THE

CHEMISTRY AND PHARMACY

OF

VEGETABLE DRUGS

Dealing with the derivation and properties of all the principal Vegetable Drugs.

By

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PREFACE

THIS book is especially designed to answer the many questions which must arise in the mind of those interested in pharmacy when making preliminary acquaintance with the numerous vegetable drugs and their galenical preparations. Thus, in the discussions of drugs of secondary importance, the items have frequently been grouped together so that, although the descriptions are individually inadequate, the reader is enabled to assess the value of the medicaments in relation to the more important drugs and thereby acquire a useful perspective knowledge of the vegetable series. The marshalling of so many separate accounts into a connected narrative has presented obvious difficulties, but every endeavour has been made to sustain the reader's interest by occasionally widening the field of view and thus introducing discussions which properly belong to subjects not ordinarily treated in a discourse professedly devoted to vegetable drugs. No allusions have been made to disturbances in the supply of commodities occasioned by the war, since such references, besides being of little avail, would, with the passage of time, lose their significance.

The present-day student of materia medica is called upon to assimilate an ever-increasing number of facts concerning newly discovered hormones and synthetic drugs, but it is important to realise that very few of the medicaments of vegetable origin have been thereby displaced, whence it is essential for the medical practitioner and the pharmacist to acquire detailed knowledge concerning them. If this volume helps to this end it will have achieved its purpose.

In writing this work the British Pharmaceutical Codex has been of great value as a source of information concerning the less common drugs. The author desires to express his thanks to Mr. T. E. Wallis, B.Sc., F.I.C., Ph.C., for kindly lending the original photographs for Figures 1, 2, 5, and 6, and to Mr. A. I. Robinson, Ph.C., for the remaining illustrations in the chapter on opium, all of which are reproduced by courtesy of the Editor of *The Pharmaceutical Journal*. All the other photographic illustrations were taken in the laboratories and warehouses of The British Drug Houses Ltd., by kind permission of the Directors, while the author is indebted to his assistant, Mr. A. H. Abbott, B.Sc., A.I.C., for help in reading the proofs and for compiling the index. Finally, the author is particularly desirous to record his grateful thanks to Mr. R. R. Bennett, B.Sc., F.I.C., a Director of The British Drug Houses Ltd., and a Member of the British Pharmacopœia Commission, for his very kindly interest and valuable advice.

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THE CHEMISTRY AND PHARMACY OF VEGETABLE DRUGS

Chapter I

CLASSIFICATION : GALENICALS : TESTS

IN the following pages it is proposed to describe medicaments occurring in the vegetable kingdom in contradistinction to medicines of mineral or animal origin and to organic drugs prepared synthetically in the laboratory. Plants which are cultivated in various parts of the world for their value as drugs owe their medicinal properties to particular constituents, to which the general term "active principle" is applied. Many of these active principles are extremely complex substances and their precise chemical nature is not yet known; but even in those cases where the constitution of the important ingredient has been discovered, it is still generally more convenient to use the product prepared by nature rather than to employ an active ingredient prepared synthetically. However, the alternative procedure of administering the isolated active principle in preference to an extract of the whole plant is often adopted.

CLASSIFICATION

In order to present a coherent account of a large number of individual products some attempt at systematic grouping is essential and in the case of vegetable drugs there would appear to be three possibilities: namely, division according to their botanical classification; the chemical nature of their active principles; or their therapeutic action.

Of these alternatives, the most precise is the botanical, and the whole assemblage might be grouped according to the natural orders to which they severally belong, but, notwithstanding its scientific basis, the method is not well suited for the purpose of presenting the subject from the practical standpoint. Thus, most vegetable drugs as met with in commerce only consist of one portion of the plant, such as the root, leaf or seed whence its taxonomical characteristics are not apparent. Again, drugs belonging to the same natural order often have nothing else in common by which they can be associated; for example, under the Leguminosæ one finds products so different, both chemically and therapeutically, as senna, liquorice, Calabar beans and cutch.

