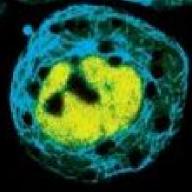
Download your free ebook on Student Consult



RANG & DALE'S Pharmacology

EIGHTH EDITION

H. P. Rang, J. M. Ritter, R. J. Flower, G. Henderson

CHURCHER LIVINGATIONE





Content Strategist: Meghan Ziegler Content Development Specialist: Alexandra Mortimer Content Coordinator: Sam Crowe, Trinity Hutton Project Manager: Joanna Souch Design: Christian Bilbow Illustrator: Peter Lamb, Antbits, Jason McAlexander Marketing Manager: Melissa Darling

Phang and DALE'S Phand Cology EIGHTH EDITION

H P Rang MB BS MA DPhil Hon FBPharmacolS FMedSci FRS Emeritus Professor of Pharmacology, University College London, London, UK

J M Ritter DPhil FRCP FBPharmacolS FMedSci Emeritus Professor of Clinical Pharmacology, King's College London, and Medical Research Director, Quintiles, London, UK

R J Flower PhD DSc FBPharmacolS FMedSci FRS Professor, Biochemical Pharmacology, The William Harvey Research Institute, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London, UK

G Henderson BSc PhD FBPharmacolS FSB Professor of Pharmacology, University of Bristol, Bristol, UK



For additional online content visit **studentconsult**





an imprint of Elsevier Limited

© 2016, Elsevier Ltd. All rights reserved.

First edition 1987 Second edition 1991 Third edition 1995 Fourth edition 1999 Fifth edition 2003 Sixth edition 2007 Seventh edition 2012

The right of H P Rang, J M Ritter, R J Flower and G Henderson to be identified as authors of this work has been asserted by them in accordance with the Copyright, Designs and Patents Act 1988.

No part of this publication 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. Details on how to seek permission, further information about the Publisher's permissions policies and our arrangements with organizations such as the Copyright Clearance Center and the Copyright Licensing Agency, can be found at our website: www.elsevier.com/permissions.

This book and the individual contributions contained in it are protected under copyright by the Publisher (other than as may be noted herein).

Notices

Knowledge and best practice in this field are constantly changing. As new research and experience broaden our understanding, changes in research methods, professional practices, or medical treatment may become necessary.

Practitioners and researchers must always rely on their own experience and knowledge in evaluating and using any information, methods, compounds, or experiments described herein. In using such information or methods they should be mindful of their own safety and the safety of others, including parties for whom they have a professional responsibility.

With respect to any drug or pharmaceutical products identified, readers are advised to check the most current information provided (i) on procedures featured or (ii) by the manufacturer of each product to be administered, to verify the recommended dose or formula, the method and duration of administration, and contraindications. It is the responsibility of practitioners, relying on their own experience and knowledge of their patients, to make diagnoses, to determine dosages and the best treatment for each individual patient, and to take all appropriate safety precautions.

To the fullest extent of the law, neither the Publisher nor the authors, contributors, or editors, assume any liability for any injury and/or damage to persons or property as a matter of products liability, negligence or otherwise, or from any use or operation of any methods, products, instructions, or ideas contained in the material herein.

ISBN:

Main edition ISBN-13 978-0-7020-5362-7

International edition ISBN-13 978-0-7020-5363-4



Working together to grow libraries in developing countries

www.elsevier.com • www.bookaid.org

Rang and Dale's Pharmacology Eighth Edition Preface

In this edition, as in its predecessors, we set out not just to describe what drugs do but also to emphasise the mechanisms by which they act. This entails analysis not only at the cellular and molecular level, where knowledge and techniques are advancing rapidly, but also at the level of physiological mechanisms and pathological disturbances. Pharmacology has its roots in therapeutics, where the aim is to ameliorate the effects of disease, so we have attempted to make the link between effects at the molecular and cellular level and the range of beneficial and adverse effects that humans experience when drugs are used for therapeutic or other reasons. Therapeutic agents have a high rate of obsolescence, and more than 100 new ones have been approved since the last edition of this book. An appreciation of the mechanisms of action of the class of drugs to which a new agent belongs provides a good starting point for understanding and using a new compound intelligently.

