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LC-MS, a Capable Integration

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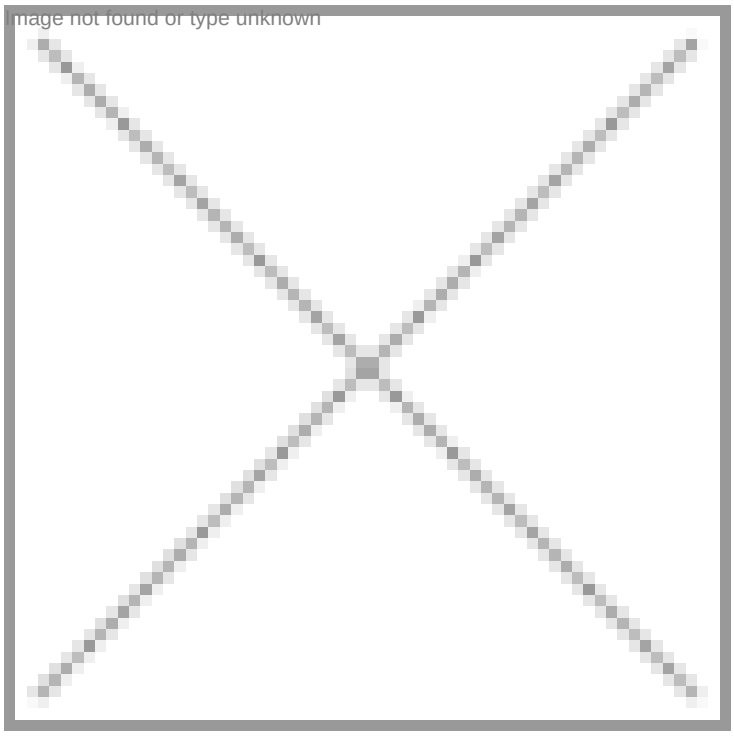

LC-MS, a Capable Integration

LC-MS has emerged as the most preferred technique for routine bioanalysis and there is no doubt that this technology will continue towards more automation and wider range of applications in the coming years.

Liquid chromatography-mass spectrometry (LC-MS), the analytical chemistry technique that combines the physical separation capabilities of liquid chromatography with the mass analysis capabilities of mass spectrometry has emerged as a powerful technique used for many applications with very high sensitivity and specificity.

The applications of LC-MS are used in innumerable analytical fields, including pesticide-residue determination. There is no doubt that LC-MS is currently competing with gas chromatography (GC)-MS for the status of reference analytical technique to determine pesticide residues and that its ever-increasing application is bound to the evolution of modern instruments and their growing performance qualities. Strategies in the drug discovery and drug development processes are undergoing radical change. For example, the contribution of pharmacokinetics to both processes is increasing. Furthermore, toxicokinetics is established as an essential part of toxicity testing. With this emphasis in the use of pharmacokinetics/toxicokinetics and the greater potencies of newer drugs, a sensitive and specific bioanalytical technique is essential, LC-MS and liquid chromatography-tandem mass spectrometry (LC-MS/MS) have emerged to fulfill that need. LC-MS/MS can be considered to be the major bioanalytical development of this decade.

LC-MS has become very common in pharmacokinetic studies of pharmaceuticals. The last few years have witnessed its extensive use in the study of proteomics. It is frequently being used in drug development at many different stages including peptide mapping, glycoprotein mapping, natural products dereplication, bioaffinity screening, in vivo drug screening, metabolic stability screening, metabolite identification, impurity identification, degradant identification, quantitative bioanalysis,

and quality control.

Technology upgradation

The last few years have seen a significant movement toward using single nanoscale LC-MS methodologies that arecapable of qualitative profiling and quantitative analysis of complex mixtures of proteins across wide concentration ranges and the main focus is in things at the lowest concentrations. Scientists are hence relying on analytical instruments for structural information on individual low-abundance proteins and simultaneously get a true fingerprint of all of the proteins in a given cell. It has become possible for LC-MS techniques to uncover 1,500 proteins in a single analysis.

The major development in MS has been the use of tandem MS-MS where a researcher can program the detector to select certain ions to fragment. The process is essentially a selection technique, but is in fact more complex. As long as there are no interferences or ion suppression, the LC separation is quite fast. It is common now to have analysis time of one minute or less by MS-MS detection, compared to over 10 minutes with UV detection.

Some of the key improvements in liquid chromatography and mass spectrometry come from better software, such as Waters Corporation's Micromass ProteinLynx Global Server 2.0, which integrates key mass informatics tools for protein identification and characterization. Such a combination of liquid chromatography, mass spectrometry, and powerful software have proved to be useful in disease target identification and drug discovery.

MS Detector for HPLC

"Quadrupole LCMS will continue to see robust demands in future"

-S Image not found or type unknown or, Shimadzu Analytical (India) Pvt Ltd

Not long ago Shimadzu pioneered the introduction of Photodiode array detectors which went on to replace the conventional UV-VIS detectors in HPLC. The launch of LCMS-2020 in 2009 by Shimadzu heralds a new era in desk top Mass Spectrometric Detectors for HPLC systems that have the capability to address the most demanding requirements in pharmaceutical and life sciences. The development of LCMS 2020 is based on Shimadzu's proven Mass Spectrometry platforms which adopted simple, easy-to-use design while maintaining superior performance.

