Atmospheric Pressure Ionization Sources: Their Use and Applicability

This white paper discusses a range of different atmospheric pressure ionization techniques: Electrospray Ionization (ESI), Atmospheric Pressure Chemical Ionization (APCI), Atmospheric Pressure Photoionization (APPI), and Atmospheric Solids Analysis Probe (ASAP), and Waters' novel UniSpray™ (US) ion source. Included is information about their ionization mechanisms, optimization, and types of small molecules for which they are most applicable.

INTRODUCTION

It can be argued that a mass spectrometer, of any geometry, is nothing without its ion source – since, without the generation of ions there is nothing for the mass spectrometer to separate and detect. Historically, ion sources were maintained at low pressure, under vacuum, to enable easy transfer of the ions into the high vacuum region of the mass spectrometer. Ions were predominantly formed by Electron Ionization (EI) or Chemical Ionization (CI), with the analytes entering the ion source in the gas phase, or being formed as gaseous species within the ion source, for example by thermal desorption. This low pressure/high vacuum requirement made coupling LC to MS particularly challenging. In 1982, Patrick J. Arpino characterized LC-MS as "*A difficult courtship*" (modelling it as the attraction between a fish and a bird – a species of the water and a species of the air).[1] The primary difficulty is that of accommodating a large volume of solvent into a region of very low pressure and the concomitant demands placed on the instrument's pumping system.

However, some 16 years after Arpino's description of LC-MS as "*An odd couple*" in the title of his 1982 paper, Bruce A. Thomson commented on the arrival, and widespread adoption, of atmospheric pressure ionization (API) to facilitate the coupling of LC to MS. Arpino's "*difficult courtship*" had become a "*happy union*" due to the advent of API.[2] Thomson's paper charts the progress of API from a novel, research-based technique to a near-ubiquitous approach for ion formation, and transfer to the gas phase, in LC-MS. Papers about API sources continue to be published regularly;[3-5] and the tale of the fish and the bird has been brought up to date in the meeting report from PittCon 2010, entitled "*The development of LC-MS – the marriage of the bird and the fish*".[6]

Since the early days of API, the development of ion sources has continued unabated, with in excess of 20 ambient (or near ambient) ionization techniques[4,5] available to the intrepid analyst. While the ion source itself is of vital importance, almost equally important is the correct selection of the most appropriate ionization source for the types of molecules being analyzed, along with relevant optimization, and knowledge about the source's expected behaviour. This white paper is intended to be used as a tool to aid in these areas. However, by necessity, many other ionization options have not been investigated. One, or more, of the ion sources not covered here might be equally appropriate for ionization of compounds mentioned in this document.

SOURCES: OVERVIEW

ELECTROSPRAY IONIZATION

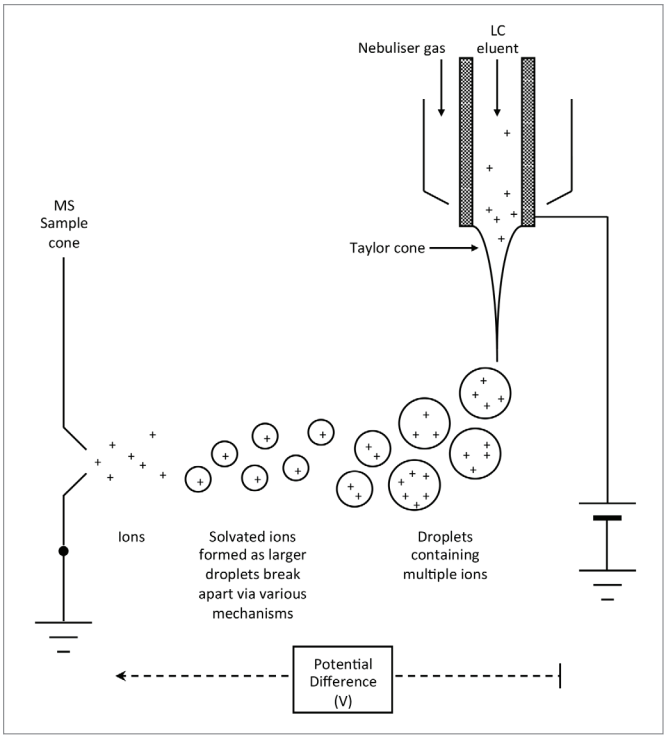


Figure 1. Schematic showing the ionization process in electrospray ionization (ESI).

Figure 1 shows a simple schematic of the ionization process in electrospray ionization (ESI). Some debate still remains regarding the precise mechanism of ion formation in ESI. Typically, molecules are believed to undergo electrochemical reactions either through redox reactions at the liquid/metal interface of the capillary tip or through acid/base reactions in solution.[7] These processes form ions in solution; the figure shows positive ions but negative ions could be generated in a similar manner.

To transfer the ions into the gas phase, two main general mechanisms are proposed:[8] the "ion evaporation mechanism" (IEM) where the electric field at the surface of highly charged, small droplets becomes sufficient to field desorb ions directly from the surface, or the "Charge Residue Model" where ions eventually become desolvated as solvent molecules leave the droplet surface. Evidence suggests that smaller ions are more likely to enter the gas phase via the IEM, whereas larger, multi-charged species are more likely to follow the CRM.[8,9] Modifications or related processes to these two mechanisms have also been proposed.[10]

