



Solubilizing Peptides

Often times the most frustrating part of working with synthetic peptides is determining the best solvent in which the peptide will dissolve. The steps outlined below provides you with a method for determining the best solvent for a synthetic peptide based on its amino acid sequence. It is best to first solubilize a small aliquot of the sample, rather than the entire sample.

- Assign a value of -1 to each acidic residue. The acidic residues are Asp (D), Glu (E), and the C-terminal -COOH.
- Assign a value of +1 to each basic residue. The basic residues are Arg (R), Lys (K), His (H), and the N-terminal -NH₂.
- Calculate the overall charge of the peptide.
- If the overall charge of the peptide is a positive value, you have a basic peptide. Initially try to dissolve the peptide in water. If the peptide does not dissolve, try 10% and higher solutions of acetic acid. If the peptide still does not dissolve, add TFA (<50ul) to solubilize the peptide and dilute to 1ml with deionized water.
- If the overall charge of the peptide is a negative value, you have an acidic peptide. Initially try to dissolve the peptide in water. If the peptide does not dissolve, add NH₄OH (<50ul) and dilute to 1ml with deionized water.
- If the overall charge of the peptide is zero, your peptide is considered neutral. Neutral peptides may require the addition of organic solvents, such as acetonitrile, methanol, or isopropanol. The addition of denaturants, such as urea or guanidinium-HCL may also be required.

Examples:

KRLMKSIEVIMPL: (+4) + (-2) = +2 This is considered a basic peptide. See step #4 above.

LVKMKSIEDPDCE: (+3) + (-5) = -2 This is considered an acidic peptide. See step #5 above.

MVSRKDLVEHRDM: (+4) + (-4) = 0 This is considered a neutral peptide. See step #6 above.