Agilent Jet Stream Thermal Gradient Focusing Technology

Electrospray ionization mass spectrometry (ESI-MS) is a sensitive technique that is used extensively for the analysis and identification of small molecules and proteins. Proprietary Agilent Jet Stream thermal gradient focusing technology optimizes ESI conditions to produce dramatic gains in sensitivity, decreasing sample size requirements, increasing sample throughput, improving assay robustness and reducing the LODs and LOQs of screening and quantitation applications.

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Agilent Jet Stream technology enhances ESI-MS sensitivity

Agilent Jet Stream thermal gradient focusing technology was developed to significantly enhance sensitivity in ESI-MS by improving the desolvation and spatial focusing of ions. Super-heated nitrogen sheath gas confines the nebulizer spray to more effectively dry ions and concentrate them in a thermal confinement zone **(Figures 1-3)**.

Desolvation reduces noise. Full confinement of the spray by the super-heated nitrogen gas eliminates sample recirculation and reduces peak tailing.

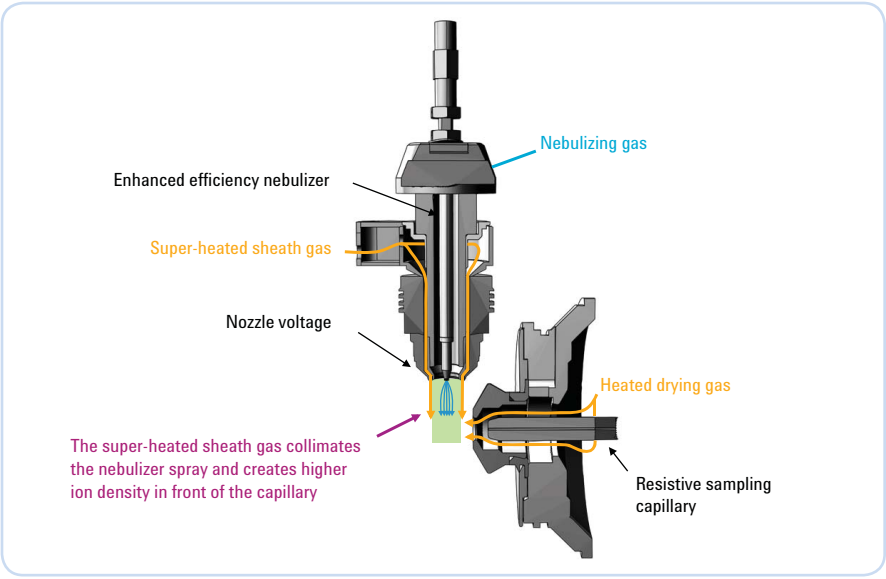


Figure 1. Agilent Jet Stream technology utilizes super-heated nitrogen to desolvate the spray and confine the electrospray plume making more ions accessible to sampling by the mass spectrometer.

