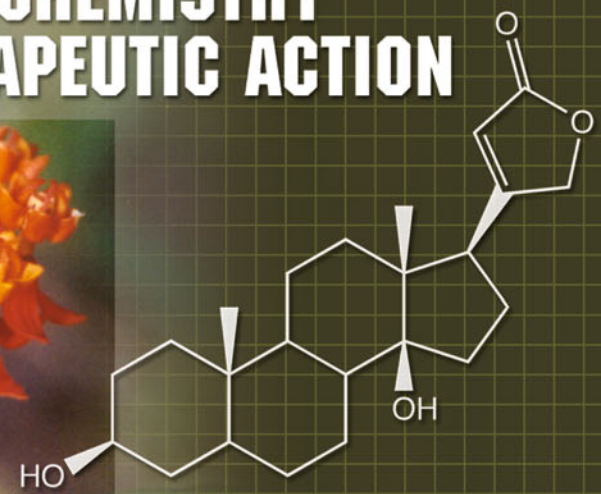
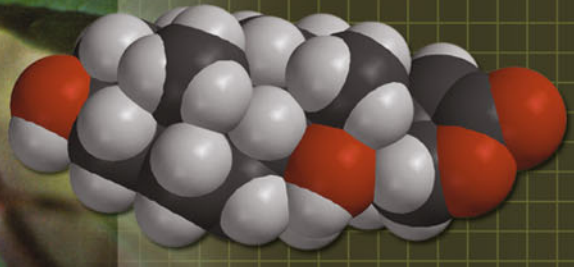
UNDERSTANDING MEDICINAL PLANTS

THEIR CHEMISTRY AND THERAPEUTIC ACTION





BRYAN A. HANSON, PhD

Understanding Medicinal Plants

Their Chemistry and Therapeutic Action

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AUTHOR'S NOTE
This book explains the chemical and pharmacological principles needed to understand how medicinal plants affect the human body. It has been written with the utmost care as to accuracy, but as an introductory work it is deliberately incomplete from a technical perspective. Although historical and current information about particular plants is given, this book is not intended as a guide to the use of medicinal plants. Before using any medicinal plant product, you should educate yourself about that particular plant and product in detail. Any information that you do not understand should be clarified before use of the product. Consultation with your regular physician or other trusted health care provider is strongly recommended. Neither the author nor the publisher is responsible for the consequences of the use or misuse of information contained in this work.

Originals of the woodcut illustrations were generously made available by the Lloyd Library and Museum, Cincinnati (www.lloydlibrary.org). Images were digitized by Celene Hawkins. Individual illustrations are shown with their sources.

Some figures were prepared using data from the Protein Data Bank (PDB), a government-funded depository of biomolecular data: Figure 4.7 is based upon PDB file 2AAI; Figure 4.9 is based upon PDB file 1BNA; and Figure 6.13 is based upon PDB file 1L0V. Figure 7.16 is based upon the model of Redinbo, Stewart, Kuhn, Champoux, and Hol (1998) published in *Science* 279: 1504-1513.

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ABOUT THE AUTHOR

Bryan Hanson, PhD, is the Julian Professor of Chemistry at DePauw University in Greencastle, Indiana, where he has taught for seventeen years. His advanced education includes a bachelor's degree in biochemistry from California State University, Los Angeles, and a PhD in chemistry from UCLA with a focus on the total synthesis of natural products. After two years of postdoctoral work with Jim White at Oregon State University, he began teaching at DePauw in 1986. Professor Hanson's research interests are in the areas of medicinal plants, natural products, and chemical ecology. His primary teaching responsibilities are in organic chemistry, biochemistry, and a course intended for nonscientists called "Medicinal Plants for Poets."

Preface

The idea for this book originated with a course I recently designed and began teaching called Medicinal Plants for Poets. The course is intended for nonscience majors, including those who are "science avoiders" and those who are taking the course only because someone *forced* them to take *something* in the sciences. When I first taught the course it was certainly a delight, but I discovered that no texts or books of any kind addressed the scientific material I wanted to cover and the audience that sat before me. Thus the idea for this work was born.

So exactly who is the audience for this book? Naturally, students in my course and similar courses are the prime audience; this book provides the necessary chemical background to support courses about medicinal plants that range in perspective from botanical to cultural and historical. And, naturally, people who want to know more about medicinal plants should read this book (and a lot of people who use medicinal plants should know more!). But what *kinds* of people might want to read this book? I believe that a wide range of people who are intrigued by science will find this book interesting—the kind of people with a natural curiosity that makes them always want to know a little more. If you regularly or even occasionally pick up a copy of *Scientific American* or *Discover* and read some of the articles, then you are probably going to enjoy this book. Because so many scientific disciplines contribute to our knowledge of medicinal plants, people who know a little about many fields, and especially those who enjoy drawing connections between different fields, are ideal readers of this book. If you consider a book that exercises your mind to be pleasure reading, then this is a book for you.

