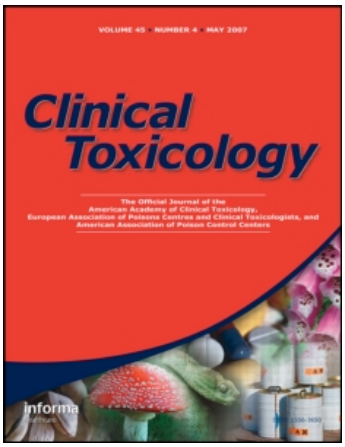

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Herbal Supplements-Drug Interactions: Scientific and Regulatory Perspectives, edited by Y. W. Francis Lam, Shiew-Mei Huang, Stephen D. HallHerb, Nutrient, and Drug Interactions: Clinical Implications and Therapeutic Strategies, edited by Mitchell Bebel Stargrove, Jonathan Treasure, Dwight L. McKee

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BOOK REVIEWS

Medical Toxicology of Natural Substances: Foods, Fungi, Medicinal Herbs, Plants, and Venomous Animals. Donald G. Barceloux, Editor, Wiley, A John Wiley & Sons Inc., 2008, 1155 pages, $195.00.

Medical Toxicology of Natural Substances is a hardcover reference text by Donald G. Barceloux, MD, the coauthor of *Medical Toxicology: Diagnosis and Treatment of Human Poisoning* (first edition, 1988), which is still a staple reference in the discipline of clinical toxicology. Barceloux combines his expertise in medical toxicology and emergency medicine with his skills as an author to address the significant and challenging natural toxins that are associated with morbidity and mortality. This is an essential reference text for medical libraries, poison and drug information centers, clinical toxicologists, and anyone who manages patients who may be exposed to natural toxins. With the increasing use of alternative medicine, this book would be a useful addition to medical practice libraries and emergency departments.

The book is divided into five sections (foodborne and microbial toxins, fungal toxins, medicinal herbs and essential oils, toxic plants, and venomous animals) and 185 chapters. There is a relatively equal distribution of content for each of the sections, with the exception of the fungal toxins section that comprises only 55 pages, but the topics are covered sufficiently. A strength of the reference is the consistency between and among chapters – each monograph follows a template, making it easier to navigate from chapter to chapter and between sections. Barceloux is the primary author, with a few chapters on food contamination, food additives, and bacteria being contributed by Cyrus Rangan, MD; therefore, the style and format of the contributions are consistent throughout. Additional strengths of the book include placing each toxin in perspective with regard to its potential morbidity and mortality, focused but comprehensive chapters, and extensive contemporary referencing. Most of the chapters are concise, and this allows the clinician to review the chapter quickly, which is especially important in the arena of acute care such as in a poison information center or emergency department where patient care decisions must be made expeditiously.

The most prominent limitation of the reference is the indexing and cross-indexing of terms, which poses a problem in searching for the various natural toxins. For example, the terms *Araceae*, *Arum*, *Epripremnum*, *Philodendron*, and *Caladium* are not indexed. To find information on these botanicals, the chapter on *Dieffenbachia species* must be reviewed. Therefore, a clinician may not be able to locate the desired information, unless they are aware that these botanicals, such as the *Dieffenbachia species*, contain oxalates, and are astute enough to find the entry in the table of contents, which diminishes the usefulness of the reference to those without botanical or toxicology expertise. Other examples that include no index terms for common botanicals are *Euphorbia pulcherrima* (Poinsettia), oak but not *Quercus*, capsaicin but not jalapeño, holly but not *Ilex*, and so on. However, using the table of contents as the search tool circumvents some of the inadequate indexing. The chapter on tickborne illness was brief, especially in view of the epidemic nature of Lyme disease; hanta virus was not included; there was no mention of West Nile Virus from mosquitoes; rabies was not covered; freshwater algae was not addressed; there was no discussion of the caustic manchineel tree (*Euphorobia cotinifolia*). However, these omissions do not diminish the importance and the overall quality of the reference.

While all the information included in this book can be found in a multitude of hard-copy references and online resources, this is the only book that combines a comprehensive review of the major natural toxins into a single, authoritative, contemporary, and easy to read reference.

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Herbal Supplements–Drug Interactions: Scientific and Regulatory Perspectives. Y. W. Francis Lam, Shiew-Mei Huang, Stephen D. Hall, Editors, Taylor & Francis Group, New York, NY, 2006, 332 pp., ISBN 0-8247-2538-7, US$ 149.95, 321 pages.

Herb, Nutrient, and Drug Interactions: Clinical Implications and Therapeutic Strategies. Mitchell Bebel Stargrove, Jonathan Treasure, Dwight L. McKee. Mosby Elsevier, St. Louis, MO, 2008, ISBN 987-00-323-02964-3, US$ 79.00, 932 pages plus reference CD.