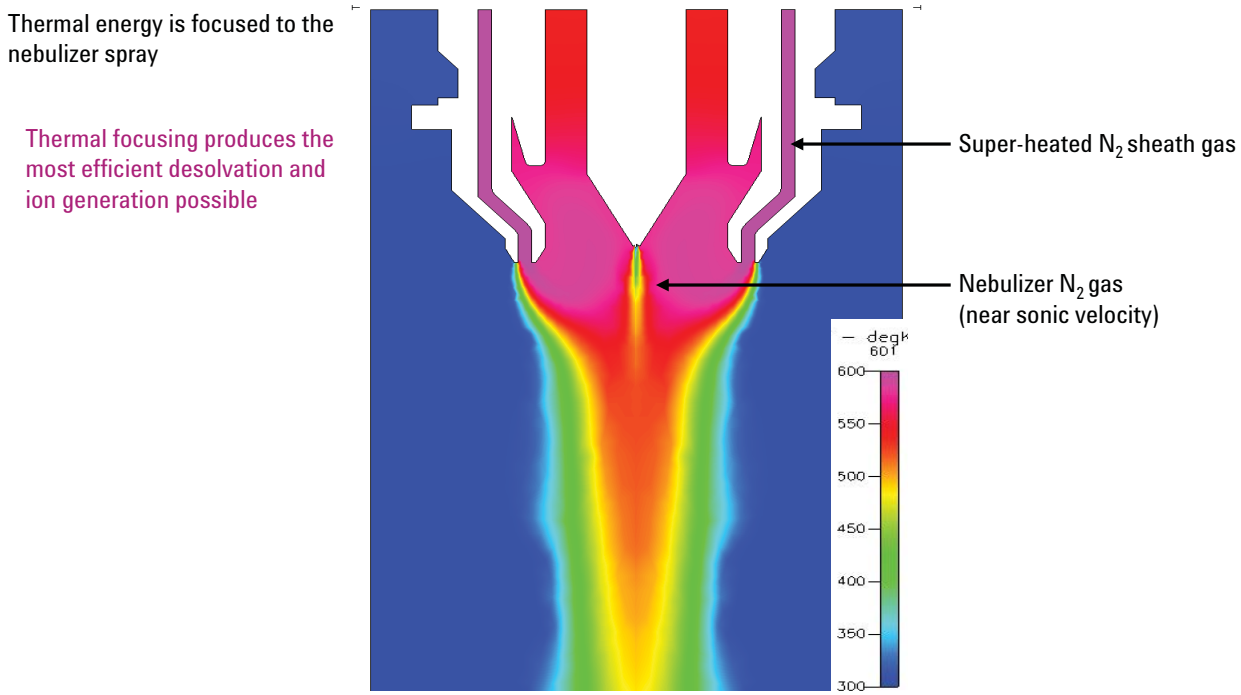


Figure 2. Simulation showing the thermal profile of the Agilent Jet Stream technology. Note the creation of a thermal confinement zone by introduction of a super-heated N_2 sheath gas.

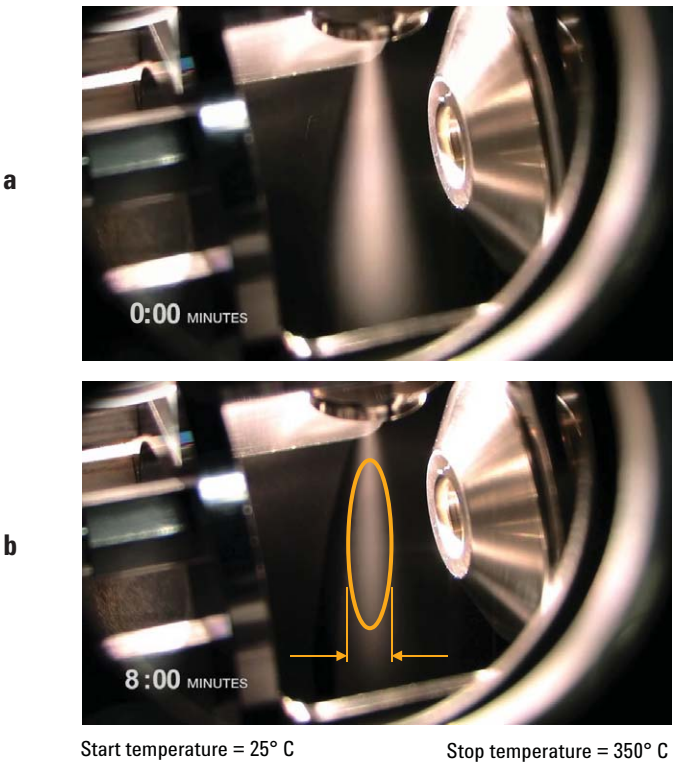


Figure 3. Time lapse images of an electrospray generated using Agilent Jet Stream technology at **(a)** 25° C and **(b)** 350° C. Less light scattering is observed in the spray at 350° C, indicating enhanced desolvation.

Improved ion production results in higher MS and MS/MS signal intensities and improved signal-to-noise ratios. On average, a 5 to 10-fold improvement in MS and MS/MS sensitivity is realized by using Agilent Jet Stream technology **(Figures 4a and 4b)**.

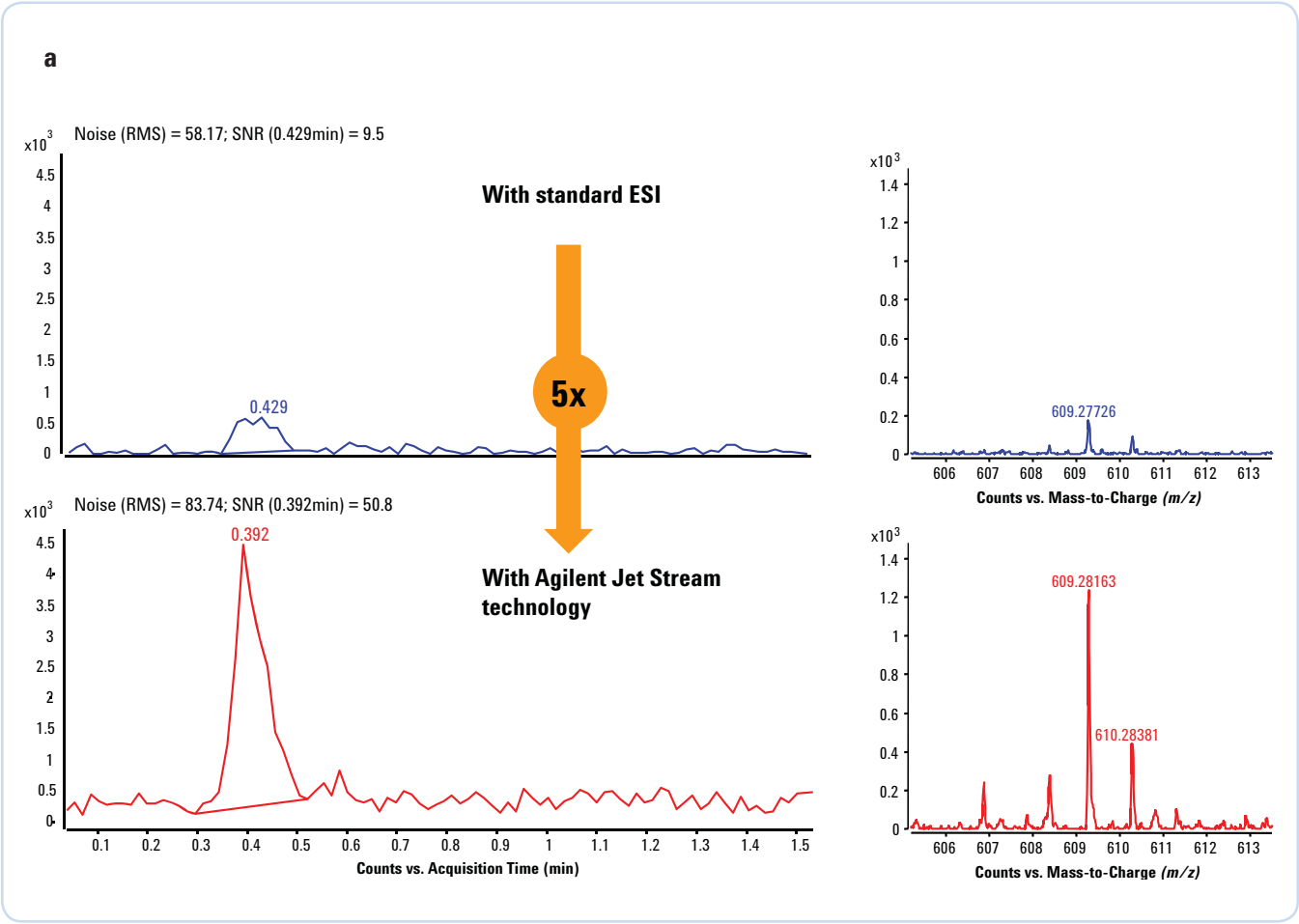


Figure 4a. Comparison of the MS spectra of a 1 pg sample of the drug reserpine obtained using conventional Agilent ESI source and Agilent Jet Stream technology on an Agilent 6530 Accurate-Mass Q-TOF LC/MS system. A 5-fold gain in signal intensity is observed with Agilent Jet Stream technology. LC conditions: Agilent 1200 LC system. Column: 2.1 x 30 mm Zorbax SB-C18, 3.5 µm; flow rate: 0.4 mL/min of 75:25 methanol/water containing 0.1% (v/v) formic acid and 5 mM ammonium formate. Agilent Jet Stream technology conditions: sheath gas temperature: 350° C; sheath gas flow: 12 L/min.

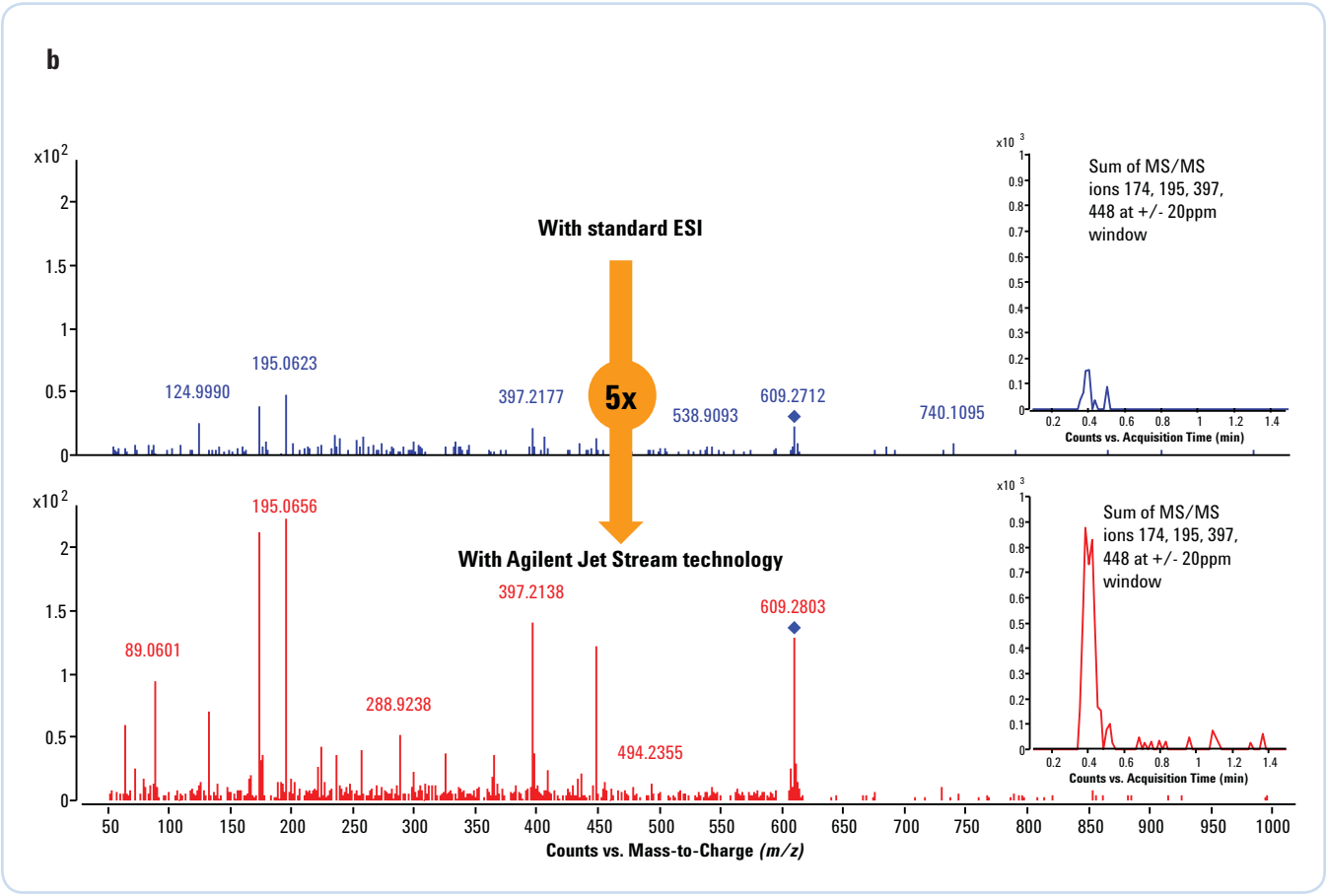


Figure 4b. Comparison of the MS/MS spectra of a 1 pg sample of the drug reserpine obtained using conventional Agilent ESI source and Agilent Jet Stream technology on an Agilent 6530 Q-TOF LC/MS system. A 5-fold gain in signal intensity is observed with Agilent Jet Stream technology. Conditions: same as for figure 4a.

The Agilent Jet Stream technology provides exceptional ESI-MS sensitivity over a wide range of flow rates. Sensitivity gains of 5-10x were seen over flow rates ranging from 50 µL/min to 2.5 mL/min, with the greatest gains typically seen at flow rates from 0.25-1.0 mL/min. Importantly, recommended operating parameters were consistent across a wide range of flow rates, reducing the need for optimization at different flow rates. The following conditions resulted in optimal results over flow rates ranging from 0.25 to 2.0 mL/min (typical flowrates for 2.1 mm ID HPLC columns):

