

# Organic Mass Spectrometry Business in India

## - Past, Present and Future

- Dr. G.Ramakrishnan

Sir J.J. Thomson invented the technique of mass spectrometry in the year 1912; however, the technique was used for molecular weight determinations only during the 1950s. Ever since, it has been one of the most fascinating technique to scientists especially as this was the most effective technique to find out the molecular weight of the compound they were studying and the sample required was only in microgram quantities. Mass Spectrometry has come a long way during the past several decades from laboratories, which were doing more research, into laboratories that do routine development work and quality control .

The commercialization of mass spectrometers started with single magnetic sector instruments with solid sample introduction to later interfacing with gas chromatographs in the late 50s. Then there came the double focusing electrostatic/magnetic sector mass spectrometers that were so large, enough to fill a whole room and these interfaced with GC gave the required results to investigators. However, for several years the sector instruments could not keep up with the speed of the capillary GCs and Quadrupole mass spectrometers became much more suited for this combined technique and this strengthened with the availability of computers. This combined with the lesser cost for quadrupole instruments resulted in an explosion in this market space in the 1970s.

In the early 1970s, when I was doing my Ph.D. in Organic Chemistry at BARC, there were very few magnetic sector instruments that I knew of and these were the single focusing

### Market Dynamics in India

- ⇒ The number of GCMS instruments sold in the country is around 100 units per annum.
- ⇒ Today there are more than 500 triple quad LCMS instruments working in India.
- ⇒ The market is adding around 80-100 triple quad LCMS instruments yearly.
- ⇒ Around 100 numbers of LCMS using the Ion Trap Technology are presently available.
- ⇒ There are nearly 60 MALDI-TOF instruments in India.
- ⇒ The market for MS instrumentation will grow by 20–25% in the coming years.

instrument CH-7 then made by Varian at the Ciba-Geigy Research Center in Mumbai, the double focusing mass spectrometer, MS30 by AEI/Kratos at the NCL Pune and the VG Micromass 70/70 Double Focusing instrument at the Chemistry Division of BARC. These MS instruments were not connected to any computers as that were not available at that time, so it was a huge task to get the mass spectrum recorded on photosensitive papers using galvanometer recorder, then look for the molecular ion peak to determine the molecular weight of the compound. There was no Chemical Ionization technique available on the instruments, so in order to confirm the molecular weight of the compound, one needed to make a derivative and then determine the molecular weight of the derivative and extrapolate the results to confirm the molecular weight of the parent compound.

The first Quadrupole instrument, Hewlett-Packard 5985 was to IPCL, Baroda in 1979 by of Blue Star, brought out the

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awareness of Quadrupole MS into India. At that time due to import restrictions, the entire process of buying of a mass spectrometer took anywhere from one to two years. Therefore if any one bought a mass spectrometer anywhere in India, it used to be a big news!! In 1981, Varian MAT sold the mass spectrometer part of the company MAT to Finnigan which became Finnigan MAT and this was represented at that time by Hinditron. It is during this period that I quit ICI research center to join Hinditron to promote the Finnigan MAT mass spectrometers. The first Finnigan MAT GCMS, Finnigan 1020B was sold to NCL, Pune in end 1981 which became operational in 1982. The introduction of HP 5970 benchtop Quadrupole GCMS and the introduction of Benchtop Quadrupole Ion Trap system ITD 70 by Finnigan MAT in 1983 became a landmark in the commercialization of mass spectrometers to the routine laboratories, especially those in Environmental, Flavor and Fragrances, Forensic Sciences, etc. The growth of this market internationally was driven by the US-EPA regulations and the stringent implementation of the laws. Since then there has been a boom in the Quadrupole and Ion Trap instruments to each and every laboratory for any type of applications for qualitative and quantitative studies.

Now there are several hundreds of single quadrupole and Ion trap mass spectrometers in various laboratories in India sold over the past several years, more so in the past 10 years. The customers who are using these instruments regularly are in the laboratories engaged in the Water analysis, Pesticide residue analysis in food, petroleum and Petrochemical, Pharma, flavor and fragrances, and in educational and research institutions. The estimated number of GCMS instruments sold in the country today is around 100 units annually and these are shared among the key players, Agilent, Perkin-Elmer, Shimadzu, Thermo Fisher and Varian almost equally.

Another key area of development has been in the area of combining the capabilities of HPLC with that of mass spectrometers. Several LC-MS interfaces were tried, but the most successful has been the Atmospheric Pressure Ionization (API/ Electrospray) invented by Dr. John Fenn of the Yale University in the early 1980s, especially due to the sensitivity that this technique could give. This technique also allowed the use of volatile and nonvolatile buffers in the HPLC methods. This interface combined with the Triple Quadrupole mass spectrometers provided the opportunity to study the metabolites in the drug discovery areas. Thus the number of Triple Quad instruments connected with HPLC started multiplying in the 90s and now in this current decade.

