Textbook of Organic Medicinal and Pharmaceutical Chemistry

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Preface

In this textbook, it is our purpose to describe, within certain chemical and pharmacologic classification, those substances used as pharmaceutic aids and as therapeutic agents. For several years, there has been a need for a textbook which would present the necessary information on organic pharmaceuticals at the undergraduate level. This volume is written for the undergraduate pharmacy student who previously has completed a regular year's course in the fundamentals of organic chemistry. The information assembled is that which is thought to be of practical value to present-day pharmacists, since it now is understood quite generally that a pharmacist should have a thorough knowledge of what a drug is, its limitations, applications, forms and uses, as well as of those characteristics which pertain strictly to its compounding.

Products used in medicine and in pharmacy have been divided, in the main, on the basis of their chemical constitution. However, since many pharmacists and teachers of pharmacists classify medicinals by pharmacologic action, some of the chapters have been prepared with this in mind. Some of these are Amines Having Parasympathomimetic Activity, Histamine and Antihistaminic Agents, Antimalarials, Amines and Amides Having Local Anesthetic Activity and Amines and Amides with Analgesic Action. As each class of organic compounds is introduced, there is a discussion of the basic principles of organic chemistry, which serves to orient the student and provide a review. Since certain terms are used in pharmacy to identify groups of pharmaceuticals, there are chapters such as Sulfur and Phosphorus Compounds, Compounds Containing Metals, Dyes, Surface-Active Agents, Antibiotics and Vitamins.

To bring about a better understanding of why certain organic compounds have been selected as pharmaceuticals and to impress on the student the importance of physical properties, a chapter was written on Physiochemical Properties in Relation to Biologic Action. Usually, the chemical properties of a compound are responsible for the method of detoxication in the body. It is desirable for the pharmacist to be aware of the mechanisms used by the body for disposing of pharmaceuticals, as this leads to increased understanding of the applications of drugs.

A modified chemical classification has been used in this textbook for two principal reasons. First of all, a course in pharmaceutical chemistry is offered most often in the junior year, following the course in organic chemistry and preceding a course in pharmacology. A complete pharmacology outline seemed illogical inasmuch as the students are less familiar with this field. Secondly, by studying the chemistry and properties of a group of chemically related pharmaceuticals, it should be easier for a student, in later years, to evaluate a newly introduced pharmaceutical product. To aid in this evaluation, those compounds of the same chemical type which also exhibited similar pharmacologic properties are discussed in the same chapter. The total number of products used in medicine is enormous, and a pharmacist should understand the chemistry and the pharmacology of chemical groups or classes and not concentrate on each compound individually.

The authors of this book have attempted to include a discussion of all products described in the U.S.P. XV, N.F. X, New and Nonofficial Remedies 1955 and Accepted Dental Remedies 1955, as well as the most important pharmaceuticals reported in

the periodical literature. A compound is identified as "U.S.P." or "N.F." when it is accepted in the current edition of the official book (U.S.P. XV, N.F. X). Where a previous edition of an official book is indicated, the compound has been dropped from later editions. Due to the fact that an organic structure may contain two or more characteristic chemical groups and often elicits several pharmacologic actions, several pharmaceuticals offer more than one possibility for classification. An attempt has been made to describe them in the most logical division.

The more modern system of indicating configuration has been used where the small capital letters D and L correlate with D- and L- glyceraldehyde. It has been recommended that the optical rotation of a compound be indicated by dextro- or levo- or by (+) or (—); the use of *d*- and *l*- should be avoided. Racemic compounds may be designated by rac-, (±) or when configuration is known by DL. However, when both configuration and rotation are known, the expression may be D(—), D(+), L(—) or L(+).

List of references and of selected topics are included at the end of each chapter.

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Introduction

The turn of the century has seen the development of most of the organic medicinal agents, a great majority of which have been produced in the past twenty years.

