

Therapeutic Dressings and Wound Healing Applications

ADVANCES IN PHARMACEUTICAL TECHNOLOGY

A Wiley Book Series

Series Editors:

Dennis Douroumis, University of Greenwich, UK

Alfred Fahr, Friedrich–Schiller University of Jena, Germany

Jürgen Siepmann, University of Lille, France

Martin Snowden, University of Greenwich, UK

Vladimir Torchilin, Northeastern University, USA

Titles in the Series

Hot-Melt Extrusion: Pharmaceutical Applications

Edited by Dionysios Douroumis

Drug Delivery Strategies for Poorly Water-Soluble Drugs

Edited by Dionysios Douroumis and Alfred Fahr

Computational Pharmaceutics: Application of Molecular Modeling in Drug Delivery

Edited by Defang Ouyang and Sean C. Smith

Pulmonary Drug Delivery: Advances and Challenges

Edited by Ali Nokhodchi and Gary P. Martin

Novel Delivery Systems for Transdermal and Intradermal Drug Delivery

Edited by Ryan Donnelly and Raj Singh

Drug Delivery Systems for Tuberculosis Prevention and Treatment

Edited by Anthony J. Hickey

Continuous Manufacturing of Pharmaceuticals

Edited by Peter Kleinebudde, Johannes Khinast, and Jukka Rantanen

Pharmaceutical Quality by Design

Edited by Walkiria S Schlindwein and Mark Gibson

***In Vitro* Drug Release Testing of Special Dosage Forms**

Edited by Nikoletta Fotaki and Sandra Klein

Forthcoming Titles:

Characterization of Micro- and Nanosystems

Edited by Leena Peltonen

Process Analytics for Pharmaceuticals

Edited by Jukka Rantanen, Clare Strachan, and Thomas De Beer

Mucosal Drug Delivery

Edited by Rene Holm

Basic Biopharmaceutics

Edited by Hannah Batchelor

Therapeutic Dressings and Wound Healing Applications

Edited by

JOSHUA BOATENG

*School of Science, University of Greenwich Medway,
Chatham Maritime, UK*

WILEY

This edition first published 2020
© 2020 John Wiley and Sons Ltd

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, except as permitted by law. Advice on how to obtain permission to reuse material from this title is available at <http://www.wiley.com/go/permissions>.

The right of Joshua Boateng to be identified as the author of the editorial material in this work has been asserted in accordance with law.

Registered Offices

John Wiley & Sons, Inc., 111 River Street, Hoboken, NJ 07030, USA

John Wiley & Sons Ltd, The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, UK

Editorial Office

The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, UK

For details of our global editorial offices, customer services, and more information about Wiley products visit us at www.wiley.com.

Wiley also publishes its books in a variety of electronic formats and by print-on-demand. Some content that appears in standard print versions of this book may not be available in other formats.

Limit of Liability/Disclaimer of Warranty

In view of ongoing research, equipment modifications, changes in governmental regulations, and the constant flow of information relating to the use of experimental reagents, equipment, and devices, the reader is urged to review and evaluate the information provided in the package insert or instructions for each chemical, piece of equipment, reagent, or device for, among other things, any changes in the instructions or indication of usage and for added warnings and precautions. While the publisher and authors have used their best efforts in preparing this work, they make no representations or warranties with respect to the accuracy or completeness of the contents of this work and specifically disclaim all warranties, including without limitation any implied warranties of merchantability or fitness for a particular purpose. No warranty may be created or extended by sales representatives, written sales materials or promotional statements for this work. The fact that an organization, website, or product is referred to in this work as a citation and/or potential source of further information does not mean that the publisher and authors endorse the information or services the organization, website, or product may provide or recommendations it may make. This work is sold with the understanding that the publisher is not engaged in rendering professional services. The advice and strategies contained herein may not be suitable for your situation. You should consult with a specialist where appropriate. Further, readers should be aware that websites listed in this work may have changed or disappeared between when this work was written and when it is read. Neither the publisher nor authors shall be liable for any loss of profit or any other commercial damages, including but not limited to special, incidental, consequential, or other damages.

