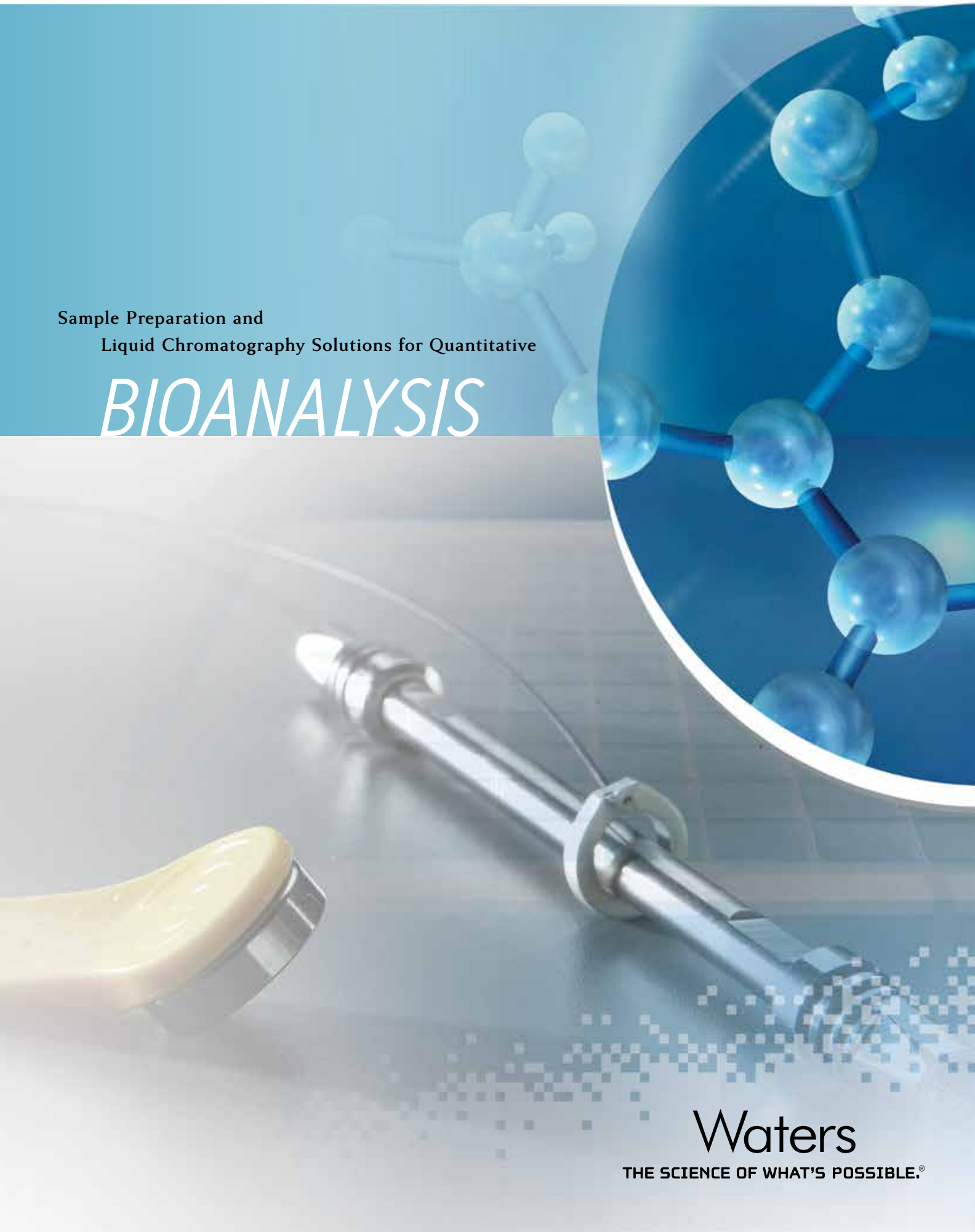


Sample Preparation and
Liquid Chromatography Solutions for Quantitative

BIOANALYSIS

Waters

THE SCIENCE OF WHAT'S POSSIBLE.®

Waters solutions for bioanalysis, which include sample preparation products, columns, analytical standards and reagents, LC systems, mass spectrometers, and software, offer the most sensitive, robust, and reproducible results. Whether you are working in the area of discovery or development, non-regulated or regulated environments, Waters system solutions comprehensively meet the converging needs of scientists, analysts, laboratory managers, and quality assurance (QA) and informational technology (IT) professionals.

