

MEDICINAL PLANT ALKALOIDS

An Introduction for Pharmacy Students

STEPHEN K. SIM

Associate Professor of Pharmacognosy
Faculty of Pharmacy
University of Toronto

Second Edition

UNIVERSITY OF TORONTO PRESS

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PREFACE TO THE SECOND EDITION

Among the medicinally useful constituents of plants, the alkaloids constitute an important group. In discussing the medicinal plant alkaloids as part of a phytochemically oriented course in pharmacognosy conducted by the author for students in Pharmacy, he was faced with the difficulty of recommending to the students a suitable reference book which would discuss, at an introductory level, the basic phytochemical aspects of the medicinally important alkaloids, particularly their properties in relation to their separation and isolation from the plant sources. Discussions of these aspects are of course to be found in the more advanced and comprehensive books on alkaloids or the special monographs on particular groups of alkaloids, as well as in various scientific journals. But these more comprehensive books and journals are generally beyond easy comprehension by undergraduate students who have not had a more elementary introduction to these subjects, and are, at any rate, rather voluminous.

The accounts and discussions given here attempt to summarize (a) the plant sources and fundamental properties of the medicinally important alkaloids, (b) the principles and certain useful methods for their separation and isolation from plant materials, and (c) some aspects of their biosynthesis. They are intended as an introduction to these aspects of the study of alkaloids, as a supplement to the relevant sections on the alkaloids in standard text-books of pharmaceutical subjects, and to provide a collateral background for related laboratory works. It is hoped that these introductory accounts may also serve to prepare the student for proceeding to independent and effective use of the more comprehensive literature on

these and other alkaloids.

Those alkaloids which are rather rarely used today for medicinal purposes have been omitted. On the other hand, a few alkaloids which are not medicinally useful but which occur in the same plant source as the medicinally useful ones or which serve to illustrate some phytochemical points are included.

Accounts of biosynthesis are confined to only four groups, namely, the Nicotiana alkaloids, the tropane alkaloids, the ergot alkaloids, and the opium alkaloids. These have been selected for discussion on the basis of their having relatively better-established experimental evidence, and on the basis of their suitability as examples for illustrating this aspect of the medicinal plant alkaloids.

Only brief indications of the principal pharmacological actions and uses are given for the purpose of relating these alkaloids to broad categories of their medicinal uses. The principal preparations in the United States Pharmacopeia, the National Formulary, the British Pharmacopoeia, and the British Pharmaceutical Codex, and a few pharmaceutical specialties are listed simply by name as examples of medicinal agents containing the alkaloids and some of their derivatives. Examples of pharmaceutical specialties are given by the names prevailing in Canada and/or the United States. Some of these preparations are not necessarily available in both countries. No exhaustive coverage is attempted for the plant sources, or for the chemical aspects, or for the medicinal preparations.

A preliminary edition was privately printed in 1964 for the use of Pharmacy students at the University of Toronto through the much appreciated

assistance of the Book Department of the University of Toronto Press. In this second edition, Chapter 7 is new. Chapters 2, 4 and 8 have been considerably revised and slightly expanded. The section on the biosynthesis of Nicotiana alkaloids in Chapter 3 has been entirely re-written. Editorial modifications and minor revisions have been made in all other chapters, and the literature references are now given at the end of each chapter.

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S. K. S.

Toronto,
July, 1965

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CHAPTER 1

INTRODUCTION

Thousands of plant species have been investigated with respect to their alkaloidal constituents. Hundreds of alkaloids have been chemically characterized, and many of these have been chemically synthesized. Most of the plant alkaloids possess in varying degrees pharmacological activities of one kind or another. However, a large number of the pharmacologically active alkaloids are not medicinally useful either because their activity is too feeble or because their toxicity is too marked. These considerations have in practice restricted the number of the medicinally useful alkaloids to a few scores or so. Those alkaloids which are pharmacologically or thereapeutically useful constitute a very important group of medicinal agents.

These introductory discussions will be largely confined to those alkaloids which are of current pharmacological or medicinal importance. A few alkaloids which are of little medicinal importance but which occur in the same plant species as the medicinally important ones and which affect the isolation and extraction of the latter are also discussed. The basic chemical aspects and properties of these alkaloids are discussed in relation to the plant sources from which they may be isolated.

It may be of interest to note that, while chemical synthesis has very largely replaced the plant source in the supply of a number of alkaloids for medicinal uses (e.g., ephedrine, quinine), in a number of other cases the plant sources continue to be the important raw material sources after chemical synthesis has been achieved, largely for economic reasons (e.g., reser-

pine, ergonovine, morphine).

It is also to be expected that from time to time fuller chemical and pharmacological studies of new as well as old alkaloids may result in the introduction of more alkaloids to medicinal use while the medicinal importance of some of the currently useful alkaloids may decrease as a result of the availability of better agents, natural or synthetic, for similar therapeutic purposes.

CHAPTER 2

ALKALOIDS - General Considerations

2.1 General Characteristics and Properties of Alkaloids

Since the isolation of morphine by Sertürner in 1817, there have been several hundred alkaloids isolated from various plants and the chemical constitutions for many of these have been elucidated. Total chemical synthesis has also been achieved for scores of these alkaloids, although in a number of these cases the biological source continues to be the most economical way of producing them. Thousands of different plant species have been investigated within the past two decades for alkaloidal constituents (18). However, only a relatively small number among all the known alkaloids are currently of importance from the therapeutic or pharmacological point of view.

The alkaloids have been traditionally treated as a group, and yet there has been no completely satisfactory definition of an alkaloid. This is so, because the term alkaloid is not a chemical designation but rather a name traditionally and conventionally accepted for a group of nitrogen-containing, basic substances from plants with rather widely different chemical constitutions. Nevertheless, there are several common features and attributes, which, to a greater or lesser degree, are associated with or possessed by the compounds commonly known as alkaloids. Among all the known alkaloids, cases of exceptions to one or more of these features can be cited. These features are as follows: (1) Alkaloids are more or less complex compounds produced by plants. (2) They contain nitrogen in the molecule. (3) Many, probably most, alkaloids are derived, in their biosynthesis, at

least partly from various amino acids as their direct precursors. (4) They are basic (alkaline) in reaction. (5) They are usually soluble in a number of immiscible organic solvents, but rather insoluble in water. (6) Many of them are precipitated by certain reagents. (7) A number of them give more or less characteristic colour reaction with certain reagents. (8) Most of them are susceptible to destruction by heat; a number of them undergo decomposition or degradation by exposure to air and/or light. (9) A great number of alkaloids show rather pronounced pharmacological actions on various organs and tissues of animals and humans.

In the following discussion of these properties, it will become obvious that these properties are of considerable practical importance in the course of extraction and isolation of alkaloids from plant materials and in the considerations of pharmaceutical production and formulation involving alkaloids.

1. Plant Source

Alkaloids occur in many different species in numerous genera and families of vascular plants as well as in certain species of fungi. It has been estimated that some fifteen per cent or more of all vascular plants contain alkaloids. A number of amines produced by animals (e.g., epinephrine) possess physical and chemical properties rather similar to those of alkaloids. By tradition and convention, these animal amines are generally not considered as alkaloids. The occurrence of alkaloids in different plant organs and tissues and their relationship to aspects of the physiology of the plants will be discussed in a later section.

2. Nitrogen in the Molecule

Alkaloids contain one or more nitrogen atoms in the molecule. A