Book Reviews

Particle-Lung Infections, Lung Biology in Health and Disease Series, Volume 143. Peter Gehr and Joachim Heyder, Eds. Marcel Dekker, Inc., 270 Madison Avenue, New York, NY 1006-0602, http://www.dekker.com/, 2000. xxi, 802 pp., illustrations. $225.00.

For more than a century the implications of environmental or occupational exposure to inhaled particulates has been a central interest in pulmonary medicine. The relationship between such exposure to particles and disease has driven research in this field, improving our understanding of lung physiology and inhalation toxicology. From a pharmaceutical perspective it should be noted that studies in environmental and occupational medicine underpin drug delivery to and through the lungs. The body of knowledge on particle-lung interaction in general may be drawn upon in considering local or systemic delivery of drugs by this route.

Professor Gehr and Heyder are leaders in the fields of aerosol research and the application of aerosols in medicine. They are ideally qualified to edit a book on the topic of particle-lung interactions and should be commended for their selection of authors for this volume. The book consists of six sections each subdivided into a total of nineteen chapters.

The first section is covered in one chapter, an overview of particle interactions with the respiratory tract. The historical review makes excellent reading for those interested in the origins of public health issues, centers of research and the geographically global nature of interest in this topic. Features of respirable particles from composition, through production to dimensions are discussed in detail. Lung deposition and clearance in different species are presented. The health effects are discussed from epidemiological and physiological perspectives. Recognizing the serious implications of exposure to ambient particulates this section concludes with a review of regulatory issues.

The second section focuses on particles interacting with the lung. There are three chapters in this section and the topics are divided into environmental, occupational and medicinal aerosols. Environmental aerosols are broadly presented as sea salt, mineral dusts and biogenic particles which may be derived from arctic, marine or continental regions. Occupational aerosols are derived from a range of industrial or commercial settings where combustion, fuming, milling, mixing, or drying takes place. Medicinal aerosol may be used for diagnostic or therapeutic purposes. Discussion of drugs is dealt with generally with respect to disease states. This was an astute approach on the part of the authors, as it will give this account relevance in spite of new developments in the field. One omission in this context is systemic delivery of drugs, which is a growing area of interest for pharmaceutical scientists.

The third section examines more closely the inhalation of particles and is divided into three chapters on deposition, retention and clearance. Any book covering inhaled aerosols requires a good account of lung deposition and this volume is no exception. By placing the theoretical account in the context of methods of evaluation of deposition and predictive mathematical modeling the authors have performed a great service to novices and summarized this area for veteran researchers in therapeutic aerosols. It is an interesting literary artifice to include a section on retention, which allows discussion of biophysical aspects of the lungs. Generally, pharmaceutical scientists overlook this topic, as lung retention of therapeutic agents is relatively short-lived. The chapter describing clearance is extremely well done covering mechanisms, kinetics, species variation and the influence of site of deposition.

Section four addresses molecular and cellular responses of the lung to inhaled particles. This is divided into five chapters dealing with gene expression, uptake by epithelial cells, responses of inflammatory cells, dendritic sentinel cells and response to aeroallergens. Each of these topics is self-explanatory as described. Again the authors have made laudable contributions which further extend the readers' understanding of the potential effects of particles in the lungs. A chapter dedicated to the immunology of the lung might have been included in this section. Elements of this topic are covered in the chapters on gene expression and inflammatory cells and also in the final section of the book. The scope of each of these chapters made it difficult for the authors to focus in detail on inflammatory mediators (the topic of an entire book in the Lung Biology in Health and Disease Series) while covering their broader topic.

Section five examines the systemic responses of the lung to inhaled particles The first two chapters of this section reiterate in greater detail issues, which were raised in section three concerning mucociliary clearance and the role of surfactant in disease associated with particle exposure. Pathophysiological and neurally mediated cardiopulmonary effects are discussed in the last two chapters.

The final section deals in three chapters with the health consequences of particle-lung interactions. These chapters address the immune effects and physiological and epidemiological evaluation of cardiopulmonary disease.

