case of relatively low-molecular weight the protonated molecule ($[M+H]^+$) was not the base peak of the mass spectrum. Fragment ions from typical neutral losses were obtained instead, such as the case of tetracycline, where the abundance of *m/z* 445 ($[M+H]^+$) is one fourth of *m/z* 410, originating from subsequent ammonia (*m/z* 428) and water neutral losses. Similar fragmentation pattern was observed in the case of related oxytetracycline, being the ammonia loss ion ($[M - NH_3 + H]^+$) with *m/z* 444 and the subsequent loss of water (*m/z* 426) more abundant than the protonated molecule. In the case of molecules with higher molecular weight lower fragmentation degree was observed. Exemplarily, spinosad yielded the two main peaks corresponding to the commercial mixture (Spinosyn A (*m/z* 732) and Spinosyn D (*m/z* 746), along with a characteristic fragment ion with *m/z* 142, corresponding to a sugar moiety as reported elsewhere[44]. Finally, in the case of erythromycin, along with the protonated molecule, two characteristic diagnostic ions of the antibiotic are also observed (*m/z* 558 and *m/z* 576).

< **Figure 4** >

Detection of low-vapor pressure explosives by LD-DBDI-MS. Many organic high explosives, particularly those found in plastic explosives, do not produce a sufficient vapor pressure to allow headspace vapor detection[45]. This is the case for both cyclo-1,3,5-trimethylenetrinitramine (RDX) (vapor pressure: 4.4 x 10^{-9} torr at room temperature) and cyclo-1,3,5,7-tetramethylenetetranitrate (HMX) (vapor pressure: 3 x 10^{-9} torr (at 100 ºC)). Both species have a very low volatility and therefore are difficult to analyze by traditional ionization methods. Diode laser DBDI-MS spectra of both RDX and HMX are shown in **Figure 5**. A 3- µL aliquot of 10 µg/mL was spotted on a glass slide (with a black ink dot at the backside) and the solvent was

allowed to evaporate for five minutes. Standard full-scan negative ion mode conditions allowed the detection of 30 ng of each explosive with signal-to-noise ratio of about 10. The identification of the target explosives in this case was accomplished by use of characteristic adducts ions formed for each compound with nitro groups: *m/z* 284 ($[M + NO_2]^-$) for RDX, and *m/z* 358 ($[M + NO_3]^-$) and *m/z* 342 ($[M + NO_2]^-$) for HMX, as it has been reported by DART[46] and LTP[15]. A thorough investigation of these adduct ions was carried out by Gapeev *et. al*. applying isotopically labeled compounds[47]. It was demonstrated that in APCI some of the RDX molecules decompose, yielding NO_2^- species which in turn cluster with other RDX molecules, thus producing abundant $[M+NO_2]^-$ cluster ions.

< **Figure 5** >

LD-DBDI-MS vs. DBDI-MS with heated substrate. In addition to the implementation of the diode laser, an alternative experiment using a heated substrate to promote thermal desorption of analytes was also implemented. As an example of this configuration, **Figure 6** shows the DBDI-MS spectra of fungicide prochloraz using a heated substrate glass slide at different operating temperatures between 100 and 200 º C. The mass spectrum presented the protonated molecule (*m/z* 376) and a main fragment (*m/z* 308), both ions showing a typical three-chlorinated isotopic pattern. There is a great increase in the signal from 100 °C to 150 °C (*ca.* one order of magnitude). At a heating temperature of 200 °C, the signal increases and the ratio protonated molecule/fragment increases, too.

< **Figure 6** >

Nine pharmaceuticals of high vapor pressure (ampicillin, ciprofloxacin, dicloxacillin, enrofloxacin, erythromycin, oxytetracycline, tetracycline, reserpine and roxithromycin) and three pesticides (spinosad, prochloraz, propazine) were selected for a comparative experiment between: (a) DBDI with heated substrate by means of a copper-block electrically heated and deposited below the glass substrate, and (b) diode laser desorption DBDI. The studied pharmaceuticals had been reported as not detected by LTP-MS[30] with heated substrate (at 120 ºC); they were also not detected by DBDI-MS when the glass substrate - where the sample is deposited - was heated at 150 °C. The minimum heating temperature to detect spinosad, ampicillin, reserpine and roxithromycin is 200 °C. Dicloxacillin was even not detected at 200 °C.

