

Second Edition

# Pharmaceutical Formulation Development of Peptides and Proteins

Edited by  
Lars Hovgaard  
Sven Frokjaer  
Marco van de Weert



CRC Press is an imprint of the  
Taylor & Francis Group, an Informa business

CRC Press  
Taylor & Francis Group  
6000 Broken Sound Parkway NW, Suite 300  
Boca Raton, FL 33487-2742

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Printed in the United States of America on acid-free paper  
Version Date: 20121003

International Standard Book Number: 978-1-4398-5388-7 (Hardback)

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Library of Congress Cataloging-in-Publication Data

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Pharmaceutical formulation development of peptides and proteins / editors, Lars Hovgaard, Sven Frøkjær, Marco van de Weert. -- 2nd ed.  
p. : cm.  
Includes bibliographical references and index.  
ISBN 978-1-4398-5388-7 (hardcover : alk. paper)  
I. Hovgaard, Lars, 1962- II. Frøkjær, Sven, 1947- III. Weert, Marco van de, 1973-  
[DNLM: 1. Peptide Biosynthesis. 2. Chemistry, Pharmaceutical--methods. 3. Protein Biosynthesis. QU 68]

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615.1'9--dc23

2012030490

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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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