Direct Analysis in Real Time (DART) – A New Ionization Technique

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Introduction

Direct analysis without sample preparation is an ultimate goal in analytical chemistry. Sample introduction has been one of the limitations of organic mass spectrometry right from the beginning. The sample had to be vaporized and introduced into the ion source maintained at high vacuum for recording electron ionization (EI) mass spectrum. In order to overcome the harsh conditions of electron ionization, another technique called chemical ionization (CI) was developed so as to get molecular weight information from labile molecules. Thermally unstable and polar molecules required field desorption (FD) technique to get ionized intact. The development of fast atom bombardment (FAB) in the early eighties paved the way for the analysis of polar and high molecular weight biomolecules. Electrospray ionization (ESI) and matrix assisted laser desorption ionization (MALDI) revolutionized mass spectrometry by enabling it to analyse very high molecular weight biomolecules. The atmospheric pressure ionization techniques, atmospheric pressure chemical ionization (APCI) and ESI covered the entire spectrum of medium polar and low molecular weight compounds to highly polar and high molecular weight biomolecules. One of the limitations in achieving high sample throughput with ESI or MALDI is the need to dissolve, extract and/or filter the sample prior to analysis. In other words, there was still the requirement of some amount of sample preparation prior to analysis. This included adequate solubility in the desired solvents and freedom from matrices such as salts and buffers. The mass spectrometrist was still looking for a technique which enabled him to present the sample in front of the mass spectrometer for analysis. Two such techniques were developed and announced in 2004 and 2005. These were the desorption electrospray ionization (DESI) and direct analysis in real time (DART).

Desorption Electrospray Ionization (DESI)

DESI was developed by Cooks and coworkers\(^1\) and uses an aqueous or methanol spray directed at an insulating sample or an analyte deposited on PTFE (Fig. 1). A mixture of liquid similar to that used in liquid chromatograph mobile phases (water-methanol) and controlled by the operating parameters similar to those for ESI conditions is used for the spray. DESI appears to be gentle enough for desorbing ions directly from animal tissue, plant tissue and biological materials. The desorbed ions can be analyzed by a commercial atmospheric pressure ionization mass spectrometer. The working species in DESI appears to be the charged droplets or the desolvated solvent ions generated in the electropray process. DESI generates secondary ions directly from the surface of the material of interest. However, the spray of solvents makes the technique a bit messy.
**Direct Analysis in Real Time (DART)**

Direct analysis in real time source was developed by Cody and Laramee. DART is a non-contact analysis technique for MS at atmospheric pressure. DART can analyse gases, liquids, solids and materials on surfaces. DART is based on the atmospheric pressure interactions of long-lived electronic excited state atoms or vibronic excited state molecules with atmospheric gases and the sample. Helium or nitrogen is used for producing the ionizing plasma. The gas flows through a chamber where an electrical discharge (corona discharge) produces ions, electrons and excited state (metastable) atoms and molecules. These metastable species, in turn, generate protonated gaseous water clusters in ambient air. The water clusters on proton exchange with the sample give rise to [M+H]^+ ions of samples. In the negative ion mode oxygen water clusters are reported to be responsible for ionizing the sample. A schematic of the DART source is given in Fig. 2. Nitrogen or helium gas is introduced into a discharge chamber in which a needle electrode is held at a potential of 2-4 kilovolts. The resulting discharge generates a plasma of ions, electrons, and excited-state species. The adjacent chamber has two perforated electrodes, which are biased to remove ions. The neutral gas molecules, including metastable species, pass through a heated chamber. The heated gas exits the source through a grid electrode, which prevents ion-ion and ion-electron recombination and acts as a source of electrons by surface Penning ionization. In addition, it acts as an electrode to promote ion drift towards the mass spectrometer atmospheric pressure inlet interface. The DART gas flow is towards the mass spectrometer inlet orifice across a gap of 5-25 mm. This gap is open to the laboratory room and the material to be analysed is held in this gap in the stream of warm gas.
When helium is used the mechanism of ionization involves predominantly the formation of ionized water clusters followed by proton transfer reactions. The helium $^2_3$S state has an energy of 19.8 eV and reacts with water efficiently with an estimated reaction cross section of 100 Å$^2$.

$$\text{He}(^2_3\text{S}) + \text{H}_2\text{O} \rightarrow \text{H}_2\text{O}^+ + \text{He} (^1\text{S}) + e^-$$

$$\text{H}_2\text{O}^+ + \text{H}_2\text{O} \rightarrow \text{H}_3\text{O}^+ + \text{OH}^-$$

$$\text{H}_3\text{O}^+ + n\text{H}_2\text{O} \rightarrow [(\text{H}_2\text{O})n\text{H}]^+$$

$$[(\text{H}_2\text{O})_n\text{H}]^+ + M \rightarrow \text{MH}^+ + n\text{H}_2\text{O}$$

