Agilent 6490 Triple Quadrupole LC/MS System with iFunnel Technology

Ultra sensitive quantitative performance

The Measure of Confidence

Agilent Technologies

Unmatched quantitative performance for the most challenging analyses

The Agilent 6490 Triple Quadrupole LC/MS System incorporates iFunnel technology to give new levels of sensitivity for the most challenging quantitative analyses in pharmaceutical, clinical, food safety, and environmental applications. The quantitative power of the 6490 Triple Quadrupole is enhanced by an extended linear dynamic range.

The 6490 Triple Quadrupole LC/MS delivers:

- 10 X increase in sensitivity
- Up to six orders of linear dynamic range
- Robust performance and operation
- Zeptomole sensitivity for the most challenging applications

The 6490 triple quadrupole has a compact benchtop design, achieved through use of a curved collision cell. The newly designed cell also helps to reduce background noise, improving overall system signal-to-noise. New high frequency quadrupole electronics enable faster scan rates and allow for narrow mass window isolation.

The new 6490 Triple Quadrupole LC/MS System with iFunnel technology – unmatched quantitative performance

The iFunnel system

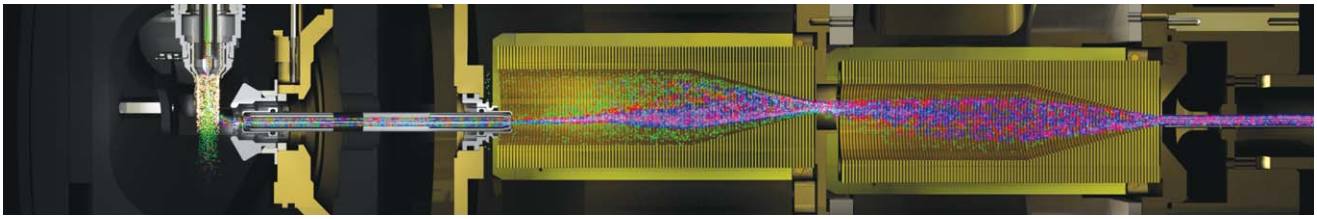

Figure 1. Agilent iFunnel technology components: Agilent Jet Stream, hexabore sampling capillary and dual stage ion-funnel.

Breakthrough iFunnel technology

The 6490 Triple Quadrupole LC/MS achieves its sensitivity from iFunnel technology, which is a combination of three fundamental innovations:

- Agilent Jet Stream technology: a precisely micro-machined sprayer surrounds ESI droplets with a sheath of super-heated gas to desolvate and concentrate ions near the MS inlet for more effective sampling
- Hexabore sampling capillary: 6 independent, parallel bores enable a much larger fraction of the ions formed in the ESI spray plume to enter the mass spectrometer ion optics
- Unique dual-stage ion funnel: efficient removal of large gas volumes and ion transfer to Q1 optics.

A schematic of this technology is shown in Figure 1.

The iFunnel technology with the hexabore capillary collects six-fold more ion laden gas than a single bore capillary and the shorter residence times of ions in the hexabore capillary lead to even higher gains in signal intensity. When comparing the 6490 Triple Quad to the 6460 Triple Quad (**Figure 2**), the 6490 Triple Quadrupole with iFunnel technology demonstrates a seven-fold gain in signal intensity for masses up to 900 *m/z* and a five-fold gain for higher masses.

Increases in signal intensity are even more pronounced for negative ions as shown in **Figure 3**. The average gain in signal intensity was 10-fold across the entire mass range of the 6490 Triple Quadrupole.