I traced the first sale of triple quadrupole LCMS sold in India and this was the VG Quattro sold by Hinditron to Astra Zeneca in Bangalore., which had API and APCI sources. The next triple Quadrupole instrument sold was perhaps the one sold by Lab

India to Pharmaceutical Education, Research and Development (PERD) center in Ahmedabad in the year 1998. Since then there has been steady streams of Triple Quad instruments sold in India with API/APCI techniques and today there are estimated 500 triple quadrupole LCMS instruments installed and working in India. This by any means is a creditable achievement to the overall industrial growth in India and to the analytical instruments industry. This triple quadrupole market has been dominated by 3 key players Applied Biosystems, Thermo Fisher and Waters. The growth has been mainly attributed to the growth of the Clinical Research Laboratories in India and more and more outsourcing of Bioanalytical work coming to India from foreign countries. Currently there are between 80-100 instruments sold in India yearly and this trend will continue for the next several years. There is an emerging trend in the use of GC-Triple Quad instruments in the analysis of pesticide residues and this may not grow to that extent as the LCMS instrumentation.

An impressive growth has been also in the area of LCMS using the Ion Trap Technology and this has been especially useful in the area of new molecule research and in the area of Impurity Profiling in the Pharma industry. The main feature of the Ion Trap technology has been in its multiple stage MS/MS capability. This product came to prominence in the late 1990s and it is impressive that India should have around 100 systems working in the country. The key players in this area have been Thermo Fisher Scientific, Bruker, Agilent and Varian. The technology is moving from the conventional 3 Dimension Trap to 2 Dimension Trap and the latter will come into prominence as it can trap more number of ions than the 3 Dimension Trap thus giving much better sensitivity. One of the major advantages of Ion Trap technology in relation to the Triple Quadrupole technology is in its capability to do ionization in multiple stages (MS/MS) by trapping a particular ion and fragmenting the same by Collision Dissociation. This is particularly useful in characterization of small organic molecules and more so in the study of proteins and peptides for sequencing.

Biochemists, who did not pay attention to the technique of mass spectrometry two decades back, cannot live without an ion trap mass spectrometer as they can also do sequencing and characterization work using this technique. The latest trend in the Ion Trap technology has been the introduction of Orbitrap by Thermo Fisher two years back. This technique is truly a unique technique in mass spectrometry field considering the last 20 years of innovations in mass spectrometry. The capability of this technique to do high resolution study to an accuracy close to the FTMS technique is quite commendable. The fact that this instrument does not require liquid helium or liquid nitrogen is making this instrument a better choice for those who require high resolution for small organic molecules



and large biomolecules. While Orbitrap is marketed only by Thermo Fisher, the key players in the FTMS have been Thermo Fisher and Bruker. As of now there are no installations of Orbitrap or FTMS in India; however, there are a few national laboratories trying to procure these types of instruments to work in the areas of Proteins and Peptides.

Another technique known as Time of Flight (TOF), though known from the mid 40s as a technique, it never took off as a viable technique, the major limitation being the computers that could keep up with the speed of scanning and the large amount of data generation. In the mid 90s this technique also started to emerge as a solution to the Biochemists and especially when the Matrix Assisted Laser Desorption Ionization (MALDI) as a sample introduction system to the TOF mass spectrometers was made available. The TOF technology today has opened up so much of instrumentation as MALDI-TOF, TOF-TOF and Q-TOF, the latter two being hybrid instrumentation using same type of analyzers or using different types. These are playing very critical parts in the Protein and Peptide Laboratories today. The information from reliable sources is that there are more than 60 instruments in India installed; these are in the Pharma, universities and national research centers. The key players in this are Applied Biosystems, Bruker and Kratos.

The future of mass spectrometry in India is very bright; the market will continue to grow. The main drivers are the growth in Pharma and Biotechnology industries, CRO business, Proteomics research in national research centers, university departments of research, etc. The other areas are the national analytical laboratories set up by the agriculture ministry and marine products export ministry, that are analyzing the food products that are exported to countries in Europe and rest of the world.; these comprise of both GCMS and LCMS instruments. What has missed my mention is the GC with high resolution magnetic sector instruments that are standard instruments for Dioxin analysis. A few laboratories have started investing in these instruments and the major players in this area are Thermo Fisher and Waters as the vendors.

The maximum chromatography instruments sold today are GCs and HPLCs. As the detection levels become more and more stringent better performances of instruments is a must. In this regard the analytical instrument manufacturers are paying a lot of attention in providing better reliable and productive instruments at competitive price to customers. As the supply of trained chemists are coming down it has also become important that these instruments are automated and easy to use software are made available. As mass spectrometer is more universal and decisive detector than any other GC and LC detectors, the market will shift more and more towards mass spectrometry. The regulatory bodies also will insist more and more on methods based on mass spectrometry. This should

lead to better growth in the mass spectrometers from a 10-15% growth per year to 20-25% in the coming years. This will enable the major vendors to establish better equipped laboratories for application and training. This should lead to better trained man power that will be available to the various industries that are investing their money in buying mass spectrometers.

Welcome one and all to the exciting world of Mass Spectrometry, the technique that will rule the coming years!! ■