For the ultimate in bioanalytical data quality, laboratory productivity, and compliance, Waters chemistries and consumables provide a comprehensive starting point for your workflow.

Sirocco™ Protein Precipitation Plate

Ostro™ SAMPLE PREPARATION PRODUCTS

OASIS® SAMPLE EXTRACTION PRODUCTS

DISCOVERY
[LEAD OPTIMIZATION]

- Many compounds
- Acceptable sensitivity
- Clean extracts
- Generic methods
- Non-regulated

EARLY STAGE DEVELOPMENT
[PRE-CLINICAL]

- Few compounds
- Increased sensitivity
- Maximum recovery
- Method development
- Regulated

LATE STAGE DEVELOPMENT
[CLINICAL]

- Targeted compounds
- High sensitivity
- Reproducibility
- Reliability
- Regulated

INCREASING SAMPLE PREPARATION CHALLENGES

XBridge® COLUMNS

XSELECT® Columns

Acquity UPLC®

CORTECS™ COLUMNS

Key Benefits:

- Unique design eliminates time-consuming steps for increased throughput
- Precipitate-free filtrate for maximum system uptime vs. classical methods
- Ideally suited for cleanliness, MS compatibility, and analyte recovery

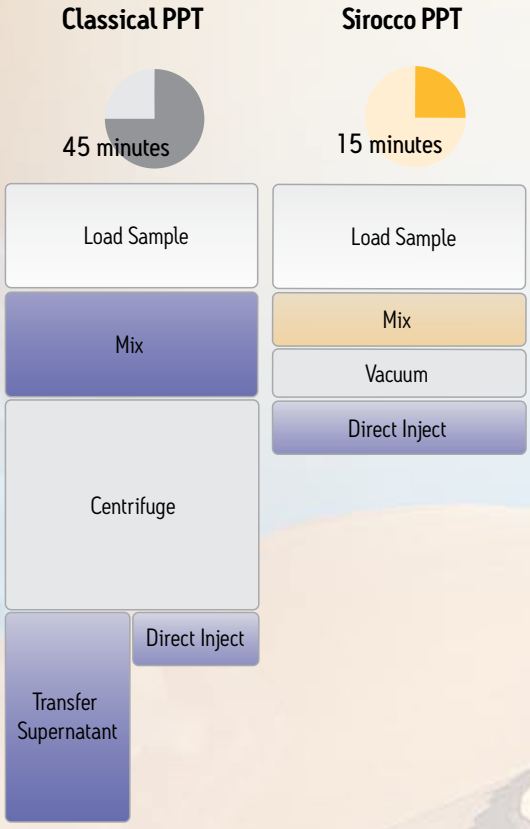
Sirocco™
Protein Precipitation Plate

SIMPLY CLEAR

The Sirocco™ Protein Precipitation (PPT) Plate eliminates additional, time-consuming sample-handling steps traditionally done with classical PPT. Unique membrane and valve-tip technology enable the analyst to carry out in-well protein precipitation followed by the final filtration step. This approach leads to efficient sample processing, resulting in clear filtrates from small sample volumes. Sirocco Plates can be automated to process large numbers of samples efficiently.