This is a well-organized volume encompassing the physics, chemistry and biology of particle-lung interactions. While the majority of readers will be those interested in environmental and occupational exposure to aerosols the contents are of interest to the pharmaceutical scientist. There have been several volumes describing delivery to the lungs and pharmaceutical aerosols but as new drugs and delivery systems are developed an understanding of particle-lung interactions will play a prominent part in therapeutic strategies.

I strongly recommend that those researchers routinely working in the field of aerosol therapy acquire this book and that others with a peripheral interest consider this a valuable reference text.

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Design and Analysis of Bioavailability and Bioequivalence Studies, Second Edition Revised and Expanded. Shein-Chung Chow and Jen-Pei Liu, Eds. Marcel Dekker, Inc., 270 Madison Avenue, New York, NY 1006-0602, http://www.dekker.com/, 1999. 584 pp., illustrations. $195.00.

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This volume is the third publication in the Biostatistics Series that is designed to provide references and textbooks in this important discipline. The goal of this volume is to present essential statistical concepts and methodologies for assessing bioequivalence of pharmaceutical products within the context of current regulatory and drug development practices. The volume is also intended to serve as a bridge between biostatisticians and pharmaceutical scientists.

The volume is organized into sixteen chapters followed by a list of references and appendices of useful statistical tables and SAS programs. Chapter 1 introduces the reader to the origin and evolution of bioavailability and bioequivalence studies in drug development, provides some information of basic biopharmaceutics and pharmacokinetics, and key statistical considerations in bioequivalence assessment that are addressed in the subsequent chapters. Chapters 2–9 are devoted to issues related to design and analysis of traditional bioequivalence studies for comparing two formulations. Information provided in these chapters is essential for understanding the key statistical concepts and assumptions underlying the current practice of bioequivalence testing. Design and analysis of studies for comparing more than two formulations is covered in chapter 10, and chapter 11 deals with bioequivalence studies based on pharmacodynamic response and clinical endpoints. In chapter 12, experimental design and analysis of certain pharmacokinetic studies such as dose proportionality and drug interaction studies are discussed. A meta-analysis approach is proposed in chapter 13 for analysis of several (independent) bioequivalence trials, and the authors postulate that this type of analysis may provide a means to evaluate bioequivalence between multiple generic products. Concepts of *Population* and *Individual* bioequivalence are introduced and discussed in chapter 14 and statistical procedures for these approaches described in chapter 15. The final chapter is devoted to a review of statistical topics in four selected FDA guidance documents.

This volume serves as a useful reference for pharmaceutical scientists and graduate students who are interested in the design and analysis of bioequivalence studies. It also provides an historical perspective on the evolution of bioequivalence test methods in the context of regulatory policies and public debates on these issues. Detailed description of current statistical concepts, methodology, and underlying assumptions are provided and exemplified. The emphasis of this volume is on statistical concepts and methodology (as it should be), so that on some occasions appears to be at the expense of underlying pharmaceutical principles. For the next edition of this volume, it is suggested that the authors consider incorporating additional discussion of underlying pharmaceutical principles and mechanisms. For example, a discussion and root-cause-analysis of "failed" bioequivalence studies will be very useful for pharmaceutical scientist who are engaged in formulation development and bioequivalence testing.

(Opinions expressed in this review are those of the author and not of the FDA).

Supervised and Unsupervised Pattern Recognition. Feature Extraction and Computational Intelligence. Evangelia Micheli-Tzanakou. CRC Press LLC., 2000 Corporate Blvd., N.W., Boca Raton, FL 33431, 2000. xxii, 371 pp., illustrations. $99.95.

If you are working on neural network and/or pattern recognition, or if you are looking for ways to extract features, classify them and match to templates from signals or images, this book is a good source to read. The book, as part of the series "Industrial Electronics Series", describes in details the application of supervised and unsupervised pattern recognition of various types of signals and images, which have been carried out in the editor/author's department. Most of the other authors are students of the editor/author. The ALOPEX (Algorithm of Pattern Extraction), developed by the author/editor and Harth in 1973, is discussed thoroughly in the various applications covered in the book. The book includes four sections and each section contains a few chapters. Each chapter is an independent report but tightly related to the topic of every section.