Those with poison center responsibilities will be attracted to the common practical topic of each of these books. Dietary supplements (defined as herbs, vitamins, minerals, amino acids, and nutritionals) are a subject of increasing frequent poison center calls, especially in regard to interactions with drugs. Emphasizing this pertinence is the rapidly growing herbal special interest group in AACT which scheduled a pre-symposium conference at NACCT in New Orleans in 2007 and whose symposium at the NACCT in Orlando in 2006 was published in *Clinical Toxicology*. Poison center educators and fellowship directors are alerted to these books about herbals and drug interactions as a topic for a teaching conference.

Francis Lam at the University of Texas at San Antonio Health Science Center, Shiew-Mei Huang of FDA's Center

for Drug Evaluation and Research, and Stephen Hall at the University of Indiana's Wiscott Memorial Hospital combine their own with well-edited chapters of other authors in *Herbal Supplements–Drug Interactions: Scientific and Regulatory Perspectives*. When contacted, Dr. Lam aptly stated "the idea of this book was conceived after I gave several international presentations on topics such as herb–drug interactions and herbal products development" adding "there is not such a book that is more focused on the science." As such, this book is intended for scientists involved in the basic study of botanical product–drug interactions and the FDA regulatory process for dietary supplements.

This book describes how botanical products interact with drugs in detail, as well as the utilization, safety, and regulatory aspects of botanical products. Specific chapters appear on drug interactions with St. John's wort, grapefruit, garlic, and other well-known examples, as well as their *in vitro* drug interaction background. Also, the special field of Traditional Chinese Medicine (TCM) is well defined in this context. Two chapters are devoted to the development of botanical products as pharmaceutical agents within the FDA framework. And this has recently come to fruition with FDA approval of a green tea extract as a drug for treatment of genital warts.

While this book is No. 162 of the Drugs and Pharmaceutical Sciences series of textbooks and monographs from the Taylor & Francis Group within the Academic Division of *Informa, plc*, it can easily stand on its own and should be encouraged into succeeding updated editions.

The Stargrove book, which has appeared more recently, is a remarkably helpful book that is immensely well organized, inclusive and consistent in section to section writing. Mitchell B. Stargrove, an ND who founded IBIS, the Integrative BodyMind Information System; Jonathan Treasure, a herbalist at the Centre for Natural Healing; and Dwight L. McKee, an MD internist, who is scientific director of Life Plus International, combined forces for this book. A large paperback with 932 pages and a reference CD, this book starts with a foreword by Tieraona Low Dog, MD, from the University of Arizona, who chairs the USP Dietary Supplements Expert Panel, and a detailed preface by the authors. The opening chapter explains the "Interactions Evaluation Guide," which is also abbreviated as a handy "Quick Guide to Interactions Evaluation System" in the front flyleaf. The interactions evaluation system establishes numbered categories and symbols that show the probability, type and clinical significance, and strength and quality of interactions. These are provided in a summary list for each herb and nutrient with the named prescription drug.

A handy guide for patient counseling on herb interactions is described in the first section of the contents from *Aloe* to *Vitex*. The vitamin section begins with β-carotene and ends with vitamin K. Mineral–drug interactions are described from boron to zinc and amino acids from arginine to tyrosine. These sections end with nutraceuticals and physiologics from 5-hydroxytryptophan to 5-adenosylmethionine (SAMe). Each section subheading, such as valerian under herbs, lists a (1) summary, (2) herb description of various forms, (3) herb use in clinical practice, (4) an interactions review, and then (5) specific herb–drug interactions. An example is valerian and benzodiazepines (probability rating 3, for "Possibly") and ending with theoretical, speculative, and preliminary interactions from research including unsubstantiated claims labeled as such. There are also "Cross-Indexes" at the back of the book for interactions by drug class, interactions by generic drug name, and interactions by drug trade name, followed by a well-executed index.

To explore the depth of this book, I looked for details, such as the eosinophilia-myalgia syndrome associated with contamination of the dimer of L-tryptophan in the accelerated manufacturing process of Showa Denka in Japan in 1989, and I found this topic well covered historically, although not referenced in the index. As well, I was pleased to encounter a detailed discussion of Bendictin (doxylamine and pyridoxine) issues that started in 1969 that were well explained and which gave rise to the famous Supreme Court decision, *Daubert v. Merrill Dow*.

The pharmacogenomic basics of why interactions occur, such as the cytochrome P450 subenzyme system, are described under summaries and interactions reviews for each herb, such as CYP 3A4 for St. John's wort. It would have been helpful for these metabolic pathways to be more globally covered in the introductory chapters and listed in the index. As well, this presents an opportunity to elucidate other basic aspects of herb and drug metabolism and excretion, such as glucuronidation, sulfation, and esterase metabolism in the liver, as well as metabolic influences from the epigenetic demethylation of single-nucleotide polymorphisms (SNPs).

