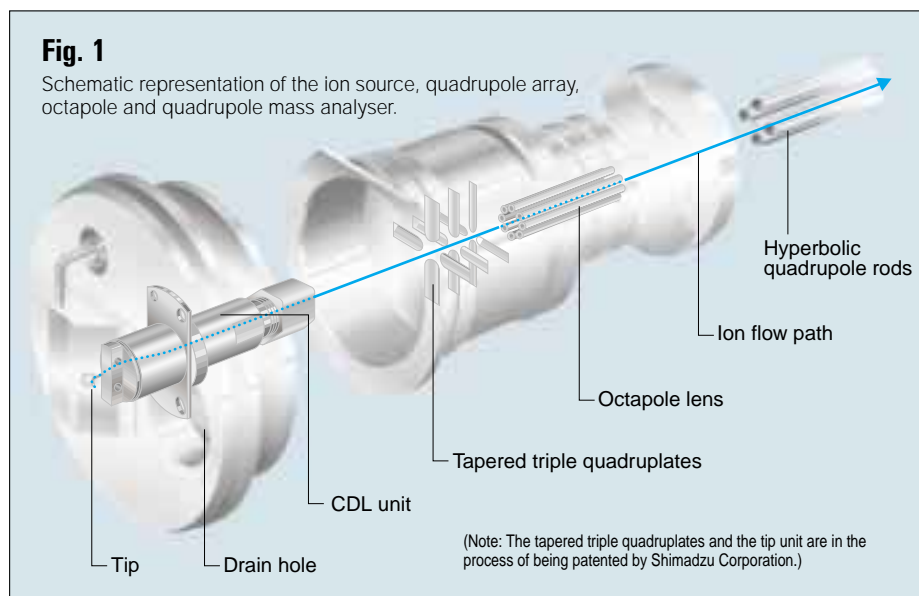


# Liquid Chromatograph Mass Spectrometer (LC/MS)

The LC/MS detects the molecular weights of a compound in just a few minutes, demonstrating its superiority for research work in the development of new drugs and analysis of the environment.



Mass spectrometry (MS) is not limited to low molecular weight detection of pharmaceutical or agrochemical products. In protein mass spectrometry the measurement of molecular mass up to 100,000 Da is now not only routine and precise but generates data on the protein secondary structure. In future, studies on structural proteomics and genomics by mass spectrometry will not be restricted to classical approaches in protein characterization and peptide sequence but will involve systems of unprecedented speed, specificity and sensitivity.

The strategic goal in LC/MS instrument development is to develop instruments that can provide a competitive advantage in sensitivity and information, whether it is simply molecular weight or in structural assignments. To meet this need Shimadzu Corporation has developed a new benchmark in innovative mass spectrometry, the LCMS-2010.

## How LC/MS works

LC/MS is typically applied to analysis of multiple component mixtures. Each component is resolved by liquid chromatography and determined by atmospheric pressure ionization mass spectrometry. Atmospheric pressure ionization mass spectrometry (API-MS) operates by ionizing sample molecules in the liquid chromatographic mobile phase to

## Introduction

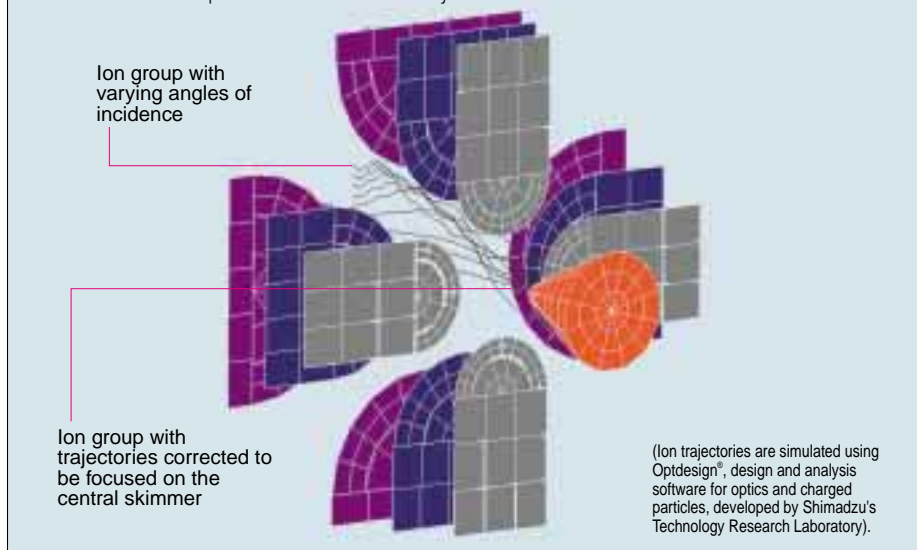
High performance liquid chromatography coupled with mass spectrometry (LC/MS) is a key enabling technology for the detection and characterization of organic molecules, providing the analytical chemist with one of the most powerful analytical tools of modern times. Mass spectrometry has had an immediate and profound effect as a consequence of the high sensitivity and the wealth of structural information for the analysis of organic compounds ranging from low molecular weight drug molecules to large molecular weight bio-polymers.

