

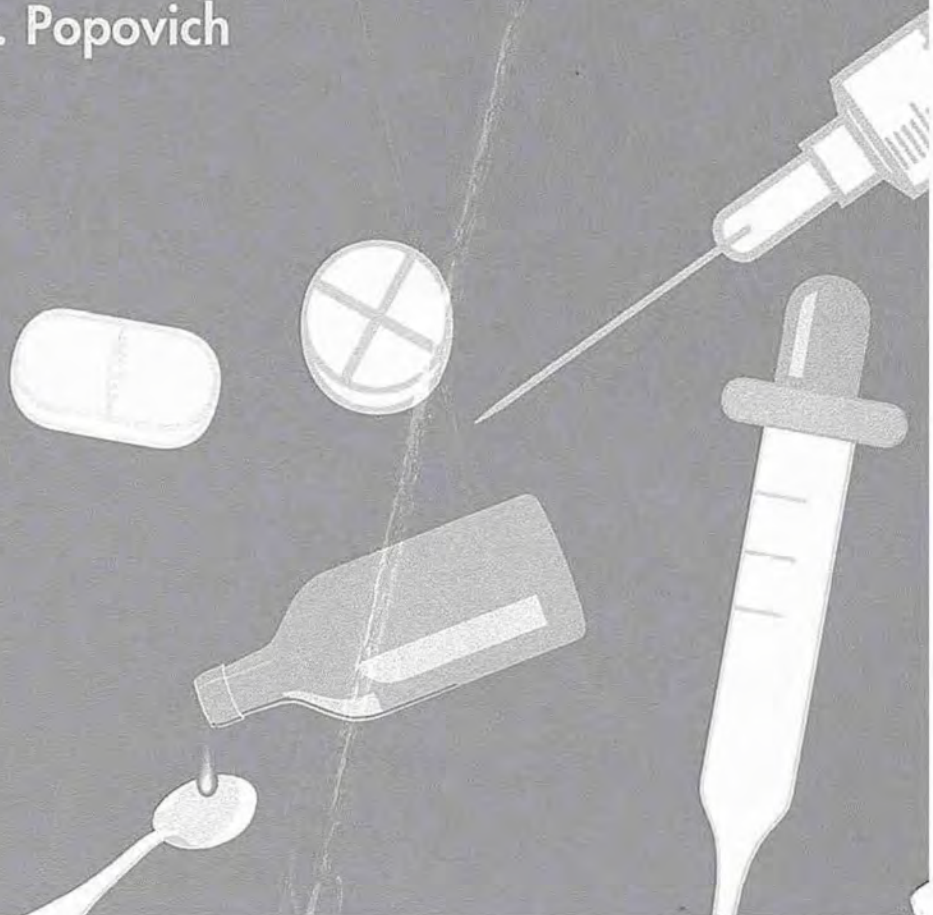
SEVENTH EDITION

# PHARMACEUTICAL DOSAGE FORMS AND DRUG DELIVERY SYSTEMS

Howard C. Ansel

Loyd V. Allen, Jr.

Nicholas G. Popovich



Editor: Donna Balado  
Managing Editor: Jennifer Schmidt  
Marketing Manager: Christine Kushner

Copyright © 1999 Lippincott Williams & Wilkins

351 West Camden Street  
Baltimore, Maryland 21201-2436 USA

227 East Washington Square  
Philadelphia, PA 19106

All rights reserved. This book is protected by copyright. No part of this book may be reproduced in any form or by any means, including photocopying, or utilized by any information storage and retrieval system without written permission from the copyright owner.

The publisher is not responsible (as a matter of product liability, negligence, or otherwise) for any injury resulting from any material contained herein. This publication contains information relating to general principles of medical care which should not be construed as specific instructions for individual patients. Manufacturers' product information and package inserts should be reviewed for current information, including contraindications, dosages, and precautions.

Printed in the United States of America

#### Library of Congress Cataloging-in-Publication Data

Ansel, Howard C., 1933–  
Pharmaceutical dosage forms and drug delivery systems / Howard C.  
Ansel, Loyd V. Allen, Jr., Nicholas G. Popovich. — 7th ed.  
p. cm.  
Includes bibliographical references and index.  
ISBN 0-683-30572-7  
1. Drugs—Dosage forms. 2. Drug delivery systems. I. Allen, Loyd V.  
II. Popovich, Nicholas G. III. Title.  
[DNLM: 1. Dosage Forms. 2. Drug Delivery Systems. QV 785 A618i 1999]  
RS200.A57 1999  
615'.1—dc21  
DNLM/DLC  
for Library of Congress

99-17498  
CIP

*The publishers have made every effort to trace the copyright holders for borrowed material. If they have inadvertently overlooked any, they will be pleased to make the necessary arrangements at the first opportunity.*

The use of portions of the text of USP23/NF18, copyright 1994, is by permission of the USP Convention, Inc. The Convention is not responsible for any inaccuracy of quotation or for any false or misleading implication that may arise from separation of excerpts from the original context or by obsolescence resulting from publication of a supplement.

