

*Scientists aren't perfect. Nobody is. In our **Technical Tips**, we can solve your most debilitating issues—from mechanics to methodology—together.*

While proteins are solvated in aqueous via polar interactions with water molecules, proteinaceous samples such as plasma are frequently analyzed for small molecular drugs and the corresponding metabolites via a technique known as **protein precipitation** (PPT).

PPT is useful for cleaning several types of matrices in industries like [food](#), [beverage](#), bioanalytical, and more. It can be performed with an organic solvent, strong acids, or salts by forcing proteins to denature and associate with other proteins rather than remain in the solution.

Protein balling and precipitation is useful for selectively removing protein from a sample or reducing the interaction of a small molecule analyte with a binding protein in plasma, like vitamin D.

Different species of plasma, from dogs, rats, humans, and monkeys, are frequently analyzed by pharmaceutical companies via PPT alone or with a combination of PPT and solid phase extraction (SPE) prior to their analytical technique.

While PPT is less selective for cleanup and requires sample dilution, it is also simpler, less expensive, and quicker than SPE.

Now, let's talk methods.

PPT Method Summary

Organic Based Precipitation Agent:

- Ideal for Ion Exchange SPE; no dilution typically required
- OK for Neutral SPE; dilution is needed to reduce organic strength prior to loading on SPE

Best Solvent: Acetonitrile

1. Add $\geq 2:1$ ratio of precipitation agent to plasma sample
2. Agitate for protein to fall out of solution; centrifuge to a pellet and remove supernatant for analysis or use high-throughput filter plate.

Aqueous Based Precipitation Agent:

- Ideal for Neutral SPE
- OK for Ion Exchange SPE; pH or salt adjustment needed prior to loading on SPE

Best Solvent: 20% TCA in water

1. Add $\geq 2:1$ ratio of precipitation agent to plasma sample
2. Agitate for protein to fall out of solution; centrifuge to a pellet and remove supernatant for analysis or use high-throughput filter plate.

BONUS Solvent: Zinc Sulfate

1. Add $\geq 2:1$ ratio of precipitation agent to plasma sample
2. Agitate for protein to fall out of solution; centrifuge to a pellet and remove supernatant for analysis or use high-throughput filter plate.

For any questions regarding PPT, email SamplePrepSupport@phenomenex.com.

More technical support:

- [Request-a-Method™](#): Contact our Method Development Team for a tailored solution!
 - [Applications](#): We have thousands of them! Search by analyte name or structure.
 - [Free Guides and Posters](#): Download free guides and posters for troubleshooting, method development, and more.
 - [Product Videos](#): See the technology in action. Watch our product videos and demonstrations.
 - [The Technical Library](#): Check out our helpful collection of technical notes, posters, webinars, how-to videos, guides, and more.
 - [Interactive Web Tools](#): Simple, interactive tools to instantly find the right products and solutions.
 - [FAQ Portal](#): Find answers to popular technical questions here.
 - [Quality and Safety Documents](#): Download your CQA, C of A, and MSDS.
 - [Product Care and Use](#): Love your products and treat them right using these handy guides.
 - [Training & On-Site Support](#): We'll come to you! Classroom training or in-lab demonstrations—you pick the topic.
 - [Troubleshooting](#): Did something go wrong? We'll fix it!
 - [Chat With Us](#): Our Phenomenex technical experts (Phenoms) are ready to chat with you about method development and technical support.
-

Related resources:

- [Monolith RP-C18e 50 x 2.0mm Column Stability Test for Protein Precipitation #5000 Injection](#)

- [Protein Precipitation Ruggedness on Kinetex 2.6µm C18 50 x 2.1mm ID \(injection no. 1000\)](#)
- [Vitamin C from Human Plasma by Protein Precipitation and LC/UV](#)
- [Finally, An Easier Protein Precipitation Solution \[Brochure\]](#)
- [Gabapentin from Plasma by Protein Precipitation and LC/MS/MS](#)
- [Protein Precipitation Protocol](#)
- [Labs Across the World Are Advancing Their Protein Precipitation \[Brochure\]](#)
- [Optimizing the Effectiveness of Plasma Protein Precipitation Using the Direct Addition Technique](#)
- [New Approaches to Protein Precipitation: Phospholipid Removal Improves Results](#)
- [Removal of Beta-Glucuronidase Enzyme from Urine Post-Hydrolysis by Protein Precipitation](#)