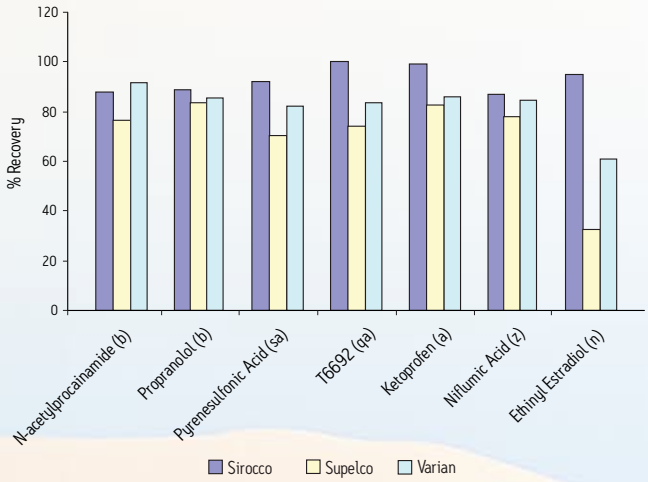
PROCESSING TIME COMPARISON

With Sirocco Plates, samples can be processed in significantly less time than with classical PPT, thus increasing laboratory throughput.



RECOVERY

The Sirocco Plate was tested for analyte recovery using seven different analytes spiked into rat plasma. The results show excellent recoveries across all analytes listed including bases (b), strong acid (sa), acids (a), neutrals (n) and quarternary amine (qa).

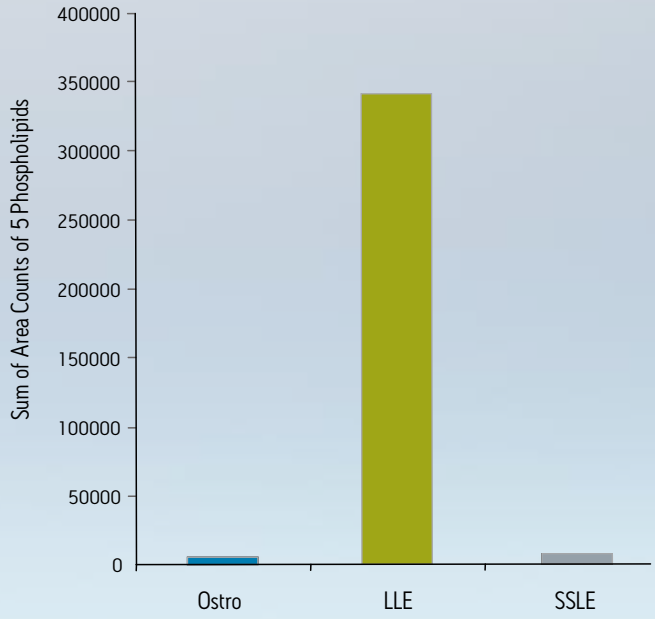


THE FASTER WAY TO CLEANER

Ostro™ Sample Preparation Products provide a novel solution for the cleanup of phospholipids in plasma and serum. Requiring minimal to no method development and using a simple protocol, this technology can be quickly implemented to optimize your laboratory's workflow. Providing cleaner, more reproducible extracts than competitive phospholipid removal devices or techniques, the Ostro 96-well Plate allows for more sensitive analyses, increased sample throughput, and reduced instrument downtime.

PHOSPHOLIPID REMOVAL

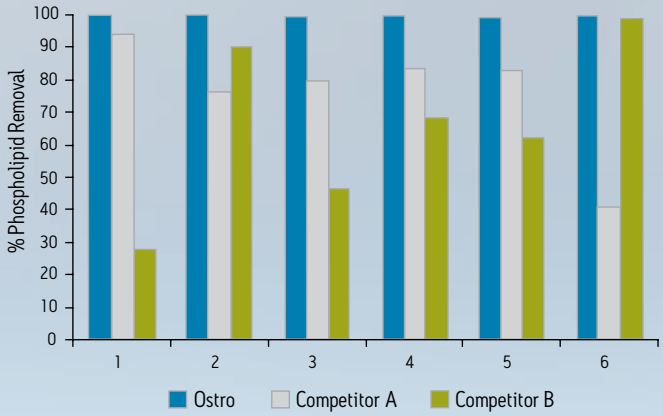
The level of 5 phospholipids remaining after sample preparation using the Ostro Plate is less than with both liquid-liquid extraction (LLE) and solid-supported liquid extraction (SSLE).



Sum of 5 abundant phosphatidylcholine containing phospholipids with m/z 496, 524, 704, 758, and 806.