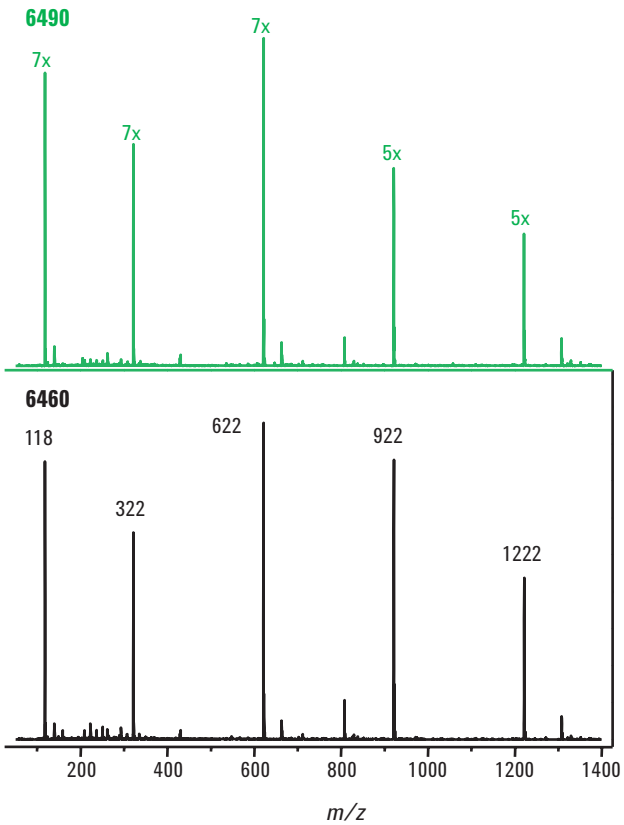

Figure 2. Signal intensities for calibration standards in positive ESI mode for the 6490 (top, green) and 6460 (bottom, black).

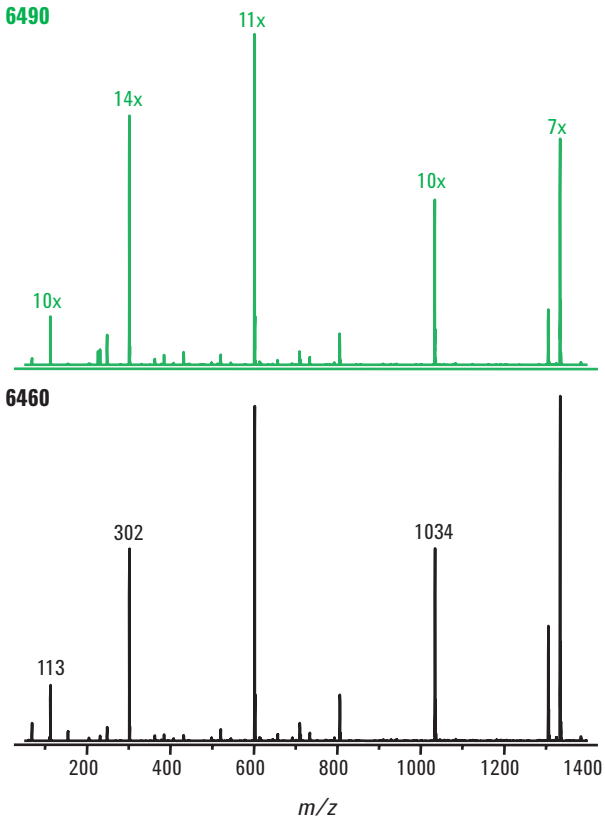

Figure 3. Ion intensities for negative calibration ions for the 6490 (top, green) and the 6460 (black, bottom).

Zeptomole sensitivity and unmatched linear dynamic range

The 6490 Triple Quadrupole with iFunnel technology delivers groundbreaking sensitivity. The first example of sub-attomole sensitivity is shown in **Figure 4** for an injection of 200 zeptomoles of verapamil on-column.

The 6490 Triple Quadrupole delivers new levels of sensitivity and also unmatched linear dynamic range. It is the first triple quadrupole LC/MS system to deliver six orders of linear dynamic range as illustrated in **Figure 5**. The excellent correlation factor (R^2 value = 0.997) underscores the wide range of linear response.