Sheath Gas Flow:	11 mL/min
Sheath Gas Temperature:	350° C
Nozzle Voltage:	600 V
Nebulizer Pressure:	30 psi
Chamber Voltage:	4 kV

(The recommended default operating parameters for the Agilent Jet Stream technology are relatively invariant with HPLC flow rate but should be optimized for best analyte response).

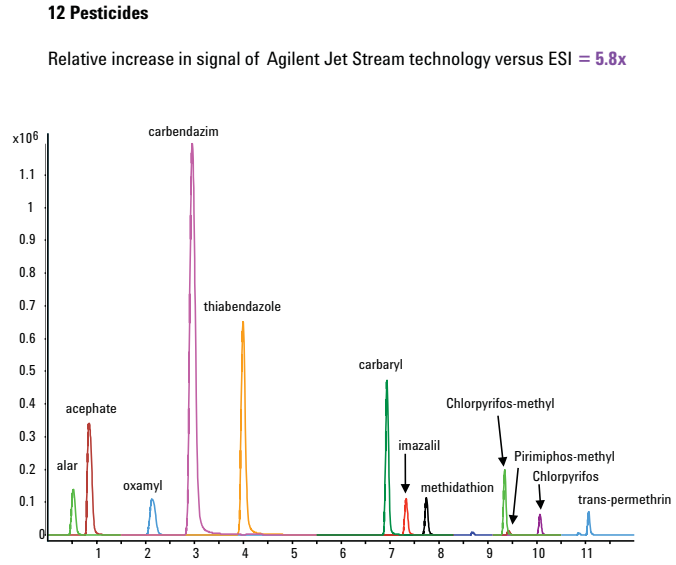
Applications

Trace Analysis of Pesticides

Sensitive and reliable analytical methods for the routine monitoring of pesticide residues are required in food safety and environmental applications. Agilent Jet Stream technology enables highly sensitive analysis of pesticides as shown in **Figure 5**. Compared to conventional ESI, an almost 6-fold improvement in sensitivity was realized.

