American Herbal Pharmacopoeia®

BOTANICAL PHARMACOGNOSY—

MICROSCOPIC CHARACTERIZATION OF BOTANICAL MEDICINES

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Coming together is a beginning. Keeping together is progress. Working together is success.

Henry Ford (1863–1947)

This text is dedicated to Paul Coates and Joseph Betz of the Office of Dietary Supplements (ODS), National Institutes of Health (NIH). They recognized the value of this work in helping to promote botanical microscopy as a quality assurance tool, provided funding, and expressed unrivaled patience in its completion. The text is also dedicated to

Professor Dr. Johannes Jurenitsch and Professor Dr. Wolfgang Kubelka of the Institute for Pharmacognosy, University of Vienna, Austria, who generously provided the technical resources and allowed Professor Dr. Reinhard Länger to develop all of the microscopic characterizations included in this work. This text would not have been possible without their vision, dedication to classical botanical pharmacognosy, and their generosity; and to

Professor Dr. Reinhard Länger, whose unrivaled skill and dedication to botanical microscopy has and will help to keep this important discipline alive for future generations.

FIGURE 1 Professor Dr. Wolfgang Kubelka (left), Prof. Dr. Reinhard Länger (center), Roy Upton (right). University of Vienna Botanical Excursion, Southern Tyrols, Italy (2000).

I do not need to expound at length the pleasure and delight that the knowledge of plants brings, since there is no one who does not know that there is nothing in life more pleasant and delightful than to wander through the woods, and over mountains and meadows, garlanded and adorned these varied, exquisite blossoms and herbs, and to gaze at them with keen eyes. This pleasure and delight is increased not a little if an understanding of their usefulness and powers is added. For there is as much pleasure and enjoyment in learning as in looking.

Leonhart Fuchs, 1542, De Historia Stirpium commentary insignes

FIGURE 2 Yarrow (*Achillea millefolium*); the signature plant of the University of Vienna. (From Woodville, W. *Medical Botany*. 1810.)

Georgina Jolliffe, BPharm, PhD, CChem, MRSC 1923–2010

To give pleasure to a single heart by a single act is better than a thousand heads bowing in prayer.

— Mahatma Gandhi

Dr. Georgina Jolliffe with her husband Dr. Geoffrey Jolliffe on Geoffrey's 80th birthday (2008).

Dr. Georgina Jolliffe, who served as a technical editor for this text, passed away before she could enjoy the fruits of her labor. According to her husband Geoffrey, Georgina worked on this text for the "sheer love of it." Georgina was fondly remembered by many students, friends, and family members as a kind and gentle soul whose academic excellence and achievements were equally matched by her personal kindness and generosity.

Dr. Jolliffe worked with AHP for a period of almost four years reviewing every aspect of the introductory chapters and providing detailed commentary on the more than 140 microscopic characterizations contained in the Atlas portion of the text. It is perhaps fitting that her last work will have been in the development of the first English-language botanical medicine text to unite classic illustrations of microscopic structures with modern microphotographs of the same structures and tissues. This work will help keep alive

one of her passions—botanical microscopy—at a time when worldwide it has been on a steady decline, and is once more on the rise. Georgina's academic excellence coupled with her practical experience was a great contribution to the text, and we are grateful that *Microscopic Characterization of Botanical Medicines* is a part of her legacy as she is now a part of the legacy of the American Herbal Pharmacopoeia.

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Foreword

American Herbal Pharmacopoeia: Botanical Pharmacognosy — Microscopic Characterization of Botanical Medicines provides an excellent historical treatment of botanical nomenclature, a review of the science of taxonomy, and strong arguments for the need, necessity, and ability to identify and standardize crude drug material. Scattered throughout the first ten chapters are numerous, excellent photomicrographs and line drawings of the microscopic features of whole and powdered drugs and photographs of whole crude materials. It is through this mechanism that the botanical nomenclature associated with plant analysis is primarily illustrated. The historical value and methodologies of this tome set the stage for the primary practical value of this book, i.e., that it provides detailed descriptions and microscopic elements of more than 135 species of widely used botanical dietary supplements and major pharmaceutical species. All of the descriptions of the included species are clearly and accurately described and the line drawings representing various microscopic features and photomicrographs are of high quality.

As one of four graduate students at the Massachusetts College of Pharmacy, it was an honor and privilege to know the now-deceased Heber W. Youngken, Sr., who taught us the elements described in this book in a course titled "Technical Microscopy." This book would have further extended my knowledge of crude drug identification if it was available at the time that I was a graduate student. I have always found that Roy Upton, the major driver for this work, has a long history of producing botanical monographs and his work and passion for botanicals has been clear, thorough, and accurate, which is exemplified in this textbook of botanical microscopy. It will soon become the major authority on the microscopic identification of crude botanical ingredients.

Norman R. Farnsworth, Ph.D., dr. hc (mult.)
UIC Distinguished Professor
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Foreword

Progress of science depends on progress in methodology.

The validity of the quotation above has been proven repeatedly during the last few decades, particularly by the development of chromatographic methods in plant sciences and pharmacognosy, from Tswett's simple column chromatography, to PC, TLC, GC, and HPLC, combined with MS and NMR. By means of these methods, new insights into the variety of secondary plant metabolites, almost inconceivable before, were obtained. Additionally, methods like DNA-analysis, aimed at the exploration of various –omics, nowadays seem to solve many problems.

However, a big mistake sometimes made by enthusiastic younger (or even more experienced) researchers is to proclaim the newest technologies as the "best," and to declare older methodologies as "classical" or "old-fashioned," and therefore no longer useful and valid. Only if a new method brings better solutions to an analytical problem should it replace its predecessors. This, for example, holds true for the replacement of paper-chromatography by modern chromatographic techniques—but it is definitely not valid for microscopy!

In the 1970s, I was a postdoc with Jack L. Beal and Raymond W. Doskotch at Ohio State University, where microscopy was no longer among the required courses for pharmacy students. This was very embarrassing for me! As a student of pharmacy at the University of Vienna I had fallen in love with the microscopy of herbal drugs. Not only did the microscope reveal an amazingly different world for me, it was also of enormous practical value. I was able to identify an unknown powder of a dried leaf, seed, or root, or even mixtures of plant materials, within a few minutes, a skill admired by botanists who could not imagine how this was possible. I came to understand why there was a disregard for microscopy in the US pharmacy curriculum when I visited US drug stores. In contrast to my home country of Austria, at that time there were almost no herbal drugs to be found among all the synthetic medications. Thus, of course, there was no need for pharmacy students and pharmacists to study and master microscopic analysis of herbal drugs.