Pharmacology is a lively scientific discipline in its own right, with an importance beyond that of providing a basis for the use of drugs in therapy, and we aim to provide a good background, not only for future doctors but also for scientists in other disciplines who need to understand how drugs act. We have, therefore, where appropriate, described how drugs are used as probes for elucidating cellular and physiological functions, even when the compounds have no clinical use.

Names of drugs and related chemicals are established through usage and sometimes there is more than one name in common use. For prescribing purposes, it is important to use standard names, and we follow, as far as possible, the World Health Organization's list of recommended international non-proprietary names (rINN). Sometimes these conflict with the familiar names of drugs (e.g. amphetamine becomes amfetamine in the rINN list), and the endogenous mediator prostaglandin I_2 - the standard name in the scientific literature - becomes 'epoprostenol' - a name unfamiliar to most scientists - in the rINN list. In general, we use rINN names as far as possible in the context of therapeutic use, but often use the common name in describing mediators and familiar drugs. Sometimes English and American usage varies (as with adrenaline/epinephrine and noradrenaline/ norepinephrine). Adrenaline and noradrenaline are the official names in EU member states and relate clearly to terms such as 'noradrenergic', 'adrenoceptor' and 'adrenal gland' and we prefer them for these reasons.

Drug action can be understood only in the context of what else is happening in the body. So at the beginning of most chapters, we briefly discuss the physiological and biochemical processes relevant to the action of the drugs described in that chapter. We have included the chemical structures of drugs only where this information helps in understanding their pharmacological and pharmacokinetic characteristics, secure in the knowledge that chemical structures are readily available online.

The overall organisation of the book has been retained, with sections covering: (1) the general principles of drug action; (2) the chemical mediators and cellular mechanisms with which drugs interact in producing their

therapeutic effects; (3) the action of drugs on specific organ systems; (4) the action of drugs on the nervous system; (5) the action of drugs used to treat infectious diseases and cancer; (6) a range of special topics such as adverse effects, non-medical uses of drugs, etc. This organisation reflects our belief that drug action needs to be understood, not as a mere description of the effects of individual drugs and their uses, but as a chemical intervention that perturbs the network of chemical and cellular signalling that underlies the function of any living organism. In addition to updating all of the chapters, we have covered the receptor-related topics of biased agonism, allosteric modulation and desensitisation in more detail in Chapters 2 and 3, as well as revamping the section on nuclear receptors. A new Chapter 27 on the pharmacology of the skin has been added, and Chapters 17 and 18 on local hormones have been revised. Additional material on cognition-enhancing drugs has been included in Chapter 48.

Despite the fact that pharmacology, like other branches of biomedical science, advances steadily, with the acquisition of new information, the development of new concepts and the introduction of new drugs for clinical use, we have avoided making the 8th edition any longer than its predecessor by cutting out-dated and obsolete material, and have made extensive use of small print text to cover more specialised and speculative information that is not essential to understanding the key message, but will, we hope, be helpful to students seeking to go into greater depth. In selecting new material for inclusion, we have taken into account not only new agents but also recent extensions of basic knowledge that presage further drug development. And where possible, we have given a brief outline of new treatments in the pipeline. Reference lists are largely restricted to guidance on further reading, together with review articles that list key original papers.

ACKNOWLEDGEMENTS

We would like to thank the following for their help and advice in the preparation of this edition: Dr Alistair Corbett, Dr Hannah Gill, Professor Eamonn Kelly, Professor Alastair Poole, Dr Emma Robinson, Dr Maria Usowicz and Professor Federica Marelli-Berg. We would like to put on record our appreciation of the team at Elsevier who worked on this edition: Meghan Ziegler (commissioning editor), Alexandra Mortimer (development editor), Joanna Souch (project manager), Brett MacNaughton (illustration manager), Peter Lamb, Antbits and Jason McAlexander (freelance illustrators), Elaine Leek (freelance copyeditor), Marcela Holmes (freelance proofreader) and Innodata Inc. (freelance indexing services).

London 2014

H. P. Rang J. M. Ritter R. J. Flower G. Henderson