Library of Congress Cataloging-in-Publication Data applied for

Hardback ISBN: 9781119433262

Cover design: Wiley

Cover images: © Kateryna Kon/Shutterstock,

© Designua/Shutterstock, © Umpaporn/Shutterstock,

© molekuul_be/Shutterstock

Set in 10/12pt, TimesLTStd by SPi Global, Chennai, India

10 9 8 7 6 5 4 3 2 1

Contents

<i>List of Contributors</i>	xiii
<i>Series Preface</i>	xvii
<i>Preface</i>	xix
1 Chronic Wound Healing: Molecular and Biochemical Basis	1
<i>Sophia Tate and Keith Harding</i>	
1.1 Introduction	1
1.2 Acute Wound Healing	1
1.3 Categories of Chronic Wound	3
1.3.1 Pressure Ulcers	3
1.3.2 Venous Stasis Ulcers	4
1.3.3 Ischaemic Ulcers	4
1.3.4 Diabetic Foot Ulcers	4
1.4 How a Chronic Wound Develops: Intrinsic Components	4
1.4.1 Cell Phenotype	5
1.4.2 Immune Cells and Inflammatory Mediators	6
1.4.3 Reactive Oxygen Species	8
1.4.4 Growth Factors	8
1.4.5 The Role of Matrix Metalloproteinases	12
1.5 How a Chronic Wound Develops: Extrinsic Factors	13
1.5.1 Infection	13
1.5.2 Nutrition	13
1.5.3 Tobacco Smoking	14
1.5.4 Hypoxia and Ischaemia–Reperfusion Injury	15
1.6 Concluding Remarks	15
References	16

2	Clinical Perspectives for Treating Chronic Wounds	21
	<i>Barun Majumder, Kirstie Lane, Diane Beck, Sandeep Singh and Duniya Majumder</i>	
2.1	Background	21
2.2	Aetiology of Diabetic Foot Ulcers	22
2.3	Standard of Care for Treatment of Diabetic Foot Ulcers	22
2.4	Commonly Used Wound Dressings for Diabetic Foot Ulcers and Their Mechanism of Action	22
2.5	Absorbent and Superabsorbent Dressings	23
2.6	Alginates	23
2.7	Films	23
2.8	Foams	24
2.9	Honeys	24
2.10	Hydrogels	25
2.11	The Role of a Split Thickness Skin Graft in Diabetic Foot Ulcers	25
2.12	Negative Pressure Wound Therapy	25
2.13	Larval Therapy	27
2.14	Clinical Case Studies from Multidisciplinary Diabetic Foot Clinic	27
2.14.1	Neuropathic Wound	27
2.14.2	Ischaemic Wound	29
2.14.3	Neuro-Ischaemic Wound	31
2.14.4	Osteomyelitis	33
2.14.5	Charcot's Foot	35
2.14.6	Necrotising Fasciitis in a Patient with Diabetes	36
2.15	Summary	39
	Acknowledgements	39
	References	39
3	Prediction, Prevention, Assessment, and Management of Skin Tears in the Aging Population	43
	<i>Kimberly LeBlanc and Karen Campbell</i>	
3.1	Introduction	43
3.2	Skin Tear Prevalence and Incidence	44
3.3	Predicting Skin Tears	45
3.4	Prevention	47
3.5	ISTAP Risk Reduction Program	49
3.5.1	General Health	49
3.5.2	Mobility	50
3.5.3	Skin	51
3.6	Assessment	52
3.7	Management	54
3.8	Treatment	54
3.9	Conclusion	55
	References	55