A detailed comparison of the results obtained is included in **Table 2**. Except in the case of the pesticide prochloraz, which yielded better results with heated substrate, the use of diode laser desorption was more rugged and effective. Typical reproducibility of the experiments with LD-DBDI-MS were in the range from 10-20% (n=3).

< **Table 2** >

Conclusions

The potential of combining diode laser desorption and dielectric barrier discharge ionization for ambient mass spectrometric interrogation of nonvolatile chemicals on surfaces has been demonstrated. Different species which were not desorbed and ionized solely by means of DBDI based ambient mass spectrometric methods were tested and successfully detected when combining DBDI with diode laser desorption. The optimization of laser spot size may be effective for improving the analytical performance of the approach and also to establish MS imaging capabilities.

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Figure captions

Figure 1. Experimental set-up of diode laser desorption dielectric barrier discharge ambient ionization mass spectrometry (LD-DBDI-MS). Different experiments were accomplished: DBDI without the use of laser; DBDI using heated substrate (glass slide heated at 150 -200 º C) and the combination laser + DBDI.

Figure 2. Diode Laser Desorption Dielectric Barrier Discharge Ambient Ionization Mass Spectrometry (LD-DBDIMS) spectrum of 1.2 μg of propazine deposited on a glass slide, using an ion trap LCQ Classic. Time dependent signal and intensities of the intact molecule and fragment ions of propazine are showed in dependence on the surface: a) without black dot under the surface, b) with black dot under the surface. c) LD-DBDI-MS time dependent signal and corresponding mass spectrum of 1.5 μg of roxithromycin deposited on a glass slide with black dot under the surface.

Figure 3. Microscope-pictures of glass slides with a black ink dot (diameter: 3000 μm) at the backside with 1 μL and 3 μL dried sample of ca. 400 mg L^{-1} propazine in methanol before and after laser desorption. Dried sample surface of a 1-μL aliquout is smaller than the black dot whereas 3-μL aliquot is larger. Bright spot (diameter: 500 μm) is an ablated area of the ink dot and the less bright spot (diameter: 1600 μm) is the area of the desorbed propazine methanol sample.

Figure 4. Diode laser desorption DBDI-MS spectrum of 1.5 μg of tetracycline (a), oxytetracycline (b), erythromycin (c) and spinosad (d) deposited on a glass slide, using an LCQ Classic ion trap.

Figure 5. Laser desorption DBDI-MS spectrum of 30 ng of non-volatile explosives HMX (a) and RDX (b) deposited on a glass slide, using an LCQ Classic ion trap in the negative ionization mode (full-scan *m/z* range 100-500).

Figure 6. DBDI mass spectra of prochloraz (0.5 μg deposited on a glass slide) obtained using heated substrate at different temperatures: 100 ºC; 150 ºC; 200 ºC.

Figures

Figure 1

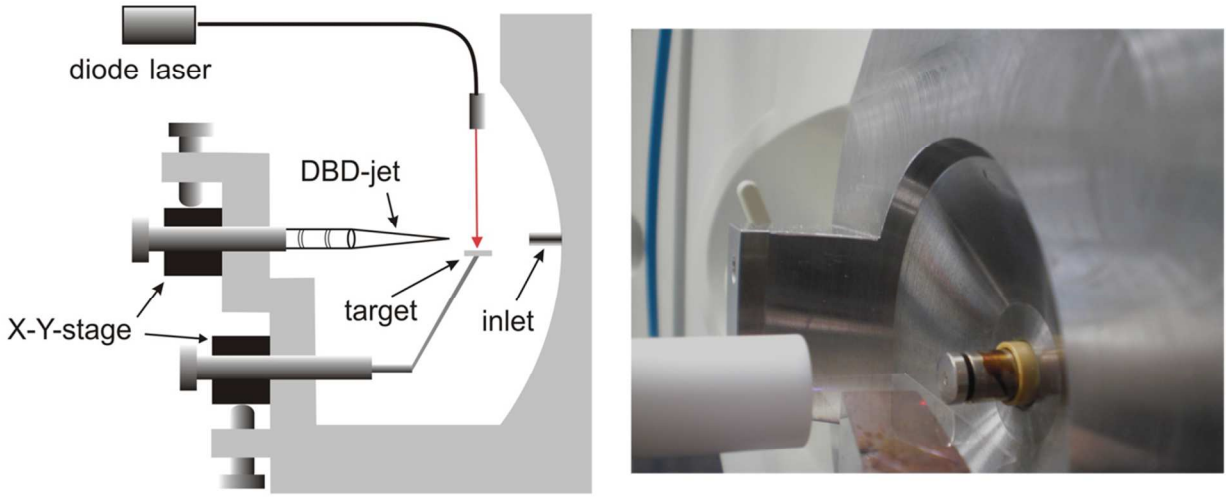


Figure 2

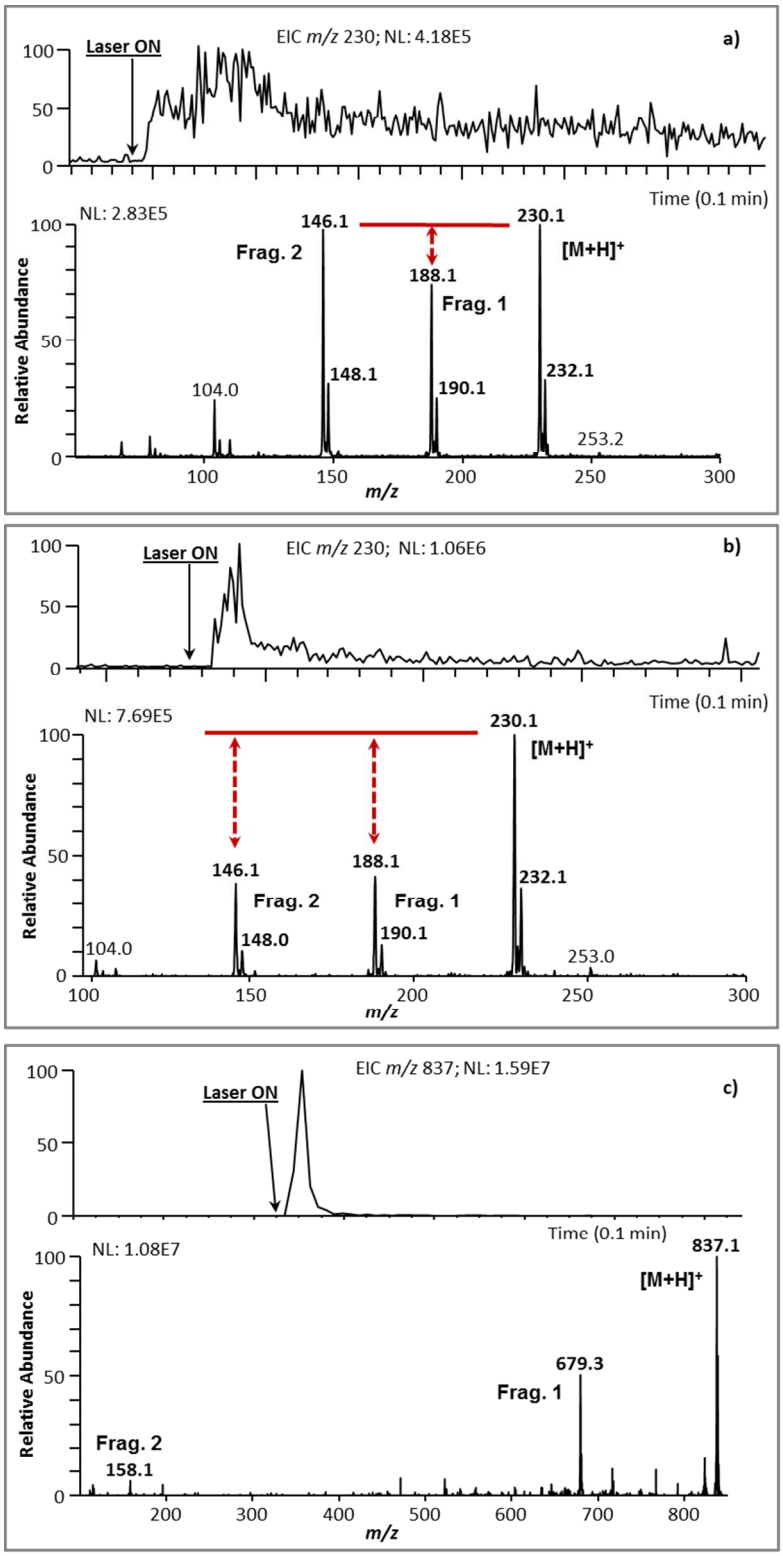

a)
EIC m/z 230; NL: 4.18E5
Laser ON
Time (0.1 min)
NL: 2.83E5
Relative Abundance
146.1
230.1
Frag. 2
[M+H]+
188.1
Frag. 1
148.1
190.1
232.1
104.0
253.2
m/z
b)
EIC m/z 230; NL: 1.06E6
Laser ON
Time (0.1 min)
NL: 7.69E5
Relative Abundance
230.1
[M+H]+
146.1
188.1
Frag. 2
Frag. 1
232.1
148.0
190.1
104.0
253.0
m/z
c)
EIC m/z 837; NL: 1.59E7
Laser ON
Time (0.1 min)
NL: 1.08E7
Relative Abundance
837.1
[M+H]+
679.3
Frag. 1
Frag. 2
158.1
m/z

