2026 Volume: 01 Issue: 07 ISSN 1671-2838 Page No: 390-399

Pharmaceutical Care and Research

https://pcrjournal.com

Review Article

Volume: 01
Issue: 07

A BRIEF REVIEW ON MASS SPECTROMETRY IN DRUG IDENTIFICATION

Aditi A. Kumbhar[1] , Dr. Prasad V. Patrekar[2], Dipak R. Phalle*[3], Omkar V. Kamble[4], Chitra G. Rajput[5], Mrudula P. More[6]

[1]Student, [2]Principal, [3]Assistant Professor, [4]Assistant Professor, [5]Assistant Professor, [6]Assistant Professor.

Eklavya College of Pharmacy, Tasgaon, Maharashtra, India.

Article Received: 23 August 2026
Article Revised: 11 September 2026
Published on: 01 October 2026

***Corresponding Author: Dipak R. Phalle**
Assistant Professor, Eklavya College of Pharmacy, Tasgaon, Maharashtra, India.

DOI: https://doi-doi.org/101555/ijpcr.6670

ABSTRACT

Mass spectrometry is an important analytical technique used for the identification and analysis of drugs and pharmaceutical substances. It is known for its high sensitivity and accuracy and can provide useful information about a compound's molecular weight and structure. This review focuses on the role of mass spectrometry in drug identification and its applications in pharmaceutical and clinical fields. An overview of the basic principles of mass spectrometry, including affinity mass spectrometry and its application in the study of interactions between drugs and biological targets. This review also describes the main components of a mass spectrometer and describes the basic concepts of mass spectrometry imaging that can study the distribution of drugs and their metabolites in tissues. Additionally, we will discuss the use of mass spectrometry for sample identification and analysis of tablets and powders. Clinical applications in the detection and analysis of drugs and related compounds are also highlighted. Overall, mass spectrometry provides a reliable and sensitive approach for drug identification and analysis. With continuous improvements in equipment and analytical techniques, this method is becoming increasingly useful in pharmaceutical research, quality control, and clinical analysis.

KEYWORDS: Drug, Pharmaceuticals, Metabolites, Mass Spectrometric Imaging, Affinity Mass Spectrometry.

INTRODUCTION

Mass spectrometry (MS) is a robust, adaptable method with uses that cover the entire range of the drug discovery and development process. MS techniques like proteomics, metabolomics, and the examination of clinical tissue samples play a crucial role in target validation discovery. Where these

methods can be employed to obtain understanding of a compound's cellular mechanism of action (MOA). For decades, MS has been pivotal in defining the structure and pharmacokinetic characteristics of compounds during lead optimization. MS is becoming more significant in the target identification phase of the drug discovery process. For instance, limited proteolysis-coupled MS is commonly employed to assess proteome-wide specificity and reveal binding sites of small molecules, while thermal proteome profiling aids in small molecule target identification, and dataindependent acquisition MS facilitates high-throughput analysis of cellular systems for comprehensive proteomics and phosphoproteomics.[1]

Principle of Affinity Mass Spectrometry

Affinity selection-MS (AS-MS) techniques assess the interaction of small molecules with their biomolecular targets, and all types of AS-MS entail the following steps:

i). An affinity selection phase, during which the protein interacts with one or more potential ligands, enabling the formation of a complex with any compound that can bind; ii). The subsequent separation of receptor–ligand complexes from the non-binding components of the mixture; and

iii). The identification of ligands through mass spectrometry (MS) or tandem mass resulting mixture is analyzed using size-exclusion chromatography. Smaller molecules of the test compound are trapped in the column, while larger entities like the target protein move through, carrying the bound compounds with them. Afterward, the bound compounds are separated and identified through LC/MS. This last phase eliminates the need for compound labeling, allowing for the analysis of individual compounds even when they are mixed. Therefore, AS-MS can be described as free of both labeling and immobilization. Compounds with a dissociation constant (Kd value) of 10 µM or less can be detected, and soluble proteins are suitable as targets. Furthermore, membrane proteins that remain in their membrane-bound states (for example, in the microsomal fractions) can be used. [2,3]

spectrometry (MS/MS).