ATMOSPHERIC PRESSURE CHEMICAL IONIZATION

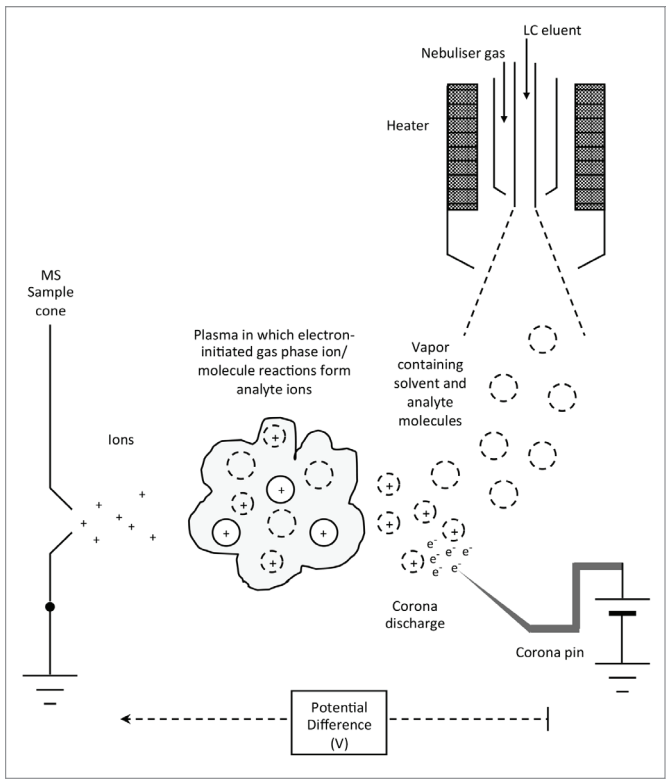


Figure 2. Schematic showing the ionization process in atmospheric pressure chemical ionization (APCI).

Figure 2 shows a simple schematic of the ionization process in atmospheric pressure chemical ionization (APCI). In contrast to ESI, APCI does not have a voltage applied to the capillary tip through which the analyte solution passes, instead it uses a corona discharge to initiate ionization in the gas phase. High energy electrons from the corona discharge cause a cascade of ion/molecule reactions that can ultimately generate positive ions related to the analyte.[11] Figure 3 illustrates the series of reactions that can take place involving atmospheric species.[12] Electrons initially ionize atmospheric species – primarily nitrogen molecules – by electron bombardment. A sequence of clustering and/or charge transfer reactions take place; finally, the protonated water clusters formed from these reactions can go on to produce positive analyte ions via charge exchange or proton exchange mechanisms. Alternatively, electrons can interact with gas phase molecules that can then go on to react with the analytes, typically via proton abstraction, resulting in the formation of negative ion species of interest.

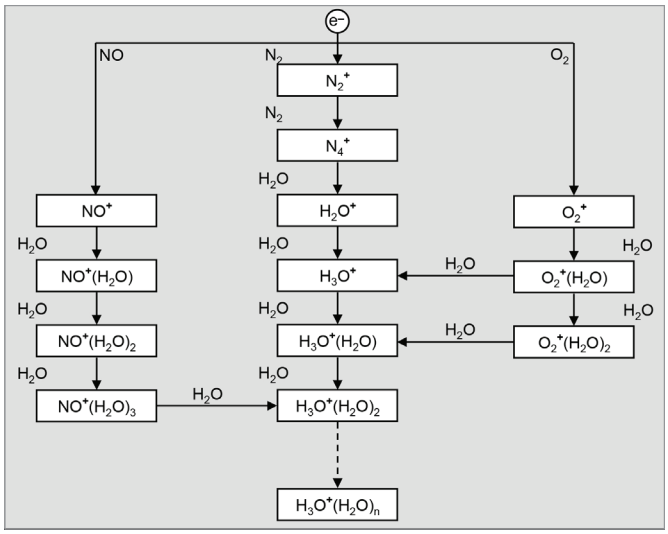


Figure 3. Schematic of reactions involving atmospheric species that can form positive ions in APCI.

ATMOSPHERIC SOLIDS ANALYSIS PROBE

The Atmospheric Solids Analysis Probe (ASAP)[13] is an ionization technique that utilizes APCI ionization mechanisms for samples that are introduced into the ion source as solid deposits, solutions, or suspensions on the tip of a small glass tube held by the probe. Heated nebulizer gas desorbs molecules from the tip of the glass tube, as shown in Figure 4.

There is no chromatographic eluent so this approach is, essentially, dry compared with classical APCI. For ASAP, ionization mechanism theories similar to those for APCI (Figure 3) can be applied, however ASAP does seem to offer a pathway (or pathways) to ionizing some species that are not so readily ionized by APCI, for example polyolefins.[14] This is possibly due to the absence of excess solvent in the source atmosphere, resulting in fewer solvent-related cluster species, which is likely to enhance charge exchange mechanisms.[15] ASAP also offers the ability to carry out some degree of thermal degradation or pyrolysis-like experiments because the nebulizer gas can be heated to in excess of 400 °C, which could be of interest in particular application areas such as polymer analysis. In addition, the ability to ramp the temperature applied in ASAP analysis enables the acquisition of boiling point profiles and simplification of highly complex samples;[16] despite no chromatographic separation, by volatilizing components according to their individual boiling points.

