Volume 7, Number 7

Biofiles

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Mass Spectrometry

Use of Proteomic Standards to Optimize Conditions for an MRM LC-MS Platform

MS for Proteins & Peptides

Metabolomics Analysis and the METLIN Metabolite Database

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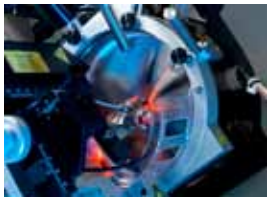
Highlights in this issue:



This issue of *Biofiles* focuses on mass spectrometry (MS) as applied to biology. MS is a particularly useful analytical method where high sensitivity is required to detect low-abundance species. Well established in chemistry for analysis of small molecules, MS has more recently been gaining greater prominence in biological research on larger biomolecules, particularly proteins. This issue features articles on MRM platform optimization with suitable proteomics standards, and on our partnership with The Scripps Center for Metabolomics on the METLIN database.

Biofilescontents

Cover: Close-up of sample injection into a mass spectrometer via electrospray ionization (ESI).

Technical content:

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Introduction

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In systems biology, two principal research platforms are proteomics and metabolomics. Mass spectrometry (MS) is a key analytical technology that has driven research in both platforms.[1-3] To facilitate MS analysis of complex biological samples, several fractionation and separation methods have been teamed with MS, such as gas chromatography, gel electrophoresis, and capillary electrophoresis.[4] In particular, the coupling of liquid chromatography (LC) with MS has created the core analytical method, LC-MS, at the heart of proteomics and metabolomics.[2] Furthermore, in the context of MS, the technique of multiple reaction monitoring/selected reaction monitoring (MRM/SRM) has long been established for small molecule studies and used in metabolite analysis for over 30 years.[3] With advances in MS instrumentation, MRM has found wider use with a different class of biomarkers: larger molecular weight species such as peptides.[5,6]

MS and "omics" studies have drilled down beyond proteomics[7-8] and metabolomics[9] to various biomolecule subclasses such as lipids,[10] glycerophospholipids,[11] and phospholipids.[12] In proteomics, beyond global protein profiles, MS has the potential to probe cellular physiology and higher-level cellular organization[6] in areas like cancer[4] and cardiovascular disease.[13] Metabolomics and MS have provided insight into such topics as aging,[14] sepsis,[15] and molecular mechanisms of cancer.[4]

This issue of *BioFiles* surveys our products for MS over a range of biomolecules. Sigma Life Science offers a wide variety of bioactive compounds, including carbohydrates, fatty acids, vitamins, hormones, and steroids, in both natural isotope and stable isotope-labeled versions. For proteomics, peptides and proteins are available as calibration standards, both individually and in mixtures. Our peptide portfolio includes custom capabilities in our AQUA™ Peptide and PEPscreen® platforms. We also provide the core reagents and products used in every MS lab, from key proteolytic enzymes and MALDI matrices to solvents and solvent additives. In the realm of chromatography, Supelco offers suitable columns and accessories for HPLC and LC-MS.

As well, this issue of *BioFiles* includes two articles on specific research topics.

- Radabaugh *et al.* address the importance of MRM method development and instrument standardization with peptides, including our MSQC1 Qual/Quant Mix.
- The recent partnership of The Scripps Center for Metabolomics with Sigma Life Science for tandem MS (MS/MS) data of metabolites is highlighted. Through the METLIN Metabolite Database, The Scripps Center for Metabolomics and Sigma provide these data publicly to interested scientists.

Sigma is proud to go beyond our second-to-none product portfolio to provide you the research tools for your MS work.

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Use of Proteomic Standards to Optimize Conditions for an MRM LC-MS Platform

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This article is adapted from the poster presentation by the above authors at the 60th ASMS Conference on Mass Spectrometry and Allied Topics, May 20-24, 2012, in Vancouver, BC, Canada.

Mass spectrometry (MS) assays and methods are continuing to gain utility in the biological sciences. Quantification of biomarkers and drug metabolites from biological fluids for use in toxicological studies, pharmaceutical development, study of disease diagnosis and progression, and monitoring of doping or drug abuse are among the many areas benefitting from advances in MS techniques and instrumentation. Of particular interest is the use of multiple reaction monitoring (MRM)-based assays to provide quantitative data from biological fluids. Employing LC-based MRM technology allows for robust and reproducible quantitation of analytes, while providing enhancements to sensitivity and specificity.

When employing this technique, it is crucial to optimize the LC-MS/MS system to achieve the best sensitivity and separation in order to provide the best results. To this end, several aspects in the system must be considered.

The first aspect is the selection of instrumentation. Triple quadrupole MS instruments are the workhorses of the technique, but one must also select an HPLC to best suit the analyses in terms of such factors as desired flow rates, trapping ability, cost, and ability to integrate with the MS.

Column selection is the next major decision. This also depends upon factors like flow rate, load, type of analyte, and column packing. Typically, for biological fluids, C-18 columns are employed. Several newer materials exist that employ either porous shell packings or sub-2 µm particles. Flow rate and column ID (internal diameter) are key aspects for consideration with respect to optimal peak shape and delay-time volume minimization. At low flow rates, one also must be very conscious of dead volume when using trapping columns to avoid gradient delays.

Once a column has been selected, flow rate and gradient optimization is done to ensure the best peak shape and resolution. Options for the source used to introduce the ions into the MS also exist and can be explored to find the best fit for specific studies.

As optimization of several aspects of the system is necessary, it is best to select a few well characterized standards for use in assessing the robustness, sensitivity, and reproducibility of an instrument. Use of a uniform standard in a MS lab allows for comparison and system quality evaluation not only within a single system, but across instruments and platforms utilized within a lab, as well as across labs.

Methods

In an effort to create an optimized system for quantification of peptides using an ABSciex 5500 QTRAP coupled to a Waters nanoACQUITY UPLC®, we evaluated sources, columns (75 µm - 200 µm ID), temperature, and flow rates (0.5 - 6 mL/min). The Supelco columns and trapping columns used in these experiments were as follows:

- Ascentis® Express column, 15 cm × 200 µm, 2.7 µm (**54261-U**)
- Ascentis Express column, 15 cm × 100 µm, 2.7 µm (**54256-U**)
- Ascentis Express column, 15 cm × 75 µm, 2.7 µm (**54219-U**)
- Ascentis Express Peptide C18 trapping column, 5 cm × 300 µm, 2.7 µm (**53546-U**)
- Ascentis Express Peptide C18 trapping column, 5 cm × 200 µm, 2.7 µm (**53545-U**)

All work was performed using MRM in the positive ion mode. For each column, several flow rates (up to ~85% of the maximum pressure for the LC system, 10,000 psi) and temperatures (ranging from 35-60 °C) were tested using a synthetic peptide mixture developed in-house. The peptide mixture allowed the retention of very hydrophobic and very hydrophilic peptides to be evaluated with various columns, flow rates, and trapping columns.

Results

The resulting chromatograms from the optimal flow rate for each respective column (based on pressure constraints, with pressure at approximately 5600 psi) are shown using the synthetic peptide mixture (see **Figure 1**). The nanoACQUITY column provided the best peak shape, but failed to retain the most hydrophilic peptide. The Supelco columns with the 75 or 100 µm ID's retained the hydrophobic peptide and provided more intense peaks, but resulted in broader peaks, most likely because of the lower flow rate constraints resulting from system pressure. Therefore, the 200 µm ID Supelco column was chosen for further optimization.

The optimal set-up was tested with MS Qual/Quant QC Mix (**MSQC1**) to assess sensitivity and limits of detection (see **Figure 2**). In addition, in an effort to translate these studies using standards to real-life experiments, serum was spiked with a non-human synthetic protein and analyzed to assess load of a complex matrix (data not shown). In all tests, peak shape, retention times, response, linearity, pressure effects, and delay time were evaluated.

MS Qual/Quant QC Mix was used to assess sensitivity and limits of detection. Two heavy-labeled peptides which are present at the lowest levels in the product were selected for integration of peak areas using MultiQuant 2.1. The 2.4 fmole on-column load provided good signal, with signal/noise levels above 5 for all transitions and above 40 for the best transitions.

Employment of both MS Qual/Quant QC Mix (**MSQC1**) and the synthetic peptide mix proved very useful in providing consistent samples with a broad retention time span for use in the optimization of the chromatographic and MS aspects of this LC-MS/MS system.

MS Qual/Quant QC Mix NEW

MS Qual/Quant QC Mix is an injection ready standard, designed with multiple reaction monitoring/selected reaction monitoring (MRM /SRM) methodology in mind. This product is optimized to assess platform characteristics, including:

- Reproducibility between runs
- System stability (drift, chromatography, signal intensity, sensitivity, etc.)
- Inter- and intra- platform and lab comparisons

Up to 100 uses based on the recommended reconstitution method

MSQC1-1VL	1 vial

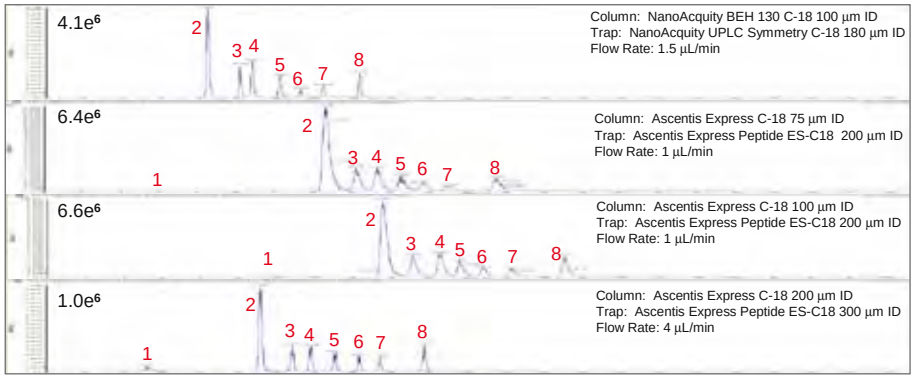

Figure 1. Comparison of Columns. The resulting chromatograms from the optimal flow rate for each respective column (based on pressure constraints) are shown using the synthetic peptide mix. The nanoACQUITY column failed to retain the most hydrophilic peptide. The Ascentis® Express columns at the 75 and 100 µm ID's retained the hydrophobic peptide and provided more signal, but resulted in broader peaks. The 200 µm ID Ascentis Express column was chosen for further optimization.

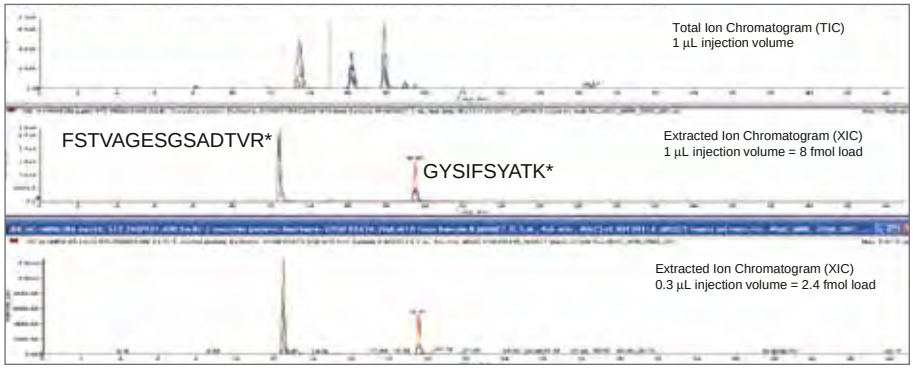

Figure 2. MS Qual/Quant QC Mix (MSQC1) Load Study. MSQC1 was used to assess sensitivity and limits of detection using the 200 µm ID Ascentis Express column. The lowest injection volume tested (0.3 mL, equal to 2.4 fmole on-column load of the selected peptides) provided good signal with signal/noise levels above 40 for the best transition for each peptide.

MS for Proteins & Peptides

Metabolic Labeling

Quantitative Proteomics Using SILAC Metabolic Labeling

Within proteomics, the combination of stable isotope labeling and MS offers researchers the distinct advantage of running a single experiment while gaining relative quantification of protein levels between multiple samples, such as stimulated vs. non-stimulated cellular states.[1] Although several methods are available, arguably the most accurate quantitative proteomic experiment is a technique commonly known as SILAC (**S**table **I**sotope **L**abeling by **A**mino Acids in **C**ell Culture).[2]

The SILAC technique calls for the growth of two separate cell cultures: one that contains only the "light" natural abundance isotopes and the other that incorporates "heavy" stable isotopes such as ^{13}C, ^{15}N and/or deuterium (see **Figure 1**). By combining the samples and performing an MS analysis, the researcher is able to gain relative protein quantification between the samples.

The products listed below include everything needed to successfully complete a SILAC experiment. Stable isotope labeled amino acids, fetal bovine serum, and depleted SILAC media are readily available. For more detailed information, visit **aldrich.com/silac**.

References

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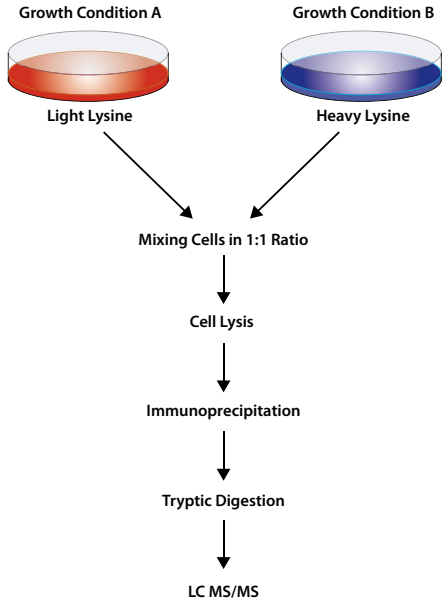

Figure 1. SILAC Workflow

99% Stable Isotope-Labeled Arginine and Lysine

Name	Isotopic Purity	Cat. No.
L-Arginine-$^{13}C_6$,$^{15}N_4$ hydrochloride, *95% (CP), 97% (L)*	99 atom % ^{13}C 99 atom % ^{15}N	608033-100MG 608033-250MG 608033-500MG
L-Arginine-$^{13}C_6$ hydrochloride, *95% (CP)*	99 atom % ^{13}C	643440-100MG
L-Arginine-$^{15}N_4$ hydrochloride, *97% (CP)*	99 atom % ^{15}N	600113-100MG
L-Lysine-$^{13}C_6$,$^{15}N_2$ hydrochloride, *95% (CP)*	99 atom % ^{15}N 99 atom % ^{13}C	608041-100MG 608041-1G
L-Lysine-$^{13}C_6$ hydrochloride, *95% (CP)*	99 atom % ^{13}C	643459-250MG

Additional Stable Isotope-Labeled Amino Acids

Name	Isotopic Purity	Cat. No.
L-Isoleucine-$^{13}C_6$,^{15}N, *95% (CP)*	98 atom % ^{13}C 98 atom % ^{15}N	608092-100MG
L-Leucine-5,5,5-d_3, *99% (CP)*	99 atom % D	486825-1G
L-Leucine-$^{13}C_6$, *95% (CP)*	98 atom % ^{13}C	605239-100MG
L-Leucine-$^{13}C_6$,^{15}N, *95% (CP)*	98 atom % ^{13}C 98 atom % ^{15}N	608068-100MG
L-Lysine-4,4,5,5-d_4 hydrochloride, *98% (CP)*	98 atom % D	616192-100MG 616192-500MG
L-Methionine-$^{13}C_5$,^{15}N, *95% (CP)*	98 atom % ^{15}N 98 atom % ^{13}C	608106-100MG 608106-250MG
L-Methionine-(*methyl*-^{13}C,d_3), *99% (CP)*	99 atom % D 99 atom % ^{13}C	299154-250MG 299154-1G

Additional Stable Isotope-Labeled Amino Acids (continued)

Name	Isotopic Purity	Cat. No.
L-Methionine-(*methyl*-d_3), *99% (CP)*	98 atom % D	300616-1G 300616-5G
L-Phenylalanine-$^{13}C_9$,^{15}N, *95% (CP)*	98 atom % ^{15}N 98 atom % ^{13}C	608017-250MG 608017-1G
L-Tyrosine-(*phenyl*-$^{13}C_6$), *99% (CP)*	99 atom % ^{13}C	489794-100MG
L-Tyrosine-$^{13}C_9$, *95% (CP)*	98 atom % ^{13}C	492868-100MG
L-Tyrosine-$^{13}C_9$,^{15}N, *95% (CP)*	98 atom % ^{13}C 98 atom % ^{15}N	607991-250MG
L-Valine-$^{13}C_5$,^{15}N, *99% (CP)*	98 atom % ^{15}N 98 atom % ^{13}C	600148-250MG 600148-1G

SILAC Depleted Media and Dialyzed Serum

Name	Description	Cat. No.
Fetal Bovine Serum	Dialyzed by ultrafiltration against 0.15 M NaCl, suitable for cell culture	F0392-100ML F0392-500ML
Dulbecco's Modified Eagle's Medium - low glucose	Liquid, suitable for cell culture, designed for SILAC applications	D9443-500ML
RPMI-1640 Medium	With L-glutamine and sodium bicarbonate. Without arginine, leucine, lysine, and phenol red, liquid, suitable for cell culture, designed for SILAC applications	R1780-500ML

Whole-Proteome Stable Isotope Labeling in Mammals (SILAM)

The use of SILAC within quantitative proteomics has become a routine technique for incorporating stable isotopes into a cell's proteome. SILAC, however, is limited to *in vitro* cell culture, which presents a major challenge. In an effort to expand the boundaries of the SILAC technology, researchers have adapted the technique to produce *in vivo* stable isotope-labeled whole proteomes.[1] This new method, known as SILAM (**S**table **I**sotope **La**beling in **M**ammals), accomplishes whole-proteome labeling using a ^{15}N-labeled feeding diet. By using this feed technique, researchers have been able to produce a rat with whole-proteome enrichments of ≥94%, including tissue with slow protein turnover and no adverse health effects.[2]

ISOTEC Stable Isotopes offers both natural abundance and ^{15}N-labeled *Spirulina*, a strain of blue-green algae that contains all 20 amino acids. The *Spirulina* can be used as a direct feeding source for the animal.

