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Surface Analysis under Ambient Conditions Using Plasma-Assisted Desorption/Ionization Mass Spectrometry

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A novel plasma-assisted desorption/ionization (PADI) method that can be coupled with atmospheric pressure sampling mass spectrometry to yield mass spectral information under ambient conditions of pressure and humidity from a range of surfaces without the requirement for sample preparation or additives is reported. PADI is carried out by generating a nonthermal plasma which interacts directly with the surface of the analyte. Desorption and ionization then occur at the surface, and ions are sampled by the mass spectrometer. The PADI technique is demonstrated and compared with desorption electrospray ionization (DESI) for the detection of active ingredients in a range of over-the-counter and prescription pharmaceutical formulations, including nonsterodial anti-inflammatory drugs (mefenamic acid, Ibugel, and ibuprofen), analgesics (paracetamol, Anadin Extra), and Beecham's "all in one" cold and flu remedy. PADI has also been successfully applied to the analysis of nicotine in tobacco and thiosulfates in garlic. PADI experiments have been performed using a prototype source interfaced with a Waters Platform LCZ single-quadrupole mass spectrometer with limited modifications and a Hiden Analytical HPR-60 molecular beam mass spectrometer (MBMS). The ability of PADI to rapidly detect active ingredients in pharmaceuticals without the need for prior sample preparation, solvents, or exposed high voltages demonstrates the potential of the technique for high-throughput screening in a pharmaceutical or forensic environment.

Desorption electrospray ionization (DESI) and direct analysis in real time (DART) are two recently introduced techniques which have successfully overcome the difficulties associated with vacuum-based analyses, such as the need for vacuum compatible samples. DESI consists of directing a pneumatically assisted electrospray onto an analyte surface, coupled with collection of the desorbed ions by the MS inlet.[1] This ambient pressure ionization method has been applied to the analysis of a wide variety of compounds including peptides,[2] proteins,[2,3] pharmaceuticals,[4−6] explosives,[7,8] controlled substances,[5,9] and others.[2,10−12] DART is another atmospheric pressure ionization technique capable of rapid surface analysis.[13] DART has been applied to the detection of pharmaceuticals, drugs of abuse, chemical warfare agents, and a multitude of other chemicals.[13] This noncontact ion source consists of a remote nonthermal plasma from which charged species are rejected with a grid system and metastable species are directed toward the surface of the analyte. Excited-state gas molecules have previously been used in ionization sources.[14−18] For example, in the metastable atom bombardment (MAB) source a metastable ion beam is generated which interacts with neutral gas-phase

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analytes and ionization occurs via a Penning ionization process in vacuo.[14] Other similar techniques include liquid surface Penning ionization (LPI), where a liquid sample is deposited onto a needle tip held at a high potential and ionized by excited argon atoms.[15,16] In atmospheric sampling glow discharge ionization (ASGDI) ionization occurs via Penning ionization when the sample is exposed to an electrical discharge.[17,18] Desorption atmospheric pressure chemical ionization (DAPCI)[19] and the related technique atmospheric pressure solids analysis probe (ASAP)[20] utilize corona discharges and operate at ambient conditions.

Ambient sampling techniques, such as DESI and DART, offer significant potential benefits over current methods for the analysis of pharmaceuticals and controlled substances which at present typically involves lengthy sample preparation. For example, solvent extraction followed by filtration and analysis via liquid chromatography mass spectrometry (LC/MS) or gas chromatography mass spectrometry (GC/MS) are commonly used to determine the presence of drugs.[21−24] The ability to rapidly identify analytes without loss of quality of the data is an important analytical challenge. The potential impact of ambient pressure ionization techniques capable of high-throughput analysis on the field of pharmaceuticals is immense.

We have recently developed a new approach to ambient surface analysis, termed plasma-assisted desorption/ionization (PADI), which is distinct from and offers advantages over DESI, DART, and related techniques. PADI consists of generating a nonthermal radio frequency-driven atmospheric pressure plasma and directing it onto the surface of the analyte without charged particle extraction. The PADI source is different from other direct ionization techniques, such as DART, DAPCI, and ASAP, in several ways. First, DART, DAPCI, and ASAP techniques utilize corona discharges, typically formed by applying several kilovolts to the tip of a sharpened electrode. This class of discharge is characterized by high-voltage/low-current characteristics which generate ions with energies extending to the full extent of the applied voltage. In contrast, the PADI source is a nonthermal atmospheric glow discharge which is characterized by a lower operating voltage and higher current characteristics than corona discharges. The PADI source operates over a lower voltage/power range (typically 300 V peak to peak and less than 5 W total applied power). This results in a truly nonthermal, or cold, plasma with an operating temperature close to that of the ambient surroundings.[25] The glow discharge is self-sustaining and results in relatively low ion energies, typically less than 5 eV and not exceeding 20 eV. In contrast to corona discharge and DESI techniques, the nonthermal plasma of PADI is cold to the touch and does not heat the sample. This in turn allows direct interaction of the plasma with thermally sensitive samples and does not require the removal of any highly energetic species as in DART. The result is a simpler, more robust source. Second, unlike DART, the surface of the analyte is in direct contact with the active part of the plasma. This direct interaction of the plasma with the sample results in surface interactions not only with metastable helium atoms, thought to be the dominant desorption/ionization mechanism in DART,[13] but also with energetic ions and radicals. Since electrons, ions, and radical species interact with surfaces in chemically specific ways, this introduces the possibility of controlling specificity by exploiting the ability to promote desired plasma−surface reactions. Selective etching of surfaces by promotion with certain radical groups is a technique long employed in low-pressure plasma processing in, e.g., the semiconductor industry.[26] A direct consequence of this is the possibility of "cleaner" mass spectra, free from spectral interferences that might otherwise mask important information. Finally, in contrast to DART and the corona discharge sources, PADI produces a visual plasma plume of submillimeter diameter that terminates in a fine point. This has distinct advantages for alignment issues.

