AIDS TO MATERIA MEDICA AND THERAPEUTICS

J. W. HADGRAFT

FIFTH EDITION

BAILLIÈRE, TINDALL & COX

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AND
THERAPEUTICS

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PREFACE TO THE FIFTH EDITION

SINCE this book was first published, the advances made in the study of pharmacology and chemotherapy have rendered obsolete the classification of drugs into organic and inorganic substances under the somewhat ambiguous title of Materia Medica. Pharmacology is now a clearly defined study and its place in the medical curriculum has undergone a corresponding change. Nevertheless, there still remains a need for a book which will indicate to the medical student the way in which drugs are formulated for use in therapeutics and the alternative preparations available. This volume of the 'Students' Aids Series' has been prepared with this object in view. It is also hoped that it will be of value to post-graduate pharmacy students entering hospital pharmacy.

The book has been completely revised in accordance with the British Pharmacopœia of 1953 and the Addendum 1955. In accordance with pharmacopœial practice, English titles have been used. Abbreviated Latin titles and proprietary names have been included where appropriate. The drugs have been arranged alphabetically but where a number of preparations form a well-defined group, these have been brought together, e.g. Antibiotics, Barbiturates, Hormones, etc.

In addition to pharmacopœial preparations, a number of drugs which have not yet received official recognition have been included. The Pharmacological Classification and Dose Tables in Part II have been re-written. Metric doses only are given for those drugs which are

commonly prescribed in the Metric system. In the case of older drugs, which are still commonly prescribed in Imperial doses, both Metric and Imperial doses are given. An Appendix on Dangerous Drugs and Poisons has been added.

The author wishes to thank Mr. J. C. Barfield for his assistance in preparing the dose-tables, Mr. C. L. Sargent and Dr. G. F. Somers for their advice and guidance and Miss J. Rolf for her assistance in preparing the manuscript.

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CONTENTS

INTRODUCTION

The British Pharmacopœia (B.P.) is a book of standards controlling the composition, purity and preparation of drugs and medicinal substances. It is issued under the direction of the General Medical Council and is authoritative throughout the British Commonwealth. Drugs included in the Pharmacopœia are said to be 'official.' This book is based on the British Pharmacopœia of 1953 and the Addendum 1955.

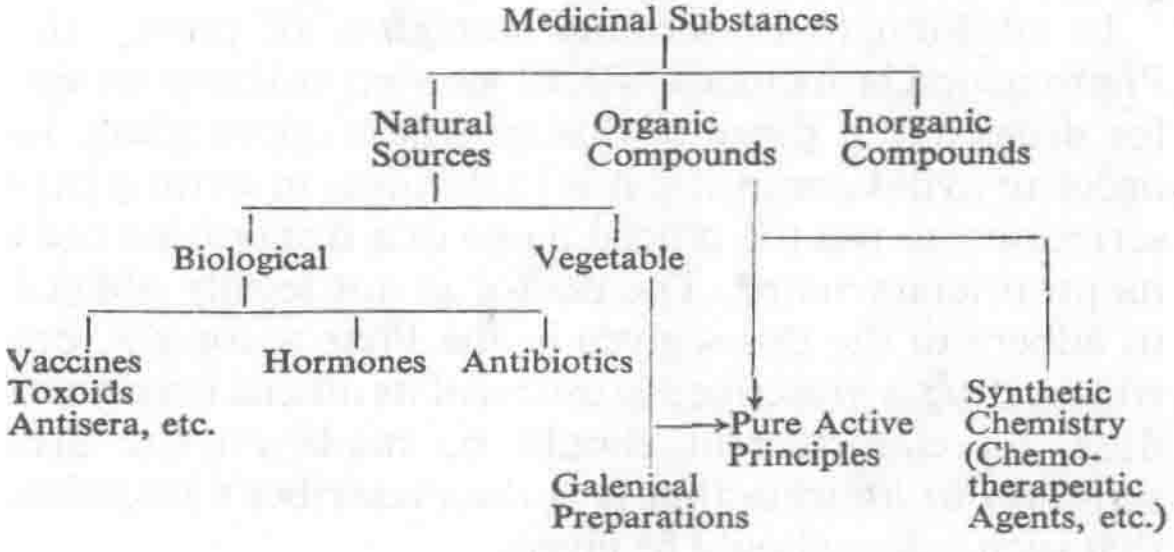
In addition to prescribing standards of purity, the Pharmacopœia includes official non-proprietary names for drugs and a range of dosage where appropriate. In order to avoid confusion it is preferable, in writing prescriptions, to use the official name of a drug rather than its proprietary name. The doctor is not legally obliged to adhere to the doses given in the Pharmacopœia, but when a drug is prescribed in excess of its official maximum dose, an endorsement should be made on the prescription to indicate that it is the prescriber's intention that such a dose should be given.