Drug Analysis in Biological Matrices

LC-MS and LC-MS/MS detection are routinely used for the analysis of drugs in biological fluids. Agilent Jet Stream technology based LC/MS analyses of four therapeutic drugs in pure solvent and in blood plasma are presented in **Figure 6**. MS analysis in biological media is often adversely affected by ion suppression, but in this particular application no such matrix effects are observed with the Agilent Jet Stream technology.



Pesticide	Optimal Temp [°C]	Signal Gain
Alar	380	5.60
Acephate	380	6.30
Oxamyl	250	5.10
Carbendazim	380	7.20
Thiabendazole	380	7.20
Carbaryl	380	6.60
Imazalil	380	8.10
Methidathion	250	5.00
Chlorpyrifos-methyl	100	6.40
Pirimiphos-methyl	380	5.50
Chlorpyrifos	380	4.00
Trans-permethrin	250	2.50
Average		**5.8x**

Figure 5. LC/MS analysis of a mixture of pesticide standards in methanol/water using Agilent Jet Stream technology on an Agilent 6460 triple quadrupole LC/MS system. The table shows the relative gain in ion signal intensities using Agilent Jet Stream technology compared to conventional ESI.

LC Conditions: Agilent 1200 LC system. Column: 2.1 x 100 mm Eclipse Plus C18, 1.8 µm; flow rate: 0.4 mL/min; gradient: water: methanol containing 0.1% formic acid and 10 mM ammonium formate. Agilent Jet Stream technology conditions: sheath gas temperature: programmed for best analyte response between 100-380° C; sheath gas flow: 10 L/min.

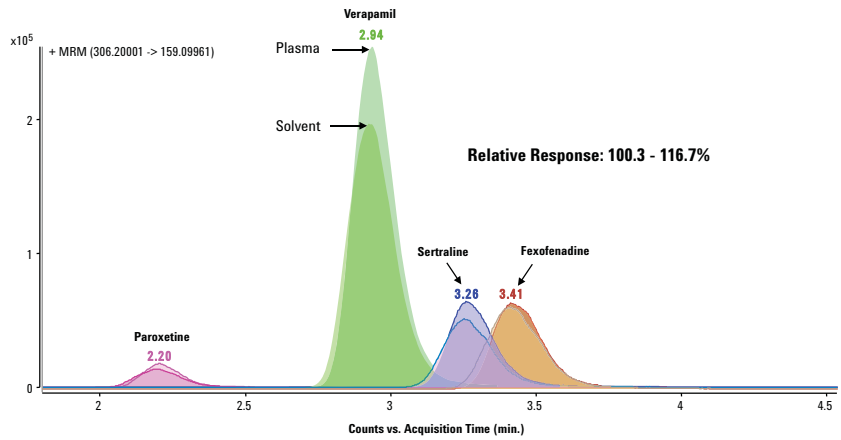


Figure 6. LC-MS analysis of four therapeutic drugs in pure solvent and in plasma on an Agilent 6460 triple quadrupole LC/MS system. LC Conditions: Agilent 1200 LC system. Column: 2.1 x 12 mm C8 guard column (5 µm) in-line with 2.1 x 100 mm C18 (3.5 µm) analytical column; gradient: acetonitrile: water (90:10 v/v).

Human Health Care Products in Drinking Water

Significant sensitivity enhancements were observed for the analysis of four pharmaceutical compounds in drinking water samples **(Figure 7)**.