Pure organic compounds, natural or synthetic, together with the so-called organometallics for the cure, mitigation or prevention of disease are the chief source of agents today. These remedial agents have had their origin in essentially three ways: (1) from naturally occurring materials of both plant and animal origin, (2) from the synthesis of organic compounds whose structures are closely related to those of naturally occurring compounds that have been shown to possess useful medicinal properties, and (3) from efforts of pure synthesis in which no attempt has been made to pattern after a known, naturally occurring compound exhibiting some activity. Many of the compounds from the first group are prepared synthetically today as a financially expedient measure. Examples of these are most of the vitamins, some sex hormones, corticometric principles, camphor and menthol. On the other hand, cardiac glycosides, quinine, atropine, penicillin, streptomycin, and epinephrine, either cannot be synthesized or can be isolated from natural sources at a cost that can compete with synthetic methods. Examples of compounds found in the second group are the large numbers of sympathomimetic drugs and local anesthetics, antispasmodics, mydriatic and myotic drugs. Examples of the third group include the synthetic antimalarials, dyes, some analgesics, mercurials, arsenicals, phenols, barbiturates, and surface active agents.

Even though the isolation and synthesis of many active constituents from animal and plant sources have been accomplished, there are new problems yet to be solved. Some of these are the isolation, proof of structure and synthesis of the active constituent of the amorphous fraction of adrenal cortex extracts; and synthesis of vitamin B_{12}, the very active, antipernicious anemia factor found in liver. These accomplishments, together with others, will add to the present large number of useful organic medicinal compounds and bring about a more complete complement of drugs.

In many cases, at present, there is no simple and direct correlation between the activity of organic compounds and their chemical structure beyond the broad generalization that compounds similarly constituted may be expected to have similar activities. This is not always true, for often a fine shade of difference in chemical structure may lie between a very active compound on the one hand and a completely inactive one on the other or even one whose activity may be antagonistic to the original model. These last compounds have received intensive research attention in recent years and usually are referred to as metabolic antagonists. The very useful sulfa drugs were shown to be metabolic antagonists. These studies are useful to the biochemist and physiological chemist, and it is hoped that new and useful medicinal agents also will be developed as a result of the extension of these studies. In other cases, each member of a whole series of compounds more or less related in structure to one another may have some activity. This can well be illustrated by sympathomimetic drugs, which include a series of compounds from the simple 2-amino heptane to epinephrine. The fact that a series of compounds, the members of which are structurally related to one another, exhibits a similarity in activity does not preclude the possibility that some other compounds, unrelated structurally, can have similar activity. For example, anesthetic properties are present not only in the cocaine or procaine type of molecule but also are found in benzyl alcohol, quinine, nupercaine, phenacaine, plasmochin and other compounds. Nevertheless, a convenient method for the study of organic medicinal agents according to a hybrid chemical classification is, in part, a desirable method of approach, because it allows the student to familiarize himself with the chemical, physical and biochemical properties of such groups. It is well to remember that the chemical and physical, and now biochemical, properties of organic compounds are functions of their structures. Therefore, much can be gained by studying medicinal agents from a structural standpoint, noting the changes in activities that are affected by structural changes.

Sometimes the activity of a drug is chiefly dependent upon its physical and chemical properties, whereas in other instances the arrangement, position and size of the groups in a given molecule are also important and lead to a high degree of specificity. In the latter case, this high degree of specificity is usually associated with the mode of action of the drug, involving enzymes or enzyme systems.

As our knowledge of enzyme systems increases, so shall the development of more perfect organic drugs be made possible. Furthermore, this increased knowledge will help us to explain the mode of action of a number of valuable organic drugs now in use.

In order to appreciate and understand organic medicinal products more fully, the student should be well grounded in such fields as organic, physical, biologic and physiologic chemistry, bacteriology, physiology and zoology.

It is not possible in a textbook of reasonable size to include a complete discussion of all subjects mentioned. Furthermore, the inclusion of commercially available forms of the medicinal compounds per se or in combination are not considered because of their nonfundamental nature. The material presented here should provide a basis for a more detailed study of the scientific literature. It is hoped that the student will make use of some of the references for this purpose.

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