Meanwhile, the wheel has turned almost completely around! Worldwide there is a dramatic increase in popularity and acceptance of herbal medicines, and the classical tools of the "traditional" pharmacognosist, in particular microscopy, are urgently needed for the assessment and quality control of plant products, be it crude herbal drugs, registered herbal medicinal products, over-the-counter herbal products, or health foods, all of which are used by large segments of the population for self-medication. While in the second half of the last century herbal medicines increasingly disappeared from pharmacopoeias, this trend is reversing as we enter the 21st century. Modern pharmacopoeias (e.g., the European Pharmacopoeia) offer new monographs on herbal drugs, including

their microscopic characterization, and the medicinal effects of new plants continue to be discovered. In contrast, there is a dramatic decline in the number of analysts capable of utilizing the advantages of microscopy!

Thus, when I first heard about the development of a text describing microscopic techniques and their application to herbal drug analysis, from the herb-enthusiastic director of the American Herbal Pharmacopoeia (AHP), Roy Upton, I was very excited about the project and immediately offered the collaboration of the Institute of Pharmacognosy, University of Vienna. In Vienna, the use of the microscope for pharmacognostical analysis is based on a longstanding tradition. Many notable pharmacognosists have worked here. Most notable among these are: Johann Adam Schmidt (1759-1809), the originator of the terms "pharmacognosis" and "pharmacodynamics," Carl Damian Schroff (1802-1887), Joseph Moeller (1848-1924), and August Emil Vogl (1833-1909). Vogl was the founder of microscopic investigation of foods and, when presented with the Hanbury medal, was described as the "Father of pharmacognosy." Vogl himself performed more than 50,000 microscopical examinations. Having studied pharmacognosy within this tradition, one of the authors of this work, Reinhard Länger, with his skill and dedication to botany and pharmacognosy, has helped to keep alive this vital discipline. Since there was no relevant modern text available in English, he enthusiastically agreed to contribute his microscopy skills both to the development of AHP monographs and to this text.

From simple practical instructions on how to conduct a microscopic analysis, particularly useful for beginners, to the selected 140 specific monographs of plant drugs on the market, there is an abundance of newly prepared photos and illustrations, altogether allowing an ideal access to the method itself and to solutions of specific problems arising with the identification of herbal drugs and their adulterations. Indeed, the book represents the passion and vitalism of traditional herbalists, combined with the scientific knowledge of academic pharmacognosists. In developing this text, the AHP and its director, Roy Upton, are helping to revitalize botanical microscopy as a unique, valuable, rapid, and cost-effective assessment tool.

Microscopy undoubtedly will, and rightfully should, be recognized for the important role it continues to play in the authentication and assessment of medicinal plants. Hopefully, AHP's microscopy text will encourage many people involved in practical plant drug analysis to once more make greater use of the microscope, and help experienced analysts solve their botanical authentication problems. It was a great pleasure and honor to collaborate with the AHP in bringing this work to fruition!

Professor Dr. Wolfgang Kubelka
Professor Emeritus
University of Vienna

Preface

The ox is slow but the earth is patient.

Ancient Chinese proverb

Almost 10 years in the making, the impetus for this text arose from a newfound and blossoming respect for the nearly departed but reemerging field of classical botanical pharmacognosy that has come to be embodied in the work of the American Herbal Pharmacopoeia® (AHP). Botanical pharmacognosy represents a focus on the botanical aspects of pharmacognosy whereby the plant and its growing habitat, harvesting, and processing conditions—rather than just the chemistry—are of central importance in ensuring the plant's medicinal efficacy. This is distinctly differentiated from modern pharmacognosy as it is typically represented in the West today.

In the former paradigm of classical botanical pharmacognosy, it is the quality of the plant, the environment in which it grew, and its myriad compounds and actions that are of utmost importance and most appropriate in the development of traditional herbal medicines that people worldwide rely upon in self-healing and traditional healing systems. In stark opposition, in modern pharmacognosy, it is the almost exclusive emphasis on the isolation of chemical compounds and specificity of an action that is centrally important for modern drug discovery and development, predominantly for commercial purposes. However, worldwide interest in traditional herbal medicines is reemerging precisely because modern drugs, whether synthetic or derived from nature, are failing to serve the health care needs of the people.

This text was developed because of the need for botanical quality assessment, which is the reason that a distinction between classical botanical and modern pharmacognosy is made. AHP's specific emphasis on botanical microscopy grew out of the fact that microscopic characterization was a cornerstone of the classical botanically descriptive discipline of nineteenth and early twentieth century pharmacognosy. So central was microscopy to pharmacognosy that Professor Norman Farnsworth, professor emeritus of the University of Illinois, Chicago, referred to microscopy as "pharmacy's unique contribution to science."

However, botanical microscopy is a dying art in North America and Europe, though it is alive and well in other, mostly developing nations. Our work in developing microscopic characterizations for AHP monographs as a fundamental identity test has underscored for us the value and importance of microscopy as a quality assessment tool. Thus, we embarked upon this project as our way of helping to preserve and reenergize this scientific discipline.

The practical genesis of this text came from discussions within the Standards Committee of the American Herbal Products Association (AHPA) on microscopy as an important analytical tool. There were suggestions to take some of our old out-of-print microscopy texts and put them into circulation once again. Concern was raised that a

number of the early microscopic characterizations were not developed from authentic specimens and were not representative of materials in trade, and that characterizations of many of the botanicals in use today were not available. Thus, it was determined that the most appropriate course of action was to begin the process of developing microscopic characterizations anew.

The technical genesis of this work evolved from original microscopy characterizations developed in the 1980s for the British Herbal Pharmacopoeia by Dr. Elizabeth Williamson, professor of pharmacy and director of practice at the School of Pharmacy, University of Reading, and formerly of the University of London School of Pharmacy. At the time, there were few texts in the modern English-language literature on microscopy, and many of the botanical ingredients used in modern herbal medicine were not included. Many of the texts also focused on powders and illustrations only and did not include cross-sections of relatively whole botanicals and photomicrograph images. Often, what was once available was out of print.

AHP was then introduced to Professor Dr. Reinhard Länger, currently of the Austrian Agency for Health and Food Safety (AGES), the Austrian equivalent of the Food and Drug Administration, and former lecturer in pharmacognosy at the Institute of Pharmacognosy of the University of Vienna. Dr. Williamson and Professor Länger are two of the leading experts on botanical microscopy in the West. AHP set out to gather botanically authenticated samples to replicate, confirm, and add to Dr. Williamson's earlier work, creating cross-sectional descriptions, illustrations, and photomicrographs. We gave particular emphasis to ensuring that characterizations were representative of the species and also gave emphasis to the differentiation between authentic plant specimens and potentially adulterating species. These two works were cross-referenced against each other as well as other works of botanical microscopy to ensure accuracy, consistency, and completeness. The culmination of this endeavor is the collection of microscopic characterizations presented in this text.