Figure 3

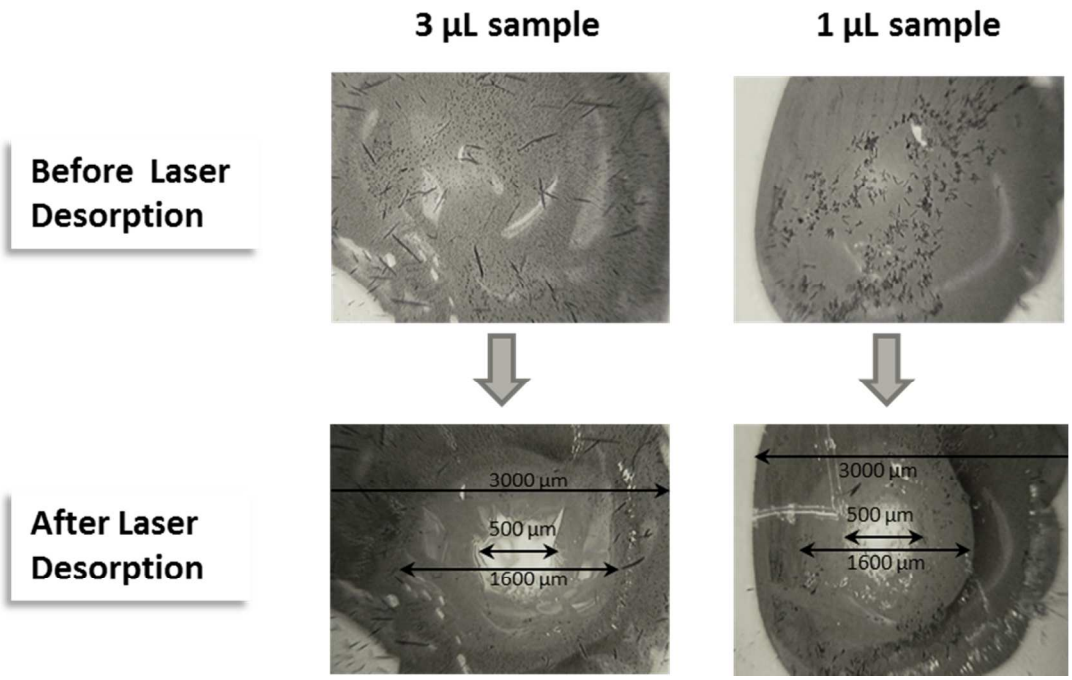

3 µL sample
1 µL sample
Before Laser Desorption
After Laser Desorption
3000 µm
500 µm
1600 µm
3000 µm
500 µm
1600 µm