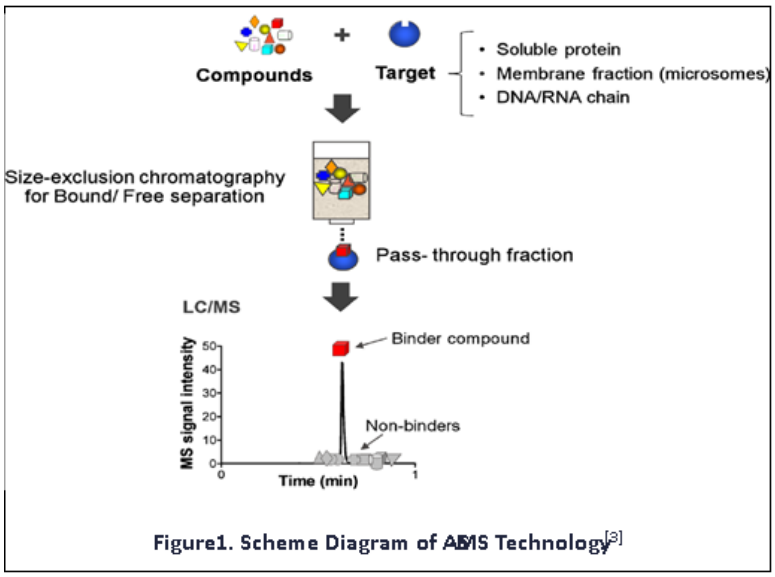


Figure1. Scheme Diagram of AS-MS Technology[3]

In AS-MS approaches (Fig. 1), compounds are combined with a specific protein, and the

Mass Spectrometric Instrumentation

MSI has its roots in physics, where it was initially utilized to investigate semiconductor surface.

The advent of MALDI-MSI in 1997 by Caprioli and colleagues sparked major advancements in methodologies, instrumentation, and software for bioanalytical purposes. These technologies were swiftly implemented in the analysis of pharmaceutical biodistribution, allowing for the correlation of molecular drug distribution maps with histological data and are now making significant impacts in areas such as molecular histology, drug distribution, and proteomics .The capacity to pinpoint compounds enables MSI to address inquiries concerning intricate distribution patterns such as penetration across the blood–brain barrier.[4,8]MSI can detect endogenous and exogenous analytes across a wide mass range, from low molecular weight drugs and endogenous compounds through to lipids and large proteins, directly from tissue samples .[6] Importantly, MSI can, by mass measurement, differentiate between drugs and metabolites formed by Phase 1 or 2 metabolism, overcoming the limitations of non-specificity encountered with autoradiography.[7]

Imaging of drugs and metabolites in tissue from animals. Most studies on drug/metabolite MSI have utilized the MALDI technique, strategy, but more recently matrix-free approaches, encompassing SIMS, NIMS, DESI, and LAESI has been explored due to their more straightforward sample preparation processes and absence of a grid. We will cover the experiments that employed (matrix-assisted laser desorption ionization MALDI,(secondary ion mass spectrometry) SIMS, NIMS, (desorption electrospray ionization) DESI and LAESI have been investigated because of their simple preparation of matrix. [5]