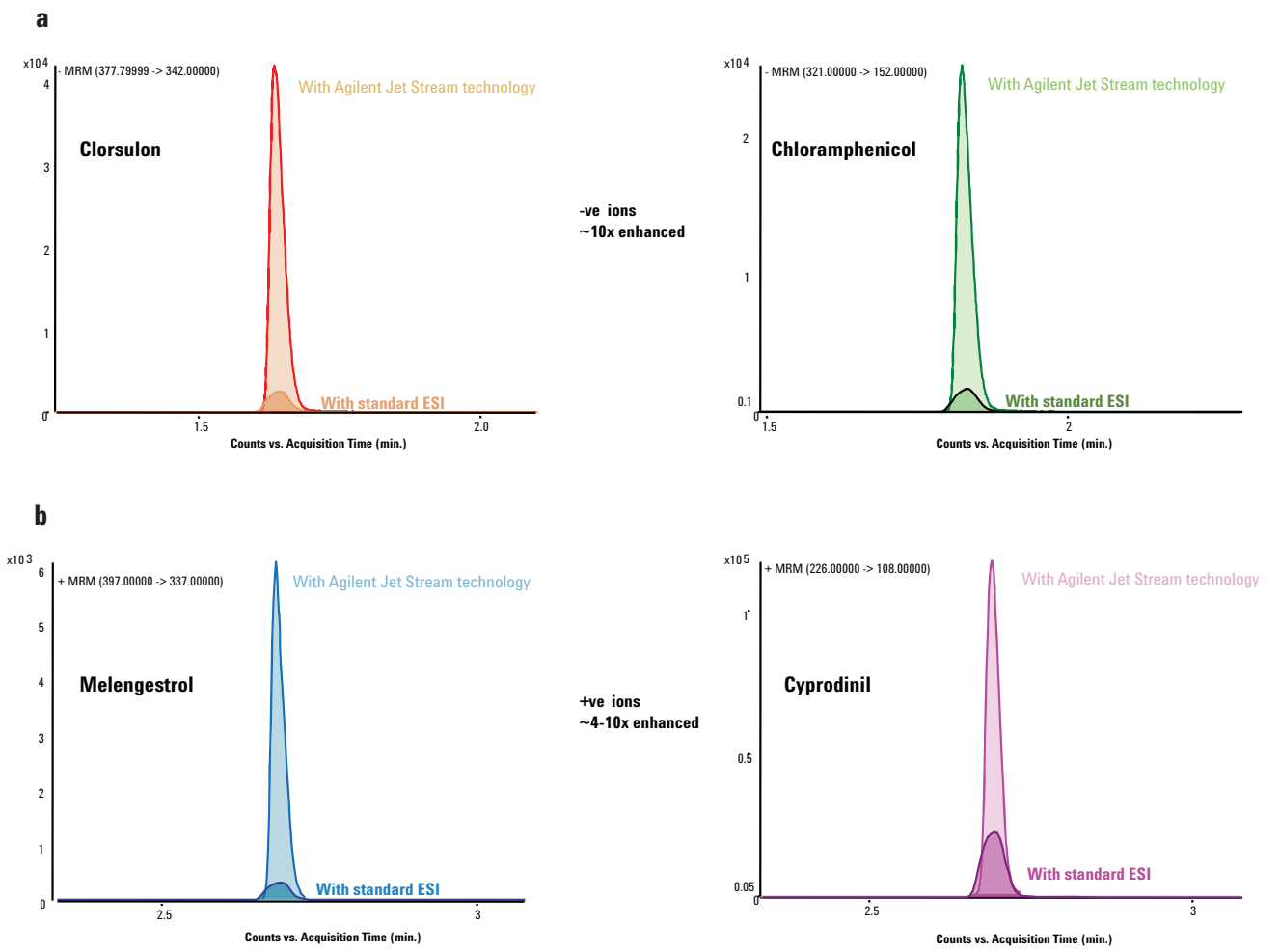


Figure 7. Pharmaceuticals spiked into potable water analyzed in **(a)** negative ion mode and **(b)** positive ion mode. Compared to conventional ESI (lower traces in each of the four graphs), Agilent Jet Stream technology enabled sensitivity improvements of approximately 10-fold in negative ion mode and between 4-to-10-fold in positive ion mode. Injected volume was 5 µL of a 50 ppb solution. LC Conditions: Agilent 1200 LC system. Column: 2.1 x 50 mm Zorbax Eclipse Plus C-18, flow rate: 0.5 mL/min, gradient: A=water, B= methanol, 5% B to 90% B. Agilent Jet Stream technology conditions: sheath gas temperature: 380° C, sheath flow: 11 L/min.

