Basic Pharmacology

Editors
R W Foster and B Cox

Basic Pharmacology

Editors
R W Foster and B Cox

With

J R Carpenter	H Schnieden
M J Dascombe	A P Silverman
M Hollingsworth	R C Small
N P Keaney	Janet Vale
G E Mawer	A H Weston
I D Morris	E T Whalley
P W Mullen	T R Wilson
J M H Rees	

The Department of Pharmacology, Materia Medica and Therapeutics, The University of Manchester

Butterworths
London Boston
Sydney Wellington Durban Toronto

United Kingdom **Butterworth & Co (Publishers) Ltd**
London 88 Kingsway, WC2B 6AB

Australia **Butterworths Pty Ltd**
Sydney 586 Pacific Highway, Chatswood, NSW 2067
Also at Melbourne, Brisbane, Adelaide and Perth

Canada **Butterworth & Co (Canada) Ltd**
Toronto 2265 Midland Avenue, Scarborough, Ontario, MIP 4SI

New Zealand **Butterworths of New Zealand Ltd**
Wellington T & W Young Building, 77-85 Customhouse Quay, 1,
CPO Box 472

South Africa **Butterworth & Co (South Africa) (Pty) Ltd**
Durban 152-154 Gale Street

USA **Butterworth (Publishers) Inc**
Boston 10 Tower Office Park, Woburn, Massachusetts 01301

All rights reserved. No part of this publication may be reproduced or transmitted in any form or by any means, including photocopying and recording, without the written permission of the copyright holder, application for which should be addressed to the Publishers. Such written permission must also be obtained before any part of this publication is stored in a retrieval system of any nature.

This book is sold subject to the Standard Conditions of Sale of Net Books and may not be re-sold in the UK below the net price given by the Publishers in their current price list.

First published 1980
© University of Manchester, Department of Pharmacology,
Materia Medica and Therapeutics 1980
ISBN 0 407 00170 0

British Library Cataloguing in Publication Data

Basic pharmacology.
1. Pharmacology
I. Foster, R W II. Cox, Barry, *b. 1937*
615'.1 RM300 80-49873

ISBN 0-407-00170-0

Typeset by Scribe Design, Gillingham, Kent
Printed and bound by Redwood Burn Limited, Trowbridge & Esher

Preface

In the thirteenth century Roger Bacon, writing in *De Erroribus Medicorum,* alleged that the typical medical man of the day was ignorant of his own simple medicine and put himself in the hands of unlearned apothecaries. There are those who would make similar allegations about the prescribers and dispensers of today's medicines. Accordingly, this book is offered in the hope that it will provide sufficient information about the drugs in current use to render such allegations groundless.

As authors of this book, the staff of the Department of Pharmacology, Materia Medica and Therapeutics at Manchester University have been able to draw on experience developed during 15 years of teaching pharmacology to students of several different disciplines. This experience gained from teaching is tempered by the fact that, as a group, the authors have variously prescribed, dispensed, scientifically investigated and even been on the receiving end of a selection of the compounds mentioned in their text.

The organization of this book is simple in concept. It is divided into sections, each section following a particular theme and being introduced by the relevant general principles – anatomical, biochemical or pharmacological. In each section the major groups of drugs relevant to the theme are discussed with detailed reference to important 'type' substances. Drugs of lesser importance are placed in proper context.

Though the format of the book is simple in concept, the realization of its content proved a formidable task. By way of example, the writing of the section concerning the actions of drugs on the central nervous system posed particular problems. This is an area where, despite a current spate of research activity, our knowledge of basic drug actions is very imprecise and to relate such actions to behavioural changes is necessarily difficult. The authors' final product for this and other sections is the result of many hours of discussion and debate.

As outlined in the introduction, this book is addressed to a wide spectrum of readers. It is to be hoped that no reader will fail to appreciate that selective toxicity (that is, the ability to chemically influence one type of biological activity without modifying any other) is the central theme of pharmacology.

Most importantly, the reader should appreciate that selective toxicity can never be absolute. Harold Kaminetsky perhaps put the dangers of chemotherapy into proper perspective yet left us with a message of hope when he suggested that there can be no really safe biologically active drugs – but there can be safe physicians.

