



21 ST EDITION

Remington

**The Science and Practice
of Pharmacy**



LIPPINCOTT WILLIAMS & WILKINS

A Wolters Kluwer Company

Philadelphia • Baltimore • New York • London
Buenos Aires • Hong Kong • Sydney • Tokyo

Editor: David B. Troy
Managing Editor: Matthew J. Hauber
Marketing Manager: Marisa A. O'Brien

Lippincott Williams & Wilkins

351 West Camden Street
Baltimore, Maryland 21201-2436 USA

530 Walnut Street
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. Manufacturer's product information and package inserts should be reviewed for current information, including contraindications, dosages and precautions.

Printed in the United States of America

Entered according to Act of Congress, in the year 1885 by Joseph P Remington, in the Office of the Librarian of Congress, at Washington DC

Copyright 1889, 1894, 1905, 1907, 1917, by Joseph P Remington

Copyright 1926, 1936, by the Joseph P Remington Estate

Copyright 1948, 1951, by the Philadelphia College of Pharmacy and Science

Copyright 1956, 1960, 1965, 1970, 1975, 1980, 1985, 1990, 1995, by the Philadelphia College of Pharmacy and Science

Copyright 2000, 2006, by the University of the Sciences in Philadelphia

All Rights Reserved

Library of Congress Catalog Card Information is available
ISBN 0-7817-4673-6

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 structural formulas from USAN and the USP Dictionary of Drug Names is by permission of The USP Convention. The Convention is not responsible for any inaccuracy contained herein.

Notice—This text is not intended to represent, nor shall it be interpreted to be, the equivalent of or a substitute for the official United States Pharmacopeia (USP) and/or the National Formulary (NF). In the event of any difference or discrepancy between the current official USP or NF standards of strength, quality, purity, packaging and labeling for drugs and representations of them herein, the context and effect of the official compendia shall prevail.

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.

Contents

Part 1 Orientation

1	Scope of Pharmacy	3
2	Evolution of Pharmacy	7
3	Ethics and Professionalism	20
4	The Practice of Community Pharmacy	30
5	Pharmacists in Industry	35
6	Pharmacists in Government	40
7	Pharmacists and Public Health	51
8	Information Resources in Pharmacy and the Pharmaceutical Sciences	64
9	Clinical Drug Literature	74
10	Research	87

Part 2 Pharmaceutics

11	Metrology and Pharmaceutical Calculations	99
12	Statistics	127
13	Molecular Structure, Properties, and States of Matter	162
14	Complex Formation	186
15	Thermodynamics	201
16	Solutions and Phase Equilibria	211
17	Ionic Solutions and Electrolytic Equilibria	231
18	Tonicity, Osmoticity, Osmolality, and Osmolarity	250
19	Chemical Kinetics	266
20	Interfacial Phenomena	280
21	Colloidal Dispersions	293
22	Coarse Dispersions	319
23	Rheology	338

Part 3 Pharmaceutical Chemistry

24	Inorganic Pharmaceutical Chemistry	361
25	Organic Pharmaceutical Chemistry	386
26	Natural Products	410
27	Drug Nomenclature—United States Adopted Names	443
28	Structure-Activity Relationship and Drug Design	468
29	Fundamentals of Medical Radionuclides	479

Part 4 Pharmaceutical Testing, Analysis, and Control

30	Analysis of Medicinals	495
31	Biological Testing	553
32	Clinical Analysis	565
33	Chromatography	599
34	Instrumental Methods of Analysis	633
35	Dissolution	672

Part 5 Pharmaceutical Manufacturing

36	Separation	691
37	Powders	702
38	Property-Based Drug Design and Preformulation	720
39	Solutions, Emulsions, Suspensions, and Extracts	745
40	Sterilization	776
41	Parenteral Preparations	802
42	Intravenous Admixtures	837
43	Ophthalmic Preparations	850
44	Medicated Topicals	871
45	Oral Solid Dosage Forms	889
46	Coating of Pharmaceutical Dosage Forms	929
47	Extended-Release and Targeted Drug Delivery Systems	939
48	The New Drug Approval Process and Clinical Trial Design	965