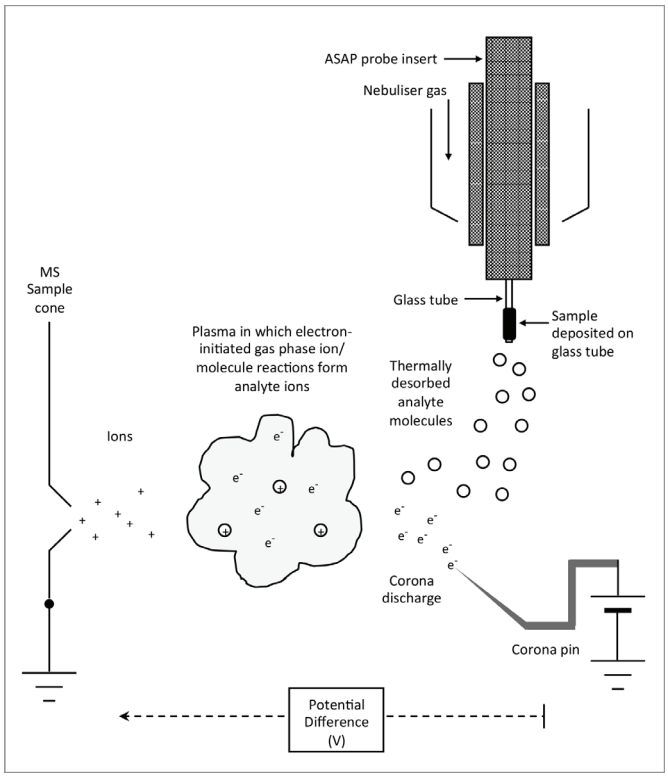


Figure 4. Schematic showing the ionization process for the atmospheric solids analysis probe (ASAP).

ATMOSPHERIC PRESSURE PHOTOIONIZATION

Figure 5 shows a simple schematic of the ionization process in atmospheric pressure photoionization (APPI). Similar to APCI, APPI is a gas phase ionization technique in which a series of gas phase ion/molecule reactions initiate ion formation. Unlike APCI, APPI does not use a corona discharge – instead, photons are emitted by a vacuum ultraviolet (VUV) lamp and photoionize gaseous species forming radical cations and electrons. The radical cations and/or the electrons can further react with other gas phase species, such as solvent molecules, to produce analyte ions.[17,18]

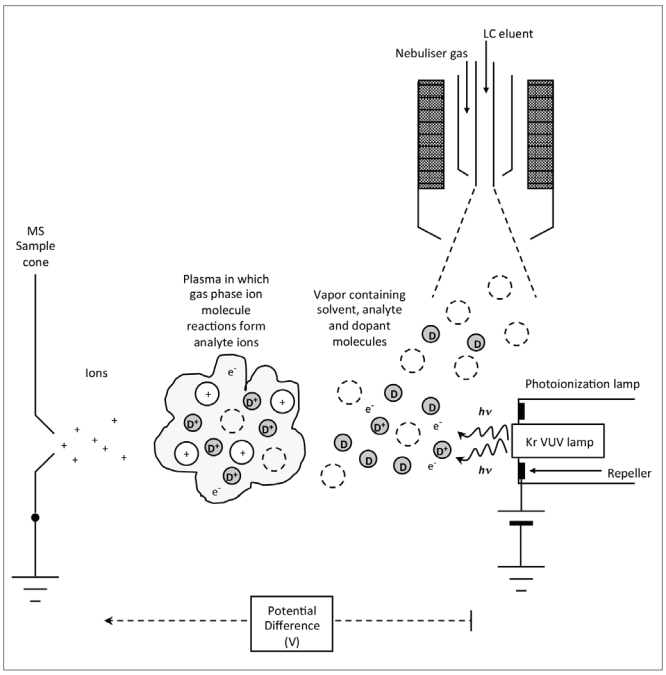


Figure 5. Schematic showing the ionization process in atmospheric pressure photoionization (APPI).

The most commonly used VUV lamp is a krypton lamp, which emits photons with approximately 10 eV energy. Any species within the atmosphere of the source can absorb the photons. If the species has an ionization energy (IE) (sometimes called ionization potential (IP)) below 10 eV it can be ionized and form radical cations and electrons. It is possible for analytes of interest to absorb photons and be photonionized directly, provided their IE is below 10 eV; however, with many samples this is statistically unlikely as the analytes are at very low concentration compared with matrix and other background species. To overcome the potential limitations of relying on direct photoionization, it is typical to add an additional solvent, known as a dopant, that has an IE below 10 eV. Examples of solvents that can be used as dopants, along with their IE and Proton Affinity (PA) values, are shown in Table 1. The dopant is easily photoionized and the resulting dopant radical cations initiate gas phase ion/molecule reactions that subsequently form analyte positive ions.

Dopant	IE (eV)[19]	PA* (kJ.mol^{-1})[19]
Acetone	9.70	812
Tetrahydrofuran (THF)	9.40	822
Benzene	9.24	750
Chlorobenzene	9.07	753
Bromobenzene	9.00	754
Toluene	8.83	784
Anisole	8.20	840

**PA: Proton Affinity*

Table 1. Gas phase ion energetics data for some typical dopant molecules.

The dopant undergoes direct photoionization, as described in this equation:

$D + h\nu \rightarrow D^* \rightarrow D^{+\cdot} + e^-$

(where D = dopant molecule and $h\nu$ is the energy of the photon).

Table 2 shows key reactions that are believed to be involved in positive ion formation in APPI. Both the IE and the PA of all species present in the ion source atmosphere can influence the ionization mechanisms.

Reaction equations†	Requirements	Type of reaction
$D^{+\cdot} + M \rightarrow D + M^{+\cdot}$	if IE (M) < IE (D)	Charge exchange
$D^{+\cdot} + S \rightarrow [D - H]^{\cdot} + [S + H]^+$	if PA (S) > PA ($[D - H]^{\cdot}$)	Proton exchange
$[S + H]^+ + M \rightarrow S + [M + H]^+$	if PA (M) > PA (S)	Proton exchange
$D^{+\cdot} + M \rightarrow [D - H]^{\cdot} + [M + H]^+$	if PA (M) > PA ($[D - H]^{\cdot}$)	Proton exchange
$M + h\nu \rightarrow M^* \rightarrow M^{+\cdot} + e^-$	if IE (M) < ~10 eV	Direct photoionization

Table 2. Key reactions for positive ion formation in APPI.

†Where: D = dopant molecules, M = analyte molecules, S = solvent molecules or solvent clusters

UNISPRAY

The ionization mechanism for the Waters UniSpray source is not yet fully characterized and several processes are believed to contribute to the highly efficient generation of ions. The source comprises a grounded capillary from which analyte solution elutes that is nebulized by high velocity nitrogen gas. The eluent spray impacts on a cylindrical, stainless steel target rod held at high voltage, typically ~0.5–4.0 kV. The impact point is optimized to be off-set from the centre of the rod and upstream of the mass spectrometer inlet, this causes the flow of the eluent spray to bend around the profile of the rod due to the Coandă effect.[20]

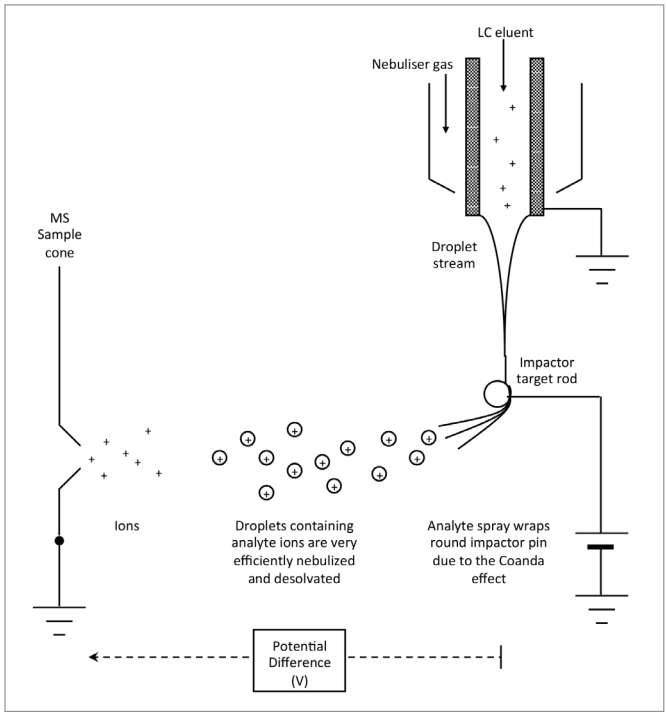


Figure 6. Schematic showing the ionization process in UniSpray.

Figure 6 shows a schematic illustrating the ionization process in UniSpray. The spectra generated when using UniSpray closely resemble those from ESI analyses so, although there is no voltage applied to the capillary tip, it is likely that the eluent contains ions formed from solution phase redox reactions and other physical processes. It is also possible that surface-based effects on the impactor rod, and additional gas phase phenomena, could further contribute to ion formation. An increase in sensitivity has been observed for UniSpray compared with other atmospheric pressure ionization techniques.[21] Investigations into ionization efficiency in ESI found that droplet size plays a role in ion production yield.[22] Therefore, it seems that a significant portion of this observed increase can be attributed to the formation of much smaller droplets when the eluent spray interacts with the impactor rod, followed by rapid ion desolvation from these smaller droplets.

SOURCES: METHODS AND EXAMPLE DATA

ACQUISITION METHODS

The performance of each source was investigated using a simple technique that did not involve any chromatography. For ESI, APCI, APPI, and UniSpray, solutions of standards, which covered a broad range of small molecules, were combined with suitable representative LC mobile phase via the on-board instrument fluidics. In the case of ASAP, the glass capillary tube was dipped directly into the solutions. Examples of representative compounds from each standard mix can be seen in Table 3.

Solvent standard solutions were prepared at suitable analytical concentrations using appropriate solvents: ~0.1–1.0 µg/mL for the small molecules mixes, ~0.1% for the engine oils, and ~1 mg/mL crude oil samples. Mobile phases were chosen according to the solubility of the analytes under consideration and the type of ionization technique being used. The following combinations were investigated:

- 1:1 H_2O:MeOH + 0.1% formic acid (FA) for all standard mixes analyzed by ESI, APCI and UniSpray
- MeOH + 0.1% FA for the OLED, FAME, and PAH mixes analyzed by ESI and APCI
- 1:9 Toluene:MeOH + 0.1% FA for all samples analyzed by APPI; the FAME, and PAH mixes analyzed by UniSpray; and the OLED mix analyzed by ESI.

UniSpray responses were evaluated at three different impactor target rod voltages: 0.5 kV, 1.0 kV, and 3.0 kV, APCI responses were evaluated at four different corona currents: 1 µA, 5 µA, 10 µA, and 12 µA, and ASAP responses were evaluated at two different corona currents: 1 µA, and 12 µA.

High resolution mass spectral data, with ion mobility, were acquired on a SYNAPT® G2-S*i* HDMS instrument. Analyte responses were evaluated using absolute response from mass corrected centroid spectra and the area under extracted ion mobility peaks. The ion source giving the highest values for both these numbers was deemed to be the best technique for the analysis of the analytes in question.

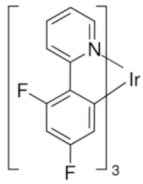
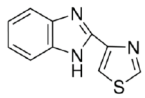
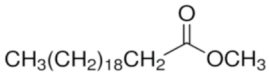
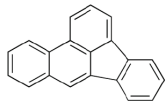
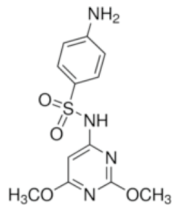
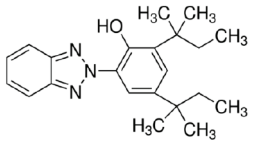
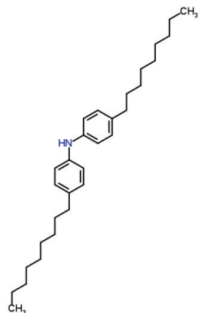
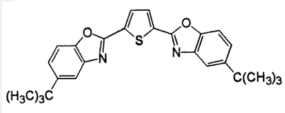
Type of samples	Example compound	Molecular formula	Relative monoisotopic mass	Structure
OLEDs	$Ir(Fppy)_3$	$C_{33}H_{18}F_6IrN_3$	761.1011	
Pesticides	Thiabendazole	$C_{10}H_7N_3S$	201.0361	
FAMEs	Methyl heneicosanoate	$C_{22}H_{44}O_2$	340.3341	
PAHs	Benzo[*b*]fluoranthene	$C_{20}H_{12}$	252.0939	
Cosmetics and Allergens (mix 1)	Sulfadimethoxine	$C_{12}H_{14}N_4O_4S$	310.0736	
Cosmetics and Allergens (mix 2)	UV 328 (Tinuvin 328)	$C_{22}H_{29}N_3O$	351.2311	
Engine oil	Oil additive (4-Nonyl-N-(4-nonylphenyl)aniline)	$C_{30}H_{47}N$	421.3709	
Polymer additives	Uvitex OB	$C_{26}H_{26}N_2O_2S$	430.1715	

Table 3. Example compounds from each type of sample mix with corresponding molecular formula, relative monoisotopic mass, and structure.

EXAMPLE DATA

Table 4 shows a summary of the responses from each ion source for the representative compounds shown in Table 3. The yellow highlighted values indicate the largest response for each compound and hence the best ion source for those types of compounds. An X indicates that there was no reliable detected response for the given compound with that ionization technique. All representative compounds formed protonated species, but the PAH compounds also formed radical cations ($M^{+\cdot}$) and the sulfadimethoxine that was chosen as representative of the cosmetics and allergens mix 1 also formed a sodium adduct ion.

	ESI$^+$		APCI$^+$		APPI$^+$		US$^+$		ASAP$^+$	
Samples	**Max. response (Peak height)**	**Max. response (Peak area)**	**Max. response (Peak height)**	**Max. response (Peak area)**	**Max. response (Peak height)**	**Max. response (Peak area)**	**Max. response (Peak height)**	**Max. response (Peak area)**	**Max. response (Peak height)**	**Max. response (Peak area)**
OLEDs *m/z* 764 $[M+H]^+$	2.87e5	23441	4.45e5	41548	2.07e5	16969	7.35e5	63698	2.94e5	40198
Pesticides *m/z* 202 $[M+H]^+$	3.78e6	375125	3.55e5	37737	2.62e5	26865	1.52e7	1552255	5.45e6	578515
FAMEs *m/z* 341 $[M+H]^+$	7.16e4	5134	1.59e5	16185	X	X	X	X	2.89e5	28585
PAHs *m/z* 253 $[M+H]^+$ (*m/z* 252) $(M^{+\cdot})$	X (1.48e6)	X (147131)	1.78e6 (7.95e5)	188870 (72772)	3.02e6 (2.34e6)	254391 (206398)	X (8.06e3)	X (670)	1.20e5 (8.25e4)	11946 (6864)
Aller. mix 1 *m/z* 311 $[M+H]^+$ (*m/z* 333) $([M+Na]^+)$	1.36e7 (4.66e6)	1433816 (491988)	2.04e6 (2.72e4)	199304 (1879)	Error during acquisition	Error during acquisition	1.41e7 (4.75e6)	1497566 (497550)	7.65e3	670
Aller. mix 2 *m/z* 352 $[M+H]^+$	4.10e6	799211	3.46e6	604629	2.13e6	207647	4.48e6	835396	1.33e6	127819
Eng. Oil *m/z* 422 $[M+H]^+$	7.83e6	812933	1.98e7	2025327	2.40e7	2547684	6.32e7	6706421	Not acquired	Not acquired
Pol. adds. *m/z* 430 $[M+H]^+$	1.58e6	156425	1.46e5	15318	2.10e5	21215	2.54e6	262162	Not acquired	Not acquired

Table 4. Summary of responses for representative compounds from each standard mix, the yellow highlighted values indicate the best responses and hence the best ionization technique for each compound.

Crude oil information has not been included in this summary table because each different ion source is discriminatory for crude oil analysis and favors ionization of certain classes of compounds over others,[15] for example ESI favorably ionizes nitrogen-containing species while APPI favorably ionizes aromatic hydrocarbons and sulfur-containing species. In practice, two (usually ESI and APPI), or more, ionization techniques are employed for crude oil analysis by mass spectrometry. Example spectra for crude oil samples are shown in Figure 7, with the most intense class identified for each ionization technique to give an indication of class coverage. Early work on the use of UniSpray for crude oil type samples reported that the compound class coverage by UniSpray is similar to that of APPI, but UniSpray appears to be more responsive for sulfur-containing compounds.[23]

