Solubilization of Peptides

Due to their individual nature, the solubilization of peptides causes sometimes unexpected troubles. With this flyer, BIOSYNTAN tries to support you in circumventing solubilization problems.

A careful look on the amino acid sequence of the peptide gives you a rough estimate of its solubility. Following table helps in classifying the amino acids and determining the nature of your peptide.

polar amino acids			nonpolar amino acids
acidic	basic	polar uncharged	hydrophobic
Asp, Glu	Lys, Arg, His	Gly, Cys, Asn, Gln, Ser, Thr, Tyr	Ala, Ile Leu, Val, Met, Pro, Phe, Trp

Peptides with a high content of **polar amino acids** show generally a good solubility in aqueous solutions at neutral pH. Using a buffered solution is recommended (PBS or TRIS buffered saline at pH 7-8). Sonication or gentle warming (<40°C) may accelerate the dilution process.

In case the peptide contains **acidic or basic amino acids**, the isoelectric point (pI) becomes relevant for the solubilization. If the pI of the peptide is close to the pH of the buffer, you will expect poorer solubility. So choose the pH of the buffer at least 2 units different to the pI of the peptide. The following calculator is a helpful tool to determine the pI of peptides:

http://web.expasy.org/compute_pi/

Peptides with a high content of **hydrophobic amino acids** (>50%) may be insoluble or only partially soluble in aqueous solutions. In this case organic solvents can assist in solubilization, e.g. dimethylsulfoxide (DMSO), acetonitrile, isopropanol or dimethylformamide (DMF). Please, keep in mind that high concentrations of these organic solvents might interfere with your assay.

Start the solubilization of the peptide by adding the organic solvent first and then dilute with water to the required concentration. Also dissolving in 6 M guanidinium hydrochloride or 8 M urea and subsequent dilution with water is an option and may be considered as a substitute for organic solvents.

Please note that peptides containing **Cys, Met or Trp** require special care to suppress oxidation. Use degassed solvents and avoid longer storage by preparing the peptide solution always freshly. **Cys-peptides** can easily form dimers at neutral or basic pH or in the presence of DMSO. Addition of thiols (DTT), or phosphanes (TCEP) reduces such disulfide bridges.

In general, always use only an aliquot of your peptide to determine the best conditions for solubilization.