Desorption Electrospray Ionization (DESI) Mass Spectrometry: A brief introduction and overview

A recent advancement in mass spectrometry is the ability to examine samples situated outside the vacuum system in the ambient environment with minimal sample preparation. This article presents an introduction to desorption electrospray ionization (DESI) mass spectrometry and an overview of recent literature and emerging methods. In DESI, electrically charged droplets are directed at the sample of interest; ions are generated of the sample constituents and are collected and mass analyzed in a standard commercial mass spectrometer. This method promises rapid, high-throughput analysis combined with the sensitivity and specificity of the mass spectrometer. Applications related to counterfeit tablet identification, metabolomics, and two-dimensional chemical imaging of biological tissues are briefly discussed.

Mass spectrometry (MS) has significant advantages in speed, sensitivity and specificity over other methods of chemical analysis, and its broad applicability has proven valuable in many different scientific fields; however, MS is limited in part by the requirements for samples to be prepared prior to analysis. In most cases, the sample must be placed in vacuum for analysis (e.g. matrix-assisted laser desorption/ionization - MALDI) or dissolved or extracted in a solvent and sprayed in atmosphere (e.g. electrospray ionization - ESI) into the mass spectrometer. The requirement for the sample to be introduced into the vacuum system poses potential problems with contamination, speed of analysis, and the ability to provide true in situ measurements. Recent advances in mass spectrometry have taken the analysis of samples outside of the vacuum environment and into atmospheric pressure where the sample is maintained under ambient conditions.(1) Desorption electrospray ionization (DESI) (2,3) (F1), developed in the laboratory of Professor R. Graham Cooks at Purdue University and now commercialized by Prosolia, Inc., is the principal method in this new family of ionization methods. F2 displays the current Omni Spray™ Ion Sources made available by Prosolia, Inc. (Indianapolis, IN). Other methods in this group of ionization techniques include electrospray laser desorption ionization (ELDI) (4), direct analysis in real time (DARTTM) (5), and the atmospheric-pressure solids analysis probe (ASAP) (6). Desorption electrospray ionization minimizes the requirements for sample preparation by enabling investigation of samples in their native environment, where the sample is free for further chemical or physical manipulation. In this new method, charged droplets and ions produced from the electrospray are directed by a high-velocity gas jet to the surface bearing the analyte. The charged droplets impact the surface where the analyte is dissolved into the electrically-charged droplets. Secondary droplets ejected from the surface are subsequently collected in the ion transfer tube or atmospheric inlet of a standard commercial mass spectrometer and are mass-analyzed.

Literature review

The DESI experiment is routinely performed in seconds and requires minimal sample preparation or treatment. These characteristics make DESI a suitable technique for rapid, in situ analysis of samples in a variety of circumstances. For example, DESI has been applied to the rapid analysis of chemical warfare agents and explosives present on common surfaces (i.e. paper, plastic, fabric, metal etc.) (7, 8). Limits of detection in these studies reached levels of picograms to femtograms for RDX (trinitrohexahydro-1,3,5-triazine), TNT (1,3,5-trinitrotoluene), and DMMP (dimethylmethylphosphonate). To date, however, the most widespread use of DESI has been for analysis of pharmaceutical formulations (i.e. tablets, ointments and liquids) without prior separation. Direct investigation of pharmaceutical tablets (9-11) and ointments (10), as well as drugs of abuse in tablet form (12, 13) and in-plant material (13) has been successfully demonstrated by a number of groups. This method provides high-throughput data with no evidence for carry-over effects (9). One important illustration is the application of DESI to rapid chemical fingerprinting of pharmaceutical tablets for identification of potentially unsafe or counterfeit tablet formulations. F3 shows the mass spectra recorded from tablets of Cialis® and a suspected counterfeit. The authentic tablet shows abundant peaks originating from pharmaceutical excipients and a less abundant peak corresponding to the intact protonated tadalafil molecule at m/z 390.2. The counterfeit tablet also shows the presence of an additional peak at m/z 475.3 identified as sildenafil (Viagra®).

High throughput DESI analysis of biological fluid samples (e.g. urine) for metabolite identification is achieving increased attention due to the potential value of information on the distributions of characteristic small molecules or biomarkers as indicators of disease. With limited sample preparation required for analysis of raw urine, a few hundred samples per hour can be analyzed using DESI-MS when biological fluids are spotted onto Whatman® grade 5 filter paper or other porous substrates. In a publication by Chen and co-workers, detection of over 80 metabolites in urine was achieved using DESI (14). Direct analysis of plant (15) and animal tissues (16) has also been demonstrated using DESI. In this application, thin tissue sections prepared for microscopy or native, freshly-cut tissue surfaces are used for DESI-MS analysis. Using electronically-controlled motion stages and a fine DESI spray, chemical imaging of surfaces is

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accomplished. Imaging mass spectrometry based on MALDI and SIMS (Secondary Ion Mass Spectrometry) has become a powerful technique for analyzing histological sections of biological tissues (17, 18). However, these techniques require that the sample be confined to the high-vacuum region of the instrument, severely limiting any further chemical or physical manipulation of the sample, a limitation not inherent in DESI studies. Using DESI, the spatial distribution of natural tissue components such as membrane phospholipids has recently been demonstrated (19). Other applications of DESI to natural surfaces occur in forensic analytics, especially in detection of explosives, toxins and drugs of abuse on the surfaces of personal items.