Herein, we describe the PADI technique and demonstrate its application for the analysis of active ingredients in a variety of common pharmaceutical drugs, making a direct comparison with DESI analysis.

EXPERIMENTAL SECTION

The pharmaceutical preparations investigated are listed in Figure 1 along with the molecular weights and formulas of the active ingredients. Paracetamol (Sterwin Medicines), ibuprofen (Galpharm Healthcare), Anadin Extra (Wyeth, U.K.), Ralgex cream (SSL International, U.K.), Ibugel (Dermal, U.K.), and Beecham's "all in one" (GlaxoSmithKline, U.K.) were purchased over the counter, and mefenamic acid tablets (Norton Healthcare, U.K.) were obtained by prescription. HPLC grade methanol was purchased from Fisher (Loughborough, Leicestershire, U.K.).

Sampling Preparation and Handling for PADI and DESI. Uncoated tablets were used as supplied, whereas coated tablets were carefully scraped with a scalpel blade prior to analysis to expose the underlying active materials. Cream formulations (ca. 10 mg) were deposited onto glass slides and spread into a thin layer using cotton-tipped safety swabs. A target plate was constructed for DESI analysis which consisted of a square of matt finished card (2 cm × 2 cm) attached to a metal post placed in close proximity to the mass spectrometer inlet. Samples (tablets or creams on glass slides) were mounted onto the matt card with double-sided tape and positioned approximately 45° to the solvent spray. For PADI analysis the sample was positioned at grazing incidence to the plasma with nonconducting tweezers typically at a distance of 1−3 mm from the source sampling inlet.

PADI Instrumentation. The PADI source consisting of a nonthermal rf plasma "needle" operating at atmospheric pressure was based upon the design of Stoffels et al.[25] This consists of a stainless steel wire, 190 mm long and 0.75 mm diameter, sharpened into a needle-like point at one end. The wire serves as a powered electrode and is placed coaxially within a ceramic tube (1.2 mm i.d., 2.5 mm o.d.) which is itself placed coaxially within a quartz tube (5 mm i.d., 7 mm o.d.). The ceramic and quartz cylinders have independent gas feeds and may be filled with the

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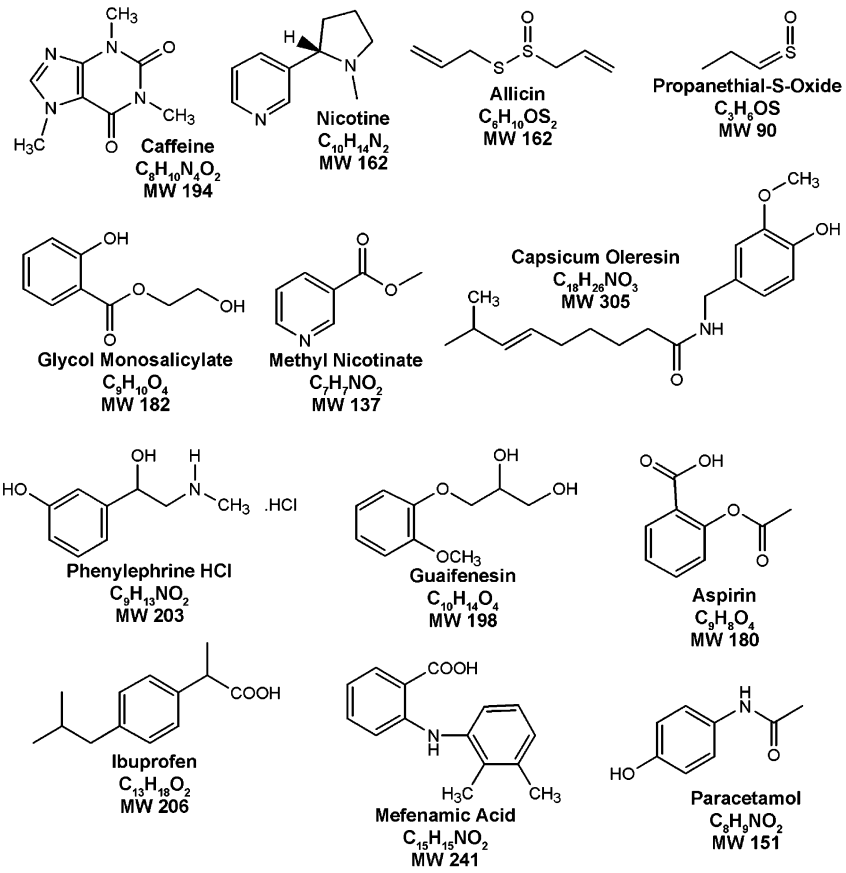

Figure 1. Structures and formulas of the analytes analyzed.