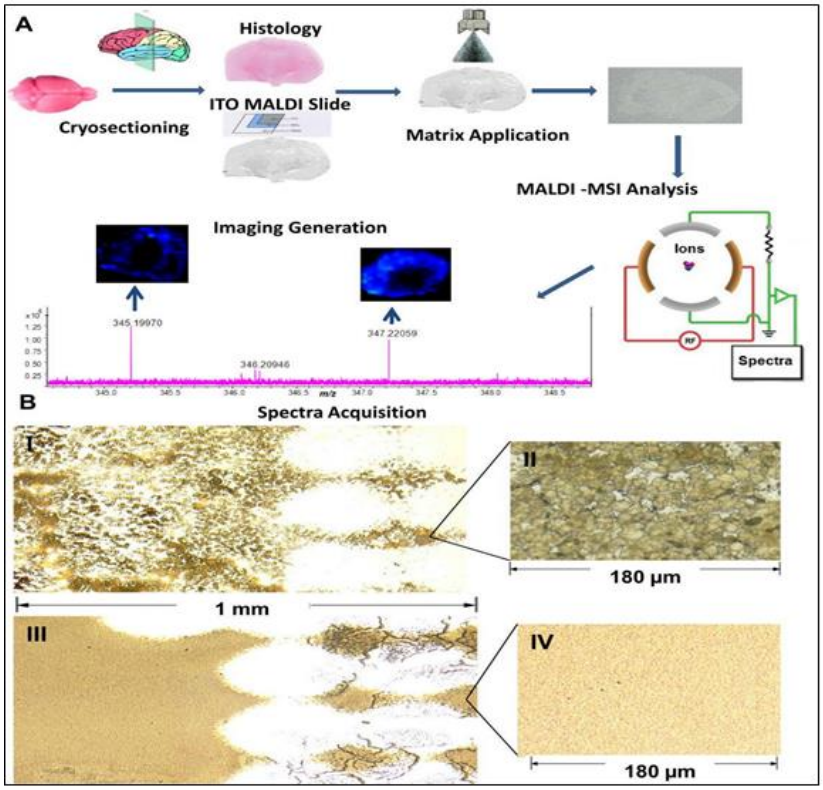


Figure2:

A). MSI process. MSI includes sample preparation, desorption and ionization of analytes, mass analysis, and registration of images. In summary, cryo-sections. Tissue samples are covered with an appropriate MALDI matrix and subsequently placed into an MSI device. A designated region of the tissue sample is examined. and gathered mass spectral data. The resulting distributions of ions are displayed as ion images. ITO, indium tin oxide. (B) Array deposition through manual spraying and sublimation. Sublimation results in the formation of smaller crystals (sub-µm) in contrast to a standard. spray-coating, with the resulting crystal sizes reaching approximately 10–20 µm. Image (×25magnifications) of a rat adrenal gland tissue slice placed on a conductive glass slide and coated with α-cyano-4-hydroxycinnamic acid (CHCA) matrix using (I) a pneumatic thin-layer chromatography sprayer (2.61 mg, complete slide) (III) sublimation (2.74 mg, complete slide). Optical image of CHCA crystals (×40 magnification) (II) created by spraying or (IV) sublimation.[4]

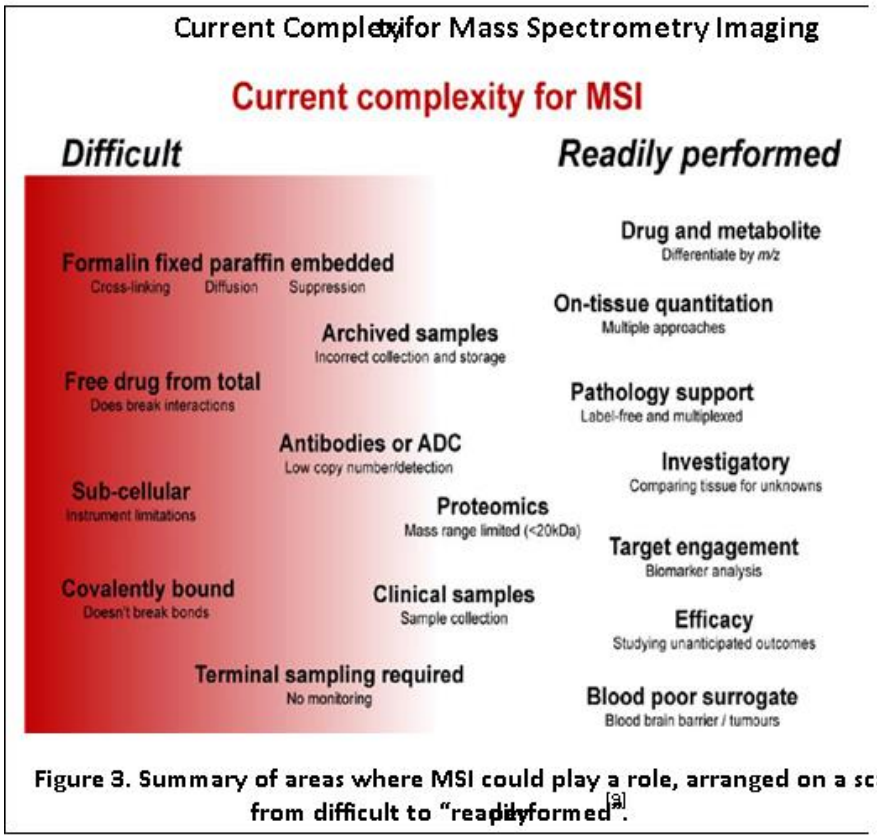


Figure 3. Summary of areas where MSI could play a role, arranged on a scale ranging from difficult to "readily performed".[3]