Figure 4

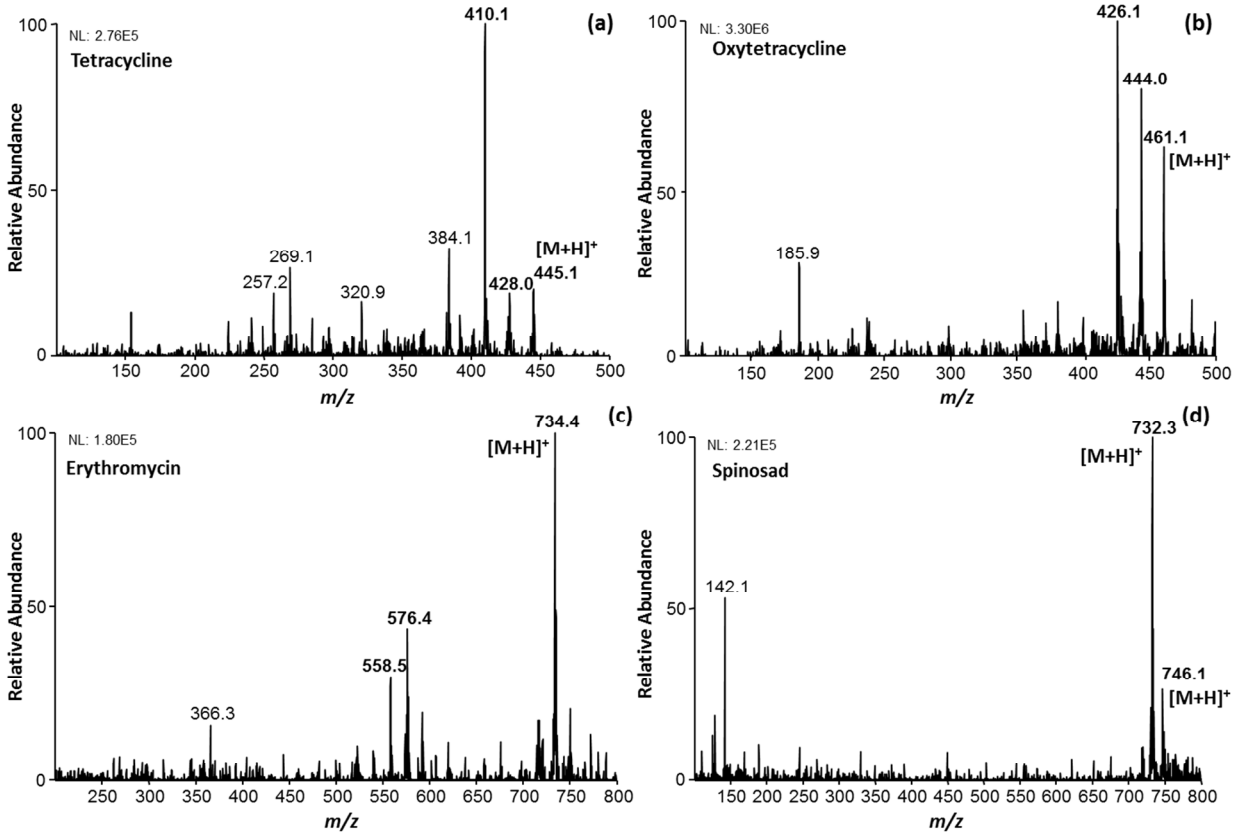

(a)
NL: 2.76E5
Tetracycline
410.1
384.1
269.1
257.2
320.9
428.0
445.1
[M+H]+
(b)
NL: 3.30E6
Oxytetracycline
426.1
444.0
461.1
[M+H]+
185.9
(c)
NL: 1.80E5
Erythromycin
734.4
[M+H]+
576.4
558.5
366.3
(d)
NL: 2.21E5
Spinosad
732.3
[M+H]+
142.1
746.1
[M+H]+
Relative Abundance
m/z