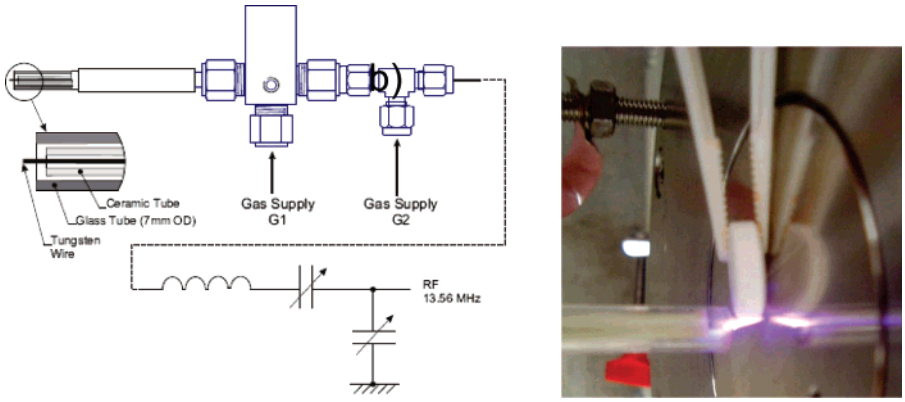

Figure 2. Schematic of the PADI probe with a photograph illustrating the source in operation.

same flowing gas, typically helium at several hundred milliliters per minute, or with helium and a second gas or mixture of gases. A radio frequency (13.56 MHz) signal is applied to the unsharpened end of the needle via a matching network. The peak-to-peak rf voltage is typically 200−500 V, and powers are typically less than 5 W. Application of this rf signal generates a cold, nonthermal plasma at the tip of the needle. The plasma is around 1 mm in diameter and may extend up to 10 mm from the tip. The plasma operates in ambient air and can be brought into direct contact with any of the surfaces under study. The action of the plasma at the sample surface produces ions from the surface material which enter the gas phase and are readily detected with a suitable mass spectrometer. A schematic illustration of the PADI source and experimental setup are shown in Figure 2.

Some PADI experiments were carried out on a Platform LCZ mass spectrometer (Waters, Manchester, U.K.) operating in positive ion mode. For all experiments the ion source block was maintained at 110 °C, and the cone voltage was set at 18 V. The Z-spray source of the instrument was removed, and the PADI probe was positioned approximately 45° to the atmospheric pressure cone inlet of the MS.

The PADI source was also interfaced to an HPR-60 molecular beam mass spectrometer (MBMS) (Hiden Analytical Ltd., Warrington, U.K.) which consists of a single-stage quadrupole mass spectrometer (QMS) with a differentially pumped three-stage inlet system.[27] The pressure reduction stages are separated by aligned skimmer cones and continuously pumped by separate turbomolecular pump sets. A free-jet expansion from atmospheric pressure

into the primary low-pressure stage is skimmed to produce a molecular beam in what is known as a Campargue source.[28] The beam is then directed into the electron impact ion source of the QMS. Ions generated via the ionization process enter the mass analyzer and are detected. PADI experiments were performed on the MBMS in both positive and negative modes of ionization. Optimum cone voltages were −30, 10, and −30 V on cones 1, 2, and 3, respectively, in positive ion mode and 0, 0, and 2 V in negative ion mode. The plasma beam was directly aligned with the mass spectrometer inlet, and the sample was inserted into the plasma using tweezers so that the beam grazed the tablet surface.

DESI Instrumentation. For DESI analysis, the standard Z-spray electrospray (ESI) probe of the platform LCZ (Waters, Manchester, U.K.) was used to deliver the solvent spray to the analyte surface. The only modification required to the instrument was the removal of the glass source cover to give access to the source region for positioning of the sample. The mass spectrometer was operated in positive ESI mode with a capillary voltage of 4.7 kV. The nitrogen gas desolvation temperature was set to 325 °C with a flow rate of 350 L/h supplied from a nitrogen generator at 100 psi (Peak Scientific, Renfrew, U.K.). The ion source block was maintained at 110 °C, and the cone voltage was set at 18 V. The sample (tablet or cream) was sprayed with a solution of methanol/water (1:1) at a flow rate of 5 μL min^{-1} using a syringe pump (WPI, Stevenage, U.K.).

RESULTS AND DISCUSSION

Optimization of PADI Operational Parameters. Optimization of the PADI technique was carried out on both the MBMS and LCZ mass spectrometers. The tip of the needle was aligned with the mass spectrometer inlet at a distance of a few millimeters (ca. 1−10), the plasma was ignited, and the sample was inserted into the beam. Adjustment of the He gas flows controlled the shape of the plasma jet; elongated plasma of about 4−5 mm was found to be optimum for PADI experimentation. This was typically obtained with gas flows in the region of 300−500 mL min^{-1}.

The main consideration with the PADI technique for the analysis of pharmaceuticals was found to be the input power. In general, the signal intensity of the protonated species of the active ingredient increased as the power increased. However, at high power (>7 W) surface erosion and charring of the tablet surface were observed. Damage to the analyte surface was virtually eliminated when the source was operated at low power (<3 W) at which setting high-quality mass spectra could readily be obtained.