Mass Spectrometry Imaging Fundamentals

Image of light while there are other figures of merit for MSI, these three are the most frequently cited in the literature. The amount of resolution and accuracy required to generate a quality image is dependent on the compounds being imaged and the complexity of the tissue. For instance, a drug with a theoretical mass of 239.1077 Da requires 419 ppm mass accuracy and 2400 mass resolution to be distinguished from isobaric molecules with mass differences of 0.1 Da or greater, and requires 4.2

ppm mass accuracy and nearly mass resolution at 240,000 to be distinguished from mass differences of 0.001 Da. Fourier transform (FT) mass spectrometers are capable of parts-per-billion mass accuracy and mass resolution greater than 1,000,000, but can be very costly and often require longer acquisition times to construct an ion image. T (TOF) instruments have resolving powers in range of 10,000 to 100,000.[9,10]

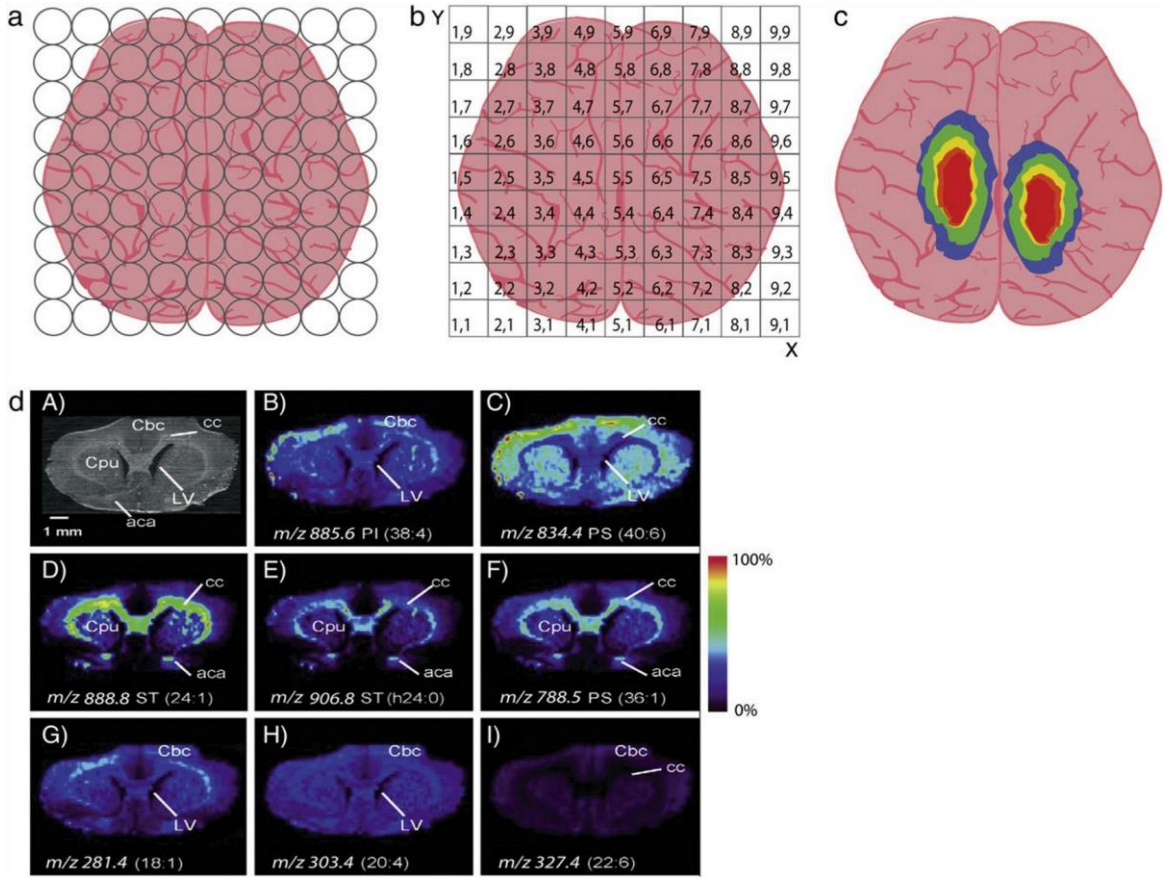


Figure 4. Production and detection of ions by mass spectrometry (a) A tissue is prepared, and mass spectra are obtained at multiple points throughout the entire tissue; (b) each sampled point is transformed into spatial coordinates and (c) an image is constructed by plotting the intensity of a particular ion at each point. (a) Images of eight different lipids simultaneously obtained from a rat brain, reprinted with permission from.[11]