4	Importance of Debriding and Wound Cleansing Agents in Wound Healing	59
	<i>Gwendolyn Cazander, Bianca K. den Ottelander, Sandra Kamga, Martijn C.H.A. Doomen, Tim H.C. Damen and Anne Marie E. van Well</i>	
4.1	What is Debridement?	59
4.2	The History of Debridement	59
4.3	Why Undertake Debridement?	60
4.4	Debridement Techniques and Wound Cleansing Agents	62
4.4.1	Mechanical Debridement	62
4.4.2	Biological Debridement	72
4.4.3	Enzymatic Debridement	74
4.4.4	Autolytic Debridement	77
4.4.5	Wound Cleansing	79
4.4.6	Other Debridement Therapies	80
4.5	What is the Future of Debridement?	81
	References	82
5	Treatment of Mixed Infections in Wounds	91
	<i>Asif Ahmed and Joshua Boateng</i>	
5.1	Introduction	91
5.1.1	Wound Healing Process	92
5.1.2	Types of Chronic Wounds	92
5.2	Prevalence of Mixed Infections	94
5.2.1	Bacterial–Fungal Interactions	95
5.2.2	Bacterial–Bacterial Interactions	98
5.2.3	Host Responses to Mixed Infections and Drug Resistance	99
5.3	Management of Mixed Infected Wounds	100
5.3.1	Clinical and Microbiological Diagnosis	101
5.3.2	Debridement and Cleansing	101
5.3.3	Antimicrobial Therapies	102
5.3.4	Hyperbaric Oxygen Therapy	104
5.3.5	Phage Therapy	104
5.4	Summary and Future Perspectives	104
	References	105
6	Treatment of Biofilms in Infected Wounds	115
	<i>Philip Debrah, Awo Afi Kwapong and Mansa Fredua-Agyeman</i>	
6.1	Introduction	115
6.2	Why and How Biofilms Form	116
6.3	Wound Biofilms	118
6.3.1	Wound Healing	119
6.4	Biofilms and Wounds	119
6.4.1	Simulation of Biofilms in Wounds	120

6.5	Treatment of Biofilms in Wounds	126
6.5.1	Biofilm Eradication	126
6.5.2	Current Treatment Protocols	128
6.6	Clinical Examples	128
6.7	Summary	128
	References	130
7	Freeze-Dried Wafers for Wound Healing	137
	<i>Shiow-Fern Ng</i>	
7.1	Introduction	137
7.2	Wafer as a Modern Wound Dressing	138
7.3	Freeze-Drying Process	139
7.4	Wafer Preparation	140
7.5	Wafer Assessments	141
7.5.1	Morphology	142
7.5.2	Swelling Index	144
7.5.3	Mechanical Properties	145
7.5.4	In Vitro Drug Release	145
7.5.5	Cell Viability	146
7.6	Wafer Biopolymers	146
7.6.1	Alginate	147
7.6.2	Chitosan	148
7.6.3	Carboxymethylcellulose	149
7.7	Conclusion	150
	References	150
8	Silver and Silver Nanoparticle-Based Antimicrobial Dressings	157
	<i>Joshua Boateng and Ovidio Catanzano</i>	
8.1	Introduction	157
8.1.1	Brief History of Silver as an Antibiotic	159
8.1.2	Mechanism of Action	160
8.1.3	Bacterial Resistance to Silver	164
8.2	Silver Dressings in Wound Healing	167
8.2.1	Silver-Based Antimicrobial Dressings	169
8.2.2	Silver Nanoparticle-Based Antimicrobial Dressings	170
8.3	Cost-Effectiveness of Silver Dressings	175
8.4	Concluding Remarks	176
	References	177
9	Hydrogel Dressings	185
	<i>Galiya S. Irmukhametova, Grigoriy A. Mun and Vitaliy V. Khutoryanskiy</i>	
9.1	Introduction	185
9.1.1	Classification by Origin of Materials Used to Prepare Hydrogels	186
9.1.2	Classification by Composition and Structure of Hydrogels	186
9.1.3	Classification by the Type of Cross-Linking	187

