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Book reviews

Biological Performances of Materials-Fundamentals of Biocompatibility
J. Black, Marcel Dekker, 2nd Edition, 1992. 390 pages., ISBN: 0-8247-8439-1

This book provides an excellent introduction to the subject of biomaterials and the various parameters that control their use. Divided into four parts and 20 chapters, that are helpfully completed with interesting general references and selected additional readings, it provides a very easy approach and familiarizes the reader with the problematic use of biomaterials. Part I briefly introduces the definitions and the issues of biocompatibility and provides some general considerations on the biological environment, with different recapitulative tables giving macroscopic values and physicochemical conditions of human body. It also deals to some pre-implantation operations, such as sterilization, of which different methods are described. Part II deals with different properties, related to physico-chemical degradation of the implanted materials in vivo, such as the swelling of polymeric carriers, leaching of degradation products, possible corrosion of metallic implants and deformation and friction of hip implants. Part III is related to the host response and the biological effects, triggerd by the implanted materials. The inflammatory process, coagulation reaction, allergic response and carcinogenesis are described, as well as the systemic distribution and excretion of materials. Finally, part IV deals with in vitro and in vivo testing methods available for evaluating new biomaterials. Standard regulations on implants complete the book advantageously, with ISO regulations and ASTM standard tables which are helpful guidelines for the testing of biomaterials.

Intended for undergraduate students courses as a textbook on biocompatibility, its use can be extended to physicians, pharmacists and engineers working in the field of medical devices.

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Biopharmaceutics of orally administered drugs
P. Macheras, C. Reppas and J.B. Dressman, Hemel Hampstead (Ellis Horwood) 1995, ISBN 0-13-108093-8.

Biopharmaceutics, the science dealing with the relationships between the formulation and routes of adminisitration of drug substances, their bioavailability, and ultimately the intensity and duration of therapeutic and toxic effects, is a broad field with many and diverse aspects. It includes hard-core science like the physics of solids and solutions or the molecular biology of membranes, enzymes and carrier proteins, and the chemistry of polymers. The craft of drug formulation is part of it, and the semi-empirical description of dissolution kinetics. It also encompasses subjects as abstract as formal kinetics and statistics. To complete the picture, even regulatory viewpoints could be included. Given the limited space of < 300 pages (the book has a total of 289), any author or group of authors has to decide, which topics to cover, and which ones to omit. Both the choice and the depth of the treatment depend upon the perceived interests and needs of imagined readers, they also reflect the writers' view of the world and priorities.

This book has four parts. The first and last one are short and have only one chapter on 'Rate parameters and physical processes relevant to absorption', and 'Statistical treatment of experimental data', respectively. In the second part, drug dissolution, release and absorption are presented in four chapters, and in part III, there are three chapters on kinetics and mechanisms of drug disposition.

This selection is not without problems. There is no way to treat the basics of (pharmaco-) kinetics on 7 pages or essential biostatistics on 14 pages. For the novice, it is not enough to define some fundamentals without elaborating them or giving at least one good example, while the expert will be bored stiff or just overlook them. The statistics of bioequivalence cannot be discussed these days without at least mentioning confidence intervals. The normal distribution, Student's t-test and linear regression are not enough.

As far as drug release and absorption are concerned, the basic equations and factors affecting dissolution

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rate profiles are discussed as well as the rationale for and fundamental aspects of extended-release systems. Considering the balance between abstract and lengthy arithmetic in Chapter 4 (e.g. the relationship between mass and surface of monodisperse spherical particles or the effect of size reduction on the surface area of cylindrical particles) and specific examples for formulation factors and physiological variables affecting the dissolution and absorption of certain certain drug substances, the former interrupt the text and carry too much weight, but the latter make this book interesting. In general, the biologically oriented sections are informative and highly readable.

This is also true for the third part on drug disposition. Although the book's title refers only to the oral route of administration, biopharmaceutics is incomplete without a close look at drug distribution, metabolism and excretion. Therefore, the three chapters on 'Protein binding', 'Distribution of drugs in the body' and 'Renal and hepatic clerances' are a valuable complement.