The British Pharmaceutical Codex (B.P.C.) is published by the Pharmaceutical Society and is intended to supplement the information of the British Pharmacopœia. It provides standards of purity for older drugs which are no longer official and new drugs which have not yet achieved pharmacopœial status. In addition, it contains information on the action and uses of both official and non-official drugs and includes formulæ for many compounded preparations. The British Pharmaceutical Codex also provides standards for surgical dressings.

The National Formulary (N.F.), published jointly by the Pharmaceutical Society and the British Medical Association, is a convenient handbook for the practising doctor. It provides essential information for prescribing official and other preparations and is the officially recognised guide for this purpose in the National Health Service.

Types of Substances Used in Medicine

Drugs and medicinal substances are derived from a variety of sources which may be summarised as follows:



Vegetable Drugs

Vegetable drugs consist of either the whole or the part of a plant which has been collected and carefully dried. They owe their activity to the presence of active principles which fall into two main groups, alkaloids and glycosides.

Alkaloids are organic compounds all containing nitrogen, having an alkaline reaction and combining with acids to form crystalline salts. A few alkaloids are liquids containing only carbon, hydrogen and nitrogen.

Most alkaloids are solids and also contain oxygen. The free alkaloidal bases are usually sparingly soluble in water but readily dissolve in alcohol and organic solvents; the salts are usually soluble in water but insoluble in organic solvents. The names of alkaloids terminate in *-ine* (cf. morphine).

Many synthetic compounds have similar chemical properties to the naturally occurring alkaloids. For example, pethidine is a synthetic drug having structural relationships to both morphine and atropine. It is used as an analgesic and antispasmodic in place of morphine. Neostigmine, having an action similar to the naturally occurring alkaloid physostigmine, is prepared by synthesis.

Glycosides are neutral in reaction, usually sparingly soluble in water and contain carbon, hydrogen and oxygen. Under the action of dilute acids or certain enzymes, they are hydrolysed to form sugars and other products which are called aglycones. When the sugar present is glucose, the substance may be called a glucoside. Thus, salicin, when boiled with dilute sulphuric acid, yields glucose and an aglycone known as saligenin. The pharmacological activity of a glycoside is due to its aglycone and not to the sugar with which it is combined. The names of glycosides are recognisable by their termination *-in* (cf. digoxin).

A few active principles are neutral in reaction but do not belong to the group of glycosides. For example, picrotoxin, derived from *Anamirta cocculus*, is a neutral active principle which is not a glycoside.

In addition to active principles, vegetable drugs contain a variety of other substances, the more important of which include the following:

Fixed Oils are esters formed by a combination of glycerol

with the higher fatty acids, usually oleic, palmitic and stearic acids. They cannot be distilled without decomposition. Fixed oils are soluble in ether and chloroform.

Soaps are salts of fatty acids and are formed by the hydrolysis of fixed oils with caustic alkalis or metallic oxides. Common fixed oils are *castor oil*, *arachis oil*, and *olive oil*.

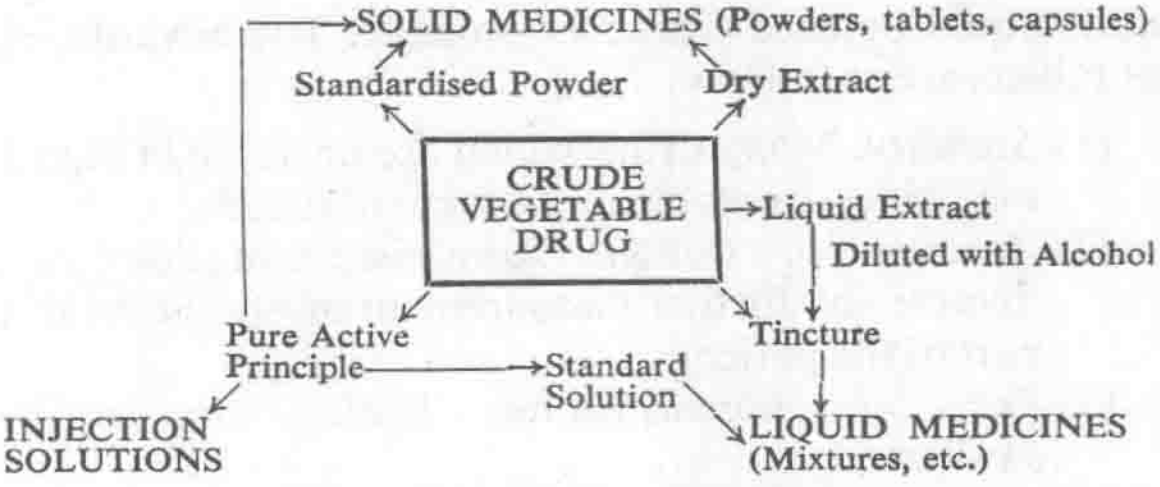
Volatile or Essential Oils, unlike the fixed oils, are volatile in steam and are prepared by steam distillation. They have pronounced, characteristic odours and leave no permanent oily mark when dropped on to paper. The essential oils vary considerably in composition but consist mainly of terpenes, complex alcohols and esters.

