Trends in Analytical Chemistry 78 (2016) 109–119

Contents lists available at ScienceDirect

Trends in Analytical Chemistry

journal homepage: www.elsevier.com/locate/trac

Biological Desorption Electrospray Ionization Mass Spectrometry (DESI MS) – unequivocal role of crucial ionization factors, solvent system and substrates

Muthu Manikandan [a], Zakayo Kazibwe [a], Nazim Hasan [b], Anbarasu Deenadayalan [c], Judy Gopal [a], Thalappil Pradeep [d], Sechul Chun [a,*]

[a] Department of Bioresource and Food Science, Konkuk University, Seoul 143-701, South Korea
[b] Department of Chemistry, Faculty of Medicine, Jazan University, Jazan 2097, Saudi Arabia
[c] Department of Immunology, National Institute for Research in Tuberculosis (ICMR), Chennai 600031, India
[d] DST Unit of Nanoscience (DST UNS), and Thematic Unit of Excellence (TUE), Department of Chemistry, Indian Institute of Technology Madras, Chennai 600 036, India

ARTICLE INFO

Keywords:
DESI MS
Solvent system
Substrates
Biological samples
Sample spotting
Analyte ionization
Molecular imprinting

ABSTRACT

DESI MS, has been successfully employed for the analysis of molecules from a wide variety of surfaces without prior sample treatment. The efficiency of DESI MS relies on various parameters. However, those that critically affect the ionization of biological samples include: the solvent system and the sample or sample spotting surfaces. These parameters gain unequivocal dominance specially whilst dealing with sensitive and intricate biological samples. This review is meant to capture the attention of the DESI-MS researchers towards the crucial role of the solvent and sample spotting surfaces for successful biological DESI-MS. This review highlights these parameters as the backbone of the breakthroughs achieved in the analysis of biological materials of plant, bacterial, animal and human origins.

Contents

1. Introduction 109
1.1. Summary of solvents and surfaces used for biological DESI MS 110
2. Milestones achieved via optimized solvent system and sample surfaces in biological DESI MS 112
2.1. Biological DESI MS for plant samples 112
2.2. Biological DESI MS for animal samples 113
3. Milestones achieved via advances through molecular imprinting 117
4. Future perspective of biological DESI MS 117
Acknowledgement 118
References 118

1. Introduction

Mass spectrometry (MS) is one of the most sophisticated techniques that measure the mass to charge ratio of molecules taking advantage of their ionization properties. The measurement of mass to charge ratio, provides detailed information of molecules, for precise identification and constant monitoring of the fate of the chemical compounds. Due to its rapidity, ease in handling and sensitivity, MS has become an unavoidable tool in various fields such as food, pharmaceutical, environmental, biological and medical sciences. In fact MS had brought about significant advancements in areas evolving around microbiology, plant science, clinical diagnostics, forensics and protein research [1–3]. Apart from that, MS also plays a key role in space research for the understanding of the molecular composition of planetary atmospheres and providing valuable information about the evolution of the planetary systems [4].

MS is broadly divided into 2 distinct categories: (i) conventional MS, where the ionization of the analyte is carried out inside the mass spectrometer and (ii) ambient MS where the ionization happens in their native environment and then is subsequently introduced into the mass spectrometer for analysis based on the mass to charge ratio of the molecules [5,6]. Due to the fact that the analytes

* Corresponding author. Tel.: 822 450 3727; Fax: +8224503726.
E-mail address: scchun@konkuk.ac.kr (S. Chun).

http://dx.doi.org/10.1016/j.trac.2016.02.013
0165-9936/

usually maintain their original chemical/physical/biological states, ambient ionization methods have made an excellent contribution towards the development of a vast variety of new mass spectrometric techniques [7, 8]. As a result, more than 25 different ambient ionization techniques have been described in literature, which have predominantly evolved from two basic instrumental techniques such as electrospray ionization (ESI)-related ambient techniques and atmospheric pressure chemical ionization (APCI)-related techniques [9]. The different techniques that have branched out from these core techniques include; desorption electrospray ionization (DESI) [7], direct analysis in real time (DART) [10], extractive electrospray ionization (EESI) [11,12], secondary electrospray ionization (SESI) [13,14] and many combinations of desorption with post ionization methods working at atmospheric pressure etc. [15].

In DESI MS, the analyte is placed just outside the mass detector capillary of the mass spectrometer. Then aqueous droplets of solvents with diameters less than 10 µm are sprayed at velocities typically in excess of 100 m/s. The sprayed droplets after hitting the sample surfaces desorb the analyte ions and are picked up along with the reflected droplets through the droplet pick up mechanism. The charged microdroplets thus formed alongwith the analyte molecules are then suctioned into an extended atmospheric pressure ion transfer capillary and subsequently enter into the mass spectrometer, getting ionized through electrospray processes resulting in the formation of singly or multiply charged ions, which are subsequently detected by a mass spectrometer [16,17].

