MERCK

LC-MS Contaminants

Avoid, identify, minimize.

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Analytical Products

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How to identify and avoid contaminants in LC-MS

(Liquid Chromatography-Mass Spectrometry)

You thought your LC-MS analysis would be straightforward, but there are peaks you didn’t expect.

In this technical bulletin, you will learn some tips on identifying LC-MS contaminants and avoiding contamination. Our 110 years of separation expertise, combined with our precision-manufactured products, give you the greatest chance of obtaining reproducible, clean data.

Introduction

A successful LC-MS assay can be defined as one that has high sensitivity, reproducibility, and efficiency while also providing an increase in sample throughput. The presence of contaminants can affect these key analytical figures of merit as well as potentially compromise the performance of the analytical U/HPLC column and/or the instrument itself.

Table 1. LC-MS performance parameters.

Parameters negatively affected by contaminants	What it is	How to minimize contaminants
Sensitivity	Lowest level of analyte detectable above background; sensitivity is reduced by ion suppression	Wash columns to mitigate column bleeding
		Effective sample preparation
		Use certified mobile phase
Reproducibility	Can mean column-to-column reproducibility or run-to-run reproducibility	Prepare sample with devices that do not introduce extractable impurities
		Run sufficient controls to verify run-to-run stability within a batch
		Remove sample components that interfere with separation, ionization and fragmentation
		Use high-quality HPLC columns
Column Lifetime	Number of injections on a column without change in selectivity and efficiency	Use a robust column with high matrix tolerance: e.g., monolithic columns have high tolerance
		Eliminate sample contaminants that adsorb strongly or ionize easily. Avoid polymers that, when fragmented, result in multiple peaks of varying m/z. Use guard column and proper sample preparation (such as centrifugation, filtration, and extraction) to remove particles and extend column lifetime.
		Fully elute/clean column after each sample

Sample components that can interfere with LC-MS results

Some biological matrices, such as plasma, contain high amounts of phospholipids. If not removed prior to chromatography, separating phospholipids from analytes of interest can require long chromatography run times and high concentrations of organic solvents. Furthermore, phospholipids can build up on analytical column, and unexpectedly elute in future runs. Drug formulation agents, such as polysorbitans and polyethylene glycol, can also interfere and cause ionization suppression.

Besides sample-derived contaminants, additional sources of contamination are sampling devices, solvent impurities, containers, sample preparation devices, volatile organics introduced as a result of handling personal care products, and even columns themselves.

Plasticizers from labware can interfere with LC-MS, resulting in the need to lengthen the chromatography run in order to resolve these peaks from analyte peaks.

A list of common contaminants, their molecular weight, and possible sources can be found in **Table 2.**

Sample components that can interfere with LC-MS results include:

- Metabolites
- Detergents
- Salts/Buffer components
- Degradation products
- Counterions
- Matrix

Table 2. List of selected contaminants observed in mass spectra (ESI, positive mode, ion mass ≤1000 Da). Refer to Appendix I for a more complete list, or one of the databases listed in the resources section on page 28.

Mono-isotopic ion mass (singly charged)	Ion type	Formula for M or subunit or sequence	Compound ID or species	Possible origin and other comments
74.06059	$[M+H]^+$	C_3H_7NO	Dimethyl formamide	Solvent
102.12827	$[M+H]^+$	$C_6H_{15}N$	TEA	Triethylamine, buffer
107.0782	$[A_2B+H]^+$	$[C_2H_4O]nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
123.09222	$[M+H]^+$	$C_7H_{10}N_2$	DMAP	Dimethylaminopyridine, solvent
153.13917	$[M+H]^+$	$C_9H_{16}N_2$	DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
214.09018	$[M+H]^+$	$C_{10}H_{15}NO_2S$	n-BBS	n-butyl benzenesulfonamide, plasticizer
242.28477	M^+	$C_{16}H_{36}N$	TBA	Tetrabutylammonium, buffer
279.15964	$[M+H]^+$	$C_{16}H_{22}O_4$	Dibutylphthalate	Plasticizer, phthalate ester
371.1018	$[M+H]^+$	$[C_2H_6SiO]_5$	Polysiloxane	Polysiloxane, followed by m/z 388
371.31614	$[M+H]^+$	$C_{22}H_{42}O_4$	DEHA	Bis(2-ethylhexyl) adipate, plasticizer
391.28484	$[M+H]^+$	$C_{24}H_{38}O_4$	Diisooctyl phthalate	Diisooctyl phthalate, plasticizer
445.12060	$[M+H]^+$	$[C_2H_6SiO]_6$	Polysiloxane	Polysiloxane, followed by m/z 462
447.2934	$[M+H]^+$	$[C_3H_6O]nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
515.41341	$[M+H]^+$	$C_{30}H_{58}O_4S$	DDTDP	Didodecyl 3,3′-thiodipropionate, antioxidant
519.13940	$[M+H]^+$	$[C_2H_6SiO]_7$	Polysiloxane	Polysiloxane, followed by m/z 536
593.15820	$[M+H]^+$	$[C_2H_6SiO]_8$	Polysiloxane	Polysiloxane, followed by m/z 610

General system care, maintenance and laboratory practice

In addition to good laboratory practices, such as wearing powder-free, nitrile gloves and monitoring laboratory air (which can contain siloxanes and phthalates), follow these tips for minimizing contamination in LC-MS.

- Flush HPLC system with organic eluent (preferably isopropanol or methanol; acetonitrile [ACN] can polymerize and block valves if system is stopped for several weeks) regularly to prevent microbial contamination. The interval of flushing depends on the eluents and buffers used and should be between two and four weeks.
- Pump debris is collected in the pump outlet filter. Some of these components can leach and be detected by MS. Replace the filter every 1–2 months or after changing from ACN to methanol (or vice versa) for lower baseline noise and general system protection.
- Filter frits attached to the inlets of the mobile phase tubing to protect the LC system from particulate matter should be made out of stainless steel. Cleaning of glass frits is time-consuming (buffer residue is hard to remove); in addition, silica and alkali are dissolved from the glass filter and form adducts $[M+X]^+$.

Sample preparation is crucial for minimizing contamination

Without sample preparation, samples contain components that are incompatible with HPLC/UHPLC/MS analyses:

- Undissolved particles/precipitates in a sample clog and reduce the life of the chromatography column.
- Sample matrices may contain many impurities, making chromatograms challenging to interpret; for example, sample matrix contains components that either elute at the same point in the LC-MS chromatogram as the analyte (potentially causing ionization suppression) or affect analyte signal intensity.
- Particles held up on the column can leach contaminants into the mobile phase (in the current sample and subsequent samples), thereby increasing background.

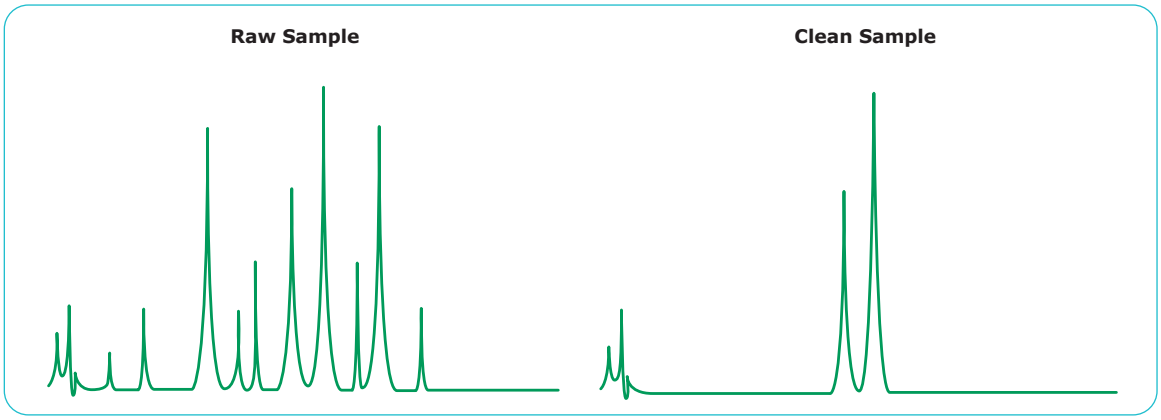

Figure 1.
Without sample preparation, the presence of contaminants in the sample results in more peaks in the chromatogram (as represented in the left hand schematic), making analysis challenging.

Select a sample preparation method that brings the sample into a solution that is free of particles. Additional points of consideration include concentrating the analyte and reducing sample complexity. For example, a plasma sample might benefit from solid phase extraction, which removes contaminants (proteins, lipids) and also concentrates the sample, whereas fruit and vegetable juices, with their high particle load, might benefit simply from dilution and filtration.

Depending on the method chosen, sample preparation may be used, for example, to selectively enrich analytes, increase analyte concentration, or remove impurities that cause ionization suppression.

How can you tell if your LC-MS analysis is suffering from ionization suppression?

Consider performing the following steps to test for ionization suppression:

1. First, assess the detector response to a calibration standard under conditions of zero ionization suppression.
2. Spike an identical concentration of this standard into prepared sample matrix. Assess the detector response again to determine the effect of ionization suppression.
3. Assess the detector response when the spiked sample prepared in step 2 is processed using the sample preparation method(s) being considered.
4. Finally, add additional calibration standard to determine if the expected increase in signal is observed.

To mitigate the interfering effects of ionization suppression, consider performing these steps:

- Dilute sample or reduce volume injected.
- Reduce ESI flow rate to the nL/min range—this will generate smaller, highly charged droplets that can resist the effects of nonvolatile salts, in case those have not been removed from the sample. Note that you should never use nonvolatile salts in the mobile phase.
- Choose a sample preparation method that removes contaminants causing ionization suppression. Using solid phase extraction instead of protein precipitation, for example, can reduce ionization suppression by phospholipids. Phospholipid removal is discussed further below.
- Change the strength of the mobile phase or the slope of the gradient, so that the analytes of interest may elute further from the solvent front and from the end of the gradient. In these regions of the chromatogram, ionization suppression is most likely to occur.

Types of sample preparation commonly used for LC-MS

Ten of the most popular sample preparation procedures currently in use (as ranked by percentage of survey respondents who reported using each method):

1. Filtration
2. Centrifugation
3. Dilution
4. Evaporation
5. pH adjustment
6. Vortexing
7. Concentration (e.g., by ultrafiltration, precipitation)
8. Sonication
9. Solid phase extraction (SPE)
10. Liquid-liquid extraction (LLE)

According to a 2013 survey of users performed by LCGC magazine, filtration was the most commonly used sample preparation method. For complex samples containing components that contribute to high background and/or interfere with analyte ionization and fragmentation, filtration alone cannot provide the sample necessary for analysis, but forms an integral part of an overall sample preparation strategy, which involves other sample preparation techniques, like extraction, centrifugation and depletion.

Sample preparation tips

Choose an appropriate membrane filter to remove particles from your sample.

The presence of particles in a sample can reduce the signal-to-noise ratio, reduce column lifetime, and increase backpressure in the LC system, potentially causing system failure. Filtration through a microporous membrane is a simple and effective method for removing particles from a sample. However, particle retention ability is different between different membranes and between different suppliers. As **Figure 2** suggests, PTFE filters with polypropylene housing consistently deliver high particle retention.

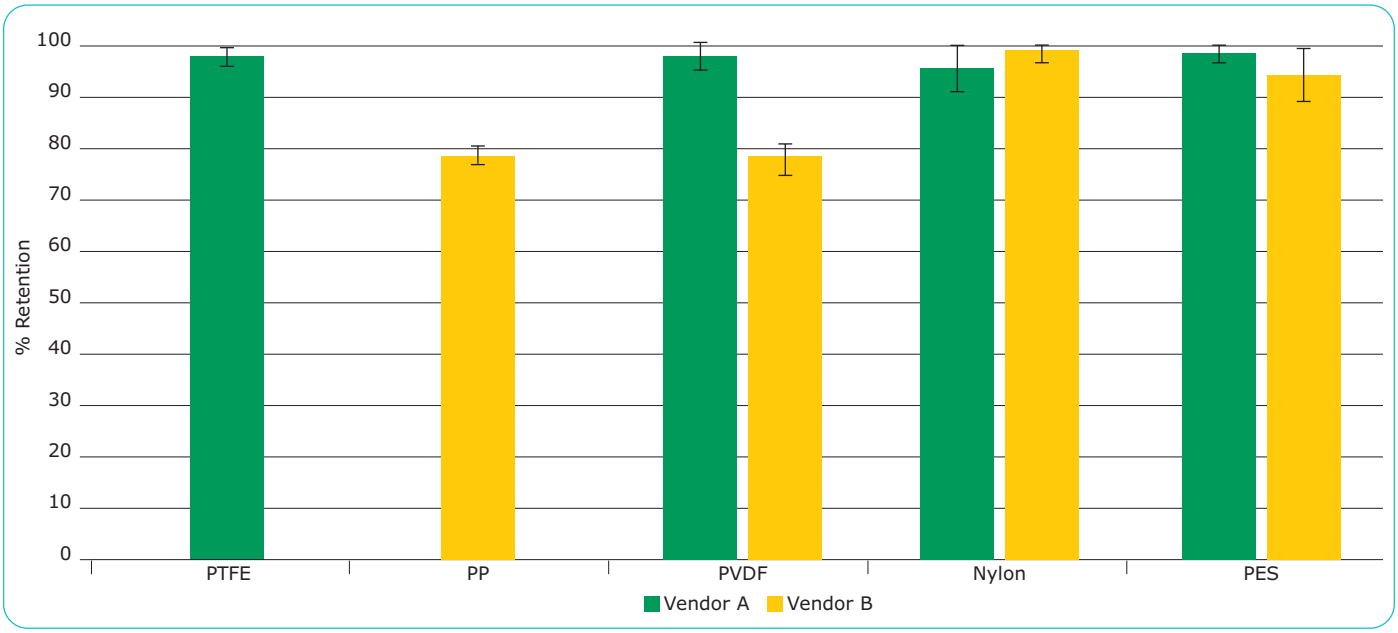

Figure 2. Particle retention ability differs between different membranes and between different suppliers. In principle, 100% of filtration membranes should retain particles. To test this hypothesis, microporous membranes from two different vendors (pore size 0.2 µm) were tested for latex particle retention following filtration of a suspension of 0.3 µm latex particles in water. PTFE=polytetrafluoroethylene; PP=polypropylene; PVDF=polyvinylidenefluoride; PES=polyethylenesulfone.

Minimize extractables (contaminants) from sample prep device

Extractable impurities can generate interfering peaks in a chromatogram or mass spectrum, making it difficult or impossible to identify or quantify analytes of interest. Therefore, it is important to use a sample preparation device that leaches minimal impurities into the sample.

Though a number of syringe filters are certified as "low-extractable" for use in high performance LC (HPLC), most of those filters are certified using HPLC coupled to detection of ultraviolet (UV) absorbance. Though this method provides information about the levels of UV-absorbing extractables coming from a filter, this information does not necessarily correlate with data obtained from an MS detector.

Select vendors now validate syringe filters using mass spectrometric analysis of extractables, which provides valuable guidance in choosing an appropriate membrane for filtering your sample.

TIP

In general, hydrophilic PTFE syringe filters provide the cleanest samples (with the lowest levels of extractable impurities). Presence of polymeric extractable impurities (such as from polypropylene syringe filters) complicate analysis of small molecular analytes.

Table 3. Overall mass spectral signal intensity for five different types of HPLC-certified syringe filters when tested using eight different solvents. The range of chemical compatibility with solvents may indicate the general level of extractables leached by a particular membrane. Millex® LCR filters, which contain hydrophilic PTFE and have broad compatibility with solvents, show the lowest level of signal intensity (and therefore background noise). On the other hand, polypropylene syringe filters from vendor A as well as nylon syringe filters from vendors A and B all show very high levels of extractables, impacting background signal.

	Hydrophilic PTFE	Polypropylene (Vendor A)	Polypropylene (Vendor B)	Nylon (Vendor A)	Nylon (Vendor B)
Reproducibility					
Range of Compatibility with Organic Solvents	Broad	Broad	Broad	Moderate	Moderate
Extractable Level	Low	High	Medium	High	High
Nature of Extractables	MW 100–400 Da	Polymeric	Variable	Polymeric-Variable	Polymeric-Variable

Consider these parameters for evaluating the suitability of a membrane filter for LC-MS:

Solvent compatibility of device

When selecting a filter, determine if constituents in the liquid being filtered will chemically attack the filter. If the filter undergoes chemical degradation, its performance will be compromised, and it may release foulants into the sample stream.

