

Second Edition

# Pharmaceutical Formulation Development of Peptides and Proteins

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# 6 Physical Instability of Peptides and Proteins

*Marco van de Weert and Theodore W. Randolph*

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## 6.1 INTRODUCTION

The biological function of peptides and proteins is highly dependent on their three-dimensional structure. Changes in that structure, which may arise due to chemical or physical processes, may alter or abolish that function, or even result in toxicity. Thus, it is of importance that a pharmaceutical formulation of therapeutic peptides and proteins retains the normal (native) structure of those peptides or proteins, or that any changes are fully reversible upon administration to the patient.

A major difference between proteins and low molecular weight drugs is the complexity of the three-dimensional structure and concomitant sensitivity toward external stress factors. The three-dimensional structure of proteins is mostly held together by noncovalent interactions, such as hydrogen bonds, salt bridges, and van der Waals forces. Any stress factor may alter these noncovalent interactions, possibly leading to new intra- or intermolecular interactions which may not be reversible upon removing the stress factor.

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