This technology is now well established in many business sec-

tors and plays a critical role as part of an accelerated development strategy. This is particularly true for one highly specialized industry, pharmaceuticals. Pharmaceutical drug development may be considered as a process that involves four key phases; drug discovery (lead identification and optimization), pre-clinical development (metabolism and toxicology), clinical development (pharmacodynamics), and finally manufacturing (QA/QC production). It is a technology that has radically transformed the dynamics of pharmaceutical drug development as it provides unequivocal identification and detection in each phase, from candidate identification to product release.

## Fig. 2 Ion trajectory through quadrupole array

Quadrupole configured as three sets of four plates (quadruplate), aligned with decreasing space between the electric poles so as to focus ion trajectories into a narrow channel.



tion studies in addition to optimizing the signal response in quantitative detection. This approach can be applied to high throughput pharmaceutical screening and in specific quantitative methods developed for target compounds.

## Outlook

There is no doubt that mass spectrometry will continue to be of central importance in the analysis of a diverse range of molecules, particularly those of biological interest. The development of innovative MS designs from Shimadzu Corporation, a global leader in analytical technology, will undoubtedly help to accelerate further exciting discoveries in the fields of drug development and life science.

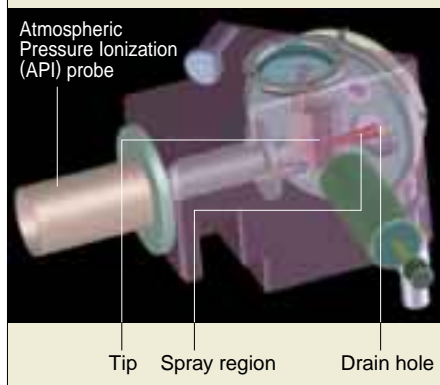
produce a beam of gaseous ions. Ionization is carried out at atmospheric pressure for two reasons; firstly, heat transfer more efficiently enhances solvent evaporation and, secondly, high electric fields do not result in strong electrical discharges that occur at reduced pressure. API-MS includes electrospray ionization (ESI) and atmospheric pressure chemical ionization (APCI). The two techniques are similar in that they ionize sample molecules to produce gaseous ions but differ in the response to sample chemistry. ESI is more suited to the analysis of ionic polar compounds, while APCI works with relatively non-polar compounds.

Once gaseous ions are formed they are electrostatically extracted into a heated capillary positioned orthogonally to the spray. Ions from the heated capillary are transmitted to the quadrupole mass analyzer using an innovative ion optic design for high ion transmission resulting in high sensitivity. The design integrates a quadrupole array with a octapole ion bridge to precisely focus ions from the ion source into the quadrupole mass analyzer (Fig. 2).

Ions from the heated capillary are transmitted to the quadrupole mass analyser using an accelerating voltage resulting in a mass spectrum often dominated by the pseudo-molecular ion with little fragmentation. When the energy acquired by the molecule exceeds the ionization potential, the excess energy is distributed inside the molecule and when the energy equals the dissociation energy for a particular chemical bond fragmentation occurs. Fragmentation provides a great deal of information about the structure of the molecule and is controlled by applying an accelerating voltage after the heated capillary. This technique of 'in source fragmentation' is particularly useful in structural elucidation and in compound verification analysis. To increase confidence in compound verification or structural confirmation multi-sequence mode supports rapid cycling of fragmentation voltages, polarity switching and acquisition mode (switching between full scan and selected ion monitoring modes) in a single injection. Multi-sequence mode is unique in its flexibility. It provides the tool for maximizing information in compound verifica-

## Fig.3 Ion source

Components separated by LC are transformed into a highly charged aerosol in the ion source by applying a high electric charge. Sample ions are then electrostatically extracted from the charged aerosol into the MS using an orthogonal source geometry. This design results in the bulk of the liquid spray draining out of the ion source.



Shimadzu High-Sensitivity Liquid Chromatograph Mass Spectrometer LCMS-2010 with LC/MS solution.