Electrons produced by Penning ionization or surface Penning ionization are rapidly thermalised by collisions with atmospheric pressure gases and undergo electron capture by atmospheric oxygen producing $\text{O}_2^-$ which reacts with the analyte to generate sample anions.

$$\text{M}^* + \text{surface} \rightarrow \text{M} + \text{surface} + e^- \quad \text{(Penning / surface Penning ionization)}$$

$$e^-_{\text{fast}} + \text{gas} \rightarrow e^-_{\text{slow}} \quad \text{(Thermalised by collision with gas)}$$

$$e^-_{\text{slow}} + \text{O}_2 \rightarrow \text{O}_2^- \quad \text{(Electron capture by atmospheric oxygen)}$$

Ion formation under DART may also involve other reactions. For example, dopants such as ammonium (from ammonium hydroxide headspace vapour) or chloride (from methylene chloride) ions can modify the chemistry of ion formation. The mechanism involved in desorption of materials from the surfaces by DART is not well understood. It is
postulated that transfer of energy to the surface by metastable atoms and molecules leads to sample desorption and ionization.\(^2\)

The mass spectra produced by DART are characterized by \(M^+\) and/or \([M+H]^+\) in positive ion mode and \(M^-\) or \([M-H]^-\) in negative ion mode. Fragment ions are also observed depending on the sample and the source conditions. The degree of fragmentation can be adjusted by the gas temperature or the MS orifice potentials. Unlike ESI, alkali metal ion attachment or doubly charged ions are not observed under DART.

**Applications**

Rapid high throughput analysis can be carried out for a variety of sample types using DART. Analysis of drug tablets is one application where direct analysis would be of extreme importance. The DART ion source has been used to analyze an extremely wide range of analytes including drugs (tablets, formulations etc), metabolites in body fluids, explosives, forensics, chemical weapon agents, synthetic organic and organometallic compounds, pesticides, toxic industrial materials, inks, dyes, foods, spices beverages, fatty acids in bacteria and also materials on surfaces such as glass, concrete, paper or currency directly.\(^3\-7\)

Some examples of such applications we have examined are given below.

Spices contain a number of specific components and their characterization can be achieved by directly analyzing them using DART MS. The rhizomes of ginger have long been valued as spice and as a herbal medicine. Dry ginger when placed in front of a DART source gives rise to the spectrum given in Fig. 3 which shows the presence of the reported sesquiterpenes, gingerols, gingerones and shogaols.

![Fig. 3 DART mass spectrum of dry ginger](image)

The spectrum shown in Fig. 4 (upper panel) was obtained when household cooking oil, sunflower oil, on a melting point capillary was placed in front of the DART source in presence of ammonium hydroxide. Ammonium hydroxide was placed in the gap below the sample. The peaks at m/z 872, 896, 998 and 900 are due to ammonium cationized triglycerides. The lower panel in Fig. 4 shows the negative ion DART spectrum of sunflower oil showing the [M-H] ions of the fatty acids present in the oil. The ions at m/z 255, 279 and 281 are due to palmitic acid, linoleic acid and oleic acid respectively. More such examples will be discussed.

Fig. 4 Positive (upper panel) and negative (lower panel) ion DART mass spectra of sunflower oil.

Conclusion

DART is a no-prep sampling technique for MS and works like a solid probe at atmospheric pressure. It operates in open air with no exposed high voltages. DART samples any material held in its ionization stream. It produces instantaneous response and does not need any solvents. Thus DART provides a means for rapid analysis of samples with no solvents or sample preparation.

References


**Dr. K. P. Madhusudanan**, born in 1947, is presently Head of Sophisticated Analytical Instrument Facility, Central Drug Research Institute, Lucknow. After obtaining his M. Sc. Degree from Kerala University in 1970 he did his doctoral research in National Chemical Laboratory, Pune and received his Ph. D. Degree in 1975. Since 1970 he has been working in the area of organic mass spectrometry. He has more than 150 research publications in national and international journals. He has been a member of the Editorial Board of *Journal of Mass spectrometry* since 1995. He was elected fellow of the National Academy of Sciences, India in 1997. He is a recipient of the ISMAS Eminent Mass Spectroscopist Award (1999). His present interests include effect of metal cationization of organic molecules, applications of mass spectrometry for the characterization of biomolecules and natural products and in drug metabolism and pharmacokinetics and also profiling of natural products and drugs by DART MS.