As interest in traditional herbal medicines grows, so does the need for the tools of classical botanical pharmacognosy. Alexander Tschirch (1856–1939), a noted pioneer in the early development of pharmacognosy and professor of pharmacognosy at the University of Bern, Switzerland, described pharmacognosy as a discipline that predated any of the branches of pharmacy. Tschirch described herbalists as the first pharmacognosists by virtue of their detailed examination and codification of medicinal plant knowledge. Thus, it is perhaps fitting that it is an *herbal pharmacopoeia* that gives emphasis to this wonderful art and science once again.

If any insult is visited upon pharmacognosists of today due to this text's overwhelming and highly biased emphasis on the botanical versus chemical or molecular aspects of modern pharmacognosy, the fault lies only with me and I offer my sincere apologies. This is our attempt to help in the revitalization of the *botanical* aspects of pharmacognosy and once again highlight the value of botanical microscopy as an important quality assurance tool, hopefully helping to bring this discipline full circle.

Roy Upton
Herbalist
Executive Director
Editor
American Herbal Pharmacopoeia®

Acknowledgments

Volunteers do not necessarily have the time; they just have the heart.

Elizabeth Andrew, author, ***On the Threshold: Home, Hardwood, and Holiness***

This work was a labor of many hands. Numerous individuals and organizations generously provided botanical samples, voucher specimens, editorial comments, and other forms of support and guidance to help make this the most comprehensive English-language work of botanical microscopy in the modern botanical pharmacognosy literature. On behalf of the authors, editors, and board of directors of AHP, we extend our sincerest thanks to those who have helped make this work one of the most seminal texts in the modern botanical microscopy literature and to return botanical microscopy to its rightful place as a valuable quality assessment tool.

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Many hands make light work.

John Heywood (1497–1580), English playwright and poet

Editor

Roy Upton, herbalist, has been working and practicing professionally as an herbalist since 1981. Trained in ayurvedic, Chinese, Caribbean, and Western herbal medicine traditions, Roy is the founder, executive director, and editor of the American Herbal Pharmacopoeia; is cofounder, past president, and current vice president of the American Herbalists Guild (AHG); and serves on the General Chapters Committee of the United States Pharmacopeia (USP) and botanical expert advisory committees of AOAC International, the American Botanical Council, and NSF International. Roy is visiting faculty for Tai Sophia (Laurel, Maryland) and lecturer for the Complementary and Alternative Medicine Program at the University of California School of Pharmacy (Los Angeles, California). Roy is also the staff herbalist for the California-based herbal supplements company Planetary Herbals and is a member of the Standards Committee of the American Herbal Products Association.

Technical Editors

Alison Graff, PhD, works as a biologist for the state of California and does private consulting in the field of rare plant conservation. From 2000 to 2006, she worked as monograph development coordinator and associate editor at AHP. Dr. Graff received her doctorate in plant ecology from Washington University and the Missouri Botanical Garden and has taught plant systematics and plant anatomy at the University of California. She worked tirelessly on facilitating the detailed editing and cross-referencing of all the microscopy descriptions, providing important contributions to a number of chapters and bringing this text to completion.

Georgina Jolliffe, BPharm, PhD, CChem, MRSC, was senior lecturer in pharmacognosy at Chelsea College (now King's College), University of London. Her interests focused on analytical work involving microscopy and chemical analysis. Her particular interest in chromatographic techniques and microscopic analysis also led to the teaching of

MSc courses in chemical analysis in the Department of Chemistry. From 1973 until her retirement, Dr. Jolliffe served on the Chromatography and Electrophoresis Group of the Analytical Division of the Royal Society of Chemistry as a committee member, vice chairman, and chairman.

Elizabeth Williamson, PhD, is a professor of pharmacy and director of practice of the School of Pharmacy, University of Reading, in the United Kingdom. She was formerly a senior lecturer in pharmacognosy at the School of Pharmacy, University of London. Dr. Williamson is editor-in-chief of *Phytotherapy Research;* a member of the Commissions of the British and European Pharmacopoeia, the Royal Pharmaceutical Society of Great Britain, the Phytochemical Society of Europe, and the Research Committee of the European Scientific Cooperative on Phytotherapy (ESCOP); and a fellow of the Linnaean Society of London. Dr. Williamson studied botanical microscopy under the noted microscopist Betty Jackson.

Contributing Editors

Wendy L. Applequist, PhD, received her PhD in botany, with a specialization in molecular systematics, from Iowa State University. She is currently an assistant curator at the Missouri Botanical Garden's William L. Brown Center, where she manages natural products discovery programs and provides botanical support to biomedical research projects dealing with medicinal plants. Dr. Applequist's research interests include quality control and sustainability of botanicals and the taxonomy of plant groups endemic to Madagascar; she is the author of *The Identification of Medicinal Plants: A Handbook of the Morphology of Botanicals in Commerce*.

Daniel Harder, PhD, is the former director of the University of California at Santa Cruz Arboretum and adjunct professor in the Department of Ecology and Evolutionary Biology at UC Santa Cruz. He obtained his BS degree in botany from the University of Wisconsin, Madison, and his PhD from the University of California, Berkeley. As director of the arboretum, he oversaw the maintenance of world-renowned collections of native plant species from Australia, New Zealand, and California and the Southern Hemisphere within a 100-acre botanical garden on the UCSC campus. Dr. Harder is an expert on plants of Asia and the Pacific Region and Africa and has published numerous papers on his research on the floras of Central Africa and Vietnam, including works on the pharmaceutical properties of plants, taxonomy, ethnobotany, and new species discoveries.

Amala Raman-Soumayanath, PhD, is an associate professor in the Department of Neurology at Oregon Health and Science University, Portland. She obtained her pharmacy degree in 1981 from Chelsea College (University of London) and registered as a pharmaceutical chemist in the United Kingdom in 1982. In 1987 she obtained her PhD from King's College, University of London, for research in drug metabolism and subsequently became senior lecturer in pharmacognosy in the Pharmacy Department, University of London. Dr. Soumayanath has been involved in course development and teaching of pharmacognosy, including microscopy, to pharmacy undergraduates. Her research covers

related areas such as phytochemistry, biological activities of natural products, and quality control issues and methods relevant to botanical products. Dr. Soumayanath's research has focused on investigating traditional plant remedies used in the treatment of vitiligo, psoriasis, and diabetes, both in terms of defining their modes of action and as sources of potential new therapeutic agents for these diseases.

