Available online at www.sciencedirect.com
SCIENCE DIRECT®
ELSEVIER
European Journal of Pharmaceutics and Biopharmaceutics 63 (2006) 369–372
European Journal of Pharmaceutics and Biopharmaceutics
www.elsevier.com/locate/ejpb

Book reviews

Jim E. Riviere (Ed.), Dermal Absorption Models in Toxicology and Pharmacology (2005, CRS Press, UK-Andover) 374 pp, £ 79.99, ISBN 0-415-70036-1

The book, Dermal Absorption Models in Toxicology and Pharmacology' edited by Jim E. Riviere is an enrichment in the field of dermal absorption. Special topics, which are normally not addressed deeply in comparable books, are presented in detailed and in a well-organized way. Chapter 1, 'Structure and Function of Skin' as well as Chapter 2 'In vitro Diffusion Cell Studies' provide relevant information of these fields in a compressed manner; however, due to the excellent citations, this does not reduce the value of these chapters. After a short introduction on perfused skin models, Chapter 3 focuses on the isolated perfused porcine skin flap (IPPSF). Advantages and disadvantages of this model are discussed and examples of the use of IPPSF like influence of biomarkers, absorption studies, and dermatopharmacokinetic studies are given. In Chapter 4, most of available in vivo models to assess skin absorption are treated. Classical experimental setups are demonstrated, e.g., surface disappearance method and tape stripping as well as newer techniques like FTIR-measurements and microdialysis. Furthermore, problems involving the use of radioactive compounds are discussed. Chapter 5 is dedicated to 'A Novel System Coefficient Approach for Systematic Assessment of Dermal Absorption from Chemical Mixtures'. This model will be of interest for all dealing with risk assessment of complex formulations. Biological-based pharmacokinetic and pharmacodynamic models of the skin are discussed in Chapter 6. Especially numerous well-chosen citations valorize this chapter. In Chapter 7, 'The Prediction of Skin Permeability Using Quantitative Structure–Activity Relationship Methods' fundamentals concerning QSAR are given and the current available methods are described briefly. Subsequently the limitations of these models are discussed. In addition, many hints on freeware programs are provided. Chapter 8 informs how dermal absorption estimations are used in risk assessment. Official guidelines and protocols concerning this topic are tabulated and critical parameters for risk assessment such as receptor fluid, use of radiolabeled substances or way of application are mentioned. Examples of risk assessment for sunscreens, hair dyes, and environmental contamination are included. Chapter 9 'Gulf War Syndrome: Risk Assessment Case Study' clearly demonstrates that chemical mixtures can severely influence dermal disposition and therefore lead to unexpected and surprising toxicological effects. Similar topics are addressed in Chapter 14 'Chemical Mixtures' where mathematical models are given to estimate the influence of interaction on skin absorption. Additionally, the potential impact of multiple interactions is discussed. Special problems of the application of volatile compounds to the skin are addressed in Chapter 10. The method described here represents a first attempt to quantitatively relate the skin disposition of volatile chemicals to their physical properties and environmental conditions. Chapter 11, 'Modeling Dermal Absorption from Soils and Powders Using Stratum Corneum Tape-Stripping In Vivo', presents efforts to model in silico the dermal absorption from soils and powders in vivo. For the model compound 4-cyanophenol reasonable consistency between experimental data and in silico is reported. Assessment efficacy of several penetration enhancers is discussed in Chapter 12. Thereby methods to investigate enhancement effects are presented and the action of special enhancers, e.g., fatty acids, terpenes, and azone, is mentioned. Tables with information on penetration enhancement with various drugs substantiate this chapter. Chapter 13 deals with 'Dermal Blood Flow, Lymphatics, and Binding as Determinants of Topical Absorption, Clearance, and Distribution'. The influence of these effects on in vitro and in vivo experiments is discussed in detail. The final Chapter 'Animal Models: A Comparison of Permeability Coefficients for Excised Skin from Humans and Animals' aims to find relationships between permeability data of different animals and humans. First results are presented relying on databases for which the data set has to match specified criteria, such as the application as aqueous solution. These databases are given in Appendix A and the sources of the permeation data in Appendix B. Furthermore, Appendix C informs on references about prior comparisons of animal skin permeability coefficient data.