9.1.4	Classification Based on the Shape and Dimensions of Hydrogels	187
9.1.5	Classification Based on the Charge of Macromolecules Forming Hydrogels	187
9.1.6	Classification Based on Functional Properties of the Hydrogels	187
9.2	Mechanism of Hydrogel Swelling	187
9.2.1	Swelling of Temperature-Sensitive Hydrogels and Their Application in Wound Healing	189
9.2.2	Swelling of Light-Sensitive Hydrogels	190
9.2.3	Swelling of Electro-Sensitive Hydrogels	191
9.3	Application of Hydrogels as Wound Dressings	191
9.4	Industrial Methods for the Synthesis of Hydrogels for Wound Dressings	193
9.4.1	Polymerization Methods	193
9.4.2	Cross-Linking of Polymers	195
9.5	Antimicrobial Hydrogels with Special Additives	198
9.6	Conclusion	200
	Acknowledgments	201
	References	201
10	Gene Therapy for the Treatment of Chronic Wounds	209
	<i>Marcos Garcia-Fuentes</i>	
10.1	Introduction	209
10.2	Pharmacodynamics of Gene Therapy in Chronic Wounds	210
10.2.1	Signalling Supplementation	210
10.2.2	Pathway Inhibition	211
10.3	Administration Routes and Methods	212
10.3.1	Systemic Delivery	212
10.3.2	Topical Delivery	212
10.3.3	Intralesional Delivery	213
10.4	Gene Delivery Systems	213
10.4.1	Physical Methods	214
10.4.2	Viral Vectors	215
10.4.3	Chemical Delivery Systems	217
10.4.4	Gene-Activated Matrices	220
10.5	Clinical Evaluation	221
10.6	Conclusion	226
	Acknowledgements	226
	References	227
11	Honey in Wound Healing	235
	<i>Emi Maruhashi</i>	
11.1	The History of Honey	235
11.2	Composition	236
11.3	Honey Research	236

11.4	Medical Grade Honey	237
11.5	Modes of Action	238
11.6	Applications and Specific Wound Types	242
11.7	Practical Considerations	246
11.8	Novel Concepts and Conclusions	247
	References	248
12	Regeneration Using Tissue Engineered Skin Strategies	255
	<i>Lucília P. da Silva, Mariana T. Cerqueira and Alexandra P. Marques</i>	
12.1	Introduction	255
12.2	Skin Physiology and Wounding	256
12.3	Skin Tissue Engineering	258
12.4	Evolving Skin Tissue Engineering Strategies	259
12.4.1	Balancing the Inflammatory Phase	261
12.4.2	Enhancement of Re-Epithelialization	263
12.4.3	Target of Dermal Matrix Synthesis and Remodeling	269
12.4.4	Re-Establishment of the Vascular Network	270
12.4.5	Innervation Shaping	280
12.4.6	Appendages and Pigmentation	281
12.5	Conclusion	282
	References	283
13	Local Delivery of Growth Factors Using Wound Dressings	291
	<i>Ovidio Catanzano and Joshua Boateng</i>	
13.1	Wound Dressings as Delivery Platforms for Growth Factors	291
13.2	Growth Factors Involved in the Wound Healing Process	292
13.3	Local Delivery of Growth Factors Using Wound Dressings	296
13.4	Integration of Platelet-Rich Plasma in Wound Dressings	299
13.5	Enhancing Local Growth Factor Expression Using Gene Therapy	300
13.6	Wound Delivery of Growth Factors from Living Systems	302
13.7	Regulatory Considerations	305
13.8	Conclusions and Future Perspectives	306
	References	307
14	Electrospinning Technologies in Wound Dressing Applications	315
	<i>Giuseppina Sandri, Silvia Rossi, Maria Cristina Bonferoni, Carla Caramella and Franca Ferrari</i>	
14.1	Introduction	315
14.2	Basic Concept and Electrospinning Set-Up	316
14.3	Parameters Affecting the Electrospinning Process	318
14.4	Process Parameters	319
14.4.1	Electric Field Strength	319
14.4.2	Flow Rate	319