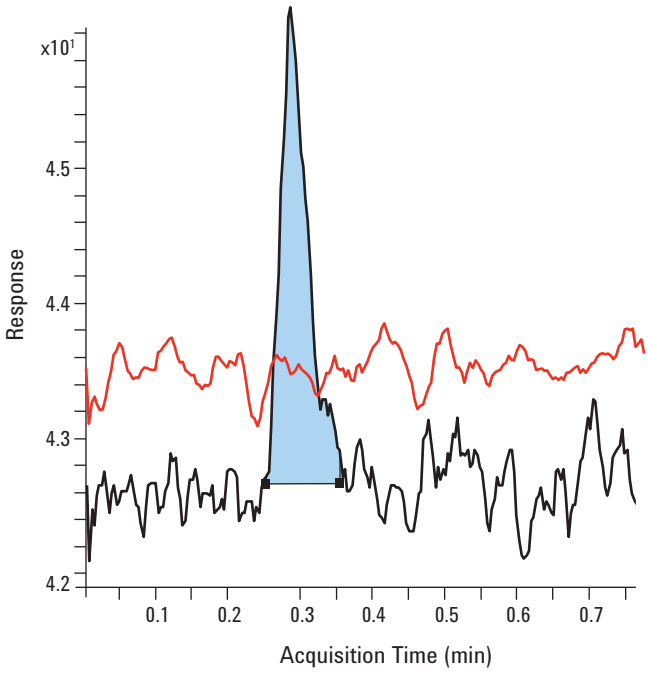

Figure 4. Verapamil ion chromatogram (MRM transition 455.3 → 164.9) for 100 attograms (200 zeptomoles) injected on-column using a 6490 Triple Quad SRM (blue). The red trace shows a blank injection.

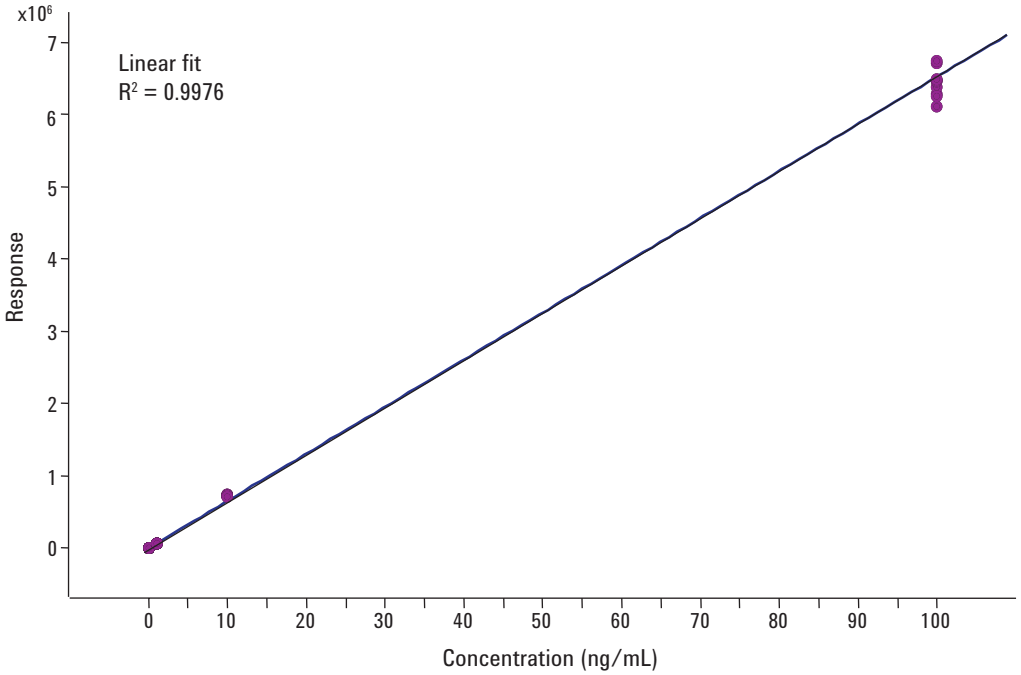

Figure 5. Linear response of verapamil from 100 attograms to 100 picograms injected on-column.

Significant performance enhancements for the determination of drugs in plasma

The quantitative performance of the 6490 Triple Quadrupole for the determination of drugs in plasma shows significant performance enhancements. **Figure 6** shows fluticasone, a synthetic steroid of the glucocorticoid family of drugs used for treating allergic conditions.

When used as a nasal inhaler or spray, the medication goes directly to the epithelial lining of the nose, and very little is absorbed into the rest of the body. Due to its low systemic levels, a high sensitivity LC/MS assay is required to determine fluticasone concentrations in human plasma.