Among the ionization techniques, DESI MS is the most significant and reliable MS technique that is being used successfully for surface analysis of various samples including those that have not been possible via ESI or any off-line solid-liquid extraction procedures. Since DESI MS operates with various mass spectrometers, the sensitivity of this technique is equivalent to or more than that of the mass spectrometer it is associated with, which is proven to be femtomoles for different molecules [18]. Therefore, the contribution of DESI MS has been undoubtedly demonstrated in various analytical applications generally without vacuum and any sample pretreatment. These include the detection of explosives, abusive drugs, direct detection of chemical warfare agents, rapid investigation of pharmaceuticals, and clustering based on sample composition, detection of pollutants for environment monitoring, analysis of metabolites from plant, animal and natural products and characterization of various chemical compounds [5, 11, 17, 19–24]. In addition to that, DESI MS technique offers tandem mass (MS^2) analysis of single compounds from a mixture of compounds which aids in the authentic identification of compounds without purification [25].

Another fascinating development in DESI MS is the monitoring of molecular ion peaks in spatial coordinates which provides valuable information with respect to 2 dimensional imaging [26] and is used primarily for medicinal and biological applications to access the distribution of metabolites, expression and toxicity of drugs. DESI MS had replaced the setback of matrix interference in renowned mass spectrometric imaging techniques like MALDI MS [27–29] by doing away without matrix usage which generally interferes substantially with small molecule detection and subsequent MS imaging. Yet with all these deliverables, there is still a huge asking from DESI MS for overcoming various hurdles and obstacles in order to make it across from the bench top to the bed side.

Although DESI MS analysis is considered as one of the most simplest ionization techniques, this technique still crucially relies on various parameters for its enhanced efficiency. These parameters include: analyte property, surface on which the analyte is spotted or placed and solvent system, and the physical parameters such as the geometry of the ion source (nebulisation capillary angle, its distance to the surface and to the MS inlet) and other settings like nebulising gas pressure and solvent flow and capillary voltage. These

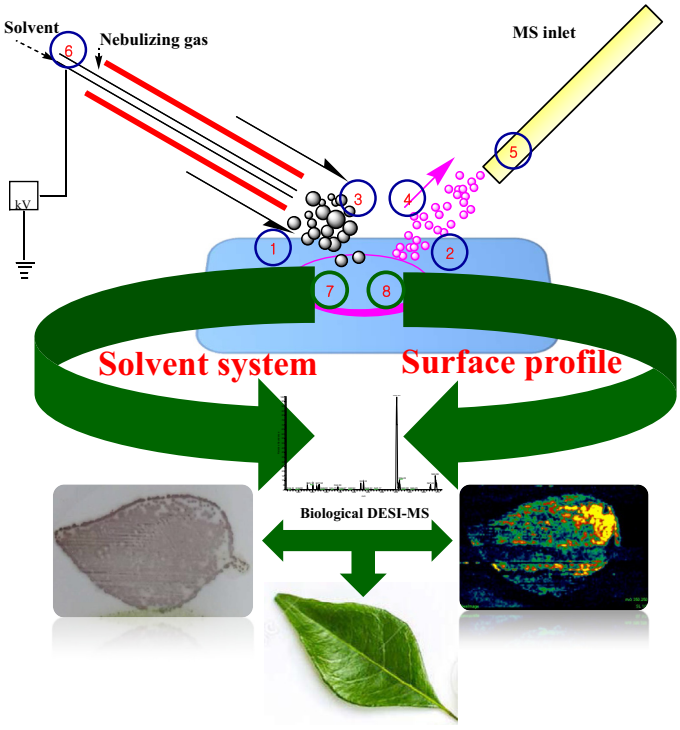

Fig. 1. Schematic diagram showing the factors affecting DESI MS analysis of biological samples, the significant factors are highlighted within blue circles and the most significant factors are highlighted using green circles. 1. Angle of the nebulizer tip to the sample surface; 2. Angle of mass spectrometer inlet from sample surface; 3. Distance between the nebulizer tip and the sample surface; 4. Distance between sample surface and mass spectrometer inlet; 5. temperature and voltage of ion transfer capillary; 6. Solvent flow rate; 7. Solvent system and 8. Sample surface.

factors in turn affect the signal intensity, signal stability and the type and extent of adduct formation. Among all the variables, for the proper ionization of an analyte molecule, the most vital is the solvent system and the sample surface profile (Fig. 1). This latter variables have often been overlooked leading to limitations in the extension of DESI MS further into complex biological analysis. In this regard, this review highlights the importance of the solvent system and the surfaces used in the biological DESI MS sample analysis. The specific reasons for their importance has been indexed in this review and the rationale behind evolution of innovative DESI MS designs and methods have been discussed in detail.

1.1. Summary of solvents and surfaces used for biological DESI MS

The most vital factor for successful biological DESI MS is the solvent system. It is evident from the tables (Table 1–3) that various solvent systems have been employed for the DESI MS analysis. The diversity of solvent systems listed in the tables with respect to a variety of biomolecules analysis either directly or after extraction from plants, bacteria, animals and human samples, show the need for careful selection of the right solvent system for a specific analyte. Fig. 2(a-c) shows the solvent system used (in percentage) for biomolecule analysis. Of the various solvent systems used, the usage of combinations of methanol and water was found to be predominating (37.9%) for molecules of plant origin, followed by pure methanol (27.58%) and methanolic solvent system with different reactive substances (20.68%) than pure methanolic spray (Fig. 2a). Although, other solvent systems such as acetonitrile, acetonitrile:water, acetonitrile with reactive substances, DMF: