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Electrospray ionization/atmospheric pressure photoionization multimode source for low-flow liquid chromatography/mass spectrometric analysis

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Analysis of several polar and non-polar compounds is performed with a newly developed dual electrospray ionization/atmospheric pressure photoionization (ESI/APPI) or ESPI source. Several variables are considered in the source, such as ESI probe heater temperature, solvent flow, dopant effects, repeller plate voltage, source geometry and photon energy (Kr vs. Ar lamp). Direct photoionization resulting in a molecular radical cation $[M]^{\cdot+}$ dominates at high temperatures (>400°C) and low flow rates (<200 μL/min). Indirect photo-induced chemical ionization (PCI) involving solvent molecules becomes important at lower temperatures and higher solvent flow rates. Indirect PCI is enhanced using an Ar lamp, which yields comparable $[M+H]^+$ signal but poorer $[M]^{\cdot+}$ signal than the Kr lamp at lower temperatures and higher flow rates. This is in support of our recent finding that the Ar lamp results in a solvent-dependent enhancement of analyte molecules via PCI. Analysis of 12 compounds in methanol under low-flow conditions (10 μL/min) demonstrates that the dual ESPI source performs favorably for most compounds versus the standard ESCI source, and significantly better than ESCI for the analysis of unstable drugs, like flurbiprofen. Several factors contributing to the benefits of the ESPI source are the shared optimal geometry for ESI and APPI sources and soft ionization of APPI versus APCI. Copyright © 2007 John Wiley & Sons, Ltd.

With increasing demands placed on current analytical systems to become more universal, there have been investigations to hybridize available technologies to better cover ever more diverse target compounds. Benefits include reduced number of parallel instruments, faster sample analysis for complex mixtures and a simplified analytical technique. Two fundamental groups of compounds are non-polar molecules (with low water solubility) and polar molecules (with high water solubility). Detection of both non-polar and polar compounds is well suited to liquid chromatography/mass spectrometry (LC/MS), and has seen considerable progress with the development of atmospheric pressure photoionization (APPI) and other variants, such as dopant-assisted APPI (DA-APPI), AP laser ionization (APLI),[3] use of different lamp energies for enhanced APPI signal,[4] and improved choices of mobile phase(s) for chromatographic separation.[5,6] There is considerable research available for reviewing the benefits of mass spectrometric techniques using different ion sources (APPI, APCI and ESI), e.g., with polyaromatic hydrocarbons,[7,8] hydrophobic peptides,[9] pesticides,[10,11] as well as fatty acids and lipids.[5,6] Our group has focused on the technique of APPI,[1,8] because it has demonstrated extended linear dynamic range,[12] enhanced sensitivity, and thus lower detection limits,[7,10,13–16] and reduced or no off-line sample cleanups[7,10] in comparison with direct atmospheric pressure chemical ionization (APCI) or electrospray ionization (ESI). Addition of a dopant to APPI (DA-APPI) to the mobile phase may further increase sensitivity.[2]

In general, among the available ionization sources, APPI performs best for non-polar compounds, while ESI performs best for polar compounds, and APCI and APPI perform comparably for moderately polar compounds.[17] This is a direct consequence of the unique ionization mechanism associated with each ion source. Given the diverse ionization mechanism of these techniques, it is logical to conclude that there are scenarios in which one source performs better than another, and indeed a combined dual source would be ideal. This has been successfully implemented and commercialized with APPI/APCI and ESI/APCI (or ESCI) dual sources.[18] There has also been investigations into combining ESI with atmospheric pressure laser ionization (APLI), with enhanced sensitivity over APPI, although it is not yet widely used due to the large size, expense and costs of the laser.[3,19] The ESI/APPI (or ESPI) dual source has been previously introduced,[20] but has required additional research to improve and validate the technology. This combination is arguably the most orthogonal combination of two ion

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sources, spanning the greatest range of compounds on the polarity scale. Our recent work on APPI of polyaromatic hydrocarbons,[4] acylglycerol lipids[5] and triacylglycerol lipids (manuscript submitted) has focused on understanding photoionization (PI) mechanisms, and we have applied this knowledge to enhance the performance of APPI sources. In addition, we have made significant improvements in the design and operation of the ESPI dual source. In this paper, we demonstrate the enhanced sensitivity of ESPI in comparison to ESCI towards the detection of several compounds, particularly under low solvent flow conditions.

EXPERIMENTAL

Chemicals and reagents

The compounds chosen in this study were selected due to their common analysis using high-pressure liquid chromatography (HPLC) mass spectrometry (MS) and their diverse polar nature, i.e. solubility. Chemicals were purchased from Aldrich Chemicals Co., Inc., (Milwaukee, WI, USA). These are (with catalog no.): benzo[*a*]pyrene (48564), cholesterol (362794), coprostan-3-one (C2152), flurbiprofen (F8514), gallic acid (G7384), hydrocortisone (286095), imipramine (10899), naproxen (284785), nimesulide (N1016), progesterone (P0130), stigmastanol (S4297) and testosterone (T5411, 1 mg/mL). Primary stock solutions were first made in dichloromethane, and were subsequently diluted to reach an end concentration of 0.1 mM in methanol, i.e., cholesterol (0.039 mg/mL), coprostan-3-one (0.039 mg/mL), flurbiprofen (0.024 mg/mL), gallic acid (0.017 mg/mL), hydrocortisone (0.036 mg/mL), imipramine (0.028 mg/mL), naproxen (0.023 mg/mL), nimesulide (0.031 mg/mL), progesterone (0.032 mg/mL) and stigmastanol (0.042 mg/mL), except benzo[*a*]pyrene (40 μM or 0.01 mg/mL) and testosterone (3.5 μM or 0.001 mg/mL), with an appropriate scaling factor applied to the data to reach 0.1 mM. To avoid further complications with solvent-analyte interactions, only methanol is used here (all analyte compounds are soluble at the concentrations studied). In certain experiments, the sample is given a dopant of 5% or 10% toluene.

Instrument, parameters and conditions

A Micromass ZQ LC/MS (Waters Corporation, Milford, MA, USA) is used for these experiments. Flow injection analysis is performed (2 μL sample loop) with an APPI single source (Syagen Technology, Inc., Tustin, CA, USA), a newly developed ESPI dual source,[20] or an ESCI dual source (Waters Corporation, Milford, MA, USA). The APPI and ESPI sources were operated with either a Kr lamp (lower energy of 10.0 and 10.6 eV photons) or an Ar lamp (higher energy of 11.6 eV photons). The mode-switching characteristics for both ESCI and ESPI are kept the same to minimize differences between sources and represent standard operating conditions for ESCI; specifically: inter-scan or inter-mode delay (time after one source turns off and another turns on) of 400 ms, inter-channel delay (time between each monitored mass signal) of 10 ms and a dwell time (time spent on each mass signal) of 50 ms. The data acquisition software used is MassLynx 4.0. For selected ion monitoring (SIM) detection, the detector monitors ion peaks of each analyte with a cone voltage of 25 V. Cone voltage is one key parameter in monitoring specific precursor or fragment ions;[5] however, only one voltage is used here to simplify this study. As solvent clusters are not accurately measured at higher cone voltages due to fragmentation,[4] solvent clusters are measured at a reduced cone voltage of 5 V. The desolvation gas flow is set to 400 L/h and the sample cone gas flow is set to 10 L/h of nitrogen.

RESULTS AND DISCUSSION

Effect of heater temperature and solvent flow

The key mechanisms for APPI that can occur for a species (M) within a solvent (S) and a dopant (D) include:

$$\text{photoionization:}\quad M + h\nu \rightarrow M^{\bullet +} + e^- \tag{1a}$$

$$\text{charge transfer:}\quad M + (D^{\bullet +} \text{ or } S^{\bullet +}) \rightarrow M^{\bullet +} + (D \text{ or } S) \tag{1b}$$

$$\text{proton transfer:}\quad M + ([D + H]^+ \text{ or } [S + H]^+) \rightarrow [M + H]^+ + (D \text{ or } S) \tag{1c}$$

$$\text{hydrogen abstraction:}\quad M^{\bullet +} + S \rightarrow [M + H]^+ + [S + H]^{\bullet} \tag{1d}$$

Mechanisms to generate dopant ions or solvent ions are numerous, but include direct thermal ionization (thermospray),[21] photoionization (e.g., dopant,[22] solvent or solvent cluster[4]), or electron ionization via thermal electrons originating from metal surfaces exposed to VUV light (observed often with low pressure ion sources[23]). While both Ar and Kr lamps used with APPI can directly ionize the target molecule and/or dopant, light from the Kr lamp often cannot directly ionize the solvent molecule due to the high ionization potential (IP) of solvents (e.g., IP = 10.85 eV for methanol).[24] This effect is observed in Fig. 1 (left), where an increase in temperature and subsequent drying of the molecule directly aid in the photoionization of analyte and dopant (either direct PI or charge transfer from $S^{\bullet +}$, resulting in $M^{\bullet +}$). At lower temperatures, where clustering is favored and solvent dimers can form more readily, the methanol solvent dimer can ionize (IP = 9.74 eV),[25] followed by ion-solvent reactions yielding a protonated dimer, and subsequent transfer of the H^+ to the analyte.[4]

Although the photon intensity from the Ar lamp is about 8× less than from the Kr lamp (explaining the low direct $M^{\bullet +}$ ion signal measured by direct APPI), the ion signal $[M+H]^+$ is comparable to the ion signal using the Kr lamp. This enhanced ion generation is believed to be a result of added photo-induced chemical ionization (PCI) of the target analyte, a result of solvent monomer ionization using an Ar lamp.[4] This is seen in Fig. 1 (right), where at higher solvent flow rates and resulting increase in solvent molecule concentration, the direct APPI signal decreases due to solvent-absorption of VUV light, whereas the indirect PCI signal slowly increases and then exceeds the direct APPI signal at a flow rate of >200 μL/min. This mechanism permits the extension of the range commonly used for APPI, providing excellent signal response of certain compounds at flows in excess of 1 mL/min.[4]

The conclusions from these experiments are: (1) an Ar lamp can be used to produce comparable results to the Kr lamp in measuring naproxen in methanol under high-flow

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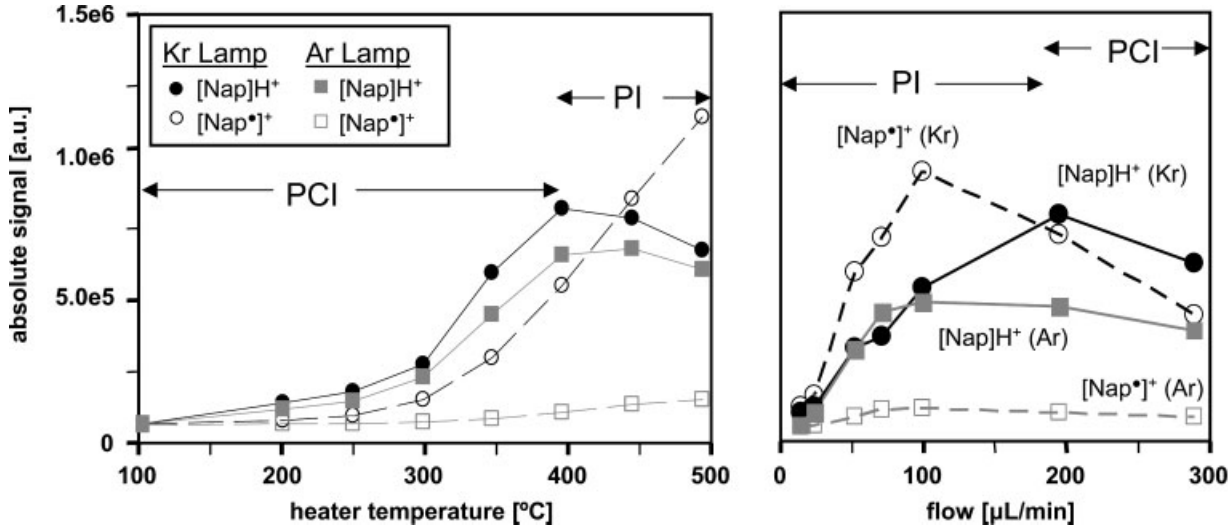

Figure 1. Analysis of naproxen (5% toluene) in methanol with a single APPI source using either a Kr or Ar lamp at (left) increasing heater temperature (set 100 µL/min) and (right) increasing solvent flow rate (set at 500°C). Photo-induced chemical ionization (PCI) dominates at lower heater temperatures or higher solvent flows, while direct photoionization (PI) dominates above 400°C or flows below 200 µL/min. Both scenarios favoring direct PI correlate to reduced solvent-cluster conditions.

conditions, despite a significantly reduced photon intensity; (2) lower temperatures lead to greater solvent clustering and reduce direct PI, $M^{\bullet+}$, but enhance indirect PCI, $[M+H]^+$; and (3) improved drying of the solvent spray from the probe tip, whether from increased temperature or lower flow, improves direct PI considerably.

Influence of the APPI source on ESI signal

One concern when combining multiple sources is the negative influence that may result from one source interfering with another. We tested two aspects of APPI that could potentially interfere with ESI: (1) influence of a commonly used dopant (5% toluene) and (2) influence of a repeller electrode (500 V) on the ESI signal. In Fig. 2 (left), we find that the ESI signals for most of the 12 compounds tested are not significantly influenced by the presence of the dopant, and in some cases dopant enhances ESI signal intensity.

Use of a repeller electrode has been previously demonstrated to enhance ion collection at reduced pressures with the photoionization technique of medium pressure laser ionization, either increasing ion intensity[26] or ion selectivity;[27] however, at atmospheric pressure, the resulting effects are influenced by solvent or solvent-cluster interactions. As seen in Fig. 2 (right), the measurement of the ESI signal with the APPI repeller electrode 'on' (constant 500 V) gives mixed results; namely, that the signal intensity of the test compounds range from half to twice their values with the repeller electrode 'off'. While the ESPI dual source is not

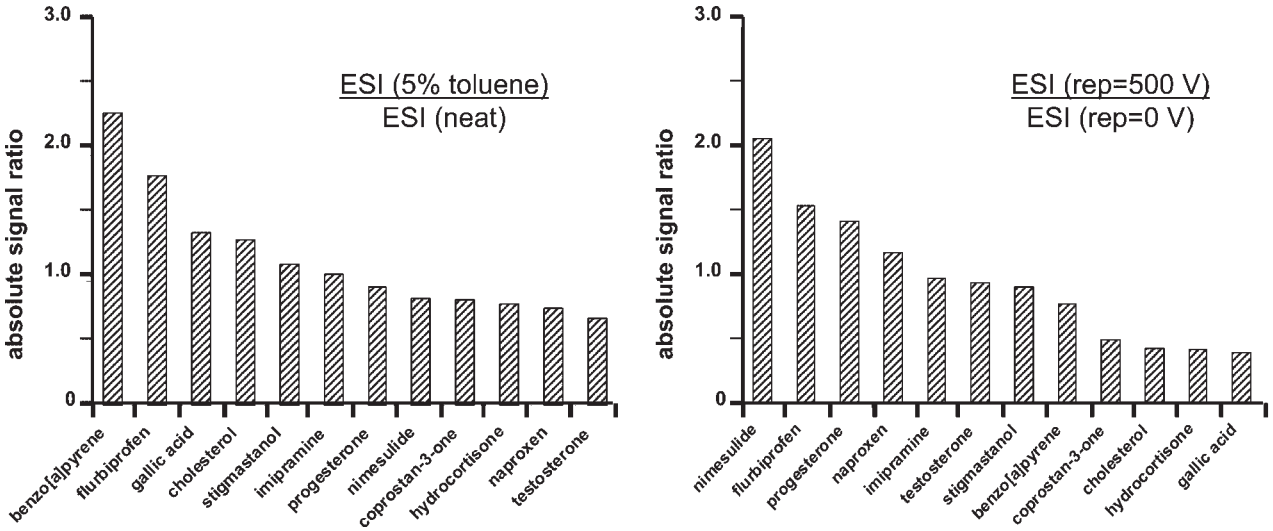

Figure 2. Comparative analysis of drugs in methanol (10 µL/min, 500°C) with a dual ESPI source using a Kr lamp. Maximum ions are chosen in each case and are measured in positive ion mode, except gallic acid. Effect of 5% toluene dopant (left) and effect of repeller electrode 'on' (500 V, right) on the ESI signal.

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expected to be operated simultaneously (currently the reflector electrode is turned off for several hundred ms before the ESI signal is measured), these results suggest that use of the repeller electrode might be advantageous in certain cases, and the user could have the option of leaving the electrode 'on' in the ESI mode if it provides better results.

Influence of spray inlet height on APPI and ESPI signals

As mentioned above, the spray temperature and solvent flow both affect the drying of the spray, and consequently the signal strength of the analyte via PI (best with a 'dry' spray) or via PCI (best with a high flow, 'cluster-rich' spray). Another factor that can be adjusted to influence the drying of the spray prior to photoionization is the distance between sample introduction (from the probe tip) and lamp surface. One potentially negative aspect is the decrease in concentration of the analyte within the spray as this distance is increased.

The right column in Fig. 3 is a basic diagram and photograph of the experiment performed. Aluminum o-rings provide an air-tight seal and extension to the position of the spray tip, with thicknesses of either ¼″ or ½″. After each stage addition, the angle of the sprayer is adjusted to maximize signal intensity. For additional information, the temperature of the vapor is measured using a thermocouple in a separate set of experiments (Monogram CN9000A, Omega Engineering, Inc., Connecticut, USA), where the lamp has been replaced by a thermocouple and an air-tight seal.

When the additional distance is added to the APPI single source (Fig. 3, top left graph), the $M^{\bullet+}$ signal (direct PI) drops with each successive stage, as would be expected by the reduced analyte concentration. The spray inlet used with the APPI single source results in a much broader spray angle than the ESI probe tip used with the ESPI dual source, resulting in the observed temperature differences at the lamp surface. The temperature of the vapor at the surface of the lamp is more affected by height increases with the ESPI source, starting at 180°C (no added distance) to 130°C at ¼″ to 120°C at ½″.

The effect on analyte signal of adding stages to the ESPI dual source, which has a much more angularly confined spray, is presented in the middle and bottom left graphs of Fig. 3. In the middle graph on the left the ESPI source is used in PI mode, and we see that the ESI probe tip is much less effective at vaporizing the spray than the inlet with the APPI single source (compare Fig. 3 top and middle left graphs). While PI signal intensity, $M^{\bullet+}$, is only slightly improved at ¼″ and then drops at ½″, we see in the middle left graph in Fig. 3 that the added distance significantly improves indirect PCI signal, $[M+H]^+$. Indeed, signal intensity of the $[M+H]^+$ ion with the ESPI source (¼″) is comparable to that of the

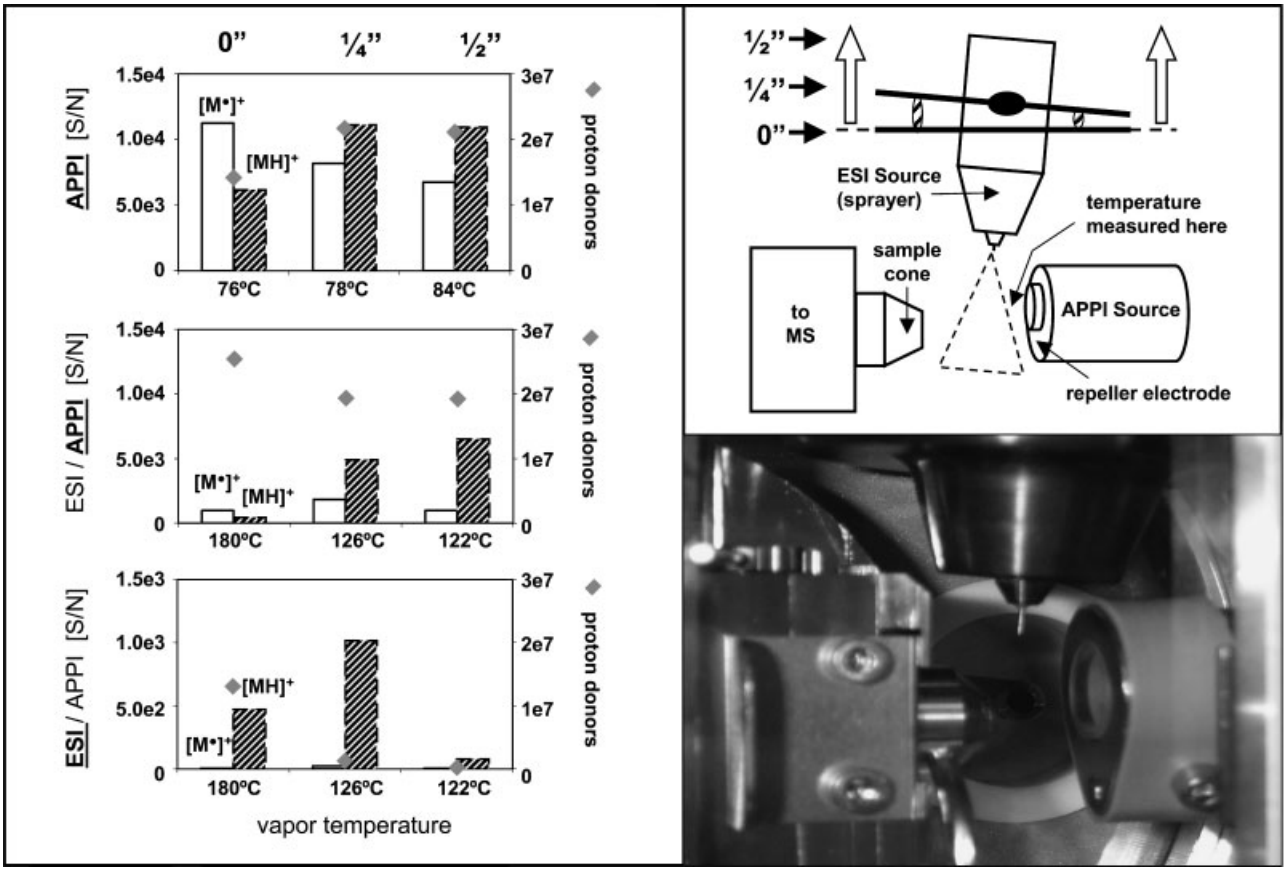

Figure 3. Effect on signal-to-noise ratio for 0.1 mM naproxen (10% toluene) with increasing ESI probe height (left graphs), with diagram and picture of source provided for reference (right column). Open boxes are radical cations (from PI, $M^{\bullet+}$) and filled boxes are protonated cations (from photo-induced CI, MH^+). The single APPI source (left top) is optimized at distance = 0″ for radical cation detection. The ESPI dual source has improved signal performance for both APPI mode (left middle) and ESI mode (left bottom) with an added distance of ¼″.

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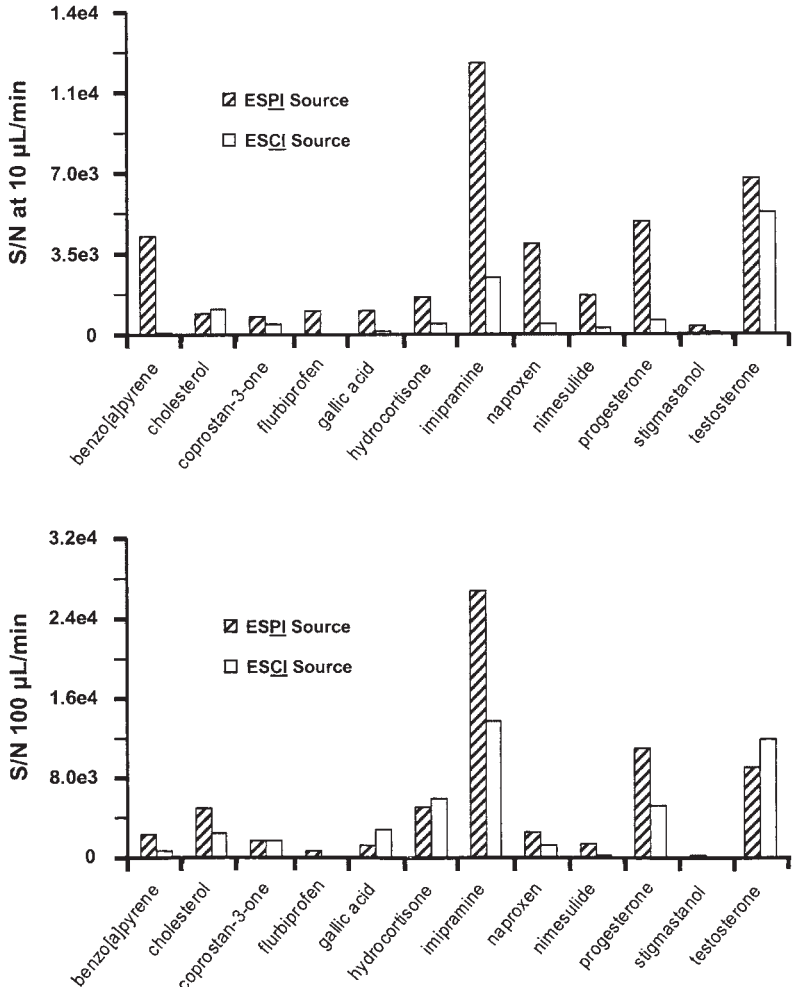
$[M+H]^+$ ion signal using the single APPI source (0″). When the total number of non-analyte, protonated species is compared to the $[M+H]^+$ signal, we see an inverse relationship, indicating an increase in potential to transfer H^+ to the analyte. This is similar to the reported dependence of $M^{\bullet+}$ and $[M+H]^+$ signal with a toluene dopant at increasing solvent flow rate reported by Kauppila *et al*.[28] In that case, the quantity of detected dopant (D^+) was observed to fall at higher flow rates, similar to our observations here with a decrease in overall proton-donating species (from dopant and solvent). Also reported by Kauppila *et al*. is that $M^{\bullet+}$ signal intensity first rises, then falls, and $[M+H]^+$ signal increases and reaches a plateau at higher flow rates – we see a similar effect with constant flow and increased spray inlet-lamp distance with both the APPI and ESPI sources (Fig. 3, left column) and also with an increase in flow rate in Fig. 1 (right).

In the bottom left graph in Fig. 3, the ESI signal for the ESPI source is measured with increasing distances, and we find that at a distance of ¼″ there is an enhancement of signal, but with ½″ the signal is significantly reduced. The measured quantity of protonating solvent and dopant species using the ESI mode drops with each stage addition, as is observed when the APPI mode is used. From these observations we find that a distance of ¼″ is the best compromise for sensitive detection by both ESI and APPI.

Comparison of ESPI vs. ESCI under low-flow conditions

The capabilities of the ESPI dual source were compared with the ESCI dual source at low flow rates of 10 and 100 μL/min for 12 test compounds. The samples were introduced as 2 μL injections of 0.1 mM in methanol (10 μL/min, 500°C heater temperature). Normal operating conditions are PI (with 5% toluene dopant) and CI without dopant; however, addition of a dopant to CI resulted in improved signal performance. In all cases, the best precursor ion was selected for comparison (either $M^{\bullet+}$ or $[M+H]^+$), except for gallic acid $[M-H]^-$ (measured in negative ion mode) and cholesterol $[M-17]^+$ (the standard measured ion for cholesterol analysis).

As seen in Fig. 4, the signal-to-noise (S/N) with the ESPI source is often an improvement over that of ESCI for these test compounds. When the ratio of APPI/APCI is compared for all compounds using the two dual sources, we see that the ESPI source is relatively best at 10 μL/min. The improved sensitivity of the ESPI dual source is a result of the shared optimum geometry of the ESI and APPI sources (so that one source or the other is not compromised), unlike the different



[ESPI] / [ESCI]

Compound	(normal)	(CI doped)
benzo[a]pyrene	87	37
cholesterol	0.8	1.3
coprostan-3-one	1.6	1.0
flurbiprofen	110	46
gallic acid	4.4	1.5
hydrocortisone	3.4	3.2
imipramine	4.8	2.8
naproxen	8.3	5.7
nimesulide	6.6	3.0
progesterone	8.3	7.7
stigmastanol	6.6	6.7
testosterone	1.3	0.9

[ESPI] / [ESCI]

Compound	(normal)	(CI doped)
benzo[a]pyrene	10	4.6
cholesterol	2.1	1.5
coprostan-3-one	1.0	1.3
flurbiprofen	69	62
gallic acid	0.4	0.3
hydrocortisone	0.8	0.6
imipramine	1.9	1.7
naproxen	2.1	2.1
nimesulide	12.0	1.3
progesterone	2.1	2.3
stigmastanol	3.4	2.5
testosterone	0.8	0.6

Figure 4. Analysis of 0.1 mM drugs in methanol with either an ESPI source (with ¼″ stage addition) in APPI mode (filled rectangles) or an ESCI source in APCI mode (open rectangles). Insert is table of ratios for ESPI/ESCI with (left column) normal operating conditions and (right column) dopant is used for both sources.

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optimum geometries of the ESI and APCI sources. Also, the generation of ions for most of the analytes is via soft photoionization with APPI, which results in less fragmentation and thus greater precursor ion detection. This is supported by the enhanced detection of the relatively unstable drug flurbiprofen using the APPI mode, which has a fluorine atom that can easily be removed under harsh ionization conditions. In this case, the APPI signal of the primary cation is at least an order of magnitude greater than the APCI signal using the ESCI source.

APCI performance is best at higher flow rates, since the primary source of charge species is the solvent itself, and thus a greater flow will directly enhance (1) the quantity of charged species within the source and (2) the resulting quantity of charges or proton transfers to the analyte, enhancing analyte detection. Under lower flow conditions, fewer charge carriers are generated. With APPI, the analyte species can be directly photoionized, permitting efficient ion generation even at lower flow rates.

Interestingly, while a dopant is not considered standard for APCI, we have found here that addition of a dopant enhances analyte detection under low-flow conditions. Presumably, the dopant provides additional charge carriers to the source, partially making up for the lack of charged solvent species at low solvent flow rates for APCI. Considering the typical operating conditions of ESPI (PI mode, with dopant) and ESCI (CI mode, no dopant) in Fig. 4 (table insert), we see that the addition of a dopant to ESCI often doubles the S/N under low-flow conditions. However, ESPI still has the advantage for most tested compounds here under these low-flow conditions.

CONCLUSIONS

Some parameters of ESPI are explored here, including temperature of spray inlet, flow of solvent and relative distance of inlet to the lamp. Ideal conditions for direct photoionization (resulting in mostly $M^{\bullet+}$) are found when the inlet spray is 'dryer', while a spray containing solvent clusters favors indirect photo-induced chemical ionization, generating mostly $[M+H]^+$. The particular emphasis of this paper is on the comparative performance of a prototype ESPI dual source to the ESCI dual source at low solvent flow rates. Under these conditions, ESPI has better performance for most compounds, with the advantage being most pronounced at the lowest flow tested, 10 μL/min. The use of a dopant and APPI repeller electrode was found to have mostly little effect on the ESI signal. In addition to advantages of reduced ion suppression with APPI and 'soft' photoionization leading to lower fragmentation, the combination of ESI and APPI appears to offer the greatest performance at low solvent flow rates.

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REFERENCES

1. Syage JA, Evans MD, Hanold KA. *Am. Lab.* 2000; **32**: 24.
2. Robb D, Covey T, Bruins A. *Anal. Chem.* 2000; **72**: 3653.
3. Constapel M, Schellenträger M, Schmitz O, Gäb S, Brockmann K, Giese R, Benter T. *Rapid Commun. Mass Spectrom.* 2005; **19**: 326.
4. Short LC, Cai S-S, Syage JA. *J. Am. Soc. Mass Spectrom.* 2007; **18**: 589.
5. Cai S-S, Syage JA. *J. Chromatogr. A* 2006; **1110**: 15.
6. Cai S-S, Syage JA. *Anal. Chem.* 2006; **78**: 1191.
7. Trösken ER, Straube E, Lutz WK, Völkel W, Patten C. *J. Am. Soc. Mass Spectrom.* 2004; **15**: 1216.
8. Hanold KA, Fischer SM, Cormia P, Miller CE, Syage JA. *Anal. Chem.* 2004; **76**: 2842.
9. Delobel A, Halgand F, Laffranchise-Gosse B, Snijders H, Laprevote O. *Anal. Chem.* 2003; **75**(21): 5961.
10. Takino M, Daishima S, Nakahara T. *J. Chromatogr. A* 2003; **1011**: 67.
11. Yoshioka N, Akiyama Y, Teranishi K. *J. Chromatogr. A* 2004; **1022**: 145.
12. Hakala K, Laitinen L, Kaukonen A, Hirvonen J, Kostianen R, Kotiaho T. *Anal. Chem.* 2003; **75**: 5969.
13. Greig M, Bolaños B, Quenzer T, Bylund J. *Rapid Commun. Mass Spectrom.* 2003; **17**: 2763.
14. Lembcke J, Ceglarek U, Fiedler G, Baumann S, Leichtle A, Thiery J. *J. Lipid Res.* 2005; **46**: 21.
15. van Leeuwen S, Hendriksen L, Karst U. *J. Chromatogr. A* 2004; **1058**: 107.
16. Takino M, Daishima S, Nakahara T. *Rapid Commun. Mass Spectrom.* 2003; **17**: 1965.
17. Syage JA. *J. Am. Soc. Mass Spectrom.* 2004; **15**: 1521.
18. Gallagher RT, Balogh MP, Davey P, Jackson MR, Sinclair I, Southern LJ. *Anal. Chem.* 2003; **75**: 973.
19. Droste S, Schellenträger M, Constapel M, Gäb S, Lorenz M, Brockmann KJ, Benter T, Lubda D, Schmitz OJ. *Electrophoresis* 2005; **26**: 4098.
20. Syage JA, Hanold KA, Lynn TC, Horner JA, Thakur RA. *J. Chromatagr. A* 2004; **1050**: 137.
21. Giuliani A, Debois D, Laprevote O. *Eur. J. Mass Spectrom.* 2006; **12**: 189.
22. Robb DB, Blades MW. *J. Am. Soc. Mass Spectrom.* 2006; **17**: 130.
23. Rohwer ER, Beavis RC, Koster C, Lindner J, Grotemeyer J, Schlag EW. *Z. Naturforsch. A* 1988; **43**: 1151.
24. *Handbook of Chemistry and Physics*, vol. 83. CRC Press: New York, 2002.
25. Tsai ST, Jiang JC, Lee YT, Kung AH, Lin SH, Ni CK. *J. Chem. Phys.* 1999; **111**: 3434.
26. Appel MF, Short LC, Benter T. *J. Am. Soc. Mass Spectrom.* 2004; **12**: 1885.
27. Short LC, Frey R, Benter T. *Appl. Spectrosc.* 2006; **60**: 208.
28. Kauppila T, Bruins AP, Kostiainen R. *J. Am. Soc. Mass Spectrom.* 2005; **16**: 1399.

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