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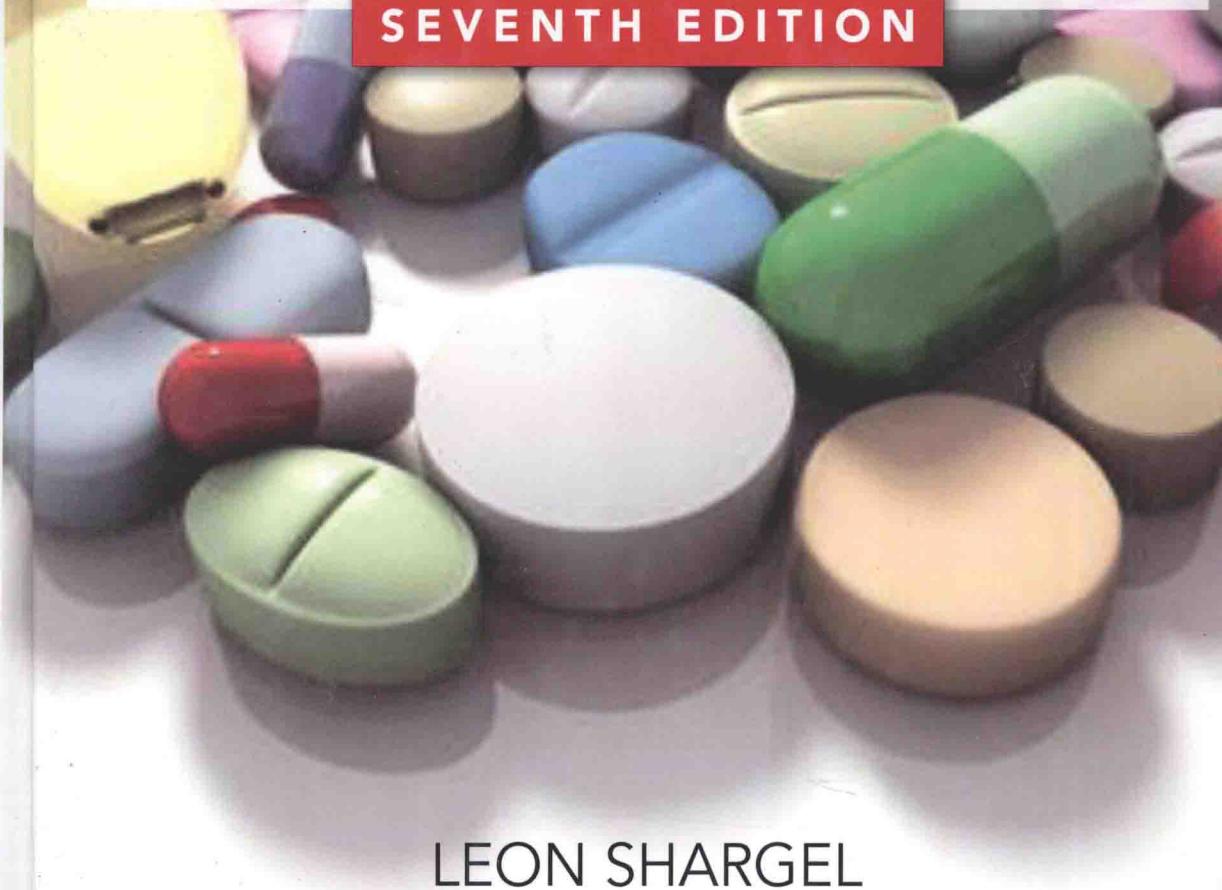
SEVENTH EDITION



LEON SHARGEL

ANDREW B.C. YU

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Applied Biopharmaceutics & Pharmacokinetics

Seventh Edition

EDITORS

Leon Shargel, PhD, RPh

Applied Biopharmaceutics, LLC
Raleigh, North Carolina
Affiliate Professor, School of Pharmacy
Virginia Commonwealth University, Richmond, Virginia
Adjunct Associate Professor, School of Pharmacy
University of Maryland, Baltimore, Maryland

Andrew B.C. Yu, PhD, RPh

Registered Pharmacist
Gaithersburg, Maryland
Formerly Associate Professor of Pharmaceutics
Albany College of Pharmacy
Albany, New York
Formerly CDER, FDA
Silver Spring, Maryland

Mc Graw Hill Education

New York Chicago San Francisco Athens London Madrid Mexico City
Milan New Delhi Singapore Sydney Toronto

