

DRUG DELIVERY

An Integrated Clinical
and Engineering
Approach

Edited by
YITZHAK ROSEN
PABLO GURMAN
NOEL ELMAN



CRC Press
Taylor & Francis Group

DRUG DELIVERY

An Integrated Clinical and Engineering Approach

Integrating the clinical and engineering aspects of drug delivery, this book offers a much needed comprehensive overview and patient-oriented approach for enhanced drug delivery optimization and advancement. Starting with an introduction to the subject and pharmacokinetics, it explores advances for such topics as oral, gastroretentive, intravitreal, and intrathecal drug delivery, as well as insulin delivery, gene delivery, and biomaterials-based delivery systems. It also describes drug delivery in cancer, cardiac, infectious diseases, airway diseases, and obstetrics and gynecology applications. Examining special clinical states requiring innovative drug delivery modifications, such as hypercoagulability often seen in pregnancy, cancer, and autoimmune diseases, the book also discusses methods for improved drug delivery in clinical settings using clinical end points, clinical trials, simulations, and other venues. It also describes the latest drug delivery advances involving nanomaterials, NEMS and MEMS devices, hydrogels, microencapsulation, lipids, stem cells, patches, and ultrasound. The book is rounded out by a chapter on the FDA regulatory and bioethical challenges involved in advancing drug delivery.

- Emphasizes an integrated clinical and engineering approach.
- Covers oral, gastroretentive, intravitreal, and intrathecal drug delivery, as well as insulin delivery, gene delivery, and biomaterials-based delivery systems.
- Describes the latest in drug delivery for cancer, cardiac, infectious diseases, airway diseases, and obstetrics and gynecology applications.
- Explores micro- and nanotechnology for drug delivery, including microneedle-mediated vaccines, microsponges, and nanoparticles as tracking systems.
- Examines special clinical states requiring innovative drug delivery modifications.
- Discusses methods for improved drug delivery in clinical settings.
- Discusses FDA regulation of drug delivery systems and bioethical challenges involved in advancing drug delivery.



CRC Press
Taylor & Francis Group
an informa business

www.taylorandfrancisgroup.com

6000 Broken Sound Parkway, NW
Suite 300, Boca Raton, FL 33487
711 Third Avenue
New York, NY 10017
2 Park Square, Milton Park
Abingdon, Oxon OX14 4RN, UK

K16126

ISBN: 978-1-4665-6594-4

90000



9 781466 565944

www.crcpress.com

DRUG DELIVERY

An Integrated Clinical and
Engineering Approach

ROSEN
GURMAN
ELMAN



Drug Delivery

An Integrated Clinical and Engineering Approach

Edited by
Yitzhak Rosen
Pablo Gurman
Noel M. Elman



CRC Press

Taylor & Francis Group

Boca Raton London New York

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

The material in this book, whether related to medicine or any other topic, should be verified as to its accuracy, currency, and preciseness by the reader. It should in no way replace any advice given by a medical professional or any other professional. None of the information provided here should be a substitute for additional reading, advice, experience, or other relevant information in any topic discussed in this book.

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

© 2017 by Taylor & Francis Group, LLC
CRC Press is an imprint of Taylor & Francis Group, an Informa business

No claim to original U.S. Government works

Printed on acid-free paper
Version Date: 20161109

International Standard Book Number-13: 978-1-4665-6594-4 (Hardback)

This book contains information obtained from authentic and highly regarded sources. Reasonable efforts have been made to publish reliable data and information, but the author and publisher cannot assume responsibility for the validity of all materials or the consequences of their use. The authors and publishers have attempted to trace the copyright holders of all material reproduced in this publication and apologize to copyright holders if permission to publish in this form has not been obtained. If any copyright material has not been acknowledged please write and let us know so we may rectify in any future reprint.

Except as permitted under U.S. Copyright Law, no part of this book may be reprinted, reproduced, transmitted, or utilized in any form by any electronic, mechanical, or other means, now known or hereafter invented, including photocopying, microfilming, and recording, or in any information storage or retrieval system, without written permission from the publishers.

For permission to photocopy or use material electronically from this work, please access www.copyright.com (<http://www.copyright.com/>) or contact the Copyright Clearance Center, Inc. (CCC), 222 Rosewood Drive, Danvers, MA 01923, 978-750-8400. CCC is a not-for-profit organization that provides licenses and registration for a variety of users. For organizations that have been granted a photocopy license by the CCC, a separate system of payment has been arranged.