In comparison, the Lam book also guides the reader on how to approach reporting herb adverse interactions in the adverse reaction reporting of FDA's *MedWatch* system (http://www.fda.gov/medwatch/). The FDA *MedWatch* system can also be searched to see whether such a reaction has been reported. Such reporting is essential for herbs where serious dietary supplements reactions are now supposed to be reported. This parallels the pharmaceutical industry, where a Phase IV equivalent or adverse reaction reporting is an FDA requirement. The Lam book also describes the fascinating interactions associated with grapefruit and other citrus fruits, common nutrients that need to be accounted for in any interaction review.

The importance of this topic was demonstrated in a recent peer-reviewed article in the *American Journal of Medicine* (Sood A. Potential for interactions between dietary supplements and prescription medications. *Am J Med* 2008; 121:207–211).

The Stargrove book is well priced considering its encyclopedic size (932 pages) and accompanying reference-containing CD. As such, I recommend this as an essential day-to-day interactions counseling reference. The authors of both books are to be congratulated on their valuable work and encouraged

to provide periodic updates of their books with IT access for subscribing professional organizations and poison centers.

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Hepatotoxicity: From Genomics to *In Vivo* and *In Vitro* Models. First Edition. Saura C. Sahu, Editor, John Wiley and Sons, Ltd., Chichester, UK, 2007, 682 pp.

As stated by the editor, the main aim of this book was to assemble an up-to-date information base on hepatotoxicity. As such, Dr. Saura C. Sahu has undertaken an excellent editorial arrangement of 26 chapters by 67 authors from eight countries. The chapters are divided between nine sections, although four of the sections each contain only one chapter. A little disappointing in this respect is the fact that Section 3 on biomarkers of hepatotoxicity is devoted to a single short chapter on mycotoxins, and the appeal of this section could have been increased by the additional inclusion of a general chapter on biomarkers of hepatotoxicity and others on drug- and chemical-induced liver injury. Also, because this work was planned primarily for research workers currently in the field of hepatotoxicity, some general readers may find the newer approaches to interpreting toxicology information (the "-omics") and the recently introduced gene technologies difficult to follow. This is particularly noticeable in Section 5 on genomics of hepatotoxicity. While those individuals active in the specialization of genomics will find the chapters in this section very rewarding, general toxicology readers may find that several of the authors do not adequately explain the concepts and bases for toxicogenomics, transcriptomics, and microarray technology, in these tightly written complex chapters.

All readers of Section 1, on models for hepatotoxicity testing, mainly in vitro, will find that it makes excellent reading for a summary of current methodologies, as does Section 2 on hepatocyte cultures. All chapters in Section 4, dealing with mechanisms of hepatotoxicity, are excellent reviews of this area, but particularly outstanding are Chapter 9, which is a general and very extensively referenced overview, Chapter 14 on cytokines and liver diseases, and Chapter 15 on bile aids as modulators of apoptosis. Section 6, containing a single chapter devoted mainly to gender and species-based differences in hepatic xenobiotic metabolism and toxicity, makes excellent reading from the viewpoints of hepatotoxicity and the influence of endogenous factors on the expression of toxicity. Section 7, on hepatocarcinogenicity, has two chapters, the first of which (Chapter 23) is a somewhat limited short discussion under the title of hepatotoxicity in oncology drug development. However, this is a disappointing chapter because it has a superficial presentation, it is more of a general paper than one related to the development of drugs for the management of oncology, and the number and range of examples of studies of hepatic adverse drug reactions is very narrow and limited. The second chapter in this section discusses a possible epigenetic mechanism for the hepatocarcinogenic potential of the antihistamine methapyrilene and is both interesting and informative reading. Section 8 contains a single chapter devoted to the hepatotoxicity of botanical supplements, a subject of current clinical interest, and although written concisely it very adequately covers general safety issues, chemical and biological characteristics, regulatory issues, and gives a wide spectrum of multiple examples. This is a readable chapter with interest to all toxicologists. The final section and chapter discusses risk analysis of hepatotoxins using physiologically based pharmacokinetic modeling. The author of this chapter writes with remarkable clarity a well-planned approach to the development and application of pharmacokinetic modeling techniques and discusses the application of these models to individual hepatotoxicants and to mixtures of hepatotoxicants. Although, as with many multi-author texts, a few chapters in this book are of less than adequate standard, overall the quality of presentation and content are excellent for a specialist subject.

The production quality of this work is high, with easy to follow tables and illustrations, and very adequately indexed. Most of the chapters have in-depth coverage of the current literature, with extensive reference lists.

As noted in the Preface, this book is directed primarily at scientists currently engaged in the field of liver toxicity. However, as a reference volume, it will also be useful to general toxicologists, particularly in the pharmaceutical, agrochemical, and general chemical industries and to those in regulatory positions. By selective reading, clinical toxicologists will find several of the chapters in this book not only of interest but also of value in practice. This applies particularly to those chapters discussing models for hepatotoxicity, mechanisms of hepatotoxicity, hepatocarcinogenicity, botanical supplements, and risk analysis.

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