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Contributors

S. Thomas Abraham, PhD
Associate Professor
Department of Pharmaceutical Sciences
College of Pharmacy & Health Sciences
Campbell University
Buies Creek, North Carolina

Michael L. Adams, PharmD, PhD
Associate Professor
Department of Pharmaceutical Sciences
College of Pharmacy & Health Sciences
Campbell University
Buies Creek, North Carolina

Antoine Al-Achi, PhD
Associate Professor
Campbell University
College of Pharmacy & Health Sciences
Buies Creek, North Carolina

Lily K. Cheung, PharmD
Assistant Professor
Department of Pharmacy Practice
College of Pharmacy & Health Sciences
Texas Southern University
Houston, Texas

Diana Shu-Lian Chow, PhD
Professor of Pharmaceutics
Director
Institute for Drug Education and Research (IDER)
College of Pharmacy
University of Houston
Houston, Texas

Philippe Colucci, PhD
Principal Scientist
Learn and Confirm Inc.
Sr. Laurent, QC, Canada

Dale P. Conner, Pharm.D.
Director
Office of Bioequivalence
Office of Generic Drugs
CDER, FDA
Silver Spring, Maryland

Barbara M. Davit, PhD, JD
Executive Director
Biopharmaceutics
Merck & Co.
Kenilworth, New Jersey

Hong Ding, PhD
Assistant Professor
Department of Immunology
Herbert Wertheim College of Medicine
Florida International University
Miami, Florida

John Z. Duan, PhD
Master Reviewer
Office of New Drug Products
Office of Pharmaceutical Quality
FDA/CDER
Silver Spring, Maryland

Murray P. Ducharme, PharmD, FCCP, FCP
President and CEO
Learn and Confirm Inc.
Sr. Laurent, QC, Canada
Professeur Associé
Faculté de Pharmacie
University of Montreal, Canada
Visiting Professor
Faculty of Pharmacy
Rhodes University, South Africa

Mathangi Gopalakrishnan, MS, PhD
Research Assistant Professor
Center for Translational Medicine
School of Pharmacy
University of Maryland
Baltimore, Maryland

Phillip M. Gerk, PharmD, PhD
Associate Professor
Department of Pharmaceutics
Virginia Commonwealth University
MCV Campus
School of Pharmacy
Richmond, Virginia

Charles Herring, BSPharm, PharmD, BCPS, CPP
Associate Professor
Department of Pharmacy Practice
College of Pharmacy & Health Sciences
Campbell University
Clinical Pharmacist Practitioner
Adult Medicine Team
Downtown Health Plaza of Wake Forest Baptist Health
Winston-Salem, North Carolina

Christine Yuen-Yi Hon, PharmD, BCOP
Clinical Pharmacology Reviewer
Division of Clinical Pharmacology III
Office of Clinical Pharmacology
Office of Translational Sciences
Center for Drug Evaluation and Research
Food and Drug Administration
Silver Spring, Maryland

Minerva A. Hughes, PhD, RAC (US)
Senior Pharmacologist
Food and Drug Administration
Center for Drug Evaluation and Research
Silver Spring, Maryland

Manish Issar, PhD
Assistant Professor of Pharmacology
College of Osteopathic Medicine of the Pacific
Western University of Health Sciences
Pomona, California

Vipul Kumar, PhD
Senior Scientist I
Nonclinical Development Department
Cubist Pharmaceuticals Inc.
Lexington, Massachusetts

S.W. Johnny Lau, RPh, PhD
Senior Clinical Pharmacologist
Food and Drug Administration
Office of Clinical Pharmacology
Silver Spring, Maryland

David S.H. Lee, PharmD, PhD
Assistant Professor
Department of Pharmacy Practice
Oregon State University/Oregon Health and Science University College of Pharmacy
Portland, Oregon

Patrick J Marroum, PhD
Director
Clinical Pharmacology and Pharmacometrics
AbbVie
North Chicago, Illinois

Shabnam N. Sani, PharmD, PhD
Assistant Professor
Department of Pharmaceutical and Administrative Sciences
College of Pharmacy
Western New England University
Springfield, Massachusetts

Leon Shargel, PhD, RPh
Manager and Founder
Applied Biopharmaceutics, LLC
Raleigh, North Carolina
Affiliate Professsor
School of Pharmacy
Virginia Commonwealth University
Richmond, Virginia

Sandra Suarez Sharp, PhD
Master Biopharmaceutics Reviewer/Biopharmaceutics Lead
Office of New Drug Products/Division of Biopharmaceutics
Office of Pharmaceutical Quality
Food and Drug Administration
Silver Spring, Maryland