H. Schnieden

此为试读,需要完整PDF请访问: www.ertongbook.com

Introduction

This book is intended for all who embark on the study of pharmacology. Most of its readers will be students of either medicine or pharmacy, whilst a few will regard pharmacology as their main or second subject. We teach all such students ourselves, think we know their needs and have attempted to satisfy the requirements of each of these groups in a single text. They have two things in common; an interest in the uses to which the drugs they study are put, and the fact that they are embarking on the study of pharmacology. Thus, we have provided a textbook which begins at the beginning, assuming only a modicum of chemistry, biology and physiology as prerequisites. It proceeds in the direction of paramedical or therapeutic rather than chemical pharmacology, assuming that the student will have access to further biology or physiology during his study. It goes far enough to cover all the introductory material; in other words, it should cover the first year of study by any of the above groups and still leave some material to launch a second year. Although newly published it has had the benefit of passing through several stages of evolution and refinement. In the form of extensive lecture notes it has been used by Manchester students for some years and we thank all our previous students who have consciously or unconsciously suggested improvements.

Perhaps the major problem encountered in the teaching of pharmacology is the large and ever-increasing number of drug names. Certainly the most frequent criticism levelled by new students is that of too many drug names. The complaint is not simply about weight of numbers but also about the apparent similarity in the names of drugs from different pharmacological groups, which for the inexperienced leads to misunderstanding and confusion. Therefore, in this book we have first defined a rigorous policy on drug names (*see below*) and, secondly, attempted an approach to the teaching of pharmacology which places a premium on understanding and reduces rote memorization to an essential minimum. This approach we call the Thematic Approach.

Rather than talk about individual chemical or therapeutic drug groups as in the traditional or systematic treatments of pharmacology, we have divided our book into sections with a common theme. We have also considered carefully the order in which these themes are presented. Thus, the book starts with a section

which has as its theme the mechanisms by which drugs act at the efferent peripheral nervous system and its effectors. This is the chosen starting point because it is in this area that mechanism of drug action is probably best understood. Also, a high proportion of the drugs mentioned in this section have therapeutic potential and the system can be used as a model to predict or infer the mechanism of action of drugs in other less well understood areas (for example central nervous system, CNS). From this starting point of drug action at a discrete well defined site the theme changes to a consideration of mechanism of drug action on tissues under endocrine or local hormonal influence. Thus, the principle of drug interaction with chemical mediators is still the theme but now a greater variety of effectors and of time scales of action is considered. The next section is that of drug action on the CNS. First, the theme is again interactions with chemical mediators, which relies heavily on the principles and concepts presented in the preceding two sections, but then a second theme is introduced, that of non-specific interactions where drug effects other than those of interaction via a specific receptor site are considered. So far the themes have been drug interactions with endogenous systems, but in the next section the theme changes to a consideration of the mechanism of drug action on parasitic cells, be they microorganisms or neoplasms. The emphasis is now on mechanisms by which parasitic cell growth or survival is selectively inhibited. At this point the student has been provided with sufficient information in pharmacology so that drugs are no longer simply names. The theme changes from that of drug action to that of drug disposition and metabolism so that an appreciation of how these factors influence drug action can be gained. At the end of the book the theme changes once again so that the Applied Section considers the practical application of drugs and illustrates how an appreciation of mechanism of action can be put to a therapeutic use. This section also brings together drugs from different sections and so hopefully counteracts compartmentalization of information, a condition to which students seem to be innately predisposed.

With the plethora of textbooks of pharmacology which are currently available the question that might justifiably be asked is 'Why another one?'. Perhaps the answer lies in the fact that among those available we could find none which was suitable for our students who were at the beginning of a study of pharmacology. Though many excellent textbooks exist at the advanced level we felt the need for a comprehensive yet simple and concise book which adhered to our principle of understanding first and foremost, memorization last and least. Hence, our reliance heavily on comprehensive lecture note handouts (mentioned elsewhere) which have now been developed into this publication.

Policy on unfamiliar words

Words which are unfamiliar to the reader may be part of the technical language of medicine or pharmacology and all such we have defined or explained on their first occurrence. A second category exists in the ordinary stock of the English language – definitions are not provided in the text and the reader is advised to consult a dictionary.

Policy on which drugs to include

We have actively sought to limit the number of different drugs described because our primary objective has been to teach the principles of the pharmacological

basis of therapeutics rather than familiarity with a rapidly ageing stock of drugs. We have therefore a narrower scope than, say, *MIMS* or the *Data Sheet Compendium* exactly as advised by the Committee of the British National Formulary. This policy is very similar to that adopted by the WHO Expert Committee reporting on The Selection of Essential Drugs.

Drugs have been categorized according to two criteria:

(1) Drugs listed in BNF (1976–78) and printed in bold type in one of the 'Notes on the use of drugs' sections are italicized, for example, *non-proprietary name.*

(2) From each pharmacological group of drugs we have chosen one which typifies the group. If its actions are understood the rest of the group, too, has been comprehended. We show these substances in sans serif type, for example, Non-proprietary name. Of course, many are also listed in the BNF and thus appear as *Non-proprietary name.*

Policy on drug names

We have used the non-proprietary names approved by the British Pharmacopoeial Commission and excluded trade names save in the very rare instances where no approved name has been assigned. For readers who are more familiar with North American terminology the US Pharmacopoeial name has been included in the index and in square brackets in the text after the first occurrence of the name. Only significant differences, however, have been declared; we have not bothered to draw special attention to systematic differences arising from different spelling conventions such as -ph- [-f-] and -oe- [-e-]. Neither did -trophin [-tropin] nor -barbitone [-barbital] seem likely to mystify our readers.