Typically, solid phase extraction (SPE) and liquid-liquid extraction (LLE) procedures are used to concentrate the analyte and to eliminate matrix effects. The extreme sensitivity of the 6490 eliminates the need for SPE and LLE, and instead allows direct analysis of crashed plasma after a four-fold dilution with water. The dilute-and-shoot method using the 6490 instrument has more than adequate sensitivity for the lowest calibration level at 5 pg/mL as shown in Figure 6. This represents only 2.5 femtograms injected on-column, with a lower limit of detection of just 1 femtogram.

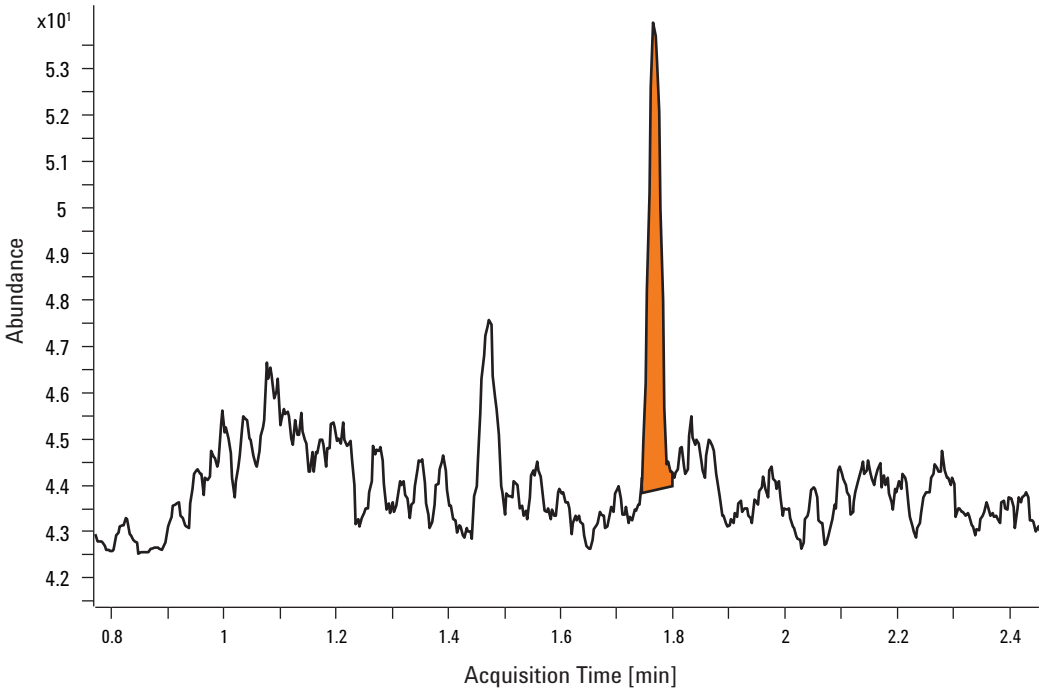

Figure 6. Fluticasone proprionate ion chromatogram (MRM transition 501.2 → 293.1) for 2.5 femtograms injected on-column using the 6490 instrument.

Outstanding assay robustness for samples in complex biological matrices

Sensitivity is important – robustness is critical. **Figure 7** shows the robustness of the 6490 for 3000 injections of verapamil (20 femtograms) in protein precipitated plasma for more than six days of continuous operation. The data shows a consistent peak response with a relative standard deviation for the peak area of less than 6%. Normally, peak area stability in plasma is shown for picogram quantities injected on-column, but this example is at levels that are more than one hundred times lower.