Microscopic Characterizations

Professor Dr. Reinhard Länger studied pharmacy at the University of Vienna from 1978 to 1983. In 1986, he obtained his PhD with a thesis on the botanical systematics of the genus *Primula* in lower Austria and, in 1997, did his habilitation in pharmacognosy at the University of Vienna. Professor Dr. Länger remained at the University of Vienna as a lecturer of pharmacy and pharmacognosy until 2006, and specialized in the teaching of botanical microscopy, while also serving as the curator of the herbarium and herb garden. He currently serves as expert and assessor for herbal medicinal products at the Austrian Medicines Agency (AGES PharmMed), the Austrian counterpart of the U.S. FDA. Unless otherwise noted, all of the microscopy images in this text were done by Professor Dr. Länger.

Research Associate and AHP Administrator

Diana Eve Swisher, MA, received her BA degree in psychology from the University of California, Santa Cruz, and her MA degree from the Mt. Madonna Institute College of Ayurveda. Ms. Swisher has been a research associate and administrator for AHP since 1998 and works tirelessly at maintaining the organizational foundation of AHP.

About the American Herbal Pharmacopoeia

There is no higher religion than human service. To work for the common good is the greatest creed.

Albert Schweitzer (1875–1965)
German theologian, philosopher, physician, and winner of the Nobel Peace Prize, 1953

AMERICAN HERBAL PHARMACOPOEIA®

The American Herbal Pharmacopoeia (AHP) is very much a work for the common good. AHP was founded in 1995 as a nonprofit 501(c)(3) educational foundation dedicated to the advancement of knowledge and quality of medicinal herbal products and herbal dietary supplements. The purpose for doing this is to break down the many barriers and fears that prevent the complete integration of herbal medicines into our health care system and our lives. Humans and plants have coevolved for many millennia, and we believe that plant-based medicines are the most appropriate therapeutic agents for human use. Environmentally, plant-based medicines represent the only sustainable pharmacologically based form of medicine on the planet.

The societal acceptance of herbal medicine can justify preservation of wild and natural habitats for medicinal plant production and generation of local economies, can provide an alternative to the chemical degradation and pollution that occur from the manufacture of conventional pharmaceuticals, and, when done optimally, can help to build a new world. It is said that the only commodity that we cannot create more of is land, but farmers do it everyday—compost replenishes the earth and medicinal plant compost rules! This is the larger goal and vision of AHP—to cultivate a deeper relationship between humans and plants through health and medicine; we very much see this as a service to humankind.

On the practical, everyday level, AHP's primary role is to develop quality control monographs and authenticated reference materials for analytical work and to produce tools such as *Microscopic Characterization of Botanical Medicines* that can be used in the quality assessment of herbal products. AHP also conducts critical reviews of the available thera-

peutic and safety data that exist on herbal medicines. This latter information is presented in the "Therapeutic Compendium" portion of AHP monographs.

AHP monographs are considerably different from most pharmacopoeial monographs, which establish and provide guidelines for identification, purity, and minimal quality along with the appropriate tests for meeting these standards. There is much more to quality assessment of herbal medicines than compliance with a set of standards or concentration of an individual constituent. Rather, all aspects of harvest and processing of the plant can affect the quality of the finished product. One cannot *test* quality into a product. As the saying goes, "Garbage in—garbage out." The quality of a plant-based product begins with quality land and growing conditions, as well as careful harvest and processing throughout every step to the finished product.

Also, compliance with an individual compound alone cannot guarantee quality and, ultimately, efficacy. AHP monographs provide several bodies of information integral to the production of a quality botanical medicine encompassing both traditional and modern knowledge. When all of these bodies of information are utilized in conjunction with established pharmacopoeial standards, the likelihood for true quality and efficacy is greater than that for compliance with the standards alone.

In addition to the establishment of specific standards, AHP monographs are designed to reeducate those involved in all aspects of the herbal products industry to both gross and subtle techniques of herbal quality assessment. Doing it once in an AHP monograph means that 500 herbal companies do not have to duplicate the work.

The "Therapeutic Compendium" is designed to present a comprehensive and critical review of the available data on the efficacy and safety of the botanicals. As with the quality and standards portion of each monograph, the "Therapeutic Compendium" similarly encompasses the authoritative traditional knowledge that most commonly forms the basis of herbal medicine use worldwide, as well as critical reviews of the available modern clinical and pharmacological data. These reviews include all available data, taking into account the full range of evidence-based criteria from meta-analyses and controlled trials to the opinions of experts. Few other sources of information provide this level of comprehensiveness, and AHP monographs truly represent a review of the totality of publicly available information—a legal requirement of the Dietary Supplement Health and Education Act (DSHEA).

The desire of the AHP is for each monograph to have the highest degree of accuracy, comprehensiveness, and clinical usefulness attainable. This is accomplished by subjecting each monograph to a multidisciplinary review that includes some of the most experienced medicinal plant experts internationally and includes botanists, herbalists, chemists, pharmacologists, pharmacognosists, pharmacists, physicians, and toxicologists. As with all pharmacopoeias worldwide, people who are dedicated to the common good of creating an herbal knowledge base for present and future generations provide the majority of the work on a volunteer basis. For all the contributions made to AHP, we are eternally grateful.

In addition to producing AHP monographs and the "Therapeutic Compendium," AHP also provides industry with a variety of botanical and chemical reference materials, designated as AHP-verified, to be used in the quality assessment of raw botanical materials and extracts. These reference materials have been independently tested and reviewed to ensure accuracy in identity, quality, and purity. AHP-verified botanical reference materials are available directly from AHP. AHP-verified chemical reference materials are developed in partnership with Chromadex (Irvine, California) and are available directly from Chromadex.

American Herbal Pharmacopoeia: Botanical Pharmacognosy—Microscopic Characterization of Botanical Medicines will be the first in a number of texts produced by AHP to focus on various aspects of botanical medicine quality assessment and classical botanical pharmacognosy.

Become a Supporting Member of AHP

In addition to the volunteer work provided, the work of AHP is made possible by revenues generated through the sale of AHP-verified botanical and chemical reference materials, and individual, organizational, and corporate memberships and tax-deductible contributions. AHP has various categories of membership, from students and institutions to corporations, and a variety of membership benefits that include a subscription to AHP monographs and our quarterly *Herbal QRS Bulletin,* which focuses on issues of herbal quality, research and safety, access to unpublished AHP materials, and the knowledge that your membership is helping to improve the integrity of herbal medicine worldwide. Membership information can be accessed at the AHP Web site (www.herbal-ahp.org).

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About *Microscopic Characterization of Botanical Medicines*

I was brought up to believe that the only thing worth doing was to add to the sum of accurate information in the world.