Trademark Notice: Product or corporate names may be trademarks or registered trademarks, and are used only for identification and explanation without intent to infringe.

Visit the Taylor & Francis Web site at
<http://www.taylorandfrancis.com>

and the CRC Press Web site at
<http://www.crcpress.com>

此为试读, 需要完整PDF请访问: www.ertongbook.com

Drug Delivery

An Integrated Clinical and Engineering Approach

Foreword

This book is a comprehensive overview in the much needed area of drug delivery. It addresses a critical unmet need, the approach of integrating the clinical and engineering disciplines for drug delivery optimization and advancement. This integration is a must, requires a patient-oriented approach, and is a key foundation in drug delivery development.

Furthermore, the book focuses on important advances and discusses how an integrated approach was used for these advances. It consists of 21 chapters, starting with a thorough introduction to drug delivery and pharmacokinetics, followed by diverse clinical examples of this integration. The book discusses the following areas and their advances: oral and intrathecal drug delivery; insulin delivery and artificial pancreas; micro- and nanotechnology for drug delivery, including applications of micro- and nanotechnology in vaccines; inflammatory diseases; airway diseases and the use of nanoparticles as tracking systems; biomaterial-based delivery systems, including chitosan and microsponges; gene delivery, cancer drug delivery with a focus on stem cells; cardiac drug delivery; intravitreal drug delivery; and drug delivery in obstetrics and gynecology as well as an important chapter on FDA regulation of drug delivery systems.

As an experienced clinician and discoverer of a new autoimmune syndrome (ASIA Syndrome), developer of novel therapeutics, publisher of numerous papers and books, and editor in chief of two journals on autoimmunity (*Autoimmunity Reviews* IF-7.95 and *Journal of Autoimmunity* IF 8.4), it is my hope that all clinicians and engineers involved in advancing drug delivery will find in this book a useful resource. Therefore, I give this book the highest recommendation.

Yehuda Shoenfeld, MD, FRCP, MaACR

*Head of Zabłudowicz Center for Autoimmune Diseases
Sheba Medical Center, Affiliated with Tel Aviv University*

Acknowledgments

We, as editors, take this opportunity to acknowledge all the contributors, editorial staff, family, and friends for greatly assisting us in making this important book publication a reality.

Editors



Yitzhak Rosen, MD, is a graduate of the Tel Aviv University of Medicine. He completed an internal medicine residency at Coney Island Hospital and is currently a fellow at the Cardiovascular Division of SUNY Downstate Medical Center in Brooklyn, New York. He has worked as a research scientist at the Institute for Soldier Nanotechnologies, Massachusetts Institute of Technology (MIT). He is also the president and CEO of Superior NanoBioSystems LLC, a biomedical company.

He has served in the Israel Defense Forces (IDF) as a medical officer and physician in militarily active areas. He completed a medical internship at the Rabin Medical Center and has worked at the Oncology Institutes of both the Rabin and the Sheba Medical Centers in Israel. He has invented a microfluidic chip platform, funded by the Defense Advanced Research Projects Agency (DARPA), for effecting extremely rapid blood typing and cross-matching for mass casualties in collaboration with the MEMS and Nanotechnology Exchange. In addition, he is the inventor of several medical ultrasound technologies.



Pablo Gurman, MD, earned his MD degree from Buenos Aires University School of Medicine in 2002, where he worked at the Pharmacology Department for 10 years. He is currently the chief medical officer at GearJump Technologies, a biotechnology company dedicated to developing innovative solutions to public health problems. Prior to this appointment, he was a research scientist at the Materials Science and Engineering Department at the University of Texas-Dallas, as well as a research collaborator at Dr. Elman's group at the Institute for Soldiers Nanotechnologies at the Massachusetts Institute of Technology (MIT). Dr. Gurman was a visiting scientist at

Argonne National Laboratory, where he worked under the artificial retina program.

Gurman's primary research interests involve micro- and nanotechnology for medical diagnostics and therapeutics, controlled release technologies, and biomaterials.