Rodney Siwale, PhD, MS
Assistant Professor
Department of Pharmaceutical and Administrative Sciences
College of Pharmacy
Western New England University
Springfield, Massachusetts

Changquan Calvin Sun, PhD
Associate Professor of Pharmaceutics
University of Minnesota
Department of Pharmaceutics
College of Pharmacy
Minneapolis, Minnesota

He Sun, PhD
President and CEO
Tasly Pharmaceuticals Inc.
Rockville, Maryland
Professor and Chairman
Department of Pharmaceutical Economics and Policy
School of Pharmaceutical Science and Technology
Tianjin University
Tianjin, P. R. China

Vincent H. Tam, PharmD, BCPS (Infectious Diseases)
Professor Department of Clinical Sciences and Administration
University of Houston College of Pharmacy
Texas Medical Center Campus
Houston, Texas

Dr. Susanna Wu-Pong, PhD
Associate Professor
Director
Pharmaceutical Sciences Graduate Program
VCU School of Pharmacy
Richmond, Virginia

Andrew B.C. Yu, PhD, RPh
Registered Pharmacist
Formerly senior reviewer, CDER, FDA
Associate Pharmaceutics Professor
Albany College of Pharmacy
Albany, New York

Corinne Seng Yue, BPharm, MSc, PhD
Principal Scientist
Learn and Confirm Inc.
Sr. Laurent, QC, Canada

Hong Zhao, PhD
Clinical Pharmacology Master Reviewer
Clinical Pharmacology Team Leader
Office of Clinical Pharmacology (OCP)
Office of Translational Sciences (OTS)
Center for Drug Evaluation and Research (CDER)
U.S. Food and Drug Administration (FDA)
Silver Spring, Maryland

HaiAn Zheng, PhD
Associate Professor
Department of Pharmaceutical Sciences
Albany College of Pharmacy and Health Sciences
Albany, New York

Preface

The publication of this seventh edition of *Applied Biopharmaceutics and Pharmacokinetics* represents over three decades in print. Since the introduction of classic pharmacokinetics in the first edition, the discipline has expanded and evolved greatly. The basic pharmacokinetic principles and biopharmaceutics now include pharmacogenetics, drug receptor theories, advances in membrane transports, and functional physiology. These advances are applied to the design of new active drug moieties, manufacture of novel drug products, and drug delivery systems. Biopharmaceutics and pharmacokinetics play a key role in the development of safer drug therapy in patients, allowing individualizing dosage regimens and improving therapeutic outcomes.

In planning for the seventh edition, we realized that we needed expertise for these areas. This seventh edition is our first edited textbook in which an expert with intimate knowledge and experience in the topic was selected as a contributor. We would like to acknowledge these experts for their precious time and effort. We are also grateful to our readers and colleagues for their helpful feedback and support throughout the years.

As editors of this edition, we kept the original objectives, starting with fundamentals followed by a holistic integrated approach that can be applied to practice (see scope and objectives in Preface to the first edition). This textbook provides the reader with a basic and practical understanding of the principles of biopharmaceutics and pharmacokinetics that can be applied to drug product development and drug therapy. Practice problems, clinical examples, frequently asked questions and learning questions are included in each chapter to demonstrate how these concepts relate to practical situations. This textbook remains unique in teaching basic concepts that may be applied to understanding complex issues associated with *in vivo* drug delivery that are essential for safe and efficacious drug therapy.

The primary audience is pharmacy students enrolled in pharmaceutical science courses in pharmacokinetics and biopharmaceutics. This text fulfills course work offered in separate or combined courses in these subjects. Secondary audiences for this textbook are research, technological and development scientists in pharmaceutics, biopharmaceutics, and pharmacokinetics.

This edition represents many significant changes from previous editions.

- The book is an edited textbook with the collaboration of many experts well known in biopharmaceutics, drug disposition, drug delivery systems, manufacturing, clinical pharmacology, clinical trials, and regulatory science.
- Many chapters have been expanded and updated to reflect current knowledge and application of biopharmaceutics and pharmacokinetics. Many new topics and updates are listed in Chapter 1.
- Practical examples and questions are included to encourage students to apply the principles in patient care and drug consultation situations.
- Learning questions and answers appear at the end of each chapter.
- Three new chapters have been added to this edition including, *Biostatistics* which provides introduction for popular topics such as risk concept, non-inferiority, and superiority concept in new drug evaluation, and *Application of Pharmacokinetics in Specific Populations* which discusses issues such as drug and patient related pharmacy

topics in during therapy in various patient populations, and *Biopharmaceutic Aspects of the Active Pharmaceutical Ingredient and Pharmaceutical Equivalence* which explains the synthesis, quality and physical/chemical properties of the active pharmaceutical ingredients affect the bioavailability of the drug from the drug product and clinical efficacy.