Some solvents may be incapable of dissolving the filter, but could be absorbed into the polymer matrix, causing it to swell over time, altering the effective pore size of the filter and changing its performance.

Lot-to-lot reproducibility of extractables level

This parameter reflects the consistency with which filters are manufactured. Since there are very few MS-certified filters, this parameter helps select the right filter for MS applications and indicates the degree of variation in levels of extractables when different lots of syringe filters are used.

Intensity of signal contribution from extractables: Total Ion Current (TIC) chromatograms

LC-MS-certified membrane filters should be supplied with a total ion current chromatogram that shows the intensity of all peaks detected under a specified set of experimental conditions, normalized to an internal standard. The TIC chromatograms can enable comparisons of extractable profiles between membranes and different filter vendors.

Type of extractables: low molecular weight, discrete peaks vs. polymeric peaks

Any type of extractables can confound downstream analysis, but the discrete peaks from low molecular weight extractables are typically less problematic than peaks from polymeric extractables, which typically show peaks separated by a common mass difference ranging over a wide m/z range. (See Appendix II for a table of mass differences of repeating units derived from common contaminating extractables.) Polymeric extractables are also difficult to remove from the sample or mass spectrometer, even after extensive cleaning of the mass spectrometer.

Adsorption of analyte to device

Because the internal surface area of polymeric microporous membranes is 100–600 times as great as the frontal surface area, there is a vast internal surface area available for nonspecific binding.

Choosing a membrane filter with low nonspecific analyte binding ensures that the overall molecular composition of the filtrate is minimally altered upon passing through the device.

Common extractable contaminants

- Polyethylene glycol (PEG)
- Metal ions (e.g., lithium, sodium, potassium, copper, platinum, iron)
- Phthalates (present in many plastics)
- Slip agents (amides)

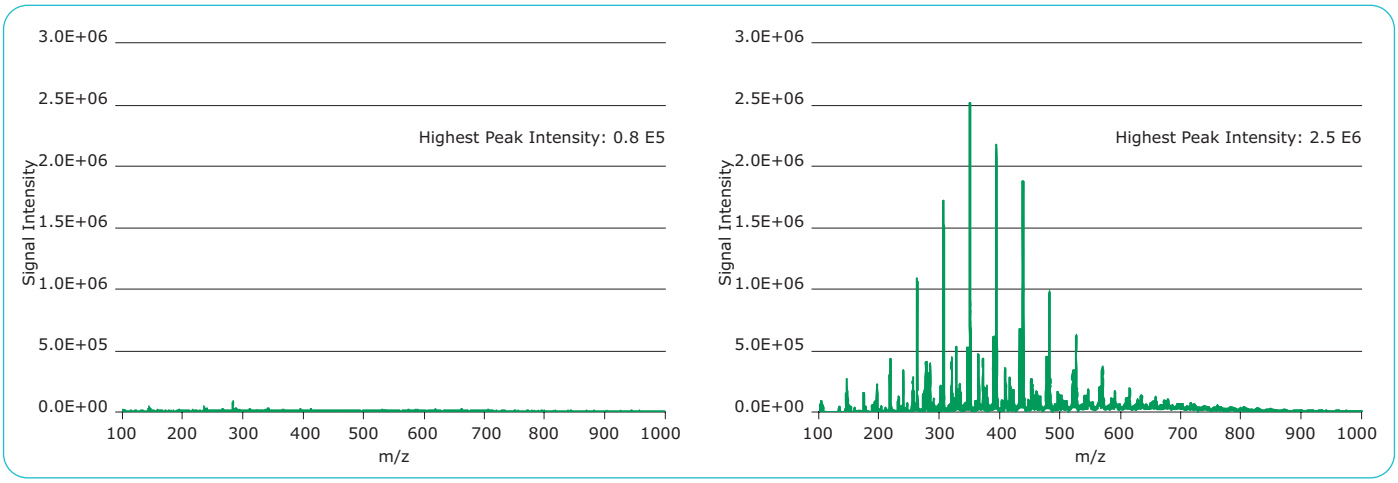

Figure 3. Few extractable impurities from Millex® LCR syringe filter (left) containing 0.45 µm pore hydrophilic PTFE membrane as detected by MS. In contrast, a syringe filter containing 0.45 µm pore polypropylene membrane (Vendor C, right) shows significant extractables. Presence of polymeric extractable impurities (from polypropylene syringe filters) complicate analysis of small molecular analytes. Millex® LCR filters showed a highest peak intensity of about 8 x 10^5 for extractable masses, whereas Vendor C polypropylene syringe filters showed extractable levels about 30 times higher (2.5 x 10^6). Such high signal intensity, which can be comparable to the signal from the analyte of interest, can make analyte quantitation very challenging.

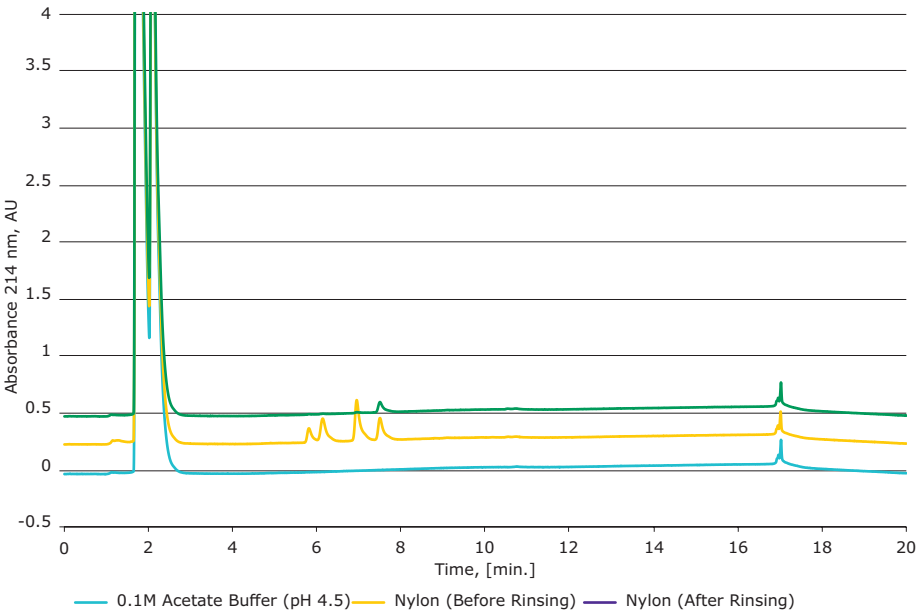

Figure 4. **Nylon syringe filters are a common source of extractables.** In this experiment, the extractable peaks seen after filtration through nylon were greatly reduced when the first milliliter of filtrate was discarded and the second milliliter was analyzed.

TIP

Prerinse the filter with sample/ solvent to reduce the extractables.

Another potential source of contamination is the syringe used to filter and/ or inject the sample. Table 4 shows the level of zinc contamination from various types of syringes.

Table 4. Level of zinc contamination with respect to syringe used.

Syringe Used	Time of Contact	Zn Contamination (ppb)
Plastic with air gap	No contact	< 10
Plastic with black piston seal	15 min.	96
Plastic with black piston seal	30 min.	171
Glass with metal Luer fitting & PTFE piston	30 min.	470

TIP

Use a plastic syringe with an air gap between the sample and the piston. Any surface that comes in contact with the sample has the potential to introduce extractables as well as contribute to analyte binding.

Ultrafiltration separates free from protein-bound analytes

Centrifugal ultrafilters, particularly devices with regenerated cellulose membrane that have defined nominal molecular weight cutoffs, are ideal for separating free from protein-bound microsolutes in serum, plasma, and other biological samples, as illustrated in **Figure 5**. This sample preparation method has been cited in LC-MS analyses for deproteinizing samples to reduce complexity or matrix interference. The method has also been used for LC-MS analyses of binding studies in new drug investigations.

TIP

If filtering many samples at a time, increase throughput while maintaining consistency by using 96-well or 384-well filter plates and a microplate-compatible vacuum manifold.

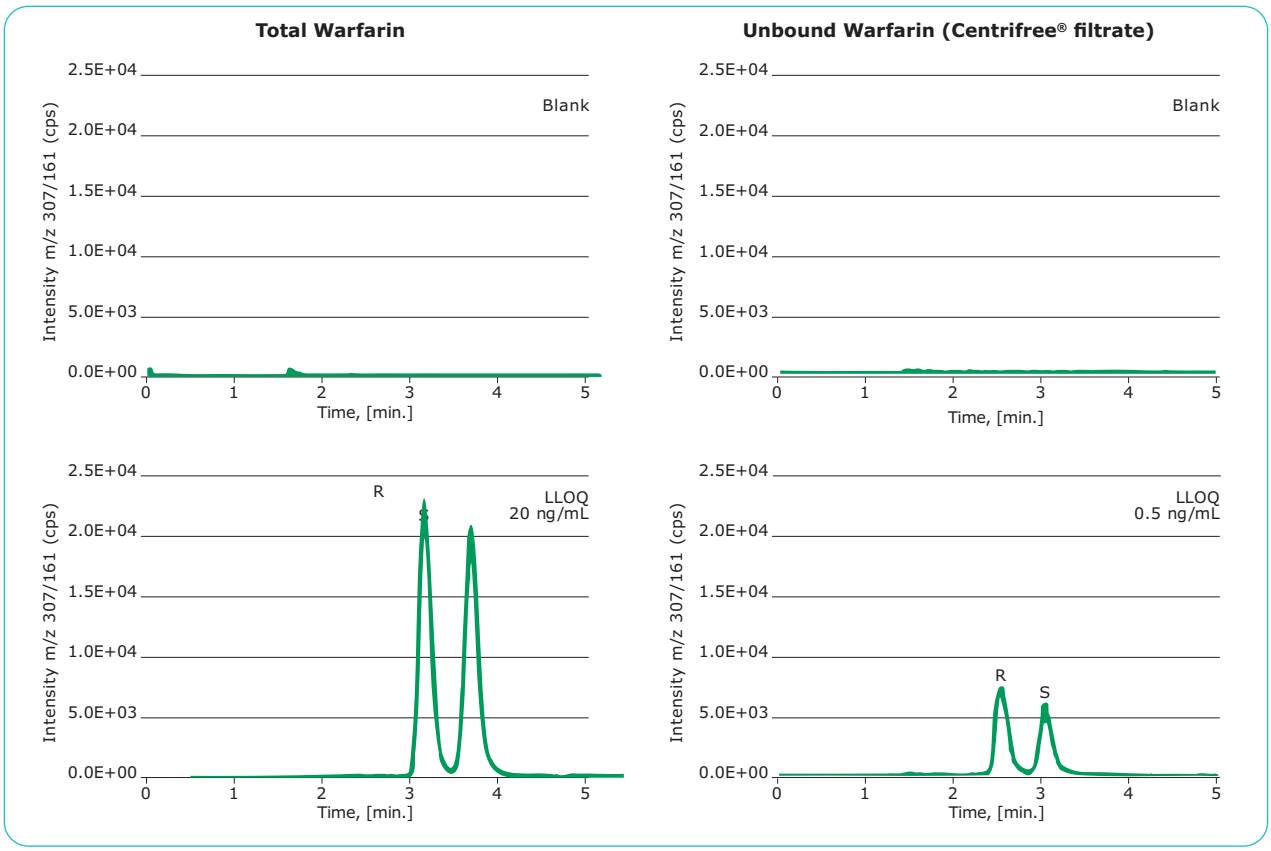

Figure 5. LC-MS analysis of total vs. free warfarin present in blank matrix (top) and human plasma samples (bottom). Unbound (free) warfarin was separated from protein-bound warfarin using centrifugal ultrafiltration devices, such as the Centrifree® device. Adapted from Jensen BP, Chin PK, Begg EJ. Quantification of total and free concentrations of R- and S-warfarin in human plasma by ultrafiltration and LC-MS/MS. Anal Bioanal Chem. 2011 Oct;401(7):2187-93.

When filtration isn't enough

For more complex sample matrices, use more specific sample preparation methods, such as solvent evaporation, protein precipitation, liquid/liquid extraction, QuEChERS, and SPE to transform samples into forms suited for LC-MS.

Some useful tools for these procedures include:

- Separatory funnel
- EXtrelut® pre-packed columns for extraction of lipophilic compounds from aqueous solutions – for sorbent-supported LLE workflows
- Solvents, acids, bases, salts – for protein precipitation
- LiChrolut® product range – for SPE
- Supel™-Select Polymeric SPE – HLB and ion-exchange phases for a wide range of applications and pH conditions
- Discovery® SPE and Supelclean™ SPE lines for a comprehensive range of reverse-phase, ion exchange, mixed mode, and normal-phase SPE products

For samples with high salt load (e.g., food, body fluids or tissue) a desalting (sample preparation step) using LiChrolut® cartridges is recommended.

Sample characteristics determine your SPE procedure

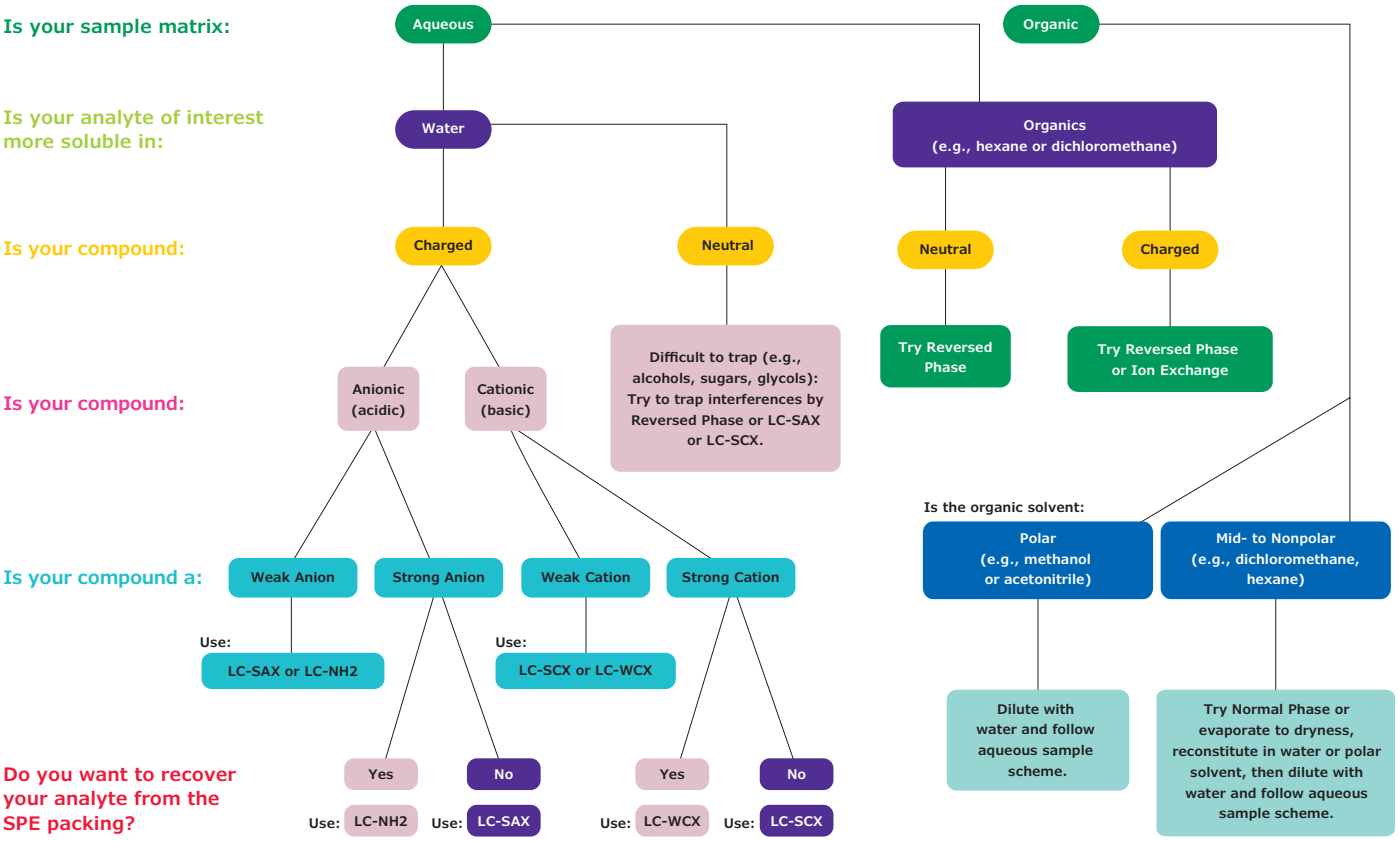

Figure 6.

