# GOODMAN and GILMAN's The Pharmacological Basis of Therapeutics

S E V E N T H E D I T I O N

# MACMILLAN PUBLISHING COMPANY

New York

COLLIER MACMILLAN CANADA, INC.

Toronto

COLLIER MACMILLAN PUBLISHERS

London



nd G ne colo s o

his work xicology, updating nism of a the addit However, same tho and aut ilman" th

bjectives ghout. A 1) the co medical tions and nportant g of empl amics to xt has be ly of the have be past five n both ba that know or thoro 1 blockers perlipop ctive pept dins and is, antihy ats, drugs crobial a s substitu ation sulf gents, ar others. Tl

illan Publis

s on pha

sign of d

COPYRIGHT © 1985, MACMILLAN PUBLISHING COMPANY, A DIVISION OF MACMILLAN, INC.

#### PRINTED IN THE UNITED STATES OF AMERICA

All rights reserved. No part of this book may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopying, recording, or any information storage and retrieval system, without permission in writing from the Publisher.

Earlier editions entitled *The Pharmacological Basis of Therapeutics* copyright 1941 and 1955, © copyright 1965, copyright © 1970, and copyright © 1975 by Macmillan Publishing Company. Earlier edition entitled *Goodman and Gilman's The Pharmacological Basis of Therapeutics* copyright © 1980 by Macmillan Publishing Company.

Macmillan Publishing Company 866 Third Avenue • New York, N.Y. 10022

COLLIER MACMILLAN CANADA, INC.

COLLIER MACMILLAN PUBLISHERS • London

Library of Congress catalog card number 85-15356

Printing: 1 2 3 4 5 6 7 8

Year: 5 6 7 8 9 0 1

P

T H
pha
app
me:
san

ogy

pos

ten

and

clin

her

all

suc

stu

Sta

org

Nev

doz

5 ye

that

a co

mol

imp

ucts

eve

rom

cho

prot

few

prec

func

imp

ing

topi

prac of th

pres

the

curr

stan

volu

and

spec

tions

In

M

T

In this textbook, reference to proprietary names of drugs is ordinarily made only in chapter sections dealing with preparations. Such names are given in SMALL-CAP TYPE, usually immediately following the official or nonproprietary titles. Proprietary names of drugs also appear in the Index.

DOCKET A L A R M Ph.D., D.Sc. Pharmacology Pharmacy, and ology, Univerine, Salt Lake

or and Head, Department of alifornia, San Jolla, Califor-

roup Research The Wellcome , Kent, United

, Sc.D.(Hon.). Chairman, Dend Professor of erve University d, Ohio

ssor of Pharma-New York, Upuse, New York

ssor and Chaircology, Univeredicine, Denver,

Dunning Dripps partment of An-Pharmacology, School of Mediania

# **CONTENTS**

PRE	FACE TO THE SEVENTH EDITION	V			
PRE	FACE TO THE FIRST EDITION	vii			
Con	NTRIBUTORS	viii			
	SECTION				
	General Principles				
	INTRODUCTION Leslie Z. Benet and Lewis B. Sheiner	1			
1.	PHARMACOKINETICS: THE DYNAMICS OF DRUG ABSORPTION, DISTRIBUTION, AND ELIMINATION  Leslie Z. Benet and Lewis B. Sheiner	3			
2.	PHARMACODYNAMICS: MECHANISMS OF DRUG ACTION AND THE RELATION- SHIP BETWEEN DRUG CONCENTRATION AND EFFECT Elliott M. Ross and Alfred G. Gilman 3				
3.	Principles of Therapeutics  Terrence F. Blaschke, Alan S. Nies, and Richard D. Mamelok	49			
	SECTION				
	Drugs Acting at Synaptic and Neuroeffector Junctional Sites				
4.	NEUROHUMORAL TRANSMISSION: THE AUTONOMIC AND SOMATIC MOTOR NERVOUS SYSTEMS  Norman Weiner and Palmer Taylor				
5.	CHOLINERGIC AGONISTS Palmer Taylor	100			
6.	Anticholinesterase Agents Palmer Taylor	110			
7.	Atropine, Scopolamine, and Related Antimuscarinic Drugs Norman Weiner 12				
8.	Norepinephrine, Epinephrine, and the Sympathomimetic Amines $Norman\ Weiner$	145			
9.	Drugs That Inhibit Adrenergic Nerves and Block Adrenergic Receptors  Norman Weiner	181			
10.	GANGLIONIC STIMULATING AND BLOCKING AGENTS Palmer Taylor	215			
11.	NEUROMUSCULAR BLOCKING AGENTS Palmer Taylor	222			