Noel M. Elman, PhD, is the CEO and founder of GearJump Technologies, LLC, a company dedicated to development of biotechnological solutions for public health applications. Dr. Elman is also a lecturer in technology and innovation at the Buenos Aires Institute of Technology. He worked at Draper Laboratory, an MIT-affiliated DoD-supported R&D center, where he was an appointed distinguished member of the technical staff. Prior to this appointment, he was a research scientist and principal investigator at the Institute

for Soldier Nanotechnologies at MIT, leading a translational research group

focused on developing technologies for biotech, biomed, and public health applications. In addition, he was appointed an Innovation Fellow at Massachusetts General Hospital. Dr. Elman's research focus is on rapid translation from idea conceptualization to experimental realization. He earned his bachelor's and master's degrees in electrical engineering at Cornell University, and his PhD degree in electrical engineering at Tel Aviv University. He performed postdoctoral studies at MIT, investigating several micro- and nanodevices for therapeutics and diagnostics.

Contributors

Lissa Nurul Abdullah

Cancer Science Institute of Singapore
National University of Singapore
Singapore

Sharifa Al-Zahrani

School of Pharmacy
Queen's University
Belfast, United Kingdom

José L. Arias

Department of Pharmacy and
Pharmaceutical Technology
Faculty of Pharmacy
University of Granada
Campus Universitario de Cartuja s/n
Granada, Spain

Shimon Ben-Shabat

Department of Clinical Pharmacology
School of Pharmacy
Faculty of Health Sciences
Ben-Gurion University of the Negev
Beer-Sheva, Israel

Luis Bruno Blanch

Medicinal Chemistry
Department of Biological Sciences
School of Sciences
National University of La Plata (UNLP)
La Plata, Argentina

María J. Blanco-Prieto

Department of Pharmacy and
Pharmaceutical Technology
School of Pharmacy
University of Navarra
Pamplona, Spain

Maximiliano L. Cacicedo

Nanobiomaterials Laboratory
Institute of Applied Biotechnology
(CINDEFI, UNLP-CONICET-CCT
La Plata)
Department of Chemistry
School of Sciences
Universidad Nacional de La Plata
La Plata, Argentina

Guillermo R. Castro

Nanobiomaterials Laboratory
Institute of Applied Biotechnology
(CINDEFI, UNLP-CONICET-CCT
La Plata)
Department of Chemistry
School of Sciences
National University of La Plata
La Plata, Argentina

SriKrishna Chandran

University Hospitals of Cleveland
Cleveland, Ohio

Mohini Chaurasia

Amity Institute of Pharmacy
Amity University
Lucknow, India

Manish K. Chourasia

Pharmaceutics Division
CSIR-Central Drug Research Institute
Lucknow, India

Edward Kai-Hua Chow

Department of Pharmacology
Yong Loo Lin School of Medicine
and
Cancer Science Institute of Singapore
National University of Singapore
Singapore

Ana Costa

CESPU

Instituto de Investigação e Formação

Avançada em Ciências e Tecnologias
da SaúdeDepartment of Pharmaceutical Sciences
Gandra-PRD, Portugal**Arik Dahan**

Department of Clinical Pharmacology

School of Pharmacy

Faculty of Health Sciences

Ben-Gurion University of the Negev

Beer-Sheva, Israel

Jonathan Daich

Superior NanoBioSystems LLC

Eyal Dassau

Harvard John A. Paulson School of

Engineering and Applied Sciences

Harvard University

Cambridge, Massachusetts

Simón Pascual-Gil de Gómez

Department of Pharmacy and

Pharmaceutical Technology

School of Pharmacy

University of Navarra

Pamplona, Spain

Paula Díaz-Herráez

Department of Pharmacy and

Pharmaceutical Technology

School of Pharmacy

University of Navarra

Pamplona, Spain

Ryan F. Donnelly

School of Pharmacy

Queen's University

Belfast, United Kingdom

Mazen M. El-Hammadi

Department of Pharmacy and

Pharmaceutical Technology

Faculty of Pharmacy

University of Granada

Campus Universitario de Cartuja s/n

Granada, Spain

and

Department of Pharmaceutics and

Pharmaceutical Technology

Faculty of Pharmacy

Damascus University

Damascus, Syria

Noel M. Elman

GearJump Technologies, LLC

Brookline, Massachusetts

Steven J. Fallows

School of Pharmacy

Queen's University

Belfast, United Kingdom

Pedro Fonte

CESPU

Instituto de Investigação e Formação

Avançada em Ciências e Tecnologias
da Saúde

Department of Pharmaceutical Sciences

Gandra-PRD, Portugal

and

REQUIMTE

Department of Chemistry

University of Porto

Porto, Portugal

Elisa Garbayo

Department of Pharmacy and

Pharmaceutical Technology

School of Pharmacy

University of Navarra

Pamplona, Spain

Julie Gehl

Department of Oncology
C*EDGE (Center for Experimental
Drug and Gene Electrotransfer)
Copenhagen University Hospital
Herlev, Denmark