Sample identification

This type of qualitative analysis includes the identification/classification/authentication of objects such as foodstuffs, products, specimens, materials, pollutions, and living organisms. Examples of such procedures include food authentication, identification of food adulteration, identification of oil spills, and identification of microorganisms. Sample identification presents.[13] Unexpected positives due to drug impurity and legal food source. Each drug has some allowed level of impurity in it, and for certain drugs, such as therapeutic grade morphine, codeine is an allowed impurity at a level of b0.15% ; thus, low levels of codeine in a specimen with high morphine concentration may be due to this

impurity. Illicit drugs may also contain impurities in variable amounts, and impurity profiling can be used to confirm consumption of certain illicit drugs. Other unique impurities can be used to confirm consumption of certain illicit drugs and impurity profiling can be used to.[14]

Tablet and Powder Analysis

An important application of MSI in pharmaceutical analysis is to image drug release systems such as stents, tablets, and powders. In 2000, Belu and colleagues analyzed three multilayer drug beads that function as controlled drug delivery systems with TOF SIMS [16]. The integrity of each layer was evaluated by imaging specific ion types for drugs (theophylline, paracetamol, prednisolone), additives and coating materials with a resolution of less than a micro meter. Each bead has a unique distribution of ingredients, and the image of the active drug shows that its distribution ranges from micrometer-sized particles in a bead section to almost homogeneous in another bead section [16]. Further more, the TOF SIMS data showed that the components of the bead did not exactly correspond to the manufacturer's specifications. TOF SIMS also analyzed drug eluting stent coatings [16,18] .A group used SIMS cluster with a source of primary ion sputterSF5 + poly atomic and a source of analysisBi3 + [17]. Depth profiles show that in stent coatings of different components, the drug sirolimus tends to disperse on the surface, forming a diffusion profile. The diffusion profile consisted of a surface region rich in drugs, a region that depletes drugs, and a constant mass composition region [17]. Another study obtained chemical images of the surface and interior of rapamycin in poly (lactic-co-glyconic acid) (PLGA) coatings using surface-sensitive electron microscopes for chemical analysis (ESCA), TOFSIMS and Raman microscopes. As the concentration of rapamycin increased from 5per cent(wt.) to 50per cent(wt.) in the rapamycin/PLGA coating, the increased separation of most of the coating was apparent.[17] However, all formulations except capcoated stent contained significant enrichment of rapamycin on the surface. The 3D spatial distribution of pharmaceutical molecules in a coronary stent coating was analyzed to visualize the distribution of drugs according to the stent effluent time.[18]

Clinical Applications

1.Measuring Drug Response and Metabolites

Histology guided MSI has been extensively applied to the study of drug response and distribution.[20,21] Combined quantitative whole-body autoradiography (QWBA) and imaging mass spectrometry to simulate an in vivo phototoxicity study of a proprietary drug candidate (Bristol-Myers Squibb Company, Princeton, NJ)within ocular tissue. QWBA reveals quantitative and tissue distribution information of radiolabeled analytes [84]. However, QWBA cannot be used to obtain information about the drug and its metabolites or degradation products. MSI is notorious for giving poor quantitative data, but can reveal information about the analyte and its products; therefore it was advantageous to combine QWBA and MSI for this study.