The grouping of drugs according to the chemical nature of their active principles is much more helpful to the student of practical pharmacy and, so far as its limitations allow, the method has been adopted in compiling this book. However, although many of the most valuable drugs have been subjected to exhaustive chemical investigation and the nature of their physiologically active constituents is well understood, there still remains a considerable number of vegetable medicaments, mostly of secondary importance but nevertheless of real value and quite extensively employed, which have not been sufficiently well examined to justify accurate chemical description.

On first consideration it might be thought that vegetable drugs could, after all, be most conveniently grouped according to their therapeutic applications, but even this method, notwithstanding its simple practical basis, is not completely satisfactory. The main difficulty attaching to this scheme lies in the fact that many of the most important drugs are employed for several different purposes : thus belladonna, according to the manner in which it is administered, behaves as an intestinal sedative, as an external anodyne or as an agent for temporarily enlarging the pupils ; again, cinchona, besides being the most important agent known to mankind for the control of malaria, is also a useful bitter tonic. On the other hand, a therapeutic classification is well suited as an aid for describing drugs which, generally, are only used for one specific purpose, and it has been adopted in this book as an adjunct to the chemical grouping. While many of the drugs discussed under a therapeutic heading may be regarded as of minor importance, this is by no means always the case, and the reader is asked to remember that, as no systematic scheme can be followed throughout, the various items are grouped in the manner which is most likely to assist in their study.

Chemical Classification

Vegetable drugs containing physiologically active principles which are referable to the chemical group known as alkaloids are by far the most important. These substances are nitrogenous bases which occur in plants combined with acids as salts and they are called alkaloids in allusion to their alkaline character. Most alkaloids are complex compounds containing carbon, hydrogen, nitrogen and generally, although not always, oxygen, and many of them have been determined chemically to be derivatives of one or other of three aromatic bases, namely, pyridine, quinoline and isoquinoline, all of which occur in coal-tar. More than two hundred vegetable alkaloids have been characterised, but only a fraction of these are employed medicinally, and many plants which have been shown to contain one or more of these bases are not used as drugs. In order to emphasise the important role which these bodies play in therapeutic science, it is only necessary to state that such products as

opium, cinchona, belladonna and ipecacuanha owe their medicinal worth to the alkaloids which they contain. General information concerning the principal alkaloidal drugs is given in Table I, and the next

TABLE I—DRUGS CONTAINING ALKALOIDS

Name	*Part of Plant Employed*	*Name of Principal Alkaloid*	*Approximate Percentage of Principal Alkaloid Present*	*Physiological Action*
Aconite ..	Root	Aconitine ..	0·2 to 0·8	Febrifuge (i.e., anti-fever).
Areca ..	Seed	Arecoline ..	—	Vermifuge (i.e., anti-worm).
Belladonna	Leaf	Hyoscyamine	0·4	Antispasmodic sedative, etc.
	Root	ditto ..	0·5 to 0·8	ditto.
Calabar bean	Seed	Physostigmine	0·15 to 0·3	Myotic.
Calumba ..	Root	Calumbamine Palmatine Jateorhizine	—	Bitter.
Cinchona ..	Bark	Quinine .. Cinchonine	3 to 5	Bitter and tonic, etc.
Coca ..	Leaf	Cocaine ..	0·1 to 1	Local anæsthetic (isolated alkaloid used).
Colchicum ..	Corm .. .. Seed	Colchicine .. ditto ..	0·3 0·5	Gout specific. ditto.
Conium ..	Leaf .. .. Fruit	Coniine ..	0·1 0·5 to 1	Sedative and antispasmodic.
Ephedra ..	Leaf and stem	Ephedrine ..	0·7	Sedative for asthma.
Ergot ..	Sclerotium ..	Ergometrine .. Ergotoxine ..	0·002 to 0·035 0·02 to 0·2	Arrests hæmorrhage.
Hydrastis ..	Rhizome ..	Hydrastine ..	2	Arrests hæmorrhage.
Hyoscyamus	Leaf	Hyoscyamine Hyoscine	0·08	Sedative.
Ipecacuanha	Root	Emetine ..	1·7	Expectorant and emetic.
Jaborandi ..	Leaf	Pilocarpine ..	0·5	Diaphoretic (i.e., producing perspiration).
Gelsemium ..	Root	Gelsemine ..	—	Nerve sedative.
Lobelia ..	Leaf and stem	Lobeline ..	—	Antispasmodic.