Figure 5

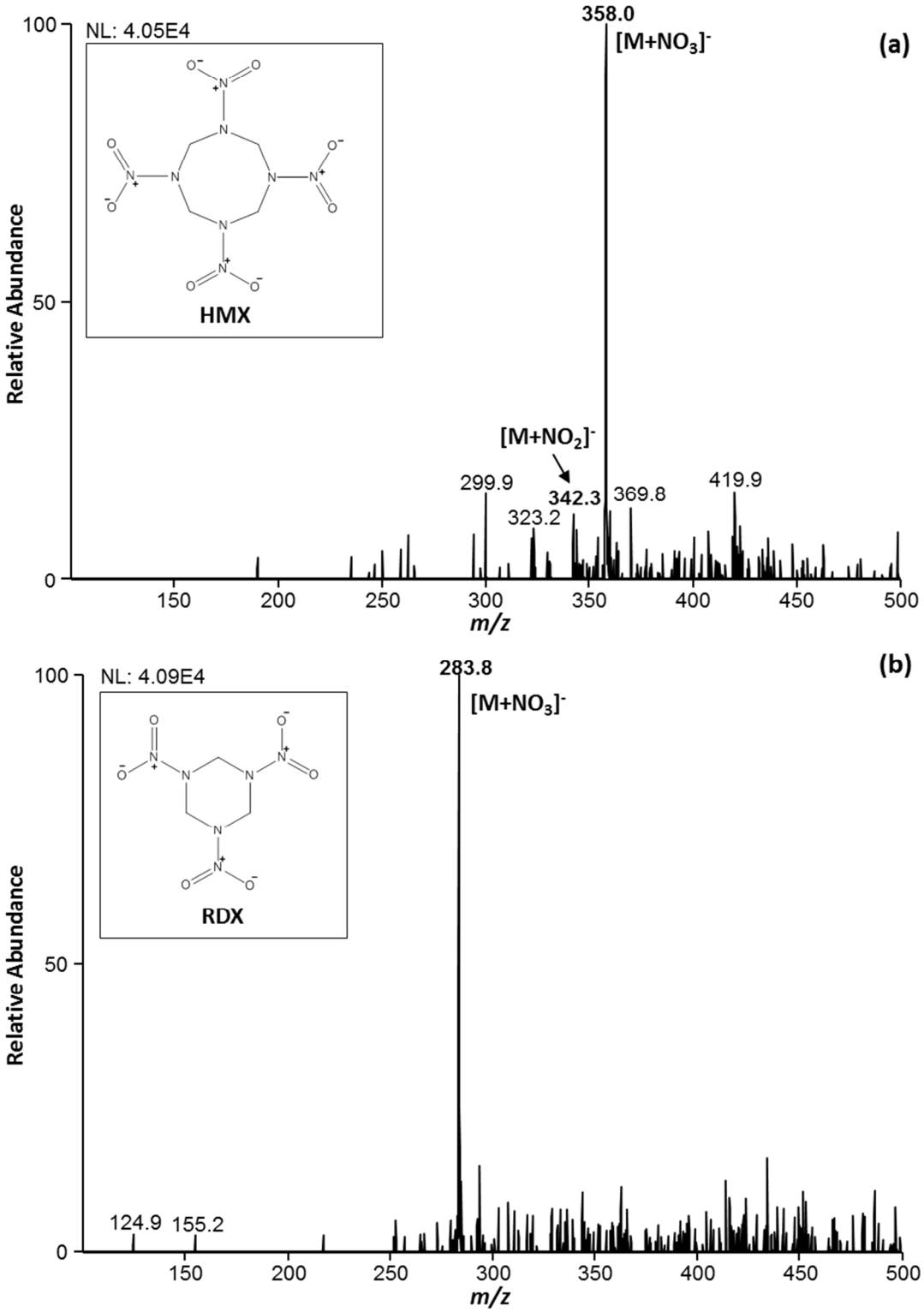