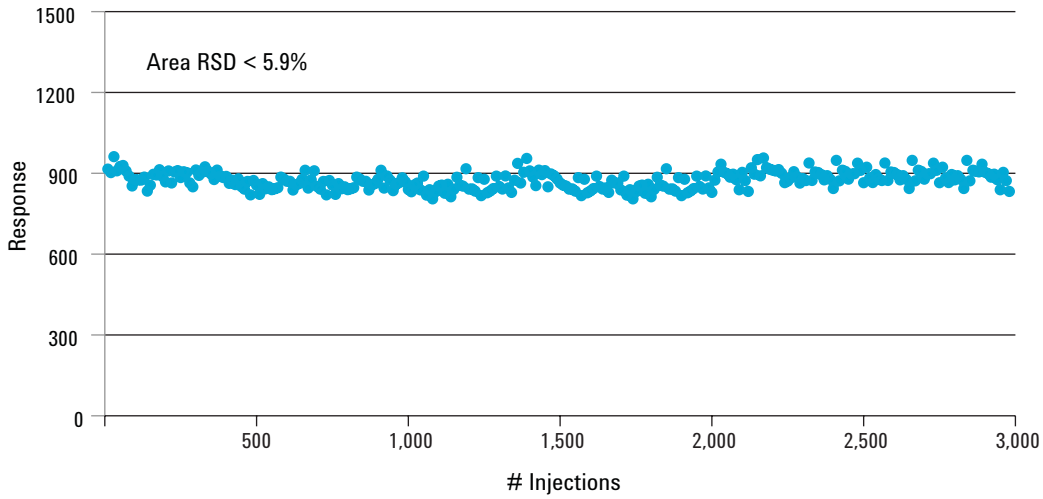

Figure 7. The 6490 Triple Quadrupole peak response for 3000 consecutive injections of verapamil in plasma (20 femtograms injected on-column).

Superb peptide quantitation with iFunnel technology

The quantitation of peptides also benefits from the impact of iFunnel technology. For example, a nine residue peptide (IEDIVTSEK) shows excellent linearity in **Figure 8** for the lowest level standard. The amount injected on a standard 2 mm i.d.-column in Figure 8 was only 28 attomoles. The strong signal intensity and low noise enabled a remarkable detection limit of approximately 1 attomole on a standard 2 mm column. The response was linear over the calibration range in the study from 28 to 2,830 attomoles and the correlation coefficient of 0.997 confirmed the good linear fit.

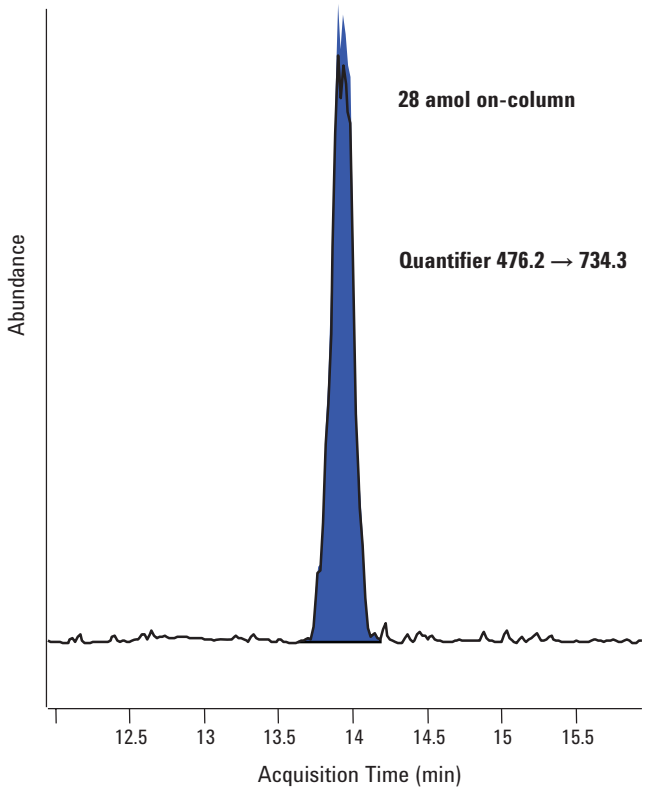

Figure 8. Extracted ion chromatogram using the transition from 476.2 to 734.3 m/z for 28 attomoles of peptide injected on-column with a conventional LC/MS system at 400 µL/min.

Standard columns offer greater throughput and method precision compared to nanoLC systems. Conventional LC methods are preferred when thousands of plasma samples must be analyzed in rigorous biomarker validation studies. For ultra-sensitive results from limited samples, the HPLC-Chip/MS with 6490 Triple Quad offers a robust alternative to nanoflow LC/MS for peptide quantitation.

The new 6490 Triple Quadrupole mass spectrometer with iFunnel technology redefines sensitivity, robustness and dynamic range for the most challenging quantitative applications. Increased ion sampling efficiency is achieved with the combination of the Agilent Jet Stream, hexabore sampling capillary and dual stage ion funnel.

For more information

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Published in USA, August 30, 2010
5990-6301EN

Agilent Technologies