49	Biotechnology and Drugs	976
50	Aerosols	1000
51	Quality Assurance and Control	1018
52	Stability of Pharmaceutical Products	1025
53	Bioavailability and Bioequivalency Testing	1037
54	Plastic Packaging Materials	1047
55	Pharmaceutical Necessities	1058

Part 6 Pharmacokinetics and Pharmacodynamics

56	Diseases: Manifestations and Pathophysiology	1095
57	Drug Absorption, Action, and Disposition	1142
58	Basic Pharmacokinetics and Pharmacodynamics	1171
59	Clinical Pharmacokinetics and Pharmacodynamics	1191
60	Principles of Immunology	1206
61	Adverse Drug Reactions and Clinical Toxicology	1221
62	Pharmacogenomics	1230
63	Pharmacokinetics/Pharmacodynamics in Drug Development	1249

Part 7 Pharmaceutical and Medicinal Agents

64	Diagnostic Drugs and Reagents	1261
65	Topical Drugs	1277
66	Gastrointestinal and Liver Drugs	1294
67	Blood, Fluids, Electrolytes, and Hematological Drugs	1318
68	Cardiovascular Drugs	1350
69	Respiratory Drugs	1371
70	Sympathomimetic Drugs	1379
71	Cholinomimetic Drugs	1389
72	Adrenergic Antagonists and Adrenergic Neuron Blocking Drugs	1399
73	Antimuscarinic and Antispasmodic Drugs	1405
74	Skeletal Muscle Relaxants	1411
75	Diuretic Drugs	1422
76	Uterine and Antimigraine Drugs	1432
77	Hormones and Hormone Antagonists	1437
78	General Anesthetics	1474
79	Local Anesthetics	1479
80	Antianxiety Agents and Hypnotic Drugs	1486
81	Antiepileptic Drugs	1501
82	Psychopharmacologic Agents	1509
83	Analgesic, Antipyretic, and Anti-Inflammatory Drugs	1524
84	Histamine and Antihistaminic Drugs	1543
85	Central Nervous System Stimulants	1551
86	Antineoplastic Drugs	1556
87	Immunoactive Drugs	1588
88	Parasiticides	1595
89	Immunizing Agents and Allergenic Extracts	1600
90	Anti-Infectives	1626
91	Enzymes	1685
92	Nutrients and Associated Substances	1688
93	Pesticides	1719

Part 8 Pharmacy Practice

A Fundamentals of Pharmacy Practice

94	Application of Ethical Principles to Practice Dilemmas	1745
95	Technology and Automation	1753
96	The Patient: Behavioral Determinants	1762
97	Patient Communication	1770
98	Patient Compliance	1782
99	Drug Education	1796

100	Professional Communications	1808	117	Documenting, Billing, and Reimbursement for Pharmaceutical Care Services	2114
101	The Prescription	1823	118	Pharmaceutical Risk Management	2124
102	Providing a Framework for Ensuring Medication Use Safety	1840	119	Integrated Health Care Delivery Systems	2130
103	Poison Control	1881		C Patient Care	
104	Drug Interactions	1889	120	Specialization in Pharmacy Practice	2155
105	Extemporaneous Prescription Compounding	1903	121	Pharmacists and Disease State Management	2163
106	Nuclear Pharmacy Practice	1913	122	Development of a Pharmacy Care Plan and Patient Problem-Solving	2170
107	Nutrition in Pharmacy Practice	1925	123	Ambulatory Patient Care	2179
108	Pharmacoepidemiology	1958	124	Self-Care	2197
109	Surgical Supplies	1968	125	Diagnostic Self-Care	2206
110	Health Accessories	1979	126	Preventive Care	2223
	B Social, Behavioral, Economic, and Administrative Sciences		127	Hospital Pharmacy Practice	2247
111	Laws Governing Pharmacy	2015	128	Emergency Medicine Pharmacy Practice	2265
112	Re-engineering Pharmacy Practice	2055	129	Long-Term Care	2272
113	Pharmacoeconomics	2070	130	Aseptic Processing for Home Infusion Pharmaceuticals	2290
114	Community Pharmacy Economics and Management ..	2082	131	The Pharmacist's Role in Substance Use Disorders	2303
115	Product Recalls and Withdrawals	2098	132	Complementary and Alternative Medical Health Care ..	2318
116	Marketing Pharmaceutical Care Services	2107	133	Chronic Wound Care	2342

Plastic Packaging Materials

Barrett E Rabinow, PhD
Theodore J Roseman, PhD



As defined by the American Society for Testing and Materials (ASTM), a plastic is a material that contains as an essential ingredient one or more polymeric organic substances of large molecular weight, is solid in its finished state and at some stage in its manufacture or processing into finished articles can be shaped by flow. The large-molecular-weight organic substance is called a polymer.

