

HANDBOOK OF
OCULAR
PHARMACOLOGY

THIRD EDITION

MARVIN B. SMITH

Handbook of Ocular Pharmacology

Third Edition

Marvin B. Smith, Ph.D.

Director of the Eye Institute Pharmaceutical Services
Pennsylvania College of Optometry



PSG Publishing Company, Inc.
Littleton, Massachusetts
1984

Library of Congress Cataloging in Publication Data
Smith, Marvin B.
Handbook of ocular pharmacology.

Bibliography: p.
Includes index.

1. Ocular pharmacology—Handbooks, manuals, etc.

I. Title. [DNLM: 1. Eye diseases—Drug therapy. WW
166 S655h]

RE994.S65 1984 615'.78 83-25019

ISBN 0-88416-451-9

First Edition © 1974

Second Edition © 1978

Third Edition © 1984

Copyright © 1984 by Marvin B. Smith

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

Printed in the United States of America.

International Standard Book Number: 0-88416-451-9

Library of Congress Catalog Card Number: 83-25019

This book is dedicated in loving memory to Isadore Smith.

About the Author

Marvin B. Smith, Ph.D. (Pharmacology), is an associate professor and Director of the Eye Institute Pharmaceutical Services. He has lectured in pharmacology, drug abuse, and pharmacy mathematics for Frankford Hospital and the Pennsylvania State University. He has also lectured to numerous groups of health care professionals in a variety of continuing education programs in the United States.

Doctor Smith has conducted research projects in ocular and systemic pharmacology and has published numerous papers in the area of ocular pharmacology and toxicology. He has been the recipient of many awards and honors which include the Eli Lilly Achievement Award, the Bristol Laboratories Award, and the Henry Fisher Memorial Pharmacology and Pharmacognosy Award. He has been a consultant to a variety of industrial, academic, professional, and educational testing organizations.

Acknowledgment

Portions of this book are revisions of original articles by the author which appeared in issues of *Optical Journal and Review of Optometry*, Chilton Way, Radnor, PA.

List of Tables

- 1-1** Selected Systemic and Ocular Pharmacology
Reference Films 7
- 2-1** Effects of Atropine in Relation to Dosage 16
- 2-2** Mg Quantity of Drug per Volume of Solution
Utilized 18
- 2-3** Estimated mg Contained in Various Volumes of
Various Percent Strength Solutions 24
- 2-4** Estimated Time (Days) a 3.75-g Tube of Ophthalmic
Ointment Will Last 25
- 6-1** Effects on a Person Taking Propranolol with Another
Drug 77
- 6-2** Drugs Utilized in Systemic Conditions Which May
Affect the Glaucomatous Eye 78
- 8-1** Ocular Diagnostic Agents 92
- 9-1** Relative Potency of Antiinflammatory Steroids 103
- 11-1** Format for Office Information on Drugs 132
- 11-2** Summary of Commonly Used Drug Types and Their
Ocular Side Effects 133
- 13-1** Selected Over-the-Counter Drugs 153

- 14-1** Selected Over-the-Counter Artificial Tears 158
- 14-2** Selected Over-the-Counter Osmotic Agents 159
- 14-3** Selected Over-the-Counter Ophthalmic Irrigation Solutions 161
- 14-4** Selected Over-the-Counter Hard Contact Lens Solutions 162
- 14-5** Selected Over-the-Counter Soft Contact Lens Solutions 165

Foreword

This Third Edition of the *Handbook of Ocular Pharmacology* is intended to outline the vast array of information on ocular pharmacology. The main objective of this revised edition is to update some of the newer innovations in drug delivery systems for ocular and systemic medications, prodrugs, beta-adrenergic blocking agents, and the constant and dynamic changes in pharmaceuticals useful in over-the-counter care and in the management of contact lenses.

This edition reviews pharmaceuticals that were not available when the previous editions were published. There also is a completely new question and answer section designed to aid clinicians in their review of basic ocular pharmacology, especially for the numerous board certification examinations they may encounter during their careers.