The book is a valuable addition to the number of texts available on biopharmaceutics, but readers should not expect to get an even view of the whole field. For some aspects, specialized literature will be required. They are also advised to ponder the question to which extent model equations depict the essence of real-life processes. The book is recommended as a text for students and workers in the field, but it should not be their only reference.

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Vaccine Design, The Subunit and Adjuvant Approach
Michael F. Powel and Mark J. Newman (Editors)
Plenum Press, New York 1995. 949 pp.; $174 (outside the U.S.). ISBN 0-306-44867-X.

It is not primarily the impressive 950 pages, but rather the considerable number of contributors (105) and, most of all, their renowned expertise that appears to guarantee the outstanding quality of this book, right at the first glance. It is certainly a privilege for this book to be prefaced by a foreword of Jonas Salk, the great inventor of the oral polio vaccine, who died unfortunately in June 1995, shortly before the book was put on the market.

The first six chapters cover immunological and formulation aspects for subunit vaccines (Chapter 1), public health implications of emerging vaccine technologies (Chapter 2), preclinical safety assessment requirements (Chapter 3), regulatory issues in vaccine design (Chapter 4), clinical considerations in vaccine trials with special reference to candidate HIV vaccines (Chapter 5), and a scientific-philosophical essay on laboratory empirism, clinical design, and social value (Chapter 6).

Chapters 7–29 address adjuvants, carriers and delivery vehicles. Chapter 7 is an extraordinary compendium of approximately 74 types or groups of vaccine adjuvants and excipients, from Alum and Freund's adjuvants to a variety of lymphokines, surfactants, polymers, vesicles, microspheres and so forth. Each monograph contains information on chemical and physical properties, source, safety/toxicity, recommended storage, uses, and adjuvant properties, and provides most valuable contact addresses. The authors (F.R. Vogel and M.F. Powell) even pointed out that it is their goal to update this compendium in 1996/1997. For this chapter alone the book is of great value for any scientist interested in vaccine formulations. A selection of these adjuvants is then treated in more detail in subsequent chapters: aluminum and calcium compounds (Chapters 8 and 9), MF59, consisting of 4.3% squalene, 0.5% Tween 80 and 0.5% Span 85 (Chapter 10), nonionic block copolymers (Chapter 11), emulsion-based muramyl dipeptide adjuvant formulations ('SAFs') (Chapter 12), virosomal and liposomal preparations (Chapters 13 and 14), vaccines based on lipid-matrices such as protein chochleate, fusogenic proteoliposomes, peptide-phospholipid conjugates (Chapter 15), various vehicles for oral immunization (Chapter 17), polymeric biodegradable microspheres (Chapters 16 and 18), nanoparticles (Chapter 19), water-soluble phosphazene polymers (Chapter 20), monophosphoryl lipid A (Chapter 21), *Quillaja* saponin QS-21 (Chapter 22), immune-stimulating complexes (ISCOMs) based on *Quillaja* saponins, cholesterol and aqueous antigen solution (Chapter 23), γ-inulin (Chapter 24), the immunostimulant loxoribine (Chapter 25), stearyl tyrosine (Chapter 26), cytokines (Chapters 27 and 28), and cytokine-containing liposomes (Chapter 29).

The remaining chapters provide selected examples of current research work on subunit vaccines focusing mainly on the chemistry and immunogenicity of the antigens. In the various contributions, the term 'subunit' embrace antigenic structures such as capsular polysaccharides and outer surface proteins of bacteria, proteins from filarial nematodes, (retro)-virus-like-particles (VLP) and retro-virus-derived particles (VDP), circumsporozoite proteins from *Plasmodium* species, antigens containing one or several epitopes prepared synthetically or biotechnologically, and cancer cell associated mucins. Conjugate vaccines of Haemophilus influenzae and Pneumococci (Chapters 30 and 31), new vaccines against lime disease and filarial nematode infections, (Chapters 32 and 33), retrovirus and retrotransposon particles for antigen presentation and delivery (Chapter 34), preerythrocytic malaria vaccines (Chapter 35), the multiple antigen peptide (MAP)-approach (Chapter 36), synthetic

peptides derived from retroviral proteins against HIV-1 and HTLV-I (human T-cell leukaemia/lymphotropic virus) infections (Chapter 37), synthetic peptides capable of eliciting specific cytotoxic T-cells (CTLs) (Chapter 38), immunotherapeutic agents based on cancer-associated mucins (Chapter 39), synthetic peptide vaccines for Schistosomiasis (Chapter 40) and synthetic hormone/growth factor vaccines for antifertility and cancer (Chapter 41) are described in detail.