14.4.3	Needle-to-Collector Distance	320
14.4.4	Collector and Needle Types	320
14.5	Solution Parameters	321
14.5.1	Molecular Weight and Polymer Concentration	321
14.5.2	Surface Tension	322
14.5.3	Conductivity/Surface Charge Density	322
14.5.4	Environmental Parameters	322
14.6	Biomedical Applications of Nanofibrous Membranes	323
14.6.1	Wound Dressings and Wound Healing	323
14.6.2	Electrospun Dressings	325
14.7	Chemicophysical and Biopharmaceutical Characterizations	325
14.8	Dressing/Scaffold Parameters Affecting Cell Functions	327
14.9	Materials for Fabricating Nanofibers	328
14.9.1	Biopolymers	328
14.10	Concluding Remarks	333
	References	333
15	The Place of Biomaterials in Wound Healing	337
	<i>Annalisa Bianchera, Ovidio Catanzano, Joshua Boateng and Lisa Elviri</i>	
15.1	Introduction to Biomaterials for Wound Healing	337
15.1.1	Definition of Biomaterials	337
15.1.2	Functional Requirements of Wound Repair Biomaterials	338
15.1.3	Classification of Biomaterials Commonly Used in Wound Healing	338
15.2	Synthetic Biomaterials for Wound Healing	339
15.2.1	Polyurethanes and their Derivatives	340
15.2.2	Poly L-Lactic Acid	340
15.2.3	Poly(Ethylene Glycol)	341
15.2.4	Polycaprolactone	341
15.2.5	Poly(Glycolic Acid) and Poly(Lactic-co-Glycolic Acid)	342
15.3	Natural Biomaterials for Wound Healing	343
15.3.1	Polysaccharide-Based Biomaterials	343
15.3.2	Protein-Based Biomaterials	348
15.4	Application of Biomaterials in Wound Healing	350
15.4.1	Traditional and Impregnated Dressings	350
15.4.2	Hydrogels	352
15.4.3	Film Dressings	353
15.4.4	Foam Dressings	354
15.4.5	Nanofiber-Based Dressings	355
15.4.6	Three-Dimensional Printed Dressings	356
15.5	New Trends in Biomaterials for Wound Healing	357
15.5.1	Extracellular Matrix-Derived Biomaterials	357
15.5.2	Tissue Engineered Skin Substitutes	357
15.6	Conclusions and Future Perspectives	358
	References	359

16	Wound Dressings and Pressure Ulcers	367
	<i>Michael Clark</i>	
16.1	Overview	367
16.2	Introduction to Pressure Ulcers	367
16.3	The Impact of Pressure Ulcers	369
16.4	Managing Pressure Ulcers	370
16.5	Wound Dressings in Pressure Ulcer Treatment	371
16.6	Pressure Ulcer Prevention and Wound Dressings	377
16.6.1	Pressure Ulcers at the Nose	378
16.6.2	Pressure Ulcers at the Heel	378
16.6.3	Pressure Ulcers at the Sacrum	378
16.7	Conclusions	380
	References	380
17	3D Printed Scaffolds for Wound Healing and Tissue Regeneration	385
	<i>Atabak Ghanizadeh Tabriz, Dennis Douroumis and Joshua Boateng</i>	
17.1	Introduction	385
17.2	3D Printing	386
17.3	Laser-Based Bioprinting	387
17.4	Jet-Based Printing	389
17.5	Extrusion-Based Printing	391
17.6	Hybrid Printing	393
17.7	Conclusions	395
	References	395
	<i>Index</i>	399

List of Contributors

Asif Ahmed, School of Science, Faculty of Engineering and Science, University of Greenwich Medway, Chatham Maritime, UK

Diane Beck, Ashford and St Peter's Hospitals NHS Foundation Trust, Chertsey, UK

Annalisa Bianchera, Interdepartmental Centre Biopharmanet-TEC, University of Parma, Italy

Joshua Boateng, School of Science, Faculty of Engineering and Science, University of Greenwich Medway, Chatham Maritime, UK

Maria Cristina Bonferoni, Department of Drug Sciences, University of Pavia, Italy

Karen Campbell, Western University, London, ON, Canada

Carla Caramella, Department of Drug Sciences, University of Pavia, Italy

Ovidio Catanzano, Department of Life Sciences, University of Trieste, Italy

Gwendolyn Cazander, Wound Expertise Center (WEC), Ikazia, Rotterdam, The Netherlands

Mariana T. Cerqueira, 3B's Research Group, I3Bs – Research Institute on Biomaterials, Biodegradables and Biomimetics, University of Minho, Headquarters of the European Institute of Excellence on Tissue Engineering and Regenerative Medicine, Barco, Guimarães; and ICVS/3B's–PT Government Associate Laboratory, Braga/Guimarães, Portugal

Michael Clark, Birmingham City University, Birmingham; and Welsh Wound Innovation Centre, Ynysmaerdy, UK

Tim H.C. Damen, Wound Expertise Center (WEC), Ikazia, Rotterdam, The Netherlands

Lucília P. da Silva, 3B's Research Group, I3Bs – Research Institute on Biomaterials, Biodegradables and Biomimetics, University of Minho, Headquarters of the European Institute of Excellence on Tissue Engineering and Regenerative Medicine, Barco, Guimarães; and ICVS/3B's–PT Government Associate Laboratory, Braga/Guimarães, Portugal