Table of Contents

1 Introduction and General Concepts of Pharmacology 1

- Experimental and Comparative Pharmacology
- Therapeutics
- Toxicology
- Prescription Drugs
- Definitions and Implications
- Reference Texts
- Reference Films
- The "Average" Person and Drug Response
- Factors Influencing Drug Response
- Route of Administration
- Prescription Writing

2 Quantitative Estimates of Doses of Ocular Diagnostic Drugs 15

- Mg from cc
- Applied Dosages
- Pediatric Dosages
- Ointment Dosages
- Dosage (Daily, Weekly, Total)

3 Chemical Reactions of Importance in Ocular Pharmacology 29

- The Anabolism and Catabolism of Acetylcholine
- The Anabolism and Catabolism of Norepinephrine
- The Anabolism and Catabolism of Carbonic Acid
- The Anabolism and Catabolism of Fibrin
- Selected Mechanism of Action of Antiinfective Agents
- Selected Chemical Toxic Reactions

4 Local Anesthetics for Topical Ocular Use 39

- History
- Prototype (Cocaine)
- Structure Activity Relationships
- Mechanism of Action
- Addition of Vasoconstrictors
- Systemic Effects
- Local Anesthetics for Topical Ocular Use
- Summary Review

5 Autonomic Drugs 47

- Autonomic Physiology
- Miotics
 - Cholinergic Drugs
 - Anticholinesterase Toxicity on the Eye
 - Summary of Cholinergic Drugs
 - Cholinesterase Inhibitors
- Adrenergic (Sympathomimetic) Drugs
- Cycloplegic (Parasympatholytic) Drugs

6 Drugs Used in the Management of Glaucoma 63

- Diagnosis:
 - Water-drinking Test
 - Mydriatic Test
 - Homatropine Test
 - Corticosteroid Test
- Treatment:
 - Miotics
 - Carbonic Anhydrase Inhibitors
 - Osmotic Diuretics
 - Prodrugs and Delivery Systems
 - Beta-adrenergic Blocking Agents
- Cure

7 Myasthenia Gravis and Ocular Pharmacology 83

- Tests
- Therapeutic Drug Treatment
- Pharmacologic Masking

8 Ocular Diagnostic Agents 89

Dyes

Local Anesthetics

Diagnosis of Systemic Disease

Nonglaucoma Diagnostic Agents:

Mecholyl Test

Gonioscopic Prism Solutions

Blanching Test

9 Antiinflammatory Agents and Decongestants 97

Antihistamines

Antiinflammatory Steroids

Decongestants

Summary

10 Antiinfective Agents of Special Importance to the Eye 111

History of Chemotherapy

Antibacterials

Antibiotics

Sulfonamides

Antivirals

Antifungals

Pediculicides

11 Ocular Side Effects of Drugs and Office Screening 119

Tranquilizers

Other CNS Agents

Analgesics

Topical Steroids

Anticholinesterases

Sympathomimetics

Belladonna Alkaloids

Cardiovascular Drugs

Diuretics

Antibiotics

Miscellaneous Agents

Hormones

Conclusion

12	Abuse Drugs: Their Potential for Ocular Disease	137
	Definition	
	Special Regulations on Controlled Drugs	
	Narcotics	
	Depressants	
	Stimulants	
	Hallucinogens	
13	Drugs Available Without Prescription	147
	OTC Sleep Aids	
	Antihistamines	
	Belladonna Alkaloids	
	OTC Ophthalmic Drugs	
	OTC Miscellaneous Agents	
14	Over-the-Counter Ophthalmic Products	157
	Artificial Tears	
	Osmolar Preparations	
	Ophthalmic Irrigation Solutions	
	Contact Lens Products	
	Over-the-Counter Abuse	
	Appendix A Sample Examination	167
	Questions	
	Answers	
	Appendix B Glossary of Terms	207
	Appendix C Topical Ophthalmic Products	215
	Appendix D Possible Side Effects of Topical Ophthalmic Products	219
	Bibliography	223
	Index	233

1

Introduction and General Concepts of Pharmacology

Pharmacology is the study of drugs; broadly speaking, it encompasses the sum total of all knowledge of drugs and their actions. For the purposes of this discussion, however, pharmacology can be divided into three basic areas of knowledge: experimental and comparative pharmacology, therapeutics, and toxicology.