REPRODUCIBILITY

Comparative % removal of total phospholipids from 6 different lots of plasma using the Ostro Plate (0.19% RSD), phospholipid removal plate from competitor A (24.5% RSD), and phospholipid removal plate from competitor B (40.9% RSD).



Key Benefits:

- Removes significantly more phospholipids than competitive products or techniques for cleaner extracts
- Improves reproducibility for more consistent, robust methods
- Increases throughput with easy-to-implement protocol

OSTro™
SAMPLE PREPARATION PRODUCTS

Key Benefits:

- Highest sensitivity for traditional pharmaceutical compounds and therapeutic peptides
- Minimal matrix effects for LC/MS/MS analyses
- Unmatched product quality, performance, and reproducibility

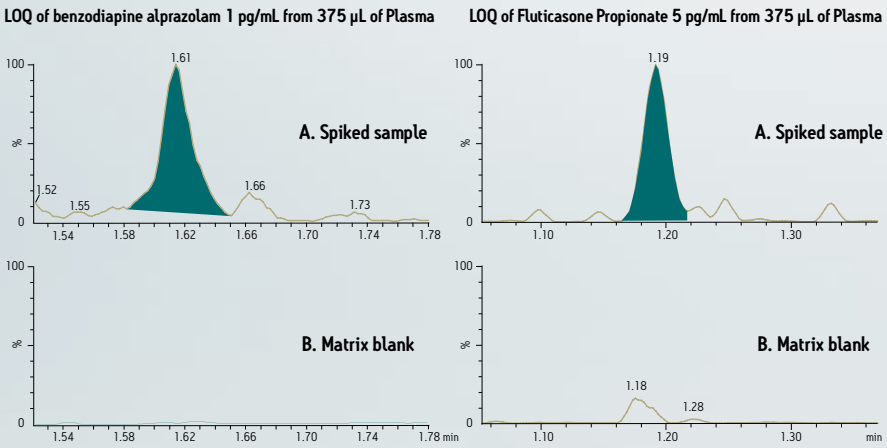
OASIS®
SAMPLE EXTRACTION PRODUCTS

SENSITIVITY IN ITS PUREST FORM

Sensitivity is one of the key requirements for a successful bioanalytical assay. Achieving optimum sensitivity requires the isolation of compounds of interest from interferences present in biological samples. The patented Oasis® Solid-Phase Extraction (SPE) Products are available in a wide array of formats and sorbents, allowing scientists to develop methodologies that are selective for the compounds of interest. Oasis Products enable scientists to create highly accurate and reproducible SPE methods that are unsurpassed in sensitivity and selectivity.

SENSITIVITY

The Oasis mixed-mode sorbents, all built upon the unique water-wettable Oasis HLB copolymer, provide dual modes of retention, enabling greater cleanup selectivity and sensitivity for both acidic and/or basic compounds—even if the sorbent in the wells runs dry. Achieve unsurpassed sensitivity with the Oasis µElution Plate which can concentrate a sample up to 15x without requiring evaporation or reconstitution.



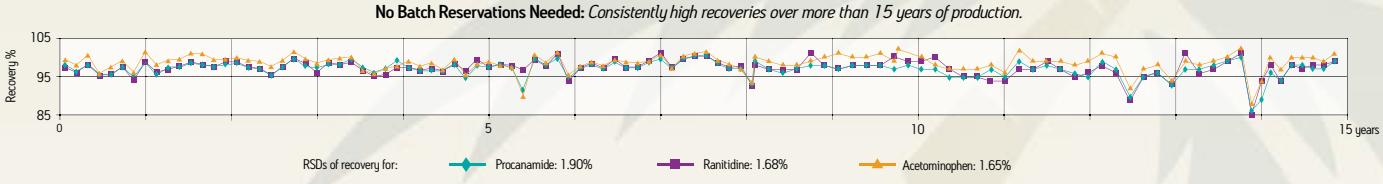
MATRIX EFFECTS

Following extraction with an Oasis mixed-mode sorbent, the matrix effects for a panel of 5 antidepressant drugs were evaluated in multiple lots of urine. The RSDs of the matrix factors were determined to be between 5.5 and 8.4%, which are well within the 15% CV limit recommended by regulatory agencies.

