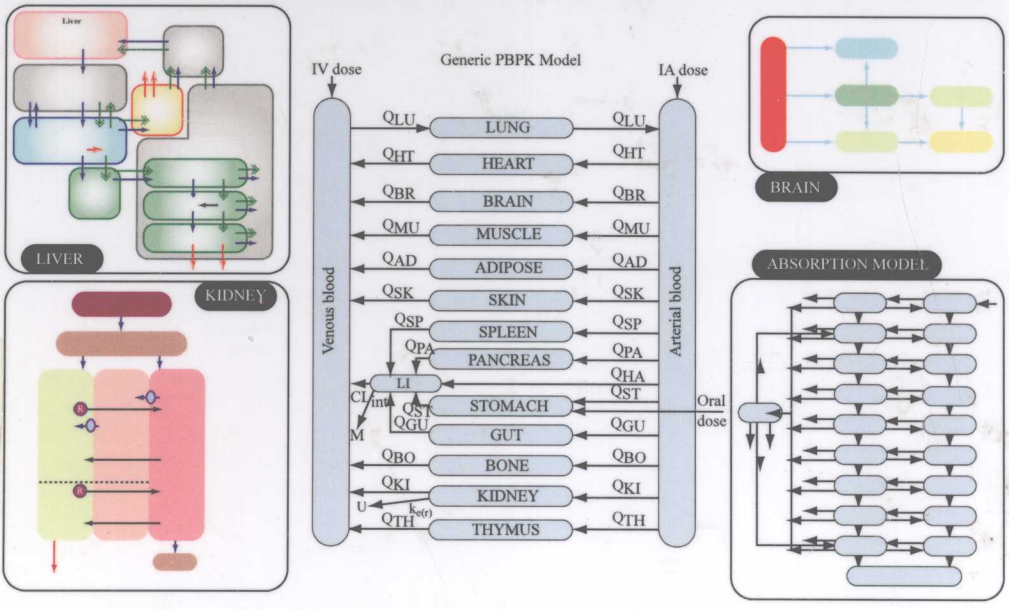
Physiologically-Based Pharmacokinetic (PBPK) Modeling and Simulations

Principles, Methods, and Applications in the Pharmaceutical Industry

Sheila Annie Peters



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Principles, Methods, and Applications in the Pharmaceutical Industry

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藏书章

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PHYSIOLOGICALLY-BASED PHARMACOKINETIC (PBPK) MODELING AND SIMULATIONS

This book is dedicated to my parents, friends, and Alfred and Christina who have always believed in me.

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PREFACE

Physiologically-based pharmacokinetic (PBPK) modeling has made rapid strides in the pharmaceutical industry in the last decade or so, thanks to an increasing awareness of the potential applications of this powerful tool. As pharmaceutical companies are working to integrate PBPK modeling into their lead selection cycle and clinical development, the availability of commercial software has played a key role in enabling even those without modeling expertise to come on board. However, this entails the risk of misuse, misinterpretation, or overinterpretation of modeling results, if the principles and underlying assumptions of PBPK modeling are not clearly understood by the users. Today, the challenge facing pharmaceutical companies is educating and training their staff to achieve an effective application of PBPK/ pharmacodynamics (PD) in projects across the value chain. In the future, providers of education should take on the responsibility of making available, modelers with appropriate skills. Given the complexity of PBPK modeling, it is certainly not an easy task for a beginner with little or no background to understand the model structure and to be aware of its limitations. The lack of a textbook on PBPK has been a further deterrent. It is hoped that this book will serve as a primary source of information on the principles, methods, and applications of PBPK modeling, exposing the power of a largely hidden and unexplored tool. Applications in the pharma sector will be the main focus, as applications in environmental toxicology and human health risk assessment have already been the subject of a previous publication.

Target audiences for the book include students and researchers in academia, apart from scientists and modelers in the pharmaceutical industry. The book can also be a resource for R&D managers in the pharmaceutical industry, seeking a quick overview of the benefits of applying PBPK modeling along the drug discovery and development value chain. An understanding of the principles of PBPK modeling by R&D management would enhance their acceptance and appreciation, which in turn can translate to effective managerial support for PBPK modeling. This book is intended to serve the interests of both the general reader, who may only want an overview of the applications of PBPK modeling without wanting an in-depth understanding of the underlying methods, and the specialist reader, who may be interested to build new models. For the general reader, keywords appear in boldface and are explained at the end of the chapters. No particular expertise is assumed in order to keep the book accessible to a diverse audience. An extensive list of bibliographic

references will help the specialist reader to build on the concepts developed in the book. A generous use of figures to illustrate concepts will help the reader gain valuable insights into this fascinating subject.

The book comprises two parts. The first part provides a detailed and systematic treatment of the principles behind physiological modeling of pharmacokinetic processes, interindividual variability, and drug interactions for small-molecule drugs and biologics. The second part exposes the reader to the powerful applications of PBPK modeling along the value chain in drug discovery and development.

SHEILA ANNIE PETERS

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S. A. P.

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PRINCIPLES AND METHODS

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