EXPERIMENTAL AND COMPARATIVE PHARMACOLOGY

Much of the literature and data in this field are concerned with the mechanism of action of drugs, or how drugs work, and the development of screening procedures to find new drugs which are both safe and effective. Since the human is useful in only relatively safe experimental systems, animals are used to model systems of human disease conditions. For example, the rabbit is often used to assess the autonomic effects of various drugs on the pupil of the eye, or to test antiinflammatory agents on the eye.

If the animal model system is successful, then the pharmacologist can predict with accuracy the effects of a drug when used clinically. Unfortunately, since pharmacology is a relatively young science, pharmacological data may become confused by apparent contradictions between human and animal studies. Hopefully, the following chapters will clarify some of these possible contradictions.

THERAPEUTICS

Therapeutics is that branch of pharmacology which concerns the use of drugs in diagnosing or treating disease.

When drugs are used to treat ocular disorders, the most rational therapy is achieved when the cause of the ocular disease is known. If, for example, an ocular lesion (e.g., ulceration) is caused by herpes simplex virus, an agent such as idoxuridine effectively inhibits the virus which causes the disease. Clinical symptoms improve because the disease source is affected. However, much ocular pharmacology and pharmacology in general is aimed at treating symptoms rather than diseases—for instance, the cause of glaucoma in many cases is unknown, but it is known that a high intraocular pressure (IOP) can produce ocular nerve damage and subsequent blindness. As a result many drugs, even agents with pharmacologically opposite effects in most cases (e.g., epinephrine and cholinomimetics), are sometimes used to treat the symptoms of glaucoma; in other words, what is treated is the elevated intraocular pressure rather than the actual cause of the disease.

However, the clinician may be faced with difficulty when trying to find diagnostic drugs listed in the general pharmacological literature. Frequently these listings are hard to find since diagnostic effects are often not major reasons for the use of the drug and since, in some cases, the diagnostic test actually induces a side effect. For example, when topical steroids are used as provocative tests for glaucoma the increased intraocular pressure expected in a glaucoma patient is actually a side effect of the drug's major use, namely as an antiinflammatory agent.

TOXICOLOGY

Toxicology is concerned with the toxic or potentially harmful effects of drugs. Many drugs have the potential for ocular iatrogenic (drug-induced) disease, a possibility which should be a constant consideration in the patient's examination.

From a practical point of view, the clinician is largely concerned with the therapeutic and toxicologic effects of drugs, which are the primary concern of this book.

PRESCRIPTION DRUGS

Prescription drugs, also called legend drugs, have stated on their labels, "Caution: Federal (U.S.A.) Law Prohibits Dispensing

Without a Prescription." The manufacturers of these drugs are required to give the clinician information on the toxicology of a drug. Since this information is often too long to put on a package label, it often is included in a "package insert" placed inside the box or container in which the drug is marketed. This package insert contains prescribing information, contraindications, adverse effects, teratological effects, incompatibilities, and storage requirements. It is considered a part of the drug's labeling. The clinician should be aware of the general meanings of these terms.

Contraindication refers to a condition in which the drug should not be used. However, it should be noted that the contraindications for a particular drug may not be absolute (unless stated) as the assumption usually is that the drug is being used alone. For example, sugar would be contraindicated in a diabetic patient. However, a diabetic patient who had taken too much insulin would require sugar administration.

Adverse (side) effects are usually undesired (untoward) effects of a particular drug; e.g., systemic antihistamines cause drowsiness as a side effect. However, sometimes the prudent clinician can utilize some adverse effects to a patient's benefit. For example, chickenpox virus sometimes starts as a lesion around the eye. It has no specific antiviral treatment other than to symptomatically decrease patient itching and discomfort. In this situation, relatively high doses of diphenhydramine (Benadryl) have been used to relieve the itching and also to produce sleep, which adds to patient comfort.

