

A large conference hall with a stage at the front. On the stage, several men are seated at a long table. Behind them is a large red backdrop with the conference title and IICMS logo. The backdrop also features a grid of small images showing various laboratory equipment and techniques. The audience, consisting of many men in white shirts, is seated at round tables in the foreground, facing the stage.

Conference on 'Frontiers in MS Technology and Emerging Applications'

About IICMS

Mass Spectrometry, once considered as a "research tool" in the hands of experts, has today become an "essential tool" encompassing all branches of science. The applications of mass spectrometry hyphenated with chromatographic techniques like liquid and gas chromatography are ever increasing. Presently several technologically advanced mass spectrometers are commercially available unraveling many innovative techniques for developing newer applications. The Indian Institute of Chromatography and Mass

Spectrometry (IICMS) is an institute established to train the scientists to fully explore these new instrumental innovations and thereby successfully overcome their application challenges.

The objective of IICMS is to develop experts by providing in-depth training on various aspects of MS techniques coupled with chromatography. The quality of the training is intended to enable the participants to develop wide range of applications starting from trace level impurity analysis to protein characterization.

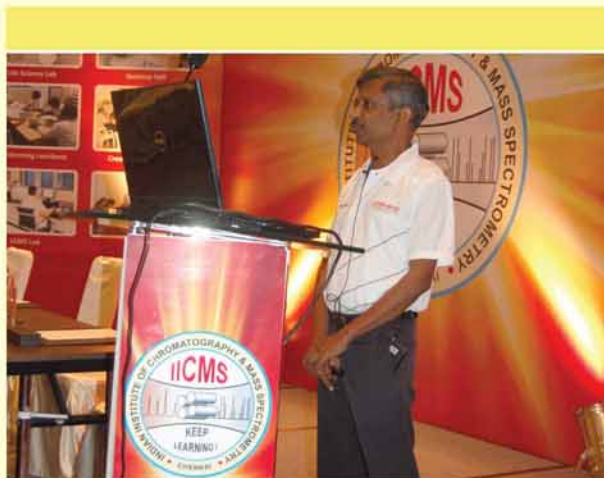
The official inauguration of IICMS took place on the 28th of November 2011 by Dr. Teruhisa Ueda, Director, Shimadzu Corporation, Japan. The inauguration was followed by the first national conference on mass spectrometry organized by IICMS.

Conference on mass spectrometry - The theme

The theme of this year's conference was on the "Frontiers in MS technology and emerging applications" and the



conference saw the confluence of over 150 scientists from all over the country. This national conference on mass spectrometry was one of the key initiatives by IICMS in "sharing the learning". Eminent speakers from the industry, national institutes and academia who have made valuable contributions through their pioneering work using mass spectrometry, addressed the huge gathering with their interesting, informative and insightful lectures.



Dr. M. Vairamani

Dean, School of Bio-Engineering,
SRM University, Kattankulathur, Chennai

Identification of unknown compounds: Challenges!

Mass spectrometry is a powerful tool to identify unknown compounds at sub micrograms where one gets the details of molecular weight, elemental composition and characteristic fragmentation pattern. Interpretation of mass spectrum can be done in comparison with commercial libraries when the mass spectrum is recorded using electron ionisation (EI) technique. Other ionisation techniques such as chemical ionisation, electron spray ionisation techniques, etc., being 'soft', provide limited fragmentation to characterize the compounds, even under MSMS mode. On the other hand direct liquid chromatography-electron impact and electron transfer dissociation techniques can give mass spectra of polar compounds to generate useful library to help to identify new compounds.



Dr. KP. Madhusudanan

Senior Scientist

Arjuna Natural Extracts Ltd, Aluva, Kerala

Ambient Mass Spectrometry and its Applications

Ambient ionisation MS is a technique in which ionisation of the analyte is achieved under ambient conditions with minimum or no sample pretreatment. The ambient sources can be directly fitted to conventional sources such as electron spray ionisation or atmospheric pressure ionisation methods. This leads to a set of different electron spray and laser desorption ionisation methods so that real time sample analysis is possible whether sample is in a liquid or solid state. Of all the techniques, desorption electron spray ionisation (DESI) and direct analysis in real time (DART) have initiated revolution in ambient mass spectrometry applications in almost all branches of science such as natural products, lipids in animal tissues, biological fluids, chemical warfare agents and so on.