Margaret Mead (1901–1978), American cultural anthropologist

Text Introduction

Microscopic Characterizations of Botanical Medicines is the first in a series of textbooks to be developed by the American Herbal Pharmacopoeia. Although each text will be complete and stand alone, the volumes will also complement each other to provide multiple methods for assessing the authenticity and quality of herbal drugs. This current work is designed to reintroduce botanical microscopy to the industry as a low-cost quality assessment tool for the physical examination of botanicals, and highlight the value of botanical microscopy as an important physical assessment tool for botanicals.

About the Characterizations in the "Botanical Microscopic Atlas"

A number of criteria need to be met for the development of microscopic characterizations to be of practical relevance to botanical identification. First, the samples used for the characterizations must be accurately identified by a botanist. Second, a variety of samples must be used and compared to ensure that the characterization encompasses the natural intraspecies variations that can occur. Last, the samples must be representative of the commercial material available in trade.

The overwhelming majority of the characterizations provided in the "Botanical Microscopic Atlas" portion of the text were developed from multiple samples that were botanically authenticated, compared against botanical samples in professional herbariums, and cross-checked against other microscopic characterizations for consistency and completeness. All samples were representative of materials in trade. Occasionally, only single botanically authenticated samples were available; nevertheless, they were cross-checked against other authoritative characterizations. This level of attention is often lacking in early American works of botanical microscopy, whose characterizations were often based on single samples that may or may not have been botanically authenticated or representative of materials in trade.

How to Use This Book

- *Format of the text:* The text is divided into two sections. The first part, "Introduction to Botanical Microscopy," provides a historical review and fundamental basis for the practical use and application of botanical microscopy as a quality assessment tool, as well as guidance on how to perform a botanical microscopic assessment and set up a botanical microscopy lab. The second part, the "Botanical Microscopy Atlas," provides the complete microscopic characterization of some of the most common species of medicinal plants in trade in North America and abroad. Before beginning or aspiring microscopists proceed to the atlas, it would be best for them to familiarize themselves with the introductory chapters, especially Chapter 6 on plant morphology and anatomy. This chapter provides a requisite understanding of the plant tissues presented in the microscopic characterizations.
- *Nomenclature:* Each microscopic characterization has been listed primarily according to the Latin botanical binomial, including the botanical authority. The botanical nomenclature is followed by the common name according to *Herbs of Commerce* (McGuffin et al. 2000) and plant part characterized, the appropriate Chinese pinyin or ayurvedic name when specifically applicable, the corresponding pharmaceutical name, and the plant family, which in some cases is diagnostically valuable.
- *Microscopic characterizations:* In addition to nomenclature, each microscopic characterization includes four parts: (1) a brief introductory paragraph on the primary medicinal use of the botanical with specific information on potential adulterants of which the microscopist should be aware; (2) a detailed text description of the microscopic characterization of the plant part in its relatively whole form, along with a listing of the primary tissues found in the same material when it is powdered; (3) illustrations of the primary tissues that are most prominent and diagnostically relevant to the microscopist; and (4) photographic images of the primary structures and tissues. The illustrations allow key elements to be highlighted, and the images provide a view of what is actually seen by the microscopist. In some cases in which adulteration is prevalent, tables have been provided that allow for an easier differentiation of the authentic from the adulterating species, and microscopic characterizations of the most prevalent adulterations are also provided.
- *Use of stains:* The microscopic characterizations provided were developed with a minimum of color reagents. The use of color reagents and stains is necessary for the detection of some tissues and they were used when needed for diagnostic purposes. However, use of such reagents increases the complexity, time, expense, and environmental burden of standard microscopic analyses and decreases reproducibility. In most cases, stains are not needed for routine microscopic identification of a species. In this text, we have used stains only when their use would provide diagnostic information that would not be gained without their use.
- *Glossary:* A glossary of terms used in botanical microscopy in general and the text specifically is included as an appendix.

Introduction

> If you look out at all the plants here, they all have something to give us; some gift; it is up to us to learn what it is.
>
> **Arona Petersen (1908–1995), herbalist, St. Thomas, U.S. Virgin Islands, 1983**

Throughout human history, the use of herbal medicines has always been central to all healing systems. Prior to our relatively recent reliance on the isolated, purified, oftentimes synthetic chemical entities dominant in modern medicine today, plants were the primary source of medicines for the majority of the world's population (Figures 1-4). This is still true today. Plants also provide the source material for a large percentage of modern drugs. Some of these medicines include well-known items such as aspirin, of which the precursor, salicin, was originally derived from the bark and leaves of willow (*Salix* spp.). Aspirin was subsequently named after the first commercial source from which salicin was derived, the botanical meadowsweet (*Filipendula ulmaria,* formerly named *Spiraea*), from which the "spir" in aspirin comes (Figure 2). Digitalis glycosides, another botanically derived category of medicines, originating from the beautiful purple foxglove (*Digitalis purpurea*), have been dominant therapeutic agents in cardiovascular medicine for more than 200 years. Quinine, derived from the bark of the cinchona tree (*Cinchona* spp.)—so named by Linnaeus (1742) after the Countess of Chincon (1638) was successfully treated with the bark for malaria—has remained a primary treatment for malaria in European culture for at least 370 years.

FIGURE 1 Ethnobotanist Dr. Michael J. Balick and herbalist/physician Dr. Rosita Arvigo discuss traditional medicines of Belize, Central America, with local herbalist Polo Romero. (Image courtesy of M. J. Balick, the New York Botanical Garden.)

FIGURE 2 Meadowsweet (*Filipendula ulmaria;* syn. *Spiraea ulmaria*), one of the original sources of aspirin from whence the "spir" in aspirin came. (From Baxter, W. 1835. *British Phaenogamous Botany.* Oxford, U.K.: J. H. Parker.)

The use of natural products in the development of modern medicines has been so prevalent that in 1996 it was estimated that as many as 50% of prescriptions dispensed in the United States contained one or more substances originally derived or modified from natural products (Robbers, Speedie, and Tyler 1996). The prevalent use of botanical drugs is further illustrated by the fact that a large number of antibiotics and antitumor drugs are derived from natural products (Cragg, Newman, and Snader 1997) (e.g., penicillin, vincristine alkaloids, taxol, etoposide, which are derived from *Staphylococcus aureus,* Madagascar periwinkle [*Catharanthus roseus*], Pacific yew [*Taxus brevifolia*], and American mayapple [*Podophyllum peltatum*], respectively). Lastly, the very word *drug* is a derivation of the Dutch *droog* or the French *drogue,* both of which refer to the drying plants hanging from the rafters of old-world apothecaries (Figure 4).