Teratological (literally, "the study of monsters") effects refer to the ability of a drug to produce birth defects. For obvious moral, ethical and legal reasons, research in this area is usually done in animal model systems, and extrapolation of the results, when applied to the human situation, is relatively unpredictable. However, the clinician should be aware of the fact that extreme caution, and careful weighing of the benefit-to-risk ratio, should be utilized when any drug is administered to a pregnant woman. Although still apparently in litigation, the drug Bendectin was voluntarily withdrawn from the market because of a number of law suits alleging teratology. Likewise, media and patient awareness of alleged dioxin teratological effects may carry over to a variety of drugs and chemicals.

Incompatibilities refer to a drug not being compatible with other drugs (chemical or pharmacological incompatibility), or physical conditions (physical incompatibility). An example of a chemical incompatibility can occur when ophthalmic AgNO_3 is used with a halogen-containing solution or a sulfonamide. In this case the AgNO_3 with the halogen or sulfonamide would cause the insoluble Ag-halogen or Ag-sulfide to precipitate, thus negating the antibacterial effect of silver. A pharmacological incompatibility occurs when one drug interferes with or causes an untoward side effect in another drug, by physiologic rather than chemical means. For example, systemic antihypertensives may be incompatible with topical beta-adrenergic blockers, as they may cause severe systemic hypotension and fainting. A physical incompatibility refers to physical conditions altering drug effectiveness. For example, epinephrine solutions deteriorate more rapidly and lose pharmacologic effectiveness when exposed to light.

DEFINITIONS AND IMPLICATIONS

A drug is anything intended for the diagnosis, mitigation, mediation, or treatment of a disease or disease process. Generally speaking, drugs are chemical compounds. It is not unreasonable, however, to suppose that soft contact lens materials could be classified as drugs since they are chemical compounds. This is especially true since hydrophilic soft lenses have been considered drug delivery systems because of their adsorptive and absorptive properties which could lend these products to use in the treatment of disease. For example, hydrophilic lenses can be presoaked in a drug solution and then placed on the eye, or a drop of drug solution can be placed on the eye with a nontreated lens. Applying a drug solution in this way could, in effect, present a greater than normal amount of drug to the eye. Another consideration is the possibility of side effects due to the use of cosmetics by contact lens patients. An additional concern is the fact that a drug applied in this manner is usually maintained in a higher volume and for a more prolonged duration.

An interesting drug is hydroxypropyl cellulose, which is similar to agents used in over-the-counter artificial tear preparations for dry eye syndromes. However, placing the hydroxypropyl

cellulose (Lacrisert) in a rod-shaped, water soluble preparation for insertion into the cul-de-sac of the eye beneath the base of the tarsus, has produced a legend drug for patients with moderate to severe dry eye syndrome. The clinician should also be aware of the fact that any over-the-counter drug can be legally considered a prescription drug if the clinician directs a patient to use the agent for a specific reason. This is especially true if the clinician commits the direction or suggestion into writing in a prescription form.

REFERENCE TEXTS

There are several books available which should aid the clinician. The following list contains some of the books which I find extremely helpful in teaching ocular pharmacology:

AMA Drug Evaluations, Third Edition. American Medical Association, 1980. Prepared by the scientific staff of the AMA, this definitive work is an indispensable pharmacological reference. Drugs have been indexed by both trade and generic names. Included are evaluations of new drugs by therapeutic classifications, along with structural formulas, adverse reactions, dosages, and combinations.

L.S. Goodman and A. Gilman, *Pharmacological Basis of Therapeutics*. New York: Macmillan, Inc., 1980. It gives detailed descriptions of most drugs and their theoretical or actual mechanisms of action. Unfortunately, the book is a generalized pharmacology text and does not give detailed descriptions specific to studying the eye as an entity. This criticism is probably true of most general pharmacology texts.

W.H. Havener, *Ocular Pharmacology*, Fourth Edition. St. Louis: The C.V. Mosby Co., 1978. A discussion of ocular pharmacology from the standpoint of how an ophthalmologist would use drugs gives many good descriptions of both the theoretical and clinical rationale for the use of ocular drugs.

M.B. Smith, *Handbook of Ocular Toxicity*. Acton, Mass.: Publishing Sciences Group, 1975. This valuable and practical book for the clinician identifies ocular symptoms produced by the use and abuse of various drugs. Every practitioner should have this book within arm's reach as an aid in documenting the patient's case history.