Resins are complex substances formed by the oxidation of volatile oils. They are insoluble in water, but soluble in alkalis and alcohol.

Gums are complex carbohydrate substances formed as exudations from certain plants. They form colloidal solutions.

Galenical Preparations are made from crude vegetable drugs. It may not be economically desirable for the active principle to be isolated in a pure state. Moreover, many vegetable drugs contain other substances which have a beneficial modifying action on the main active ingredient. The galenical preparations include standardised powders, extracts and tinctures (see Part II).

The general scheme showing how preparations, of varying degrees of purity, are derived from vegetable drugs may be represented as follows:



Routes of Administration

The main routes of administration of drugs are as follows:

(1) By mouth (oral administration)
(2) By the rectum (rectal administration)
(3) By inhalation
(4) By injection (parenteral administration)
(5) By implantation

Oral Administration

In the routine administration of drugs, oral administration is adopted wherever possible. Many preparations, however, are not administered by mouth because they are inactivated if given by this route. Examples of such preparations are the hormones (except thyroxine, sex hormones and suprarenal cortical hormones), heparin, vaccines and sera.

Other preparations are unabsorbed on oral administration but, nevertheless, may be given by mouth to obtain a local action in the intestines or bowel. Such preparations include liquid paraffin, magnesium sulphate, succinylsulphathiazole and streptomycin.

Solid drugs are given by mouth in the form of tablets, capsules, pills and cachets. Liquid preparations for oral administration include mixtures, elixirs and emulsions (see Part II). The tablet is the most suitable preparation

and should be used whenever possible. The advantages of tablets are as follows:

(1) *Stability*. Many drugs which are unstable in liquid medicines are stable in the form of tablets.
(2) *Accuracy of Dosage*. Administration does not involve any further measurement of dosage on the part of the patient.
(3) *Ease of Administration*. Tablets are easily swallowed.
(4) *Low Cost*. Tablets are cheap to produce on a large scale. They are cheaper than capsules.
(5) *Coating*. Tablets may be suitably coated with sugar or other materials where necessary.
(6) *Convenience of Supply*. Tablets occupy a small bulk.
(7) *Efficiency*. Properly made tablets readily disintegrate in the alimentary tract releasing the drug for absorption. For this reason, they are far superior to pills, which are no longer as commonly used as they were.

Sublingual Administration. A few substances are well absorbed by the sublingual epithelial cells and are best administered by either chewing a tablet or allowing it to dissolve under the tongue. Glyceryl trinitrate and isoprenaline sulphate are examples of this class of drugs.

Rectal Administration

Some drugs are well absorbed by the rectum and may be conveniently administered by this route. Enemas are liquid preparations for rectal use and, for the administration of drugs, should not exceed 2 fluid ounces in volume. Hypnotic drugs such as chloral hydrate and paraldehyde may be given in this way. A suitable vehicle for this purpose is normal saline or 2·5 per cent. mucilage of starch. Large volume enemas consisting of

a pint or more of liquid are not used for drug administration but may be used for other purposes.

Suppositories are solid preparations for rectal use and most commonly consist of the drug dissolved or dispersed in oil of theobroma, a solid fat which melts at body temperature thus releasing the drug. Suppositories may be used for the administration of alkaloidal salts such as morphine sulphate.

Inhalation

Volatile substances, when inhaled, may be well absorbed from the nasopharynx and lungs. This forms the route of administration of general anæsthetics such as ether and trichloroethylene. Amyl nitrite is also administered by this route and for the purpose is enclosed in crushable glass capsules (vitrellæ) which have a covering of lint and can be crushed between the fingers.

Occasionally, drugs may be administered by intranasal insufflation—e.g. cyanocobalamin (vitamin B_{12}) may be given by this method and is well absorbed by the nasal mucosa.