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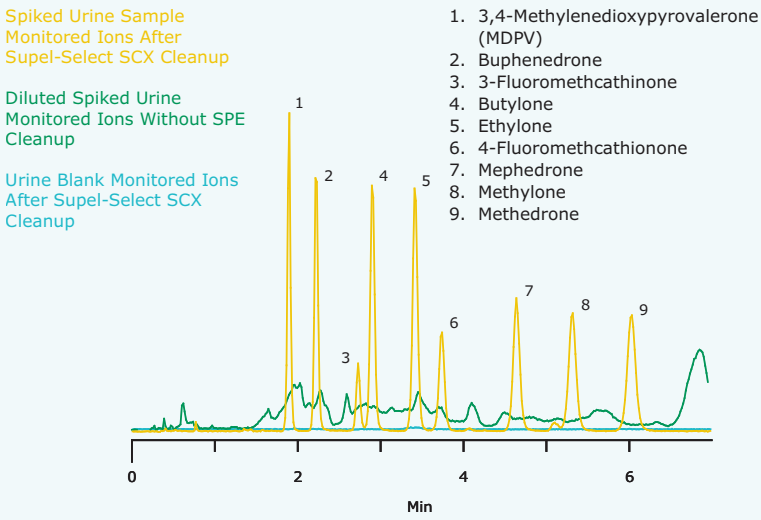
for all of your solid phase extraction needs

Interference Removal Using Supel Select SCX SPE Cartridges to Analyze Illicit Bath Salts in Urine

The analysis of bath salts from urine samples is demonstrated using polymeric SPE sample preparation, followed by hydrophilic interaction liquid chromatography (HILIC) analysis with TOF-MS detection. Supel™-Select SCX SPE is used for the processing and sample cleanup of the urine samples. The figure below illustrates the monitored bath salt ions in a spiked urine sample after SPE cleanup (yellow), in a diluted spiked urine sample without cleanup (green) and in a urine blank after Supel™ Select SCX cleanup (blue). Notice the chromatogram containing the bath salts in the spiked urine sample after SPE cleanup contains no interfering peaks. Therefore, the effectiveness of the Supel™ Select SCX cleanup is demonstrated and the analysis is more robust and reliable.

Figure 7. LC-MS Analysis of Cathinones (Bath Salts) on the Ascentis® Express HILIC (Si) Column

sample/matrix:	1 mL urine spiked to 100 ng/mL of bath salt mixture
SPE tube:	Supel™-Select SCX, 30 mg/1 mL (54240-U)
conditioning:	1 mL 1% formic acid in acetonitrile, then 1 mL water
sample addition:	1 mL spiked urine
washing:	1 mL water, 1 mL 1% formic acid in acetonitrile, 1 mL water
elution:	2 mL 10% ammonium hydroxide in acetonitrile
column:	Ascentis® Express HILIC (Si), 10 cm x 2.1 mm I.D., 2.7 µm (53939-U)
mobile phase:	(A) 5 mM ammonium formate acetonitrile; (B) 5 mM ammonium formate water; (98:2, A:B)
flow rate:	0.6 mL/min
pressure:	127 bar
column temp:	35 °C
detector:	MS, ESI+, 100-1000 m/z
injection:	1 µL
sample:	200 ng/mL in acetonitrile



Protein precipitation, followed by filtration, is often an effective, simple way to reduce the complexity of the sample matrix (**Figure 8**). For this process, it can be advantageous to use a filter plate, which enablaes precipitation and filtration in a single device, eliminating the need for sample transfer and thereby improving analyte recovery.

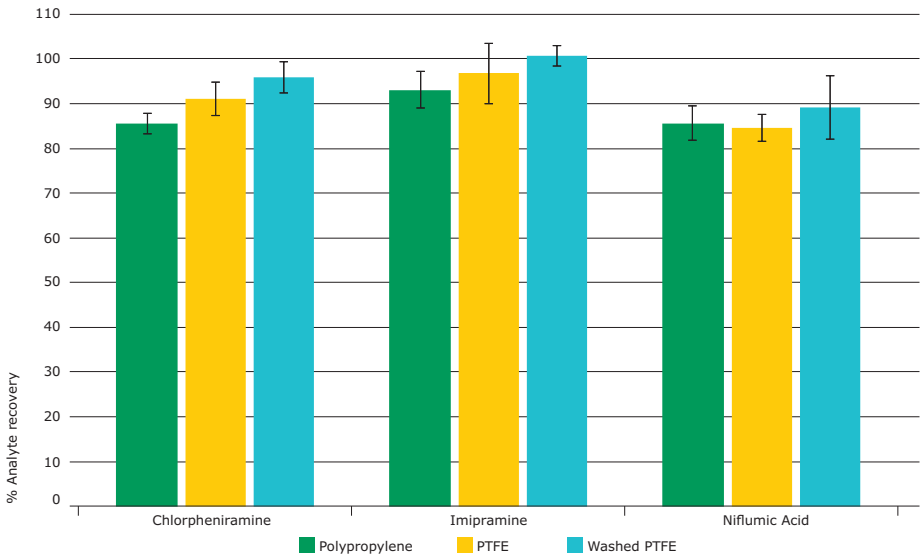


Figure 8. Analyte recovery after protein precipitation. Three different drugs (chlorpheniramine, imipramine and niflumic acid) were spiked into plasma at various concentrations. Protein precipitation was carried out using 1:4 water:acetonitrile as the precipitating solvent. The samples were filtered through various multiwell filter plates with polypropylene, PTFE, and washed PTFE (washed with solvent). Drug recovery in the filtrate was determined using LC-MS/MS analysis of the filtrate.

TIP

Prepare samples for nano LC-MS using ZipTip® pipette tips (**Figure 9**). This sample preparation microdevice is a 10 µL pipette tip with a 0.6 or 0.2 µL bed of chromatography media fixed at its end with no dead volume. It is ideal for concentrating and purifying samples for sensitive analyses such as nano LC-MS or MALDI-ToF MS.

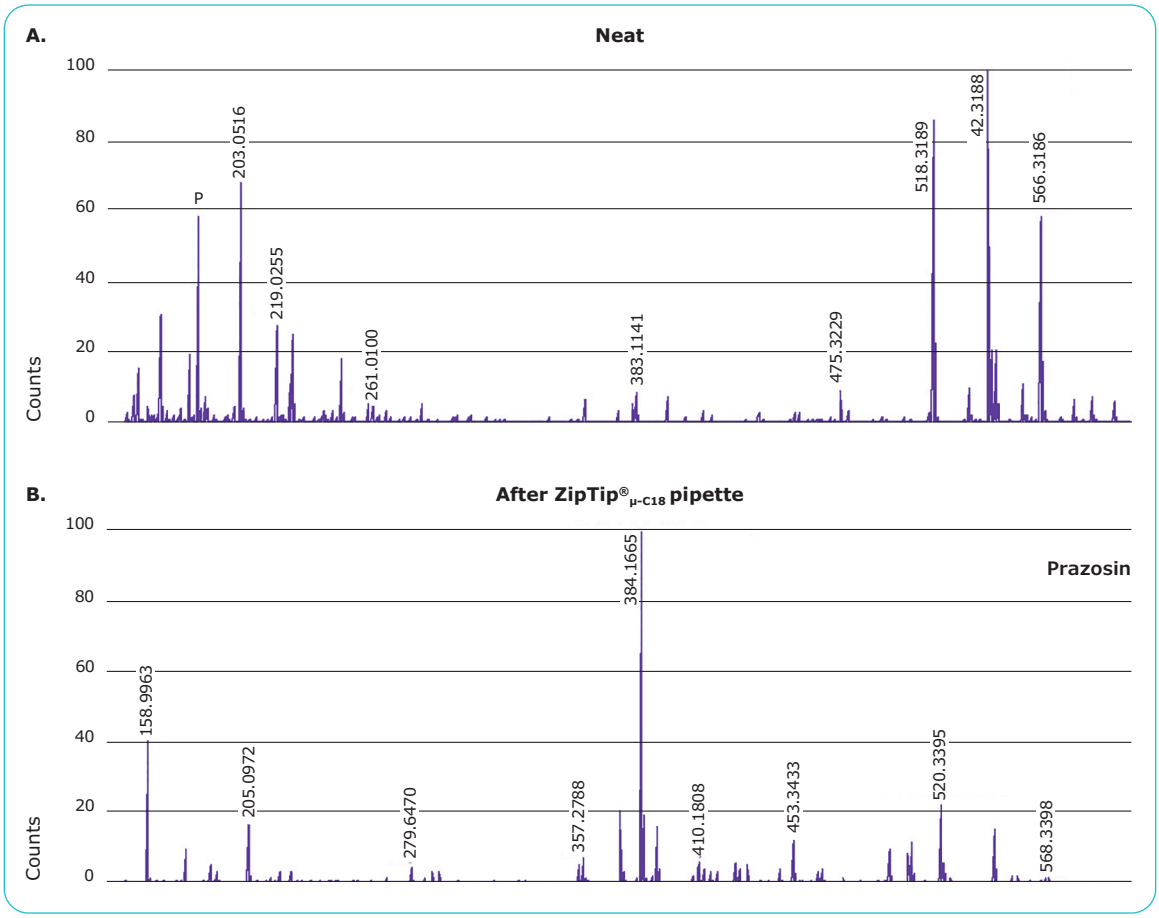


Figure 9. ZipTip® pipette tips increase sensitivity of mass spectrometric analysis. Plasma sample from rat dosed with 10 mg/kg prazosin was injected into an LTQ/Orbitrap mass spectrometer by nanoelectrospray (a) before and (b) after preparation using a C18 ZipTip® pipette tip. Adapted from Erve JCL et al, Rapid Commun. Mass Spectrom. 2008; 22: 3015–3026.

Phospholipids: a concern or LC-MS analysis of small molecules in biological matrices

Phospholipids are present as a major component of all cell membranes.

They are therefore present in all biological sample matrices including serum, plasma and whole blood and can be a problem in LC-MS analysis of small molecules because they often co-elute and ionize along with the analytes of interest. This co-elution results in ion suppression (an erroneous decrease) of the MS signal that can cause variability and impact LC-MS result accuracy. Even if phospholipids do not co-elute with the analyte of interest, they can accumulate on your analytical column.

Phospholipid removal techniques:

To overcome the problem of phospholipid-induced ion suppression, some analysts try traditional SPE. Traditional SPE often requires time-consuming and complex method development, but still only removes nominal amounts of phospholipids. A variety of products designed specifically for the removal of both proteins and phospholipids are now commercially available, including HybridSPE® plates and cartridges (**Figure 10**).

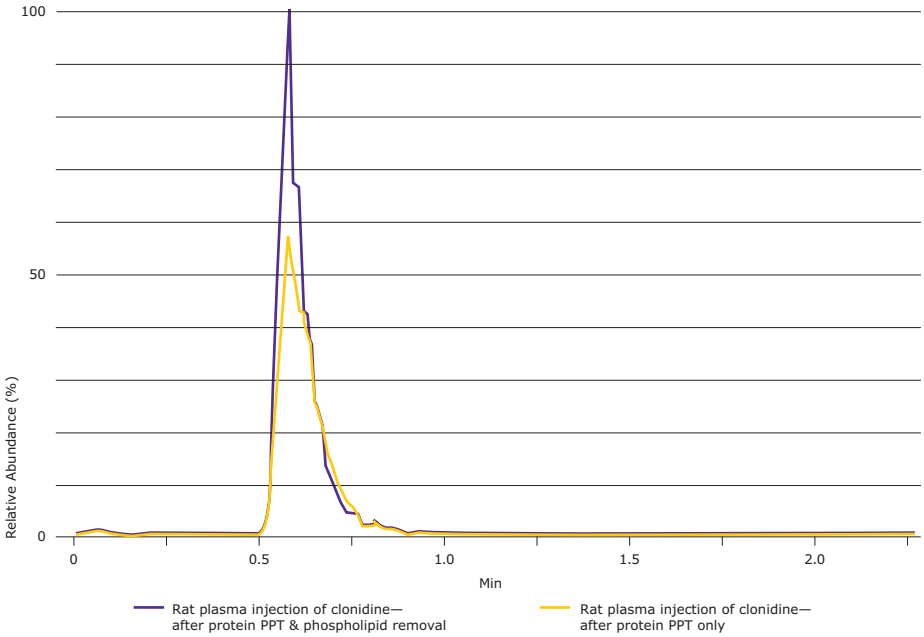


Figure 10. Removing phospholipids can improve the signal-to-noise ratio in LC-MS.

Table 5. Guide to Sample Preparation Tools

Description	Cat. No.
Millex® Syringe Filters	
Millex®-LCR Filter, 0.45 µm, Hydrophilic PTFE, 33 mm, non-sterile, 50/pk	**SLCR033NS**
Millex®-LCR Filter, 0.45 µm, Hydrophilic PTFE, 33 mm, non-sterile, 250/pk	**SLCR033NB**
Millex®-LCR Filter, 0.45 µm, Hydrophilic PTFE, 33 mm, non-sterile, 1000/pk	**SLCR033NK**
Millex®-LCR Filter, 0.45 µm, PTFE, 13 mm, non-sterile, 100/pk	**SLCRX13NL**
Millex®-LCR Filter, 0.45 µm, PTFE, 13 mm, non-sterile, 1000/pk	**SLCRX13NK**
ZipTip® Pipette Tips	
ZipTip® with 0.6 µL C 4 resin, 8/pk	**ZTC04S008**
ZipTip® with 0.6 µL C 4 resin, 96/pk	**ZTC04S096**
ZipTip® with 0.6 µL C 4 resin, 960/pk	**ZTC04S960**
ZipTip® with 0.2 µL C 18 resin, 8/pk	**ZTC18M008**
ZipTip® with 0.2 µL C 18 resin, 96/pk	**ZTC18M096**
ZipTip® with 0.2 µL C 18 resin, 960/pk	**ZTC18M960**
ZipTip® with 0.6 µL C 18 resin, 8/pk	**ZTC18S008**
ZipTip® with 0.6 µL C 18 resin, 96/pk	**ZTC18S096**
ZipTip® with 0.6 µL C 18 resin, 960/pk	**ZTC18S960**
ZipTip® with 0.6 µL strong cation resin, 8/pk	**ZTSCXS008**
ZipTip® with 0.6 µL strong cation resin, 96/pk	**ZTSCXS096**
Samplicity® Filtration Systems	
Millex®-LCR Filters for Samplicity G2, 0.45 µm Hydrophilic PTFE, 250/pk	**SAMP2LCRB**
Millex® -LG Filters for Samplicity G2, 20 µm Hydrophilic PTFE, 250/pk	**SAMP2LGNB**
Millex®-HV Filters for Samplicity G2, 0.45 µm Hydrophilic PVDF, 250/pk	**SAMP2HVNB**
Millex®-GV Filters for Samplicity G2, 22 µm Hydrophilic PVDF, 250/pk	**SAMP2GVNB**
Samplicity® G2 Filtration System, Bold Blue	**SAMP2SYSB**