Analyte	% RSD of Matrix Factors
Amitriptyline	6.03
Nortriptyline	5.53
Imipramine	8.36
Desipramine	7.15
Doxepin	5.96

QUALITY

Waters careful process design and stringent quality controls have set a new standard in batch-to batch and lot-to-lot reproducibility for SPE sorbents. This enables scientists to develop robust, accurate, and precise bioanalytical methods.



EXTREME FLEXIBILITY AND EXCEPTIONAL SELECTIVITY

Due to the increased sensitivity, improved throughput, and exceptional assay reliability provided by UPLC® Technology, this system is now the platform of choice for bioanalytical assays. With four different column technologies and different particle substrates and over twenty sub-2-µm column chemistries available for small molecules and biotherapeutic applications, Waters has a wide range of column solutions to meet your application needs.

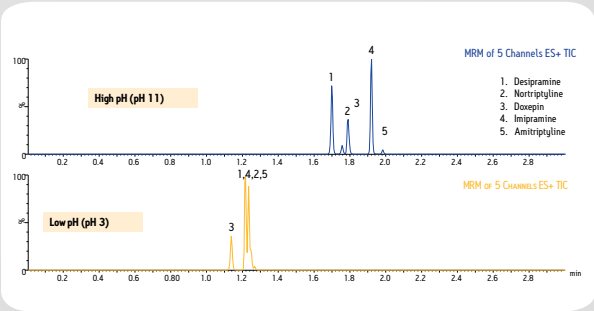
As a starting point, we recommend Waters BEH C_{18}, CSH™ C_{18}, and BEH HILIC columns as they offer the flexibility to address the bioanalytical needs for the widest range of compounds. For HPLC-MS systems, we suggest the same column chemistries in our e***X***tended ***P***erformance [***XP***] 2.5 µm Columns format for maximum resolution and throughput that can also provide a bridge from HPLC to UPLC technologies.

With the introduction of CORTECS™ Columns, based on a new silica-based solid-core particle, we add a new dimension to ultra performance chromatographic separations, with high efficiency, high resolution, and reduced analysis time separations. CORTECS columns are available in C_{18}, C_{18}+, and HILIC chemistries.

BEH Technology™

BEH C_{18}

- Universal starting point for method development and screening for small and large molecules
- Maximum flexibility and a wide pH range (1–12)
- Long column lifetimes

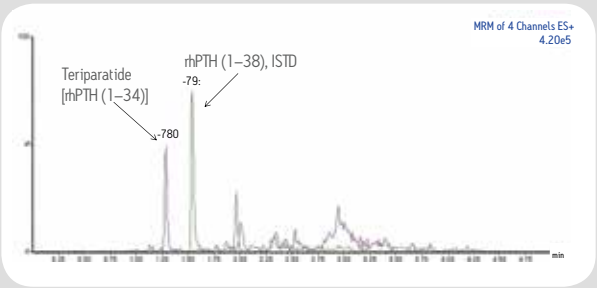


Comparison data between low and high pH.

CSH™ Technology

CSH C_{18}

- Alternative selectivity for method development and screening
- Superior peak shape and loading capacity for basic compounds
- Exceptional stability at low and high pH



UPLC separation of Teriparatide (MW4117) and internal standard from a 125 pg/mL extracted human plasma sample, using an ACQUITY UPLC CSH 2.1 x 50 mm Column.

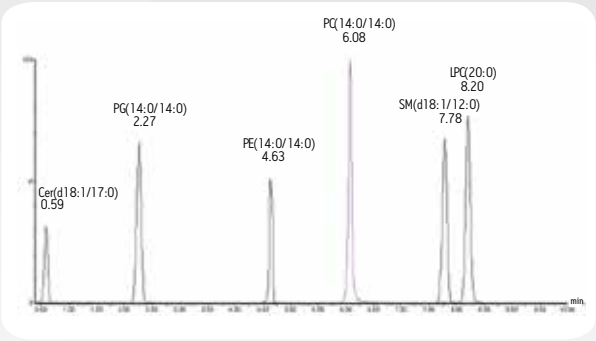
Key Benefits:

- Maximize laboratory productivity by reducing analysis time while improving data quality
- Reach lower limits of detection by enabling higher MS response with narrow chromatographic peaks
- Improve sample characterization by reducing MS suppression due to residual matrix components

BEH Technology™

BEH HILIC

- Ideal column for highly polar analytes and other difficult separations including lipids
- Complimentary selectivity
- Exceptional chemical stability and peak shape compared to silica columns

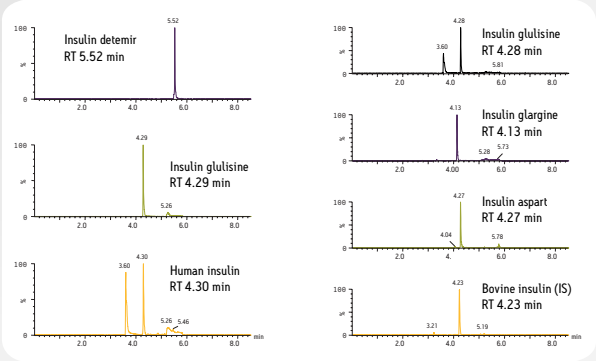


HILIC UPLC chromatogram of lipid standards.

SOLID-CORE PARTICLE TECHNOLOGY

CORTECS C_{18}

- Silica-based solid core particle technology column
- Maximum efficiency and maximum resolution
- Ultimate peak capacity with the ACQUITY UPLC® System



UPLC-MS/MS chromatogram for human insulin, five insulin analogs, and bovine insulin (IS).

XBridge® COLUMNS

XSELECT® Columns

CORTECS™ COLUMNS

Acquity UPLC®

PRECISE FORMULATION AND ABSOLUTE TRACEABILITY

Waters understands the importance of high quality analytical standards and reagents for ensuring continuous analytical instrumentation performance and workflow success. As a result, Waters now offers standards and reagents that are pure, precisely formulated, reproducible, and traceable to exact specifications.

From system performance standards to application specific standards, Waters provides the right product for optimal results.

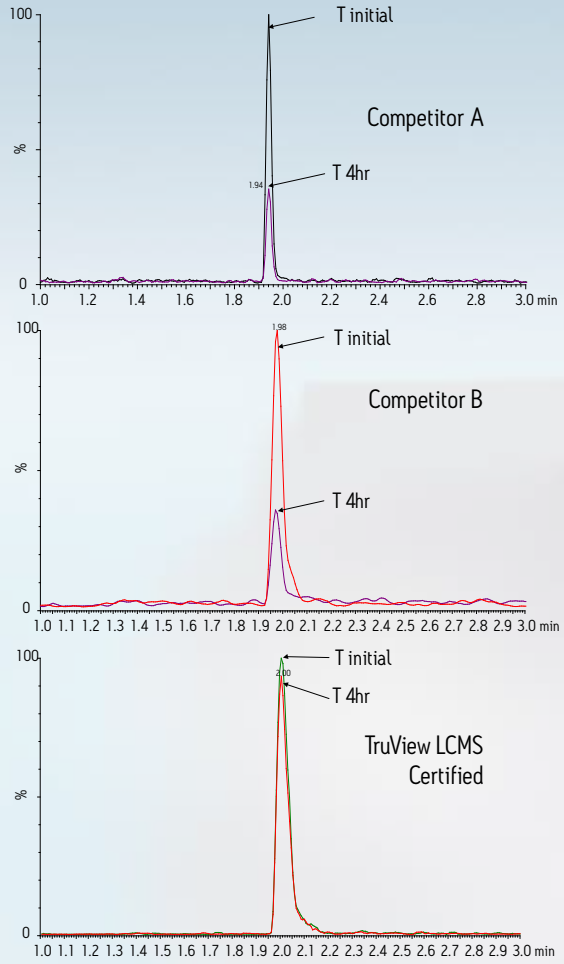
Key Benefits:

- Reduce variability in the laboratory
- Streamline the laboratory process
- Increase confidence in analytical results and reproducibility
- Provide absolute standard traceability

Analytical Standards and Reagents Catalog, Literature Code: 720004231EN

CERTIFIED FOR CONFIDENCE

Waters understands the importance of auto sampler vials and plates for the performance of analytical instrumentation. Quality vials are essential for reliable analytical results. All Waters Certified Vials are tested by LC or LC-MS to assure quality and cleanliness. The test results confirm the vials, cap, and septa have been properly manufactured, handled, and packaged, and are free from any potential contaminants which could result in chromatographic ghost peaks.