In contrast to PADI, there are several operational parameters related to the DESI source which need to be optimized in order to effectively generate and detect ions. These include the high voltage applied to the ESI, solvent flow rate, and distances to the MS inlet.[1,2,6] The most critical variables for DESI analysis are the angles between the sample, MS sampling cone, and the ESI spray. Plasma to MS inlet angles over the range of 30−90° were investigated on the LCZ mass spectrometer. The scope of angles examined was limited by spatial parameters due to the physical dimensions of the prototype PADI source. For PADI interfaced with the LCZ mass spectrometer these angles were found not to be critical. However, PADI combined with the MBMS generated higher signal intensities when the angle of the plasma to MS inlet was 0°. Overall, the setup and optimization of the PADI source was found to be considerably less time-consuming and critical than for the DESI source. The integration of the PADI source is therefore straightforward for mass spectrometers having an atmospheric pressure inlet, requiring minimal modification and permitting control of voltages directly from vendor software. This distinct advantage of PADI may be exploited for pharmaceutical and, potentially, forensic applications where rapid screening is essential.

PADI with Molecular Beam Mass Spectrometry Detection. The objective of this work was to evaluate PADI as an ambient pressure surface analysis technique. To achieve this PADI was combined with an MBMS for the analysis of a range of pharmaceutical preparations. Figure 2b shows a photograph of the PADI source interfaced with the MBMS for the sampling of a paracetamol tablet.

Typical data obtained for the detection of active ingredients of pharmaceuticals using PADI interfaced with the MBMS operated in positive ion mode are shown in Figure 3a−c. All spectra were acquired from approximately 1 s of experimental data. Tablet and gel formulations were examined including nonsterodial anti-inflammatory drugs such as mefenamic acid, ibuprofen tablets (data not shown), and Ibugel. For each of the compounds the expected protonated molecules were observed with high signal intensity. For example, the active ingredient of a generic mefenamic acid tablet (500 mg of mefenamic acid) was evident at m/z 242 (Figure 3a). Ibugel contains the active component ibuprofen at the 5.0% level (w/w); this was observed as a protonated molecule at m/z 207 (Figure 3b). Simultaneous detection of multiple ingredients was assessed by the rapid analysis of Beecham's "all in one", an "over-the-counter" cold and flu remedy which contains the three actives paracetamol (250 mg), guaifenesin (100 mg), and phenylephrine hydrochloride (5 mg). The two main active ingredients were observed as protonated species, guaifenesin at m/z 199 and paracetamol at m/z 152 (Figure 3c). The base peak at m/z 124 was due to fragmentation of guaifenesin.

The ability of the technique to operate in both negative and positive ion modes is of particular importance to the pharmaceutical industry because many drug formulations may contain both basic and acidic molecules with a range of polar and nonpolar properties. Paracetamol, ibuprofen, and aspirin tablets were selected as examples to demonstrate PADI for the detection of the active ingredients using the negative ion mode. The mass spectra generated are shown in Figure 3d−f. For all these compounds the deprotonated ion of the active ingredient was observed with high signal intensities. For example, abundant peaks at m/z 150 and m/z 205 correspond to deprotonated paracetamol and ibuprofen, respectively. The negative ion mass spectrum obtained for aspirin using PADI is shown in Figure 3f. As expected, the deprotonated molecule $[M - H]^-$ for the active ingredient at m/z 179 was observed. In-source CID of this ion resulted in the fragment at m/z 137, which is consistent with DESI analysis of aspirin.[29] DESI negative ion mass spectra were obtained

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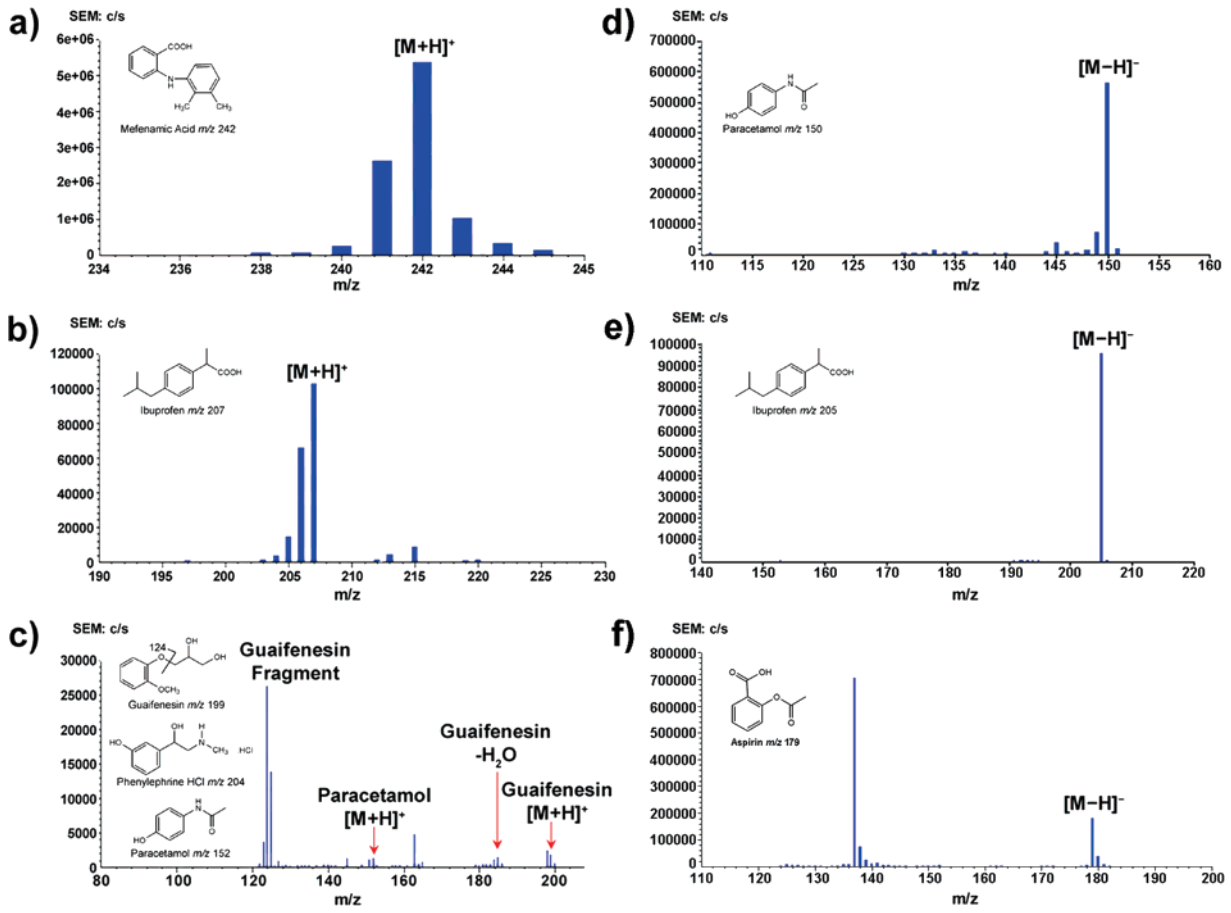

