



ESTROGENS AND ANTIESTROGENS

BASIC
AND
CLINICAL
ASPECTS

EDITORS

ROBERT LINDSAY

DAVID W. DEMPSTER

V. CRAIG JORDAN

Estrogens and Antiestrogens

Basic and Clinical Aspects

Editors

Robert Lindsay, M.B.Ch.B., Ph.D., F.R.C.P.

*Chief, Internal Medicine
Professor of Clinical Medicine, Columbia University
Clinical Research Center and Regional Bone Center
College of Physicians and Surgeons
Helen Hayes Hospital
West Haverstraw, New York*

David W. Dempster, Ph.D.

*Professor of Clinical Pathology, Columbia University
Director, Clinical Research Center
and Regional Bone Center
Helen Hayes Hospital
West Haverstraw, New York*

V. Craig Jordan, Ph.D, D.Sc.

*Director, Breast Cancer Research Program
Robert H. Lurie Cancer Center
Professor of Cancer Pharmacology
Northwestern University Medical School
Chicago, Illinois*



Lippincott - Raven

P U B L I S H E R S

Philadelphia • New York

Acquisitions Editor: Danette Knopp
Developmental Editor: Juleann Dob
Manufacturing Manager: Dennis Teston
Production Manager: Jodi Borgenicht
Production Editor: Jeff Somers
Cover Designer: Karen Quigley
Indexer: Lisa Mulleneaux
Compositor: Lippincott-Raven Electronic Production
Printer: Maple Press

© 1997, by Lippincott-Raven Publishers. All rights reserved. This book is protected by copyright. No part of it may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means—electronic, mechanical, photocopy, recording, or otherwise—without the prior written consent of the publisher, except for brief quotations embodied in critical articles and reviews. For information write **Lippincott-Raven Publishers, 227 East Washington Square, Philadelphia, PA 19106-3780.**

Materials appearing in this book prepared by individuals as part of their official duties as U.S. Government employees are not covered by the above-mentioned copyright.

Printed in the United States of America

9 8 7 6 5 4 3 2 1

Library of Congress Cataloging-in-Publication Data

Estrogens and anti-estrogens : basic and clinical aspects / editors, David W. Dempster, Robert Lindsay, V. Craig Jordan.

p. cm.

Includes bibliographical references and index.

ISBN 0-397-51719-X (alk. paper)

1. Estrogen—Antagonists—Physiological effect. 2. Estrogen—Physiological effect. I. Dempster, David W. II. Lindsay, Robert, Ph.D. III. Jordan, V. Craig (Virgil Craig)

[DNLM: 1. Estrogens-pharmacology. 2. Estrogen Antagonists—pharmacology. WP 522 E808 1997]

RM295.E883 1997

615'.366—dc21

DNLM/DLC

for Library of Congress

Care has been taken to confirm the accuracy of the information presented and to describe generally accepted practices. However, the authors, editors, and publisher are not responsible for errors or omissions or for any consequences from application of the information in this book and make no warranty, express or implied, with respect to the contents of the publication.

The authors, editors, and publisher have exerted every effort to ensure that drug selection and dosage set forth in this text are in accordance with current recommendations and practice at the time of publication. However, in view of ongoing research, changes in government regulations, and the constant flow of information relating to drug therapy and drug reactions, the reader is urged to check the package insert for each drug for any change in indications and dosage and for added warnings and precautions. This is particularly important when the recommended agent is a new or infrequently employed drug.

Some drugs and medical devices presented in this publication have Food and Drug Administration (FDA) clearance for limited use in restricted research settings. It is the responsibility of the health care provider to ascertain the FDA status of each drug or device planned for use in their clinical practice.

Contents

Contributing Authors	ix
Foreword by <i>Jack Gorski</i>	xi
Preface	xiii
Acknowledgments	xv

Section I: Structure and Function

1. History of the Estrogen Receptor Concept and Its Relation to Antiestrogens <i>Elwood V. Jensen</i>	3
2. The Origin of Antiestrogens <i>V. Craig Jordan</i>	9
3. Chemistry: Structure and Function Relationships <i>Timothy M. Willson</i>	21
4. Metabolism of Antiestrogens <i>V. Craig Jordan, Michael Piette, and Angela Cisneros</i>	29
5. Mode of Action at the Cellular Level with Specific Reference to Bone Cells <i>John A. Robinson and Thomas C. Spelsberg</i>	43
6. The Postmenopausal State and Estrogen Deficiency <i>Rogério A. Lobo</i>	63

Section II: Target Tissues

7. Estrogenic Effects on the Central Nervous System: Clinical Aspects. <i>Barbara B. Sherwin</i>	75
8. Effects on the Cardiovascular System: Basic Aspects <i>Thomas B. Clarkson and Mary S. Anthony</i>	89
9. Effects on the Cardiovascular System: Clinical Aspects <i>Alison J. Cooper and John C. Stevenson</i>	119
10. Effects on Bone and Mineral Metabolism: Basic Aspects <i>Russell T. Turner</i>	129
11. Clinical Effects of Estrogens and Antiestrogens on the Skeleton and Skeletal Metabolism. <i>Felicia Cosman, David W. Dempster, and Robert Lindsay</i>	151

12. Clinical Implications of Target Organ–Specific Actions of Selective Antiestrogens	165
<i>Alan E. Wakeling</i>	
13. Effects on Breast Cancer: Clinical Aspects	175
<i>Kathleen I. Pritchard</i>	
14. Estrogenic and Antiestrogenic Actions of Tamoxifen in the Female Reproductive Tract	211
<i>P.G. Satyaswaroop</i>	
15. Effects on the Reproductive Tract: Clinical Aspects	223
<i>T. Scott Jennings and William T. Creasman</i>	
16. Estrogens, Antiestrogens, and the Urogenital Tract	243
<i>Con J. Kelleher and Linda Cardozo</i>	
Section III: Treatment	
17. The Complexity of Selective Estrogen Receptor Modulation: The Design of a Postmenopausal Prevention Maintenance Therapy	261
<i>Jennifer MacGregor, Debra A. Tonetti, and V. Craig Jordan</i>	
Subject Index	279

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.