To inquire about Stable Isotopes pricing and availability, email us at **isosales@sial.com.**

References

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Whole Proteome Labeling Products

Algal lyophilized cells-^{15}N (*spirulina*) NEW

738352

Algal lyophilized cells (*spirulina*)

741094

Gel Electrophoresis

ProteoSilver™ Plus Silver Stain Kit

Conveniently packaged, extremely stable, and highly sensitive, ProteoSilver™ Plus is an ideal product for any protein scientist. This kit contains prepared solutions of silver staining reagents along with detailed instructions to achieve optimal results. With a detection limit of 0.1 ng/mm^2 of protein (BSA) and an extremely low background, ProteoSilver Plus leads to superior detection of low abundance proteins.

ProteoSilver Plus is also MALDI-MS compatible and does not contain glutaraldehyde, which crosslinks lysine residues, resulting in inaccurate spectra. This kit contains two additional reagents for destaining an excised protein spot, for those wishing to perform further characterization through tryptic digestion and MALDI-MS analysis.

Features and Benefits

- **Premixed and preweighed** solutions reduce time and cost of purchasing and preparing individual components
- **Optimized protocols** help establish conditions for best results
- **High sensitivity and low background** ensure very low abundance proteins can be detected and resolved from other proteins
- **MALDI Compatible -** Protein spots of interest can be further characterized by mass spectrometry
- **Room Temperature Stability** allows easy and convenient storage

1 kit sufficient for 25 mini-gels (10 × 10 cm)

Components

ProteoSilver™ Silver Solution 25 mL
ProteoSilver™ Sensitizer 25 mL
ProteoSilver™ Developer 2 2.5 mL
ProteoSilver™ Stop Solution 125 mL
ProteoSilver™ Destainer A 125 mL
ProteoSilver™ Destainer B 125 mL
ProteoSilver™ Developer 1 125 mL

PROTSIL2-1KT 1 kit

LUCY® Protein Dyes

LUCY® fluorescent dyes are a reliable, convenient, and economical set of alternative staining reagents to silver staining techniques and other fluorescent staining methods. The dyes have good to high sensitivity for detection of proteins and rapid, robust staining for all types of SDS gels. Protein staining by LUCY dyes does not interfere with subsequent MALDI-MS.

- LUCY 506 is recommended for high sensitivity staining with a detection limit of 3 ng protein per band.
- LUCY 565 is used in neutral gel-staining, e.g., before Western blotting. It has a sensitivity of ~5 ng protein per band and a linear response up to 4,000 ng per band.
- LUCY 569 has a broad linear response between ~5 and 6,000 ng protein per band.

The LUCY Starter kit provides sample quantities of all three fluorescent dyes for staining evaluation and comparison.

LUCY® 506 solution

LUCY 506 is provided as a 5000× stock solution in DMF (5 mg/ml).

fluorescence.....λ_{ex} 504 nm, λ_{em} 515 nm in aqueous buffer pH 8.3 with SDS and BSA

68721-500UL	500 µL

LUCY® 565 solution

LUCY 565 is provided as a 5000× stock solution in DMSO (5 mg/ml).

fluorescence.....λ_{ex} 565 nm, λ_{em} 584 nm in aqueous buffer pH 8.3 with SDS and BSA

43772-500UL-F	500 µL

LUCY® 569 solution

LUCY 569 is provided as a 5000× stock solution in DMSO (5 mg/ml).

fluoresce nce.....λ_{ex} 565 nm, λ_{em} 581 nm in aqueous buffer pH 8.3 with SDS and BSA

41629-500UL-F	500 µL

LUCY® Starter Kit

The LUCY Starter Kit contains three fluorescent protein stains for SDS-PAGE gels.

Components

LUCY® 506 (Sigma 68721) 50 µL
LUCY® 565 (Sigma 43772) 50 µL
LUCY® 569 (Fluka 41629) 50 µL

51153-1KT	1 kit

Proteolytic Enzymes

Trypsin

Trypsin from porcine pancreas

▸ Proteomics Grade, Dimethylated

Specifically prepared and extensively purified to provide optimal digests for proteomic applications, this highly stabilized trypsin performs impressively in both solution and in-gel digests. Trypsin is a pancreatic serine endoprotease which specifically hydrolyzes peptide bonds at the carboxyl side of arginyl and lysyl residues. The lysine residues of proteomics grade trypsin have been reductively methylated, resulting in a product that is resistant to autolysis. The product has been treated with TPCK to remove chymotryptic activity, further purified through affinity chromatography, and lyophilized, resulting in convenient use and highly specific cleavage. This product is also applicable to mass spectrometry work.

T6567-20UG	20 µg
T6567-5X20UG	5 × 20 µg
T6567-1MG	1 mg

Trypsin Singles, Proteomics Grade

Experience all of the advantages of Proteomics Grade Trypsin in a convenient, single-use 1 µg package.

Features and Benefits

- Convenient, single-use 1 µg size
- Eliminates repetitive pipetting
- Reductively methylated to minimize autolytic activity
- TPCK treated to quench chymotryptic activity
- Extensively purified

activity: ≥10,000 BAEE units/mg protein
average mol wt 23.29 kDa
optimum pH.....~8.0

Components

Trypsin Solubilization Reagent
Trypsin Reaction Buffer
Trypsin Singles, Proteomics Grade, Enzyme 96 x 1 ug

T7575-1KT	1 kit

Trypsin Spin Columns

▸ for proteomics

Enjoy all of the advantages of Proteomics Grade Trypsin in a 15-minute digestion. A staple of MS sample preparation, efficient tryptic digestion is essential to successful proteomic analyses. While traditional digests require up to 18 hours, the same digest can be accomplished in only 15 minutes using the Trypsin Spin Column, Proteomics Grade.

This ultra-micro spin column contains highly purified, TPCK-treated porcine trypsin immobilized on a spherical 20 µm silica support, chemically modified to minimize non-specific adsorption. This product is ideal for rapid protein digestion of small volumes (100 µl or less). Eluted peptides are ready for MS analysis, and require no additional clean-up.

Components

Trypsin Spin Columns 10 each
Collection Tubes 20 each
Enzyme Reaction Buffer 25 ml

TT0010-10EA	10 ea

Trypsin from bovine pancreas

[9002-07-7]
mol wt 23.8 kDa

▸ suitable for protein sequencing, lyophilized powder

vial = 100 µg

T8658-1VL	1 vial

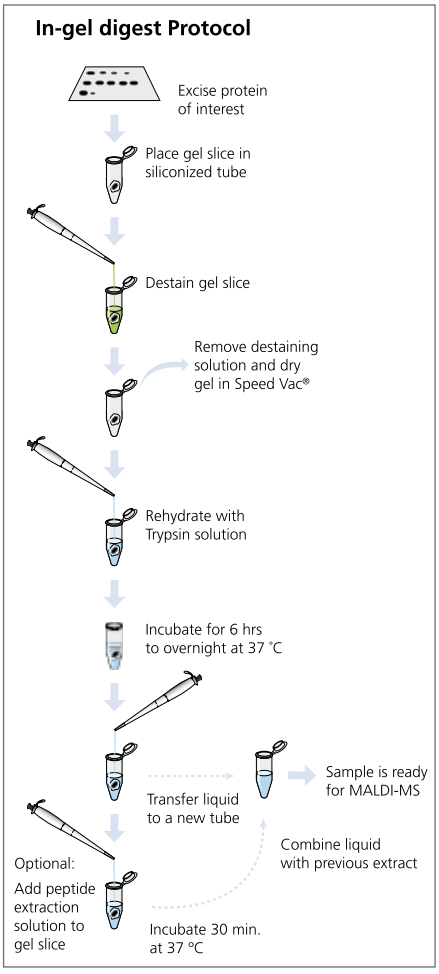
Trypsin Profile IGD Kit

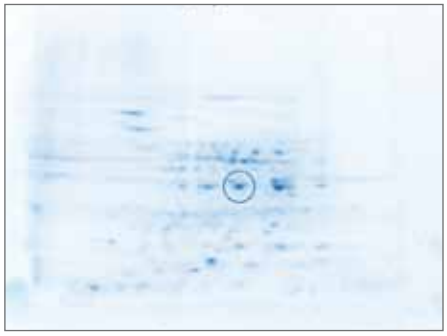
The Trypsin Profile IGD Kit enables fast, efficient, and complete in-gel tryptic digestion of up to 100 excised protein spots. Digested proteins are ready for MALDI-MS and require no additional preparation. Because the Trypsin Profile IGD Kit contains Proteomics Grade Trypsin, a higher sequence coverage and fewer ambiguous autolytic peaks are observed in MALDI spectra.

Features and Benefits

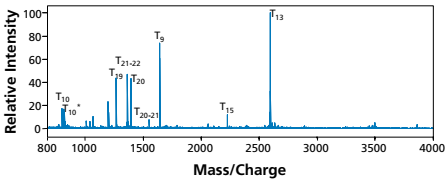
- Faster destaining than with alternative in-gel digest kits
- Includes 100% of the reagents needed to destain, digest, and extract proteins/peptides of interest
- Compatible with Coomassie, SYPRO® Orange, SYPRO Ruby, and ProteoSilver™ Stained gels
- Resulting samples are ready for analysis by MALDI-MS or HPLC-MS

1 kit sufficient for ≤100 applications





A solution of 2.5 mg/ml *E. coli* cells (EC-1) in Cellular and Organelle Membrane Solubilizing Reagent of ProteoPrep® Total Extraction Sample Kit (Cat. No. PROTTOT) was sonicated, then reduced with tributyl phosphine and alkylated with iodoacetamide (Cat. No. PROTRA). 109 µg of protein was loaded on a 7 cm, pH 4-7, IPG strip, focused for 50,000 volt hours, then run on a 4-20% Tris-Glycine SDS PAGE gel at 150 volts for 70 min. The gel was then stained with EZBlue™ (Cat. No. G1041). A random spot was then excised and tryptically digested using the Trypsin Profile IGD Kit (Cat. No. PP0100)



The sample was desalted using a ZipTip™ C18 pipette tip from Millipore and eluted directly onto the MALDI target using the MALDI matrix (α-cyano-4-hydroxycinnamic acid, 10 mg/ml in 70% ACN, 0.03% TFA). MALDI analysis was performed in the reflection positive ion mode. The resulting monoisotopic masses were searched against the NCBI database at a tolerance of 150 ppm. The protein was identified as outer membrane protein 3a from *E. coli* with the matched peptides providing 30% sequence coverage.

Components

Destaining Solution Reconstituted 75 ml
Trypsin Reaction Buffer
Aldrich Biotech Grade Acetonitrile
Trypsin Solublization Reagent
Peptide Extraction Solution
Trypsin, Proteomics Grade

PP0100-1KT	1 kit

Arg-C

Endoproteinase Arg-C is a serine endoprotease from mouse submaxillary gland which hydrolyzes peptide bonds at the carboxyl side of arginyl (Arg) residues. Arg-C also exhibits esterase and amidase activities. This product is HPLC purified.

Endoproteinase Arg-C from mouse submaxillary gland

[82047-85-6]

- suitable for protein sequencing, lyophilized powder

vial = 5 µg

P6056-1VL	1 vial

Asp-N

Endoproteinase Asp-N is a metallo-endoprotease which hydrolyzes peptide bonds on the N-terminal side of aspartic acid and cysteic acid residues. This product is isolated from a mutant strain of *Pseudomonas fragi* and is HPLC purified.

Endoproteinase Asp-N from *Pseudomonas fragi* mutant strain

[9001-92-7]

- suitable for protein sequencing, lyophilized powder

vial = 2 µg

P3303-1VL	1 vial

Glu-C

Endoproteinase Glu-C from *Staphylococcus aureus* strain V8 is a serine endoprotease which hydrolyzes peptide bonds at the carboxyl side of glutamyl (Glu) and aspartyl (Asp) residues. The specificity of Glu-C is dependent upon the buffer and pH used, as well as the structure around the potential cleavage site.

- In ammonium acetate (pH 4.0) or ammonium bicarbonate (pH 7.8), Glu-C preferentially cleaves Glu bonds.
- In phosphate buffer (pH 7.8), Glu-C cleaves at either Glu or Asp.
- No cleavage will occur if a proline residue is on the carboxyl side.

Endoproteinase Glu-C from *Staphylococcus aureus* V8

V8 Protease [66676-43-5]

- suitable for protein sequencing, lyophilized powder

≥85% (HPLC)

P6181-50UG	50 µg

Lys-C

Endoproteinase Lys-C is a serine endoprotease which hydrolyzes peptide bonds at the carboxyl side of lysine (Lys) residues. This product is isolated from from *Lysobacter enzymogenes* and is HPLC purified.

Endoproteinase Lys-C from *Lysobacter enzymogenes*

[72561-05-8]

- suitable for protein sequencing, lyophilized powder

vial = 5 µg

P3428-1VL	1 vial

Protease Profiler™ Kit

Protease Profiler™ Kit

For detailed characterization of proteins of interest, increase your protease selection with the Protease Profiler. The Protease Profiler provides four proven alternative proteases in addition to Proteomics Grade Trypsin, an enzyme solublization reagent, and an enzyme reaction buffer. Each component has been stringently purified and qualified for MALDI-MS to ensure optimal performance. Characterize with greater flexibility, perform double enzymatic digestions, and explore alternative cleavage sites with the Protease Profiler.

- **Double Enzymatic Digestion -** An initial digestion may result in peptide fragments greater than 5 kDa, often above the optimal detection range for most MS systems/instruments. A second digestion using a protease with different specificity results in cleavage of the large peptides, generating smaller peptides suitable for MS.
- **Explore Alternative Proteases -** Trypsin may be incompatible with some protein samples. Find the protease best suited to your protein of interest and improve the quality of your data.
- **Perform Either Solution or Gel-based Digests -** Optimized protocols and reagents for both digest conditions are provided, enabling flexibility in your analysis.