xi

SECTION

## Drugs Acting on the Central Nervous System

12.	Neurohumoral Transmission and the Central Nervous System Floyd $E.\ Bloom$			
13.	HISTORY AND PRINCIPLES OF ANESTHESIOLOGY  Theodore C. Smith and Harry Wollman			
14.	4. GENERAL ANESTHETICS Bryan E. Marshall and Harry Wollman			
15.	LOCAL ANESTHETICS J. Murdoch Ritchie and Nicholas M. Greene	302		
16.	THE THERAPEUTIC GASES  Theodore C. Smith, Jeffrey B. Gross, and Harry Wollman Oxygen, Carbon Dioxide, Helium, and Water Vapor			
17.	Hypnotics and Sedatives Stewart C. Harvey	339		
18.	THE ALIPHATIC ALCOHOLS  J. Murdoch Ritchie	372		
19.	Drugs and the Treatment of Psychiatric Disorders $Ross\ J.\ Baldessarini$			
20.	Drugs Effective in the Therapy of the Epilepsies  Theodore W. Rall and Leonard S. Schleifer			
21.	Drugs for Parkinson's Disease, Spasticity, and Acute Muscle Spasms  Joseph R. Bianchine	473		
22.	OPIOID ANALGESICS AND ANTAGONISTS  Jerome H. Jaffe and William R. Martin			
23.	Drug Addiction and Drug Abuse Jerome H. Jaffe	532		
24.	CENTRAL NERVOUS SYSTEM STIMULANTS  Strychnine, Picrotoxin, Pentylenetetrazol, and Miscellaneous Agents (Doxapram, Nikethamide, Methylphenidate)	582		
25.	CENTRAL NERVOUS SYSTEM STIMULANTS (Continued) Theodore W. Rall	589		

#### SECTION

The Methylxanthines

# IV

#### Autacoids

	Introduction	William W. Douglas	604
26.	HISTAMINE AND 5-HYDROXYTRYPTAMINE ANTAGONISTS	(SEROTONIN) AND THEIR William W. Douglas	605
27.	POLYPEPTIDES—ANGIOTENSIN, PLASMA KININ	s, and Others William W. Douglas	639
28.	PROSTAGLANDINS, PROSTACYCLIN, THROMBOX		660



o ti

m in

tic pr

m

fro

ca

is the the

trei

and pra

tion

dru para

end antiantipres ager mus agor place cluditical indiv

784

V

236

260

276

302

322

339

372

387

446

473

491

532

582

589

604

605

639

660

oom

man

man

eene

lman

irvey

tchie

arini

leifer

JSCLE

chine

1artin

Jaffe

Franz.

gents

. Rall

ouglas Their

ouglas

ouglas

IENES

Vane

Drug T	Therapy	of	Inflar	nmation
--------	---------	----	--------	---------

29. Analgesic-Antipyretics and Anti-Inflammatory Agents; Drugs Employed in the Treatment of Gout

Roderick J. Flower, Salvador Moncada, and John R. Vane 674

VI

#### Cardiovascular Drugs

- 30. DIGITALIS AND ALLIED CARDIAC GLYCOSIDES

  Brian F. Hoffman and J. Thomas Bigger, Jr. 716
- 31. Antiarrhythmic Drugs J. Thomas Bigger, Jr., and Brian F. Hoffman 748
  32. Antihypertensive Agents and the Drug Therapy of Hypertension
- 33. Drugs Used for the Treatment of Angina; Organic Nitrates, Calcium Channel Blockers, and  $\beta$ -Adrenergic Antagonists

  Philip Needleman, Peter B. Corr, and Eugene M. Johnson, Jr. 806

Peter Rudd and Terrence F. Blaschke

34. Drugs Used in the Treatment of Hyperlipoproteinemias

Michael S. Brown and Joseph L. Goldstein 827

VII

#### Water, Salts, and Ions

35. AGENTS AFFECTING VOLUME AND COMPOSITION OF BODY FLUIDS

Gilbert H. Mudge 846

VIII

## Drugs Affecting Renal Function and Electrolyte Metabolism

- INTRODUCTION Gilbert H. Mudge and Irwin M. Weiner 879
- 36. DIURETICS AND OTHER AGENTS EMPLOYED IN THE MOBILIZATION OF EDEMA FLUID Irwin M. Weiner and Gilbert H. Mudge 887
- 37. AGENTS AFFECTING THE RENAL CONSERVATION OF WATER

  Richard M. Hays 908
- 38. INHIBITORS OF TUBULAR TRANSPORT OF ORGANIC COMPOUNDS

  Irwin M. Weiner and Gilbert H. Mudge 920

# DOCKET

# 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.