TABLE I—DRUGS CONTAINING ALKALOIDS—*continued.*

Name	*Part of Plant Employed*	*Name of Principal Alkaloid*	*Approximate Percentage of Principal Alkaloid Present*	*Physiological Action*
Nux vomica	Seed	Strychnine ..	1·2	Tonic.
Opium ..	Latex ..	Morphine ..	11	Narcotic and sedative.
		Codeine ..	1·5	
Pomegranate	Bark	Pelletierine ..	0·2	Anthelmintic (i.e., tending to expel intestinal worms).
Stavesacre ..	Seed	Delphinine ..	1	Destroys pediculi.
		Delphisine		
Stramonium	Leaf	Hyoscyamine	0·2 to 0·4	Antispasmodic.

eight chapters of this book are devoted to an account of such of these as conveniently conform to a chemical classification.

Another highly important group of active principles characterising certain vegetable drugs are known as glucosides. These compounds are distinguished by their property of undergoing decomposition in the presence of dilute mineral acids, or of certain enzymes, with the formation of a sugar and a residual substance of varying complexity. As an example, mention may be made of salicin, which occurs in willow bark : in aqueous solution this substance is hydrolysed by the enzyme emulsin, dextrose and saligenin being produced. The hydrolysing enzymes usually exist in the same parts of the plants as the glucosides, but the latter are not decomposed under natural conditions, because the glucosides and the enzymes are situated in separate cells and are thus kept apart by the walls of the cellular tissue. One of the most important drugs in this class is digitalis, or foxglove. The leaves of this plant contain complicated glucosides characterised by their property of stimulating the action of the heart, and thus it is invaluable to the physician in treating cases of cardiac failure.

Certain glucosides, when hydrolysed by means of dilute mineral acid or an enzyme, yield hydrocyanic acid (prussic acid) as one of the products of decomposition: thus, amygdalin, which occurs in bitter almonds, gives rise to hydrocyanic acid, dextrose and benzaldehyde. In small doses hydrocyanic acid is a useful digestive stimulant, and a group of vegetable products containing this particular type of glucoside are discussed together in this book under the heading of Cyanogenetic Drugs.

There is yet another class of glucosides of some importance in pharmacy known as the saponins. These substances form a soap-like froth when

shaken with water, and even extremely dilute solutions exhibit the phenomenon after being vigorously agitated. The saponins are powerful protoplasmic poisons and many are strongly sternutatory; on hydrolysis they yield various sugars, together with non-toxic compounds termed sapogenins. A separate chapter is devoted to a description of the more important vegetable drugs which owe their value to the saponins they contain.

The purgative drugs—cascara sagrada, frangula, rhubarb, senna and aloes—all contain principles which are closely allied in chemical constitution and are known as the emodins. These substances are chemical derivatives of anthraquinone which, in turn, is formed by the oxidation of anthracene, a hydrocarbon which occurs in the last portion of the distillate from coal-tar. The emodin of senna is trihydroxymethyl-anthraquinone, while that of rhubarb is dihydroxymethyl-anthraquinone, this latter substance being termed chrysophanic acid. The characteristic emodin of aloes, tetrahydroxymethyl-anthraquinone, or barbaloin, is known to exist in the plant as a glucoside, being combined with the sugar arabinose.

A large number of vegetable drugs contain physiologically active resins, and among these the most important are the purgatives, jalap, podophyllum and scammony root. Resins occur as solid, amorphous and generally vitreous masses having a conchoidal fracture and are insoluble in water and acids, but soluble in alcohol, ether and oil of turpentine. They dissolve in alkalis to form compounds of the nature of soap, being, with certain exceptions, again precipitated from the aqueous solutions of these on the addition of mineral acids.

The active constituents of a number of astringent vegetable drugs are referable to the tannins which is a generic name given to the naturally occurring derivatives of poly-hydroxybenzoic acids. Some tannins appear to contain derivatives of catechol, and are termed phlobo-tannins in contradistinction to those tannins originating from pyrogallol. Phlobotannins are characterised by the readiness with which they yield a red precipitate of phlobophane when their aqueous solutions are boiled with hydrochloric acid.