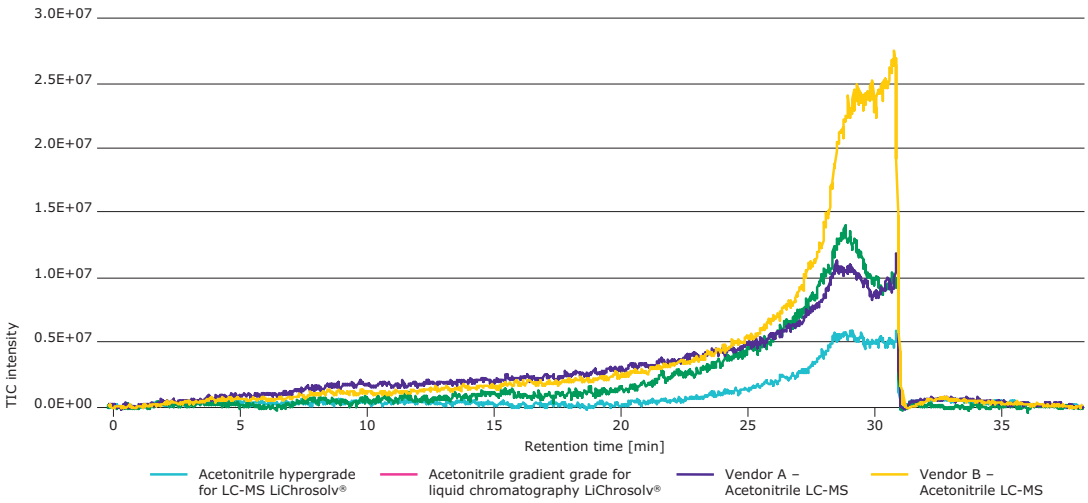
Description	Cat. No.
Ultrafree®-MC and –CL Centrifugal Microfiltration Units	
Ultrafree®-MC Filter, 0.22 µm Hydrophilic PTFE, 25/pk	**UFC30LG25**
Ultrafree®-MC Filter, 0.45 µm Hydrophilic PTFE, 25/pk	**UFC30LH25**
Ultrafree®-CL Filter, 0.22 µm Hydrophilic PTFE, 25/pk	**UFC40LG25**
Ultrafree®-CL Filter, 0.45 µm Hydrophilic PTFE, 25/pk	**UFC40LH25**
Centrifree® Ultrafiltration Device with Ultracel® Membrane	**4014**
MultiScreen® Filter Plates	
MultiScreen® Solvinert 96-well Plate, 0.45 µm Hydrophilic PTFE, 50/pk	**MSRLN0450**
MultiScreen® Deep Well Solvinert 96-well Plate, 0.45 µm Hydrophilic PTFE, 10/pk	**MDRLN0410**
Solid Phase Extraction	
EXtrelut® NT 20 pre-packed columns for extraction of lipophilic compounds from aqueous solutions (20 mL sample)	**115096**
LiChrolut® RP-18 E (40 – 63 µm) 500 mg 3 mL standard PP-tubes 50 extraction tubes per package	**119849**

Table 6. HybridSPE Cartridges and 96-well Plates

Description	Qty.	Cat. No.
Well Plates		
HybridSPE®-PLus 96-well Plate, 50 mg/well	1	**575659-U**
	20	**575673-U**
HybridSPE®-PL, Small Vol. 96-well Plate, 15 mg/well	1	**52794-U**
	20	**52798-U**
HybridSPE®-PLus 96-Well Plate Essentials Kit (contains: 96-well Plate, 50 mg/well, 1 cap mat , sealing film, and collection plate)	1	**52818-U**
SPE Cartridges		
HybridSPE®-PL Ultra Cartridge, 30 mg/1 mL	100	**55269-U**
HybridSPE®-PL Cartridge, 30 mg/1 mL	100	**55261-U**
	200	**55276-U**
HybridSPE®-PL Cartridge, 500 mg/6 mL	30	**55267-U**

Proper mobile phase preparation to minimize contaminants

For LC-MS, use the highest quality of pure solvents and reagents and avoid further contamination by careful handling. Any impurity could cause signal suppression and/or adduct formation with target molecules and therefore decrease sensitivity (signal-to-noise ratio) and/or increase complexity of the mass spectrum.



Chromatographic conditions	
System	Bruker Esquire 3000+ ion trap MS
Detection	Pos. ESI-MS, m/z range 50 – 2000
Flow rate	1.0 mL/min
Mobile phase	A: Water (Cat. No. 115333) B: Various ACN qualities as indicated in the graphics
Gradient	0 min 98% A, 30 min 0% A, 38 min 98% A
Temperature	25 °C

Figure 11. Combined TICs of the blank runs of four different acetonitrile qualities. All solvents were delivered to the MS source via an LC system.

Hypergrade and gradient grade solvents minimize contaminant peaks

Figure 9 illustrates the influence of LiChrosolv® acetonitrile quality on the background noise intensity in mass spectra. Supelco® solvents labeled “hypergrade for LC-MS LiChrosolv®” are dedicated for use with MS systems and deliver minimized contaminant peaks, ion suppression, adduct formation and background noise and therefore maximize sensitivity. Gradient grade solvent quality (labeled “gradient grade for liquid chromatography LiChrosolv®”) are suitable for LC-UV gradient runs.

Use ultrapure water (bottled or freshly purified)

Ultrapure water for LC-MS applications can be either bottled or freshly delivered from a water purification system. The choice is mainly determined by daily consumption. Demineralized tap water is not recommended for use in combination with LC-MS setups because of possible system contamination. The quality of LiChrosolv® bottled water for chromatography and freshly purified ultrapure water produced from a Milli-Q® lab water purification system is consistently high and generally independent of the regularity of use.

Ultrapure water quality is perfectly suitable for the production of mobile phase, buffers, blanks, standards preparation, sample dilution, glassware rinsing or extraction used in these critical applications.

Careful storage and handling of water are critical to prevent contamination during drawing. **Figure 12** displays total ion currents (TICs) of Milli-Q® ultrapure water drawn at different points in time: Directly on Monday (after system standby over the weekend), on the same day after discarding several liters prior to ultrapure water collection, and after four days of daily use. Generally, it is recommended to flush the system every morning by drawing and discarding a few liters prior to water collection.

TIP

For your most sensitive LC-MS analyses, we recommend replacing the 0.22 µm filter at the point-of-delivery (POD) of your Milli-Q® ultrapure water system with an LC-Pak® polisher. The LC-Pak® polisher contains C18 silica and is optimized for the most sensitive organic analyses.

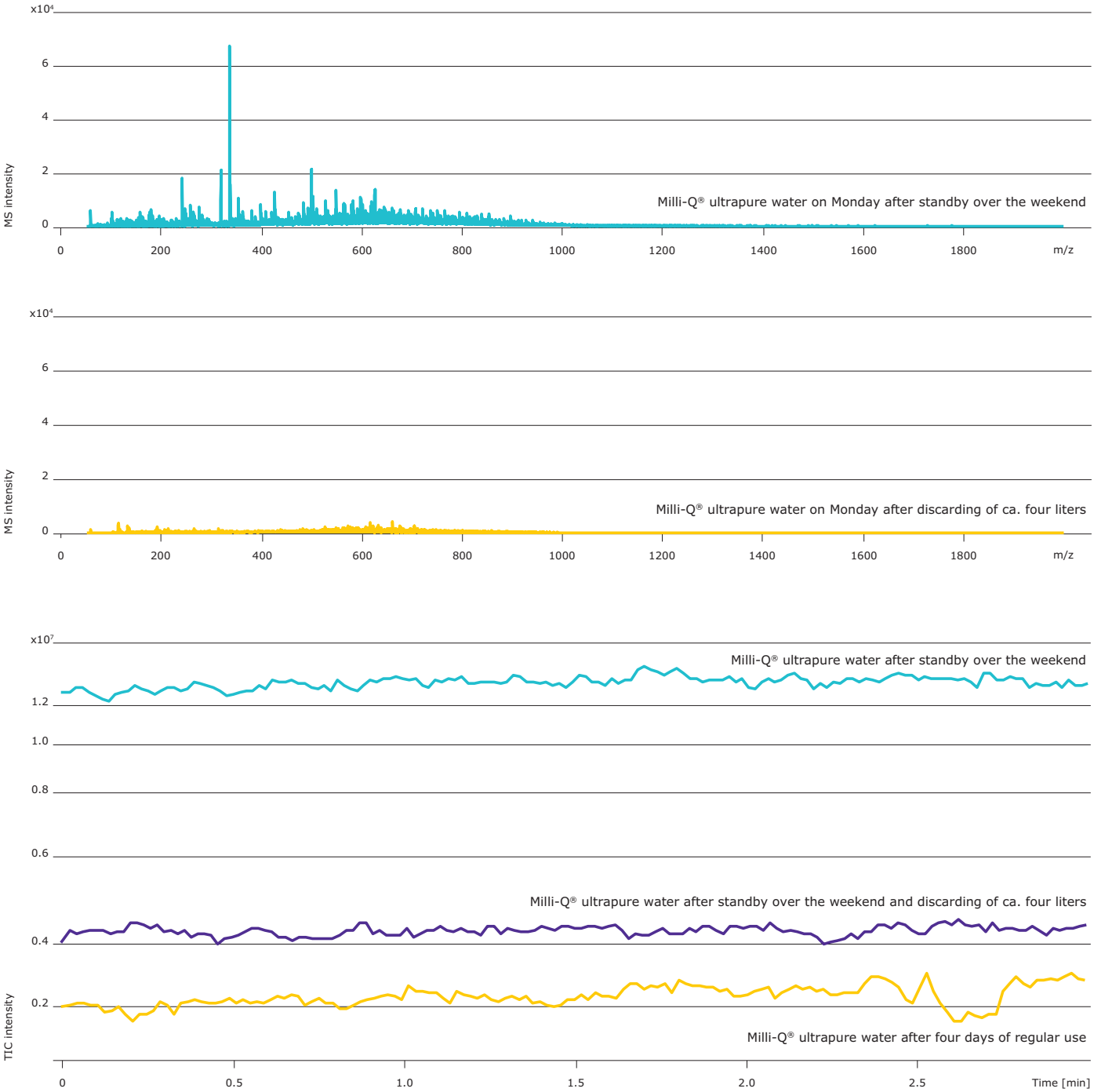


Figure 12. Exploiting the full potential of Milli-Q® ultrapure water systems via proper handling. Top: MS spectra of two samples of ultrapure water delivered at different points of time; bottom: TICs of the same samples and one additional sample. All analyses were performed via direct injection of the preconcentrated solvents into the MS operated in positive ESI mode.

Solvent storage

Tips for maintaining your solvent purity:

- Store all eluents (water and organic) in surface-treated amber glass bottles (original packaging of all Supelco® LC-MS grade solvents) or in borosilicate glass (if solvents have to be decanted).
- Select a solvent storage system that is appropriate for usage volume and withdrawal frequency (**Table 7**).
- Do not use standard glass bottles; silica and alkali dissolve and form adducts $[M+X]^+$ with analytes.
- Use Supelco® HPLC bottle caps/adapters with tube connections and membrane filter mounted directly on the original brown glass bottle. This protects both solvents and environment.
- Avoid decanting; it is a possible source of contamination.
- Avoid improvised repairs for fixing solvent tubing; this may cause leakages and/or release of contaminants to the eluents.
- Do not use plastic devices (bottles, funnels, etc.) to handle or store solvents, buffers, etc. Solvents extract additives (anti-static agents, stabilizers, plasticizers) from plastic, a source of contaminant ghost peaks and increased background noise.

Table 7. Select solvent storage options based on volume of usage and frequency of withdrawal to minimize contamination

Solvent storage systems	Storage container volume
Bottle top adapters for directly connecting solvent bottles to LC system	1 L, 2.5 L, 4 L (for infrequent withdrawal)
Stainless steel barrel with adapter for direct withdrawal	10 L, 30 L (for frequent withdrawal)
Stainless steel barrel directly connected to LC system	
Central storage of stainless steel barrels with adapters to supply solvent to multiple different laboratories	

Using water as a mobile phase?

Keep in mind these additional considerations:

- Keep 5% organic solvent in your eluent if chromatographic conditions allow. This avoids microbial contamination of bottle, tubing and LC system.
- Keep 5% of aqueous eluent in the organic mobile phase to avoid buffer precipitation in the system, e.g., in valves, and subsequent tedious cleaning procedures.

Solvent container cleaning: avoid the dishwasher

Dishwashers are standard laboratory equipment, but they are operated using chemicals such as strong bases and surfactants. Strong bases can lead to dissolution of silica and alkali from glassware and cause the formation of adducts $[M+X]^+$ with analytes, while traces of surfactants remain on the glass surface after the cleaning process and decrease MS sensitivity by increasing background noise.

The easiest way to avoid dishwashing is “cleaning” of all equipment via simple evaporation of both solvents and additives. All chemicals dedicated to the application in LC-MS are volatile; therefore, this procedure is straightforward as long as chemicals are highly pure and microbial growth can be eliminated. In case of equipment contamination, flushing with LiChrosolv® solvents or Milli-Q® ultrapure water or organic hypergrade solvents has to be performed to achieve sustainable cleaning.

Buffers and additives

When working with buffer to adjust pH of eluents, keep in mind:

- Use volatile salts (such as ammonium formate, ammonium acetate, or trimethylamine). Nonvolatile salts (e.g., phosphates, borates, sulfates or citrates) precipitate in and block the MS source, requiring tedious cleaning procedures.
- Total ionic strength of the eluent should not exceed 20 mM. Adjust buffer concentration in the aqueous solvent accordingly. Buffers for LC-MS should be prepared using the purest salt and acid/base quality available. If possible, avoid working with an ammonium bicarbonate buffer. The salt is often highly contaminated — see comparison with ammonium acetate (**Figure 13**).

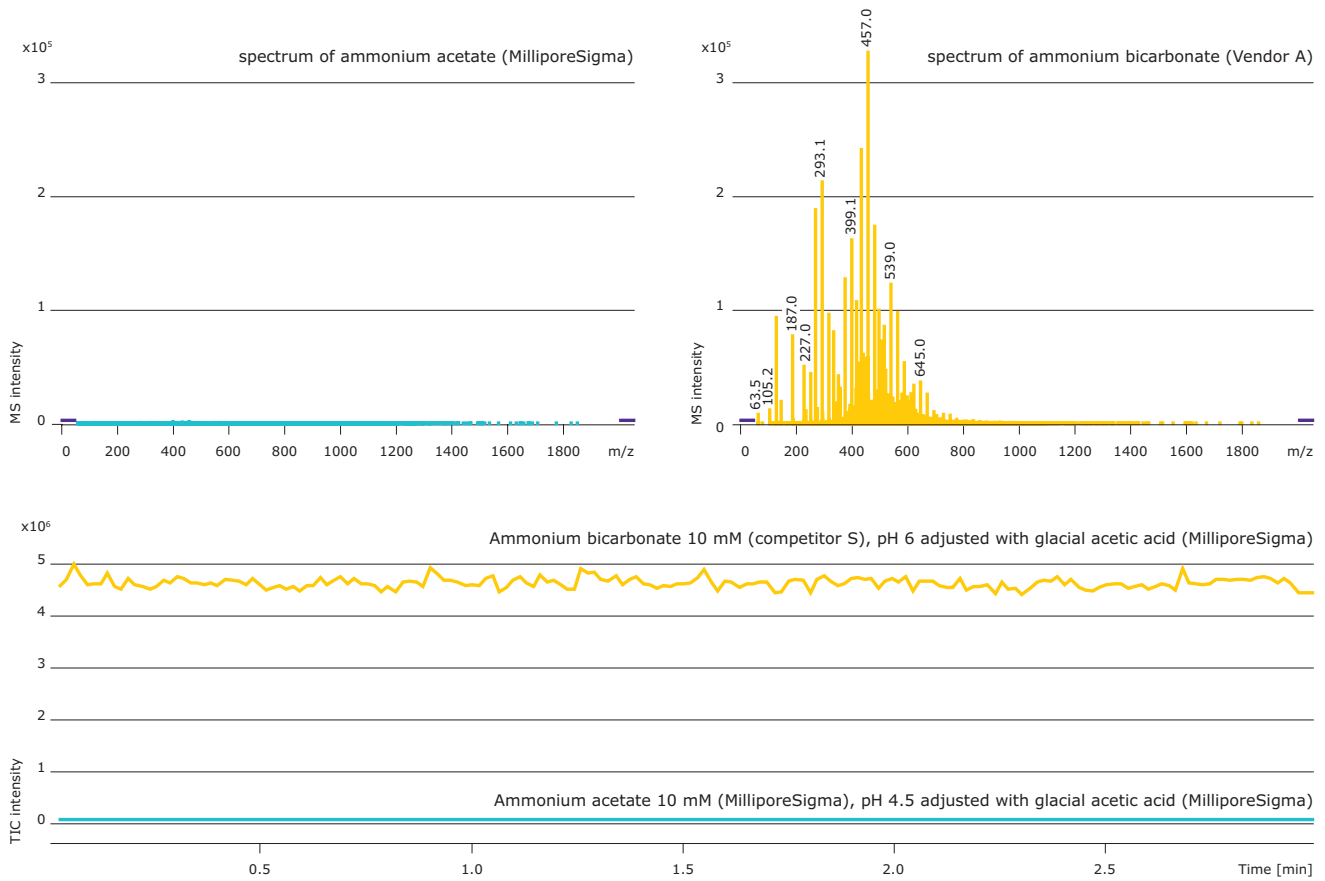


Figure 13. Comparison of MS spectra (top) and TIC chromatograms (bottom) of the two buffer systems, ammonium bicarbonate and ammonium acetate. Both mixtures were prepared using Milli-Q® ultrapure water and the same acetic acid source and were analyzed via direct injection into the mass spectrometer operated in positive ESI mode. Note the high MS background signals observed when utilizing ammonium bicarbonate as a buffer.

