

Degradation Pathways of Therapeutic Peptides in Aqueous Solutions and Strategies to Improve Stability

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Abstract

A number of hormones, enzymes, antitumor agents, antibiotics and neurotransmitters are peptides. Nowadays, peptides are used as therapeutic agents against diverse disease areas such as neurological, endocrinological and hematological disorders. Therapeutic peptides pose a number of challenges for pharmaceutical scientists regarding their formulation and delivery. The sensitivity of many peptides to enzymatic breakdown and their poor ability to pass absorbing membranes typically results in a poor bioavailability following non-parenteral administration. Therefore, parenteral administration is the most commonly used route for systemic delivery of peptide drugs. However, therapeutic peptides are often unstable in aqueous solution limiting their shelf life. The lack of physical and chemical stability may lead to significant degradation during processing and storage of the (aqueous) formulations. Although a dry powder for reconstitution may overcome the lack of physical and chemical stability, from an economic point of view aqueous liquid formulations are preferred. In this presentation the main peptide stability problems in solution will be introduced following known strategies to inhibit peptide degradation, including recent research on improving peptide stability in liquid formulations. In conclusion, the most useful stabilization approaches are optimizing the pH and the type of buffer. Co-solvency, air exclusion, and viscosity enhancement can also be useful to reduce the degradation rate.