The use of plastics in the health care industry has grown at a very rapid rate since the 1960s. This phenomenal growth is due primarily to the wide flexibility in choice of properties offered by plastics. However, because of the wide range of properties of plastics, judicious selection must be made for the intended application.

Prior to the recognition of the potential use of plastics in health care practice, glass was the predominate material used in the primary packaging of pharmaceutical products. Glass has a definite advantage in being a relatively unreactive and an inert substance (although leachable aluminum and glass particles or delamination have occasionally posed problems). As such, it can be used in contact with many critical products, either dry or liquid. It provides excellent protection against water vapor and gas permeation, and it can withstand steam sterilization (autoclaving) without incurring physical distortion. Two definite disadvantages of glass in the field of packaging, however, are its fragility and weight. Because of these negative aspects, coupled with the many positive attributes of plastics, significant inroads for the use of plastic in pharmaceutical packaging have been made. Today, for example, plastics are being used in the following primary packaging areas, where in the 1960s only glass could be considered: syringes, bottles, vials, and ampules.

There are many other significant medical uses that, without the use of plastics, would never have been technically feasible. A few examples include indwelling catheters, prosthetic devices, tracheotomy tubes, unit dose packaging, and flexible containers for intravenous, irrigation, and inhalation solutions, as well as for the collection of blood. An additional use for plastics is in secondary container packaging (ie, packaging that is not in direct contact with the product itself). This particular use normally involves plastic films of various types and thicknesses used for tamper-proof overwrapping, whereas the previously mentioned devices normally are fabricated by molding or extrusion of the finished part.

Selection of the appropriate materials for a packaging application should be performed with an understanding of the intended overall design of the package. The requirements should be specified with regard to customer usage, regulatory approval, marketing presentation, toxicological considerations,

manufacturability, sterility, and, very importantly, protection of the pharmaceutical product or device during transportation, storage, and use. These functional requirements then must be analyzed in terms of the stress requirements they impose on the material, permitting translation of those requirements into material properties. A target material profile is developed by assigning required values of design and performance properties that predict or correlate with the container functions. Likely candidate materials are determined by comparing their properties with the property profile derived from the functional requirements. A prototype is built and tested via functionally oriented tests such as maintenance of product stability, simulated usage and storage tests, and customer focus groups. These concepts are embodied in ISO 11607.¹ Material properties affecting functional performance are described below.

MATERIAL PROPERTIES

Mechanical Properties

Important mechanical properties in plastic packaging materials are:

Tensile strength—the maximum force needed to pull apart a specimen of material, divided by its cross-sectional area. Elongation is the percentage change over original length at breaking point and measures a film's ability to stretch.

Impact strength—a measure of the ability to withstand shock-loading, in which a specimen receives a blow from a swinging pendulum, for example. Fracture will occur if the impact force exceeds the limit of elasticity of the material. Glass, for example, has a much lower impact strength than many plastics, although it has appreciable tensile strength.

Tear strength—measured both as the force necessary to initiate a tear and force to propagate a tear. Propagation of tear is undesirable in shipping sacks but desirable in tear tapes. Orientation of the material can affect results, because the polymer chains can be aligned along a particular direction during manufacturing, thus conferring greater strength in that direction.

Stiffness—the resistance of bending where deflection against a load can be measured.

Flex resistance to the development of pinholing and fracture, when subjected to repeated flexing or creasing, is important in shipping applications. Unsupported aluminum foil, unless it is heavy gauge, is prone to this failure mode.

Coefficient of friction or slip—relates to the ease with which one material will slide over another. Passage of films through

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.