Delivering the ultimate in measurement speed and sensitivity, the compact LCMS-2020 mass spectrometer offers faster measurements and higher detection sensitivity for quicker and more accurate analysis of trace impurities, environmental pollutants, and contaminants in different sample matrices. When combined with a Prominence ultra-fast LC (UFLC/UFLCXR) the system helps analysts achieve the ultimate in separation performance and productivity.

The single quadrupole system of LCMS-2020 uses a patented **ultrafast(UF)** technology providing significantly higher sensitivity than any other single quadrupole analyzer and offers unique cost effective solutions to a range of analytical requirements such as mass identification, process monitoring, mass based purification etc. The new **UFscanning** technology achieves measurement speeds of 15,000 u/sec without sacrificing sensitivity or resolution, thus obtaining the best chromatography for the fastest LC conditions.

UFSwitching technology of LCMS-2020 enables switching between positive and negative ion modes in 15 milliseconds so even the fastest LC peaks can be analysed in both modes, thus increasing productivity. Innovative ion optics with the newly developed Qarray® ion optical system provide superior sensitivity, repeatability, and linearity, achieving 50% to 300% greater sensitivity than any other single quadrupole analyzer for substances most commonly measured. Users can inject less and keep the analyzer cleaner, longer.

LCMS-2020 enables improved high mass operation with sensitivity increased by more than 500 percent for masses above 1,000. In addition to better performance, the LCMS-2020 allows easier maintenance, permitting users to replace the ionization unit and inlet capillary to the MS from the LC, without breaking the vacuum. The ESI method typically used for LCMS can be replaced with APCI, which is suitable for neutral compounds, or with a dual ionization source (DUIS) for simultaneous operation of both ionization modes, quickly and without tools.

The new Shimadzu LCMS-2020 with its breakthrough technology is the world's most sensitive, fastest scanning and fastest polarity switching single quadrupole mass spectrometric detector available. The launch of LCMS-2020 recently at Delhi attracted a large number of Mass Spectroscopists from the Pharmaceutical Industry.

The strength of single quadrupole mass spectrometric detectors lies not only in their adoption by HPLC users but also by the pharmaceutical industry as a whole. Applications on DMPK (Drug Metabolism and Pharmacokinetics) and compound screening are particularly well suited for single quadrupole LCMS. Besides its high resolution and accuracy, LCMS is also a high-throughput technique capable of meeting a number of pharmaceutical industry's needs from R&D from analytical services, to method development and quality control. With increases in Pharmaceutical R&D spending and advancements in drug development, single quadrupole LCMS will continue to see robust demands in future.

Market scenario

In 2008, Waters introduced its Xevo family, the new range of mass spectrometers for most demanding applications. The company's IntelliStartTM technology was first introduced with the ACQUITY SQD and TQD systems. The technology automatically ensures that the instrumentation is ready to use and automatically generates methods for the quantification of trace analytes in samples.

â€œEasy to operate and reliable instrumentation can make a significant contribution in helping a scientist to be more productive. LC-MS/MS is a very powerful analytical tool that can benefit a wide range of different businesses. Today we

recognize that within many organizations a broad range of scientists need to access LC-MS/MS instrumentation,â€? said Kochu Sankar, general manager, Marketing, Waters India.
The most common technology platforms used in laboratories around the world for detecting chemical contaminants such as melamine in food are 'hyphenated' systems that combine chromatography with mass spectrometry.
â€œToday, LC-MS QQQ methods are available for detection of melamine. While the limit of detection (LOD) is significantly lower than that of the GC-MS method, the LOQ is still relatively high. Solid phase extraction during sample preparation and IEC, LC-MS-MS methods simplify the sample preparation process since no derivatization is necessary, and they provide confirmation and quantification in one step,â€? opined Dr. Jerry Zweigenbaum, market development specialist, LC-MS, Agilent Technologies.
According to Ajit Srivastava, business manager-LC-MS, Agilent Technologies, the latest development in this field is the 'microfluidic-based nanoflow HPLC-Chip'. HPLC-chip provides fast chromatography, the best sensitivity and excellent reproducibility in retention time, which are crucial for quantitation analysis. The system has superior usability and is ideally suited for 'walk up to' lab environment. The HPLC-Chip/QQQ system can achieve sensitivity in the low attomole range with five orders of magnitude in dynamic range. To achieve best quantitation and specificity, excellent chromatography separation and retention time reproducibility are crucial.

Future technologies
Although the use of LC-MS for bioanalysis began only some ten years ago, growth in the development and applications of this technology has been phenomenal. The performance to cost ratio of the necessary equipment is being improved continuously. The advent of the ion-trap as a tandem MS quantitative detector for routine bioanalysis probably represents a notable breakthrough in terms of performance-cost ratio, despite some compromise in performance such as sensitivity and precision, when compared to triple-quadrupole instruments. Today, instrument manufacturers are more focused on their product range and the equipment is increasingly dedicated to specific applications. Also, with the advances in pumping technology, electronics and software control, instrument manufacturers are able to design machines that are smaller, simpler to use and with a much better performance to cost ratio.
A new generation of LC-MS interfaces that are more amenable to the use of non-volatile buffers and ion pairing reagents are being developed. The technology for automated sample preparation continues to improve. As the range of available packing materials for solid-phase extraction increases, more and more bioanalytical methods will be based on this extraction approach. In the near future, automated SPE systems or on-line precolumn switching capabilities are expected to become an integral part of a bioanalytical LC-MS/MS system. Other automated SPE methodology will be based on immunoaffinity columns and other molecular recognition approaches. Development of the technology will therefore continue towards more automation and to include an even wider range of applications.

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