Components

Trypsin (Sigma T6567) 20 ug
Endoproteinase Asp-N (Sigma P3303) 2 ug
Endoproteinase Glu-C (Sigma P6181) 25 ug
Endoproteinase Lys-C (Sigma P3428) 5 ug
Endoproteinase Arg-C (Sigma P6056) 5 ug
Enzyme Solublization Reagent 1 ml
Enzyme Reaction Buffer 25 ml

PP0500-1KT	1 kit

Calibration Standards

Universal Proteomics Standards

Universal Proteomics Standard Set

The Universal Proteomics Standard (UPS) Set is intended to standardize and/or evaluate mass spectrometric (e.g., LC-MS/MS, MALDI-TOF-MS, etc.) and electrophoretic analysis conditions prior to the analysis of complex protein samples. Potential uses include:

- Bracketing critical experimental datasets for confirming the robustness of analysis methods.
- Comparison of MS or other proteomic data that are generated in different labs using a variety of analytical strategies and instruments.
- Identifying limitations of proteomics analysis systems and search algorithms.
- An external reference to assist with the evaluation of data derived from poorly defined samples.

The Universal Proteomics Standard (UPS) Set was developed in collaboration with the Association of Biomolecular Resource Facilities (ABRF) Proteomics Standards Research Group (sPRG). This protein mixture was extensively evaluated and reported under the direction of ABRF's sPRG during a comprehensive 2005/2006 study. The findings of the study were presented at the ABRF 2006 and US HUPO 2006 conferences.

Components

Universal Proteomics Standard 1 vial
Trypsin (Sigma T6567) 20 ug

UPS1-1KT	1 kit

Proteomics Dynamic Range Standard Set

The Proteomics Dynamic Range Standard Set can be used to standardize and/or evaluate mass spectrometric and electrophoretic analysis conditions prior to the analysis of complex protein samples.

The Proteomics Dynamic Range Standard Set is produced from a mixture of 48 individual human source or human sequence recombinant proteins, each of which has been selected to limit heterogeneous post-translational modifications (PTMs). The protein standard is formulated from 6 mixtures of 8 proteins to present a dynamic range of 5 orders of magnitude, ranging from 50 pmoles to 500 amoles. Each protein has been quantitated by amino acid analysis (AAA) prior to formulation.

concentration.....10.6 µg/ampule protein

Components

Proteomics Dynamic Range Standard 1 vial
Trypsin (Sigma T6567) 20 µg

UPS2-1SET	1 set

Peptide Mixture

MS Qual/Quant QC Mix NEW

MS Qual/Quant QC Mix is an injection ready standard, designed with multiple reaction monitoring/selected reaction monitoring (MRM / SRM) methodology in mind. This product is optimized to assess platform characteristics, including:

- Reproducibility between runs
- System stability (drift, chromatography, signal intensity, sensitivity, etc.)
- Inter- and intra- platform and lab comparisons

Up to 100 uses based upon the recommended reconstitution method

MSQC1-1VL	1 vial

MALDI Standards Kits

ProteoMass™ Peptide and Protein MALDI-MS Calibration Kit

This kit features a convenient selection of pre-qualified standard peptides, proteins, matrices, and solvents for calibrating and testing matrix assisted laser desorption ionization (MALDI) mass spectrometers. Configured for analyzing complex mixtures of proteins and peptides (700 to 66,000 Da), MSCAL1 is ideal for evaluating unknown samples or samples containing a broad range of molecular masses. Applications include calibration, tuning, and sensitivity testing of MALDI instruments from all manufacturers.

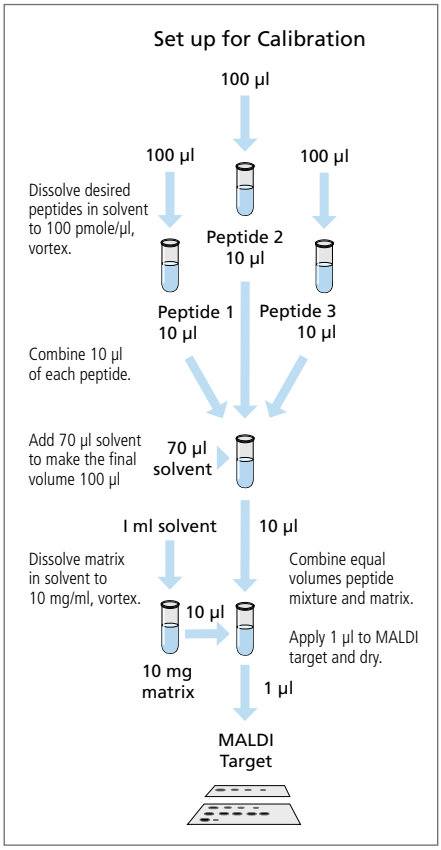
Components

ProteoMass™ Bradykinin Fragment 1-7 MALDI-MS Standard (Sigma B4181) 1×10 nmol
ProteoMass™ P14R MALDI-MS Standard (Sigma P2613) 1×10 nmol
ProteoMass™ ACTH Fragment 18-39 MALDI-MS Standard (Sigma A8346) 1×10 nmol
ProteoMass™ Insulin chain B oxidized MALDI-MS Standard (Sigma I6154) 1×10 nmol
ProteoMass™ Insulin MALDI-MS Standard (Sigma I6279) 1×10 nmol
ProteoMass™ Cytochrome c MALDI-MS Standard (Sigma C8857) 1×10 nmol
ProteoMass™ Apomyoglobin MALDI-MS Standard (Sigma A8971) 1×10 nmol
ProteoMass™ Albumin MALDI-MS Standard (Sigma A8471) 1×10 nmol
ProteoMass™ Aldolase MALDI-MS Standard (Sigma A9096) 1×10 nmol
ProteoMass™ Angiotensin II MALDI-MS Standard (Sigma A8846) 1×10 nmol
α-Cyano-4-hydroxycinnamic acid (Sigma C8982) 4×10 mg
Sinapinic acid (Sigma S8313) 4×10 mg
Trifluoroacetic acid 30 mL
Acetonitrile 30 mL
Trifluoroacetic acid solution 1% 4 mL

MSCAL1-1KT	1 kit

ProteoMass™ Peptide MALDI-MS Calibration Kit

This kit features a convenient selection of pre-qualified standard peptides, matrices, and solvents for calibrating and testing matrix assisted laser desorption ionization (MALDI) mass spectrometers. Configured specifically for peptide applications (in the mass range of 700 to 3500 Da), MSCAL2 is ideal for analysis of tryptic fragments or post-source decay studies. Applications also include calibration, tuning, and sensitivity testing of MALDI instruments from all manufacturers.



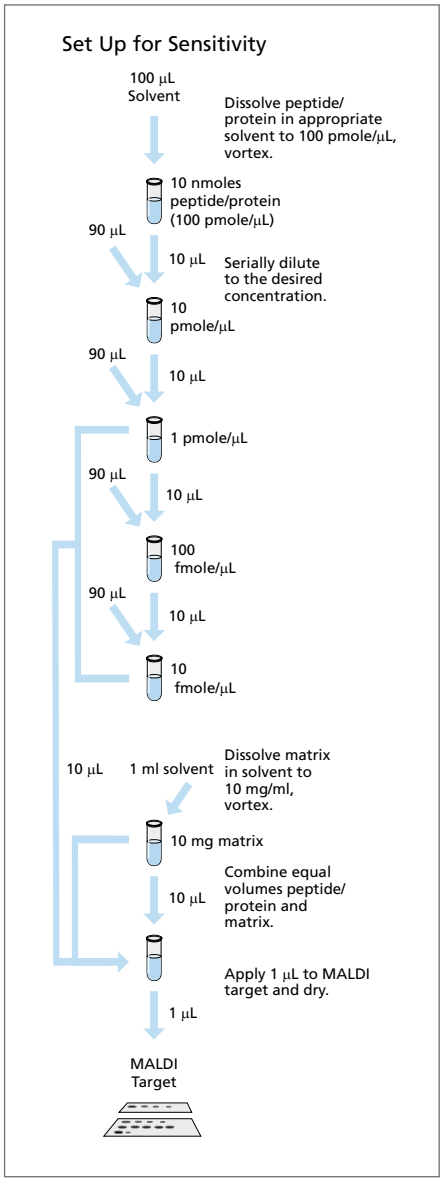
Components

ProteoMass™ Bradykinin Fragment 1-7 MALDI-MS Standard (Sigma B4181) 2×10 nmole
ProteoMass™ Angiotensin II MALDI-MS Standard (Sigma A8846) 2×10 nmole
ProteoMass™ P14R MALDI-MS Standard (Sigma P2613) 2×10 nmole
ProteoMass™ ACTH Fragment 18-39 MALDI-MS Standard (Sigma A8346) 2×10 nmole
ProteoMass™ Insulin chain B oxidized MALDI-MS Standard (Sigma I6154) 2×10 nmole
Trifluoroacetic acid 30 mL
Acetonitrile 30 mL
Trifluoroacetic acid solution 1% 4 mL
α-Cyano-4-hydroxycinnamic acid (Sigma C8982) 8×10 mg

MSCAL2-1KT	1 kit

ProteoMass™ Protein MALDI-MS Calibration Kit

This kit features a convenient selection of pre-qualified standard proteins, matrices, and solvents for calibrating and testing matrix assisted laser desorption ionization (MALDI) mass spectrometers. Configured specifically for applications in the mass range of 5 to 66 kDa, MSCAL3 is ideal for most protein studies. Applications include calibration, tuning, and sensitivity testing of MALDI instruments from all manufacturers.



Components

ProteoMass™ Insulin MALDI-MS Standard (Sigma I6279) 2×10 nmol
ProteoMass™ Cytochrome c MALDI-MS Standard (Sigma C8857) 2×10 nmol
ProteoMass™ Apomyoglobin MALDI-MS Standard (Sigma A8971) 2×10 nmol
ProteoMass™ Aldolase MALDI-MS Standard (Sigma A9096) 2×10 nmol
ProteoMass™ Albumin MALDI-MS Standard (Sigma A8471) 2×10 nmol
Sinapinic acid (Sigma S8313) 8×10 mg
Trifluoroacetic acid 30 mL
Acetonitrile 30 mL
Trifluoroacetic acid solution 1% 4 mL

MSCAL3-1KT	1 kit

ProteoMass™ MALDI Calibration Kit for LTQ XL and LTQ Hybrids

The ProteoMass MALDI Calibration Kit for LTQ XL™ and LTQ hybrids enables calibration of Thermo Scientific ion trap and ion trap-based hybrid mass analyzers equipped with MALDI sources in positive and negative ion mode. It covers a mass range from m/z 144 to m/z 3,657, and is therefore usable for calibrations between m/z 50 and 4000.

Features and Benefits

Discover the Advantages for Yourself!

- Developed and qualified specifically for use with the Thermo Scientific LTQ XL and LTQ hybrid mass spectrometers with MALDI source
- Contains high purity, low alkali metal solvents and recrystallized matrix
- Conveniently packaged, freeing you from time-consuming purification and weigh-up steps, allowing you to focus on acquisition of quality data

Components

α-Cyano-4-hydroxycinnamic acid 5 x 5 mg
ProteoMass™ Calibrant Mix, Normal Range 5 vials
ProteoMass™ Calibrant Mix, High Range 5 vials
ProteoMass™ Angiotensin II, Sensitivity Standard 2 x 500 pmols
Trifluoroacetic acid 4 ml
Acetonitrile 30 ml
Ethanol (Sigma E7023) 10 ml

MSCAL4-1KT	1 kit

ESI Calibration Kits

ProteoMass™ LTQ/FT-Hybrid ESI Pos. Mode CalMix NEW

The ProteoMass ESI Calibration Kit for LTQ based Hybrids, positive ion mode calibration solution, enables calibration of Thermo Scientific hybrid instruments equipped with ESI source in positive ion mode. It covers a mass range from m/z 138 to m/z 1822, and is, therefore, usable for calibrations between m/z 50 and 2000.

Features and Benefits

Discover the Advantages for Yourself!

- Ready-to-use
- Developed and qualified specifically for use with the LTQ based Thermo Scientific hybrid instruments (LTQ FT, LTQ FT Ultra, and LTQ Orbitrap series) with ESI source and Thermo Scientific Exactive
- Conveniently packaged, freeing you from time consuming mixing and dilution steps, allowing you to focus on acquisition of quality data

Components

Met-Arg-Phe-Ala Acetate
Caffeine
Ultramark 1621

MSCAL5-1EA	pkg = 1 × 10 mL	1 ea
MSCAL5-10EA	pkg = 10 × 10 mL	10 ea

ProteoMass™ LTQ/FT-Hybrid ESI Neg. Mode CalMix NEW

The ProteoMass ESI Calibration Kit for LTQ based Hybrids, Negative Ion Mode Calibration Solution, enables calibration of Thermo Scientific hybrid instruments equipped with ESI source in negative ion mode. It covers a mass range of m/z 265 to m/z 1880, and is, therefore, usable for calibrations between m/z 50 and 2000.

Features and Benefits

Discover the Advantages for Yourself!

- Ready-to-use
- Developed and qualified specifically for use with the LTQ based Thermo Scientific hybrid instruments (LTQ FT®, LTQ FT Ultra®, and LTQ Orbitrap™ series) with ESI source and Thermo Scientific Exactive
- Conveniently packaged, freeing you from time-consuming mixing and dilution steps, allowing you to focus on acquisition of quality data

Components

Ultramark 1621
Sodium dodecyl stearate
Taurocholic acid sodium salt

MSCAL6-1EA	pkg = 1 × 10 mL	1 ea
MSCAL6-10EA	pkg = 10 × 10 mL	10 ea

Individual Protein & Peptide Calibration Standards

The ProteoMass™ MALDI-MS Standards are peptide calibration standards designed for MALDI-MS instruments. Each vial contains 10 nmole of peptide.

ProteoMass™ Bradykinin Fragment 1-7 MALDI-MS Standard

Bradykinin fragment 1-7, mass spec standard

- vial = 10 nmol, monoisotopic mol wt 756.3997 Da

B4181-5X1VL	5 × 1 vial

ProteoMass™ Angiotensin II MALDI-MS Standard

Angiotensin II, mass spec standard

- vial = 10 nmol, monoisotopic mol wt 1,045.5423 Da

A8846-5X1VL	5 × 1 vial

ProteoMass™ $P_{14}R$ MALDI-MS Standard

P14R PPPPPPPPPPPPPR

- vial = 10 nmol, monoisotopic mol wt 1,532.8582 Da

P2613-5X1VL	5 × 1 vial

ProteoMass™ ACTH Fragment 18-39 MALDI-MS Standard

Adrenocorticotropic hormone fragment 18-39 Arg-Pro-Val-Lys-Val-Tyr-Pro-Asn-Gly-Ala-Glu-Asp-Glu-Ser-Ala-Glu-Ala-Phe-Pro-Leu-Glu-Phe [53917-42-3]

- vial = 10 nmol, monoisotopic mol wt 2,464.1989 Da

A8346-5X1VL	5 × 1 vial

ProteoMass™ Insulin chain B oxidized MALDI-MS Standard

Insulin Chain B Oxidized from bovine pancreas
FVNQHLCGSHLVEALYLVCGERGFFYTPKA [30003-72-6]
$C_{157}H_{232}N_{40}O_{47}S_2$ FW 3495.89

- vial = 10 nmol, monoisotopic mol wt 3,493.6513 Da

I6154-5X1VL	5 × 1 vial

ProteoMass™ Insulin MALDI-MS Standard

Insulin from bovine pancreas [11070-73-8]
$C_{254}H_{377}N_{65}O_{75}S_6$ FW 5733.49

- vial = 10 nmol, monoisotopic mol wt 5,729.6087 Da

I6279-5X1VL	5 × 1 vial

ProteoMass™ Cytochrome c MALDI-MS Standard

Cytochrome c from equine heart; Cytochrome c from horse heart [9007-43-6]

- vial = 10 nmol, $(M+H^+)$ 12,361.96 Da, calculation

C8857-5X1VL	5 × 1 vial

ProteoMass™ Apomyoglobin MALDI-MS Standard

Apomyoglobin, mass spec standard

- vial = 10 nmol, $(M+H^+)$ 16,952.27 Da, calculation

A8971-5X1VL	5 × 1 vial

ProteoMass™ Aldolase MALDI-MS Standard

- vial = 10 nmol, average mol wt 39,211.28 Da, calculation

A9096-5X1VL	5 × 1 vial

ProteoMass™ Albumin MALDI-MS Standard

Albumin, bovine, mass spec standard

- vial = 10 nmol, average mol wt 66,429.09 Da, calculation

A8471-5X1VL	5 × 1 vial

Met-Arg-Phe-Ala acetate salt

MRFA [67368-29-0] $C_{23}H_{37}N_7O_5S$ FW 523.65

- ≥90% (HPLC)

A marker in an unambiguous method for sequencing tetrapeptides using FAB, MI, and collisional activation spectra in combination.