Buffer pH is generally adjusted via a titration with the respective acid or base and monitored with a pH electrode. The unavoidable contamination of the buffer solution with alkali ions from the pH electrode can be decreased by using a miniaturized system available from several suppliers. Unlike standard equipment with a diameter of approximately 10 mm, the diameter of miniaturized electrodes is only 3 mm.

Buffers not only adjust the pH and ionize a target molecule [M], they can also form adducts [M+buffer], e.g., with ammonium, alkali, halogens, formate or acetate. This leads to the detection of additional peaks in the MS spectrum. Even a complete suppression of the analyte signal is possible when the vapor pressure of the resulting adduct (mainly alkali) is decreased significantly. As a result of this phenomenon and in order to keep the ESI source clean, volatile buffers are recommended.

TIP

Avoid using TFA. Trifluoroacetic acid (TFA) is widely used as an ion pairing reagent to improve the liquid chromatographic separation of peptides or proteins when using standard UV for detection. However, TFA can cause strong ion suppression in mass spectrometry (mainly in negative ESI mode) and also contaminates the LC-MS system. Formic acid (0.1%) is commonly used instead as a mobile phase modifier that is compatible with LC-MS.

Table 8. Guide to Mobile Phase Preparation Reagents

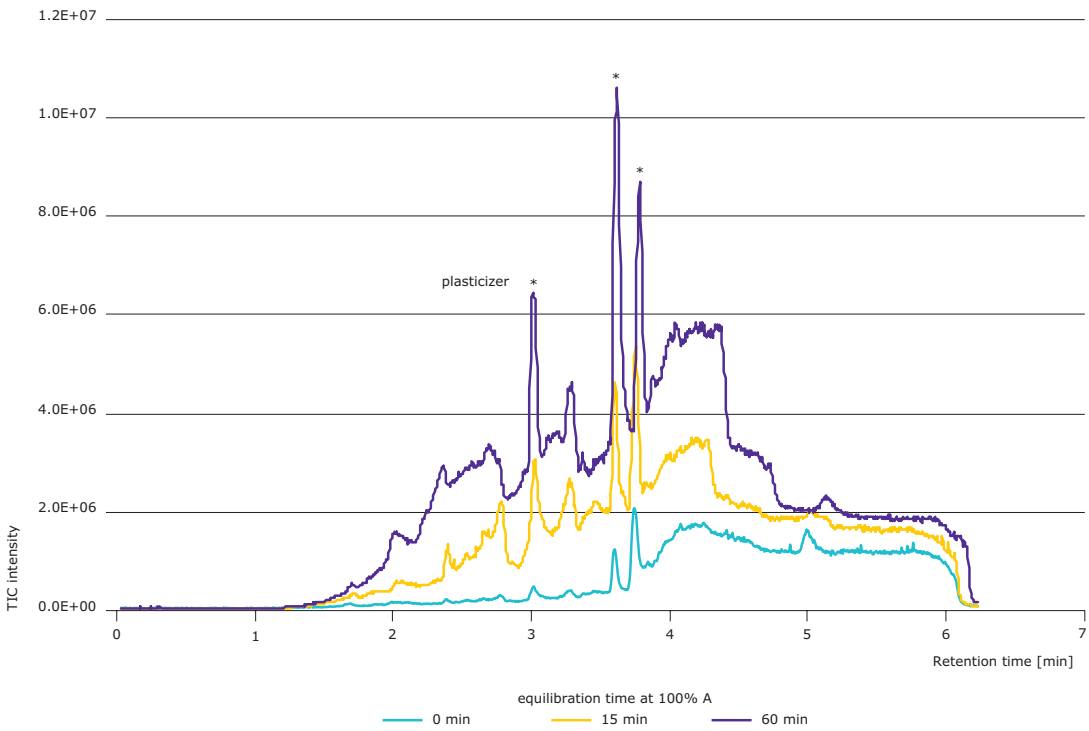
Description	Cat. No.
Milli-Q® Water Purification Solutions	
Milli-Q® IQ 7000 ultrapure water system	**ZIQ7000T0**
Milli-Q® IQ 7003/05/10/15 pure and ultrapure water system	**ZIQ7005T0**
LC-Pak® Application-Specific Polisher	**LCPAK00A1**
LiChrosolv® Solvents	
Acetonitrile hypergrade for LC-MS LiChrosolv®	**100029**
Methanol hypergrade for LC-MS LiChrosolv®	**106035**
Ethanol gradient grade for liquid chromatography LiChrosolv®	
2-Propanol gradient grade for liquid chromatography LiChrosolv®	**101040**
Toluene for liquid chromatography LiChrosolv®	**108327**
Water for chromatography LiChrosolv® (LC-MS)	**115333**
Suprapur® Inorganic Acids and Bases	
Acetic acid (glacial) 100% Suprapur®	**100066**
Ammonia solution 25% Suprapur®	**105428**
Formic acid 98–100% Suprapur®	**111670**
Hydrochloric acid 30% Suprapur®	**100318**
Other Reagents	
Acetic acid (glacial) 100% anhydrous for analysis EMSURE® ACS, ISO, Reag. Ph Eur	**100063**
Ammonia solution 28–30% for analysis EMSURE® ACS, Reag. Ph Eur	**105423**
Ammonium acetate for analysis EMSURE® ACS, Reag. Ph Eur	**101116**
Dichloromethane for organic trace analysis UniSolv®	**106454**
Formic acid 98–100% for analysis EMSURE® ACS, Reag. Ph Eur	**100264**
n-Hexane for organic trace analysis UniSolv®	**104369**
n-Pentane for organic trace analysis UniSolv®	**107288**
Petroleum benzine boiling range 40–60°C for organic trace analysis UniSolv®	**116740**
2-Propanol for analysis EMSURE® ACS, ISO, Reag. Ph Eur	**109634**

*Contact your local representative for detailed ordering information.

For even more LC-MS solvents and reagents, visit: **SigmaAldrich.com/lc-ms**

TIP

Avoid equilibrating columns with more than 10 column volumes of mobile phase (or one blank gradient run with subsequent equilibration). Contaminants in solvents and additives can accumulate on a stationary phase. **Figure 14** shows this effect for plasticizers dissolved in the eluent on a reversed phase column after equilibration for 0, 15 and 60 minutes. While these compounds would become eluted as very broad peaks under isocratic conditions (and cause an increased background noise), they elute as distinct, intensive peaks under gradient conditions and can interfere with analyte signals. Instead, run samples immediately after two or three blank runs to ensure that the system is stable prior to sample analysis.



Chromatographic conditions	
System	Bruker Esquire 6000plus
Detection	Pos. ESI-MS, TICs
Flow rate	0.4 mL/min
Mobile phase	A: Water (Cat. No. 115333) / acetonitrile (Cat. No. 100029) 95/5 (v/v) + 0.1 % formic acid (Cat. No. 100264) B: Acetonitrile + 0.1% formic acid
Gradient	0 min 100% A, 3 min to 95% B, 5 min at 95% B, then back to 100% A
Temperature	25°C
Sample	Plasticizers (*) were added by the immersion of plastic tubing in aqueous solvent B

Figure 14. Accumulation of contaminants on an HPLC column for various periods of time and elution via a gradient profile.

Effects of column choice on LC-MS performance

For samples available in small amounts (such as plasma or serum) or where analyte concentrations are low, a setup consisting of both highly sensitive separation and MS detection techniques is necessary for proper identification of the target molecules.

Suboptimal column choice and misuse of the column could decrease the signal-to-noise ratio and increase background noise.

Tips for proper column choice:

1. **Refer to comprehensive column selection guides** for full guidance on selecting a column with optimal stationary phase and dimensions and to match method specifications. Column selection guides can be found at: **SigmaAldrich.com/hplc**
2. **Pick column in accordance with eluent pH.** Using an eluent pH that is too high (e.g., >8) can dissolve the backbone of silica-based HPLC columns. Using a pH that is too low (<2) can strip the stationary phase (C18, etc.). Both options can lead to additional signals in your spectrum, increased background noise and/or signal suppression. Both scenarios may decrease column lifetime.
3. **Consider using polymeric columns for highly alkaline samples.** Polymeric columns are more stable at high pH than silica columns, where the silica may dissolve. However, polymeric columns possess smaller phase ratios and therefore, lower resolution. In addition, they are prone to swelling in organic solvents, leading to changed chromatographic characteristics. Furthermore, due to micropores in the stationary phase, column performance may be lower as compared to silica-based columns.
4. **Highly endcapped stationary phases** are another good option for sample analysis at high pH. Endcapping leads to more pH-stable columns.
5. **Column diameter influences the sensitivity of the analysis.** The sensitivity increases with decreasing column internal diameter (or increasing mass of the injected sample). For example, when changing from a 4.6 mm i.d. column to a 0.1 mm i.d. capillary column, sensitivity theoretically increases by a factor of approximately 2000 (**Table 9**). Hence, a combination of capillary chromatography coupled to mass spectrometry may be the best combination for high sensitivity analysis. However, it is important to note that extra-column effects may impact signal-to-noise ratio when column diameter is decreased—for example, the system dwell volume, dead volume in the system, the ability of the system pump to deliver accurate gradient and the volume of the detector cell can all result in peak broadening and loss of sensitivity.

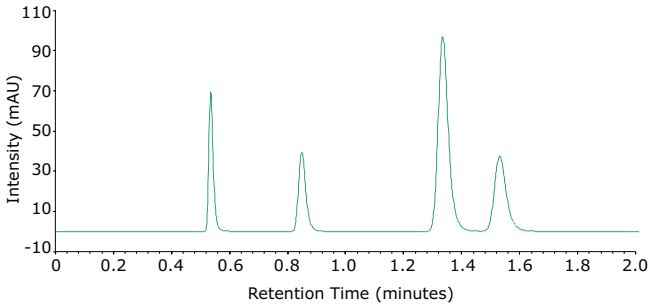
Table 9. Effect of decreasing column diameter on flow rate and relative sensitivity.

Column i.d. (mm)	Typical flow rate (µL/min)	Relative sensitivity
4.6	1000 – 6000	1
2.0	200 – 800	5.3
0.2	0.5 – 20	530
0.1	0.4 – 3	2100
0.05	0.1 – 0.8	8500

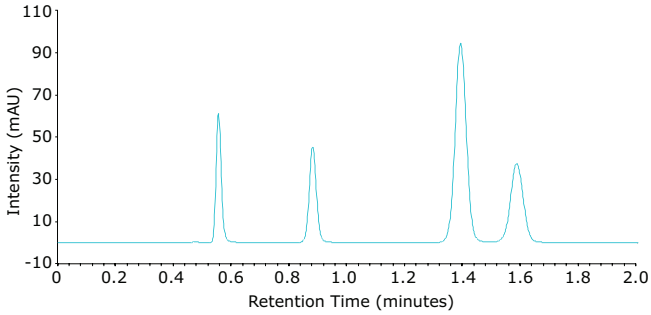
6. If the sample and analyte allow for HILIC chromatography, consider using HILIC instead of reversed phase columns. In HILIC chromatography, analysis is performed under highly organic conditions (e.g., 80% acetonitrile and 20% aqueous buffer) and polar compounds elute later than in reverse phase chromatography. Under these conditions, the eluent is vaporized more easily in the MS source, resulting in better sensitivity (signal-to-noise ratio).

Tips for column usage

1. Wash columns after each use with appropriate strong eluent to remove all adsorbed compounds. (See “Column bleeding” and **Figure 16**.)
2. Use the column at proper operating temperature (refer to each column User Guide) in order to avoid loss of stationary phase or dissolution of column backbone, both of which contribute to the appearance of additional signals on the spectrum that may interfere with analysis.
3. You can use a guard column (usually either 5 mm or 10 mm long) directly in front of the main column to protect the column against contamination (such as particles, sample matrix). Guard columns should be changed frequently in order to keep system backpressure low and in order to maximize the lifetime of the analytical column.



Chromatographic conditions		
Column	Chromolith® Performance RP18 endcapped 100-4.6 mm	
Mobile Phase	Acetonitrile/Water 40/60 (v/v)	
Flow Rate	4.0 mL/min	
Pressuer	86 - 40 = 46 bar	
Detection	UV 254 nm	
Temperature	23 °C	
Injection Volume	1 µL	
Sample	1. Biphenyl-4,4’-diol	3.1 mg
	2. Biphenyl-2,2’-diol	20.8 mg
	3. Biphenyl-4-ol	12.5 mg
	4. Biphenyl-2-ol	11.1 mg in 100 mL A/W 50/50



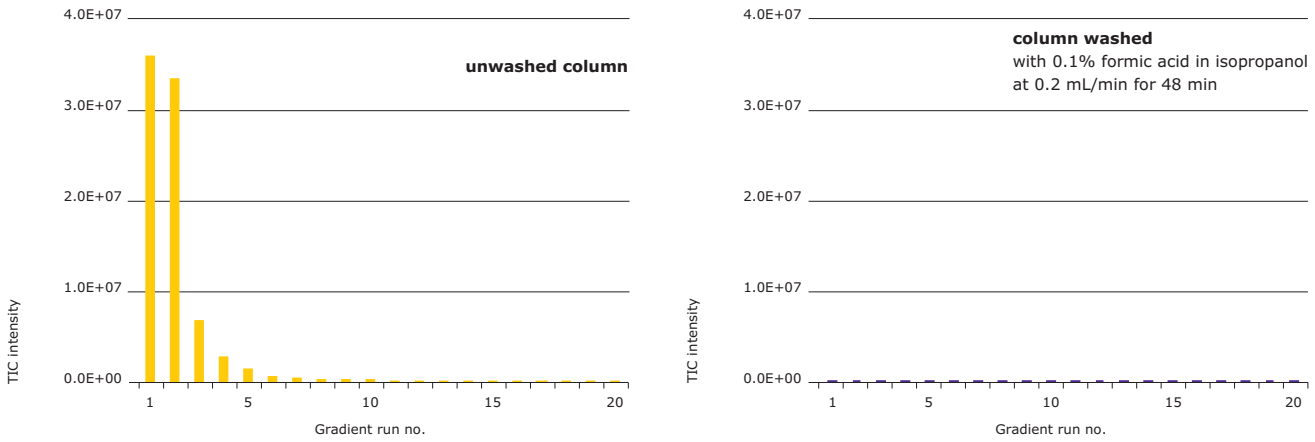
Chromatographic conditions		
Column	Chromolith® Performance RP18 endcapped 100-3 mm	
Mobile Phase	Acetonitrile/Water 40/60 (v/v)	
Flow Rate	1.7 mL/min	
Pressure	65 - 15 = 50 bar	
Detection	UV 254 nm	
Temperature	23 °C	
Injection Volume	0.4 µL	
Sample	1. Biphenyl-4,4’-diol	3.1 mg
	2. Biphenyl-2,2’-diol	20.8 mg
	3. Biphenyl-4-ol	12.5 mg
	4. Biphenyl-2-ol	11.1 mg in 100 mL A/W 50/50

Figure 15. Decreasing column diameter may improve sensitivity. Typical fast separation of four compounds in less than two minutes using a Chromolith® 4.6 mm i.d. column at a flow rate of 4 mL/min (left). The same separation was achieved on a Chromolith® 3 mm i.d. column (right). Both chromatograms exhibit excellent column efficiency and peak resolution, however the 3 mm i.d. column demonstrates improved sensitivity at just 1.7 mL/min, thus saving 57% of solvents.

Column bleeding

The stationary phase of every HPLC column (except for normal phase systems) is made out of covalently bound organic entities altering its physical properties. Depending on the quality of both phase modification and a subsequent washing step, these entities (e.g., octadecyl, cyano, phenyl) can be stripped off the column during a chromatographic run and cause weak to severe interfering signals.

This unwanted phenomenon is referred to as “column bleeding” and leads to a decreased sensitivity in MS. It can be avoided by flushing the column prior to analysis using isopropanol and 0.1% formic acid as a solvent at half optimum flow for one hour. This process removes unbound or weakly bound organic entities, minimizes column bleeding and hence increases sensitivity by decreasing background noise (**Figure 16**).



Chromatographic conditions	
System	Bruker Esquire 6000plus mass spectrometer with ion trap and electrospray ionization (ESI) source
Detection	Pos. ESI-MS, m/z range 50 – 600
Flow rate	0.4 mL/min
Mobile phase	A: Milli-Q® water from water purification system + 0.1% formic acid 98 – 100% for analysis EMSURE® (Cat. No. 100264) B: Acetonitrile hypergrade for LC-MS LiChrosolv® (Cat. No. 100029) + 0.1% formic acid
Gradient	0 min 95% A, 3 min 5% A, 5 min 5% A
Temperature	25 °C

Figure 16. Column washing can compensate for column bleeding. Total ion current (TIC) of a competitor column after 20 gradient runs: left– unwashed column; right– column washed with 0.1% formic acid in isopropanol at 0.2 mL/min for 48 min.

