FUNDAMENTALS OF DRUG DELIVERY

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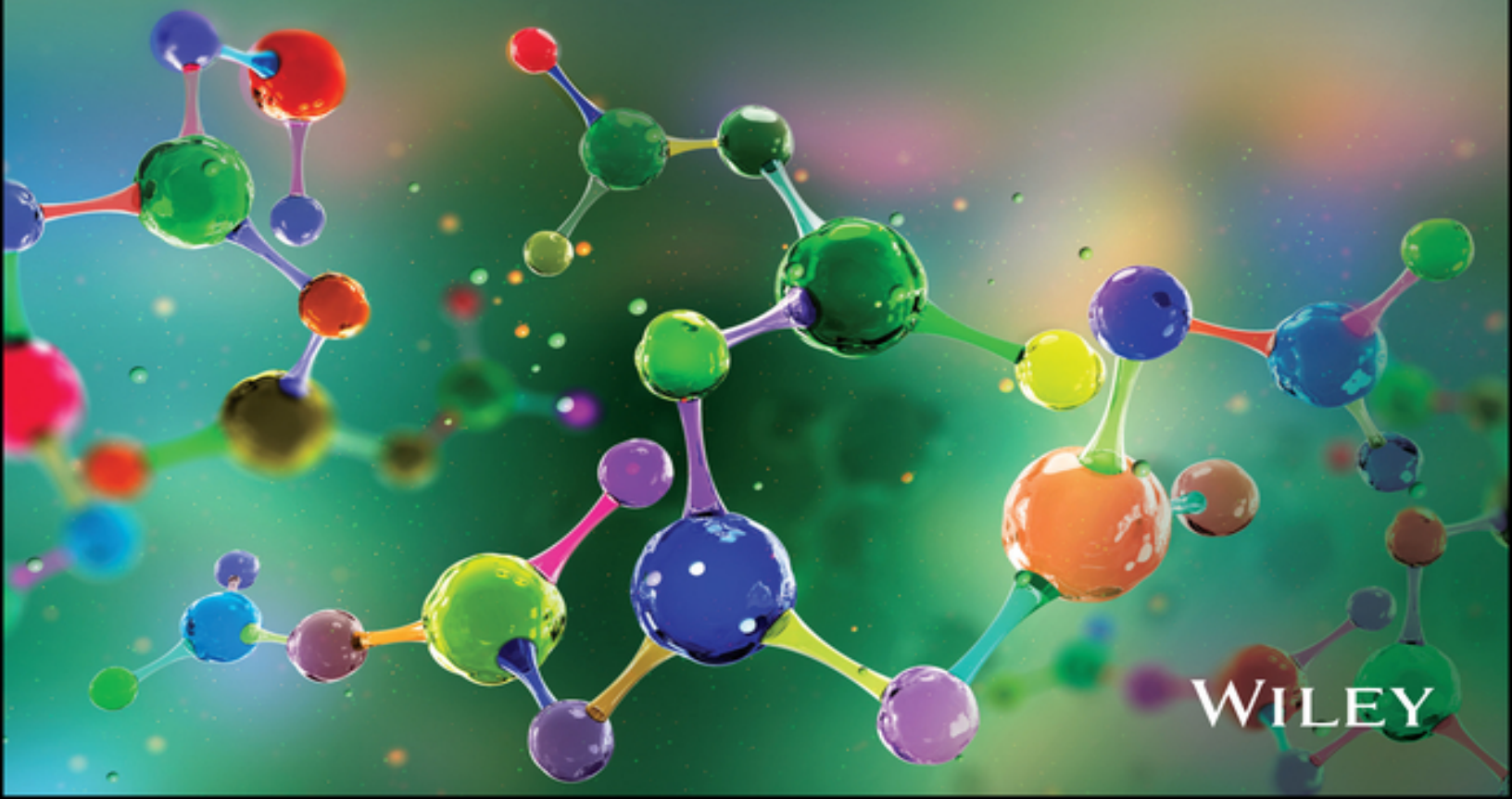