M1170-1MG	1 mg
M1170-5MG	5 mg

Phosphopeptide MS Standards

For phosphopeptide analysis and workflow verification

The MS PhosphoMix products are used to test the strengths and weaknesses of phosphopeptide enrichment techniques, sample processing, and MS-based phosphoproteomics workflows. The MS PhosphoMix products consist of 25 mono-, di-, tri-, and tetraphosphorylated synthetic peptides formulated into 3 uniquely designed mixtures (MS PhosphoMix 1, 2, and 3). Each mixture is available in natural (light) and isotopically labeled (heavy) versions, making the set of products highly amenable to quantitative analyses and allowing users to compare recovery between workflows or enrichment techniques.

Each mixture includes phosphopeptides with a broad range of characteristics, including peptide ionizability (both ESI and MALDI), molecular weight, chromatographic retention time, charge state, and isoelectric point. The mixtures were designed to include complimentary peptides with the same or similar amino acid sequences, but where the number of phosphorylated residues and the site-specific locations of phosphorylation vary.

MS PhosphoMix products are ideal for use as internal reference materials to gauge overall platform performance (e.g. recovery, sensitivity, repeatability) during routine phosphopeptide analysis. Visit **sigma.com/phosphomix** to download the MS PhosphoMix FASTA file of all phosphopeptide sequences and to access composition, phosphorylation site, and monoisotopic mass data for each standard mixture.

MS PhosphoMix 1 Light

pkg = 200 pmole total phosphopeptides

MSP1L-1VL	1 vial

MS PhosphoMix 1 Heavy

pkg = 200 pmole total phosphopeptides

MSP1H-1VL	1 vial

MS PhosphoMix 2 Light

pkg = 200 pmole total phosphopeptides

MSP2L-1VL	1 vial

MS PhosphoMix 2 Heavy

pkg = 200 pmole total phosphopeptides

MSP2H-1VL	1 vial

MS PhosphoMix 3 Light

pkg = 200 pmole total phosphopeptides

MSP3L-1VL	1 vial

MS PhosphoMix 3 Heavy

pkg = 200 pmole total phosphopeptides

MSP3H-1VL	1 vial

Peptide Derivatization Products

ProteoMass™ Guanidination Kit

▶ For improving MALDI-MS sensitivity and increasing sequence coverage

One MS0100 kit is sufficient for 96 reactions.

The ProteoMass Guanidination Kit allows you to enhance MALDI-MS sensitivity, increase sequence coverage, and identify peptides with greater confidence. Following proteolytic digestion, peptides with C-terminal Arginine residues are ionized preferentially over peptides with C-terminal Lysine residues, leading to compromised sequence coverage and limited confidence during peptide mass fingerprint analysis. The ProteoMass Guanidination Kit efficiently and conveniently converts C-terminal Lysine residues to homoarginine, increasing MALDI signal strength and producing enhanced sequence coverage.

Features and Benefits

- Identify more samples with greater accuracy and confidence
- Increase throughput and save time - only 35 minutes to use the kit vs. 2 hours using traditional methods
- Compatibility – compatible with 1D or 2D PAGE gel bands or spots, as well as complex cell extracts

Components

O-methylisourea hemisulfate
Base Reagent
Stop Solution
Control Peptide

MS0100-1KT	1 kit

Glycine ethyl ester hydrochloride

Ethyl glycinate hydrochloride GEE [623-33-6]

$NH_2CH_2COOC_2H_5 \cdot HCl$ FW 139.58

▶ 99%

Glycine ethyl ester (GEE) is used in conjunction with *N*-(3-Dimethylaminopropyl)-*N'*-ethyl-carbodiimide (EDC) for carboxyl-footprinting studies of proteins. The GEE/EDC protocol effects specific derivatization of glutamate and aspartate carboxyl side chains on intact proteins. This reaction is readily done under aqueous conditions at physiological pH.[1,2]

Lit cited: 1. Zhang, H.; et al., *Mol. Cell. Proteomics* **10**, (2011); 2. Zhang, H.; et al., *Int. J. Mass Spectrom.* **312**, 78-86 (2012);

G6503-5G-A	5 g
G6503-100G-A	100 g
G6503-500G-A	500 g

N-(3-Dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride

EDAC; EDC hydrochloride; *N*-Ethyl-*N'*-(3-dimethyl-aminopropyl)carbodiimide hydrochloride; WSC hydrochloride [25952-53-8] $C_8H_{17}N_3 \cdot HCl$ FW 191.70

Water soluble condensing reagent. EDAC is generally utilized as a carboxyl activating agent for amide bonding with primary amines. In addition, it will react with phosphate groups. EDAC has been used in peptide synthesis; crosslinking proteins to nucleic acids; and preparation of immunoconjugates as examples. Typically, EDAC is utilized in the pH range 4.0-6.0 without buffers. In particular, amine and carboxylate buffers should be avoided.

E1769-1G	1 g
E1769-5G	5 g
E1769-10G	10 g
E1769-25G	25 g

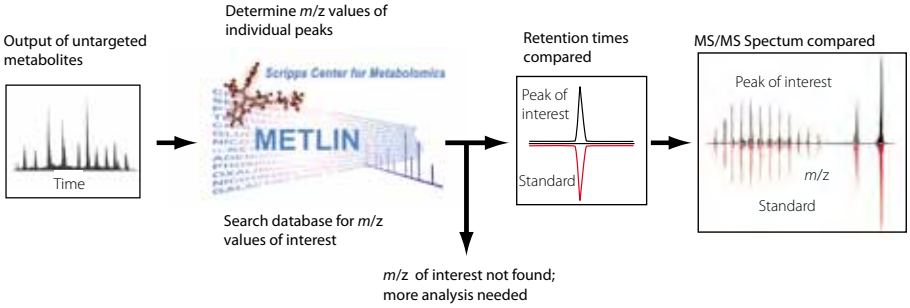
Metabolomics Analysis and the METLIN Metabolite Database

Melissa Fields, Product Specialist

Metabolomics is an emerging field in "-omics" research and has been gaining momentum as a discovery platform in pharmaceutical and diagnostic research. In fact, most biomarkers are metabolites and have been used for decades to assess disease or disease risk.[1] Identifying novel metabolite biomarkers and discerning their biological roles are essential to discovering new methods for disease diagnosis as well as identifying new therapeutic targets. With technological advancements in analytical instrumentation and methods, the ability to rapidly measure thousands of metabolites within a single sample has now been realized.

Metabolomics analyses generally employ one of two approaches: targeted or untargeted metabolomics. Targeted metabolomic analysis involves the measurement of specific known metabolites in a sample, usually within a defined pathway or related group of compounds. This approach can be useful to screen for a group of metabolites implicated as signals for disease, such as diabetes, or to screen newborns for inborn errors in metabolism.

Untargeted metabolomic analysis is global in scope and provides an unbiased metabolic profile of both known and unknown metabolites within a sample.[2] This technique is used in a broad range of applications, including nutritional assessments and the investigation into biomarkers for disease and toxicological effects.[3] The untargeted metabolomic method can generate extremely large amounts of data, which require software programs and databases for processing. Using bioinformatics software such as XCMS to detect and align features of the LC/MS data can help simplify the process.[4] Any feature of interest is identified by searching the m/z value of the compound in a database, such as METLIN. A database match should be confirmed by comparison of retention times and MS/MS data to a standard compound.[2]



The Untargeted Metabolomic Workflow

The workflow involves determining the *m/z* values for peaks within a biological sample, then searching METLIN for the *m/z* value of interest. Once the peak of interest is identified, comparison of retention times and tandem MS to a standard compound is required.

The METLIN Metabolite Database was created in 2004 through the efforts of Dr. Gary Siuzdak and his lab at the Scripps Center for Metabolomics and Mass Spectrometry. METLIN is a freely accessible, web-based database to assist researchers in metabolite identification by providing metabolite structural information along with high-resolution tandem mass spectrometry (MS/MS) spectra.[5] METLIN currently contains over 64,000 compounds with annotations and structures, with corresponding MS/MS spectra available on >10,000 compounds.

Sigma Life Science is proud to be working together with the Scripps Center for Metabolomics to expand the library of tested metabolites within the METLIN Metabolite Database. The tandem mass spectrometry data generated by Scripps are available in the METLIN Metabolite Database and on Sigma product webpages. METLIN also provides links to Sigma metabolite pages to simplify the identification and ordering process of standard compounds.

For additional information on METLIN and the collaboration between Sigma and Scripps Center for Metabolomics, please visit **sigma.com/metlin**.

References

1. Likie, V., Metabolites: A novel platform for converging research on metabolism and metabolomics. *Metabolites*, **1,** 1-2 (2011).
2. Patti, G., *et al.* Innovation: Metabolomics: the apogee of the omics trilogy. *Nat. Rev. Mol. Cell Biol.*, **13(4),** 263-269 (2012).
3. Kamleh, M.A., *et al.* Metabolic profiling in disease diagnosis, toxicology and personalized healthcare. *Curr. Pharm. Biotechnol.* **12(7),** 976-995 (2011).
4. Tautenhahn, R., *et al.* XCMS Online: A web-based platform to process untargeted metabolomic data. *Anal. Chem.*, **84**, 5035-5039 (2012).
5. Smith, C.A., *et al.* METLIN: A metabolite mass spectral database. *Ther. Drug Monit.* **27(6),** 747-751 (2005).

Stable Isotope Labeled Bioactive Compounds

Stable isotope labeled compounds are used as internal standards for various MS techniques and within many applications. With chemical and ionization properties nearly identical to their unlabeled counterparts, stable isotope labeled compounds are often considered the top choice for an internal standard. Furthermore, the labeled standard and the analyte of interest can be easily differentiated by the mass shift between the two compounds, which is ideally three or more units.[1]

Although availability is a significant challenge surrounding the use of stable isotope labeled standards, ISOTEC Stable Isotopes offers a large selection of labeled products suitable for this purpose. Labeled standards have been utilized within numerous applications, including quantification of cholesterol in a clinical setting,[2] vitamin D within baby formula,[3] and B vitamins in human milk.[4] Labeled internal standards have also been employed in research on the diagnosis of Graves disease[5] and hypertension,[6] the study of fatty acid oxidation,[7] and the analysis of androgenic steroids in wastewater.[8]

MS standards from ISOTEC have high chemical and isotopic purities with labeling patterns including ^{13}C, ^{15}N, and deuterium. The ^{13}C and/or ^{15}N labels do not exchange within the mass spectrometer source, providing further advantage.[1]

Visit **aldrich.com/isotec** to find additional stable isotope labeled standards.

References

1. Vogeser, M. and Seger, C., Pitfalls associated with the use of liquid chromatography-tandem mass spectrometry in the clinical laboratory. *Clin. Chem.*, **56**, 1234-1244 (2010).
2. Edwards, S.H., *et al.*, Proposed serum cholesterol reference measurement procedure by gas chromatography-isotope dilution mass spectrometry. *Clin. Chem.*, **57**, 614-622 (2011).
3. Sullivan, D., Infant formula and adult/pediatric nutritional methods approved First Action using the AOAC voluntary consensus standards process. *J. AOAC Int.*, **95**, 1-4 (2012).
4. Hampel, D., *et al.*, Ultra-performance liquid chromatography tandem mass-spectrometry (UPLC-MS/MS) for rapid, simultaneous analysis of thiamin, riboflavin, flavin adenine dinucleotide, nicotinamide and pyridoxal in human milk. *J. Chromatogr. B*, **903**, 7-13 (2012).
5. Higashi, T., *et al.*, Stable isotope-dilution liquid chromatography/tandem mass spectrometry method for determination of thyroxine in saliva. *J. Chromatogr. B*, **879,** 1013-1017 (2011).
6. Taylor, P.J., *et al.*, Measurement of aldosterone in human plasma by semiautomated HPLC-tandem mass spectrometry. *Clin. Chem.*, **55**, 1155-1162 (2009).
7. Mohammad, M.A., *et al.*, Galactose promotes fat mobilization in obese lactating and nonlactating women. *Am. J. Clin. Nutr.*, **93**, 374-381 (2011).
8. Backe, W.J., *et al.*, Analysis of androgenic steroids in environmental waters by large-volume injection liquid chromatography tandem mass spectrometry. *Anal. Chem.*, **83**, 2622-2630 (2011).

Caffeine and Caffeine Metabolites

Name	Isotopic Purity	Assay	Cat. No.
5-Acetylamino-6-amino-3-methyluracil-(*ring*-$^{13}C_4$,$^{15}N_2$, *amino*-^{15}N)	98 atom % ^{15}N 99 atom % ^{13}C	98% (CP)	**705578-1MG** **705578-5MG**
Caffeine-(*trimethyl*-$^{13}C_3$)	99 atom % ^{13}C	99% (CP)	**485365-1G**
Caffeine-(*trimethyl*-d_9)	99 atom % D	99% (CP)	**725625**
1,3-Dimethyluric acid-2,4,5,6-$^{13}C_4$-1,3,9-$^{15}N_3$	98 atom % ^{15}N 99 atom % ^{13}C	98% (CP)	**705632-1MG** **705632-5MG**
1,7-Dimethyluric acid-2,4,5,6-$^{13}C_4$-1,3,9-$^{15}N_3$	98 atom % ^{15}N 99 atom % ^{13}C	98% (CP)	**705640-1MG** **705640-5MG**
1,7-Dimethylxanthine-2,4,5,6-$^{13}C_4$-1,3,9-$^{15}N_3$	99 atom % ^{13}C 98 atom % ^{15}N	98% (CP)	**705381-2MG** **705381-5MG**
1,7-Dimethylxanthine-(*dimethyl*-d_6)	98 atom % D	98% (CP)	**705373-2MG** **705373-5MG**
3,7-Dimethylxanthine-(*dimethyl*-d_6)	98 atom % D	98% (CP)	**705357-2MG** **705357-5MG**
3-Methyluric acid-2,4,5,6-$^{13}C_4$, 1,3,9-$^{15}N_3$	98 atom % ^{15}N 99 atom % ^{13}C	98% (CP)	**705616-2MG** **705616-5MG**
7-Methyluric acid-2,4,5,6-$^{13}C_4$, 1,3,9-$^{15}N_3$	98 atom % ^{15}N 99 atom % ^{13}C	97% (CP)	**705624-2MG** **705624-5MG**
1-Methylxanthine-2,4,5,6-$^{13}C_4$, 1,3,9-$^{15}N_3$	99 atom % ^{13}C 98 atom % ^{15}N	98% (CP)	**705195-2MG** **705195-5MG**
3-Methylxanthine-2,4,5,6-$^{13}C_4$, 1,3,9-$^{15}N_3$	98 atom % ^{15}N 99 atom % ^{13}C	98% (CP)	**705217-2MG** **705217-5MG**

Caffeine and Caffeine Metabolites (continued)

Name	Isotopic Purity	Assay	Cat. No.
1-Methylxanthine-(*methyl*-$^{13}C,d_3$)	99 atom % ^{13}C 98 atom % D	97% (CP)	705209-1MG 705209-5MG
7-Methylxanthine-2,4,5,6-$^{13}C_4$, 1,3-$^{15}N_2$ (partial ^{15}N labeling at N_9)	99 atom % ^{13}C 98 atom % ^{15}N (based on $^{15}N_2$)	98% (CP)	705225-2MG 705225-5MG
1,3,7-Trimethyluric acid-2,4,5,6-$^{13}C_4$-1,3,9-$^{15}N_3$	99 atom % ^{13}C 98 atom % ^{15}N	98% (CP)	705667-2MG 705667-5MG