Writing this book was a great excuse to read more deeply on many interesting topics, and this has enriched me as a scientist. My own training is in organic chemistry and biochemistry, with some pharmacology thrown in on the side. Questions about nature have always interested me, and I find attractive the insights that these fields provide. I have chosen a career in teaching at a liberal arts college, where criti-

cal-thinking skills in varied contexts are emphasized. All of these aspects come together in this book; it's primarily a guide to thinking critically about medicinal plants.

Although this book is not intended as a consumers' guide by any means, once you have read this book you will be a lot more savvy about interpreting the claims you hear about medicinal plants and their actions on the human body. *Understanding Medicinal Plants* is not intended to be comprehensive but rather to convey some of the fundamental chemistry, biology, and pharmacology needed to understand the molecules in a medicinal plant and how they can affect your body. I try to get the basic information out there quickly and then explain why understanding a concept is important. As a check and reinforcement, I apply these concepts to actual cases. I want you to know what the important questions are and have some basic conceptual answers to these questions. I've carefully chosen some suggested readings and placed them at the end of selected sections for those of you who want to follow up on a particular topic.

Anytime one writes about a technical subject—especially one that touches on several scientific disciplines—the challenge is to balance rigor with readability. *Understanding Medicinal Plants* aims for the middle ground between a technical publication which assumes its reader is highly trained and a book for the popular press which oversimplifies the material. Although I have limited the depth of many topics, all of the information I have provided is factually sound, and I've tried to avoid simplifying in such a way that it misleads. What you learn in this book can safely be used as a basis for further learning, and I hope that's just what you'll do.

I've tried to draw out the beauty inherent in these complex topics in an accessible, user-friendly way. When you are done reading, I hope you will feel that I have achieved this goal. If the notion of beauty in complexity seems strange, consider the following quote from E. O. Wilson, a highly respected Harvard professor, champion of biodiversity preservation, and author of numerous books:

> The cutting edge of science is reductionism, the breaking apart of nature into its natural constituents. The very word, it is true, has a sterile and invasive ring, like a scalpel or catheter. Critics of science portray reductionism as an obsessional disorder. . . . Practicing scientists, whose business is to make verifiable discoveries, view reductionism in an entirely different way: It is the

> search strategy employed to find entry points into otherwise impenetrably complex systems. Complexity is what interests scientists in the end, not simplicity. Reductionism is the way to understand it. *The love of complexity without reductionism makes art; the love of complexity with reductionism makes science.*[1]

This *is* a book about science; in fact, it's about some of the most complex sciences working together to teach us about medicinal plants. If you don't already, I hope you will learn to love the pleasure of teasing understanding out of complexity, and be stimulated to dig deeper on various topics.

NOTE

1. Edward O. Wilson, *Consilience: The Unity of Knowledge* (New York: Knopf, 1998), p. 54, emphasis added.

Acknowledgments

Writing a book is a considerable undertaking that goes much more smoothly with the support of interested colleagues, as well as students who challenge you to make things just a little clearer. I am fortunate to know all sorts of helpful people, and thanks are due to several individuals. Early encouragement on the project was provided by my occasional collaborator Mike Flannery of the Lister Hill Library of Medicine at the University of Alabama at Birmingham. I am grateful to Dave Roberts of DePauw for his assistance in preparing quality space-filling style figures and to Robin DiRocco for assistance in preparing the bibliography. My son Keith Hanson selected the terms for the glossary and drafted the initial definitions. Keith, Kit Newkirk (a friend with a lifelong interest in medicinal plants), and Maureen Bonness (a fellow educator in the field of medicinal plants) carefully read drafts and provided much needed guidance. I am also thankful for the not-always-subtle feedback received from the students in several offerings of my Medicinal Plants for Poets class who used various drafts of the book along the way. Kyle Danforth, using his keen eye, undertook the tedious task of checking all of the chemical structures for accuracy. A great deal of research was necessary to provide the latest information, and Bizz Steele and Angie Battin of the interlibrary loan office at DePauw University were exceptional at locating and promptly providing the many references I sought. Other important resources were provided by the able staff of the Lloyd Library in Cincinnati. The Faculty Development Committee at DePauw provided both funding and time for the writing, which made reasonable progress possible. Finally, I greatly appreciate the helpful editors and staff at The Haworth Press. Thanks to all!