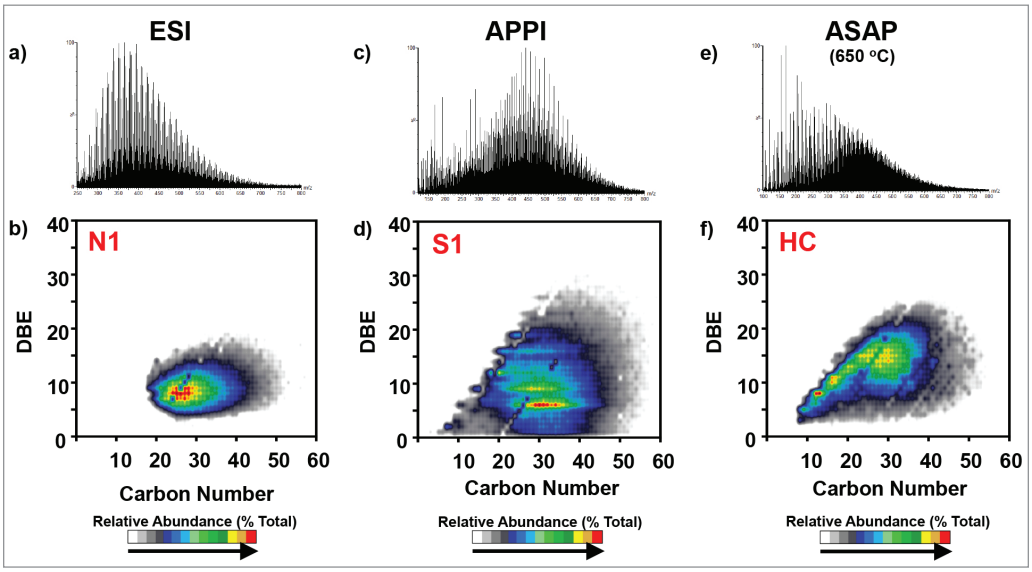


Figure 7. Illustrative crude oil data showing (a) ESI mass spectrum with (b) the most intense class for ESI indentified as the N1 class; (c) APPI mass spectrum with (d) the most intense class for APPI identified as the S1 class; (e) ASAP mass spectrum, produced at 650 °C, with (f) the most intense class for ASAP identified as the HC (hydrocarbon) class.

Table 5 shows data focussing on the small compound mix of polymer additives. Responses for all components of this mix are shown for the four liquid flow ion sources under investigation. In each case, the most intense ion observed is given, with the colour of the text indicating the type of ion: black = protonated molecule, blue = sodiated molecule, red = hydride ion abstraction, and brown = radical cation. The highlighted yellow values indicate the largest response for each compound and hence the best ion source for that particular compound.

			APCI+		APPI+		ESI+		US+	
Name	Formula	Relative Monoisotopic Mass (neutral)	Ion Observed	Ion Intensity (µA on pin)	Ion Observed	Ion Intensity	Ion Observed	Ion Intensity	Ion Observed	Ion Intensity (kV on pin)
Diethyl phthalate	$C_{12}H_{14}O_4$	222.0892	X	X	X	X	$[M+Na]^+$	2.91e5	$[M+Na]^+$	1.49e6 (0.5 kV)
Tinuvin P	$C_{13}H_{11}N_3O$	225.0902	$[M+H]^+$	1.92e6 (1 µA)	$[M+H]^+$	1.35e6	$[M+H]^+$	1.41e6	$[M+H]^+$	2.01e6 (3.0 kV)
Dibutyl sebacate	$C_{18}H_{34}O_4$	314.2457	X	X	X	X	$[M+Na]^+$	1.10e6	$[M+Na]^+$	5.72e6 (0.5 kV)
Diphenyl phthalate	$C_{20}H_{14}O_4$	318.0892	X	X	X	X	$[M+Na]^+$	4.24e5	$[M+Na]^+$	3.17e6 (0.5kV)
2-hydroxy-4-octyloxy benzophenone	$C_{21}H_{26}O_3$	326.1882	$[M+H]^+$	1.47e5 (1 µA)	$[M+H]^+$	2.06e5	$[M+H]^+$	3.45e5	$[M+H]^+$	4.47e5 (3.0kV)
Tinuvin 327	$C_{20}H_{24}ClN_3O$	357.1608	$[M+H]^+$	1.07e6 (1 µA)	$[M+H]^+$	1.25e6	$[M+H]^+$	1.03e6	$[M+H]^+$	8.62e5 (3.0 kV)
TCP	$C_{21}H_{21}O_4P$	368.1177	$[M+H]^+$	2.04e5 (1 µA)	$[M+H]^+$	2.80e5	$[M+H]^+$	1.29e6	$[M+Na]^+$	6.23e6 (0.5 kV)
Uvitex OB	$C_{26}H_{26}N_2O_2S$	430.1715	$[M+H]^+$	1.46e5 (1 µA)	$[M+H]^+$	2.10e5	$[M+H]^+$	1.58e6	$[M+H]^+$	2.54e6 (3.0 kV)
Cyasorb 2908	$C_{31}H_{54}O_3$	474.4073	$[M+H]^+$	4.79e4 (1 µA)	$[M+H]^+$	4.74e4	$[M+H]^+$	1.15e5	$[M+Na]^+$	1.45e5 (0.5 kV)
Irganox 1076	$C_{35}H_{62}O_3$	530.4699	$[M-H]^+$	5.80e3 (1 µA)	$M^{+\cdot}$	6.32e4	$[M+Na]^+$	5.86e5	$[M+Na]^+$	1.94e6 (0.5 kV)
Irganox 245	$C_{34}H_{50}O_8$	586.3506	$[M+Na]^+$	1.21e4 (1 µA)	$[M+H]^+$	1.43e4	$[M+Na]^+$	1.46e6	$[M+Na]^+$	9.98e6 (0.5 kV)
Irganox 1098	$C_{40}H_{64}N_2O_4$	636.4866	$[M+H]^+$	3.24e4 (1 µA)	$[M+H]^+$	5.18e4	$[M+Na]^+$	5.93e5	$[M+Na]^+$	4.36e6 (0.5 kV)
Tinuvin 360	$C_{41}H_{50}N_6O_2$	658.3995	$[M+H]^+$	2.02e5 (1 µA)	$[M+H]^+$	2.13e5	$[M+H]^+$	4.91e5	$[M+H]^+$	3.50e5 (3.0 kV)
Ethanox 330 (Irganox 1330)	$C_{54}H_{78}O_3$	774.5951	$[M-H]^+$	9.04e3 (1 µA)	$M^{+\cdot}$	1.97e4	$[M+Na]^+$	4.47e4	$[M+Na]^+$	8.23e4 (0.5kV)
Uvinul 3030	$C_{69}H_{48}N_4O_8$	1060.3472	X	X	X	X	$[M+Na]^+$	6.72e3	$[M+Na]^+$	1.01e4 (0.5 kV)
Irganox 1010	$C_{73}H_{108}O_{12}$	1176.7841	X	X	X	X	$[M+Na]^+$	8.81e3	X	X