Carbohydrates

Name	Isotopic Purity	Assay	Cat. No.
D-Fructose-$^{13}C_6$	99 atom % ^{13}C	99% (CP)	587621-500MG
D-Glucose-1,2,3-$^{13}C_3$	99 atom % ^{13}C	99% (CP)	720127
D-Mannitol-$^{13}C_6$	99 atom % ^{13}C	99% (CP)	605492
D-Ribose-2,3,4,5-$^{13}C_4$	99 atom % ^{13}C	99% (CP)	605484
D-Sorbitol-$^{13}C_6$	99 atom % ^{13}C	99% (CP)	605514
Sucrose-$^{13}C_{12}$	99 atom % ^{13}C	99% (CP)	605417-100MG
α,α–Trehalose-$^{13}C_{12}$	99 atom % ^{13}C	99% (CP)	738921
Xylitol-$^{13}C_5$	99 atom % ^{13}C	98% (CP)	740934
D-Xylose-$^{13}C_5$	98 atom % ^{13}C	99% (CP)	666378

Fatty Acids

Name	Isotopic Purity	Assay	Cat. No.
Arachidonic-5,6,8,9,11,12,14,15-d_8 acid	(Minimum 7.45 D per molecule)	98% (CP)	735000-5MG 735000-10MG 735000-50MG 735000-100MG
Butyric acid-$^{13}C_4$	99 atom % ^{13}C	99% (CP)	723894
Decanoic-10,10,10-d_3 acid	99 atom % D	99% (CP)	616125
cis-4,7,10,13,16,19-Docosahexaenoic-21,21,22,22,22-d_5 acid	(Minimum 5D/molecule, Partial deuteration on C_{20})	98% (CP)	733326-1MG 733326-5MG
cis-5,8,11,14,17-Eicosapentaenoic acid-19,19,20,20,20-d_5	(Minimum 5D per molecule, Partial deuteration on C_{18})	98% (CP)	734322-1MG 734322-5MG
Heptanoic-5,6,7-$^{13}C_3$ acid	99 atom % ^{13}C	98% (CP)	606499
Heptanoic-d_{13} acid	98 atom % D	99% (CP)	617040
trans-9-Hexadecenoic acid-1,2,3,7,8-$^{13}C_5$	99 atom % ^{13}C	95% (CP)	722774
6-Hydroxyhexanoic acid-$^{13}C_6$	99 atom % ^{13}C	95% (CP)	750875
Lauric-d_{23} acid	98 atom % D	99% (CP)	451401-1G
Linoleic acid-$^{13}C_{18}$	99 atom % ^{13}C	97% (CP)	605735-100MG
Myristic acid-1,2-$^{13}C_2$	99 atom % ^{13}C	99% (CP)	490865-500MG
Myristic acid-13,13,14,14,14-d_5	98 atom % D	99% (CP)	614165
Myristic acid-$^{13}C_{14}$	99 atom % ^{13}C	99% (CP)	605689
Myristic-d_{27} acid	98 atom % D	99% (CP)	366889-1G
trans-6-Octadecenoic acid-1,2,3,4,5-$^{13}C_5$	99 atom % ^{13}C	97% (CP)	722847
trans-9-Octadecenoic acid-1,2,3,7,8-$^{13}C_5$	99 atom % ^{13}C	95% (CP)	722790
trans-11-Octadecenoic acid-1,2,3,9,10-$^{13}C_5$	99 atom % ^{13}C	97% (CP)	722855
Octanoic acid-1,2,3,4-$^{13}C_4$	99 atom % ^{13}C	99% (CP)	493163-1G
Octanoic acid-$^{13}C_8$	99 atom % ^{13}C	99% (CP)	605727
Octanoic acid-8,8,8-d_3	99 atom % D	99% (CP)	616095
Octanoic-d_{15} acid	98 atom % D	99% (CP)	448214-1G
Oleic acid-1,2,3,7,8-$^{13}C_5$	99 atom % ^{13}C	99% (CP)	749079
Oleic acid-1,2,3,7,8,9,10-$^{13}C_7$	99 atom % ^{13}C	96% (CP)	646458
Oleic acid-$^{13}C_{18}$	99 atom % ^{13}C	99% (CP)	490431-100MG
Palmitic acid-1,2,3,4-$^{13}C_4$	99 atom % ^{13}C	99% (CP)	489611-1G
Palmitic acid-5,6,7,8-$^{13}C_4$	99 atom % ^{13}C	99% (CP)	605700
Palmitic acid-15,15,16,16,16-d_5	98 atom % D	99% (CP)	616109

Fatty Acids (continued)

Name	Isotopic Purity	Assay	Cat. No.
Palmitic acid-$^{13}C_{16}$	99 atom % ^{13}C	99% (CP)	605573-100MG
Palmitic acid-d_{31}	98 atom % D	99% (CP)	366897-100MG 366897-1G
Palmitoleic acid-$^{13}C_{16}$	99 atom % ^{13}C	97% (CP)	724173
Potassium oleate-1,2,3,7,8-$^{13}C_5$	99 atom % ^{13}C	98% (CP)	739693
Potassium palmitate-$^{13}C_{16}$	99 atom % ^{13}C	99% (CP)	605751
Stearic acid-$^{13}C_{18}$	99 atom % ^{13}C	99% (CP)	605581-100MG
Stearic acid-18,18,18-d_3	98 atom % D	99% (CP)	490393-250MG
Stearic-d_{35} acid	98 atom % D	99% (CP)	448249-250MG 448249-1G
Valeric acid-3,4,5-$^{13}C_3$	99 atom % ^{13}C	98% (CP)	637122

Fatty Acid Derivatives

Name	Isotopic Purity	Assay	Cat. No.
Cholesteryl linoleate-$^{13}C_{18}$	99 atom % ^{13}C	95% (CP)	729663
Cholesteryl-26,26,26,27,27,27-d_6 linoleate	98 atom % D	97% (CP)	729515
Cholesteryl oleate-$^{13}C_{18}$	99 atom % ^{13}C	95% (CP)	729523
Cholesteryl-26,26,26,27,27,27-d_6 oleate-1,2,3,7,8,9,10-$^{13}C_7$	98 atom % D 99 atom % ^{13}C	97% (CP)	729671
rac-Glyceryl-2,3-di(oleate-$^{13}C_{18}$)-1-palmitate	99 atom % ^{13}C	95% (CP)	741388
rac-Glyceryl-d_5-2,3-dioleate-1-palmitate	98 atom % D	95% (CP)	730076
rac-Glyceryl-d_5-2-linoleate-3-oleate-1-palmitate	98 atom % D	95% (CP)	730068
Glyceryl 1-oleate-$^{13}C_{18}$-2,3-dioleate	99 atom % ^{13}C	97% (CP)	741086
rac-Glyceryl-2-oleate-$^{13}C_{18}$-3-oleate-1-palmitate	99 atom % ^{13}C	95% (CP)	741124
Glyceryl-d_5 trilinoleate	98 atom % D	97% (CP)	729507
Glyceryl tri(octanoate-d_{15})	98 atom % D	99% (CP)	617121
Glyceryl-$^{13}C_3$ trioleate	99 atom % ^{13}C	99% (CP)	605638-500MG
Glyceryl tri(palmitate-1-^{13}C)	99 atom % ^{13}C	99% (CP)	425907-1G
Glyceryl tri(palmitate-d_{31})	98 atom % D	99% (CP)	616966
Glyceryl tri(palmitate-d_{31})	98 atom % D	99% (CP)	660698
2-Linoleoyl-1-palmitoyl-*rac*-glycero-3-phosphocholine-(*trimethyl*-d_9)	98 atom % D	95% (CP)	730033
2-Oleoyl-1-palmitoyl-*rac*-glycero-3-phosphocholine-(*trimethyl*-d_9)	98 atom % D	97% (CP)	730041
1-Palmitoyl-2-stearoyl-*rac*-glycero-3-phosphocholine (trimethyl-d_9)	98 atom % D	97% (CP)	749176

Steroids and Hormones

Name	Isotopic Purity	Assay	Cat. No.
Aldosterone-2,2,4,6,6,21,21-d_7	(variable deuteration on C17) 98 atom % D (based on d_7)	98% (CP)	706035-1MG 706035-2MG 706035-5MG
4-Androstene-3,17-dione-2,3,4-$^{13}C_3$ solution	98 atom % ^{13}C	98% (CP)	730645-1ML
Chenodeoxycholic acid-2,2,4,4-d_4	98 atom % D	98% (CP)	614122-500MG
Cholesterol-2,2,3,4,4,6-d_6	97 atom % D	98% (CP)	488577-100MG
Cholesterol-2,3,4-$^{13}C_3$	99 atom % ^{13}C	98% (CP)	749478-2MG 749478-5MG
Cholesterol-25,26,27-$^{13}C_3$	99 atom % ^{13}C	99% (CP)	707678
Cholesterol-26,26,26,27,27,27-d_6	98 atom % D	97% (CP)	679046
Cholic acid-2,2,3,4,4-d_5	98 atom % D	98% (CP)	614106
Cholic acid-2,2,4,4-d_4	98 atom % D	98% (CP)	614149-500MG
Cortisone-2,2,4,6,6,12,12-d_7	97 atom % D	98% (CP)	705586-5MG
Dehydroepiandrosterone-2,2,3,4,4,6-d_6	85 atom % D	98% (CP)	709549-5MG 709549-10MG
Dehydroepiandrosterone-2,2,3,4,4,6-d_6 sulfate sodium salt	85 atom % D (Min. 5D/molecule)	98% (CP)	723266-1MG 723266-5MG 723266-10MG

Steroids and Hormones (continued)

Name	Isotopic Purity	Assay	Cat. No.
Deoxycholic acid-2,2,4,4-d_4	98 atom % D	98% (CP)	**614130**
11-Deoxycortisol-2,2,4,6,6-d_5	98 atom % D	-	**710784-1MG** **710784-5MG**
Dihydrotestosterone-2,3,4-$^{13}C_3$ solution	99 atom % ^{13}C	98% (CP)	**730637-1ML**
3, 3′-Diiodo-L-thyronine-(*phenoxy*-$^{13}C_6$) (T2)	99 atom % ^{13}C	97% (CP)	**719528-1MG** **719528-5MG** **719528-10MG**
3,3′-Diiodo-L-thyronine (T2)	-	98% (CP)	**719536-1MG** **719536-5MG** **719536-10MG**
17β-Estradiol-2,3,4-$^{13}C_3$	99 atom % ^{13}C	98% (CP)	**719552-1MG** **719552-5MG** **719552-10MG**
17β-Estradiol-2,4,16,16,17-d_5	97 atom % D	-	**613967**
Estriol-2,3,4-$^{13}C_3$	99 atom % ^{13}C	98% (CP)	**731668-100UG** **731668-250UG** **731668-500UG** **731668-1000UG**
Estrone-2,3,4-$^{13}C_3$	99 atom % ^{13}C	98% (CP)	**719544-1MG** **719544-5MG** **719544-10MG**
Glycocholic-2,2,4,4-d_4 acid	98 atom % D	98% (CP)	**739723**
Hydrocortisone-9,11,12,12-d_4	98 atom % D	98% (CP)	**705594-5MG** **705594-10MG**
16-α-Hydroxyestrone-2,3,4-$^{13}C_3$	99 atom % ^{13}C	98% (CP)	**731641-100UG** **731641-250UG** **731641-500UG** **731641-1000UG**
17α-Hydroxyprogesterone-2,3,4-$^{13}C_3$	98 atom % ^{13}C	98% (CP)	**738093-1MG** **738093-5MG**
3-Iodothyronamine-(*ethylamino*-1,1,2,2-d_4) hydrochloride	98 atom % D	98% (CP)	**709557-1MG**
4-Methoxy-^{13}C,d_3-estradiol	98 atom % D 99 atom % ^{13}C	98% (CP)	**705713-1MG**
2-Methoxy-^{13}C,d_3-estradiol	98 atom % D 99 atom % ^{13}C	98% (CP)	**705829-1MG**
2-Methoxy-^{13}C,d_3-estrone	98 atom % D 99 atom % ^{13}C	98% (CP)	**705705-1MG**
4-Methoxy-^{13}C,d_3-estrone	99 atom % ^{13}C 98 atom % D	98% (CP)	**705691-1MG**
Pregnenolone-20,21-$^{13}C_2$-16,16-d_2	99 atom % ^{13}C 98 atom % D	98% (CP)	**739545-1MG** **739545-5MG**
Pregnenolone-20,21-$^{13}C_2$-16,16-d_2 sulfate sodium salt	99 atom % ^{13}C 98 atom % D	98% (CP)	**740985-1MG** **740985-5MG**
Progesterone-2,3,4-$^{13}C_3$	99 atom % ^{13}C	98% (CP)	**737143-1MG** **737143-5MG**
Testosterone-2,3,4-$^{13}C_3$ solution	99 atom % ^{13}C	98% (CP)	**730610-1ML**
3α,5β-Tetrahydroaldosterone	-	98% (CP)	**750026-1MG** **750026-5MG**
3,3′,5′-Triiodothyronine-(*diiodophenyl*-$^{13}C_6$) hydrochloride	99 atom % ^{13}C	95% (CP)	**709719-1MG** **709719-5MG**
3,3′,5-Triiodothyronine-(*tyrosine ring*-$^{13}C_6$) hydrochloride	99 atom % ^{13}C	95% (CP)	**709611-1MG** **709611-5MG**

To inquire about Stable Isotopes pricing and availability, email us at **isosales@sial.com.**