Philip Debrah, Department of Pharmaceutics and Microbiology, School of Pharmacy, University of Ghana, Accra, Ghana

Bianca K. den Ottelander, Wound Expertise Center (WEC), Ikazia, Rotterdam, The Netherlands

Martijn C.H.A. Doomen, Wound Expertise Center (WEC), Ikazia, Rotterdam, The Netherlands

Dennis Douroumis, School of Science, Faculty of Engineering and Science, University of Greenwich, Chatham Maritime, UK

Lisa Elviri, Food and Drug Department, University of Parma, Italy

Franca Ferrari, Department of Drug Sciences, University of Pavia, Italy

Mansa Fredua-Agyeman, Department of Pharmaceutics and Microbiology, School of Pharmacy, University of Ghana, Accra, Ghana

Marcos Garcia-Fuentes, Center for Research in Molecular Medicine and Chronic Diseases (CIMUS), Universidad de Santiago de Compostela, Spain

Atabak Ghanizadeh Tabriz, School of Science, Faculty of Engineering and Science, University of Greenwich, Chatham Maritime, UK

Keith Harding, Division of Population Medicine, Cardiff University School of Medicine, Cardiff, UK

Galiya S. Irmukhametova, Faculty of Chemistry and Chemical Technology, al-Farabi Kazakh National University, Almaty, Kazakhstan

Sandra Kamga, Wound Expertise Center (WEC), Ikazia, Rotterdam, The Netherlands

Vitaliy V. Khutoryanskiy, School of Pharmacy, University of Reading, UK

Awo Afi Kwapong, Department of Pharmaceutics and Microbiology, School of Pharmacy, University of Ghana, Accra, Ghana

Kirstie Lane, West Byfleet Health Centre, West Byfleet, UK

Kimberly LeBlanc, Wound Ostomy Continence Institute/Association of Nurses Specialized in Wound Ostomy Continence, Ottawa, ON, Canada

Barun Majumder, Ashford and St Peter's Hospitals NHS Foundation Trust, Chertsey, UK

Duniya Majumder, Lanarkshire, Glasgow, UK

Alexandra P. Marques, The Discoveries Centre for Regenerative and Precision Medicine, Headquarters at University of Minho, Barco, Guimarães, Portugal

Emi Maruhashi, University of Lisbon, Lisbon, Portugal

Grigoriy A. Mun, Faculty of Chemistry and Chemical Technology, al-Farabi Kazakh National University, Almaty, Kazakhstan

Shiow-Fern Ng, Centre for Drug Delivery Research, Faculty of Pharmacy, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

Silvia Rossi, Department of Drug Sciences, University of Pavia, Italy

Giuseppina Sandri, Department of Drug Sciences, University of Pavia, Italy

Sandeep Singh, Ashford and St Peter's Hospitals NHS Foundation Trust, Chertsey, UK

Sophia Tate, University Hospital of Wales, Cardiff and Vale University Health Board, Cardiff, UK

Anne Marie E. van Well, Wound Expertise Center (WEC), Ikazia, Rotterdam, The Netherlands

Series Preface

The series *Advances in Pharmaceutical Technology* covers the principles, methods and technologies that the pharmaceutical industry uses to turn a candidate molecule or new chemical entity into a final drug form and hence a new medicine. The series will explore means of optimizing the therapeutic performance of a drug molecule by designing and manufacturing the best and most innovative of new formulations. The processes associated with the testing of new drugs, the key steps involved in the clinical trials process and the most recent approaches utilized in the manufacture of new medicinal products will all be reported. The focus of the series will very much be on new and emerging technologies and the latest methods used in the drug development process.

The topics covered by the series include the following:

Formulation: The manufacture of tablets in all forms (caplets, dispersible, fast-melting) will be described, as will capsules, suppositories, solutions, suspensions and emulsions, aerosols and sprays, injections, powders, ointments and creams, sustained release and the latest transdermal products. The developments in engineering associated with fluid, powder and solids handling, solubility enhancement, colloidal systems including the stability of emulsions and suspensions will also be reported within the series. The influence of formulation design on the bioavailability of a drug will be discussed and the importance of formulation with respect to the development of an optimal final new medicinal product will be clearly illustrated.