Table 5. Summary of responses for the polymer additives mix comparing the responses of the four liquid flow ion sources. The yellow highlighted values indicate the best responses and hence the best ionization technique for each compound.

SOURCES: DISCUSSION AND GUIDANCE

DISCUSSION

The data presented above clearly indicates that, where ESI would normally be the ionization technique of choice, UniSpray is the best ion source to use. In general, for the solvent standards tested, UniSpray gave a better response than any of the other ion sources – except in cases where the test compounds are known to be highly non-polar, for example PAHs. The evidence presented here suggests that the ions in UniSpray might not be formed via different mechanisms compared with ESI because the same types of ions are formed with UniSpray and ESI. Instead, it seems that the efficiency of droplet desolvation plays a key role, as discussed in early work on UniSpray.[20]

In the UniSpray analyses, the optimal voltage for the analysis depended upon the type of ion that predominates: sodiated molecules or protonated molecules. For the compounds used in this work, sodiated species gave a better response with a lower voltage applied to the impactor target pin – in this case 0.5 kV, whereas protonated species gave a better response with an applied voltage of 3.0 kV. For the two techniques that use a corona discharge pin, APCI and ASAP, the choice of applied corona current was also evaluated. In general, a lower corona current value was suitable for simpler samples and solvent standards. The more complex the sample the higher the required corona current, for example, for the analysis of crude oil and petroleum samples the required corona current can be around 10–15 µA to maintain a reliable sample signal.[15] In addition, ASAP typically seems to produce a better response with a slightly higher corona current than APCI for the same sample.

While UniSpray and ESI both offered good coverage of the compounds analysed in this work, there were some types of compounds that required alternative options more applicable to non-polar samples. ASAP offered excellent coverage for both polar and non-polar molecules and is a good option for fast, triage-like MS analyses. Furthermore, APPI is well recognised as being the most appropriate ion source for highly aromatic species such as PAHs and related compounds,[24,25] which was also found to be the case in this work.

GENERAL GUIDANCE

In practice, the choice of ionization technique might be limited by the ion source or sources available to the analyst. Typically, ESI is the source of choice for most LC-MS analyses. Even though ESI might not be the most applicable ionization technique based on the compound chemistry, i.e. the technique that gives the most intense response, it will often give a sufficient response for a broad range of compounds. From early investigations, it seems that UniSpray offers a similar level of broad coverage with an enhanced response compared to ESI for most compounds studied.

However, if more than one source option is available, the following information is intended as a general guidance to help in the selection of the most applicable ion source for a particular analysis. Table 6 shows a summary of typical structural characteristics that make different compounds amenable to ionization by particular ion sources, along with some illustrative examples of compounds. Suggested compounds will not necessarily be uniquely ionized by the stated ion sources, for example vitamin B12 is not only ionized by APPI it can also be ionized using ESI.

Ion Source	Appropriate Structural Characteristics	Example Compounds/Classes
UniSpray or ESI	Polar molecules, e.g. containing oxygen or nitrogen atoms, hydroxyl groups, amine groups, carboxyl groups, etc. that can form ions in solution	Pesticides, e.g. tebuconazole, thiabendazole Veterinary drugs, e.g. flubendazole, oxolinic acid
APCI or ASAP	Non-polar species particularly with non-aromatic ring structures	Steroids, e.g. 17α-hydroxyprogesterone Biocide compounds, e.g. tributyltin chloride Phytosterols, e.g. campesterol
APPI or ASAP	Non-polar aromatic species or species with regions of delocalized electron density. Species with chromophores	PAHs, e.g. pyrene, anthracene Vitamin B12 UV stabilizers, e.g. Tinuvin compounds
ASAP	Some saturated species	Low molecular weight poly(ethylene) FAMEs, e.g. methyl heneicosanoate

Table 6. Structural characteristics of compounds that make them amenable to ionization by particular ion sources along with illustrative example compounds

SOURCE OPTIMIZATION AND USE GUIDANCE

- ASAP
  - Acquire using corona current rather than corona voltage
  - Evaluate several different corona currents including higher values, for example 10 µA
  - For a rapid, triage-like sample analysis, a 30-second ballistic temperature ramp can be used to volatilize the sample and evaluate what ions can be seen
  - For separation according to the boiling point profile of the sample, a slower temperature ramp can be used
- APPI
  - In most cases a dopant will enhance the ionization process
  - Start by trying toluene as a dopant, this will typically work well. If required, try other dopants according to their IE and the IE of your analyte or analytes
  - For exact mass data acquisitions, the dopant can be prepared 1:1 dopant:MeOH with leucine enkephalin dissolved in the MeOH so that a lock mass ion will be acquired in Function 1. The leucine enkephalin ion can be used for internal mass correction
  - Use a low to medium repeller voltage, for example 0.5 kV
  - Ensure that the lamp is pushed all the way into the source housing (position 2 on the source housing)
  - APPI shows a better response with lower flow rates
  - The dopant flow rate should, ideally, be in the range 10–50% of the eluent flow rate