Vitamins

Name	Isotopic Purity	Assay	Concentration	Cat. No.
Biotin-(*ring*-6,6-d_2)	98 atom % D	97% (CP)	-	**705268-5MG** **705268-10MG**
1α,25-Dihydroxyvitamin D_2 solution	-	98% (CP)	5 µg/mL in ethanol	**739901-1ML**
1α,25-Dihydroxyvitamin D_2 solution	-	95% (CP)	50 µg/mL in ethanol	**739898-1ML**
1α,25-Dihydroxyvitamin D_2 solution	-	98% (CP)	100 µg/mL in ethanol	**739677-1ML**
1α,25-Dihydroxyvitamin D_2 (6,19,19-d_3) solution	99 atom % D	95% (CP)	5 µg/mL in ethanol	**739855-1ML**
1α,25-Dihydroxyvitamin D_2 (6,19,19-d_3) solution	99 atom % D	95% (CP)	50 µg/mL in ethanol	**739863-1ML**
1α,25-Dihydroxyvitamin D_2 (6,19,19-d_3) solution	99 atom % D	95% (CP)	100 µg/mL in ethanol	**739871-1ML**
1α,25-Dihydroxyvitamin D_3 (6,19,19-d_3)	97 atom % D	96% (CP)	-	**705942-1MG**
1α,25-Dihydroxyvitamin D_3 (6,19,19-d_3) solution	97 atom % D	96% (CP)	5 µg/mL in ethanol	**740551-1ML**
1α,25-Dihydroxyvitamin D_3 (6,19,19-d_3) solution	97 atom % D	96% (CP)	50 µg/mL in ethanol	**740543-1ML**
1α,25-Dihydroxyvitamin D_3 (6,19,19-d_3) solution	97 atom % D	96% (CP)	100 µg/mL in ethanol	**740578-1ML**
3-*epi*-25-Hydroxyvitamin D_3	-	98% (CP)	-	**705993-1MG**
3-*epi*-25-Hydroxyvitamin D_3 solution	-	98% (CP)	50 µg/mL in ethanol	**739928-1ML**
3-*epi*-25-Hydroxyvitamin D_3 solution	-	98% (CP)	100 µg/mL in ethanol	**739936-1ML**
3-*epi*-25-Hydroxyvitamin D_3 (6,19,19-d_3)	98 atom % D	98% (CP)	-	**751316-1MG**
3-*epi*-25-Hydroxyvitamin D_3 (6,19,19-d_3) solution	98 atom % D	98% (CP)	50 µg/mL in ethanol	**751324-1ML**
3-*epi*-25-Hydroxyvitamin D_3 (6,19,19-d_3) solution	98 atom % D	98% (CP)	100 µg/mL in ethanol	**751332-1ML**
25-Hydroxyvitamin D_2 solution	-	98% (CP)	5 µg/mL in ethanol	**740233-1ML**
25-Hydroxyvitamin D_2 solution	-	98% (CP)	50 µg/mL in ethanol	**740225-1ML**
25-Hydroxyvitamin D_2 solution	-	98% (CP)	100 µg/mL in ethanol	**740217-1ML**
25-Hydroxyvitamin D_2 (6,19,19-d_3)	97 atom % D	98% (CP)	-	**705497-1MG**
25-Hydroxyvitamin D_2 (6,19,19-d_3) solution	97 atom % D	98% (CP)	5 µg/mL in ethanol	**740209-1ML**
25-Hydroxyvitamin D_2 (6,19,19-d_3) solution	97 atom % D	98% (CP)	50 µg/mL in ethanol	**740195-1ML**
25-Hydroxyvitamin D_2 (6,19,19-d_3) solution	97 atom % D	98% (CP)	100 µg/mL in ethanol	**740071-1ML**
25-Hydroxyvitamin D_2 (25,26,27-$^{13}C_3$) solution	99 atom % ^{13}C	98% (CP)	50 µg/mL in ethanol	**752266-1ML**
25-Hydroxyvitamin D_2 (25,26,27-$^{13}C_3$) solution	99 atom % ^{13}C	98% (CP)	100 µg/mL in ethanol	**752258-1ML**
25-Hydroxyvitamin D_3 solution	-	98% (CP)	5 µg/mL in ethanol	**739669-1ML**
25-Hydroxyvitamin D_3 solution	-	98% (CP)	50 µg/mL in ethanol	**739642-1ML**
25-Hydroxyvitamin D_3 solution	-	98% (CP)	100 µg/mL in ethanol	**739650-1ML**
25-Hydroxyvitamin D_3 (6,19,19-d_3)	97 atom % D	98% (CP)	-	**705888-1MG**
3-*epi*-25-Hydroxyvitamin D_2	-	98% (CP)	-	**753149-1MG**
3-*epi*-25-Hydroxyvitamin D_2 solution	-	98% (CP)	50 µg/mL in ethanol	**753548-1ML**
3-*epi*-25-Hydroxyvitamin D_2 solution	-	98% (CP)	100 µg/mL in ethanol	**753556-1ML**
25-Hydroxyvitamin D_3 (6,19,19-d_3) solution	97 atom % D	98% (CP)	5 µg/mL in ethanol	**739626-1ML**
25-Hydroxyvitamin D_3 (6,19,19-d_3) solution	97 atom % D	98% (CP)	50 µg/mL in ethanol	**739618-1ML**
25-Hydroxyvitamin D_3 (6,19,19-d_3) solution	97 atom % D	98% (CP)	100 µg/mL in ethanol	**739596-1ML**
Pyridoxal-(*methyl*-d_3) hydrochloride	98 atom % D	98% (CP)	-	**705187-1MG** **705187-5MG**
Pyridoxamine-methyl-d_3 dihydrochloride	98 atom % D	98% (CP)	-	**705322-1MG** **705322-5MG**
Riboflavin-dioxopyrimidine-$^{13}C_4$,$^{15}N_2$	98 atom % ^{15}N 99 atom % ^{13}C	97% (CP)	-	**705292-1MG** **705292-5MG**
Thiamine-(*4-methyl*-^{13}*C-thiazol-5-yl*-$^{13}C_3$) hydrochloride	99 atom % ^{13}C	98% (CP)	-	**731188-2MG** **731188-5MG** **731188-10MG**
α-Tocopherol-(*ring-5,7-dimethyl*-d_6)	98 atom % D	98% (CP)	-	**731234-2MG** **731234-5MG** **731234-10MG**
Vitamin B_5 (*di*-β-*alanine*-$^{13}C_6$,$^{15}N_2$) calcium salt	98 atom % ^{15}N 99 atom % ^{13}C	97% (CP)	-	**705837-5MG** **705837-10MG** **705837-20MG**
Vitamin D_2 solution	-	98% (CP)	100 µg/mL in ethanol	**740306-1ML**
Vitamin D_2 (6,19,19-d_3) solution	97 atom % D	98% (CP)	100 µg/mL in ethanol	**739847-1ML**

Vitamins (continued)

Name	Isotopic Purity	Assay	Concentration	Cat. No.
Vitamin D_2 (6,19,19-d_3) solution	97 atom % D	98% (CP)	1 mg/mL in ethanol	**739839-1ML**
Vitamin D_3 solution	-	98% (CP)	100 µg/mL in ethanol	**740292-1ML**
Vitamin D_3(6,19,19-d_3) solution	97 atom % D	97% (CP)	100 µg/mL in ethanol	**740284-1ML**
Vitamin D_3(6,19,19-d_3) solution	97 atom % D	97% (CP)	1 mg/mL in ethanol	**731285-1ML**
Vitamin D_2 (6,19,19-d_3)	97 atom % D	98% (CP)	-	**705489-1MG**
Vitamin E acetate-(*trimethyl*-d_9)	98 atom % D	98% (CP)	-	**615366**
Vitamin K-d_7*(5,6,7,8*-d_4, *2-methyl*-d_3*)*	98 atom % D	98% (CP Sum of E & Z Isomers)	-	**705470-1MG** **705470-5MG**
Vitamin K_3-d_8	98 atom % D	97% (CP)	-	**737836-50MG**

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Reference

1. Ciccimaro, E. and Blair, I.A. Stable-isotope dilution LC-MS for quantitative biomarker analysis. *Bioanalysis,* **2(2),** 311-341(2010).

Name	Isotopic Purity	Assay	Cat. No.
Fmoc-Ala-OH-^{15}N	98 atom % ^{15}N	99% (CP)	**489905-1G**
Fmoc-Ala-OH-$^{13}C_3$	99 atom % ^{13}C	99% (CP)	**605131-1G**
Fmoc-Ala-OH, $^{13}C_3$,^{15}N	99 atom % ^{13}C 98 atom % ^{15}N	99% (CP)	**667064**
Fmoc-Ala-OH-3,3,3-d_3	99 atom % D	99% (CP)	**485888-1G**
Fmoc-Arg(Pbf)-OH-$^{13}C_6$,$^{15}N_4$	98 atom % ^{15}N 98 atom % ^{13}C	97% (CP)	**653659**
Fmoc-Asn(Trt)-OH-$^{13}C_4$, $^{15}N_2$	98 atom % ^{15}N 99 atom % ^{13}C	95% (CP)	**668753**
Fmoc-Asp(OtBu)-OH-$^{13}C_4$,^{15}N	98 atom % ^{13}C 98 atom % ^{15}N	97% (CP)	**683639**
Fmoc-Gln-(Trt)-OH-$^{13}C_5$,$^{15}N_2$	98 atom % ^{15}N 98 atom % ^{13}C	97% (CP)	**663956**
Fmoc-Gly-OH-1-^{13}C	99 atom % ^{13}C	99% (CP)	**605182-1G**
Fmoc-Ile-OH-^{15}N	98 atom % ^{15}N	99% (CP)	**578622-250MG**
Fmoc-Ile-OH-$^{13}C_6$,^{15}N	98 atom % ^{15}N 98 atom % ^{13}C	98% (CP)	**597228-250MG**
Fmoc-Leu-OH-^{15}N	98 atom % ^{15}N	98% (CP)	**485950-1G**
Fmoc-Lys(Boc)-OH-$^{13}C_6$,$^{15}N_2$	98 atom % ^{13}C 98 atom % ^{15}N	97% (CP)	**653632**
Fmoc-Phe-OH-$^{13}C_9$,^{15}N	98 atom % ^{13}C 98 atom % ^{15}N	98% (CP)	**651443-100MG** **651443-500MG**
Fmoc-Pro-OH-$^{13}C_5$,^{15}N	98 atom % ^{15}N 98 atom % ^{13}C	99% (CP)	**651451**
Fmoc-Ser(*t*Bu)-OH-^{15}N	98 atom % ^{15}N	99% (CP)	**609145-100MG**
Fmoc-Ser(tBu)-OH-$^{13}C_3$,^{15}N	99 atom % ^{13}C 98 atom % ^{15}N	99% (CP)	**658928**
Fmoc-Thr(tBu)-OH-^{15}N	98 atom % ^{15}N	99% (CP)	**658162**
Fmoc-Tyr (t-Bu)-OH-$^{13}C_9$,^{15}N	98 atom % ^{15}N 98 atom % ^{13}C	97% (CP)	**658898**
Fmoc-Val-OH-$^{13}C_5$,^{15}N	98 atom % ^{13}C 98 atom % ^{15}N	99% (CP)	**642886**

To inquire about Stable Isotopes pricing and availability, email us at **isosales@sial.com.**

Sample Cleanup

Supel-Tips Pipette Tips

The Supel-Tips SPE product line is designed for the micro-scale extraction, concentration, and recovery of small molecules and biological macromolecules. These 10 µL polypropylene pipette tips contain a sorbent bed bonded at the working end of the tip using an inert high-purity adhesive. The bed acts as a solid phase extraction (SPE) medium to adsorb molecules of interest from the sample matrix. Subsequently, the concentrated and desalted analytes are eluted for downstream analysis.

Supel-Tips offer:

- Superior recovery
- Exceptional binding capacity and enhanced affinity
- Excellent sorbent bed stability for cleaner samples
- Fast and effective analyte retention/elution

Supel-Tips Zr or Ti Pipette Tips

Application: microextraction of phosphopeptides and other phosphate-containing molecules

- Stationary Phase: Zirconia-silica or Titania-silica composite
- Particle Size: 50-60 µm
- Pore Size: 300 Å
- Capacity: 1 µg monophosphopeptide-1

Supel-Tips C18 Pipette Tips

Application: microextraction and desalting of peptides and proteins

- Stationary Phase: C18 bonded onto spherical silica
- Particle Size: 50-60 µm
- Pore Size: 200 Å
- Capacity: 17 µg Insulin chain B, oxidized; 17 µg β-Amyloid; 7.6 µg Bradykinin fragment 1-7

Supel-Tips Carbon Pipette Tips

Application: microextraction of oligosaccharides and other sugar-containing macromolecules

- Stationary Phase: graphitized carbon adsorbent
- Particle Size: 50-60 µm
- Pore Size: 175 Å
- Capacity: 10.2 µg Maltohexose; >10 µg Glycopeptide (mol. wt. 1300-3500)

	Qty.	Cat. No.
Supel-Tips Zr Pipette Tips		
volume 10 µL	96 ea	**54266-U**
Supel-Tips Ti Pipette Tips		
volume 10 µL	96 ea	**54263-U**
Supel-Tips C18 Pipette Tips		
C18 bonded on spherical silica, endcapped, volume 10 µL	96 ea	**TPSC18-96EA**
Supel-Tips Carbon Pipette Tips		
volume 10 µL	96 ea	**54227-U**

ZipTips

Ziptip and Ziptip micro

The ZipTip is a 10 µL (P-10) pipette tip with a bed of chromatography medium fixed at its end such that there is no dead volume. It is intended for purifying and concentrating femtomoles to picomoles of protein, peptide, or oligonucleotide samples prior to analysis, providing better data quality. The sample is aspirated and dispensed through the ZipTip to bind, wash, and elute. Recovered samples are contaminant-free and eluted in 0.5-4 µL for direct transfer to a MS target or vial.

ZipTip C18 is a 10 µL pipette tip with a ~0.6 µL bed of chromatography medium fixed at its end to avoid dead volume. ZipTip Micro-C18 is a 10 µL pipette tip with a ~0.2 µL bed of chromatography medium fixed at its end such that there is no dead volume. Both are ideal for concentrating and purifying peptides, proteins or oligonucleotides in seconds prior to MS, HPLC, capillary electrophoresis and other analytical techniques.

	Qty.	Cat. No.
Millipore® Ziptips		
C18	8 ea	**Z720038-8EA**
C18	96 ea	**Z720070-96EA**
C18	960 ea	**Z720046-960EA**
Micro-C18	8 ea	**Z719986-8EA**
Micro-C18	96 ea	**Z720003-96EA**
Micro-C18	960 ea	**Z720011-960EA**

HybridSPE®-Phospholipid

HybridSPE-Phospholipid (HybridSPE-PL) combines the simplicity of protein precipitation with the selectivity of SPE for the targeted removal of phospholipids in biological plasma/serum (see **Figure 1**).

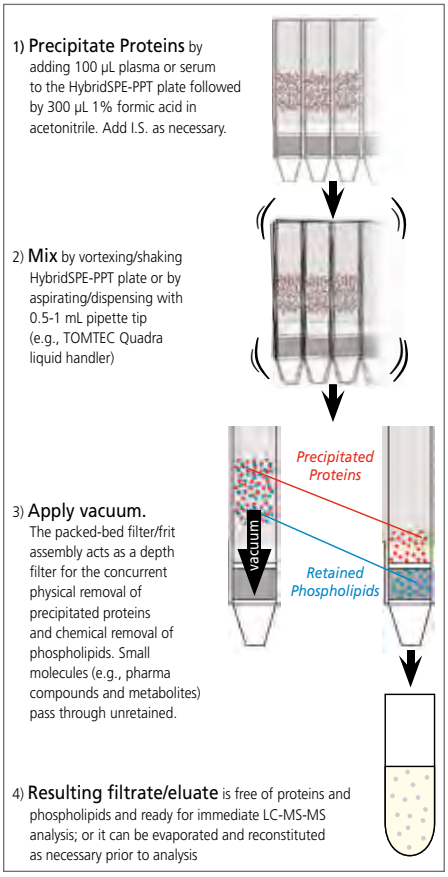


Figure 1. HybridSPE-PPT In-well Method for Targeted Phospholipid Removal from Plasma/Serum

The technology utilizes a zirconia-coated particle and exhibits selective affinity toward phospholipids while remaining non-selective towards a range of basic, acidic, and neutral compounds. The phospholipid retention mechanism is based on a highly selective Lewis acid-base interaction between the proprietary zirconia ions (functionally bonded to the HybridSPE stationary phase) and the phosphate moiety consistent with all phospholipids (see **Figure 2**).

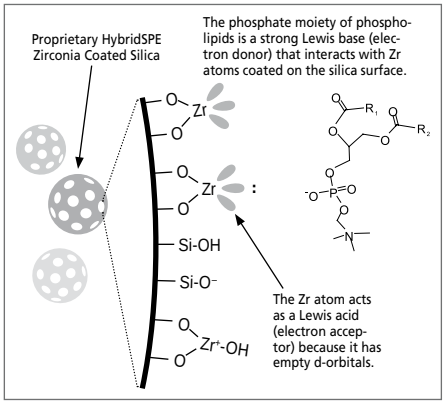


Figure 2. Lewis Acid-Base Interactions Between HybridSPE Zirconia Ions and Phospholipids

- Combines the simplicity of protein precipitation and selective SPE for targeted removal of phospholipids
- Typically >98% removal of phospholipids and precipitated proteins
- Minimal or no method development required

LC Accumulation of Phospholipids

With advances in LC-MS technology, many analysts are decreasing LC run time by incorporating ballistic gradients and sub-2 µm HPLC column particles. However, when coupled with standard protein precipitation methods (e.g., plasma:acetonitrile, 1:3 v/v), ballistic gradients are often inadequate at purging the column of phospholipids. As a result, phospholipids can build on the column, potentially changing the LC retention selectivity and eluting uncontrollably downstream in an injection run sequence, causing unpredictable ion-suppression effects and poor reproducibility. In addition, sub-2 µm HPLC columns are more prone to clogging than larger particle size columns (2.7-5.0 µm).

A series of reversed-phase gradient LC-MS injections was performed on samples after standard protein precipitation and on samples prepared using HybridSPE-PL. The phosphonate moiety of phospholipids (m/z 184) was monitored for performance.

The standard protein precipitation technique shows substantial phospholipid build-up after 20 injections (**Figure 3**, top panel). However, sample cleanup with HybridSPE-PL shows complete removal of phospholipids and no phospholipid build-up (**Figure 3**, middle panel).

Unlike traditional protein precipitation techniques that use centrifugation to remove precipitated proteins, HybridSPE-PL 96-well plates contain a series of filters that allows users to remove proteins and phospholipids concurrently, preventing phospholipid buildup on the LC column and reducing column backpressure (**Figure 3**, bottom panel).

