

Peptide Solubility

Description

Peptides are complex biomolecules. Depending on the amino acid composition each peptide is unique with regard to its chemical and physical properties. Although some peptides are easy to dissolve in aqueous solutions, a common problem encountered is very low solubility or even insolubility of peptides, especially of peptides with stretches of hydrophobic amino acids.

General guideline to prepare peptide solutions:

As the amino acid composition determines the properties of every individual peptide, testing of peptide solubility with a small amount of product is recommended!

Allow the peptide to warm to room temperature (preferably in a desiccator) before reconstituting. Always use sterile water or buffer (PBS, Tris or phosphate, pH 7) for preparation of solutions. For peptides containing Cys, Met or Trp, that are rapidly susceptible to oxidation, oxygen-free solvents should be used.

Solubility can also be facilitated by careful warming (< 40°C) or sonication. If the pH of the solution has to be increased, only very weak bases should be used in order to prevent immediate inactivation by racemisation or side reactions.

Guideline for hydrophobic peptides

If a product proves insoluble in water / buffer due to high hydrophobicity, addition of DMSO (dimethylsulfoxide) may be necessary:

In such cases dissolve the peptide in the smallest possible volume of a 50% (v/v) DMSO / water mixture and subsequently add water / buffer until the desired concentration is achieved. If product precipitates again during this process and cannot be re-dissolved by adding DMSO, lyophilization is required and another attempt of solubilization is needed.

If DMSO interferes with your experimental system, DMF (dimethylformamide) or acetonitrile can serve as alternative solvents.

Prediction of peptide solubility in aqueous solutions

The influence of the amino acid sequence on the chemical and physical characteristics of an individual peptide is vast. Thus, we can only give some general guidelines for solubility prediction:

Peptides shorter than 5 residues are usually soluble in water or aqueous buffer, except if the whole sequence consists of hydrophobic amino acids (like W, L, I, F, M, V, Y).

Hydrophilic peptides containing >25% charged residues (like D, K, R, H, E) and <25% hydrophobic amino acids are usually soluble in water or aqueous buffer.

Hydrophobic peptides containing 50% and more hydrophobic residues may be insoluble or only partly soluble in aqueous solutions. In this case we recommend using organic solvents like DMSO, DMF or acetonitrile.

Peptides containing a very high (>75%) proportion of D, E, H, K, N, Q, R, S, T, Y are capable of building intermolecular hydrogen bonds (cross-linking), thus forming gels in aqueous solutions. These peptides should either be treated according to the instructions for hydrophobic peptides or by changing the pH value if possible.

To minimise solubility problems, optimization of the peptide sequence may be necessary!

Parameters influenced by the amino acid composition of a peptide

Depending on the peptide sequence, some amino acids or peptide properties directly influence physical and / or chemical behaviour of peptides.

Among these one can find peptide solubility, peptide stability and peptide charge.

Please refer to the tables below for amino acid classifications:

Solubility in aqueous solutions

Hydrophilic amino acids	Intermediate	Hydrophobic amino acids
D, E, H, K, N, Q, R, S, T, hydroxy-proline, pyro-glutamic acid	C, G	A, F, I, L, M, P, V, W, Y, alpha-amino butyric acid, beta-amino alanine, norleucine

Peptide stability

Subject to oxidation under relatively mild conditions	subject to de-amidation, de-hydration, cyclisation to pGlu	subject to degradation during peptide preparation
C, M	N, Q, C-terminal amides N-terminal Q	M, W

Peptide charge

	positive	negative
	K, R, H, N-terminus of peptide	D, E, Y, C-terminus of peptide

Product offering

As special service we offer an optional Peptide Solubility Test Service.

Please refer to current price list at www.thermo.com/peptides or contact our team at services.biopolymers@thermo.com for further information.

In addition to these offices, Thermo Fisher Scientific maintains a network of representative organizations throughout the world.

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