2.Biomarker discovery and validation

The discovery and validation of biomarkers, along with other lab- oratory and clinical evaluations, contribute to the assessment of disease severity, disease progression, and treatment response.[23] Gene expression profiling was the prominent source of biomarker discovery, but more recently, protein expression profiling has explored in this field [24], and lipidomics has been gaining popularity.[25]

3. Protein Biomarkers

Changes in protein levels in tissue may be correlated with the state of disease .These protein levels can be monitored not only to reveal the type of disease, but also the severity of the disease. MSI is becoming a powerful tool for biomarker discovery mainly because it can study tissue proteomics while maintaining spatial distribution , allowing direct comparison with its histology [26]. MSI can be applied simultaneously to multiple tissues, allowing more in-depth study of target diseases and potential biomarkers .[27]

4. Lipid Biomarkers

Lipidomics has become increasingly well-known in clinical uses. In a manner akin to protein biomarker discovery, lipidomics seeks to characterize. Characterize lipid molecules in tissues and connect this information to illness. countries, in addition to various uses. [28] Proteomics seeks to define and measure the cellular functions indicating gene expression, in contrast, lipidomics (a branch of metabolomics) examines the molecular metabolic byproducts and is most aligned with patient phenotype, creating Lipidomics is a significant area of research.[29]

5. Small Molecule Biomarkers

Tiny molecule indicators Ambient ionization techniques may likewise be employed to investigate and detect biomarkers in malignant tissues.[22] Dill and colleagues. utilized DESI-MSI to investigate human bladder cancer and create a statistical model technique for differentiating between malignant and benign tissue specimens alongside conventional histological recognition techniques.[31] The researchers employed a sample training set to establish the most effective predictive attributes and a test/validation dataset for assessment the effectiveness of their statistical model on typical samples. There existed 20 pairs of cancerous and nearby normal human bladder samples of tissue utilized in this research. DESI-MSI data indicated considerable alterations in glycerol phosphor inositols, glycerol phosphoserines, and fatty acids in the cancerous and healthy tissue samples.[32]

CONCLUSION

Mass spectrometry has become an important method for drug identification and analysis due to its sensitivity, accuracy, and ability to provide detailed molecular information. The development of various mass spectrometry techniques has increased their usefulness in pharmaceutical research and drug analysis. Affinity mass spectrometry helps understand drug target interactions, and improved equipment allows for faster and more accurate analysis. Mass spectrometry imaging also provides valuable information about the distribution of drugs and metabolites in biological tissues. The use of

mass spectrometry for sample identification, tablet and powder analysis, and clinical applications demonstrates the importance of mass spectrometry in the pharmaceutical field. Although the high cost of equipment and the need for trained personnel may be limitations, current technological developments are making this method more efficient and useful. Overall, mass spectrometry is a reliable and versatile method for drug identification and is expected to continue to be an important analytical tool in pharmaceutical research, quality control, and clinical research.

REFERENCES

1. M. Emilia Duenas, R. E Peltier-Heap, M. Leveridge, R. S Annan, F. H Buttner and M' Trost, "Advances in high throughput mass spectrometry in drug discovery 2011", page no.1.
2. D.Allen Annis, E. Nickbarg , X. Yang, Micheal R Ziebell and C. E Whitehurst, "Affinity selection mass spectrometry screening technology for small molecule drug discovery chemical biology 2007", page no.518.
3. T. Motayaji, "Resolution of small molecule drug discovery by affinity selection mass spectrometry technology", Received 15 Sep 2019.
4. D. F. Cobice , R. J. A Goodwin, P.E . Andex , A. Nillson, C.L. Mackay and P. Andrew, " Future technology insight; mass spectrometry imaging as a tool in drug research and development". Page no. 3268-3269
5. J. proteonomics, " Mass spectrometry imaging for drugs and metabolites", Published Nov 2011.
6. W. RE, Manitpisitkul P (2001), "Kinetic theory of cassette dosing in drug discovering , screening drug metabolites" , Dispos29:957-966
7. W. EM, Himmon AB (2013) "Imaging mass spectrometry from tissue sections to cell cultures advance delivery" Review65:1039-1055
8. Liu X, Ide JL, Norton I, Marchiooni, MA Ebling MC, Liu LJ Etal(2013) " Molecular imaging of drug transit through the blood brain barrier with MLDI mass spectrometry imaging".
9. A. Nilsson, Richard J.A Goodwin, M. Shariathorji, T. Villina tou peter I.H.Webborn and Per. E. Andren , " Mass spectrometry imaging in drug development
10. G. Glauser, N. Veyrat, B. Rochat, J.L.Wolfender, T.C. Turlings, "Ultra high pressure liquid chromatography mass spectrometry for plant metabolomics a systematic comparison of high resolution quadrapole time of flight and single state orbitap" MS, J. Chrpmatp.A(2012).