The one-day event comprised of two sessions, the morning session focused on instrumentation needs, chemical sciences and the afternoon session addressed life science applications. Each session ended with panel discussions where brainstorming amongst the speakers and participants resulted in sharing of MS knowledge and applications.

An initiative of this magnitude will definitely require tremendous support from various institutions. IICMS is currently under a memorandum of understanding (MoU) with the leading educational institutions in the country like IIT-Madras, Central Leather Research Institute (CLRI), Pondicherry University and Madras University. One of the most significant collaborations is with Shimadzu, to set up the IICMS lab in Guindy, Chennai. Dr. Venkat Manohar, Director, IICMS and Mr. Tsuguo Kishida, Managing Director, Shimadzu Asia Pacific (SAP) signed on the dotted line and exchanged the MoU. Mr. Kishida was happy to share that “IICMS will be a great platform for the younger generation to learn mass spectrometry with a “hands-on” perspective to build their confidence levels“

Speaker's Highlights

The first speaker for the conference was Dr. Teruhisa Ueda. Dr. Ueda, who is currently the Director of the



analytical instrument division in Shimadzu, gave a comprehensive insight of the “World of Shimadzu” starting with the simple analytical balances all the way to

the state of the art mass spectrometers. In his presentation he dealt upon the importance of MS technology in today's world and how Shimadzu, as one of the leading manufacturers of mass spectrometers, was constantly innovating to provide the highest sensitivity, specificity and speed in all their MS instruments, to meet the ever growing challenges of MS users.

Following his talk Dr. Vairamani, Dean, Bioengineering department, SRM University, laid out the challenges involved in characterizing unknown compounds, which is usually done by comparing the spectral data with the library. This is available mostly only for the Electron Ionization method. However in LC/MS we use soft ionization techniques such as electron spray ionization (ESI) and atmospheric pressure chemical ionization (APCI), which do not give the fingerprint of the molecule. Dr. Vairamani in his lecture explained how this could be effectively addressed by using the EI technique to characterize unknown molecules. In LC/MS the sample preparation plays a very important role in analysis and



most of problems can be solved if sample preparation is done effectively. What if we could analyze a sample as it is without going through sample preparation process? To build upon this question, Dr. KP. Madhusudhan, Senior Scientist, Arjuna Natural Extracts Ltd, Aluva, elaborated on ambient ionization techniques such as Desorption Electrospray Ionization (DESI) and Direct Analysis in Real Time (DART) that are predominantly used today in the analysis of Natural products, lipids, biological fluids and chemical warfare agents. Some of the applications that he showed truly reflected the emerging applications



Dr. M. V. Suryanarayana

Vice President, API R&D

Matrix Laboratories Limited, Hyderabad

Impurity Profiling in Pharmaceuticals

Regulatory Authorities emphasize on the identification of impurities in pharmaceuticals to establish biological safety. Identification of impurities is done by variety of Chromatographic and Spectroscopic techniques, either alone or in combination with other techniques. There are different methods for detecting and characterizing impurities with other techniques. Various Analytical techniques, Hyphenated techniques have revolutionized not only separation but structural identification of impurities. Use of Mass Spectrometry in impurity profiling is discussed with a few case studies.



Dr. Tausif Ahmed

Asst. Director, Translational Research (M&S)
Piramal Life Sciences Ltd, Mumbai

Application of LC-MS in PK & PD

Mass spectrometry has made tremendous advancement during the last decade. The progress has led to the advent of entirely new instruments/technologies and has revolutionized the analysis small and large molecules. Today, with the advent of high-throughput discovery programs across the industry, LC-MS is being used during initial screening of compounds as the high throughput tool for ranking in in-vitro DMPK assays for its activities and possible identification of the new drugs. The late stage development applications include quantification of drugs/metabolites in plasma and other matrices using validated bioanalytical methods. Further, LC-MS is potentially applied to understand biomarkers, including markers for drug response, toxicity, mechanism of action and/or markers of disease. Advances in LC-MS instrumentation ultimately result into reduction of time and cost of drug development process.

of mass spectrometry.