Figure 3. Typical positive ion mode PADI-MBMS spectra obtained for the rapid detection of active pharmaceutical ingredients in (a) a generic mefenamic tablet (500 mg of mefenamic acid), (b) Ibugel (5% ibuprofen w/w), (c) "Beecham's all in one" (250 mg of paracetamol, 100 mg of guaifenesin, and 5 mg of phenylephrine hydrochloride) and typical negative ion mode PADI-MBMS spectra obtained for (d) a paracetamol tablet (500 mg of paracetamol), (e) a generic ibuprofen tablet (200 mg of ibuprofen), and (f) an aspirin tablet (300 mg of aspirin).

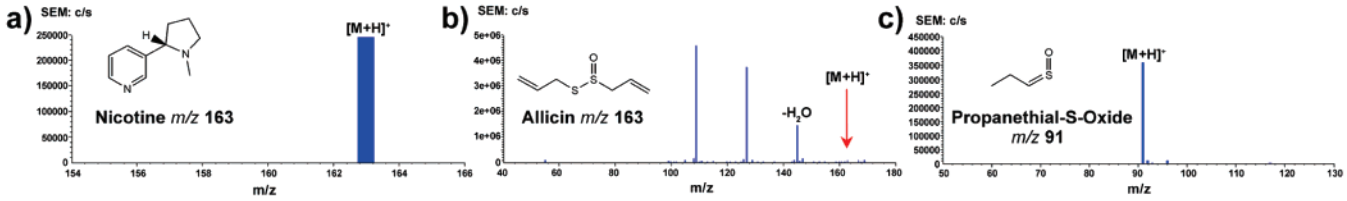

Figure 4. PADI-MBMS spectra obtained for the detection of (a) nicotine in tobacco, (b) allicin in freshly sliced garlic, and (c) propanethial-S-oxide in freshly cut onion.

for paracetamol, ibuprofen, and aspirin (data not shown) which were comparable with the PADI spectra.

PADI was also applied to the analysis of naturally occurring plant alkaloids. One such example is nicotine which is present in tobacco. A small amount of dried tobacco was held in nonconductive tweezers and positioned in the plasma beam in the same way as solid tablets. No detrimental effects were seen to the tobacco. Results were comparable to those reported for the analysis of nicotine via DESI and DART.[4] The protonated molecule of nicotine was observed at m/z 163 with high signal intensity, shown in Figure 4a. Other plant materials examined by PADI MS have included the vegetable alliums, garlic and onion (Figure 4, parts b and c). No sample preparation was required, apart from slicing the onion or garlic clove prior to analysis. Allicin, the predominant thiosulfate in freshly cut garlic (3.2−4.8 mg g^{-1}, <30 μmol)[30] was detected with high abundance at m/z 163, and propanethial-S-oxide was observed as a protonated species at m/z 91 for freshly cut onion. This unstable volatile compound forms through the decomposition of sulfenic acids generated by enzymes released when the onion tissue is damaged and is difficult to analyze by conventional mass spectrometric techniques.[31]

A wide range of samples has thus far been analyzed using PADI, including a variety of over-the-counter drug formulations. Table 1 lists examples with the m/z values for the most prominent ions observed. Those shown in bold correspond to protonated

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Table 1. Examples of Other Analytes Examined by PADI MS with *m/z* Values Observed[a]

sample	major *m/z* observed
paracetamol and codeine dual active tablets	**152**, 303
Boots Paracetamol Extra (paracetamol and caffeine)	**195**, 152, 110
aspirin	**181**, 163, 139, 121
muscle rub ointment (menthol and methyl salicylate)	**153**, **155**
chlorodiazepoxide	**300**
Tyrozet	**166**, 138, 120
Benylin (guaifenesin and levomenthol)	**199**
glucosamine sulfate	159
Betnovate (betamethasone valerate)	225

[a] Bold denotes protonated molecules of the active ingredients.

molecules of the active ingredients. Cough medicines, creams, and ointments were smeared onto a glass slides or foil prior to analysis. In the case of the dual-active tablet paracetamol and codeine the protonated molecule of paracetamol was detected at *m/z* 152 and the corresponding dimer $[2M + H]^+$ at *m/z* 303. This is consistent with results obtained for the DESI analysis of a Solphadeine Max tablet, which contains the same active ingredients.[4] Interestingly, the dimer was not observed for the analysis of paracetamol and caffeine tablets. This difference in results may be explained by the influence of excipients and irreproducible positioning of the sample in the plasma beam using tweezers.