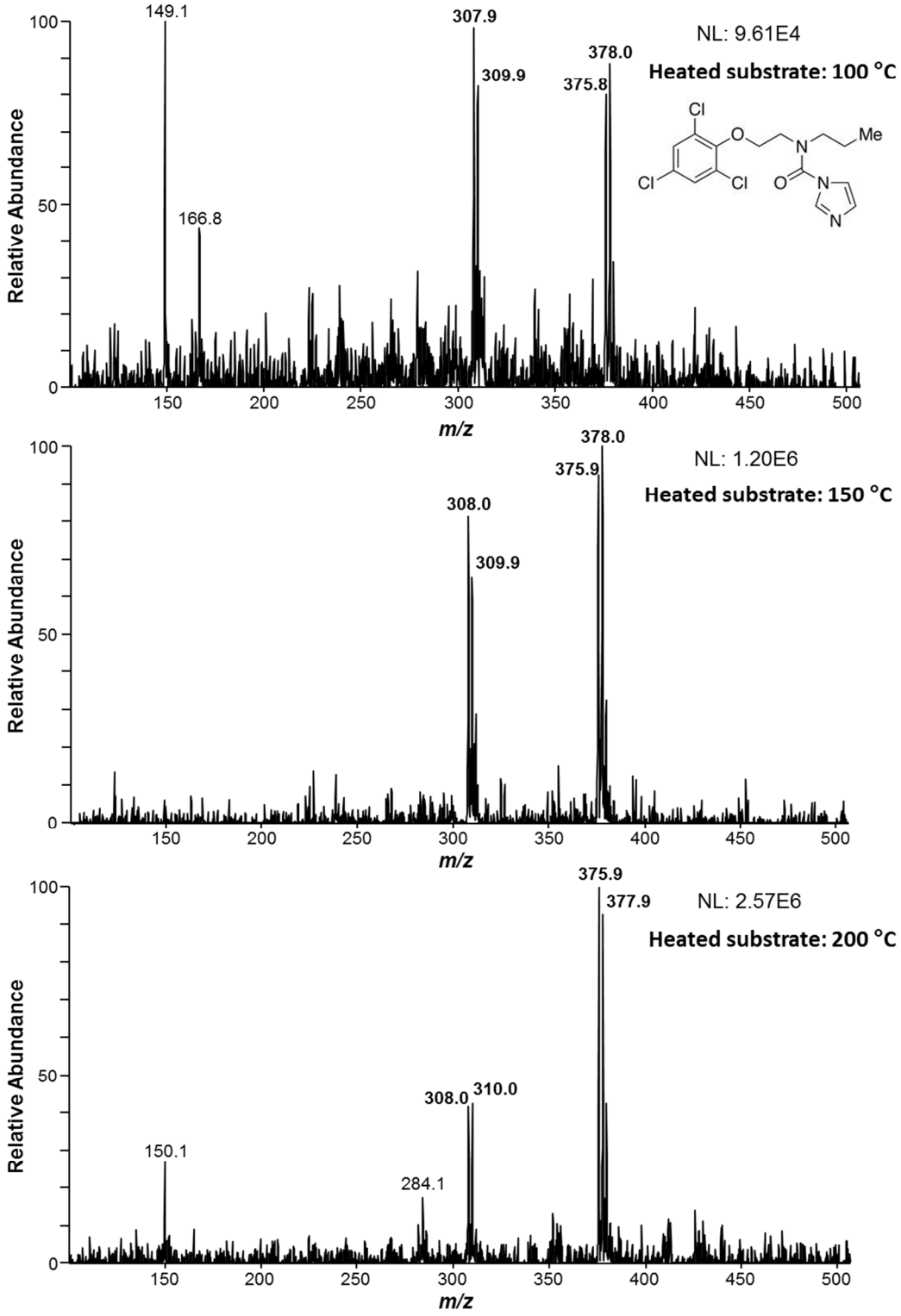