In conclusion, I have little doubt that this book will become a standard reference for future development of vaccine formulations, although the editors point out rightly that 'this field is evolving rapidly and, by definition, the information provided will not long remain current'. I recommend this book to all pharmaceutical scientists interested or working in the field of vaccines. It is not only a reality that several subunit vaccines and adjuvant/delivery systems have appeared on the market over the past 5 years, e.g. Hib-Conjugates, HepA bound to liposomes (virosomes), HBsAg bound to alum and acellular pertussis vaccines, but it is also my strong conviction that many more subunit vaccines and a great variety of adjuvants and delivery systems will make their breakthrough in the very near future. Moreover, new vaccines may no longer be treated exclusively as 'biologicals', but considered as common drug formulations requiring corresponding quality standards and controls. Therefore, new vaccines may also be given more emphasis in undergraduate pharmaceutical education; in addition to be treated briefly in microbiology and phamacology courses, they should also be discussed in galenics, biopharmaceutics, and pharmaceutical chemistry and analytics.

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Inhalation Aerosols, Physical and Biological Basis for Therapy

Anthony J. Hickey (Editor), Lung Biology in Health and Disease, Vol. 94, Marcel Dekker, New York, 1996, 511 pp, ISBN 0-8247-9702-7

My long search for a decent introductory text to pharmaceutical aerosols led me by chance to this work. It is without doubt the best comprehensive text on the biopharmaceutics of aerosols and pulmonary drug delivery. Although it is a multi-authored work, the style is remarkably uniform and the book is very readable and well referenced. As Hickey notes in the Preface, his intention was to present the chemistry of formulation, the physics of aerosol generation, aerodynamic behaviour and implications for lung deposition to derive implications for therapy. He has completely succeeded in this intention, and presents a balanced pharmaceutical and medical overview of the subject.

Although the book is divided into three sections, aerodynamic behaviour, biological considerations, and pharmaceutics and pharmaceutical technology, the reader will find many common themes and implied cross-references. Under aerodynamic behaviour we find a straightforward description of particle deposition in the human airways, followed by a short consideration of the problems of hygroscopic materials. The following chapter on mathematical aerosol models is brief and free from complicated mathematics. It presents a descriptive overview of the historical development of lung/aerosol models, being effectively referenced. As to be expected in a series of medical texts, the second section entitled biological considerations is lengthy. All of the points of relevance to biopharmaceutics are mentioned. There is a description of the physiology and pharmacology of the airways followed by considerations of solute transport following deposition and drug metabolism within the lungs. The bioavailability and pharmacokinetics of inhaled drugs are succinctly presented. The chapter on the therapeutic uses of lung aerosols mentions delivery of genes, but does not sufficiently stress the importance of protein delivery to the lungs. But this is understandable, the chapter being written by two physicians.

The third section entitled 'Pharmaceutics and Pharmaceutical Technology' represents almost half of the book and is an excellent introduction and reference to formulation problems. In separate chapters the various aerosol devices are considered: atomisers and nebulizers, ultrasonic aerosol generators, NMIs and DPIs. There are also chapters on the spray drying and supercritical fluid particle generation techniques, and interfacial phenomena and phase behaviour in MDIs.

This is the ideal introduction to the subject of aerosol technology in pharmaceutics. It can be given to a new graduate student starting work in the field, or be read by an industrial pharmacist just starting to work with aerosols. I recommend the book highly. Of course, to keep up to date with the new developments in this vital field of pharmaceutics and drug delivery, one still needs the books of proceedings Aerosol Drug Delivery, currently up to volume 5.

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