
Preface

Drug metabolism and transport is a crucial function in the discipline of pharmaceutical sciences, an arena that is vast, ever improving, and extremely dynamic. The kinetics of drug metabolism and transport is an indispensable scientific branch in this field. The editors have different experiences that have developed their passion for the topic of kinetics of drug metabolizing enzymes and transporters.

One of the editors developed an internal learning program within the department geared mostly to teaching scientists at all levels to think more intuitively and to apply these kinetic principles in their every day work. The heightened awareness resulted in tangible benefits, from improved design of experiments, better justification of experimental approaches, and more in-depth data analysis, with greater insight into mechanisms.

For one of us, the drive toward gaining a deeper understanding of enzyme kinetics stemmed from one simple question—“how is a rate of substrate depletion different from clearance in microsomal incubations?” Knowing how each of the kinetic parameters is derived is an important step toward understanding the limitations and applications of an assay, be it *in vitro*, *in vivo*, or *ex vivo*. These assays make up the everyday “tool box” of today’s drug metabolism and pharmacokinetics scientist, either during the discovery of new chemical entities or drug characterization of clinical candidates. Therefore, a strong grasp of the kinetics that occurs in each of these assays is essential for seamless integration of such assays (*in vitro* to *in vivo*) and their realistic application in drug discovery and development.

One editor, specifically trained in pharmacokinetics, has gained an appreciation for enzyme kinetics while conducting research on drug metabolism. Enzyme kinetic concepts are utilized regularly in modeling metabolic elimination of drugs, as well as in overall nonlinear drug disposition models. Additionally, understanding basic concepts such as different enzyme–substrate–inhibitor interaction schemes, deriving appropriate equations, and interpreting kinetic parameters correctly is critical for gaining a deep knowledge of the subject. Appreciation of these aspects on the one hand helps in application of fundamental concepts to real-life scientific questions and on the other hand forms the foundation of extending our understanding of the basic science of enzyme structure and function. The didactic nature of this book will greatly aid all levels of academic and industry scientists in reviewing basic concepts, as well as in applying these concepts to practical research questions.

A primary goal for this book, from the editors’ point of view, was to focus on the very practical aspects of applying enzyme kinetic principles. This book is divided into five parts. Part I provides the fundamental principles of enzyme kinetics. What are K_m and V_{max} ? How are these parameters derived? While these are fundamental concepts dealt with in other texts, what do they really mean from a drug metabolism and transport perspective? This book aims at answering this question. Part II of the book focuses on the kinetics of oxidative and conjugative drug metabolizing enzymes and drug transporters. Part III considers some modeling approaches for both drug metabolizing enzymes and transporters, as well as novel systems biology approaches. Understanding of variability—intrinsic and extrinsic—is dealt with in Part IV and is considered crucial from “design of experiments” to “interpretation of results.” This subject is tackled from a kinetics perspective.

Finally in Part V, case studies provide real-life examples, conversations between supervisor and scientist, and current outlooks, which provide opportunities from which we can all learn. Overall, this book is conceptualized as a teaching tool for a novice, nonmathematically trained scientist and to help supervisors in training these scientists on fundamental concepts. In addition, the book provides insights into applying these concepts, especially geared to those who deal with enzyme kinetics on a daily basis.

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