Chapter 1

Introduction

> Almost all aspects of life are engineered at the molecular level, and without understanding molecules we can only have a very sketchy understanding of life itself.
>
> Francis Crick

Interest in alternatives to modern medicine has never been higher than it is now, and a large part of that interest revolves around the use of medicinal plants. One can purchase a wide variety of herbal products at virtually any drugstore or all-purpose retailer. Television and magazine ads proclaim the virtues of garlic, ginkgo, and ginseng. You probably know people who regularly use herbal supplements, and you may have used them yourself.

If you have picked up this book and read this far, you are probably the kind of person who has, at one time or another, wondered exactly how drinking an herbal tea can help prevent cancer, or how taking *Echinacea* capsules can help you beat a cold.[1] Perhaps you have heard that red wine and dark chocolate can help prevent cardiovascular diseases such as heart attacks and strokes, and have wondered how such a wonderful thing is possible—though most people don't need excuses to enjoy wine and chocolate!

If so, then you are asking the very questions scientists ask, and how to think about these questions and understand the answers is the subject of this book. Let's look at a common example to illustrate what I mean. Almost certainly you have heard of the plant St. John's wort, which is recommended for the treatment of mild depression. Some of

Hypericum perforatum. (*Source:* Woodville, William. *Medical Botany* containing systematic and general descriptions, with pl.s of all the medicinal plants, indigenous and exotic, comprehended in the catalogues of the material medica; as published by the Royal College of Physicians of London and Edinburgh; accompanied with a circumstantial detail of their medicinal effects, and of the diseases in which they have been most successfully employed. London: printed and sold for the author by J. Phillips, 1790, Vol. 1, pl. no. 10.)

the questions you and scientists of various ilk might ask about this plant include the following:

- Does St. John's wort actually treat depression?
- How can I identify St. John's wort when I see it?
- What time of year should I collect the plant?
- What part of the plant should I collect?
- How much of the plant should I take, and how should I take it?
- What are the active ingredients in the plant?
- How do the active ingredients work?
- Can I overdose or poison myself by taking too much?
- Can the plant be dangerous if I'm pregnant or have high blood pressure?

The detailed answers to these questions would require the expertise of a number of different types of scientists:

- Physicians and statisticians would determine if the plant is actually effective in treating depression.
- Botanists would help with the identification of the plant.
- Pharmacologists and chemists would help determine what time of year and what plant part to collect, as well as help the physicians with dosage issues.
- Chemists would isolate and identify the active ingredients.
- Chemists, pharmacologists, physiologists, and perhaps molecular biologists would help us figure out how it works.
- Toxicologists and physicians could take this information one step further to help us understand whether the plant might poison us or have side effects.

As you can see, with all these "-ologists," the study of medicinal plants is a busy field (academics call it interdisciplinary). Still other scientific fields might be relevant: ethnobotanists and anthropologists to help interpret the medicinal plant knowledge of other cultures, pharmacognocists[2] who would contribute in a variety of ways, and so on.

I'm certainly not prepared to discuss all of these areas, but I point them out to illustrate the nature of medicinal plant investigations. In fact, the previous questions only scratch the surface, as St. John's

wort has other interesting properties besides being an antidepressant. Regarding its antidepressant activity, however, scientists are still not completely certain which molecule is responsible. For many years it was thought that the antidepressant activity of St. John's wort was due to a molecule called hypericin, though now other molecules are under consideration (see Figure 1.1). My point is that even after identifying hypericin (or anything else) as an active ingredient, scientists will have many more questions, such as how to analyze a plant or a pill for its hypericin content.

So this book is about *questions* about medicinal plants, particularly questions about what's in them and how they work—in other words, *understanding* medicinal plants. It is intended for nonscientists, and I have tried to write for this audience. I have tried to maintain rigor but keep the writing accessible through careful explanation and careful choice of examples. *Understanding Medicinal Plants* is not the place to find information about specific herbs for particular medical conditions; many books about that topic are already available. Rather, my goal is to provide a basic knowledge of the concepts and principles needed to understand what kinds of molecules are in a medicinal plant and how they exert their influence on the human body. This may be everything you want to learn about right now, but should you eventually want to investigate a particular plant further, you will have an excellent foundation so that you can ask the right kinds of questions, and understand the answers. Although this book is about how to think about and understand medicinal plants, what you will learn can be applied to any molecules used as drugs, whether they come from a plant, a fungus, a bacterium, or even a pharmaceutical company's laboratory.