Therapeutic Classification

As already indicated, certain important drugs which are employed for one specific and well-defined purpose will be described under a therapeutic heading, even though the chemical nature of the active principle may be known. Thus, considering the drugs listed in Table I, it is more convenient for the purposes of study to include areca and pomegranate bark in a chapter devoted to a description of medicaments used for the expulsion of parasitic worms rather than endeavour to associate them with those containing alkaloids. Again, although the active principles of calumba are alkaloidal in chemical nature, it is more

usual to regard it as an important member of the group known as bitters, thus linking it with gentian, which owes its therapeutic value to the glucosides which it contains.

Again, the therapeutic classification is more convenient for those vegetable drugs employed as carminatives since the volatile oils upon which the action of most of them depend differ widely in chemical nature. Another objection to presenting a chemical grouping of the carminative drugs arises in the case of ginger which, although a highly important member of the series, owes its activity not to its volatile oil but to a complex mixture of phenolic substances collectively termed gingerol.

As further examples which can only be classified on a therapeutic basis may be mentioned such chemically diverse substances as mustard and capsicum which are both useful rubefacients. Among expectorants, ipecacuanha and squill are probably the most important, but as both these drugs are of great value for other purposes they have been described in relation to the chemical character of their active constituents, while a separate chapter is devoted to an account of the numerous other vegetable substances which are similarly employed for the stimulation of the respiratory tract. Finally, it may be remarked that so little is known concerning the chemistry of many minor vegetable drugs that a rational chemical classification of them would be impossible.

THE PREPARATION OF GALENICALS

It has already been observed that vegetable drugs as sold in commerce usually consist of some particular part separated from the whole plant such as the root, leaf, bark or whatever portion has been found by experience to possess therapeutic value in greatest degree. Some important drugs consist of juices or other exudations, but whatever the original substance may be it is necessary that it should be reduced to some form convenient for administration as a medicine. Occasionally the dried and powdered drug can be used, but more generally it is necessary to prepare an extract with some suitable solvent. The selection of the solvent is important, and the choice should be so made that the preparation contains the maximum amount of active principle coincident with the minimum proportion of physiologically inert material. The preparations so made are termed galenicals, and the manufacture of most of these follow general principles.

Methods of Powdering Drugs

After the plant material has been dried it is usually necessary, except in the case of soft exudations, to reduce it to powder before the galenicals can be made. For small-scale work an iron mortar and pestle is usually all that is required, but for manufacturing purposes various types of grinding mills have been devised. Mention may be made of the ball mill which consists

of a hollow cylindrical vessel horizontally mounted on bearings. This cylinder, made of unglazed porcelain or steel, is charged with the drug to be ground together with several balls also made of porcelain or steel; on being rotated by motor power the drug is gradually reduced to a fine powder.

Another type of mill is known as the end-runner and consists of a mechanically revolving mortar containing a pestle mounted on a vertical shaft and free to revolve by friction with the sides of the mortar (Fig. 1).

Fig. 1.—A SMALL END-RUNNER MILL USED FOR GRINDING SAMPLES OF DRUGS PREPARATORY TO THEIR ANALYSIS

Yet another type of mill called the edge-runner consists of two heavy wheel-shaped granite stones which are connected to a common axle and run on a shallow stationary granite bed. When the central shaft is made to revolve by a power motor the two granite rollers are moved with it and run on the bed and over any drug placed in their path. The motion of the stones forces the drug out on either side of the track, but it is brought back into the path of the stones by scrapers revolving on the same axis (Fig. 2).

In preparing galenicals the fineness of the powder is important, and it is therefore necessary to pass the material through standardised sieves as shown in Fig. 3.

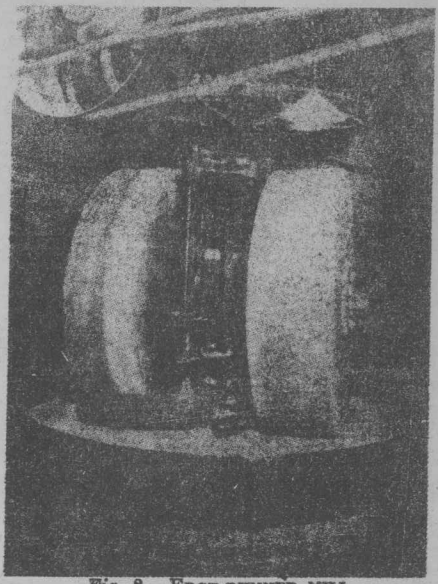

Fig. 2.—EDGE-RUNNER MILL
Each revolving stone weighs about 2½ tons.