Comparison of PADI with DESI. A wide range of pharmaceutical tablet drug formulations were successfully analyzed using PADI-MBMS. However, further mass spectrometric experiments were performed to compare PADI with DESI for the analysis of a range of compounds including pharmaceutical tablets, creams, and gels. PADI and DESI generated similar data on a comparable time scale, and no significant carryover effects were observed. However, in general PADI spectra were cleaner, displaying less fragmentation than the DESI spectra, and the active ingredients were observed with higher signal intensity.

a. Paracetamol. A generic paracetamol tablet was analyzed by both PADI and DESI interfaced with a single-quadrupole mass spectrometer (Waters Platform LCZ). A comparison of the data obtained by each technique is shown in Figure 5. The base peak in both spectra corresponds to the protonated molecule of the active ingredient at *m/z* 152. This was observed with higher signal intensity in the PADI spectrum. The fragment ion seen in the DESI spectrum at *m/z* 110 corresponds to the loss of ketene, and this is consistent with results observed by Chen et al.[32] However, the fragment was not observed in the PADI spectrum indicating that PADI is potentially a softer ionization technique for some analytes.

b. Ibuprofen. Ibuprofen is a nonsterodial anti-inflammatory drug used to relieve moderate pain and inflammation. PADI and DESI mass spectra obtained for the analysis of this drug in tablet form containing 200 mg of the active ingredient are shown in Figure 6. In the DESI analysis, the expected protonated

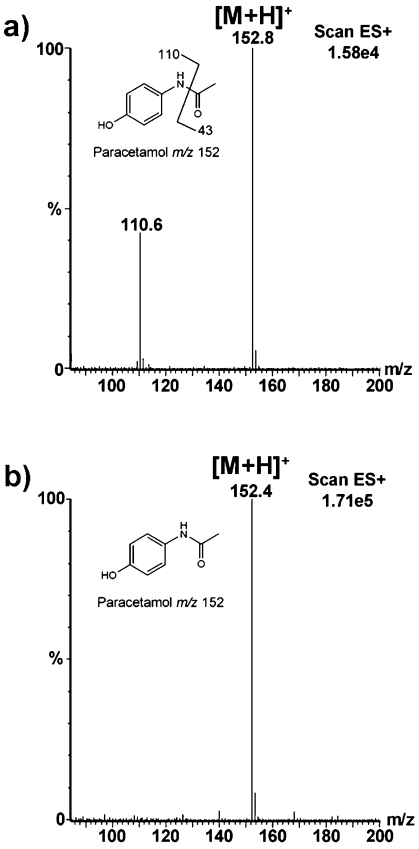

Figure 5. Analysis of the active ingredient of a generic paracetamol tablet (500 mg of paracetamol) by (a) DESI and (b) PADI.

molecule of the active ingredient at *m/z* 207 was not observed due to fragmentation of the molecule via in-source CID at 18 V cone voltage. The base peak at *m/z* 161 was due to the loss of a neutral fragment (HCOOH, formic acid) from *m/z* 207. However, with PADI analysis the active ingredient was observed as a protonated species with high signal intensity. Loss of the carboxyl group from the protonated molecule was also observed in the PADI MS.

c. Anadin Extra. A solid Anadin Extra tablet containing aspirin (300 mg), paracetamol (200 mg), and caffeine (45 mg) was analyzed by PADI and DESI. The resulting spectra are shown in Figure 7. All three active ingredients are evident as protonated species in the resulting PADI spectrum, paracetamol at *m/z* 152, aspirin at *m/z* 181, and caffeine at *m/z* 195. The protonated molecule of aspirin was absent in the DESI mass spectrum, which is consistent with results obtained by Williams et al.[33] The base peak in both spectra at *m/z* 121 corresponds to the loss of acetic acid from protonated aspirin. Further fragment ions indicating the loss of CH_2CO and the loss of water from aspirin were seen in the PADI spectra at *m/z* 139 and 163, respectively. Loss of water from aspirin has been previously reported for both DESI and DART analysis.[4]

d. Ralgex Cream. DESI and PADI have also been applied to the analysis of ointments and creams. Ralgex, a cream used for the treatment of muscular pain, is one such example. This contains the active ingredients glycol monosalicylate 10% w/w, methyl

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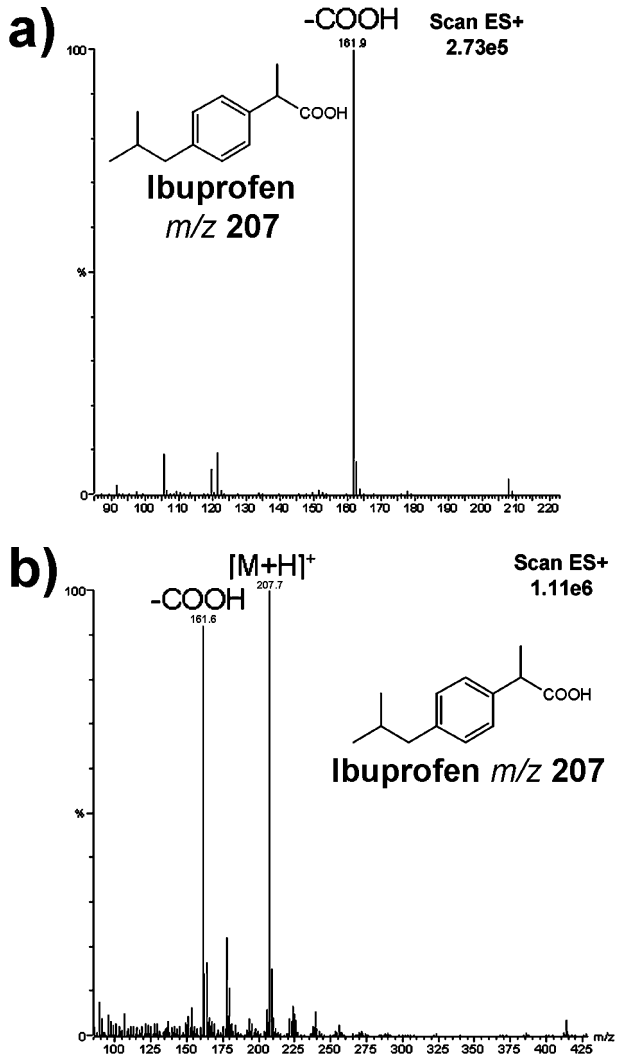

Figure 6. Rapid sampling of a generic ibuprofen tablet (ibuprofen 200 mg) by (a) DESI and (b) PADI.

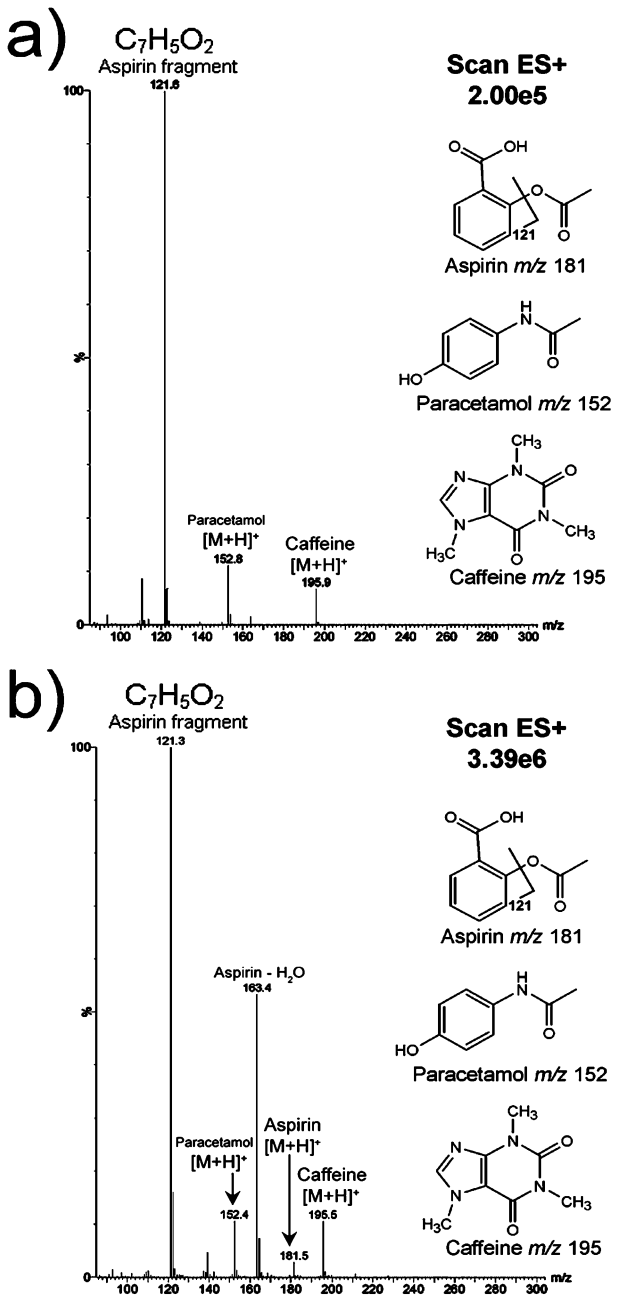

Figure 7. Analysis of Anadin Extra (200 mg of paracetamol, 300 mg of aspirin, and 45 mg of caffeine) by (a) DESI and (b) PADI mass spectrometry.

nicotinate 1% w/w, and capsicum oleoresin 0.12% w/w. A thin layer of the cream was smeared onto a glass slide and positioned into the source region of the mass spectrometer as previous described. Figure 8b shows the PADI spectrum which was generated in ca. 3 s. Glycol monosalicylate and methyl nicotinate were detected as singly charged protonated molecules at m/z 183 and 138, respectively. The base peak at m/z 121 is formed by the cleavage of the carbonyl bond of glycol monosalicylate as indicated in Figure 8. Other ions observed in the spectra at low abundance are likely to be from additives in the cream. The resulting DESI spectrum for the analysis of Ralgex from a glass slide is shown in Figure 8a. Glycol monosalicylate and methyl nicotinate were again observed as protonated species along with the fragment ion at m/z 121. Abundance of the ions in relation to each other was significantly different for DESI and PADI.

Mechanisms of Desorption and Ionization. The mechanisms of desorption and ionization in the PADI method will be the focus of further work, and we comment here only briefly on what are likely to be the most important contributions. Positive ionization mechanisms are thought to include a combination of direct electron impact ionization, metastable Penning ionization, and ion−molecule reactions. The He(2^3S) metastable state has an energy of 19.8 eV, and it is well-known that such species can induce desorption from surfaces of either neutral molecules or ions.[34]

$$\mathrm{He}(2^3\mathrm{S}) + \mathrm{M} \rightarrow \mathrm{M}^+ + \mathrm{He}(1^1\mathrm{S}) + \mathrm{e} \qquad (1)$$

The reaction of the helium(2^3S) state with water is very efficient,[35] and we suggest that analyte ionization mechanism

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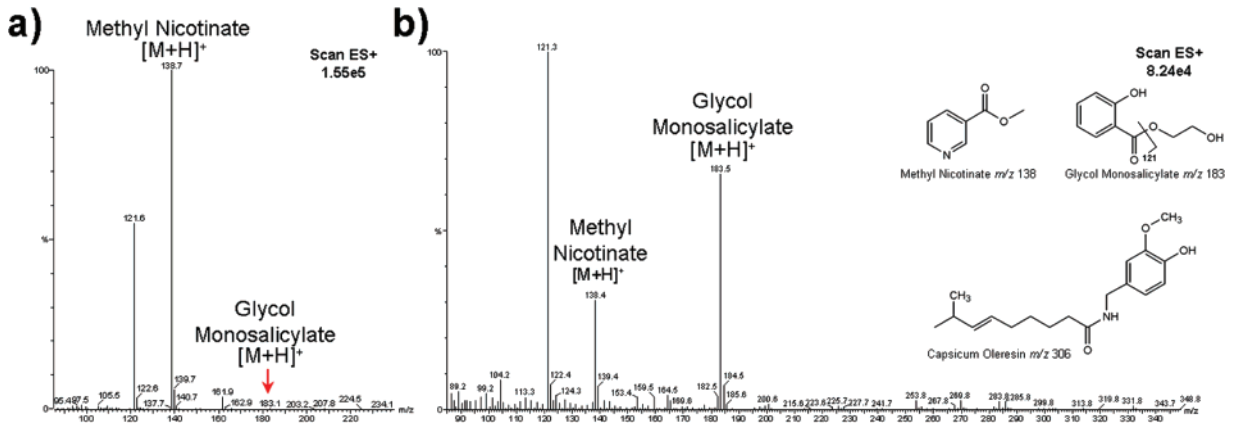

Figure 8. Analysis of Ralgex cream (glycol monosalicylate 10% w/w, methyl nicotinate 1% w/w, capsicum oleoresin 0.12% w/w) from a glass slide by (a) DESI and (b) PADI mass spectrometry.

in PADI proceeds via combination of ionized water cluster formation and proton-transfer reactions:

$$\mathrm{He}(2^3\mathrm{S}) + n\mathrm{H_2O} \rightarrow \mathrm{H_3O^+(H_2O)}_{n-2} + \mathrm{OH^-} + \mathrm{He}(1^1\mathrm{S}), \quad n > 1 \quad (2)$$

$$\mathrm{H_3O^+(H_2O)}_n + \mathrm{M} \rightarrow \mathrm{MH^+} + (n+1)\mathrm{H_2O} \quad (3)$$

This mechanism is supported by observations of both M^+ and MH^+ fragments and also $H_3O^+(H_2O)_n$ clusters from the PADI source (data not shown) and predicts that each mechanism plays a part in the ionization of analytes in this technique. Negative ion formation is thought to proceed via direct and dissociative electron attachment to oxygen species, producing, e.g., O_2^-, which then react with analyte molecules to produce predominantly $[M - H]^-$ groups. These and other core negative ion species have been measured from the PADI source and previously in similar discharges.[36]

Desorption processes are less well understood, but we believe that a combination of energy transfer from metastable helium, ion impact, and radical−surface interactions contribute to the mechanisms in the PADI technique. The action of radicals at surfaces has long been exploited in low-pressure plasma techniques and is known to be effective in similar high-pressure discharges.[37] This is a clear advantage of PADI over other ambient techniques since it presents the possibility of harnessing the selective reaction mechanisms long established and utilized in low-pressure plasma processing techniques.

CONCLUSION

In conclusion, we have introduced PADI, a new technique for surface chemical analysis, and have demonstrated the potential of this method for the rapid analysis of pharmaceuticals. Results have shown that the coupling of PADI with the MBMS system is effective for generating high-quality data from various pharmaceutical formulations, such as tablets and creams, and suggests that the methodology has potential for future applications. The PADI source can be easily interfaced to mass spectrometers which have an atmospheric pressure inlet. For the work presented here, no alterations were necessary to the MBMS instrument and the only modification to the LCZ mass spectrometer was to remove the existing ESI source and override the source interlock to enable control of the MS via the vendor software.

As with DESI, PADI is an ionization technique which requires no sample preparation prior to analysis. It is simple, fast, and capable of high-throughput analysis. However, the main advantages of the latter method is the ease of operation, minimal requirements for optimization of operating parameters, and the lack of need for solvents which is beneficial for pharmaceutical and forensics applications. PADI is less angle-dependent than DESI, in respect of the sample to the mass spectrometer inlet and also the angle of the sample surface to the electrospray or plasma probe. This enables faster setup and analysis with less dependence upon the sample under investigation. This initial study has shown that PADI has considerable potential as a valuable and versatile tool for forensic, pharmaceutical, and biological applications. The technique is sensitive, tolerant to contaminants, and cross-contamination is negligible.

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