- APCI
  - Acquire using corona current rather than corona voltage
  - Evaluate several different corona currents including higher values, for example 10 µA. In general, for less complex samples, values up to 5 µA should be sufficient
  - The amount of water in the source may effect the ionization efficiency since water clusters play a role in the ionization mechanism for APCI
- UniSpray
  - Try several different impactor pin voltages to optimize for the compounds of interest
  - Always check for sodium adducts since these are formed very readily for many of the compounds investigated in this work
  - Optimizing the position of the spray onto the surface of the impactor pin is very important. Ensure it is slightly off center from the MS inlet to utilize the Coandă effect

CONCLUSION

In conclusion, to assist with ion source selection, Figure 8 shows a simple decision flow chart giving a suggested sequence in which the ionization techniques could be considered. This acknowledges that ESI is likely to be the first choice for most day-to-day analyses and, where it is available, UniSpray should also be evaluated as an early option. If chromatographic separation is not required then ASAP would be the recommended technique of choice since it offers very broad coverage of compound classes and can be evaluated in a matter of minutes to ascertain its applicability for the analysis. The other alternative, where chromatography is not required, is to use infusion and follow the same decision pathway as that suggested for LC-MS analysis.

Overall, for a problem-solving laboratory, having a wide range of ion sources available would be beneficial to enable the ionization of the broadest range of different molecules. Once an appropriate ion source for a particular analysis has been identified the selected technique can be routinely implemented; however, if new ionization techniques are developed, such as UniSpray, these might offered improved responses for established analyses.

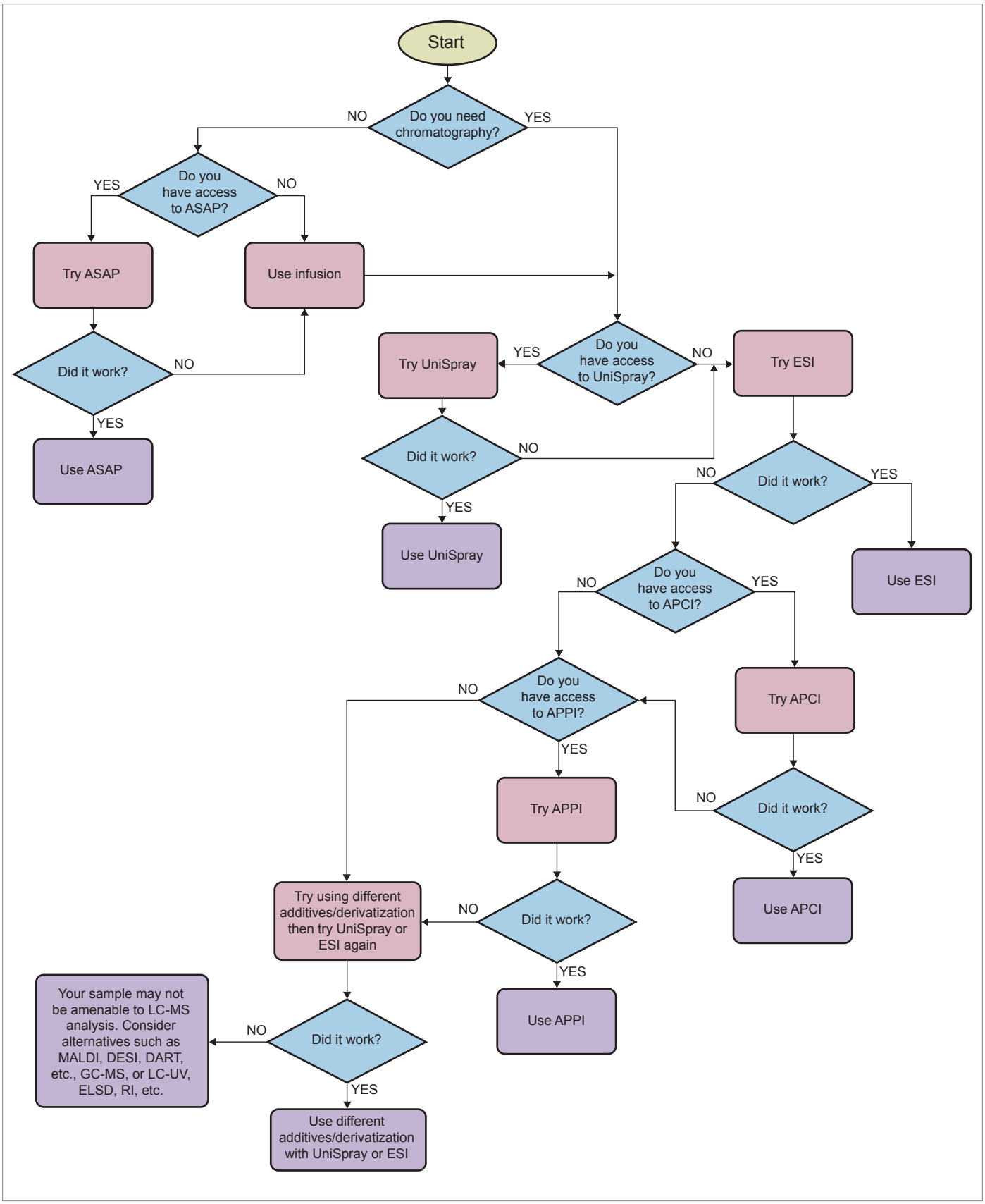


Figure 8. Decision flow chart showing suggested workflow when choosing the most appropriate ion source.

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