Drug Delivery and Targeting
for Pharmacists and Pharmaceutical Scientists

Edited by

Anya M. Hillery
Department of Health Sciences
Saint Louis University
Madrid Campus, Spain

Andrew W. Lloyd
School of Pharmacy and Biomolecular Sciences
University of Brighton
UK

and

James Swarbrick
President, PharmaceuTech Inc
Pinehurst, NC
USA

London and New York
## Contents

Preface ix  
Acknowledgements xi  
Corresponding Authors xiii  

### Section 1: Introduction to Advanced Drug Delivery and Targeting

#### Chapter 1: Drug Delivery: The Basic Concepts  
Anya M. Hillery  
1.1 Introduction 2  
1.2 The concept of bioavailability 3  
1.3 The process of drug absorption 6  
1.4 Pharmacokinetic processes 30  
1.5 Timing for optimal therapy 33  
1.6 Drug delivery considerations for the 'new biotherapeutics' 37  
1.7 Conclusions 46  
1.8 Further reading 47  
1.9 Self-assessment questions 48  

#### Chapter 2: Drug Delivery: Market Perspectives  
Paul Evers  
2.1 Introduction 50  
2.2 Commercial importance of advanced drug delivery technologies 50  
2.3 Market analysis 54  
2.4 Industry evolution and structure 60  
2.5 Further reading 61  
2.6 Self-assessment questions 62  

#### Chapter 3: Advanced Drug Delivery and Targeting: An Introduction  
Anya M. Hillery  
3.1 Terminology of drug delivery and targeting 64  
3.2 Rate-controlled release in drug delivery and targeting 65  
3.3 Drug targeting systems 69  
3.4 Dosage forms for advanced drug delivery and targeting systems 70  
3.5 Routes of administration 72  
3.6 Strategies to increase drug absorption 78  
3.7 Conclusions 81  
3.8 Further reading 81  
3.9 Self-assessment questions 81  

#### Chapter 4: Rate Control in Drug Delivery and Targeting: Fundamentals and Applications to Implantable Systems  
Hongkee Sah and Yie W. Chien  
4.1 Introduction 84  
4.2 Advantages and disadvantages of implantation therapy 85  
4.3 Biocompatibility issues 87  
4.4 Non-degradable polymeric implants 88  
4.5 Biodegradable polymeric implants 99  
4.6 Implantable pumps 107  
4.7 Conclusions 113  
4.8 Further reading 114  
4.9 Self-assessment questions 114
Chapter 5: Drug Targeting Systems: Fundamentals and Applications to Parenteral Drug Delivery
Daan J.A. Crommelin, Wim E. Hennink and Gert Storm

5.1 Introduction 118
5.2 Soluble carriers for targeted drug delivery 127
5.3 Particulate carriers for drug targeting 131
5.4 Pharmaceutical aspects of carrier systems 139
5.5 Conclusions and prospects 142
5.6 Further reading 142
5.7 Self-assessment questions 143

Section 2: Routes of Drug Delivery

Chapter 6: Oral Drug Delivery
Vincent H.L. Lee and Johnny J. Yang

6.1 Introduction 146
6.2 Structure and physiology of the GI tract 146
6.3 Physiological factors affecting oral bioavailability 150
6.4 Formulation factors affecting oral bioavailability 158
6.5 Advantages and disadvantages of oral drug delivery 163
6.6 Current technologies in oral drug delivery 166
6.7 New and emerging technologies in oral drug delivery 170
6.8 Conclusion 182
6.9 Further reading 182
6.10 Self-assessment questions 183

Chapter 7: Oral Trans-Mucosal Drug Delivery
Janet Hoogstraate, Luce Benes, Sophie Burgaud, Françoise Horriere and Isabelle Seyler

7.1 Introduction 186
7.2 Structure and physiology of the oral mucosa 186
7.3 Physiological factors affecting oral transmucosal bioavailability 189
7.4 Formulation factors affecting oral transmucosal bioavailability 192
7.5 Advantages and disadvantages of oral transmucosal drug delivery 193
7.6 Current technologies for oral transmucosal drug delivery 196
7.7 New and emerging technologies for oral transmucosal drug delivery 198
7.8 Conclusions 205
7.9 Further reading 205
7.10 Self-assessment questions 206

Chapter 8: Transdermal Drug Delivery
M. Begoña Delgado-Charro and Richard H. Guy

8.1 Introduction 208
8.2 Structure and physiology of the skin 208
8.3 Factors affecting transdermal bioavailability 211
8.4 Advantages and disadvantages of transdermal drug delivery 216
8.5 Current technologies for transdermal drug delivery 217
8.6 New and emerging technologies for transdermal drug delivery 229
8.7 Conclusions 233
8.8 Further reading 234
8.9 Self-assessment questions 235
Section 3: Future Directions of Drug Delivery and Targeting

Chapter 14: Plasmid-based Gene Therapy
Ram I. Mahato and Eric Tomlinson
14.1 Introduction 372
14.2 Gene expression systems 374
14.3 Gene delivery systems 377
14.4 Biodistribution and pharmacokinetics 383
14.5 Clinical applications of gene therapy 389
14.6 Conclusion 395
14.7 Further reading 396
14.8 Self-assessment questions 396

Chapter 15: Integrating Drug Discovery and Delivery
David Bailey and Andrew W. Lloyd
15.1 Introduction 400
15.2 Combinatorial chemistry 400
15.3 High-throughput screening 404
15.4 Genomics 405
15.5 Proteomics 413
15.6 Pharmacogenomics and pharmacoproteomics 415
15.7 Exploiting proteomics and genomics in drug targeting 416
15.8 Bioinformatics 417
15.9 Conclusions 418
15.10 Further reading 418
15.11 Self-assessment questions 419

Chapter 16: New Generation Technologies
Hongkee Sah, Yie W. Chien, Haesun Park, Sun-Joo Hwang, Kinam Park and Andrew W. Lloyd
16.1 Introduction 422
16.2 Rationalising drug design, discovery and delivery 422
16.3 The challenge of chronopharmacology 427
16.4 Epilogue 440
16.5 Further reading 441
16.6 Self-assessment questions 441

Appendix 443

Index 445