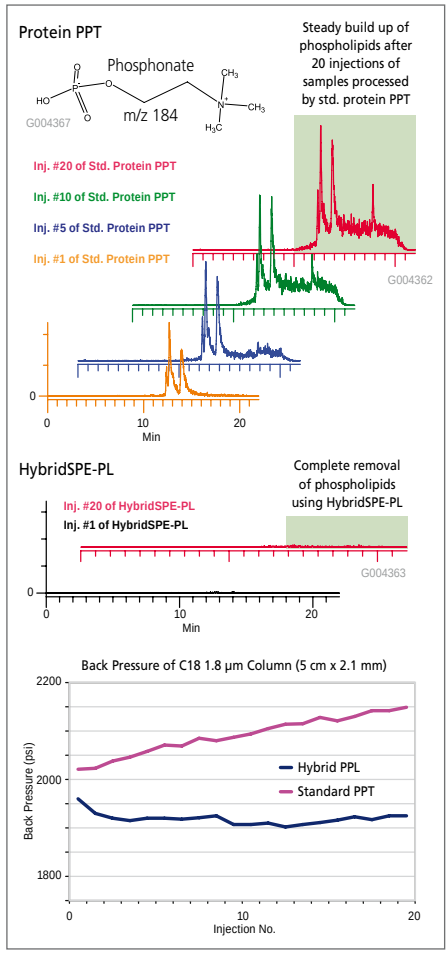


Figure 3. Comparative Gradient RP LC-MS of Blank Plasma Samples, Standard Protein Precipitation vs. HybridSPE-PL Treatment

Featured Products

	Qty.	Cat. No.
HybridSPE®-Phospholipid		
96-well Plate, volume 2 mL	1 ea	575656-U
96-well Plate, volume 2 mL	20 ea	575657-U
Cartridge, volume 1 mL	100 ea	55261-U
Cartridge, volume 1 mL	200 ea	55276-U
96-well Plate, volume 0.8 mL	1 ea	52794-U
96-well Plate, volume 0.8 mL	20 ea	52798-U
Cartridge, volume 6 mL	30 ea	55267-U
HybridSPE®-Phospholipid Ultra		
cartridge, volume 1 mL	100 ea	55269-U

Protein Precipitation

96-Well Protein Precipitation Filter Plate

The 96-well protein precipitation filter plate is ideal for removing precipitated proteins from biological plasma/serum. The plate consists of a 0.2 µm hydrophobic graded filter/frit. Biological plasma is first added to the 96-well plate followed by a protein precipitating agent (e.g., acetonitrile). After a brief mixing step, vacuum is applied to the plate, and the filter/frit removes precipitated proteins from the sample. The resulting filtrate is ready for further processing and/or analysis.

volume.....2 mL

55263-U	1 ea

Supel™ QuE for QuECHERS Method

The "QuEChERS" method (**Qu**ick, **E**asy, **Ch**eap, **E**ffective, **R**ugged, and **S**afe) has emerged as a sample prep technique popular in the area of multi-residue pesticide analysis in food and agricultural products.

In QuEChERS methodology, food/agricultural samples are first extracted with an aqueous miscible solvent (e.g., acetonitrile) in the presence of high amounts of salts (e.g., sodium chloride and magnesium sulfate) and/or buffering agents (e.g., citrate) to induce liquid phase separation and stabilize acid- and base-labile targets, respectively. Upon shaking and centrifugation, an aliquot of the organic phase is subjected to further cleanup using SPE. Unlike traditional methods using SPE tubes, in dispersive SPE, cleanup is facilitated by mixing bulk amounts of SPE (e.g., Supelclean™ PSA, ENVI-Carb™, and/or Discovery® DSC-18) with the extract. After sample cleanup, the mixture is centrifuged. The resulting supernatant can either be analyzed directly, or subjected to minor further treatment before analysis.

The Supel QuE line of vials and centrifuge tubes contains pre-determined amounts of salts and SPE sorbents to support the most common method configurations used today for QuEChERS.

Visit **sigma-aldrich.com/quechers** for more information and to view the complete line of QuEChERS products.

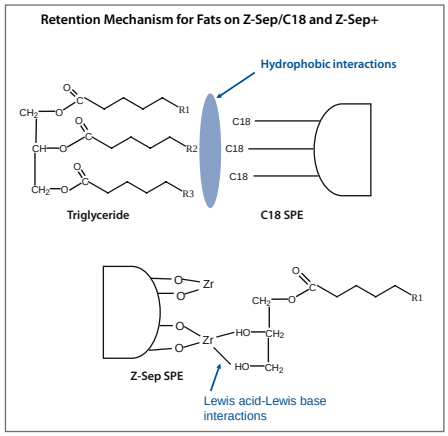
Supel QuE Z-Sep for Fat Removal in Difficult Matrices

The patented zirconia-coated silica particles of Supel QuE Z-Sep sorbents selectively remove more fat and color from sample extracts than traditional phases for QuEChERS methods. Lipid retention is based on two synergetic interactions:

- The interaction between the polar group of the lipid and the proprietary bonded ion-exchange group of the sorbent.
- The interaction between the hydrophobic chains of the lipid and the hydrophobic group of the sorbent (either that of the C18 or Z-Sep+).

Supel Z-Sep+ is recommended for cleanup of samples containing >15% fat. Z-Sep/C18 is generally preferred for samples containing <15% fat.

- Significantly diminishes fatty matrix interferences and various colors
- Provides more robust LC/MS and GC/MS methods by eliminating problematic matrix interferences
- Can replace C18 and PSA phases in current methods without additional method development



	Qty.	Cat. No.
Supel™ QuE		
Z-Sep/C18 Tube	100 ea	55284-U
Z-Sep+ Tube	50 ea	55296-U

LC-MS Columns

LC-MS Columns

As an integral part of Sigma-Aldrich, Supelco is a leading manufacturer of HPLC and UHPLC columns for the analysis of proteins and peptides. Products for biopolymer separations include such innovative and established brands as Ascentis® Express and Discovery® BIO for reversed phase and HILIC separations, and the industry-leading TSKgel® brand of columns for size exclusion, ion exchange, and hydrophobic interaction.

In addition to the columns listed here, find additional columns with different internal dimensions (ID) at **sigma.com/hplc**.

Ascentis® Express Technology

Ascentis Express Fused-Core® columns are high-speed HPLC columns based on a new particle design. The Fused-Core or core-shell particles consist of a thin porous shell of high-purity nano-sized silica particles surrounding a non-porous, silica core. This particle design exhibits very high column efficiency because of the shallow diffusion path in the 0.5 µm thick porous shell and the small overall particle size of 2.7 µm. Fused-Core particles have the same efficiency as smaller porous particles at half the back pressure, which makes it possible to use Ascentis Express columns in traditional HPLC as well as ultra-high pressure UHPLC systems. Ascentis Express columns are available with silica particles in 90 Å and 160 Å pore sizes.

Ascentis Express UHPLC Columns

90 Å pore size Ascentis Express columns are recommended for fast and efficient separations of low molecular weight compounds (<2000 Da), either by Reversed Phase or Hydrophilic Interaction Chromatography (HILIC).

Ascentis Express C18 Capillary HPLC Columns

L (cm)	I.D. (µm)	Pore Size (Å)	Cat. No.
particle size 2.7 µm			
5	75	90	**53982-U**
5	100	90	**53985-U**
5	200	90	**53989-U**
5	300	90	**53992-U**
5	500	90	**53998-U**
15	75	90	**54219-U**
15	100	90	**54256-U**
15	200	90	**54261-U**
15	300	90	**54271-U**
15	500	90	**54273-U**

Ascentis Express C18 Narrow Bore HPLC Columns

L (cm)	I.D. (mm)	Pore Size (Å)	Cat. No.
particle size 2.7 µm			
2	2.1	90	**53799-U**
3	2.1	90	**53802-U**
7.5	2.1	90	**53804-U**
5	2.1	90	**53822-U**

Ascentis Express OH5 HILIC Columns

The OH5 bonded stationary phase moiety in Ascentis Express OH5 columns is a highly polar ligand that contains 5 hydroxyl groups tethered to the silica via a novel proprietary linkage phase chemistry. The phase is designed to provide enhanced HILIC partitioning and limited ion exchange retention.

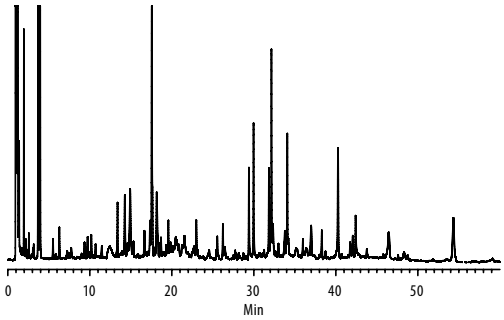
Ascentis Express OH5 HPLC Columns

L (cm)	I.D. (mm)	Cat. No.
particle size 2.7 µm		
2	2.1	**53779-U**
3	2.1	**53748-U**
5	2.1	**53749-U**
7.5	2.1	**53755-U**
10	2.1	**53757-U**
15	2.1	**53764-U**

Ascentis Express Reversed Phase Columns for Peptide Analysis

Peptides up to about 20 kDa are best analyzed on 160 Å pore size Ascentis Express Peptide ES C18 columns.

column: Ascentis Express Peptide ES-C18, 10 cm x 4.6 mm I.D. (53324-U)
mobile phase A: 0.1% (w/v) TFA in water
mobile phase B: 0.1% TFA (w/v) in 40:60 water:acetonitrile
gradient: initial = 3% B to 100% B in 53 min.
flow rate: 1.0 mL/min
temp.: 30 °C
det.: UV at 215 nm
injection: 20 µL



Carbonic Anhydrase Tryptic Digest on an Ascentis Express Peptide ES-C18 Column

Ascentis Express Peptide ES C18 Capillary HPLC Columns

L (cm)	I.D.	Pore Size (Å)	Cat. No.
particle size 2.7 µm			
5	75 µm	160	**53543-U**
5	100 µm	160	**53544-U**
5	200 µm	160	**53545-U**
5	300 µm	160	**53546-U**
5	500 µm	160	**53547-U**
5	1.0 mm	160	**53548-U**
15	75 µm	160	**53549-U**
15	100 µm	160	**53552-U**
15	200 µm	160	**53553-U**
15	300 µm	160	**53554-U**
15	500 µm	160	**53558-U**
15	1.0 mm	160	**53561-U**

Ascentis Express Peptide ES C18 Narrow Bore HPLC Columns

L (cm)	I.D. (mm)	Pore Size (Å)	Cat. No.
particle size 2.7 µm			
3	2.1	160	**53299-U**
5	2.1	160	**53301-U**
7.5	2.1	160	**53304-U**
10	2.1	160	**53306-U**
15	2.1	160	**53307-U**
10	4.6	160	**53324-U**

Discovery® BIO Columns for Protein Analysis by Reversed Phase

The selectivity and the efficiency offered by Discovery BIO Wide Pore reversed phase columns give maximum resolving power for complex mixtures of proteins, natural or synthetic peptides, and peptide maps.

Exceptional pH stability allows full use of mobile phase pH to adjust the separation. Discovery BIO Wide Pore columns are available packed with 3 or 5 µm porous particles that are functionalized with alkyl-bonded phase ligands. Discovery BIO Wide Pore columns deliver:

- A choice of selectivity with C5, C8, and C18 phase chemistries
- Enhanced stability and lifetime of C5 alkyl ligands compared to conventional C4 phases
- No-bleed LC/MS properties
- Guaranteed reproducibility from run-to-run, column-to-column, and batch-to-batch
- Scalability from capillary to preparative dimensions.

Discovery BIO Wide Pore C18 HPLC Columns

L (cm)	I.D. (mm)	Pore Size (Å)	Cat. No.
particle size 3 µm			
5	0.18	300	**65603-U**
5	0.32	300	**65526-U**
10	0.32	300	**65527-U**
5	0.5	300	**65517-U**
10	0.5	300	**65518-U**
5	1.0	300	**65504-U**
10	1.0	300	**65506-U**
5	2.1	300	**567200-U**
10	2.1	300	**567201-U**
15	2.1	300	**567202-U**

HPLC Columns For Proteins

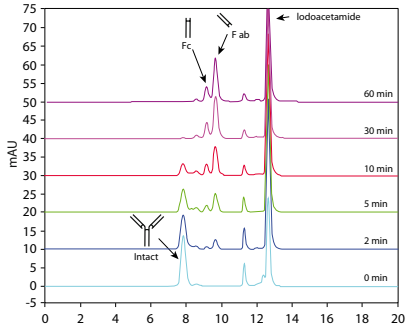
TSKgel® Gel Filtration Chromatography Columns

In 1977, Tosoh introduced the TSKgel SW-type product line (10 µm), the first silica-based gel high performance gel filtration columns for proteins. Since then, TSKgel SWxl (5 µm) and later TSKgel SuperSW columns (4 µm) have become synonymous with analyzing protein molecular weight, first in the emerging field of biotechnology and currently in the development of biotherapeutics.

Featuring ultra-efficient 4 µm particles, TSKgel SuperSW2000 and SuperSW3000 provide higher efficiency than 5 µm TSKgel G2000SWxl columns. The narrow 4.6 mm column inner diameter reduces buffer consumption and is ideal for sample-limited applications. To benefit fully from the high efficiency of 4 µm columns, and because the column diameter of TSKgel SuperSW columns is 4.6 mm, it is important to minimize the amount of dead volume in the HPLC system.

TSKgel SuperSW2000 columns are best suited for peptides and recombinant proteins up to a molecular mass of ~100 kDa. Larger proteins, including monoclonal antibodies and antibody drug conjugates require the larger pore size available in TSKgel SuperSW3000 columns. Depending on the mass of the therapeutic protein, either column can be used successfully to determine protein aggregates.

Column: TSKgel G30000SW$_{XL}$, 7.8 mm ID x 30 cm
Mobile phase: 20 mmol/L phosphate buffer + 0.3 mol/L NaCl, pH 7.0
Flow rate: 1.0 mL/min
Detection: UV @ 280 nm
Temperature: room temperature
Injection vol.: 10 µL
Concentration: 0.24 g/L



HPLC of Papain Digestion of IgG on a TSKgel SuperSW3000 Column

Product Name	L (cm)	I.D. (mm)	Pore Diameter (Å)	Particle Size (µm)	Cat. No.
TSKgel® SuperSW2000 Size Exclusion HPLC Column	30	4.6	125	4	**818674**
TSKgel® SuperSW3000 Size Exclusion HPLC Column	30	4.6	250	4	**818675**

TSKgel Ion Exchange Chromatography Column

TSKgel DEAE-5PW and SP-5PW columns are methacrylate-based anion and cation exchange columns, respectively, each containing 10 µm spherical particles. TSKgel DEAE-5PW columns are packed with porous hydrophilic polymer beads which are surface-modified with a weak anion exchanger. TSKgel SP-5PW columns are packed with porous hydrophilic polymer beads which are surface-modified with a strong cation exchanger.

Both column types are used for the separation and analysis of proteins, nucleotides, nucleosides, and other biologically active molecules. The nominal pore size of 1000 Å allows unhindered access for proteins with a molecular mass of up to 1 MDa.

Product Name	L (cm)	I.D. (mm)	Particle Size (µm)	Cat. No.
TSKgel® DEAE-5PW Anion Exchange HPLC Column	7.5	2	10	**818757**
TSKgel® SP-5W Cation Exchange HPLC Column	7.5	2	10	**818758**

TSKgel Hydrophobic Interaction Chromatgraphy Columns

Both hydrophobic interaction chromatography (HIC) and reversed-phase liquid chromatography separate on the basis of protein hydrophobicity and allow selective binding and desorption of proteins. However, HIC operates at significantly lower binding energy and uses aqueous mobile phases. These characteristics are less likely to disturb protein conformation. HIC thus generally provides better activity recovery.

TSKgel Ether-5PW and Phenyl-5PW, resin-based columns provide different hydrophobicities for chromatographic optimization. TSKgel Ether-5PW and Phenyl-5PW columns provide quality access to larger molecules with low diffusion coefficients and are stable in either acid or caustic cleaning regimens. Ether-5PW and Phenyl-5PW packings are based on TSKgel G5000PW resin - 10 µm particles with a 1000 Å pore size.

TSKgel Ether-5PW has intermediate hydrophobicity and is recommended for purifying very hydrophobic proteins. It is an excellent choice for separating hydrophobic molecules such as membrane proteins or monoclonal antibodies such as IgG or IgM.

