
Prodrugs

Biotechnology: Pharmaceutical Aspects

Ronald T. Borchardt and C. Russell Middaugh, Series Editors

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R.T. Borchardt, E.H. Kerns, C.A. Lipinski, D.R. Thakker, B. Wang

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Volume V: *Prodrugs: Challenges and Rewards, Parts 1 and 2*

V.J. Stella, R.T. Borchardt, M.J. Hageman, R. Oliyai, H. Maag, J.W. Tilley

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Prodrugs: Challenges and Rewards

Part 1

 Springer



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Preface

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The astute reader will recognize that this concept is as applicable now as it was in the 1950s. At present we use terms such as “drugability” or the need for “drug-like” properties to describe the requirement to incorporate these properties so that the complex synthetic molecules of today can be clinically tested and potentially commercialized. In the mid-1980s, with the advent of molecular biology and the availability of pure protein targets, many new chemical entities were found to be effective at the molecular/receptor level but ineffective as molecules of commercial value. Maximizing binding often led to molecules so chemically constrained that drug-like properties could no longer be built in without significantly compromising activity. Some have referred to this as the “high affinity trap.” Of necessity, this began to change. The papers and talks given by C.A. Lipinski and his collaborators made medicinal chemists aware that high throughput screening for drug-like properties should be performed in parallel with molecular/receptor screens so that leads and, ultimately, drug candidates had a better chance of clinical success.

Therefore, in the two parts of this book, we attempt to present the current status of the prodrug concept and its many applications and to highlight its many successes in overcoming the formulation and delivery of problematic drugs. Dictated by the quantity of material, this book is divided into two parts.

The first part is composed of chapters that address the ability of prodrugs to overcome biopharmaceutical challenges resulting from poor permeability of polar drug entities, poor aqueous solubility of oral and parenteral drugs, inadequate targeting of the drug to the brain or particular diseased tissues, etc. This part was specifically directed to teams responsible for the design and delivery of problematic drugs in which the flaw in the parent drug was clearly identified and a prodrug solution sought. Approved and marketed prodrug examples as well as experimental and research concepts are presented.

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Our goal, therefore, in editing and contributing to this book is to provide sufficient examples and supporting literature to introduce this topic to the novice as well as to help the professional in the design of prodrugs. We hope our enthusiasm for this topic is obvious and infective with a full recognition of the challenges and rewards that prodrugs can bring.

Valentino J. Stella, Ph.D.
For the editors

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