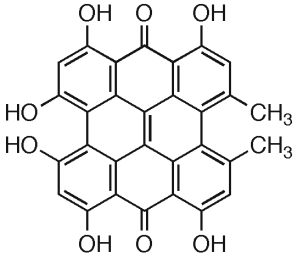

FIGURE 1.1. Hypericin, a molecule found in St. John's wort *(Hypericum perforatum).*

Understanding Medicinal Plants is organized as follows. In Chapter 2 we will learn to interpret the symbolism of chemical structures, such as the diagram of hypericin in Figure 1.1. These diagrams often scare people away from further reading on chemical topics, so it is well worth the time to try to demystify it. We will also talk about the naming of molecules and consider the enormous range of chemical structures that are possible.

In Chapter 3 we will look at just enough background on chemical bonding that we can begin to understand molecular properties such as the shape of a molecule. Shape turns out to be critical in understanding how a drug works on a molecular level, so we must have some appreciation of this area.

Chapter 4 is a catalog of sorts, in which examples of the different chemical families found in plants are given. This is good information to browse through at first and turn to later when more specific information on a particular family is needed (or it can be skipped entirely).

Chapter 5 looks at chemical behavior that is relevant to medicinal substances obtained from plants. We will examine acid-base behavior and such techniques as spectroscopy to see how they can be used to help isolate and identify substances from plants. Then we will turn to exploring the antioxidant properties of medicinal plants, which will bring us back to chocolate and red wine.

Chapter 6 discusses how plant drugs and toxins move through the body and act on specific molecules. We will first look at some general principles that affect how a drug is absorbed, distributed through the body, and eventually excreted in some form. We will then move to a molecular view of what happens once a drug reaches its final place of action (referred to as its target). Material covered in the earlier chapters will be essential to understanding these sections.

Finally, in Chapter 7, we will look at several case studies of medicinal plants and apply all we have learned to understand how these plants work. With the possible exception of Chapter 4, you'll probably want to read the chapters in order.

Before we launch into this material, however, I feel I would be misleading you if I didn't mention something about my beliefs about medicinal plants, because they color my approach to the topic. The word *beliefs* has a religious air about it and, indeed, many people believe that medicinal plants have some special, mystical properties because they are natural, or organic, or God given. For similar reasons, some

folks reject anything considered a "chemical" because they believe them to be fundamentally bad, or they reject mainstream medicines because they are synthetic. Indeed, we have much to learn about medicinal plants; in some cases whole herbs, as opposed to extracts or purified materials, *are* better. But is also true that nature contains many, many toxic substances, so we should not label plants and natural, herbal treatments as superior in all cases. Like it or not, virtually everything in the world is a chemical or is composed of chemicals. In fact, the entire point of this book is to help you think about these kinds of issues and use your knowledge effectively.

The eminent pharmacognocist Varro Tyler liked to point out that a great percentage of conventional modern medicines actually come from plants, and he argued convincingly that "rational herbal medicine is conventional medicine" (Robbers and Tyler, p. 15). In other words, while many people consider herbs to be alternative medicine, they really are quite conventional when you examine history and current practice. Tyler also identified ten criteria that are characteristic of what he called "paraherbalism," which he considered a pseudoscience. If the difference between rational herbalism and paraherbalism interests you, and I hope it does, be certain to see the introduction to his book *Herbs of Choice* for more information (details are given in the suggested reading).

I'd like to briefly emphasize one other concept that should be kept in mind at all times. The art of healing is complex and multifaceted. In any culture, healing practices are part psychological and symbolic, part physiological. Psychological and cultural influences on healing are fascinating topics and important to understanding the use of medicinal plants, both historic and modern. Much has been written on these topics, and I hope you have or will read some of the fine works available. In this book, however, the focus is on the physiological actions of medicinal plants. My hope for you, the reader, is that by learning some of the chemistry and pharmacology of medicinal plants, you can move toward a deeper understanding of how to evaluate what you hear about medicinal plants.

SUGGESTED READING

Balick, M. J. and Cox, P. A. (1997). *Plants, people, and culture: The science of ethnobotany.* New York: Scientific American Library. A very readable descrip-

tion about how plants affect culture, and how we Westerners "discover" medicinal plants.

Blumenthal, M., Goldberg, A. and Brinkmann, J. (eds.) (2000). *Herbal medicine: Expanded Commission E monographs.* Boston: Integrative Medicine Communications. This is an excellent source to begin digging into individual herbs on a more technical level.

Robbers, J. E. and Tyler, V. E. (1999). *Tyler's herbs of choice: The therapeutic use of phytomedicinals.* Binghamton, NY: The Haworth Herbal Press. One of the best books about what herbs to use for what conditions; also discusses paraherbalism and rational herbalism.

Sumner, J. (2000). *The natural history of medicinal plants.* Portland, OR: Timber Press. A potential companion to this book which presents a botanical/ecological perspective.