Artificial neural networks, or simply neural networks, are constituted with interconnected units or neurons that can be implemented with hardware devices or simulated with computer. Connected neurons form different layers among which there are one input layer, one output layer, and at least one middle layer. The systems take a pattern of data as input, pass through middle layers for processing, and output results. Each neuron sums all inputs to it and outputs the proceeded information to other neurons. The connection between two neurons, called synapse, is characterized by the strength (i.e. synaptic weight) that controls how the two neurons affect each other. In order to recognize a signal or an image, the synaptic weights are needed to be assigned. This involves the training and learning step before an artificial neural network becomes applicable. There are two ways to carry out the training step. The first one is supervised training where the information about the correct or desired output for each input training pattern is given. The second one is unsupervised training where no such information is available. Using self-learning or self-organizing approaches is one of the ways implemented in the unsupervised training. Another issue in pattern recognition is how to represent input data and how to extract features from input data. This book investigates these issues carefully and reports many outstanding and inspiring work.

The four sections of this book are carefully edited. The first section describes overview on classifiers and especially the nonparametric regression approaches. Subjects of neural networks are reviewed. A system for handwritten digit recognition is well explained. Other feature extraction methods, such as wavelet analysis, invariant moments, entropy, ceps-

trum analysis and fraction dimension, are covered in one chapter. The second section focuses on the unsupervised neural networks and fuzzy neural networks, Their applications to handwritten character recognition, as well as recognition of normal and abnormal visual evoked potentials, are discussed in following chapters. The third section discusses issues of advanced neural network architectures and their applications such as classification of mammograms and a visual ophthalmologist system. A 3D neural network architecture is introduced as well. The last section incorporates general applications and simulations in various fields of signal and image analysis and recognition including speaker identification, face recognition, and biological and machine vision. Implementation of the neural networks with hardware devices is also thoroughly discussed.

In summary, this book, "Supervised and Unsupervised Pattern Recognition", is neither a tutorial nor textbook of pattern recognition. Rather it is an excellent source of knowledge of the state of the art of feature extraction, supervised and unsupervised learning and training schemes in addition to various notable finds and exciting applications of signal and image analysis and recognition. Because it is relatively independent, each chapter provides its own insight into an individual discussion. Nevertheless, all chapters are well suited into each section and the book would provide advanced readers with in-depth guidance and inspiring ideas as to new applications of signal and image analysis and recognition.

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Vaccine Adjuvants. Preparation Methods and Research Protocols. Derek T. O'Hagan, Ed. Humana Press, 999 Riverview Drive, Suite 208, Totowa, NJ 07512, http://www.humanapress.com, 2000. x, 342 pp., illustrations. $99.50.

This book is a welcome addition to the rapidly expending field of immunological adjuvant. The editor has done an outstanding job in persuading experts both from the industry and academic institutions to contribute in a wide range of topics on vaccine adjuvants. This book should be valuable for researchers working in the area of vaccine development for infectious diseases, cancer, autoimmune diseases, and modulation of reproduction and animal productivity.

Three chapters, An Overview of Adjuvant Use; Harmful and Beneficial Activities of Immunological Adjuvants; and Transcutaneous Immunization, provide excellent basic information that should be of interest to both new and established researchers in the area of vaccine development. Other chapters are focused on a single adjuvant with an aim to suggest specific conditions where a particular adjuvant may be preferred. Alternative choices are also provided to assist researchers to select an adjuvant according to their specific needs. The step-wise method of antigen and adjuvant formulation provided in this book should be useful to researchers who are not expert on that particular adjuvant. Overall, this is an excellent comprehensive book on vaccine adjuvants.

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Solid-State Chemistry of Drugs, Second Edition. Stephen R. Byrn, Ralph R. Pfeiffer, and Joseph G. Stowell, Eds. SSCI, Inc., 3065 Kent Avenue, West Lafayette, IN 47906-1076, http://ssci-inc.com 1999. xvii, 574 pp., illustrations. $165.00.