Illicit Drugs in Urine

Agilent Jet Stream technology was used for LC/MS detection and quantitation of the illicit drug MDMA in urine **(Figure 8)**. Significant sensitivity gains were seen with the use of Agilent Jet Stream technology versus standard ESI.

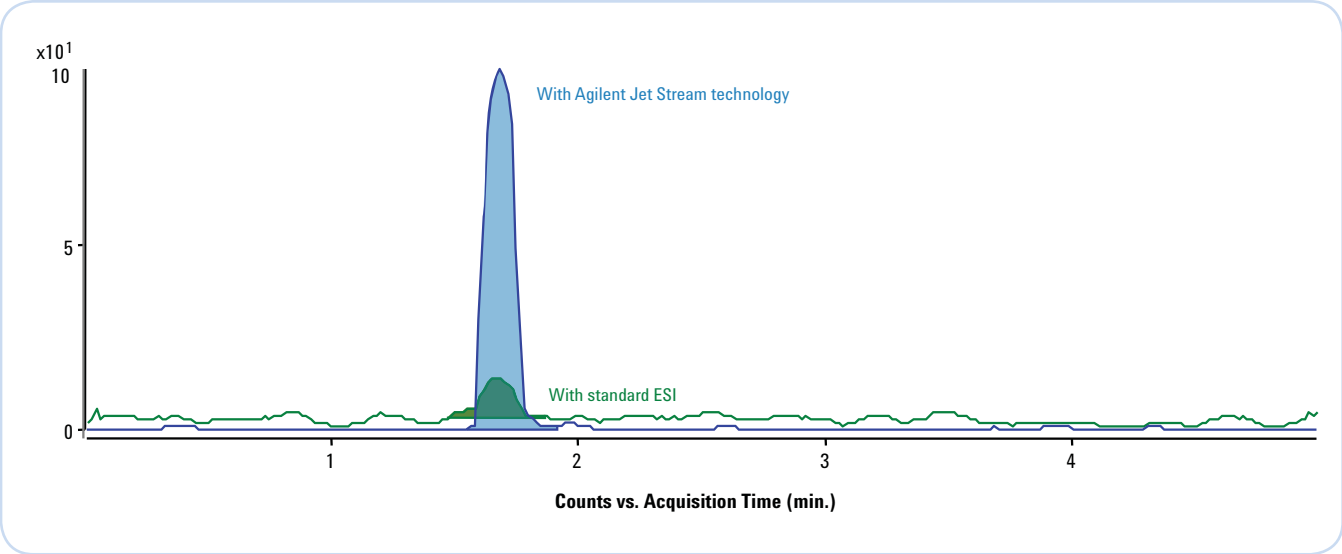


Figure 8. Analysis of MDMA spiked into urine (50 fg on-column) by standard ESI (green trace) and Agilent Jet Stream technology (blue trace) on an Agilent 6460 Triple Quad LC/MS system. LC Conditions: Agilent 1200 LC system. Column: Zorbax Eclipse Plus C-18 (2.1 x 50 mm, 1.8 µm), flow rate: 0.5 mL/min, gradient: A=water with 0.1% formic acid, B= acetonitrile with 0.1% formic acid, 5% B to 100% B.

Conclusions

Agilent Jet Stream thermal gradient focusing technology enables a 5-10 fold sensitivity improvement over ESI at conventional flow rates (50 µL/min-2.5 mL/min). Dramatically improved ion desolvation and confinement of the spray by a thermal gradient yield improved ion generation and sampling efficiencies for significantly increased signal and reduced noise. Agilent Jet Stream technology is suited for today's most demanding applications—it provides maximum sensitivity for the analysis of pharmaceutical compounds to support drug development applications and trace-level pesticide and chemical analysis to assure environmental quality and food safety.

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