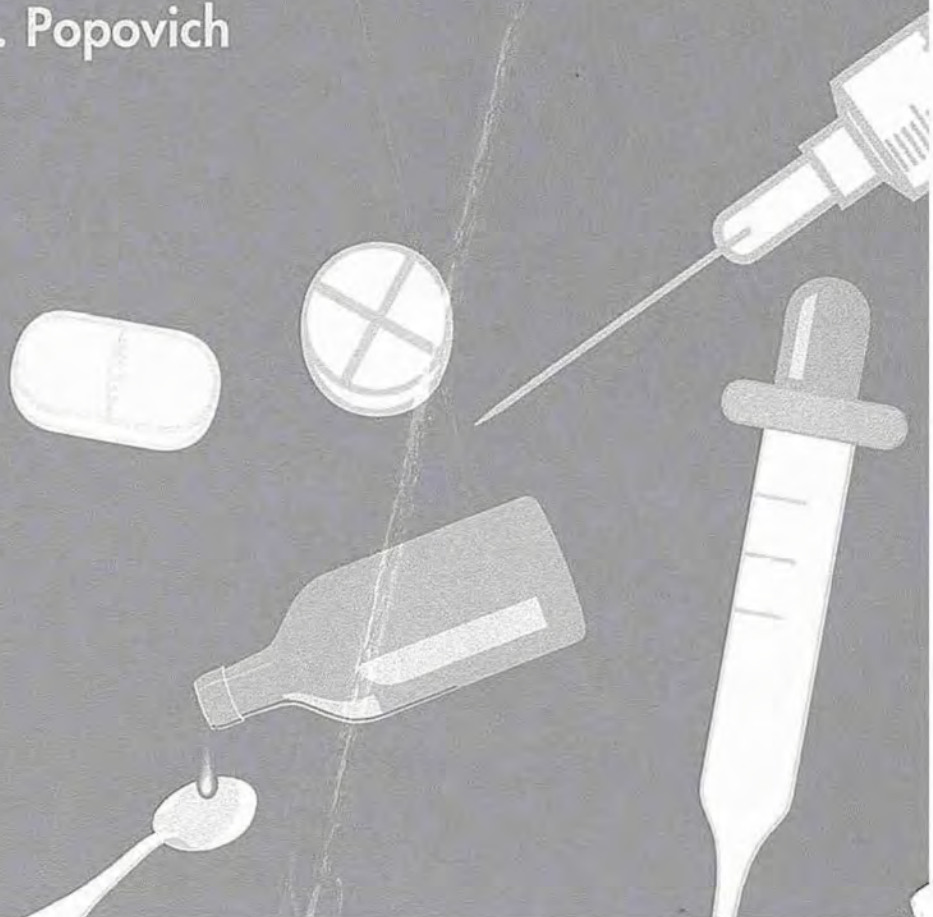


SEVENTH EDITION
**PHARMACEUTICAL
DOSAGE FORMS
AND DRUG
DELIVERY SYSTEMS**

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

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

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

DISPERSE SYSTEMS

Chapter at a Glance

Suspensions	Gels and Magmas
Reasons for Suspensions	Colloidal Dispersions
Features Desired in a Pharmaceutical Suspension	Terminology Related to Gels
Physical Features of the Dispersed Phase of a Suspension Dispersion Medium	<i>Classification and Types of Gels</i>
Preparation of Suspensions	Preparation of Magmas and Gels
Sustained-Release Suspensions	Examples of Gelling Agents
Extemporaneous Compounding of Suspensions	Gel Formulation Considerations
Packaging and Storage of Suspensions	Examples of Magmas and Gels
Examples of Oral Suspensions	<i>Bentonite Magma, NF</i>
<i>Antacid Oral Suspensions</i>	<i>Aluminum Hydroxide Gel, USP</i>
<i>Antibacterial Oral Suspensions</i>	<i>Milk of Magnesia, USP</i>
Examples of Other Suspensions	<i>Starch Glycerite</i>
<i>Otic Suspensions</i>	<i>Lubricating Jelly Formula</i>
<i>Rectal Suspensions</i>	<i>Clear Aqueous Gel with Dimethicone</i>
Dry Powders for Oral Suspension	<i>Poloxamer Gel Base</i>
Emulsions	Proper Administration and Use of Disperse Systems
Purpose of Emulsions and of Emulsification	Aerosols
Theories of Emulsification	Advantages of the Aerosol Dosage Form
Preparation of Emulsions	The Aerosol Principle
<i>Emulsifying Agents</i>	Aerosol Systems
<i>The HLB System</i>	<i>Two-phase Systems</i>
<i>Methods of Emulsion Preparation</i>	<i>Three-phase Systems</i>
<i>Continental or Dry Gum Method</i>	<i>Compressed Gas Systems</i>
<i>English or Wet Gum Method</i>	Aerosol Container and Valve Assembly
<i>Bottle or Forbes Bottle Method</i>	<i>Containers</i>
<i>Auxiliary Methods</i>	<i>Valve Assembly</i>
<i>In Situ Soap Method</i>	Metered Dose Inhalers (MDIs)
<i>Microemulsions</i>	Filling Operations
Stability of Emulsions	<i>Cold Filling</i>
<i>Aggregation and Coalescence</i>	<i>Pressure Filling</i>
Examples of Oral Emulsions	<i>Testing the Filled Containers</i>
<i>Mineral Oil Emulsion</i>	Packaging, Labeling, and Storage
<i>Castor Oil Emulsion</i>	Proper Administration and Use of Pharmaceutical Aerosols
<i>Simethicone Emulsion</i>	Topical Aerosols
	Vaginal and Rectal Aerosols

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.