We were pleasantly surprised by the small number of significant differences; there was an era of fundamental differences, witness paracetamol [acetaminophen] and pethidine [meperidine], but modern drugs are deliberately being assigned the same name on both sides of the Atlantic.

Pharmacology, like most other scientific disciplines, is developing rapidly and the perennial problem of any text is that of keeping 'up to date'. We intend to make regular revisions of this book and will be helped in deciding the timing of these by the close connection, expressed in 'Aims and Objectives' below, with the BNF. Thus, stimuli for revision will be either a major advance in the understanding of the mechanism of action of any group of drugs, or significant therapeutic advances expressed as new inclusions in the BNF of drugs worthy of 'type substance' status.

We should be happy to receive suggestions for improvement from users of the book.

We thank John Carpenter for preparing the diagrams, and Professor Malcolm Rowlands for help with Section 5, Sybil McCartney for typing the manuscript and all our colleagues for the time invested in evolving common policies and in proof reading.

AIMS AND OBJECTIVES

The aim of this book is to provide the sound pharmacological basis on which could be built a rational approach to therapeutics.

By the end of the book the reader should:

- Recognize most of the British Pharmacopoeial names of drugs (and their United States Pharmacopoeial equivalents, if different) appearing in bold type in the 'Notes on the use of drugs' section of the *British National Formulary* (BNF, latest edition),
- Be able to group together those drugs with common pharmacological properties and name one which typifies the group;
- Know the site and mechanism of action of each 'type substance';
- Know the pharmacological properties of each 'type substance' which are relevant to its therapeutic use, with special emphasis on those which can be deduced from a knowledge of the site and mechanism of action;
- Be aware of the nature (but not the detail) of the therapeutic application of each group of drugs;
- Know the common or serious side (or toxic) effects of each 'type substance' when used therapeutically, especially those which can be deduced from the pharmacological properties;
- Be able to place new drugs within the classificatory framework provided by the book.

List of abbreviations

ACh	acetylcholine
AChE	acetylcholinesterase
ACTH	adrenocorticotrophic hormone, corticotrophin
ADH	antidiuretic hormone
ATP	adenosine triphosphate
AV	atrioventricular
bd	(lit bis die) twice daily
BNF	*British National Formulary*
BP	blood pressure
C.	Corynebacterium
cAMP	cyclic adenosine monophosphate
cf	(lit confer) compare
ChE	cholinesterase
Ci	Curie
Cl.	Clostridium
CNS	central nervous system
CoA	coenzyme A
COMT	catechol O-methyl transferase
CSF	cerebrospinal fluid
CTZ	chemosensitive trigger zone
DHF	dihydrofolate
DNA	desoxyribonucleic acid
DOPA	dihydroxyphenylalanine
E.	Escherichia
EC50	concentration of drug evoking a half maximal effect
ECF	extracellular fluid
ECT	electroconvulsive therapy
EEG	electroencephalogram
epp	end plate potential
epsp	excitatory post-synaptic potential
FEV_1	forced expiratory volume in one second
FFA	free fatty acid
FSH	follicle stimulating hormone

g	gram
GABA	γ-aminobutyric acid
GFR	glomerular filtration rate
GH	growth hormone
H.	Haemophilus
h	hour
HCG	human chorionic gonadotrophin
HMG	human menopausal gonadotrophin
5-HT	5-hydroxytryptamine
HWY	hundred woman years
Hz	Hertz (1 Hertz is 1 cycle per second)
Ig-	immunoglobulin-
im	intramuscular
IUD	intrauterine device
iv	intravenous
k-	kilo- (10^3)
ℓ	litre
LH	luteinizing hormone
lit	literally
log	logarithm
LSD	lysergic acid diethylamide
M.	Mycobacterium
m	metre
m-	milli-(10^{-3})
mac	minimum anaesthetic concentration
MAO	monoamine oxidase
MFO	mixed function oxidase
mic	minimum inhibitory concentration
μ	micro (10^{-6})
min	minute
mol	mole (gram molecular weight)
mRNA	messenger ribonucleic acid
MW	molecular weight
N.	Neisseria
n-	nano- (10^{-9})
NA	noradrenaline
NADPH	nicotinamide adenine nucleotide phosphate (reduced)
P.	Plasmodium
P-	partial pressure
Pa-	arterial blood partial pressure
PG	prostaglandin
Ps.	Pseudomonas
qv	(lit quod vide) which see
R	registered trade name
RNA	ribonucleic acid
S.	Salmonella
SA	sino–atrial
sc	subcutaneous
SRS-A	slow-reacting substance of anaphylaxis
Staph.	Staphylococcus

