Book Reviews

Integrated Drug Discovery Technologies. Edited by Houng-Yau Mei and Anthony W. Czarnik. Marcel Dekker, Inc., New York. 2002. xii + 577 pp. 16 × 24 cm. ISBN 0-8247-0649-8. $175.

This book presents an overview of the many new chemical, biochemical, biological, and screening paradigms and their integration that are being applied to the modern discovery and screening of potential new drug products. Following an introductory chapter, this multidisciplinary book with 48 contributors is divided into three major parts: Part I. From Gene to Screen; Part II. High-Throughput Screening; Part III. High-Throughput Chemistry.

In the Introduction, Wendell Wierenga reviews the almost overwhelming challenges involved in discovering and developing new therapeutic agents. He divides drug discovery into five categories, i.e., modifying the structure of known drugs, screening natural product and chemical inventories in laboratory models of diseases, proteins as therapeutics, modifying the structure of natural substances that affect natural substrates such as enzymes or receptors, and computer-aided drug design. The first two categories represent the major history of drug discovery through the 1970s. The final three have come into prominence during the past 15 years or so. Proteins and peptides became a target for drug discovery with the advent of molecular biology in the late 1970s. Modification of natural substrates is likewise an area of recent intense research; however, many of these are peptides or peptidomimetics that are characterized by poor pharmacokinetics and delivery-related challenges. Structure-based computer-aided drug design emerged in the 1980s and now is widely used in the search for new therapeutic agents. Rapid, automated, high-volume techniques and instrumentation and novel biological and chemical sources of diversity, as well as the generation of molecular targets through biotechnology, have revolutionized the way in which screening is conducted. Combinatorial chemistry has provided an enormous number of diverse screening sources.

It seems likely that integration of the methods of drug discovery with the newer screening paradigms and the vast testing sources available from a multitude of combinatorial libraries will contribute greatly to the next generation of therapeutic agents. Indeed, the past decade has witnessed the most dramatic change in the pursuit of new drugs in the history of drug discovery. As noted in Chapter 2, there are three basic components necessary for the discovery of new drug products, i.e., meaningful targets for drug intervention, methods to screen compounds for their effect on the targets, and compounds for testing.

Identification of novel targets has been greatly enhanced by the recent explosion of genomics, proteomics, bioinformatics, and information technologies. Thus, it is estimated that of the 80 000 to 150 000 human genes there may be as many as 10 000 targets for developing drugs of value in treating the most common multifactorial diseases. Part I, Chapters 2−8, focuses on genomics, proteomics, and associated methodologies in the identification of screening targets and on the investigation of the properties of genes and proteins that may lead to interventions in the treatment of disease.

Part II, Chapters 9−15, considers high-throughput screening (HTS), which has become the core of discovery operations in most pharmaceutical companies. Dramatic developments in genetic engineering and molecular biology have resulted in biochemical and cellular assays reflecting mechanistic responses. Such assays are specific and economical and permit the screening of much larger numbers of test compounds than conventional whole organism pharmacological models. HTS involves the integrated technologies that permit the rapid evaluation of millions of compounds annually in scores of bioassays in the pursuit of new drugs. The three objectives of HTS, namely, de novo discovery, hit development, and screening for absorption, distribution, metabolism, elimination, and toxicity properties (the major causes of drug failure of screening "hits"), are considered in this part.

With the dramatic increase in the ability to test large numbers of compounds resulting from HTS, the demand for large, complex, and structurally diverse chemical libraries continues to grow. The approach of medicinal and synthetic chemists in addressing this challenge is the subject of Part III, Chapters 16−20, which presents reviews of combinatorial chemistry, new synthetic methodologies, supports for solid-phase synthesis, the NMR "tool kit" for compound characterization, and materials management.

The book includes a list of contributing authors, and it concludes with an adequate subject index. All chapters are appropriately referenced with timely, up-to-date references.

In summary, this is a first of its kind book. It presents a current, state-of-the-art overview of the drug discovery process that is being employed by most pharmaceutical research companies. It features the most current advances in drug discovery technologies by addressing new methodologies from biology, chemistry, and the computational sciences that offer the hope of permitting the identification of new therapeutic agents more quickly and more effectively. *Integrated Drug Discovery Technologies* will be of interest to all—chemists, biologists, and administrators—who are concerned with the discovery of new drug products.

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Chinese and Related North American Herbs: Phytopharmacology and Therapeutic Values. By Thomas S. C. Li. CRC Press, Boca Raton, FL. 2002. iv + 589 pp. 16 × 24 cm. $169.95 ISBN 1-58716-128-1. $169.95.

This book mainly consists of three extensive tables. It would be very useful if this book could be published in a searchable electronic form. Table 1 presents information on the major constituents and therapeutic values of more than 1800 species of Chinese medicinal herbs. Unfortunately, the most authoritative book in this area, the 10-volume "Zhong Hua Ben Cao" (Chinese Material Medica) published in 1999 was not used as a reference.

The readers should be aware that major constituents listed for several herbs in Table 1 may not be accurate or contain the most up-to-date information. As an example, in the table, allicin was listed as a major constituent of *Allium chinense* Max, *A. odorumn* L., *A. sativum* L., *A. fistuluscum*, etc.; however, allicin is known to be specific to *Allium sativum* L. and not to other species.

Tables 2 and 3 list a total of 700 North American herbs belonging to the same species or genus as Chinese herbs and a comparison of active ingredients and claimed therapeutic values. These two tables are the highlight of this book and provide unique and useful information. It can be used by natural product chemists and pharmaceutical chemists to identify useful North American herbs that may have documented therapeutic values similar to those of closely related Chinese herbs.

This book also contains three appendices totaling 200 pages. The first appendix cross-references Chinese and scientific herbal names. Appendices 2 and 3 list major chemical components and their Chinese and North American herbal sources, respectively. Again, the chemistry is probably not the strong aspect of this book. Many of the chemical components listed in these two appendices, such as amino acids, anthocyanin, ash, calcium, D-glucose, essential oils, fatty acids, fatty oil, etc., are too general and have very little value.

Despite some shortcomings, this book is a good reference guide for interested scientists dealing with both Chinese and North American herbs.

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