Overview of U/HPLC columns for LC-MS

For LC-MS, particulate HPLC columns, preferably based on high purity Type B silica, are widely used.

1. Small particles deliver high separation efficiency/ peak capacity
2. Suitable for cleaner samples and MS, after removal of matrix components

Typical fully porous particulate columns:

Purospher® STAR HPLC and UHPLC columns are available with particle sizes of 2 µm, 3 µm and 5 µm in various column modifications providing high efficiency, extended pH stability (pH 10.5) for RP-18e and RP-8e and stability in aqueous mobile phases.

Ascentis® and Discovery® HPLC columns are available with 3 µm and 5 µm particle sizes and a very broad range of column chemistries providing selectivity for the separation of almost every compound.

Titan® UHPLC columns based on monodisperse particles of 1.9 µm particle size provide very high efficiency due to a more consistent packed bed.

HILIC is superior for the separation of polar hydrophilic molecules, i.e., many of the endogenous molecules.

SeQuant® ZIC®-HILIC/cHILIC/pHILIC bonded zwitterionic stationary phases combine perfectly with ESI-MS detection due to the applied solvents and additives. A significant increase in sensitivity in comparison with reversed phase chromatography can be achieved. Strongly retained polar analytes can be removed from HILIC columns by changing to a more polar eluent.

Superficially porous particulate columns for maximum resolution and speed:

Fused-core® columns feature narrower particle size distribution and shorter diffusion path compared to fully porous particles. The result is increased resolution, added sensitivity and faster runs.

Ascentis® Express HPLC and UHPLC columns provide about 40% more efficiency in comparison to columns with fully porous particles of the same size. This performance enhancement is applicable to all HPLC instruments (in addition to UHPLC systems). Particle sizes of 2 µm, 2.7 µm and 5 µm are available with a very broad range of modifications, all excellently suitable for LC-MS use.

BIOshell™ HPLC and UHPLC columns deliver maximum speed and efficiency for the separation of biomolecules on both UHPLC and HPLC systems. The Fused-Core® superficially porous silica particles with pore sizes from 90 Å up to 1000 Å allows superior separation of glycans as well as very large proteins. In particular, a pore size of 1000 Å shows very clear advantages over common 300 Å pores for the separation of very large proteins in biotherapeutic drug development such as monoclonal antibodies (mAbs) or proteins with molecular weights greater than 100 kDa.

The advantages of Fused-Core® columns are:

- Maximum speed and efficiency on both UHPLC and HPLC systems (particle sizes: 2 µm, 2.7 µm and 5 µm)
- 40% more efficiency in comparison to Fully Porous Particles (FPP) of same particle size
- UHPLC columns with 2 µm particles (pressure stable 1000 bar)
- Column dimensions from 0.075 mm ID (capillary columns) to 4.6 mm ID (analytical HPLC columns)
- Very broad range of column chemistries

Monolithic silica columns have high matrix tolerance

The analysis of samples with high matrix load requires tedious and time-consuming sample preparation steps. For cost-effective investigations, sample handling has to be kept as short as possible and combined with robust LC columns displaying a high matrix tolerance and long lifetime. The 50-2 mm monolithic silica column is well-suited for fast gradient run liquid chromatography, and the applied low flow rates make it the perfect choice for MS detection. Analysis of matrix-rich samples, such as food or tissue, can be performed on this robust column type without the need for a guard column or tedious and complex sample preparation procedures.

The advantages of Chromolith® monolithic silica columns are:

- Exceptional robustness or lifetime—described as number of injections—enabling cost savings
- High matrix tolerance decreases tedious sample preparation steps, speeds up all processes and allows for fast and simple HPLC analyses
- Very low column back-pressure, fast analytical speed and high reproducibility on standard HPLC systems as well as using UHPLC instruments

Consult a column selection guide today!

SigmaAldrich.com/hplc

Effects of Reference Material choice on LC-MS performance

How to choose the correct reference material quality grade for your needs?

Who uses reference materials?

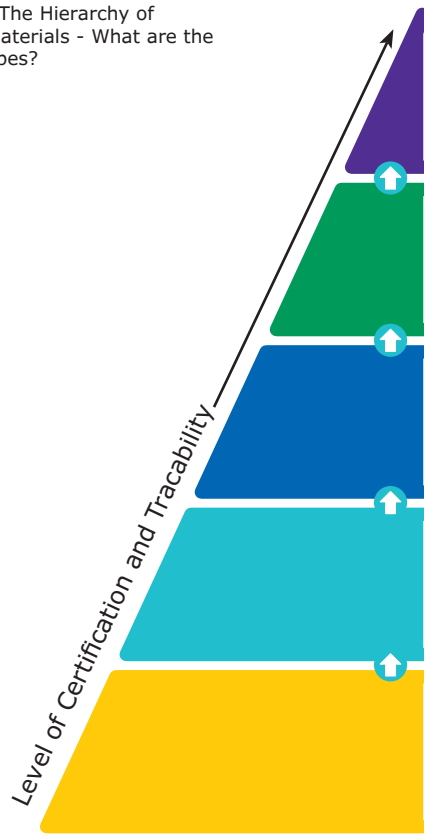
Reference materials are a critical component of the analytical testing workflow and can help to avoid or identify contaminants. Through calibration of measurement systems, validation of methods, and quality control programs, reference materials ensure accuracy in testing. Proper selection of the right reference material for the laboratory's testing application is important, because results are only as accurate as your reference. Therefore it is important to understand the five major quality grades of reference materials.

ISO 17034 and quality grades of standards, reference materials and certified reference materials

The reference material hierarchy includes four major quality grades, from national metrology and other primary standards to Certified Reference Materials (CRMs), Reference Materials (RMs) and Analytical Standards. Level of certification and traceability requirements increase for each higher level. Where national governments give standardization to the top level, specific ISO guidelines provide standardization for CRMs and RMs. These ISO requirements include ISO 17034, ISO/IEC 17025 and ISO Guide 31.

Reference material producers must meet these ISO requirements to manufacture CRMs or RMs. For both of these quality grades, Certificates of Analysis must be provided, and the information contained within is defined by the aforementioned ISO guidelines. The quality specifications for the last two levels are defined by each individual producer rather than by a national government or ISO accreditations specific to CRMs and RMs.

Figure 17. The Hierarchy of Reference Materials - What are the Different Types?



National Metrology Standard (e.g. NIST, JRC, NMI Australia)

Compendial Standard (e.g. USP, EP, BP, JP, IP)

- Issued by an authorized body
- Considered to provide the highest level of accuracy & traceability

Certified Reference Material (CRM) (ISO 17034, 17025)

- Considered to provide the highest level of accuracy, uncertainty, and traceability to an SI unit of measurement
- Manufactured by an accredited Reference Material Producer

Reference Material (RM) (ISO 17034)

- Fulfilling ISO requirements which are less demanding than for CRMs
- Manufactured by an accredited Reference Material Producer

Analytical Standard (ISO 9001)

- Certificate of Analysis available
- Level of certification varies

Reagent Grade / Research Chemical

- May come with a Certificate of Analysis
- Are not characterised for use as reference materials

What is measured in each grade of reference material?

Purity and Identity of the material are typically included in the Certificate of Analysis for each of the five quality grades. Content and Stability are required for the primary standards or ISO-defined CRM and RM.

Analytical standards and research chemicals may or may not include these two parameters as their inclusion is dependent on the producer. Analytical Standards can also in some cases be Quality Control materials compliant with ISO Guide 80.

Homogeneity is required for the primary standards, CRM, and RM, but this parameter will not be found with the lower quality grades. Uncertainty and Traceability information are limited to just the primary standards and CRM. In the pharmaceutical world, secondary standards can be CRMs or RMs, but here, there are two different types of traceability – to the SI unit of measurement for the ISO-defined CRM as well as traceability to the primary compendial standard, which is a requirement specific to pharmaceutical secondary standards.

Table 10. The Hierarchy of Reference Materials – What's the Difference?

Parameter	NMI Standard	Compendial Standard	CRM	RM	Analytical Standard	Research Chemical
Purity	✓	✓	✓	✓	✓	✓
Identity	✓	✓	✓	✓	✓	✓
Content	✓	✓	✓	✓	maybe	
Stability	✓	✓	✓	✓	✓	
Homogeneity	✓	✓	✓	✓		
Uncertainty	✓		✓			
Traceability	✓		✓	✓		
Type	Primary Measurement Standard or Primary Standard (Pharma)		Primary or Secondary Standard (Pharma)	Secondary Standard (Pharma)		

Choose the correct reference material for your testing purpose

For instrument qualifications and calibrations, establishing and maintaining traceability is critical. The selected reference material should help the laboratory achieve this. In daily routine system suitability applications, it might be important to qualify something that is practical and easy to use, yet reliable and cost effective for everyday use. In method validation, it's critical to use highly accurate and precise materials to show that the laboratory method is accurate and precise. For identity and screening purposes, important attributes of reference materials include proven authenticity and identity. For quantitation, assays, or stability assessment, stable and accurate reference materials are needed.

Table 11

Type of test	Use of Ref. Mat.	Examples	Requirements of the Ref. Mat.
Instrument qualification / Calibration	Establish system performance Measurement accuracy	Annual qualifications Routine balance calibrations	Traceable
Routine calibration / System suitability	Daily / weekly System / method specific Establish routine performance	Pre-use balance calibrations System performance checks for LC-UV/MS; GC-FID…	Qualify as suitable for use
Method validation	Accuracy Precision Specificity & interferences LOD/LOQ & Linearity	Pharma QC; Environmental testing Standards of the analyte(s), interferences, impurities	Accurate Traceable
Identity	Comparison of unknown to known	Incoming raw materials in pharma, food etc. Screening tests	Authenticity
Content or assay	Quantitation of analytes	Pesticide/toxin limits Pharma QC - API content	Certified content Traceable
Stability assessment	Monitor product stability	Pharma QC	Stable, homogenous
Internal Quality Control	Method accuracy	Routine quantitation of analytes - pharma/pesticides/diagnostics	Certified content Traceable

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Which quality grade is the best fit for purpose?

Fit for purpose decisions in selection of reference materials can depend on several factors, from regulatory requirements, availability, and type of testing application to level of accuracy and sample matrix.

Table 12. Fit for Purpose Guidance in Standard Selection

Type of Test	NMI Standard	Compendial Standard	CRM	RM	Analytical Standard	Reagent Chemical	Attribute
Instrument qualification / Calibration	✓	✓	✓				Traceability & Accuracy
Routine calibration/ System suitability	✓	✓	✓	✓	maybe		Qualified standard (Primary or secondary)
Method validation	✓	✓	✓	✓			Accuracy, Precision, Bias
Identity	✓	✓	✓	✓	✓	✓	Authenticity
Content or assay	✓	✓	✓	✓	maybe		Qualified standard
Stability assessment	✓	✓	✓	✓	maybe		Qualified standard
Internal Quality Control	✓	✓	✓	✓	maybe		Qualified standard
Regulatory / Accreditation	✓	✓	✓	✓			Qualified standard

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Appendix I.

Common mass spectrometry contaminants and their sources

This list of potential interfering or contaminant ions in mass spectrometry (ESI positive mode, mass ≤1000 Da) is adapted from an excerpt of "Interferences and contaminants encountered in modern mass spectrometry" Bernd O. Keller, Jie Sui, Alex B. Young and Randy M. Whittal Analytica Chimica Acta 627, Issue 1, 3 October 2008, Pages 71-81. However, we have updated the masses listed in the previous publication by calculating the singly charged monoisotopic ion mass of each listed ion based on its molecular formula.

Mono-isotopic ion mass (singly charged)	Ion type	Formula for M or subunit or sequence	Compound ID or species	Possible origin and other comments
33.0340	$[M+H]^+$	CH_3OH	Methanol	Acetonitrile, solvent
42.0344	$[M+H]^+$	CH_3CN	ACN	Acetonitrile, solvent
59.0609	$[M+NH_4]^+$	CH_3CN	ACN	Acetonitrile, solvent
63.0446	$[A_1B+H]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
64.0163	$[M+Na]^+$	CH_3CN	ACN	Acetonitrile, solvent
65.0603	$[M_2+H]^+$	CH_3OH	Methanol	Methanol, solvent
74.0606	$[M+H]^+$	C_3H_7NO	Dimethyl formamide	solvent
74.0606	$[A_1B_1+H]^+$	$(CH_3CN)_n(CH_3OH)_m$	Acetonitrile/Methanol	ESI solvents
77.0603	$[A_1B+H]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
79.0218	$[M+H]^+$	C_2H_6OS	DMSO	Dimethylsulfoxide, solvent
83.0609	$[M_2+H]^+$	CH_3CN	Acetonitrile	ESI solvents
85.0265	$[A_1B+Na]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
85.0594	$[M+H]^+$	C_2D_6OS	d6-DMSO	d6-Dimethylsulfoxide, solvent
88.0399	$[A_1B_1+H]^+$	$(CH_3CN)_n(HCOOH)_m$	Acetonitrile/Formic Acid	ESI solvents
96.0425	$[A_1B_1+Na]^+$	$(CH_3CN)_n(CH_3OH)_m$	Acetonitrile/Methanol	ESI solvents
99.0422	$[A_1B+Na]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
101.0841	$[M+H]^+$	$C_5H_{10}NO$	NMP	N-methyl 2-pyrrolidone; solvent, floor stripper
101.0005	$[A_1B+K]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
101.0037	$[M+Na]^+$	C_2H_6OS	DMSO	Dimethylsulfoxide, solvent
101.0814	$[A_2B_2+H]^+$	$[MeOH]_n[H_2O]_m$	Methanol/Water	ESI solvents
102.0555	$[A_1B_1+H]^+$	$(CH_3CN)_n(CH_3COOH)_m$	Acetonitrile/Acetic Acid	ESI solvents
102.1283	$[M+H]^+$	$C_6H_{15}N$	TEA	Triethylamine, buffer
103.9561	$[M+_{63}Cu]^+$	C_2H_3N	ACN	Acetonitrile, solvent
104.9928	$[M+Na]^+$	$C_2H_3O_2Na$	Sodium acetate	ESI solvents
105.0429	$[M_2+Na]^+$	C_2H_3N	ACN	Acetonitrile, solvent
41.0265	$[M+_{65}Cu]^+$	C_2H_3N	ACN	Acetonitrile, solvent
107.0708	$[A_2B+H]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
115.0161	$[A_1B+K]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
115.0871	$[A_1B_1+H]^+$	$(CH_3CN)_n(C_3H_7NO)_m$	Acetonitrile/ Dimethylformamide	solvent
120.0483	$[M+CH_3CN+H]^+$	C_2H_6OS	DMSO	Dimethylsulfoxide, solvent
122.0817	$[M+H]^+$	$C_4H_{11}NO_3$	TRIS	TRIS, buffer
123.0633	$[A_2B_2+Na]^+$	$[CH_3OH]_n[H_2O]_m$	Methanol/Water	ESI solvents
123.0922	$[M+H]^+$	$C_7H_{10}N_2$	DMAP	Dimethylaminopyridine, solvent
124.0374	$[A_1B_1+Na]^+$	$(CH_3CN)_n(CH_3COOH)_m$	Acetonitrile/Acetic Acid	ESI solvents
129.0528	$[A_2B+Na]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
130.1596	$[M+H]^+$	$C_8H_{19}N$	DIPEA	Diisopropylethylamine, solvent
132.9054	M^+	Cs	Cs-133	Cesium, from Cesium Iodide used as calibrant
133.1076	$[A_3B_2+H]^+$	$[CH_3OH]_n[H_2O]_m$	Methanol/Water	ESI solvents
135.1021	$[A_2B+H]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
137.0749	$[M+CH_3CN+NH_4]^+$	C_2H_6OS	DMSO	Dimethylsulfoxide, solvent
142.0303	$[M+CH_3CN+Na]^+$	C_2H_6OS	DMSO	Dimethylsulfoxide, solvent
144.1752	$[M+H]^+$	$C_9H_{21}N$	TPA	Tripropylamine, solvent
144.9827	$[M_2+_{63}Cu]^+$	CH_3CN	ACN	Acetonitrile, solvent, together with m/z 147
145.0267	$[A_2B+K]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
146.0694	$[M_3+Na]^+$	CH_3CN	ACN	Acetonitrile, solvent
146.9809	$[M_2+_{65}Cu]^+$	CH_3CN	ACN	Acetonitrile, solvent, together with m/z 145
147.1134	$[A_2B_2+H]^+$	$(CH_3CN)_n(CH_3OH)_m$	Acetonitrile/Methanol	ESI solvents
149.0239	$[f+H]^+$	$C_8H_4O_3$	Pthalic Anhydride	fragment ion originating from phthalate esters