It's a well-known fact that the pharmaceutical industry globally is going through a challenging phase of complex regulations while at the same time witnessing an atmosphere of tremendous opportunities in both the emerging and developed markets. As regulators tighten the product standards the need for characterization and impurity profiling at very low levels was increasingly being felt.

Dr. M.V. Suryanarayana, Vice President - API R&D, Matrix presented an overview of the importance of understanding impurities or related substances with respect to regulatory requirements. Touching upon both the chemistry and safety aspects of impurity profiling, he explained about the various sources of impurities in drug products such as raw materials, manufacturing process, by products, stability and degradation, storage and packing conditions. His presentation on case studies was



an illustrative live example of how mass spectrometry played a vital role in characterizing the impurities at trace level concentration.

Having heard the importance of impurity analysis at trace levels from Dr. Suryanarayana, Dr. Saranjit Singh, professor and head, pharmaceutical analysis, NIPER, took over the dais to present a series of MS methodology that leads to characterization of compounds at trace levels be it related substances, impurity, degraded products or metabolites and emphasized how the host of MS technologies in total could lead to characterization of molecules unambiguously. He brought into attention of

the participants the role of LC/NMR coupled with mass spectrometry. In this context he further shared with audience how such state of art technology was also complex to attain meaningful information's and the need of trained manpower. He gave a couple of examples on how HRMS could distinguish between molecules that have very close values differing in millidaltons. Another important aspect covered by Dr. Saranjit Singh in his talk was the detection and characterization of synthetic steroidal and non-steroidal anti-inflammatory drugs in Indian Ayurvedic/herbal products using LC/MS, a study that was very important from the perspectives of quality control and spurious products detection for the benefit of consumers.

A panel discussion was setup with all the speakers, chaired by Dr. Vairamani. It was very informative and participants had a free exchange of ideas/comments through the question and answer sessions. This session



further helped the participants to discuss some of the key issues with respect to specific applications. Since all the panel members were experts in their own areas, the participants derived immense benefits from this kind of panel discussions.

After having spent presentations and discussions on sample preparation, impurity profiling, and stability and degradation issues, the afternoon session focused on the life science applications of mass spectrometry.

The first speaker for the afternoon was Dr. Tausif Ahmed, Assistant Director, Translational Research (M&S),



Dr. Y. Ravindra Kumar

Director (Analytical research)
Dr. Reddys Laboratories Ltd, Hyderabad

Role of NMR and Mass spectrometry in structural characterization of organic molecules

Characterization of quality and stability of bulk drugs/pharmaceutical formulations is the core activity in modern drug analysis. This includes a group of analytical activities like detection, identification, structure elucidation and quantitative determination of organic and inorganic impurities as well as residual solvents. Due to the rapid development of the analytical methodologies available for this purpose and the similarly rapid increase of the demands as regards the purity of drugs, it is an important task to give a summary of the problems and the various possibilities offered by modern analytical chemistry for their solution. NMR and mass spectrometry will play a vital role in characterization of critical structures in organic chemistry with their hyphenation with liquid chromatography. Different case studies are presented by proving the importance of these two techniques together.



Dr. V. V. Vaidyanathan

Associate Director - Assay & DMPK
Syngene International Ltd, Bangalore

Metabolite profiling using LC-MS/MS

Understanding which metabolites are likely to be formed in vivo is essential for interpreting pharmacology, pharmacokinetics and toxicology data. Metabolite profiling is also very critical during lead optimization as it helps to identify metabolic hot spots. Species differences in Phase I and Phase II metabolism should also be known for successful drug development. Metabolites can be investigated in a number of different matrices including microsomal incubations, hepatocyte incubations, expressed enzyme incubations or plasma samples. We use modern LC-MS/MS technology to study compound metabolism. Case studies will be presented where identification of metabolites early in discovery phase helped us to optimize compounds and dosing strategies in discovery programs.