Leon Shargel
Andrew B.C. Yu

Preface to First Edition

The publication of the twelfth edition of this book is a testament to the vision and ideals of the original authors, Alfred Gilman and Louis Goodman, who, in 1941set forth the principles that have guided the book through eleven editions: to correlate pharmacology with related medical sciences, to reinterpret the actions and uses of drugs in light of advances in medicine and the basic biomedical sciences, to emphasize the applications of pharmacodynamics to therapeutics, and to create a book that will be useful to students of pharmacology and to physicians. These precepts continue to guide the current edition.

As with editions since the second, expert scholars have contributed individual chapters. A multiauthored book of this sort grows by accretion, posing challenges editors but also offering memorable pearls to the reader. Thus, portions of prior editions persist in the current edition, and I hasten to acknowledge the contributions of previous editors and authors, many of whom will see text that looks familiar. However, this edition differs noticeably from its immediate predecessors. Fifty new scientists, including a number from out-side. the U.S., have joined as contributors, and all chapters have been extensively updated. The focus on basic principles continues, with new chapters on drug invention, molecular mechanisms of drug action, drug toxicity and poisoning, principles of antimicrobial therapy and pharmacotherapy of obstetrical and gynecological disorders. Figures are in full color. The editors have continued to standardize the organization of chapters: thus, students should easily find the basic physiology, biochemistry, and pharmacology set forth in regular type; bullet points highlight important lists within the text; the clinician and expert will find details in extract type under clear headings.

Online features now supplement the printed edition. The entire text, updates, reviews of newly approved drugs, animations of drug action, and hyper links to relevant text in the prior edition are available on the Goodman & Gilman section of McGraw-Hill's websites, *AccessMedicine.com* and *AccessPharmacy.com*. An Image Bank CD accompanies the book and makes all tables and figures available for use in presentations.

The process of editing brings into view many remarkable facts, theories, and realizations. Three stand out: the invention of new classes of drugs has slowed to a trickle; therapeutics has barely begun to capitalize on the information from the human genome project; and, the development of resistance to antimicrobial agents, mainly through their overuse in medicine and agriculture, threatens to return us to the pre-antibiotic era. We have the capacity and ingenuity to correct these shortcomings.

Many, in addition to the contributors, deserve thanks for their work on this edition; they are acknowledged on an accompanying page. In addition, I am grateful to Professors Bruce Chabner (Harvard Medical School/Massachusetts General Hospital) and Björn Knollmann (Vanderbilt University Medical School) for agreeing to be associate editors of this edition at a late date, necessitated by the death of my colleague and friend Keith Parker in late 2008. Keith and I worked together on the eleventh edition and on planning this edition. In anticipation of the editorial work ahead, Keith submitted his chapters before anyone else and just a few weeks before his death; thus, he is well represented in this volume, which we dedicate to his memory.

Laurence L. Brunton

About the Authors

Dr. Leon Shargel is a consultant for the pharmaceutical industry in biopharmaceutics and pharmacokinetics. Dr. Shargel has over 35 years experience in both academia and the pharmaceutical industry. He has been a member or chair of numerous national committees involved in state formulary issues, biopharmaceutics and bioequivalence issues, institutional review boards, and a member of the USP Biopharmaceutics Expert Committee. Dr. Shargel received a BS in pharmacy from the University of Maryland and a PhD in pharmacology from the George Washington University Medical Center. He is a registered pharmacist and has over 150 publications including several leading textbooks in pharmacy. He is a member of various professional societies, including the American Association Pharmaceutical Scientists (AAPS), American Pharmacists Association (APhA), and the American Society for Pharmacology and Experimental Therapeutics (ASPET).

Dr. Andrew Yu has over 30 years of experience in academia, government, and the pharmaceutical industry. Dr. Yu received a BS in pharmacy from Albany College of Pharmacy and a PhD in pharmacokinetics from the University of Connecticut. He is a registered pharmacist and has over 30 publications and a patent in novel drug delivery. He had lectured internationally on pharmaceutics, drug disposition, and drug delivery.

Contents