FIGURE 3 Eighteenth century apothecary. The apothecaries of early centuries predominantly consisted of crude herbal drugs and preparations prepared from them. It was not uncommon for an apothecary to stock more than 1,000 different plants. The original word for drug is derived from the old Dutch *droog* or the French *drogue* referring to the herbs hanging to dry from apothecary rafters. (From Thompson, C. J. S. 1929. *The Mystery and Art of the Apothecary*. London: John Lane The Bodley Head Ltd.)

A Renaissance of Traditional Herbal Medicine

More relevant to the subject of botanical microscopy than the development of modern drugs from natural products is the widespread and increasing use of traditional botanical medicines as an integral part of national health care systems by both developed and developing nations. Developing nations continue to rely on traditional healing systems partially because of cultural practices and preferences, as well as limited access to other medical options, the higher cost or side effect profile associated with modern medicines, or the inability of modern medicines to deal effectively with chronic degenerative conditions. It has been repeatedly estimated by the World Health Organization (WHO) that

approximately 80% of the world's population continues to rely on traditional medical practices, including herbal medicines, as their primary form of health care.

The now seminal surveys of Eisenberg et al. (1993, 1998) showed clearly that American consumers are actively seeking traditional healing practices as an alternative or complement to therapies offered by conventional medical practitioners, including a greater number of patient visits to alternative care practitioners. This is a staggering phenomenon when one really thinks about it. In their 1993 survey, Eisenberg and colleagues reported that approximately 34% of Americans had utilized some form of "alternative" therapy in the previous 12 months. In Canada, the same 34% of ambulatory surgery patients reported using herbal medicines. In the 1998 survey of Eisenberg et al., the numbers of Americans using complementary and alternative (CAM) therapies increased to more than 42%, and a 2008 survey by Barnes, Bloom, and Nahin reported that approximately 40% of Americans use some type of CAM therapy and that use of nonvitamin and nonmineral preparations was most prevalent. These authors further reported that more than 14% of respondents had used ginseng, almost 16% used flax seed oil, and nearly 20% used echinacea.

In the same timeframe, dietary supplement use rose substantially, with herbal supplement use increasing more than any other CAM modality. In 1984, dietary supplement sales through retail outlets were reported at $8.8 billion. In 2000, dietary supplement sales rose to an estimated $15.7 billion, and in 2003 to $18.8 billion—an increase of more than 100% in the past 10 years (reported by Bardia et al. 2007).

Use of herbal medicine is equally widespread internationally. Germany has a long history of use of herbal medicines; hundreds of plant-based medicines are on the market, and a large number of German physicians prescribe botanical medicines regularly. In 1997, Germany maintained the largest economic market for herbal medicines in Europe at $3.5 billion, or approximately 25% of the world's then estimated $14 billion market for herbal medicines (Yuan and Gruenwald 1997).

A worldwide trend in the increased desire for plant-based medicines perhaps is best exemplified in international legislative initiatives for natural medicine products. These include the establishment of the Dietary Supplements Health and Education Act (DSHEA) in the United States, the Natural Health Products Directive of Canada, and the Traditional Medicines Directive throughout the European Union. These initiatives are accompanied by increasing recognition of natural medicine practitioners. Similar trends are also evident in China, Hong Kong, and India, where interest, research, and consumer use of traditional Chinese and ayurvedic medicines are continually rising. In the United States, this has frequently been referred to as an *herbal renaissance* and it is evident that this renaissance is international in scope.

A seminal driving factor of alternative medicine use, according to the early 1993 survey, was that a substantial amount of unconventional therapy was reportedly used for health promotion or disease prevention in contrast to use for principal medical conditions. This suggests a different health care paradigm by users of natural therapies that seeks the promotion of health and disease prevention through the use of what can be characterized as gentler therapies in contrast to taking more heroic measures once disease occurs.

The Herbal Trade Past and Present

Historically, two major pathways for medicinal plant trade and use have coexisted. One track consists of relatively small quantities of herbs gathered by traditional herbalists for use in their local healing practices. The other consists of a network of wholesalers and retailers dealing in large quantities of local or exotic plants for domestic or international commerce. The traditional herbalist pathway offers a relatively direct link between identification, harvest conditions, and processing of an herb, and the consuming individual and community at large. The herbalist has a vested interest in procuring the correct herb of sufficient quality to elicit the desired medicinal effect. If he or she does not, his or her livelihood as a community herbalist will suffer.

In contrast, when herbs, especially exotics, are sourced through a commercial trader or traders, multiple batches of the same plants are typically picked at multiple locations, at different times, under varying collecting and processing conditions, and with variable degrees of care. Often, different batches are traded through a myriad of dealers and eventually are pooled together: good with bad, fresh with old, correct with incorrect, clean with dirty. In this case, there is much less selectivity than is generally applied by the local herbalist and a much greater chance for intentional or unintentional adulterations, impurities, contaminations, and substandard herbal medicines. Thus, in the worldwide trade of medicinal plants, testing methodologies are essential for ensuring the authenticity, purity, and quality of the finished medicinal product.

With the centralization of the medical profession and increased industrialization, the role of the herbalist became less important in Western Europe and North America. By the eighteenth and nineteenth centuries, the practice of ensuring drug quality, which was still mostly plant based, and the practice of medicine were largely the physician's province. At the same time, medical botany was an important subject in the curriculum of early physicians. With the growing international trade of medicinal plants, quality control became less centralized away from local herbalists and herb purveyors and was subject to less connection with the source of the medicine and less direct oversight. This disconnection between the biosystem in which the plant is grown and those involved in harvesting or

FIGURE 4 Harvesting the ayurvedic herb brahmi (*Bacopa monnieri*) at Shastry's Estate, Hosagunda, in the Shivmoga district of Karnataka in southern India. (Image courtesy of Sebastian Pole, Pukka Herbs, Bristol, United Kingdom.)

dispensing a medicine makes the task of ensuring identity, purity, and quality more difficult—sometimes impossible. The greater the disconnect from the source and the more hands medicinal raw plant materials move through, the greater the potential for poor-quality materials and the need for more sophisticated means of testing.

Increased Need for Classical Pharmacognosy and Skills of the Herbalist

As the desire for herbal medicine grows, there is a need to rekindle and continue to develop the traditional herbal assessment skills that were historically so prevalent, while at the same time utilizing the most modern of analytical methodologies where applicable. Since the reemergence of interest in herbal medicine in the United States in the 1960s, issues of quality control have been relegated to the herbal products industry, oftentimes with too little integration of botanists, herbalists, or pharmacognosists, and too little application of either traditional or modern assessment skills. The domestic herbal products industry and, ultimately, consumers, have suffered greatly for this oversight.