11. J.M.Wiseman, D.R. Ifa, Q.Y.Song, R. Glooks, " Tissue imaging atmospheric pressure using desorption electrospray ionization (DESI)" MS Angew.Chem,In+ Ed.. Engl45 (2006) 7188-7192.
12. Christopher B. Lietz, Erin Gemperline , Lingjun Li, " Qualitative and quantitative MS imaging drug metabolites", 2013.
13. L. milman, "General principle of identification by mass spectrometry; trends in analytical chemistry", 2015
14. Chao Yuan, Derrick Chen, Sihe Wand, " Drug conformation by MS: Identification criteria and complicating factors" , Department of clinical pathology, Cleveland 44195 USA.
15. Chien- Hua Chaing , Hei- Hwa Lee, Bai- Hsiun, Chen, Yi-Ching Lin, Yu- Ying Chao
16. LihHuang, "Using ambient Mass Spectrometry and LC-MS/MS for rapid detection and identification of multiple illicit street drugs" , 2019
17. Belu A, Davies, Newton J, Patel N, ToF, " SIMS characterization and imaging of controlled release drug delivery system", analytical chemistry 200: 72:5625-5638
18. Mohoney C, Fahey A, three dimentional compositional analysis of drug eluting stents coatings using clester secondary ion mass spectrometry", analytical chemistry 2008:80:624-632
19. Fisher G. Belu, A. Mohnet, C. Wormath, K. Sanadon , " Three dimentional time of flight secondary ion mass imaging of pharmaceutical in a coronary stent coating as a function of elution time", Analytical Chem. 2009.81-9930-9940
20. Tyler Greer, Robert Sturm and Lingiun Li, "MS Imaging for drug and metabolites", department of chemistry and school of pharmacy 18 Nov 2011.
21. Drexler DM, Tannehill-Gregg SH, Wang LF, Brock BJ. Utility of quantitative wholebody autoradiography (QWBA) and imaging mass spectrometry (IMS)by matrix-assisted laser desorption/ionization (MALDI) in the assessment ofocular distribution of drugs. J Pharmacol Toxicol Methods 2011;63:205-8.
22. Greer T, Sturm R, Li LJ. Mass spectrometry imaging for drugs and metabolites. J Proteomics 2011;74:2617-31
23. Hui Ye, Erin Gemperline, Lingjiun Li, A vision for better health: Mass Spectrometry Imaging for clinical diagnostics 2013, Page no(16,17).
24. Young SP, Piraud M, Goldstein JL, et al. Assessing disease severity in Pompe disease: the roles of a urinary glucose tetrasaccharide biomarker and imaging techniques. Am J Med Genet C Semin Med Genet 2012;160C:50-8.

25. Meding S, Nitsche U, Balluff B, et al. Tumor classification of six common cancer types based on proteomic profiling by MALDI imaging. J Proteome Res2012;11:19962003.
26. Postle AD. Lipidomics. Curr Opin Clin Nutr Metab Care 2012;15:127-33.
27. Seeley EH, Caprioli RM. Imaging mass spectrometry: towards clinical diagnos- tics. Proteomics Clin Appl 2008;2:1435-43.
28. Cazares LH, Troyer DA, Wang BH, Drake RR, Semmes OJ. MALDI tissue imaging:
29. from biomarker discovery to clinical applications. Anal Bioanal Chem 2011;401:17-27.
30. Postle AD. Lipidomics. Curr Opin Clin Nutr Metab Care 2012;15:127-33.
31. Thomas A, Lenglet S, Chaurand P, et al. Mass spectrometry for the evaluation of cardiovascular diseases based on proteomics and lipidomics. Thromb Haemost 2011;106:20-33.
32. 30.Weaver CM, Liebman M. Biomarkers of bone health appropriate for evaluating functional foods designed to reduce risk of osteoporosis. Br J Nutr 2002;88: S225-32.
33. 31. Gamez-Pozo A, Sanchez-Navarro I, Calvo E, et al. PTRF/Cavin-1 and MIF proteins are identified as non-small cell lung cancer biomarkers by label-free proteomics. PLoS One 2012;7