Liquid Extracts

An extract is a preparation made by separating the soluble matter of the vegetable tissues by means of water or alcohol, or a mixture of the two. It is usually prepared by moistening the dried and powdered drug with the appropriate solvent and then packing the mixture into a percolator. When the liquid commences to pass through, the lower orifice of the percolator is closed, and the drug is allowed to macerate (soak) for a specified time, after which percolation is continued until the drug is exhausted. The percolate is then evaporated to a suitable volume and filtered. If water has been employed for the extraction, alcohol must be added to the final product in order to arrest fermentation.

Fig. 3.—SIFTING POWDERED LIQUORICE ROOT WITH THE AID OF A MECHANICAL SIEVE
The tray carrying the sieves is suspended on steel straps and oscillated by means of a power-driven eccentric.

Some liquid extracts are standardised by chemical analysis so that they shall contain a specified percentage of the active principle of the drug. When this is not possible, 1000 millilitres of the extract is made from 1000 grammes of air-dried drug; one fluid part of such a preparation should contain the active principles of one part by weight of the drug and it is known as a "one-in-one" extract.

Fig. 4.—A LARGE SIZE PERCOLATOR USED FOR MAKING LIQUID EXTRACTS AND TINCTURES
This percolator holds 500 lb. of powdered drug.

When making liquid extracts of drugs which are not easily exhausted, the first part of the percolate is reserved and the latter part evaporated to the consistency of a paste, which is then dissolved in the reserved portion and the liquid extract finally adjusted to the required volume. Sometimes this practice is necessary in order to avoid loss of active principles when evaporating the percolate. The first part of the percolate always contains the major portion of the active principle, so that it is sometimes advisable to set this aside and only submit the later portions of the percolate to the action of heat.

A deposit of colouring matter and inert substances always separates from freshly made liquid extracts, and it is therefore necessary that they should be set aside for some time and then filtered.

Dry Extracts

These preparations find a wide application in the manufacture of pills. They occur as dry free-running powders or granules. The preliminary percolation of the drug is conducted in the same manner as when making liquid extracts, but the evaporation of the liquor is continued until a little taken out of the pan and cooled on a slab is found to be of the desired consistency. While the extract is hot, bubbles of water vapour will rise to the surface, forming a froth which may be removed by skimming ; the extract beneath the scum will be smooth and bright.

When cold, the hard extract is removed, usually by momentarily heating again to soften the outer layer of extract in contact with the pan, and then pulverised.

It is frequently necessary to evaporate the liquors under reduced pressure in order that the temperature shall not rise so high that the active principles are destroyed. For this purpose, vacuum stills with removable heads are employed. When evaporation is conducted under reduced pressure it is often advantageous suddenly to increase the vacuum towards the end of the operation ; this causes the extract to froth vigorously, and when in this condition the last traces of water are readily removed.

Tinctures

A tincture is an alcoholic solution of the soluble matter of a drug. Tinctures often contain the extractive material of more than one drug and they are then termed compound tinctures. They are much weaker preparations than the extracts and find a wide application, since the appropriate dose, being relatively large, is easily measured. The method of preparing tinctures varies with the character of the drug, some being made by maceration, some by percolation and others by diluting liquid extracts or dissolving solid extracts in alcohol of the appropriate strength.

To prepare a tincture by maceration the powdered drug is mixed with the whole of the solvent, and after standing with occasional shaking for a week the liquid is strained off. The solid material which remains, termed the marc, is then pressed and the liquid thus obtained is added to the bulk of the tincture, which is clarified by subsidence or filtration.