Piramal Life Sciences Ltd, Mumbai. He has done extensive work using the MSin Drug metabolism/ Pharmacokinetic studies (DMPK), Pharmacokinetics/ Pharmacodynamics (PK/PD) modeling, POP-PK, simulations and first-in-human (FIH) dose prediction. Dr. Tausif who developed various bioanalytical methods, explained the utility of different types of mass spectrometers and sample processing methods and illustrated the use of these techniques in early discovery ADME, late development, and biomarker method validation and protein quantitation. The challenges in biomarker assay methods and LC/MS/MS analysis of proteins, peptide quantitation were also discussed.

When a drug is taken it interacts with the body tissues or fluids and undergoes metabolism and need to be studied extensively for the course of their metabolism with identification/quantitation of the metabolites as an important aspect of drug discovery. Dr. V.V. Vaidyanathan, Associate Director (Assay & DMPK), Syngene



International Ltd, Bangalore in his talk emphasized on the use of LC/MS as a method of choice for metabolite analysis due to its superior specificity, sensitivity and efficiency. He illustrated the value of quantitative analysis, an integral part of developing bioanalytical methods, through triple quadrupole mass spectrometers. He brought into the attention of the audience about the useful applications of the new generation Ion Trap-Time of Flight (IT-TOF) technologies used extensively for detailed profiling and structure elucidation of metabolites. The step wise approach towards metabolite profiling was explained, whether it was in-vitro or in-vivo analysis. One of the key issues in bioanalysis was sample

preparation, that is extraction of active ingredient from biological matrix. In this context he laid importance on the value of different methods of extraction such as protein precipitation method, liquid-liquid extraction and solid phase extraction. He also showed the types of metabolic reactions and associated mass changes that could be used for tracking the metabolism pathways.

If these metabolites are going to be active or cause toxicity effects, its activity need to curtailed by modifying the chemistry aspects. It's very important to have a complete characterization of metabolites for this reason for which we will need a conformation of the structure of the compounds. Dr. Y. Ravindrakumar, Director-Analytical Research, Dr. Reddy's laboratories Ltd, Hyderabad in his presentation explained in detail about the role of NMR as a complementary technology for LC/MS in obtaining the structural conformations. He



presented five case studies elucidating the use of NMR to arrive at the unambiguous structures of unknown organic compounds in drug substances.

Irrespective of the diverse applications of a mass spectrometry and type of mass spectrometer technology used in analysis, the core issue in a mass spectrometer is its sensitivity.

Arvind Thyagarajan, Business Development Manager, Spinco Biotech shared the various innovations in LC/MS technology by major manufacturers in enhancing sensitivity. As in most sequence of operations, maximum performance benefits could be obtained with improvements at the beginning of the sequence. So in his



Dr. Saranjit Singh

Professor and Head,
Department of Pharmaceutical Analysis,
NIPER, S.A.S. Nagar, Punjab

Utilizing LC-MS tools to effectively characterize degradation impurities

There has been a sea of change in analytical challenges for industry in recent years. From earlier focus on analysis of major components, the emphasis has shifted to characterization and quantitative determination of trace level impurities, drug-drug/drug-excipient interaction products, metabolites, drug adulterants in herbals, etc. As the structural elucidation at low concentrations is time consuming under conventional process, hyphenated tools such as LC-MS, LC-NMR, etc., are being extensively applied for this purpose. In fact, unequivocal characterization of majority of the related substances at trace level is possible using LC-MS alone. The strategy involves establishment of fragmentation pathway of the drug and related substances using ion trap and MS/TOF systems as well as H/D exchange experiments. The strategy, very successfully employed, will be highlighted through select case studies.