Parenteral Administration

This is a general term applied to the various methods of introducing a drug by injection through the skin. This may be done at various levels.

Intracutaneous (*Intradermal*) *Injection*, in which an injection is made into the surface layers of the skin, is confined mainly to the introduction of test solutions in diagnostic tests, e.g. Schick Test Toxin.

Subcutaneous (*Hypodermic*) *Injection* is used to obtain more nearly the maximal effects of a given dose of a drug than can be obtained by oral administration. The sensory nerve endings are localised in the subcutaneous

tissues and this route, therefore, is too painful for the administration of a number of drugs.

Intramuscular Injection is less painful than subcutaneous injection and is used for drugs which are too irritant to be given subcutaneously—e.g. penicillin preparations. Since the blood supply to the muscles is richer, soluble drugs diffuse more readily on intramuscular injection.

Insoluble drugs injected into the muscle will provide a reserve from which the drug will be slowly released and produce a more prolonged effect. For example, procaine penicillin is a sparingly soluble salt which is more slowly absorbed than the more soluble salts of penicillin.

Intravenous Injection produces the most rapid effect since the drug is introduced directly into the blood stream and is therefore of value in urgent cases, e.g. the administration of ouabain in cardiac failure. It is the least painful of the routes of injection. Examples of drugs given intravenously are thiopentone sodium and the soluble sulphonamides. The intravenous route is also used for the introduction of large volumes of solutions for the replacement of body fluids—e.g. normal saline.

Owing to the rapidity of action, intravenous injection is dangerous if used for some drugs. For example, acetylcholine, and drugs having a similar action such as carbachol, may cause death by inhibiting the heart if given by intravenous injection.

Intrathecal Injection is used for the administration of drugs employed in the treatment of meningitis, e.g. streptomycin sulphate and penicillin sodium. The soluble sulphonamides must never be given by this route. Since the cerebrospinal fluid has no defence mechanisms against bacterial invasion, it is essential that the strictest aseptic technique be adopted in making intrathecal injections.

Implantation

In the case of certain hormones, a very prolonged action may be obtained by implanting a sterile pellet of the substance in the subcutaneous tissues—e.g. deoxycortone acetate may be given by implantation in the maintenance treatment of Addison's disease. Effects lasting several months may be obtained by this method of administration.

Frequency of Administration

Drugs which are rapidly absorbed and excreted, such as the salicylates and the sulphonamides, must be given frequently—e.g., three- or four-hourly—so as to maintain a constant concentration of the drug in the blood.

Drugs which are absorbed and excreted slowly can be given less frequently. Digitalis, for instance, is effective if given in one daily dose. It is traditional rather than essential to give slowly acting drugs in three divided doses daily.

Where it is desired to secure a rapid concentration of a drug in the body, in order that its therapeutic effect may be exerted as early as possible, large doses should be given over a short period, followed by considerably smaller maintenance doses. The sulphonamides are given in this way.

In the case of cumulative drugs, such as digitalis, where, for instance, large initial doses may be necessary in a case of auricular fibrillation, caution should be exercised in the administration of the maintenance dosage, or otherwise cumulative toxic effects may be produced.

Prescribing

Prescriptions were traditionally written in Latin, but it is now increasingly the practice to use English

following the introduction of English main titles for monographs in the B.P. 1953. The National Formulary 1955 reintroduced abbreviated Latin titles and, for this reason, abbreviated Latin names are given, where appropriate, in this book. Whatever the convention followed, it is most important that a prescription should not be ambiguous in any way so that the prescriber's intention may be carried out without difficulty.

It is preferable to use the Metric system of weights and measures wherever possible. There is, however, a large number of established drugs which are still prescribed in doses based on the Imperial system. The apothecary symbols which were formerly used in writing prescriptions should no longer be used. In this connection the British Pharmacopœia of 1932 made the following recommendation:

'In prescriptions the symbol ℥i is often used to represent 60 grains and also to represent 1 fluid drachm; and the symbol ʒi to represent 480 grains, sometimes 437·5 grains. Since these symbols are misleading prescribers should cease to employ them. Instead of them, solids should be prescribed in grains (gr.) and ounces (oz.), and liquids in minims (min.) and fluid ounces (fl. oz.). In order to avoid the possibility of confusion between gramme and grain, the symbol G. should be used in prescriptions as a contraction for gramme.'

Combination of Drugs in a Prescription

Prescriptions should be kept as simple as possible and nowadays it is seldom necessary for a preparation to be formulated in writing a prescription. Where this is necessary, however, care should be taken not to combine active drugs with other substances which will cause their deterioration.