If the percolation process is used, the powdered drug is well moistened with the menstruum, and after about 4 hours the mixture is packed in a percolator and more solvent added. When the solvent commences to drop from the percolator the outlet is closed and sufficient menstruum is added to leave a layer above the drug. After macerating thus for 24 hours, percolation is continued until three-fourths of the volume required has been collected. The marc is then transferred to a press (Fig. 5) and the expressed liquid added to the original percolate and the mixture diluted to the required volume and clarified. Since the tissues of vegetable drugs expand when moistened with water or alcohol, it is important that only wetted material should be introduced into the percolator.

Fig. 5.—HYDRAULIC PRESS FOR RECOVERING RESIDUAL LIQUID FROM MARCS

Fresh Infusions

There are two kinds of infusions, known as fresh and concentrated. A fresh infusion is made by pouring upon the drug cold or boiling water, and at the expiration of 15 or 30 minutes straining off the resulting liquid. The drug may be either powdered or broken into small pieces according to its character. The marc is not pressed after the clear liquid has been strained off. Fresh infusions must be used within 12 hours from the time of their preparation. Special pots, containing a perforated cup to hold the drug, are employed for preparing infusions. This cup is suspended in the upper part of the pot and as the water becomes charged with the extractive matter it sinks and the drug is constantly exposed to fresh portions of less saturated liquid.

Concentrated Infusions

Concentrated infusions, which are used for the extemporaneous preparation of ordinary infusions, are approximately eight times stronger

than their corresponding fresh infusions. The name "infusion" as applied to these preparations is not quite accurate, since they all contain alcohol added as a preservative. They are prepared either by maceration or percolation on principles similar to those adopted in making liquid extracts.

Decoctions

These preparations are made by mixing the drug in coarse powder or small pieces with cold water, heating the mixture until the water boils, and allowing to simmer gently for a prescribed time varying from 10 to 30 minutes. After cooling, the liquid is strained and diluted to the desired volume.

Other Pharmaceutical Preparations

There are other pharmaceutical preparations especially applicable to individual drugs which will be mentioned in the more detailed account which is to follow.

PHARMACOPŒIAS

It will readily be understood that consignments of drugs of plant origin are liable to vary considerably in quality. They are subject to the influence of climatic conditions and the quality of the soil in which they are grown. Furthermore, there is always the possibility of spurious material, similar in outward appearance, being offered for sale. These contingencies have to be carefully guarded against by manufacturing chemists dealing with these commodities. Again, it is most important that physicians should be assured that the galenicals which they prescribe shall be

Fig. 6.—DETERMINATION OF THE ASH FOR JUDGING QUALITY OF VEGETABLE DRUGS (1)
A quantity of an air-dried drug is first weighed.

prepared to known standards of strength. This uniformity is achieved by the publication in all civilised countries of pharmacopœias. In these books, standards are defined as to the quality of raw drugs and the strength of galenicals. As certain drugs become obsolete and new remedies are discovered, the pharmacopœias become out of date, and it is therefore necessary to issue fresh standards to suit the changed conditions.

The present British Pharmacopœia was published under the direction of the General Medical Council and is dated 1932. Great care is essential in preparing a book of this character, since it is necessary to consult the highest authorities on medicine, pharmacology, pharmacognosy, pharmacy and chemistry. The British Pharmacopœia 1932 occupies 713 closely printed pages and was produced by the Pharmacopœia Commission, consisting of seven members and a secretary, with the assistance of six sub-committees. Wherever possible, definite standards of quality are fixed and methods of chemical analysis are described. Every test and every statement has been the subject of careful discussion. In order to keep abreast of recent advances in medicine, pharmacy and chemistry and to meet changing conditions of supply five Addenda to the Pharmacopœia have been published.

Fig. 7.—DETERMINATION OF THE ASH (2)
The ash is burnt over a bunsen burner until all the organic material has been completely burnt away.

GENERAL TESTS FOR CRUDE DRUGS

In judging the quality of vegetable drugs, it is often useful to apply certain empirical tests, such as the determination of the percentage of residue left after incineration (the ash), and the percentage of extractive material yielded to alcohol or water. General appearance and botanical characteristics must also be considered, and in the case of powdered drugs of all kinds, a microscopical examination of the histological elements is important in order to detect possible adulteration with foreign material; this work demands considerable patience