Fortunately, Asia in general has maintained a very strong connection with the traditional knowledge regarding collection and processing of herbal medicines, so the greatest majority of herbal medicines that are produced are consistent with those used historically. In a similar but technical fashion, much of Western Europe has utilized the most sophisticated of analytical techniques for ensuring optimum harvest times, drying times, and processing conditions for producing high-quality herbal medicines. In actuality, the combination of traditional herbal assessment skills coupled with modern analytical methodologies will provide the greatest assurance of botanical ingredient quality, whether herbs are used as ingredients in dietary supplements, conventional foods, cosmetics, or botanical medicines.

Synergism in Plant-Based Medicines

To the modern pharmacognosist, the identification, purification, molecular elucidation, and biological effects of a plant compound for purposes of commercial drug development are most seminal. To the herbalist or natural health care practitioner, an herbal medicine should be like a fine wine. The gestalt of qualities possessed by an herb or herbal formula and its multitude of actions are considered important to facilitate a healing process. This idea of synergism of herbal medicines has been popularly touted but can remain elusive to the research chemist who is used to one compound with one activity.

The alkaloid berberine is widely known for its local antibacterial activity. Relatively recently, Stermitz, Lorenz, et al. (2000) and Stermitz, Tawara-Matsuda, et al. (2000) (reported by Kinghorn 2001) found that the antibacterial activity of berberine derived from the traditionally used Native American botanical *Berberis fremontii* against resistant *Staphylococcus aureus* was potentiated by the presence of two other constituents contained within the plant: the flavonolignin 5′-methoxyhydnocarpin and the porphyrin pheophorbide *a* (Figure 5). Although both compounds potentiated the activity of subthreshold concentrations of berberine, neither elicited any antibiotic activity alone (Kinghorn 2001).

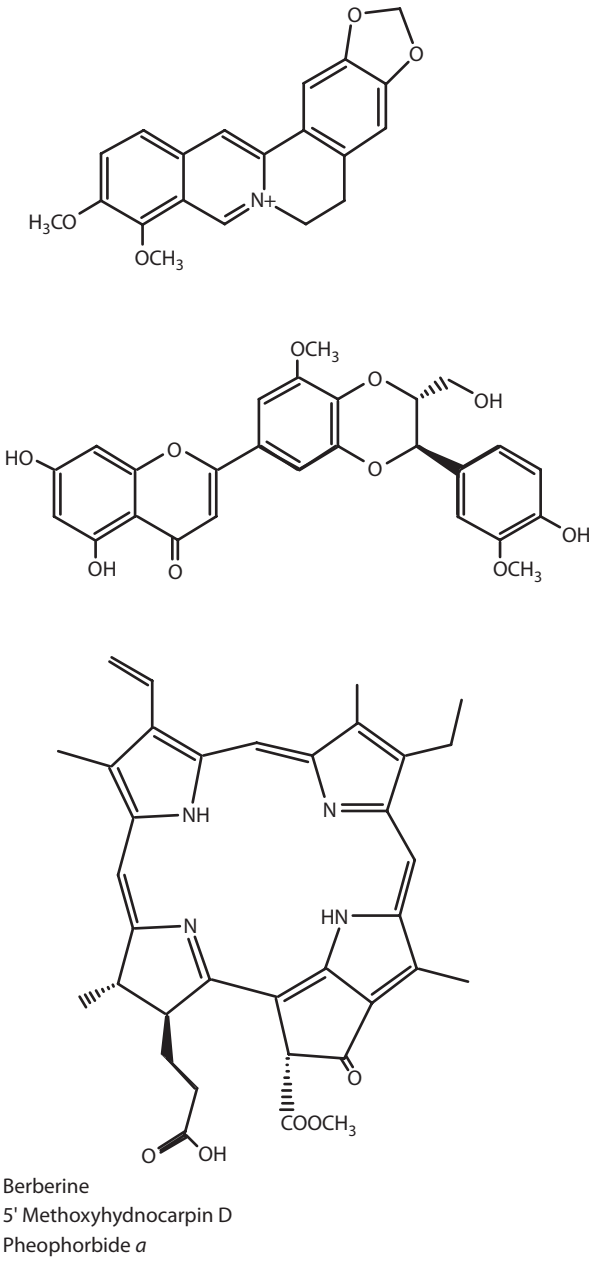

FIGURE 5 **An example of synergism whereby the antibacterial activity of the alkaloid berberine is enhanced by the presence of and co-occurring compounds in *Berberis fremontii.* (Modified from Kinghorn, D. A. 2001. *Journal of Pharmacy and Pharmacology* 53:135–148.)**

At a satellite conference of the American Society of Pharmacognosy, Wagner (2004) reported that herbal medicine potentially represents a cutting edge of medicine due to the inherent multitargeted, multicomponent nature of herbal preparations. Wagner provided three examples of the multitargeted nature of herbal medicines. He compared such strategies to the use of multi-ingredient pharmaceutical cocktails that are now prevalent in modern medicine for the treatment of hypertension, cancer, and AIDS.

The first, using the herbal antidepressant St. John's wort (*Hypericum perforatum*) as an example, described the multiple actions associated with St. John's wort that may

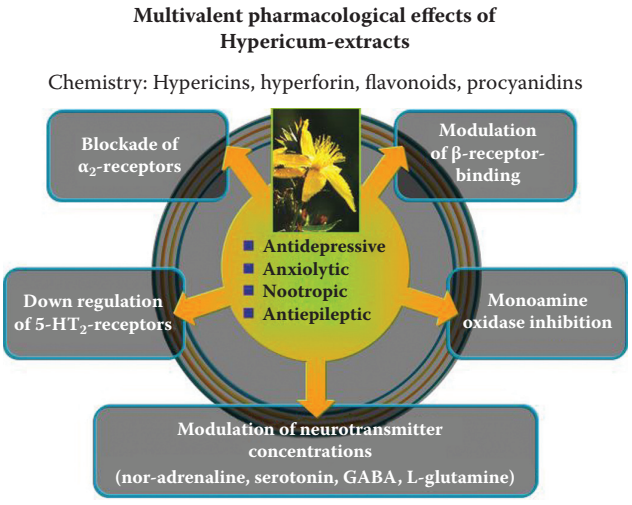

FIGURE 6 Example of St. John's wort (*Hypericum perforatum*) showing that multiple actions may contribute to the herb's clinical efficacy as an antidepressant and anxiolytic. (From Wagner H. 2004. *Revival of Pharmacognosy. Classical Botanical Pharmacognosy*. Satellite Symposium: Annual Meeting of the American Society of Pharmacognosy, Phoenix, AZ.)

contribute to its putative clinical antidepressant and anxiolytic effects (Figure 6). These actions included the blockade of α_2-receptors, down regulation of serotonin receptors, and modulation of a variety of neurotransmitters. The second example used garlic and highlighted the variety of different therapeutic actions associated with garlic's various constituents (Figure 7). The third example showed how a multi-ingredient herbal compound can address the numerous underlying manifestations of a condition, with the herbal ingredients contributing not just one, but rather a multiple of activities that are beneficial for the condition (Figure 8).