Drug Delivery: The use of various excipients and their role in drug delivery will be reviewed. Among the topics to be reported and discussed will be a critical appraisal of the current range of modified-release dosage forms currently in use and also those under development.

The design and mechanism(s) of controlled release systems including macromolecular drug delivery, microparticulate controlled drug delivery, the delivery of biopharmaceuticals, delivery vehicles created for gastrointestinal tract targeted delivery, transdermal

delivery and systems designed specifically for drug delivery to the lung will all be reviewed and critically appraised. Further site-specific systems used for the delivery of drugs across the blood–brain barrier including dendrimers, hydrogels and new innovative biomaterials will be reported.

Manufacturing: The key elements of the manufacturing steps involved in the production of new medicines will be explored in this series. The importance of crystallization; batch and continuous processing, seeding; and mixing including a description of the key engineering principles relevant to the manufacture of new medicines will all be reviewed and reported. The fundamental processes of quality control including good laboratory practice, good manufacturing practice, Quality by Design, the Deming Cycle, regulatory requirements and the design of appropriate robust statistical sampling procedures for the control of raw materials will all be an integral part of this book series.

An evaluation of the current analytical methods used to determine drug stability, the quantitative identification of impurities, contaminants and adulterants in pharmaceutical materials will be described, as will the production of therapeutic bio-macromolecules, bacteria, viruses, yeasts, molds, prions and toxins through chemical synthesis and emerging synthetic/molecular biology techniques. The importance of packaging including the compatibility of materials in contact with drug products and their barrier properties will also be explored.

Advances in Pharmaceutical Technology is intended as a comprehensive one-stop shop for those interested in the development and manufacture of new medicines. The series will appeal to those working in the pharmaceutical and related industries, both large and small, and will also be valuable to those who are studying and learning about the drug development process and the translation of those drugs into new life-saving and life-enriching medicines.

Dennis Douroumis
Alfred Fahr
Jürgen Siepmann
Martin Snowden
Vladimir Torchilin

Preface

Wounds and their effective healing constitute a common and current global medical concern with several challenges, including the increasing incidence of obesity and type 2 diabetes, an ageing population that has increased the incidence of chronic (difficult to heal) wounds, and the requirement for more effective but also cost-effective dressings. Wounds can be chronic or acute and can result from burns, amputation, surgical procedures, or underlying medical conditions. Innovative dressings that take an active part in wound healing in a more rapid manner and at reasonable cost are currently an unmet public health need. Although there are several dressings on the market, not all of them take an active part in wound healing; instead, they depend on the body's natural physiological tissue processes, which are normally compromised in patients with underlying medical conditions and in those who are highly traumatized, such as combat personnel and mass casualties.

Therefore, interest has shifted in academic research laboratories, industry, and general clinical practice towards more advanced therapeutic dressings that are biologically active and usually involve multi-disciplinary approaches spanning molecular biology, biomaterial/polymer science, biochemistry, formulation science, and biopharmaceutics. These include medicated dressings, biomaterial-based biological dressings (biological and naturally derived), tissue-engineered scaffolds, as well as nanotechnology.

This book systematically covers various aspects of the above advanced wound healing therapies and is divided into three main themes. The book comprises 17 chapters written by various authors who are widely recognized in their fields of expertise. The first six chapters focus on the physiological and molecular basis of wounds and their healing, including the various types of chronic wounds as well as some of the complicating and risk factors, such as infections and dead tissues, and how to manage these from a clinical perspective. Chapters 7–9 focus on advanced moist modern dressings such as wafers and hydrogels as well as on nanotechnology-based silver dressings. Finally, Chapters 10–17 address more advanced and novel approaches to wound healing, including gene therapy-based dressings, tissue engineering, delivery of growth factors, electrospun dressings, biomaterial-based dressings,

and the use of three-dimensional (3D) printed scaffolds embedded with cells and other active entities that take part in tissue regeneration.

Most importantly, I would like to personally thank all of the authors for their willingness to contribute to this book in the first place, and for preparing their chapters with due diligence and a sense of purpose to meet the agreed deadlines.

Joshua Boateng