This second edition of the book gives a broad overview of some key aspects of solid-state chemistry of drugs and other organic molecules. This book is not only useful for pharmaceutical scientists, but also for researchers in other disciplines, such as chemical engineering, materials science, and physical chemistry. With the solid-state being the most common phase for drugs, this book is especially useful for students and scientists new to the field as well as for researchers who seek a thorough review of the recent developments in the field of solid-state chemistry. The goal of the authors of this book is to provide a basic understanding of the solid-state properties of pharmaceutically active compounds and to make the readers aware of challenges, issues and pitfalls that can arise during the development and manufacture of a drug product. The entire book is divided into five parts and 22 chapters.

The first part of the book gives a general overview of the field of solid-state chemistry of drugs. In this section, the authors have introduced specific subjects, which are discussed in detail in subsequent chapters. The basic concepts of the crystalline state, the various forces involved in crystal packing, the process of crystallization, the properties of amorphous solids, the physical and chemical transformation of drugs, and the role of solid-state technology in pharmaceutical industry, are discussed succinctly and clearly. The second part of the book briefly describes the various methods of analysis for the characterization of the solid-state properties of drugs. The specific questions posed by scientists while characterizing a new drug substance and the various methods available to address some of the specific problems are reviewed systematically in this section. The analytical techniques discussed in this section are X-ray crystallography, X-ray powder diffractometry, microscopy, thermal methods of analysis, and solid-state nuclear magnetic resonance (NMR) spectroscopy. Though some of these techniques are not discussed in detail, the practical applications of each of these techniques to help answer some specific problems are well addressed. The readers are given an ample list of references to help them learn more about a particular technique.

The third part of the book discusses the structure and properties of the most frequently encountered solid forms of drug substances, such as polymorphs, solvates and amorphous forms. Polymorphs of some broad chemical classes of drugs, such as sulfonamides, steroids and barbiturates, are discussed in detail. The fourth part of the book discusses some of the current problems faced by the pharmaceutical industry, especially physical transformations, such as polymorphic transitions and desolvations. If they occur in the final dosage form, these transformations may result in alterations of the physical properties and dissolution rate, and perhaps bioavailability, of the drug. The effect of pharmaceutical processing on the phase transformations is discussed briefly. In particular, as-

pects, such as the effect of crystal packing and hydrogen bonding on the desolvation mechanisms, are discussed and reviewed. The fifth section of the book focuses on the various chemical transformations that may occur in the solid state. Some of the solid-state reactions that are discussed are oxidations, hydrolyses, decompositions, photochemical reactions, and thermal reactions. All these reactions affect the chemical stability of solid pharmaceuticals, both as bulk drugs and in formulations. At the end of this section, some miscellaneous topics are discussed, which are expected to attract more interest in the future. Such examples include various aspects of crystallization, molecular mobility of solids, role of defects in solid-state reactions, solid-state stability of protein pharmaceuticals, and prediction of crystal structures and polymorphs. The last chapter discusses the regulatory aspects of drugs in the solid state. It would probably be more useful to include a separate chapter on regulatory aspects perhaps following the chapter on reaction kinetics. The various decision trees presented are of great practical importance to scientists in the pharmaceutical industry and hence need special attention.

The authors can be complimented on the relatively small number of errors. However, there is some confusion on pages 24 and 25, where the y-axis labels on Figures 1.17 and 1.18 indicate "moles of water" and "% water content", respectively, whereas the figure legends indicate "Idealized vapor pressure versus relative humidity plot" and "Vapor pressure versus relative humidity diagrams for three hydrates of sodium cefazolin", respectively, for the two figures. The moles of water and vapor pressure should not be used interchangeably. Also, in Table 16.5, on page 337, forms I and II of hydrocortisone 21-butanoate ester are interchanged. According to the text, form I was crystallized from 2-propanol and belongs to the space group $P6_1$, whereas form II was crystallized from toluene and belongs to space group $P2_12_12_1$. Another minor error is noticed in Table 16.5 where forms I of the 21-butanoate and 21-pentanoate esters of 9α-fluorohydrocortisone are shown to be crystallized from ethanol, whereas 342, paragraph 2, indicates that both the esters were crystallized from methanol. Apart from these minor errors, the book is very clearly written and well organized.