In summary, this is a well-written book which addresses many aspects in dermal toxicology and pharmacology. For detailed information references are well

selected. The book is highly recommended for graduate students and researchers in industry and academia looking for fundamental information on the exciting fields of skin absorption, skin toxicology, skin risk assessment, and skin pharmacology. It was a pleasure for me to go through the book!

Ulrich Schäfer*
Department of Biopharmaceutics and Pharmaceutical Technology, Building A 4.1, Saarland University, 66123 Saarbrücken, Germany
E-mail address: ufs@mx.uni-saarland.de

Available online 9 March 2006

* Tel.: +49 681 302 2019; fax: +49 681 3024677.
doi:10.1016/j.ejpb.2006.01.008

Mark C. Rogge, David R. Taft (Eds.), Preclinical Drug Development, Drugs and the Pharmaceutical Sciences Series (vol. 152, 2005, Taylor & Francis, Boca Raton) ISBN 0-8247-0293-X

The selection of drug molecules for development from an abundance of potential candidates is a key element of preclinical development programs. Effective molecule assessment programs facilitate more productive and informative absorption, disposition, and safety data, and help guard against unexpected pharmacokinetics and toxicities in clinical testing. Furthermore, experimental in vitro predictive methods for assessing tissue permeability, cellular transport, and organ toxicity have reduced the number of animals used in preclinical drug development while simultaneously providing further mechanistic insights into transport, metabolism, and toxicity of potential new candidate drugs. Thus, drug molecules periodically pass through decision gates predefined by carefully selected criteria as a strategy to terminate drug development as early as possible where appropriate to reduce unexpected late clinical stage failure and thus provide opportunities for more viable drug candidates to move forward in the development pipeline.

The scope of the text covers the general elements of preclinical drug development and introduces the reader to these scientific disciplines.

Chapter two encompasses interspecies differences in physiology and pharmacology between animal and human populations. The discussion also focusses on interspecies pharmacokinetic differences including absorption, metabolism, distribution, protein binding, and biliary excretion. Chapter three extends this discussion to the use of transgenic animals for preclinical drug development. This includes also disease models for evaluating biological activities of new drugs. Due to their fundamental differences, the pharmacokinetics/ADME of small and large molecules (protein pharmaceuticals) are described in separate chapters. Other chapters include preclinical pharmacokinetic–pharmacodynamic modeling and simulation, factors related to the formulation and route of administration influencing drug permeability and absorption, membrane transporters, and in vitro/isolated organ systems in the assessment of pharmacokinetics and non-clinical toxicity evaluations. Furthermore, the role of the ICH and the technical requirements for the registration of pharmaceuticals for human use in current toxicology practices is discussed including case studies of Celecoxib (Celebrex®), Trastuzumab (Herceptin®), Rituximab (Rituxan®), and Infliximab (Remicade®). Chapter 11 is a survey on the application of pathology in the safety assessment of compounds pointing out the involvement of pathologists during different phases of a toxicity/carcinogenicity study. It is demonstrated that, e.g., early microscopic assessment of nonhuman tissues may reveal subtle toxicity and subsequently lead to a timely discontinuation of the development project. Finally, in Chapter 12, the principles of toxicogenomics and its implications for preclinical drug development are discussed. Due to the fact that modulation of gene expression is of paramount importance in the mechanisms of drug-induced toxicity, major efforts are being made to determine the relevance of gene expression in response to drug exposure.

Overall, most chapters are starting points for understanding the scientific foundation needed to move a drug candidate into clinical trials. While there are additional textbooks that are more focussed and advanced on specific scientific disciplines, they should be regarded as complementary.

Peter Langguth*
Pharmaceutical Technology and Biopharmaceutics, Institute of Pharmacy, Johannes Gutenberg-University, D-55099 Mainz, Germany
E-mail addresses: langguth@mail.uni-mainz.de

Available online 28 February 2006

* Tel.: +49 6131 392 5746; fax: +49 6131 392 5021.
doi:10.1016/j.ejpb.2006.02.001

Stanley H. Nusim (Ed.), Active Pharmaceutical Ingredients Development, Manufacturing, and Regulation, Drugs and the Pharmaceutical Sciences (vol. 151, 2005, Taylor & Francis, Boca Raton) ISBN 0-8247-0293-X

Organic chemicals (Active Pharmaceutical Ingredients, "APIs"), generally synthetic and not of biotechnological origin such as fermentation products, are the subject of this book. Historically these compounds are also referred to as Bulk Drug Substances (BDS) which are determined to be used in a final pharmaceutical dosage form.