Arvind Thyagarajan

Business Development Manager
IICMS, Chennai

Innovations in LC/MS technology in enhancing sensitivity

Since its invention 100 years ago, mass spectrometer has played and continues to play a prominent role in the science of the day. Mass spectrometer has encompassed all branches of science, thanks to the advancements in technology. Irrespective of the field of application, one of the most crucial factors in determining a mass spectrometer's capability is its sensitivity. Many commercial manufacturers of mass spectrometer continue their innovative approach to maximize the overall sensitivity of the instrument coupled with chromatographic techniques. Coupling of liquid chromatography with mass spectrometer continues to remain as a big challenge to obtain highest sensitivity in mass spectrometer. This presentation gives an overview of various innovations in LC/MS technology in achieving highest possible sensitivity.

talk Arvind shared the innovations in the interface and ion optics in a MS that lead to great rewards in sensitivity. He also showed how "attogram" level detection, (10^{-18} gm) has been possible with the Shimadzu LCMS-8030 triple quadrupole system with its advanced interface, optics and collision cell technology.

Similar to the discussions arranged in the morning sessions, a second panel discussion was organized in the evening chaired by Dr. Venkat Manohar. The interactions between the speakers and participants helped to mutually set right some of the issues in bioanalytical methods. These kinds of discussions specific to bioanalysis could form a basis for a future white paper discussion in India,



similar to the one arranged by international communities annually at Canada and USA involving global CRO council.

After an entire day of informative and insightful talks, Dr. Manohar concluded in his vote of thanks by saying that "The mission of IICMS is to impart knowledge in chromatography and mass spectrometry and develop experts of tomorrow in these areas. True to our mission statement, IICMS has made a modest beginning by organizing this one-day seminar with speakers of international repute in the field of MS over several decades. Having gained the strength and confidence from the overwhelming response from all participants, in future IICMS will host the MS conference annually".

"Let good thoughts come to me from all directions"

- Rig Veda

About IICMS

Indian Institute of Chromatography & Mass Spectrometry LLP (IICMS) is a premier institute, focused in developing experts of chromatography & mass spectrometry through training. It collaborates with academic institutions, national laboratories and industries conducting research programs in mass spectrometry. IICMS carries out its own research program in oncology. It offers a seamless connectivity between academy and industry.

Mission

Develop experts of tomorrow in chromatography & mass spectrometry.



About Dr. Venkat Manohar

Dr. Venkat Manohar is the Director of Indian Institute of Chromatography & Mass Spectrometry (IICMS) who has been practicing analytical science over a period of more than three and half decades at various multinational companies. Prior to this assignment, he has been Senior Vice President in Piramal Life Sciences Limited (PLSL), Mumbai for the past six and half years, responsible for the entire analytical facility for drug discovery research as well as a diagnostic research laboratory. He has obtained Ph.D. in Physics from University of Madras. During his tenure at PLSL, more than six new molecules in various therapeutic areas had been filed for IND and all of them are in Phase I / Phase II clinical trials. In addition to these, he has developed expertise in confocal microscopy coupled with Raman Spectroscopy, FTIR microscope to characterize surface molecules through Chemical Microscopy. His hobby is sharing the learning!



www.iicms.in



Synthetic Laboratory



Brainstorming conclaves



HPLC Laboratory



Information Centre



Creative environment



MS Laboratory



Seminar hall



Genomics Laboratory



Indian Institute of Chromatography and Mass Spectrometry

IICMS is a premier institute developing experts in chromatography & mass spectrometry (CMS) through training. It offers a seamless connectivity between academy and industry.

Dr. Venkat Manohar
Director, IICMS



- To conduct two day/three day workshops to the scientists/analysts of industries and other research institutes
- To offer specific in-house to industries to meet their specific requirements
- State-of-the-art seminar hall as well as small conclaves for 'team brain-storming'
- Information centre having standard books on chromatography, mass spectrometry and related areas
- HPLC laboratory equipped with series of modern HPLCs to gain 'true hands-on' through training
- Modern mass spectrometry laboratory having single quad, triple quads and HRMS mass spectrometer to get an 'insight' in mass spectrometric analysis.
- Synthetic laboratory not only to synthesize novel molecules but to make compounds to learn different facets of chromatography & mass spectrometry

Courses & workshops

- Two day workshop on 'Advanced course on Liquid chromatography'
- Two day workshop on 'Introduction to LC/MS and quantification using LC/MS/MS'
- Three day course on 'Advanced course on liquid chromatography and mass spectrometry'
- Two day workshop on 'GLP Bio-analysis using LC/MS/MS'

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