Ammonium Acetate or Triethylamine TEA Use with Cogent HPLC Columns - Tips and Suggestions

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Using Ammonium Acetate in HPLC, ANP, and LC-MS Workflows – Technical Guidance

Ammonium acetate is one of the most commonly selected additives for Aqueous Normal Phase (ANP) chromatography and LC-MS because it offers a rare combination of near-neutral pH, high solubility in mixed aqueous–organic environments, and full MS volatility.

In ANP methods—particularly on Cogent TYPE-C™ silica-hydride columns—ammonium acetate helps maintain ionization of organic acids, which enhances retention and peak shape while supporting the electrostatic surface interactions that define ANP selectivity.

While ammonium acetate is extremely useful, it also comes with important technical considerations. It is not soluble in neat acetonitrile, meaning analysts must include at least 5–10% water in the mobile phase to prevent precipitation and ensure consistent ionization conditions. Failure to dissolve the salt completely can introduce micro-particulates, unstable retention, and erratic MS response. Filtering the prepared mobile phase is strongly recommended to remove any undissolved solids.

A critical system consideration is that ammonium acetate is believed to adsorb to silica-based stationary phases, altering the surface chemistry and potentially shifting retention behavior. For this reason, once used with a column, that column should be dedicated exclusively to ammonium-acetate-based methods to maintain consistent and predictable chromatography. This mirrors similar recommendations for other adsorbing modifiers such as TEA.

In LC-MS applications, buffer concentration must be carefully managed. Concentrations above 10 mM may significantly increase nebulizer and ion source buildup, requiring more frequent cleaning. Even at 10 mM, some accumulation is expected, but growth is manageable when proper water content—≥5% DI water in solvent B—is maintained.

During negative ionization mode, ammonium acetate is often the preferred additive, whereas formic or acetic acid may be more suitable for positive mode. Analysts should avoid unnecessarily high buffer concentrations since ammonium acetate may reduce MS signal sensitivity relative to simple acid-only mobile phases, especially for compounds that ionize readily on their own.

When to Use Ammonium Acetate:

- Developing ANP methods where organic acids must remain ionized.
- LC-MS workflows requiring volatile buffering at near-neutral pH.
- Methods where silica-hydride surfaces benefit from controlled surface charge formation.

When to Avoid or Use Caution:

- When strict column interchangeability is required between different method types.
- When high MS sensitivity is needed for easily ionized analytes.

- When running fully organic mobile phases without water (solubility concern).

CAUTION: You should be sure not to exceed the pH limit of any silica based HPLC column because these materials become increasingly soluble at increasing pH (this can lead to voids).

NOTE 1: Our research has shown though that TEA can be used to obtain advantageous changes in chromatography in under certain conditions. Data has demonstrated improved peak shape and selectivity for simple sugars when using TEA with Cogent columns. This effect is thought to be due at least partly to an ion-pairing mechanism of the TEA on the surface of the material.

NOTE 2: With ammonium acetate, a near-neutral pH is obtained with this additive, so it is a popular choice for keeping most organic acids ionized, which is generally preferred for ANP methods. In addition, it is LC-MS compatible, in contrast to a near neutral pH phosphate buffer.

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