此为试读,需要完整PDF请访问: www.ertongbook.com

Str.	Streptococcus
$t_{1/2}$	half time, half life
THC	tetrahydrocannabinol
THF	tetrahydrofolate
Tr.	Treponema
tRNA	transfer RNA
TSH	thyroid stimulating hormone, thyrotrophin
UK	United Kingdom
UV	ultraviolet
+ve	positive
−ve	negative
viz	(lit videlicet) namely
v/v	volume per unit volume
w/v	weight per unit volume

Abbreviations specific to the drug disposition section are on page 225.

Contents

1
Drug action on the efferent peripheral nervous system and its effectors

INTRODUCTION

Studies of drug effects exerted upon the peripheral nervous sytem or the cells which it innervates can provide an excellent introduction to mechanisms of drug action, the rationale behind the use of drugs as investigative tools or as therapeutic agents and the methods by which drug actions are measured. Furthermore, such studies will provide a working base from which to approach the pharmacology of other, perhaps more complex, physiological systems such as the brain.

Learning objectives

In common with other sections of this book, the drugs chosen for discussion are included in preparations listed by the BNF or constitute pharmacological tools of particular importance. For each drug mentioned you should know:

- Its mechanism of action and the changes in effector cell activity evoked both *in vitro* and *in vivo*;
- Its interactions with other pharmacological agents;
- Something of its therapeutic or scientific usage – and the rationale behind that usage;
- Something of its undesirable effects.

Consideration of these four items will not give the reader a complete understanding of the pharmacology of a given drug. By reference to other sections of this book, he should seek knowledge of the drug's handling by the body (absorption, disposition and elimination) and whether it has actions on physiological systems which are outside the scope of this section.

Clinical applications

Many of the drugs described in this section are clinically useful. They may be used:

(1) To modify physiological processes and thus permit an operative or other procedure, for example, Tubocurarine (page 23);
(2) As aids in the diagnosis of disease, for example, *Edrophonium* (page 38); and
(3) In the symptomatic treatment of disease, for example, ***Propranolol*** (page 51).

It is important to realize that (with the exception of some antibiotics – *Table 1.3*) the agents mentioned in this section cannot be used to effect radical cure of disease.

Anatomy and physiology of the (efferent) peripheral nervous system and its effectors

Before we can understand how drugs produce their effects in the body we must have a thorough understanding of the anatomy and physiology of the relevant organ systems.

The nervous system can be subdivided as shown in *Figure 1.1.*

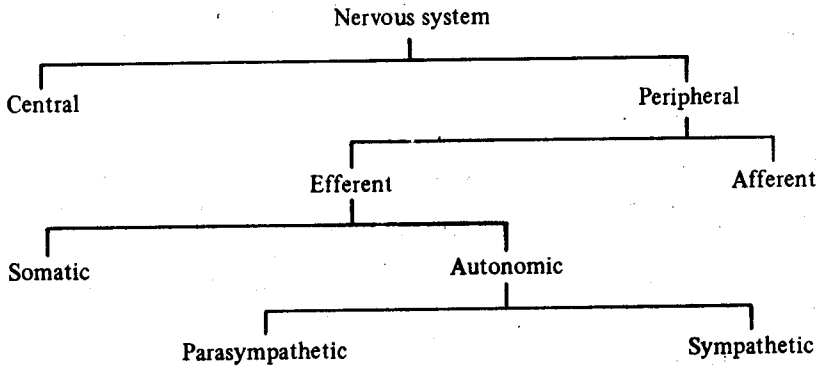

Figure 1.1 *Subdivision of the nervous system*

The central nervous system (CNS) comprises the brain and spinal cord. The peripheral nervous system lies outside the skull and vertebral column and comprises 12 pairs of nerves which emerge from the brain stem (cranial nerves) plus 31 pairs of nerves which emerge from the spinal cord (spinal nerves).

Peripheral neurones which carry impulses towards the CNS are called afferent neurones. Those which carry impulses away from the CNS are called efferent neurones.

Some cranial nerves consist of only afferent neurones, some of both afferent and efferent neurones and some of only efferent neurones. For the major part of their length, the spinal nerves consist of both afferent and efferent neurones and

此为试读,需要完整PDF请访问: www.ertongbook.com