This philosophy is consistent with that of an overwhelming majority of traditional herbal practitioners. Some herbal formulas, such as the legendary three-fruit *Triphala* compound of ayurveda (Figure 9), have been in continuous use for more than 2,300 years (ca. third century BCE). Traditional Chinese herbalists have been using the same gynecological formula, *si ni tang,* for more than 700 years. Even the United States has herbal formulas that have been in use continuously for more than 100 years (e.g., *Trifolium Compound*, *Composition Powder*).

In traditional herbal medicine and in early pharmacognosy a tremendous emphasis was placed on the proper sourcing of botanical raw materials, botanical identification, and the organoleptic profile of the material. To the traditional herbal practitioner, the primary, secondary, and tertiary effects of a single herb, or the multiple effects of herbal combinations, were carefully applied according to the individual needs of a patient. Just as the quality of a wine cannot be judged by its resveratrol or proanthocyanidin content, the quality of an herbal medicine cannot be judged by the concentration of a particular compound. It is both necessity and knowledge that unite the worlds of plants and humans. To allow this knowledge to die or fall into disuse is to forget our relationship with the natural world. Traditional herbalists, ethnobotanists, and perhaps early pharmacognosists understood these concepts clearly. Understanding this approach is the only way one can truly come to understand the value and importance of herbal medicine to humankind

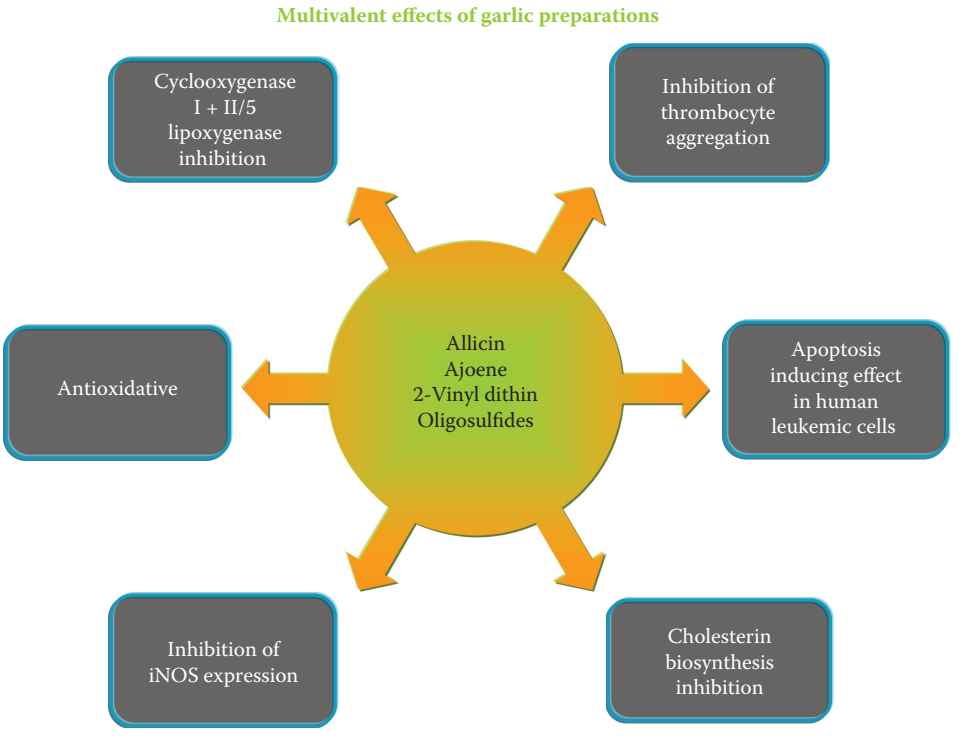

FIGURE 7 Example of garlic (*Allium sativum*) constituents showing that multiple compounds are associated with a myriad of activities in botanical products. (From Wagner H. 2004. *Revival of Pharmacognosy. Classical Botanical Pharmacognosy*. Satellite Symposium: Annual Meeting of the American Society of Pharmacognosy, Phoenix, AZ.)

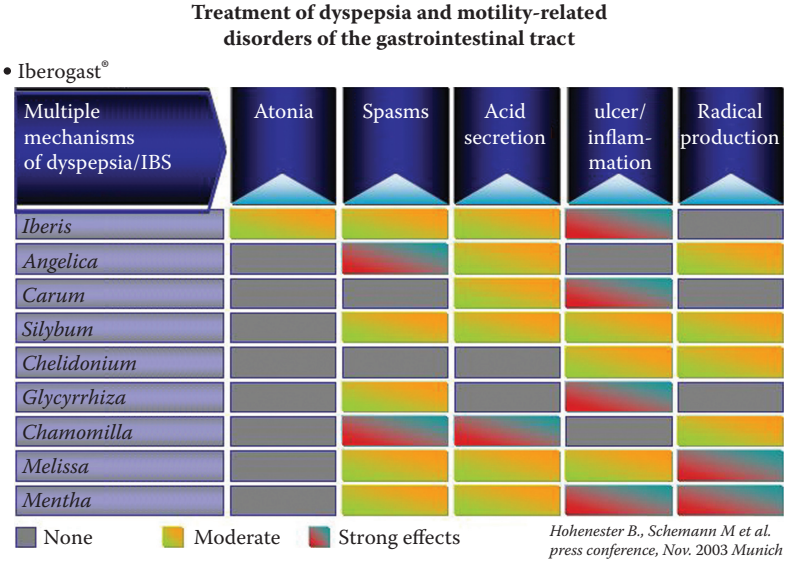

FIGURE 8 Example of the multiple effects of a multiple-herb compound contributing to a variety of activities that address various manifestations of a disorder (e.g., irritable bowel syndrome). (From Wagner H. 2004. *Revival of Pharmacognosy. Classical Botanical Pharmacognosy*. Satellite Symposium: Annual Meeting of the American Society of Pharmacognosy, Phoenix, AZ.)

FIGURE 9 Fruits of the 2,300-year-old *triphala* compound of ayurveda consisting of amla (*Phyllanthus emblica*), behada (*Terminalia bellerica*), and harada (*Terminalia chebula*). (Image courtesy of Prashanti de Jager, Lucknow, India.)

and the manner in which plant-based medicines more closely unite us with Earth and the biological principles of our breathing biosystem.

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