A majority of the work reported on DESI and MS have been recorded using commercial quadrupole ion trap mass spectrometers. However, the common use of ion trap mass spectrometers is not a consequence of method since its implementation simply requires an atmospheric interface, although certain interface geometries have proven to perform better. In addition to use with ion trap mass spectrometers, DESI has been combined with triple quadrupoles (12), quadrupole time-of-flight instruments (11), ion mobility/time-of-flight (10, 20), a prototype Orbitrap instrument (21), and a hybrid quadrupole linear ion trap instrument (22). DESI has also been combined with a field-portable mass spectrometer for analysis of chemical warfare agent simulants, explosives, and environmental toxins present on a variety of surfaces (23). The subject of field-portable instrumentation based on MS or ion mobility has received increased attention owing to the possibilities of direct, in situ analysis. The combination of the specificity and sensitivity inherent in MS instrumentation and rapid, direct ionization under ambient conditions by DESI presents a very powerful approach to the problems faced in homeland security and environmental monitoring applications.

Emerging applications

An emerging capability of DESI is its ability to be automated for high-throughput monitoring and molecular imaging of biological tissues. The ability to record molecular information and its spatial distribution simultaneously from a sample or surface through imaging DESI-MS is proving to be a particularly powerful approach for analysis of biological tissues, especially when limited preparation of the surface is required and the sample is under ambient conditions. The limited sample preparation allows for higher throughput and the ability to record information on samples in situ. The development of imaging mass spectrometry by DESI was described recently (24, 25) and its application to tissue imaging with a spatial resolution of <400 µm was also demonstrated (24). F4 shows selected ion images of particular lipid species in a 10µm coronal section of rat brain. Each image consists of 112 x 39 pixels (4368 full mass spectra) with a pixel dimension of 150µm x 300µm. In the images shown in F4, distinct anatomical features are distinguished based on the chemical maps of two lipids. By acquiring full mass spectra for each image point (pixel) the information content in each pixel is greatly increased. In this case, the specific distributions of multiple analytes detected from the tissue surface are simultaneously acquired. In other studies, the lateral spatial resolution obtained when tested by analyzing an ink pattern on photographic paper was approximately 200 µm (25).

Clearly, applications which retain the ability to record the tissue distributions of exogenous compounds and their associated metabolites would be of tremendous advantage in the development of pharmaceuticals. Chemical imaging by DESI has this capability and is advantageously applied to label-free detection of drugs and metabolites in tissue (26). DESI-MS imaging has the following advantages over the conventional whole-body autoradiography approach: 1) no radioactive label is required; and 2) allows simultaneous detection of the parent drug compound and metabolites in tissue. DESI also retains the advantages of speed and specificity inherent in the mass spectrometry experiment. The fact that matrix solutions are not required to be deposited onto the tissue surface also presents a significant advantage over the MALDI technique. The two methods, however, are complementary in that MALDI is primarily suited for detection of large molecules such as peptides and proteins, and DESI is well suited for detection of small molecules such as lipids, metabolites and drug molecules.

Mass spectrometry-based methodologies are becoming increasingly utilized in early-phase discovery of molecular markers for cancer diagnosis. Molecular discovery in disease processes and integration into diagnostic pathology is currently underway, and development of new technologies should allow for faster integration. There are many foreseeable opportunities in diagnostic and surgical pathology that could take advantage of the sensitivity and specificity of MS-based technologies – especially those that provide both molecular weight identity and spatial information directly from the biopsied tissue. Such applications are very early in development; however, preliminary results are promising for distinguishing diseased and non-diseased tissue based on their chemical signatures obtained by DESI-MS (16, 27). In these studies qualitative changes in the lipid profiles were obtained that distinguished the tumor from the non-tumor region of a biopsied liver adenocarcinoma tissue.

Chemical imaging by DESI-MS is still, however, in its infancy. Ongoing research in the area is addressing questions concerning sensitivity, compound-specific ionization yields, tissue-specific ion suppression, and effects of solvent composition on ionization yields. Insight into these experimental variables should improve method reproducibility and allow for quantitative information to be obtained.

Conclusions

DESI-MS offers unique advantages over traditional MS approaches. These include: (1) minimal sample preparation; (2) sample maintenance under ambient conditions outside the vacuum system; (3) rapid, high-throughput analysis; (4) the ability for in situ detection; and (5) label-free chemical imaging with basic instrumentation requirements. The advantages offered by DESI-MS should lend it useful in the pharmaceutical industry in support of testing for cleaning validations to rapid, counterfeit tablet profiling to label-free chemical imaging of drug compounds in tissues.
References


F1. Schematic diagram of the DESI experiment.

F2. Omni Spray™ Ion Sources. (A) Thermo Scientific LCQ models (B) Thermo Scientific LTQ and Ion Max™ compatible instruments (C) Bruker/Agilent (D) MDS Sciex (E) ABI/Waters
F3. Direct tablet analysis for rapid fingerprinting counterfeit and authentic drug tablet formulations.

![Diagram of m/z vs Relative Abundance for sildenafil and tadalafil in counterfeit and genuine tablets.]

F4. Selected ion images of phosphatidylcholine (PC) species in a 10µm coronal section of rat brain. 

bregma -5.0 A) PC (32:0) [M+K]+ m/z 772.3 B) PC (36:1) [M+K]+ m/z 826.4.