To purchase additional copies of this book call our customer service department at (800) 638-3030 or fax orders to (301) 824-7390. International customers should call (301) 714-2324.

99 00 01 02  
1 2 3 4 5 6 7 8 9 10



# Contents

---

<b>Preface</b>	v
<b>Acknowledgments</b>	vii
<b>Section I. PRINCIPLES OF DOSAGE FORM DESIGN AND DEVELOPMENT</b>	
<b>1</b> Introduction to Drugs and Pharmacy	1
<b>2</b> New Drug Development and Approval Process	23
<b>3</b> Dosage Form Design: Pharmaceutic and Formulation Considerations	60
<b>4</b> Dosage Form Design: Biopharmaceutic and Pharmacokinetic Considerations	101
<b>5</b> Current Good Manufacturing Practices and Good Compounding Practices	142
<b>Section II. SOLID DOSAGE FORMS AND MODIFIED-RELEASE DRUG DELIVERY SYSTEMS</b>	
<b>6</b> Powders and Granules	164
<b>7</b> Capsules and Tablets	179
<b>8</b> Modified-Release Dosage Forms and Drug Delivery Systems	229
<b>Section III. SEMI-SOLID AND TRANSDERMAL SYSTEMS</b>	
<b>9</b> Ointments, Creams, and Gels	244
<b>10</b> Transdermal Drug Delivery Systems	263

<b>Section IV. PHARMACEUTICAL INSERTS</b>	
<b>11</b> Suppositories and Inserts	279
<b>Section V. LIQUID DOSAGE FORMS</b>	
<b>12</b> Solutions	296
<b>13</b> Disperse Systems	346
<b>Section VI. STERILE DOSAGE FORMS AND DELIVERY SYSTEMS</b>	
<b>14</b> Parenterals	397
<b>15</b> Biologicals	450
<b>16</b> Ophthalmic Solutions and Suspensions	469
<b>Section VII. NOVEL AND ADVANCED DOSAGE FORMS, DELIVERY SYSTEMS, AND DEVICES</b>	
<b>17</b> Radiopharmaceuticals	487
<b>18</b> Products of Biotechnology	503
<b>19</b> Novel Dosage Forms and Drug Delivery Technologies	535
<b>Appendix</b>	
Systems and Techniques of Pharmaceutical Measurement	552
<b>Index</b>	563

# CAPSULES AND TABLETS

## Chapter at a Glance

### Capsules

#### *Hard Gelatin Capsules*

- The Manufacture of Hard Gelatin Capsule Shells
- Capsule Sizes
- Preparation of Filled Hard Gelatin Capsules
- Developing the Formulation and Selection of Capsule Size
- Filling Hard Capsule Shells
- Capsule Sealing
- Cleaning and Polishing Capsules

#### *Soft Gelatin Capsules*

- Preparation of Soft Gelatin Capsules
- Utilization of Soft Gelatin Capsules

#### *Compendial Requirements for Capsules*

- Added Substances
- Containers for Dispensing Capsules
- Disintegration Test for Capsules
- Dissolution Test for Capsules
- Weight Variation
- Content Uniformity
- Content Labeling Requirement
- Stability Testing
- Moisture Permeation Test

#### *Official and Commercially Available Capsules Inspecting, Counting, Packaging, and Storing Capsules*

### Tablets

#### *Types of Tablets*

- Compressed Tablets (C.T.)
- Multiple Compressed Tablets (M.C.T.)
- Sugar-Coated Tablets (S.C.T.)
- Film Coated Tablets (F.C.T.)
- Gelatin-Coated Tablets
- Enteric-Coated Tablets (E.C.T.)
- Buccal or Sublingual Tablets
- Chewable Tablets

#### Effervescent Tablets

- Molded Tablets (M.T.)
- Tablet Triturates (T.T.)
- Hypodermic Tablets (H.T.)
- Dispensing Tablets (D.T.)
- Immediate Release Tablets (I.R.)
- Instant Disintegrating/Dissolving Tablets
- Extended Release Tablets (E.R.)

#### Vaginal Tablets

#### *Compressed Tablets*

#### *Quality Standards and Compendial Requirements*

- Compressed Tablet Manufacture
- Wet Granulation
- All-in-One Granulation Methods
- Dry Granulation
- Tableting of Granulation
- Direct Compression Tableting
- Tablet Dedusting

#### *Chewable Tablets*

#### *Molded Tablets*

#### *Tablet Coating*

- Sugarcoating Tablets
- Film-coating Tablets
- Enteric Coating
- Fluid-Bed or Air Suspension Coating
- Compression Coating

#### *Impact of Manufacturing Changes on Solid Dosage Forms*

#### *Official and Commercially Available Tablets*

#### *Packaging and Storing Tablets*

#### *Oral Administration of Solid Dosage Forms*

#### *Other Solid Dosage Forms for*

#### *Oral Administration*

- Lozenges
- Pills

# Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

## Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

## Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

## Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

## API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

## LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

## FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

## E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.