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$$\widetilde{M}_{1,R} = \tau - \frac{1}{6} - \frac{2}{\pi^2}\sum_{n=1}^{\infty}\frac{(-1)^n \exp[-n^2\pi^2\tau]}{n^2}$$

Chapter 19

Fundamentals of Drug Delivery

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Preface

Effective, controlled drug delivery has the potential to greatly impact the therapeutic outcome, clinical benefit, and safety of drugs in a wide range of diseases and health conditions. There are a large number of potentially useful drugs with limited effectiveness and/or safety concerns due to poor drug delivery. This may occur because a physiologically relevant concentration is not delivered to the target site, does not remain in contact for a sufficient period, or causes adverse effects because of the resulting high blood concentrations associated with indiscriminate release. Controlled drug delivery systems are designed to carry the drug and release it at the target site in a timely manner, facilitating its absorption and optimizing its physiological action. An effective controlled drug delivery system improves efficacy and safety by controlling the rate, time, and place of drug release within the body, thereby minimizing dose requirements and the potential to interact with non-target body sights that can contribute to undesirable side effects. Drug delivery has evolved from relatively simple systems to modern technologies designed to personalize medicines that have biologically precise drug release in response to real-time monitoring of body parameters.

Controlled drug delivery system development is rapidly evolving with an ever-increasing focus on advanced technologies that bring together a wide range of skilled professions including pharmaceutical scientists, chemical, mechanical, and electrical engineers, chemists, physicists, and clinicians. It is an exciting field that has helped to advance clinical outcomes in almost every health condition, ranging from negating the need for cold-chain storage thus

allowing medicines to be transported to the most remote parts of the world, to precision targeting of drugs in cancer treatment. This book is designed to provide an insight into the fundamentals of drug delivery and the important processes in the development of controlled drug delivery systems.

The book is divided into three parts.

Part 1 (Chapters 1–8) introduces the concept of drug delivery and provides a perspective into the challenges, opportunities, and fundamental processes involved in the development of controlled drug delivery systems. It includes a historical perspective and a peek into the future of drug delivery. There is a focus on the drug development process, including the selection of pharmaceutical candidates and evaluation of their physicochemical characteristics with emphasis on the relevance to dosage form design. The role and application of mathematical modeling and the influence of drug transporters in pharmacokinetics and drug disposition complete this section.

Part 2 (Chapter 9–13) is focused on particular challenges in controlled drug delivery and advanced delivery technologies. This includes delivery systems for biologicals, an increasing drug category that presents enormous therapeutic opportunities and equally enormous delivery challenges. The application and recent advances in cell-mediated drug delivery are discussed, and there is a series of chapters on nanotechnology that include fundamentals, applications for targeted delivery, and discussion of the toxicological and safety issues.

Part 3 (Chapters 14–20) provides a “top to bottom” critique of the common administration routes for controlled drug delivery. Each chapter begins with a short introduction and then a more detailed discussion of the physiology pertinent

to each administration route, focusing on the barriers to drug delivery. Controlled drug delivery systems that have been evaluated for each route are then discussed before some conclusions summarizing the state-of-the-art and potential future developments. Each chapter includes comprehensive references at the time of writing for those wishing to read the primary literature. *Controlled* drug delivery systems imply that control over dosing resides in the formulation with control over drug release and predictable drug delivery. However, it is apparent that, given the complexities of the biological barriers present for the administration routes, in several cases control over drug delivery arises predominantly from the biological barrier. Although strategies have been developed to reduce these barriers – for example the use of penetration enhancers – it is contentious whether these approaches truly allow *controlled* drug delivery. However, in seeking to provide a comprehensive critique of the current literature, such partially controlled systems have been considered.

We express our thanks to the authors who have contributed to this book. In each case, the chapters are authored by well-respected researchers in the field who have generously provided their knowledge and experience, and continue to contribute to advancing research in their fields. We are also grateful to Jonathan Rose and his team at Wiley who have brought the concepts and chapters to fruition, and shown remarkable patience in dealing with editors who agree with Albert Einstein that “time is an illusion”.

Australia
June 2021

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