NL: 4.05E4
358.0
[M+NO3]-
(a)
HMX
[M+NO2]-
299.9
342.3
323.2
369.8
419.9
Relative Abundance
m/z
NL: 4.09E4
283.8
[M+NO3]-
(b)
RDX
124.9
155.2
Relative Abundance
m/z

Figure 6


149.1
307.9
309.9
378.0
375.8
166.8
NL: 9.61E4
Heated substrate: 100 °C
Cl
O
N
Me
Cl
Cl
O
N
N
Relative Abundance
m/z
378.0
375.9
308.0
309.9
NL: 1.20E6
Heated substrate: 150 °C
375.9
377.9
NL: 2.57E6
Heated substrate: 200 °C
308.0
310.0
150.1
284.1

Tables

Table 1. Main features and configuration of DBD based ambient ionization sources: LTP and DBDI

	LTP-MS [15]	DBDI [28]
Format	Probe	LC-MS interface / Probe
Voltage (amplitude)	2-5 kV	2-5 kV
Pulse frequency	2 -5 KHz	20 KHz
Distance between electrodes	2.7 mm	12 mm
Inner diameter	3.75 mm	0.5 mm
External diameter	6.35 mm	1.2 mm
Dielectric thickness	2.6 mm	0.7 mm
Operating Helium Flow	0.1-0.5 L/min	0.2 L/min
Pin (grounded) electrode diameter	1.57 mm	-

Table 2. Comparative evaluation of different experiments performed using LD-DBDI-MS and DBDI-MS with a heated substrate.

Compound	Measured ion	Analyte response				
		LD-DBDI[1]	DBDI-MS w/ heated substrate			
		Laser (2.6 W)	100 ºC	150 ºC	200 ºC	250 ºC
Pharmaceuticals:						
Ampicillin (0.5 µg)	*m/z* 186 (fragment)	3.7×10^5	n.d. [2]	n.d.	3.3×10^4	n.t. [3]
Dicloxacillin (0.5 µg)	*m/z* 212 (fragment)	8.6×10^4	n.d.	n.d.	n.d.	n.d.
Enrofloxacin (0.5 µg)	*m/z* 316 (fragment)	4.2×10^6	n.d.	n.d.	1.0×10^5	1.3×10^5.
Reserpine (0.46 µg)	*m/z* 609 ($[M+H]^+$)	1.6×10^7	n.d.	n.d.	1.2×10^6	n.t.
Roxithromycin (0.47 µg)	*m/z* 837 ($[M+H]^+$)	8.7×10^6	n.d.	6.0×10^4	1.6×10^6	3.5×10^6
Tetracycline (0.5 µg)	*m/z* 445 ($[M+H]^+$)	4.9×10^5	n.d.	n.d.	5.3×10^5	1.8×10^5
Pesticides:						
Propazine (0.40 µg)	*m/z* 230 ($[M+H]^+$)	1.3×10^6	n.d.	5.1×10^5	1.4×10^5	n.t.
Prochloraz (0.5 µg)	*m/z* 376 ($[M+H]^+$)	1.2×10^5	8.8×10^4	1.6×10^6	2.6×10^6	1.0×10^6
Spinosad (0.5 µg)	*m/z* 732 ($[M+H]^+$)	2.3×10^5	n.d.	n.d.	n.t.	n.t.

[1]: Substrate at room temperature before laser desorption
[2]: non detected
[3]: not tested