Comparison of loss of sample between Waters TruView™ LCMS Certified Vials and competitive vials. TruView LCMS Certified Vials are recommended for ng/mL concentrations and lower.

Key Benefits:

- Compatible with all autosamplers
- Specially designed vials and plates for limited sample volumes
- Complete selection of vial sizes and materials

CERTIFIED LCMS CERTIFIED TruView™ LCMS CERTIFIED

Waters TruView LCMS Certified Vials White Paper, Literature Code: 720004097EN
Waters LCMS Certified Vials White Paper, Literature Code: 720001517EN

SOLUTIONS FOR THE WAY YOU'LL WORK TOMORROW

Tomorrow's pharmaceuticals will need to be more targeted, effective, safer, and get approved and to market faster than ever. To succeed in that world, you'll need technology that is designed to support continuous improvement and a technology partner who truly understands your methods and goals. Only one company offers both: Waters.

For regulated laboratories, Waters offers the Regulated Bioanalysis Platform Solution, a fully integrated platform for quantitative bioanalysis. It delivers robust assays with the highest sensitivity. The platform brings together industry-leading technology for every stage of analysis with a fully networked, scalable informatics system that gives you a tremendous advantage in data management and reporting for compliance and validation. These are technologies that Waters continually innovates, upgrades, and improves. They're the best today. They'll be even better tomorrow.

Sample

Blood
Plasma
Serum
Urine
Tissue
Biological Fluids

Sample Preparation

Sirocco Protein Precipiration Plate
Ostro Sample Preparation Plate
Oasis Sample Extraction Cartridges and Plates

Columns

BEH Technology™ (ACQUITY UPLC and XBridge® Columns)
CSH Technology (ACQUITY UPLC and XSelect® Columns)
Solid-core Particle Technology (CORTECS Columns)

Liquid Chromatography System

ACQUITY UPLC I-Class
ACQUITY UPLC H-Class

Key Benefits:

- Advanced, analytical software for increased MS sensitivity
- Adaptive workflows to help you function as a unified team
- Sample preparation tools for purity, consistency, and quality
- Better tools for ever-increasing regulatory demands

Mass Spectrometer

Xevo® TQD
Xevo TQ-S

Data Management

UNIFI® Software
MassLynx® Software

SALES OFFICES:

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Australia 61 2 9933 1777
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Brazil 55 11 4134 3788
Canada 1 800 252 4752
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Denmark 45 46 59 8080
Finland 358 9 5659 6288
France 33 1 30 48 72 00
Germany 49 6196 400 600
Hong Kong 852 2964 1800
Hungary 36 1 350 5086
India 91 80 2837 1900
Ireland 353 1 448 1500
Israel 9723 3731391
Italy 39 02 265 0983
Japan 81 3 3471 7191
Korea 82 2 6300 4800
Mexico 52 55 52 00 1860
The Netherlands 31 76 508 7200
Norway 47 6 384 6050
Poland 48 22 101 5900
Portugal 351 21 893 61 77
Puerto Rico 1 787 747 8445
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Singapore 65 6593 7100
Spain 34 93 600 9300
Sweden 46 8 555 115 00
Switzerland 41 56 676 7000
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References

1. E. Chambers, D. M. Wagrowski-Diehl, Z. Lu, J. R. Mazzeo J., Systematic and comprehensive strategy for reducing matrix effects in LC/MS/MS analyses. Chromatogr. B 852 (2007) 22–34.

www.waters.com/BA

Waters

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January 2014 720003931EN AO-IGS