Table 5

Some common sample preparation problems by extraction type

Type of Sample Preparation	*Common problems and outcomes*
Solid Phase Extraction (SPE)	Elute analytes to waste instead of autosampler vials or collection plate – no or low peak areas
Solid Phase Extraction	Silica based SPE stationary phase dries out during extraction (selected cartridges/wells) – low, inconsistent peak areas. Polymer based SPE media is not sensitive to drying out.
Liquid-Liquid Extraction	Contamination of organic layer with the interface between aqueous/organic layers during transfer – interfering peaks, ion suppression, low peak areas, LC overpressure from injected particulate
Liquid-Liquid Extraction	Emulsion – no or low peak areas, extraction may need to be repeated if unable to break emulsion
Protein precipitation with filtration plates or phospholipid removal plates	Clogging of selected wells, no filtration – no peaks, no liquid in well of collection plate
Manual protein precipitation	Insufficient precipitation, delayed precipitation in autosampler vial, insufficient mixing, insufficient centrifugation - LC overpressure from injected particulate
Protein precipitation (serum, plasma), Simple dilution (urine, CSF)	Insufficient matrix removal – variable ion suppression, shortened column lifetimes, shortened MS/MS maintenance-free intervals