TSKgel Phenyl-5PW is more hydrophobic and is highly recommended to use in screening for the selectivity, retention, and recovery of most biomolecules.

Product Name	L (cm)	I.D. (mm)	Particle Size (µm)	Cat. No.
TSKgel® Ether-5PW Hydrophobic Interaction Chromatography (HIC) Column	7.5	2	10	**818760**
TSKgel® Phenyl-5PW Hydrophobic Interaction Chromatography (HIC) Column	7.5	2	10	**818759**

MALDI Matrices Selection Table

Matrix-**a**ssisted **l**aser **d**esorption/**i**onization (MALDI) has expanded MS into the analysis of high molecular weight, non-volatile, and thermally labile compounds, such as intact proteins and oligonucleotides. Moreover, it has become an important technique in proteomics research.[1-3] Further significant applications of MALDI-MS include the analysis of polymers, glycans, lipids, and metabolites. MALDI requires relatively little sample preparation and is more amenable to topological imaging compared to other forms of MS ionization.

A typical MALDI matrix substance is an aromatic acid with a chromophore that absorbs strongly at the wavelength of the incident laser. The MALDI technique generally involves mixing the sample with a matrix substance, followed by crystallization by different techniques on the MALDI sample plate. The crystallized sample-matrix mixture is irradiated by laser light, usually UV. As the matrix absorbs the light energy, it vaporizes into the gas phase, resulting in an indirect ionization of the sample molecules.[4-6]

Choosing a suitable matrix of high quality is the key to the success of a MALDI-MS experiment. Organic impurities can lead to extraneous peaks, especially in the low mass range. Trace levels of ions, especially Na^+ and K^+, form adducts with sample molecules. These adducts differ in mass according to the number of positive ions and complicate the MS spectrum. Since the matrix substance is generally applied in large excess to the sample, a very high purity is even more crucial. The MALDI Matrices Selection Table below facilitates choosing the appropriate matrix for the class of molecules under investigation.

References

1. Karas, M., *et al.*, Matrix-assisted ultraviolet laser desorption of non-volatile compounds. *Int. J. Mass Spectrom. Ion Proc.*, **78**, 53-68 (1987).
2. Hillenkamp, F., and Peter-Katalinic, J. (eds.), *MALDI MS. A Practical Guide to Instrumentation, Methods and Applications*, Wiley-VCH (2007).
3. Aebersold, R., and Mann, M., Mass spectrometry-based proteomics. *Nature*, **422**, 198-207 (2003).
4. Dreisewerd, K., The desorption process in MALDI. *Chem. Rev.*, **103**, 395-425 (2003).
5. Karas, M., and Krüger, R., Ion formation in MALDI. *Chem. Rev.*, **103**, 427-439 (2003).
6. Knochenmuss, R., and Zenobi, R., MALDI ionization: The role of in-plume processes. *Chem. Rev.*, **103**, 441-452 (2003).

Description	Purity	Abbrev-iation	Proteins	Peptides	Glycans	Oligonuc-leotides	Polymers	Lipids	Analytes	Note	Pack Sizes	Cat. No.
9-Aminoacridine	≥99.5%	9-AA						✓	Metabolites		1 g	**92817**
Aminopyrazine	≥99.0%	AP							Small carbohydrates		10 × 10 mg, 1 g	**89132**
3-Aminoquinoline	≥99.0%	3-AQ			✓						1 g	**07336**
Anthranilic acid	≥99.0%	2-AA			✓	✓					1 g	**10678**
6-Aza-2-thiothymine	≥99.0%	ATT	✓	✓	✓	✓			Non-covalent complexes		1 g, 5 g	**82393**
4-Benzyloxy-α-cyanocinnamic acid	≥99.0%								PAH-DNA adducts		250 mg	**38368**
Caffeic acid	≥99.0%		✓	✓							1 g, 5 g	**60018**
α-Cyano-4-hydroxycinnamic acid	≥99.0%	CHCA	✓	✓	✓						250 mg, 1 g	**70990**
α-Cyano-4-hydroxycinnamic acid puriss. p.a.	≥99.5%, Ultra pure	CHCA	✓	✓	✓						10 × 10 mg	**39468**
α-Cyano-4-hydroxycinnamic acid	suitable for MALDI-TOF	CHCA	✓	✓	✓						10 × 10 mg	**C8982**
α-Cyano-4-hydroxycinnamic acid butylamine salt	≥99.0%	BA-CHCA		✓			✓			Ionic Liquid Matrix	100 mg, 1 g	**67336**
α-Cyano-4-hydroxycinnamic acid diethylammonium salt	≥99.0%	DEA-CHCA		✓			✓			Ionic Liquid Matrix	1 g	**55341**
α-Cyano-4-hydroxycinnamic acid *N*-ethyl-*N*,*N*-diisopropylammonium salt	≥99.0%	DIEA-CHCA	✓	✓	✓		✓			Ionic Liquid Matrix	10 × 10 mg	**18211**
α-Cyano-4-hydroxycinnamic acid *N*-tert-butyl-*N*-isopropyl-*N*-methylammonium salt	≥99.0%	IMTBA-CHCA	✓	✓						Ionic Liquid Matrix	10 × 10 mg	**94190**

MALDI Matrices Selection Table (continued)

Description	Purity	Abbrev-iation	Proteins	Peptides	Glycans	Oligonuc-leotides	Polymers	Lipids	Analytes	Note	Pack Sizes	Cat. No.
α-Cyano-4-phenylcinnamic acid	≥99.0%								PAHs		10 × 10 mg	**89759**
2′,5′-Dihydroxyacetophenone	≥99.5%	2,5-DHAP	✓	✓	✓						250 mg, 1 g	**89415**
2′,6′-Dihydroxyacetophenone	≥99.5%	2,6-DHAP	✓	✓	✓			✓			1 g, 5 g	**37468**
2,5-Dihydroxybenzoic acid	≥99.0%	DHB	✓	✓	✓		✓	✓	Organic molecules		10 mg, 250 mg, 1 g	**85707**
2,5-Dihydroxybenzoic acid	≥99.5%, Ultra pure	DHB	✓	✓	✓		✓	✓	Organic molecules		10 × 10 mg	**39319**
Dithranol	≥98.5%	DIT					✓	✓	Dendrimers		250 mg, 1 g	**10608**
trans-Ferulic acid	≥99.0%	FA	✓	✓							1 g, 5 g	**46278**
Ferulic acid *N*-ethyl-*N*,*N*-diiso-propylammonium salt	≥98.0%	DIEA-F			✓					Ionic Liquid Matrix	10 × 10 mg	**94155**
Glycerol	≥99.0%		✓	✓	✓					Liquid Matrix	5 mL	**49771**
(4-Hydroxybenzylidene) malonitrile BioXtra	≥99.0%						✓				10 × 10 mg, 250 mg	**95712**
2-(4-Hydroxyphenylazo) benzoic acid	≥99.5%	HABA	✓	✓	✓		✓				1 g, 5 g	**54793**
3-Hydroxypicolinic acid	≥99.0%	3-HPA				✓			Oligo-saccharides		250 mg, 1 g	**56197**
trans-3-Indoleacrylic acid	≥98.5%	IAA					✓				250 mg	**38472**
Isovanillin	≥99.5%								Small organic molecules		1 g	**59927**
2-Mercaptobenzothiazole	≥99.0%	MBT	✓	✓			✓				250 mg	**76154**
Nicotinic acid	≥99.5%		✓	✓		✓					250 mg, 1 g	**72311**
4-Nitroaniline	≥99.0%		✓	✓				✓		Liquid Matrix	250 mg, 1 g	**72681**
2-Picolinic acid	≥99.5%		✓			✓					1 g	**39245**
Salicylamide	≥99.0%					✓					1 g	**84228**
Sinapic acid	≥99.0%	SA	✓	✓					Dendrimers, Fullerenes		1 g, 5 g	**85429**
Sinapic acid	≥99.5%, Ultra pure	SA	✓	✓					Dendrimers, Fullerenes		10 × 10 mg	**49508**
Succinic acid	≥99.5%		✓	✓			✓				1 g, 5 g	**14078**
Super-DHB BioReagent	≥99.0%	Super-DHB	✓	✓	✓		✓			9:1 mixture of DHB and 2-hydroxy-5-meth-oxy-benzoic acid	10 × 10 mg, 1 g, 5 g	**50862**
2′,4′,6′-Trihydroxyaceto-phenone monohydrate	≥99.5%	THAP	✓	✓	✓	✓					1 g, 5 g	**91928**
Universal MALDI Matrix			✓	✓					Organic molecules	1:1 mixture of DHB and CHCA	1 g	**50149**

Solvents, Blends, And Additives

In most MS analyses, extraction techniques and chromatographic separations (GC or LC) are applied prior to sample introduction into the mass spectrometer, in order to remove matrix components such as lipids and salts. In particular, alkali ions tend to form adducts with many compounds and interfere with most of the typical ionization techniques (ESI, MALDI), leading to reduction in MS detection sensitivity. Organic impurities lead to additional peaks and further complicate chromatograms of biological samples.

For reasons such as these, all solvents and additives in chromatography mobile phases should be of the highest quality and should not contain any salts or other organic impurities. Sigma-Aldrich's LC-MS Ultra and LC-MS solvents and additives are tested for applicability in LC-MS and are manufactured to the highest quality. CHROMASOLV® LC-MS solvents are designed specifically with low content (<100 ppb) of adduct-forming impurities such as calcium, magnesium, potassium, and sodium. CHROMASOLV LC-MS solvents are also run through specific UV-spectroscopic quality control tests. Packaging of the solvents is deliberately selected to maintain the quality and to ease the preparation of mobile phases.

Solvents

Ultra-LC

Name	Grade	Suitability	Assay	Cat. No.
Acetonitrile	LC-MS Ultra CHROMASOLV®	suitability for UHPLC-MS passes test	≥99.9%, GC	14261-1L 14261-2L
Methanol	LC-MS Ultra CHROMASOLV®	suitability for UHPLC-MS passes test	≥99.9%, GC	14262-1L 14262-2L
Water	LC-MS Ultra CHROMASOLV®	suitability for UHPLC-MS passes test	-	14263-1L 14263-2L

LC-MS

Name	Grade	Suitability	Assay	Cat. No.
Acetonitrile	LC-MS CHROMASOLV®	suitability for LC-MS in accordance	≥99.9%	34967-250ML 34967-1L 34967-6X1L 34967-2.5L 34967-4X2.5L 34967-4X4L 34967-20L
Ethyl acetate	LC-MS CHROMASOLV®	suitability for LC-MS passes test	≥99.7%, GC	34972-1L-R 34972-2.5L-R
Methanol	LC-MS CHROMASOLV®	suitability for LC-MS passes test	≥99.9%	34966-1L 34966-6X1L 34966-2.5L 34966-4X2.5L 34966-4X4L 34966-20L
2-Propanol	LC-MS CHROMASOLV®	suitability for LC-MS in accordance	≥99.9%	34965-1L 34965-6X1L 34965-2.5L 34965-4X2.5L
Water	LC-MS CHROMASOLV®	suitability LC/MS (reserpine test) complies	-	39253-1L-R 39253-4X4L-R 39253-20L-R

Solvent Blends

LC-MS

Name	Grade	Suitability	Assay	Cat. No.
Acetonitrile with 0.1% acetic acid	LC-MS CHROMASOLV®	LC-MS tested	0.093-0.107% acetic acid basis ≥99.5%	34678-2.5L-R
Acetonitrile with 0.1% ammonium acetate	LC-MS CHROMASOLV®	LC-MS tested	≥98% acetonitrile basis, GC	34669-2.5L-R
Acetonitrile with 0.1% formic acid	LC-MS CHROMASOLV®	LC-MS tested	≥99.5%, GC	34668-2.5L-R
Acetonitrile with 0.1% formic acid and 0.01% trifluoroacetic acid	LC-MS CHROMASOLV®	LC-MS tested	≥99.5%, GC	34676-2.5L-R
Acetonitrile with 0.1% trifluoroacetic acid	LC-MS CHROMASOLV®	LC-MS tested	>99.5%, GC	34976-2.5L-R
Methanol with 0.1% acetic acid	LC-MS CHROMASOLV®	LC-MS tested	≥99.5%, GC	34672-2.5L-R
Methanol with 0.1% ammonium acetate	LC-MS CHROMASOLV®	LC-MS tested	≥99.5%, GC	34670-2.5L-R
Methanol with 0.1% formic acid	LC-MS CHROMASOLV®	LC-MS tested	≥99.5%, GC	34671-2.5L-R
Methanol with 0.1% trifluoroacetic acid	LC-MS CHROMASOLV®	LC-MS tested	≥99.5%, GC	34974-2.5L-R
Water with 0.1% acetic acid	LC-MS CHROMASOLV®	LC-MS tested	-	34675-2.5L-R
Water with 0.1% ammonium acetate	LC-MS CHROMASOLV®	LC-MS tested	-	34674-2.5L-R
Water with 0.1% formic acid	LC-MS CHROMASOLV®	LC-MS tested	-	34673-2.5L-R
Water with 0.1% formic acid and 0.01% trifluoroacetic acid	LC-MS CHROMASOLV®	LC-MS tested	-	34677-2.5L-R
Water with 0.1% trifluoroacetic acid	LC-MS CHROMASOLV®	LC-MS tested	-	34978-2.5L-R

Eluent Additives

Ultra-LC

Name	Grade	Suitability	Assay	Cat. No.
Ammonium acetate	-	suitability for UHPLC-MS in accordance	≥99.0%, T (calc. on dry substance)	14267-25G
Ammonium formate	-	suitability for UHPLC-MS in accordance	≥99.0%, NT (calc. on dry substance) ≥99.0%	14266-25G
Formic acid	LC-MS Ultra, eluent additive for UHPLC-MS	UHPLC-MS passes test	~98%, T	14265-1ML 14265-2ML
Trifluoroacetic acid	LC-MS Ultra, eluent additive for UHPLC-MS	UHPLC-MS passes test	≥99.0%, GC ≥99.0%	14264-1ML 14264-2ML

LC-MS

Name	Grade	Suitability	Assay	Cat. No.
Acetic acid	eluent additive for LC-MS	LC-MS in accordance miscibility in accordance	-	49199-50ML-F
Ammonium acetate	eluent additive for LC-MS for mass spectrometry	LC-MS in accordance	≥99.0%, T (calc. on dry substance)	73594-25G-F 73594-100G-F
Ammonium bicarbonate	eluent additive for LC-MS	LC-MS in accordance	-	40867-50G-F
Ammonium fluoride	eluent additive for LC-MS	LC-MS in accordance	≥98.0% (F)	52481-50G
Ammonium formate	eluent additive for LC-MS	LC-MS in accordance	≥99.0%, NT (calc. on dry substance)	55674-50G-F
Ammonium hydroxide solution	eluent additive for LC-MS	LC-MS in accordance	-	44273-10X1ML-F 44273-100ML-F
Ammonium formate	for mass spectrometry	-	≥99.0%, NT (calc. on dry substance) ≥99.0%	70221-25G-F 70221-100G-F
Formic acid	eluent additive for LC-MS	LC-MS complies	~98%, T	56302-10X1ML-F 56302-10X1ML 56302-50ML-F 56302-1L-GL 56302-1L-GL-F 56302-1L-F
1,1,1,3,3,3-Hexafluoro-2-propanol	eluent additive for LC-MS	LC-MS complies	≥99.8%, GC	42060-10X1ML 42060-50ML
Potassium citrate tribasic monohydrate	eluent additive for LC-MS	LC-MS in accordance	≥99.5%, NT	77843-50G
Propionic acid	eluent additive for LC-MS	LC-MS in accordance	≥99.5%, GC	49916-50ML-F
Triethylamine	eluent additive for LC-MS	LC-MS complies	≥99.5%, GC	65897-50ML-F
Trifluoroacetic acid	eluent additive for LC-MS	LC-MS passes test	≥99.0%, GC	40967-10X1ML-F 40967-10ML-F 40967-5X10ML-F 40967-1L-F
2,2,2-Trifluoroethanol	eluent additive for LC-MS	LC-MS complies	≥99.8%, GC	05841-10X1ML 05841-50ML

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