In each of the chapters of the book, the basic concepts have been well substantiated with figures, tables, well-drawn illustrations and various case examples. There is an extensive bibliography of references at the end of each chapter. A glossary, which clearly explains the various terms used, is included at the end of the book. The book is dedicated to Peggy Etter who has made seminal contributions in the area of hydrogen bonding and has been especially influential in the development of graph set theory to classify the different types of hydrogen bonds that can be formed in organic solids. Overall, this book provides a comprehensive review of varied aspects of the solid-state chemistry of drugs and is highly recommended as a reference book for all pharmaceutical scientists interested in the solid state.

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Books Received

Analysis

Affinity Chromatography: Methods and Protocols, Methods in Molecular Biology, Volume 147. Pascal Bailon, George K. Ehrlich, Wen-Jian Fung, and Wolfgang Berthold, Eds. Humana Press, 999 Riverview Drive, Suite 208, Totowa, NJ 07512, http://www.humanapress.com, 2000. x, 230 pp., illustrations. $79.50.

Biomaterials and Bioengineering

Biomaterials and Bioengineering Handbook. Donald L. Wise, Ed. Marcel Dekker, Inc., 270 Madison Avenue, New York, NY 1006-0602, http://www.dekker.com/, 2000. x, 920 pp., illustrations. $235.00.

Pharmaceutics

Pharmaceutical Emulsions and Suspensions, Drugs and the Pharmaceutical Sciences, Volume 105. Francoise Nielloud and Gilberte Marti-Mestres, Eds. Marcel Dekker, Inc., 270 Madison Avenue, New York, NY 1006-0602, http://www.dekker.com/, 2000. xi, 637 pp., illustrations. $195.00.

Pharmaceutical and Clinical Calculations, Second Edition. Mansoor A. Khan, Ph.D., and Indra K. Reddy, Ph.D., Eds. Technomic Publishing Co., Inc., P.O. Box 3535, 851 New Holland Avenue, Lancaster, PA 17604-9961, http://www.techpub.com, 2000. xiii, 396 pp., illustrations. $84.95.

Controlled Drug Delivery. Designing Technologies for the Future, ACS Symposium Series 752. Kinam Park and Randall J. Mrsny, Eds. American Chemical Society, Publications Division, 1155 16th Street, N.W., Washington, D.C. 20036, 2000. xii, 459 pp., illustrations. $150.00.

Therapeutics

Medical Management of Diabetes Mellitus. Jack L. Leahy, Nathaniel G. Clark, and William T. Cefalu, Eds. Marcel Dekker, Inc., 270 Madison Avenue, New York, NY 1006-0602, http://www.dekker.com/, 2000. xxiii, 738 pp., illustrations, $99.75. (This book is divided into five parts: (I) overview; (II) signs, symptoms, diagnosis, and diabetes types; (III) therapies; (IV) complications; and (V) special settings. This is an excellent reference book for those who are involved in the development of insulin delivery systems).

Drugs: Synonyms & Properties. G. W. A. Milne, Ed. Ashgate Publishing Company, 131 Main Street, Burlington, VT 05401, http://www.ashgatechem.com, 2000. xx, 1267 pp., illustrations. $250.00.

Platinum-Based Drugs in Cancer Therapy. Lloyd R. Kelland and Nicholas P. Farrell, Eds. Humana Press, 999 Riverview Drive, Suite 208, Totowa, NJ 07512, http://www.humanapress.com, 2000. xii, 341 pp., illustrations. $145.00.

Molecules, Miracles and Medicines. Andrew Lasslo, Ph.D., Warren H. Green, Inc. 8356 Olive Boulevard, St. Louis, MO 63132, www.iwc.com/whgreen, 2000. ix, 89 pp. $12.95, paper.

Others

Gone for Good: Tales of University Life after the Golden Age. Stuart Rojstaczer. Oxford University Press, 2001 Evans Road, Cary, NC 27513, www.oup-usa.org, 1999. x, 187 pp. $22.00.

Ethical Issues in Biomedical Publication. Anne Hudson Jones and Faith McLellan, Eds. The Johns Hopkins University Press, 2715 N. Charles Street, Baltimore, MD 21218-4319, www.press.jhu.edu, 2000. xx, 374 pp., illustrations. $22.50.

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