Pablo Gurman

Gur&Gor LLC
Revere, Massachusetts

Yael Hants

Department of Obstetrics and
Gynecology
Hadassah–Hebrew University Medical
Center, Ein Kerem
Jerusalem, Israel

Sarit Helman

Department of Obstetrics and
Gynecology
Shaare Zedek Medical Center
Jerusalem, Israel

Mark Ihnen

Kentucky Eye Care
Louisville, Kentucky

Germán A. Islan

Nanobiomaterials Laboratory
Institute of Applied Biotechnology
(CINDEFI, UNLP-CONICET-CCT
La Plata)
Department of Chemistry
School of Sciences
Universidad Nacional de La Plata
La Plata, Argentina

Sanjay K. Jain

Pharmaceutics Research Project
Laboratory
Department of Pharmaceutics
Dr. Hari Singh Gour University
Sagar, Madhya Pradesh, India

Ridhima Juneja

Department of Chemistry
University of Delhi
Delhi, India

Stephen Kuperberg

SUNY Downstate Medical Center
Department of Critical Care and
Pulmonary Medicine
Brooklyn, New York

Jennifer Lane

Drexel University College of Medicine
Philadelphia, Pennsylvania

Maelíosa T. C. McCrudden

School of Pharmacy
Queen's University
Belfast, United Kingdom

Ellis Meng

Department of Biomedical Engineering
Ming Hsieh Department of Electrical
Engineering
University of Southern California
Los Angeles, California

Vivek K. Pawar

Pharmaceutics Division
CSIR-Central Drug Research Institute
Lucknow, India

Mahyar Pourriahi

SUNY Downstate Medical Center
Department of Medicine
Brooklyn, New York

Felipe Prósper

Hematology, Cardiology and Cell
Therapy
Clínica Universidad de Navarra and
Foundation for Applied Medical
Research
University of Navarra
Pamplona, Spain

Masturah Bte Mohd Abdul Rashid

Department of Pharmacology
Yong Loo Lin School of Medicine
National University of Singapore
Singapore

Aaron Richler

Brookdale University Hospital
Brooklyn, New York

Yitzhak Rosen

SUNY Downstate Medical Center
Department of Medicine,
Cardiovascular Division
Brooklyn, New York

and

Superior NanoBioSystems LLC
New Jersey

Indrajit Roy

Department of Chemistry
University of Delhi
Delhi, India

Omar Saleh

Department of Ophthalmology
Jordan University of Science and
Technology
Irbid, Jordan

Bruno Sarmiento

CESPU
Instituto de Investigação e Formação
Avançada em Ciências e Tecnologias
da Saúde
Department of Pharmaceutical Sciences
Gandra-PRD, Portugal

and

INEB
Institute of Biomedical Engineering
University of Porto
Porto, Portugal

Shlomit Schaal

Department of Ophthalmology and
Visual Sciences
University of Massachusetts Medical
School
Worcester, Massachusetts

Komal Sethi

Department of Chemistry
University of Delhi
Delhi, India

Roya Sheybani

Department of Biomedical Engineering
University of Southern California
Los Angeles, California

Satish Shilpi

Pharmaceutics Research Project
Laboratory
Department of Pharmaceutical Sciences
Dr. Hari Singh Gour University
Sagar, Madhya Pradesh, India

and

Department of Pharmaceutics
Ravishankar College of Pharmacy
Bhopal, Madhya Pradesh, India

Joseph Shivers

Columbia University College of
Physicians and Surgeons
New York, New York

David Shveiky

Department of Obstetrics and
Gynecology
Hadassah–Hebrew University Medical
Center, Ein Kerem
Jerusalem, Israel