Mono-isotopic ion mass (singly charged)	Ion type	Formula for M or subunit or sequence	Compound ID or species	Possible origin and other comments
150.1283	$[M+H]^+$	$C_{10}H_{15}N$	Phenyldiethylamine	solvent
151.0970	$[A_3B+H]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
153.1392	$[M+H]^+$	$C_9H_{16}N_2$	DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
155.0895	$[A_3B_2+Na]^+$	$[CH_3OH]_n[H_2O]_m$	Methanol/Water	ESI solvents
157.0357	$[M_2+H]^+$	C_2H_6OS	DMSO	Dimethylsulfoxide, solvent
157.0841	$[A_2B+Na]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
158.9646	$[M+Na]^+$	$C_2F_3O_2Na$	NaTFA	Sodium trifluoroacetate, salt
163.0395	$[M-CH_3OH+H]^+$	$C_{10}H_{10}O_4$	Dimethyl phthalate	Phthalate esters, plasticizer
163.1334	$[M+H]^+$	$C_8H_{18}O_3$	DGBE	Diethylene glycol monobutyl ether, cpd. In scintillation cocktail
169.0953	$[A_2B_2+Na]^+$	$(CH_3CN)_n(CH_3OH)_m$	Acetonitrile/Methanol	ESI solvents
170.1188	$[M_2+H]^+$	C_2D_6OS	d6-DMSO	d6-Dimethylsulfoxide, solvent
171.0058	$[f+Na]^+$	$C_8H_4O_3$	Phthalic anhydride	from phthalate esters, plasticizer
173.0580	$[A_2B+K]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
173.0790	$[A_3B+Na]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
179.0176	$[M_2+Na]^+$	C_2H_6OS	DMSO	Dimethylsulfoxide, solvent
181.1229	$[M+H]^+$	$C_{11}H_{16}O_2$	BHA	Butylated hydroxyanisole, antioxidant additives
183.0810	$[M+H]^+$	$C_{13}H_{10}O$	DPK	Diphenyl ketone
183.1444	$[A_4B_3+H]^+$	$[CH_3OH]_n[H_2O]_m$	Methanol/Water	ESI solvents
185.1154	$[M+Na]^+$	$C_8H_{18}O_3$	GE	glycol ether
186.2222	$[M+H]^+$	$C_{12}H_{27}N$	TBA	Tributylamine, solvent
189.0529	$[A_3B+K]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
193.1440	$[A_3B+H]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
195.0657	$[M+H]^+$	$C_{10}H_{10}O_4$	Dimethyl phthalate	Phthalate esters, plasticizer
195.1232	$[A_4B+H]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
203.1048	$[M+Na]^+$	$C_{11}H_{16}O_2$	BHA	Butylated hydroxyanisole, antioxidant additives
205.1263	$[A_4B_3+Na]^+$	$[CH_3OH]_n[H_2O]_m$	Methanol/Water	ESI solvents
214.0902	$[M+H]^+$	$C_{10}H_{15}NO_2S$	n-BBS	n-butyl benzenesulfonamide, plasticizer
215.1259	$[A_3B+Na]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
217.1052	$[A_4B+Na]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
221.1905	$[M+H]^+$	$C_{15}H_{24}O$	BTH	Butylated hydroxytoluene, Antioxidant
225.1967	$[M+H]^+$	$C_{13}H_{24}N_2O$	DCU	N,N'-Dicyclohexylurea
231.0999	$[A_3B+K]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
231.1167	$[M+NH_4]^+$	$C_{10}H_{15}NO_2S$	n-BBS	n-butyl benzenesulfonamide, plasticizer
233.0791	$[A_4B+K]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
236.0721	$[M+Na]^+$	$C_{10}H_{15}NO_2S$	n-BBS	n-butyl benzenesulfonamide, plasticizer
239.1495	$[A_5B+H]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
239.2254	$[(M.H_{35}Cl)_2\text{-}Cl]^+$	$C_6H_{15}N$	TEA.HCl	Triethylamine-hydrochloride, buffer
241.2224	$[(M.H_{37}Cl)_2\text{-}Cl]^+$	$C_6H_{15}N$	TEA.HCl	Triethylamine-hydrochloride, buffer
242.2848	M^+	$C_{16}H_{36}N$	TBA	Tetrabutylammonium, buffer
243.1174	M^+	$C_{19}H_{15}$	Trityl cation	Trityl cation, [Ph3C]+
243.1725	$[M+Na]^+$	$C_{15}H_{24}O$	BTH	Butylated hytroxytoluene, Antioxidant additives
251.1858	$[A_4B+H]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
251.2011	$[AB_1+H]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
257.0316	$[M_3+Na]^+$	C_2H_6OS	DMSO	Dimethylsulfoxide, solvent
261.1314	$[A_5B+Na]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
265.2168	$[AB_1+H]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
267.1725	$[M+H]^+$	$C_{12}H_{27}O_4P$	TBP	Tributylphosphate
273.1279	M^+	$C_{20}H_{17}O$	MMT	Monomethoxytrityl cation
273.1678	$[A_4B+Na]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
273.1830	$[AB_1+Na]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
277.1053	$[A_5B+K]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
279.0939	$[M+H]^+$	$C_{18}H_{15}OP$	TPO	Triphenylphosphine oxide
279.1596	$[M+H]^+$	$C_{16}H_{22}O_4$	Dibutylphthalate	Plasticiser, phtalate ester
279.2300	$[AB_1+Na]^+$	$[C_{14}H_{28}O][C_2H_4O]_n$	Triton®, reduced	X-100R, X-114R, X-405R, or X-45R Detergents
281.0517	$[M+H\text{-}CH_4]^+$	$[C_2H_6SiO]_4$	Polysiloxane	Polysiloxane, (neutral methane loss from m/z 297)
282.2797	$[M+H]^+$	$C_{18}H_{35}NO$	Oleamide	Slip agent in polyethylene films
283.1757	$[A_6B+H]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
284.2953	$[M+H]^+$	$C_{18}H_{37}NO$	Stearamide	Slip agent in polyethylene films
287.1987	$[AB_1+Na]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
288.2539	$[M+H]^+$	$C_{16}H_{33}NO_3$	n,n-DDA	n,n-bis(2-hydroxyethyl) dodecanamide, anti-static agent
289.1417	$[A_4B+K]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether

Mono-isotopic ion mass (singly charged)	Ion type	Formula for M or subunit or sequence	Compound ID or species	Possible origin and other comments
293.2457	$[AB_1+Na]^+$	$[C_{15}H_{30}O][C_2H_4O]_n$	Triton®, reduced	101R Detergents
295.2273	$[AB_2+H]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
297.0830	$[M+H]^+$	$[C_2H_6SiO]_4$	Polysiloxane	Polysiloxane, followed by m/z
301.1416	$[M+Na]^+$	$C_{16}H_{22}O_4$	Dibutylphthalate	Dibutylphthalate, plasticizer
304.2616	$[M+Na]^+$	$C_{18}H_{35}NO$	Oleamide	Slip agent in polyethylene films
305.1576	$[A_6B+Na]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
306.2773	$[M+Na]^+$	$C_{18}H_{37}NO$	Stearamide	Slip agent in polyethylene films
309.2277	$[A_5B+H]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
309.2430	$[AB_2+H]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
315.2535	$[M+H]^+$	$C_{18}H_{34}O_4$	DBS	Dibutyl sebacate, plasticizer
317.1155	$[M+K]^+$	$C_{16}H_{22}O_4$	Dibutylphthalate	Dibutylphthalate, plasticizer
317.2093	$[AB_2+Na]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
321.1316	$[A_6B+K]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
323.2562	$[AB_2+Na]^+$	$[C_{14}H_{28}O][C_2H_4O]_n$	Triton®, reduced	X-100R, X-114R, X-405R, or X-45R Detergents
325.2590	$[M_2+H]^+$	$C_8H_{18}O_3$	DGBE	Diethylene glycol monobutyl ether, cpd. In scintillation cocktail
327.0786	$[M+H]^+$	$C_{18}H_{15}O_4P$	TPP	Triphenyl phosphate, flame retardant in plastics
327.2019	$[A_7B+H]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
331.2097	$[A_5B+Na]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
331.2249	$[AB_2+Na]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
337.1190	$[M+H]^+$; ($_{120}$Sn)	$C_{13}H_{28}O_2S_n$	Tributyl tin formate	Tributyl tin formate, catalyst
337.2719	$[AB_2+Na]^+$	$[C_{15}H_{30}O][C_2H_4O]_n$	Triton®, reduced	101R Detergents
338.3423	$[M+H]^+$	$C_{22}H_{43}NO$	Erucamide	Erucamide, (Cis-13-docosenoic amide)
339.2535	$[AB_3+H]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
347.1836	$[A_5B+K]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
349.1838	$[A_7B+Na]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
353.2692	$[AB_3+H]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
355.0705	$[M+H\text{-}CH_4]^+$	$[C_2H_6SiO]_5$	Polysiloxane	Polysiloxane, (neutral methane loss from m/z 371)
355.3688	$[M\text{-}Cl]^+$	$C_{22}H_{47}N_2OCl$	PATC	Palmitamidopropyl-trimonium chloride, personal care products additive
360.3242	$[M+Na]^+$	$C_{22}H_{43}NO$	Erucamide	Erucamide, (Cis-13-docosenoic amide)
361.2355	$[AB_3+Na]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
365.1578	$[A_7B+K]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
367.2696	$[A_6B+H]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
367.2824	$[AB_3+Na]^+$	$[C_{14}H_{28}O][C_2H_4O]_n$	Triton®, reduced	X-100R, X-114R, X-405R, or X-45R Detergents
368.4256	$[M\text{-}Cl]^+$	$C_{25}H_{54}NCl$	BTAC-228	Behentrimonium chloride, personal care product additive
371.1018	$[M+H]^+$	$[C_2H_6SiO]_5$	Polysiloxane	Polysiloxane, followed by m/z 388
371.2281	$[A_8B+H]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
371.3161	$[M+H]^+$	$C_{22}H_{42}O_4$	DEHA	Bis(2-ethylhexyl) adipate, plasticizer
371.3161	$[M+H]^+$	$C_{22}H_{42}O_4$	DOA	Dioctyl adipate, plasticizer
375.2511	$[AB_3+Na]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
381.2981	$[AB_3+Na]^+$	$[C_{15}H_{30}O][C_2H_4O]_n$	Triton®, reduced	101R Detergents
383.2797	$[AB_4+H]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
388.1284	$[M+NH_4]^+$	$[C_2H_6SiO]_5$	Polysiloxane	Polysiloxane, (see m/z 371)
389.2515	$[A_6B+Na]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
391.2848	$[M+H]^+$	$C_{24}H_{38}O_4$	Diisooctyl phthalate	Diisooctyl phthalate, plasticiser
393.2101	$[A_8B+Na]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
397.2954	$[AB_4+H]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
405.2255	$[A_6B+K]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
405.2617	$[AB_4+Na]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
409.1840	$[A_8B+K]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
411.3086	$[AB_4+Na]^+$	$[C_{14}H_{28}O][C_2H_4O]_n$	Triton®, reduced	X-100R, X-114R, X-405R, or X-45R Detergents
413.2668	$[M+Na]^+$	$C_{24}H_{38}O_4$	Diisooctyl phthalate	Diisooctyl phthalate, plasticiser
415.2543	$[A_9B+H]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
419.2773	$[AB_4+Na]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
425.3114	$[A_7B+H]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
425.3243	$[AB_4+Na]^+$	$[C_{15}H_{30}O][C_2H_4O]_n$	Triton®, reduced	101R Detergents
427.3060	$[AB_5+H]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
429.0893	$[M+H\text{-}CH_4]^+$	$[C_2H_6SiO]_6$	Polysiloxane	Polysiloxane, (neutral methane loss from m/z 445)
429.2407	$[M+K]^+$	$C_{24}H_{38}O_4$	Diisooctyl phthalate	Diisooctyl phthalate, plasticiser
437.2363	$[A_9B+Na]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
441.3216	$[AB_5+H]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
445.1206	$[M+H]^+$	$[C_2H_6SiO]_6$	Polysiloxane	Polysiloxane, followed by m/z 462

Mono-isotopic ion mass (singly charged)	Ion type	Formula for M or subunit or sequence	Compound ID or species	Possible origin and other comments
447.2934	$[A_7B+Na]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
449.2879	$[AB_5+Na]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
449.3856	$[M_2+H]^+$	$C_{13}H_{24}N_2O$	DCU	N,N'-Dicyclohexylurea
453.2102	$[A_9B+K]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
453.3441	$[M+H]^+$	$C_{24}H_{44}N_4O_4$	nylon	Cyclic oligomer of polyamide 66, (adipic acid/hexylmethylene diamine condensation)
454.2933	$[M+CH_3CN+Na]^+$	$C_{24}H_{38}O_4$	Diisooctyl phthalate	Diisooctyl phthalate, plasticiser
455.3349	$[AB_5+Na]^+$	$[C_{14}H_{28}O][C_2H_4O]_n$	Triton®, reduced	X-100R, X-114R, X-405R, or X-45R Detergents
459.2805	$[A_{10}B+H]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
462.1471	$[M+NH_4]^+$	$[C_2H_6SiO]_6$	Polysiloxane	Polysiloxane (see m/z 445)
463.2673	$[A_7B+K]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
463.3036	$[AB_5+Na]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
469.3505	$[AB_5+Na]^+$	$[C_{15}H_{30}O][C_2H_4O]_n$	Triton®, reduced	101R Detergents
471.3322	$[AB_6+H]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
481.2625	$[A_{10}B+Na]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
483.3533	$[A_8B+H]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
485.3478	$[AB_6+H]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
493.3141	$[AB_6+Na]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
494.5665	$[M-Cl]^+$	$C_{34}H_{72}NCl$	DPDMA	Dipalmityldimethylammonium chloride, catalyst, personal care products additive
497.2364	$[A_{10}B+K]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
499.3611	$[AB_6+Na]^+$	$[C_{14}H_{28}O][C_2H_4O]_n$	Triton®, reduced	X-100R, X-114R, X-405R, or X-45R Detergents
484.3376	$[M+H-CH_4]^+$	$[C_2H_6SiO]_7$	Polysiloxane	Polysiloxane, (neutral methane loss from m/z 519)
503.3068	$[A_{11}B+H]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
505.3353	$[A_8B+Na]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
507.3298	$[AB_6+Na]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
513.3767	$[AB_6+Na]^+$	$[C_{15}H_{30}O][C_2H_4O]_n$	Triton®, reduced	101R Detergents
515.3584	$[AB_7+H]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
515.4134	$[M+H]^+$	$C_{30}H_{58}O_4S$	DDTDP	Didodecyl 3,3'-thiodipropionate, antioxidant
519.1394	$[M+H]^+$	$[C_2H_6SiO]_7$	Polysiloxane	Polysiloxane, followed by m/z 536
521.3092	$[A_8B+K]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
522.5978	$[M-Cl]^+$	$C_{36}H_{76}NCl$	SPDMA	Stearyl-palmityldimethylammonium chloride, catalyst, personal care product additive
525.2887	$[A_{11}B+Na]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
529.3740	$[AB_7+H]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
531.4083	$[M+H]^+$	$C_{30}H_{58}O_5S$	DDTDP	Didodecyl 3,3'-thiodipropionate oxidized to sulfoxide, antioxidant
531.4777	$[M+H]^+$	$C_{35}H_{62}O_3$	Irganox	Irganox 1076, antioxidant in synthetic polymers, antioxidant
536.1659	$[M+NH_4]^+$	$[C_2H_6SiO]_7$	Polysiloxane	Polysiloxane (see m/z 519)
537.3403	$[AB_7+Na]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
537.8796	$[M_6-6H+{}_3Fe+O]^+$	$C_2H_4O_2$	Acetic acid-Fe-O-complex	during ESI with metal tips and acetic acid
541.2626	$[A_{11}B+K]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
541.3952	$[A_9B+H]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
543.3873	$[AB_7+Na]^+$	$[C_{14}H_{28}O][C_2H_4O]_n$	Triton®, reduced	X-100R, X-114R, X-405R, or X-45R Detergents
547.3330	$[A_{12}B+H]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
547.4032	$[M+H]^+$	$C_{30}H_{58}O_6S$	DDTDP	Didodecyl 3,3'-thiodipropionate oxidized to sulfone, antioxidant
550.6291	$[M-Cl]^+$	$C_{38}H_{80}NCl$	DSDMA	Distearyldimethylammonium chloride, catalyst, personal care products additive
551.3560	$[AB_7+Na]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
553.3903	$[M+Na]^+$	$C_{30}H_{58}O_5S$	DDTDP	Didodecyl 3,3'-thiodipropionate oxidized to sulfoxide, antioxidant
553.4597	$[M+Na]^+$	$C_{35}H_{62}O_3$	Irganox	Irganox 1076, antioxidant in synthetic polymers, antioxidant
555.8902	$[M_6-6H+H_2O+3Fe+O]^+$	$C_2H_4O_2$	Acetic acid-Fe-O-complex	during ESI with metal tips and acetic acid
557.4029	$[AB_7+Na]^+$	$[C_{15}H_{30}O][C_2H_4O]_n$	Triton®, reduced	101R Detergents
559.3846	$[AB_8+H]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
563.3771	$[A_9B+Na]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
569.3149	$[A_{12}B+Na]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
573.4003	$[AB_8+H]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
577.1269	$[M+H-CH_4]^+$	$[C_2H_6SiO]_8$	Polysiloxane	Polysiloxane, (neutral methane loss from m/z 593)
579.3511	$[A_9B+K]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
581.3666	$[AB_8+Na]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents

Mono-isotopic ion mass (singly charged)	Ion type	Formula for M or subunit or sequence	Compound ID or species	Possible origin and other comments
585.2888	$[A_{12}B+K]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
587.4135	$[AB_8+Na]^+$	$[C_{14}H_{28}O][C_2H_4O]_n$	Triton®, reduced	X-100R, X-114R, X-405R, or X-45R Detergents
591.3592	$[A_{13}B+H]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
593.1582	$[M+H]^+$	$[C_2H_6SiO]_8$	Polysiloxane	Polysiloxane, followed by m/z 610
595.3822	$[AB_8+Na]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
597.9007	$[M_7\text{-}6H+3Fe+O]^+$	$C_2H_4O_2$	Acetic acid-Fe-O-complex	during ESI with metal tips and acetic acid
599.4370	$[A_{10}B+H]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
601.4292	$[AB_8+Na]^+$	$[C_{15}H_{30}O][C_2H_4O]_n$	Triton®, reduced	101R Detergents
603.4108	$[AB_9+H]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
610.1847	$[M+NH_4]^+$	$[C_2H_6SiO]_8$	Polysiloxane	Polysiloxane (see m/z 593)
613.3411	$[A_{13}B+Na]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
615.4043	$[M+H]^+$	$C_{32}H_{58}N_2O_7S$	CHAPS	3-[(3-Cholamidopropyl)dimethylammonio] -1-propanesulfonate
617.4265	$[AB_9+H]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
621.4190	$[A_{10}B+Na]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
621.9735	$[M_6\text{-}6H+3Fe+O]^+$	$C_3H_6O_2$	Propionic acid Fe-O complex	during ESI with metal tips and acetic acid
625.3928	$[AB_9+Na]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
629.3151	$[A_{13}B+K]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
631.4397	$[AB_9+Na]^+$	$[C_{14}H_{28}O][C_2H_4O]_n$	Triton®, reduced	X-100R, X-114R, X-405R, or X-45R Detergents
635.3854	$[A_{14}B+H]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
637.3929	$[A_{10}B+K]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
639.4084	$[AB_9+Na]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
645.4554	$[AB_9+Na]^+$	$[C_{15}H_{30}O][C_2H_4O]_n$	Triton®, reduced	101R Detergents
647.4370	$[AB_{10}+H]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
651.1456	$[M+H\text{-}CH_4]^+$	$[C_2H_6SiO]_9$	Polysiloxane	Polysiloxane, (neutral methane loss from m/z 667)
657.3673	$[A_{14}B+Na]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
657.4789	$[A_{11}B+H]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
661.4527	$[AB_{10}+H]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
667.1769	$[M+H]^+$	$[C_2H_6SiO]_9$	Polysiloxane	Polysiloxane, followed by m/z 684
669.4190	$[AB_{10}+Na]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
673.3413	$[A_{14}B+K]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
675.4659	$[AB_{10}+Na]^+$	$[C_{14}H_{28}O][C_2H_4O]_n$	Triton®, reduced	X-100R, X-114R, X-405R, or X-45R Detergents
679.4116	$[A_{15}B+H]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
679.4608	$[A_{11}B+Na]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
679.5122	$[M+H]^+$	$C_{36}H_{66}N_6O_6$	nylon	Cyclic oligomer of polyamide 66, (adipic acid/hexylmethylene diamine condensation)
683.4346	$[AB_{10}+Na]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
684.2035	$[M+NH_4]^+$	$[C_2H_6SiO]_9$	Polysiloxane	Polysiloxane (see m/z 667)
689.4816	$[AB_{10}+Na]^+$	$[C_{15}H_{30}O][C_2H_4O]_n$	Triton, reduced	101R Detergents
691.4633	$[AB_{11}+H]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
695.4348	$[A_{11}B+K]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
701.3936	$[A_{15}B+Na]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
705.4789	$[AB_{11}+H]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
713.4452	$[AB_{11}+Na]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
715.5208	$[A_{12}B+H]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
717.3675	$[A_{15}B+K]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
719.4921	$[AB_{11}+Na]^+$	$[C_{14}H_{28}O][C_2H_4O]_n$	Triton®, reduced	X-100R, X-114R, X-405R, or X-45R Detergents
723.4378	$[A_{16}B+H]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
725.1644	$[M+H\text{-}CH_4]^+$	$[C_2H_6SiO]_{10}$	Polysiloxane	Polysiloxane, (neutral methane loss from m/z 741)
727.4608	$[AB_{11}+Na]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
733.5078	$[AB_{11}+Na]^+$	$[C_{15}H_{30}O][C_2H_4O]_n$	Triton®, reduced	101R Detergents
735.4895	$[AB_{12}+H]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
737.5027	$[A_{12}B+Na]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
741.1957	$[M+H]^+$	$[C_2H_6SiO]_{10}$	Polysiloxane	Polysiloxane, followed by m/z 758
745.4198	$[A_{16}B+Na]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
749.5051	$[AB_{12}+H]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
753.4766	$[A_{12}B+K]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
757.4714	$[AB_{12}+Na]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
758.2223	$[M+NH_4]^+$	$[C_2H_6SiO]_{10}$	Polysiloxane	Polysiloxane (see m/z 741)
761.3937	$[A_{16}B+K]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
763.5184	$[AB_{12}+Na]^+$	$[C_{14}H_{28}O][C_2H_4O]_n$	Triton®, reduced	X-100R, X-114R, X-405R, or X-45R Detergents
767.4640	$[A_{17}B+H]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether

Mono-isotopic ion mass (singly charged)	Ion type	Formula for M or subunit or sequence	Compound ID or species	Possible origin and other comments
771.4871	$[AB_{12}+Na]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
773.5626	$[A_{13}B+H]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
777.5340	$[AB_{12}+Na]^+$	$[C_{15}H_{30}O][C_2H_4O]_n$	Triton®, reduced	101R Detergents
779.5157	$[AB_{13}+H]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
789.4460	$[A_{17}B+Na]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
793.5313	$[AB_{13}+H]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
795.5446	$[A_{13}B+Na]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
798.5884	$[M_2+NH_4]^+$	$C_{24}H_{38}O_4$	Diisooctyl phthalate	Diisooctyl phthalate, plasticiser
801.4976	$[AB_{13}+Na]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
803.5438	$[M_2+Na]^+$	$C_{24}H_{38}O_4$	Diisooctyl phthalate	Diisooctyl phthalate, plasticiser
805.4199	$[A_{17}B+K]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
807.5446	$[AB_{13}+Na]^+$	$[C_{14}H_{28}O][C_2H_4O]_n$	Triton®, reduced	X-100R, X-114R, X-405R, or X-45R Detergents
809.4875	$[AB_{10}+Na]^+$	$[C_{18}H_{34}O_6][C_2H_4O]_n$	Tween®	Tween® 20
811.4903	$[A_{18}B+H]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
811.5185	$[A_{13}B+K]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
815.5133	$[AB_{13}+Na]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
819.5177	$[M_2+K]^+$	$C_{24}H_{38}O_4$	Diisooctyl phthalate	Diisooctyl phthalate, plasticiser
821.5602	$[AB_{13}+Na]^+$	$[C_{15}H_{30}O][C_2H_4O]_n$	Triton®, reduced	101R Detergents
823.5419	$[AB_{14}+H]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
831.6045	$[A_{14}B+H]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
833.4722	$[A_{18}B+Na]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
837.5575	$[AB_{14}+H]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
845.5238	$[AB_{14}+Na]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
849.4461	$[A_{18}B+K]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
851.5708	$[AB_{14}+Na]^+$	$[C_{14}H_{28}O][C_2H_4O]_n$	Triton®, reduced	X-100R, X-114R, X-405R, or X-45R Detergents
853.5137	$[AB_{11}+Na]^+$	$[C_{18}H_{34}O_6][C_2H_4O]_n$	Tween®	Tween® 20
853.5864	$[A_{14}B+Na]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
855.5165	$[A_{19}B+H]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
859.5395	$[AB_{14}+Na]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
865.5501	$[AB_{10}+Na]^+$	$[C_{22}H_{42}O_6][C_2H_4O]_n$	Tween®	Tween® 40
865.5864	$[AB_{14}+Na]^+$	$[C_{15}H_{30}O][C_2H_4O]_n$	Triton®, reduced	101R Detergents
867.5681	$[AB_{15}+H]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
869.5604	$[A_{14}B+K]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
877.4984	$[A_{19}B+Na]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
881.5838	$[AB_{15}+H]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
889.5501	$[AB_{15}+Na]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
889.6464	$[A_{15}B+H]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
891.5657	$[AB_{10}+Na]^+$	$[C_{24}H_{44}O_6][C_2H_4O]_n$	Tween®	Tween® 80
893.4724	$[A_{19}B+K]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
893.5814	$[AB_{10}+Na]^+$	$[C_{24}H_{46}O_6][C_2H_4O]_n$	Tween®	Tween® 60
897.5399	$[AB_{12}+Na]^+$	$[C_{18}H_{34}O_6][C_2H_4O]_n$	Tween®	Tween® 20
899.5427	$[A_{20}B+H]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
903.5657	$[AB_{15}+Na]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
905.6803	$[M+H]^+$	$C_{48}H_{88}N_8O_8$	nylon	Cyclic oligomer of polyamide 66, (adipic acid/hexylmethylene diamine condensation)
909.5763	$[AB_{11}+Na]^+$	$[C_{22}H_{42}O_6][C_2H_4O]_n$	Tween®	Tween® 40
909.6127	$[AB_{15}+Na]^+$	$[C_{15}H_{30}O][C_2H_4O]_n$	Triton®, reduced	101R Detergents
911.5943	$[AB_{16}+H]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
911.6283	$[A_{15}B+Na]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
921.5246	$[A_{20}B+Na]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
925.6100	$[AB_{16}+H]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
927.6022	$[A_{15}B+K]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
933.5763	$[AB_{16}+Na]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
935.5919	$[AB_{11}+Na]^+$	$[C_{24}H_{44}O_6][C_2H_4O]_n$	Tween®	Tween® 80
937.4986	$[A_{20}B+K]^+$	$[C_2H_4O]_nH_2O$	PEG	Polyethylene glycol, ubiquitous polyether
937.6076	$[AB_{11}+Na]^+$	$[C_{24}H_{46}O_6][C_2H_4O]_n$	Tween®	Tween® 60
939.6232	$[AB_{16}+Na]^+$	$[C_{14}H_{28}O][C_2H_4O]_n$	Triton®, reduced	X-100R, X-114R, X-405R, or X-45R Detergents
941.5661	$[AB_{13}+Na]^+$	$[C_{18}H_{34}O_6][C_2H_4O]_n$	Tween®	Tween® 20
947.5919	$[AB_{16}+Na]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
947.6882	$[A_{16}B+H]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
953.6025	$[AB_{12}+Na]^+$	$[C_{22}H_{42}O_6][C_2H_4O]_n$	Tween®	Tween® 40
953.6389	$[AB_{16}+Na]^+$	$[C_{15}H_{30}O][C_2H_4O]_n$	Triton®, reduced	101R Detergents
955.6205	$[AB_{17}+H]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
969.6362	$[AB_{17}+H]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents

Mono-isotopic ion mass (singly charged)	Ion type	Formula for M or subunit or sequence	Compound ID or species	Possible origin and other comments
969.6702	$[A_{16}B+Na]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
977.6025	$[AB_{17}+Na]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents
979.6181	$[AB_{12}+Na]^+$	$[C_{24}H_{44}O_6][C_2H_4O]_n$	Tween®	Tween® 80
981.6338	$[AB_{12}+Na]^+$	$[C_{24}H_{46}O_6][C_2H_4O]_n$	Tween®	Tween® 60
983.6494	$[AB_{17}+Na]^+$	$[C_{14}H_{28}O][C_2H_4O]_n$	Triton®, reduced	X-100R, X-114R, X-405R, or X-45R Detergents
985.5923	$[AB_{14}+Na]^+$	$[C_{18}H_{34}O_6][C_2H_4O]_n$	Tween®	Tween® 20
985.6441	$[A_{16}B+K]^+$	$[C_3H_6O]_nH_2O$	PPG	Polypropylene glycol, ubiquitous polyether
991.6181	$[AB_{17}+Na]^+$	$[C_{15}H_{24}O][C_2H_4O]_n$	Triton®	101 Detergents
997.6287	$[AB_{13}+Na]^+$	$[C_{22}H_{42}O_6][C_2H_4O]_n$	Tween®	Tween® 40
997.6651	$[AB_{17}+Na]^+$	$[C_{15}H_{30}O][C_2H_4O]_n$	Triton®, reduced	101R Detergents
999.6470	$[AB_{18}+H]^+$	$[C_{14}H_{22}O][C_2H_4O]_n$	Triton®	X-100, X-114, X-405, or X-45 Detergents

Appendix II.

Monoisotopic ion masses of commonly observed repeating units in LC-MS

Positive ion

Mass difference	Origin
14.0157	-$[CH_2]$-, alkane chains, waxes, fatty acids, methylation
15.9949	O, oxidation
18.0106	H_2O, water clusters
28.0313	-$[C_2H_4]$-, natural alkane chains such as fatty acids
32.0262	CH_3OH, methanol clusters
41.0266	CH_3CN, acetonitrile clusters
42.0470	-$[C_3H_6]$-, propyl repeating units, propylation
44.0262	-$[C_2H_4O]$-; polyethylene glycol, PEG, and related components such as Triton®- and Tween®-containing buffers
49.9968	-$[CF_2]$-, from perfluoro compounds
53.0032	NH_4Cl salt adducts/clusters
56.0626	-$[C_4H_8]$-, butyl repeating units, butylation
57.9586	NaCl, sodium chloride clusters
58.0419	-$[C_3H_6O]$-; polypropylene glycol and related compounds, PPG, and related compounds
63.0320	$CHOONH_4$, ammonium formate adducts/clusters
67.9874	$NaHCO_2$, sodium formate clusters
67.9874	CHOONa, sodium formate adducts/clusters
72.0395	-OH replacement with -$OSi(CH_3)_3$,(=$[C_3H_8Si]$), trimethylsiloxane, endcapping reagent
73.9326	KCl adducts/clusters
74.0188	-$[O\text{-}Si(CH_3)_2]$-, polysiloxane, silicone rubber polymer (typical series at m/z's 355, 429, 503, 593, 667, 741, 815)
78.0139	C_2H_6OS, DMSO adducts/clusters, dimethylsulfoxide solvent
82.0031	$NaCH_3CO_2$, sodium acetate clusters
84.0516	C_2D_6OS, deuterated DMSO adducts/clusters, NMR solvent
135.9748	$NaCF_3CO_2$, sodium trifluoroacetate clusters
162.0528	-$[C_6H10O_5]$-, polysaccharides residues
226.1681	-$[C1_2H_{22}N_2O_2]$-, cyclic oligomers from polyamide 66 (series observed with m/z 453, 679, 905)
259.8099	CsI, cesium iodide clusters, used as calibration

Notes

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