# FUNDAMENTALS OF DRUG DELIVERY

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## **Table of Contents**

<u>Cover</u>

<u>Title Page</u>

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**Preface** 

List of Contributors

<u>Part I: Product Design, the Essence of Effective</u> <u>Therapeutics</u>

<u>1 Challenges and Innovations of Controlled Drug</u> <u>Delivery</u>

1.1 Background

1.2 Parenteral Dosage Forms

1.3 Oral Route and Delivery Systems

1.4 Nasal Drug Delivery

1.5 Pulmonary Drug Delivery

1.6 Transdermal Drug Delivery

1.7 Ocular Drug Delivery

1.8 Drug Delivery System Development Process

1.9 Conclusion

<u>References</u>

<u>2 Challenges in Design of Drug Delivery Systems</u>

2.1 Drug Properties to be Considered in Design of Controlled Release Products

2.2 Physicochemical Factors that Need to be Considered in Design of CRDDS

2.3 Biopharmaceutical Properties that Deserve Consideration in Design of Controlled Release Products 2.4 Conclusion

**References** 

<u>3 Drug Delivery of the Future (?)</u>

3.1 Introduction

3.2 Therapeutic Indicators

3.3 Drugs of the Future

<u>3.4 Delivering the Drugs of the Future</u>

3.5 A View to the Longer Term?

3.6 Conclusion

<u>References</u>

<u>4 The Pharmaceutical Drug Development Process:</u> <u>Selecting a Suitable Drug Candidate</u>

<u>4.1 The Oral Drug Candidate: How to Get There</u> and Questions to Answer

<u>4.2 Challenges for Selecting a Topical Drug</u> <u>Candidate</u>

<u>4.3 Percutaneous Flux as a Surrogate</u> <u>Measurement of Skin Tissue Concentration</u>

<u>4.4 Learnings from Past Topical Drug</u> <u>Development of Factors Affecting Efficacy</u>

4.5 Dermal

Pharmacokinetics/Pharmacodynamics

4.6 Assessment of Systemic Exposure

<u>4.7 Screening Cascade Approach to Select a</u> <u>Dermal Drug Candidate</u>

<u>4.8 Opportunities for Repurposing Molecules</u> <u>into Dermally Active Treatments for</u> <u>Cosmeceutical or Pharmaceutical Approaches</u>

4.9 Conclusion

**<u>References</u>** 

5 Preformulation and Physicochemical Characterization Underpinning the Development of Controlled Drug Delivery Systems

5.1 When Is a Controlled Drug Delivery System Needed?

5.2 Optimizing Drug Characteristics

5.3 Defining the Product Profile

5.4 Preformulation and Physicochemical Characterization Underpinning Development of CDD

5.5 Conclusion

<u>References</u>

<u>6 Mathematical Models Describing Kinetics</u> <u>Associated with Controlled Drug Delivery Across</u> <u>Membranes</u>

<u>6.1 Introduction</u>

6.2 Model Solutions

6.3 Solution Methods

<u>References</u>

7 Understanding Drug Delivery Outcomes: Progress in Microscopic Modeling of Skin Barrier Property, Permeation Pathway, Dermatopharmacokinetics, and Bioavailability

7.1 Introduction

7.2 Governing Equation

7.3 Input Parameters

7.4 Application

7.5 Perspective

<u>References</u>

<u>8 Role of Membrane Transporters in Drug</u> <u>Disposition</u> 8.1 Introduction

8.2 Distribution of Major Drug Transporters in Human Tissues

8.3 Role of Drug Transporters in Drug Disposition

8.4 Closing Remarks

<u>References</u>

Part II: Challenges in Controlled Drug Delivery and Advanced Delivery Technologies

9 Advanced Drug Delivery Systems for Biologics

9.1 Introduction

9.2 Considerations in Biologics Product

<u>Development</u>

9.3 Administration Routes for Biologics Delivery

9.4 Conclusion

<u>References</u>

<u>10 Recent Advances in Cell-Mediated Drug Delivery</u> <u>Systems for Nanomedicine and Imaging</u>

10.1 Introduction

<u>10.2 Cell Types and Modification for</u> <u>Therapeutic Agent Delivery</u>

<u>10.3 Imaging and Tracking of Cell-Based</u> <u>Delivery Systems</u>

<u>10.4 Cell-Mediated Drug Delivery Systems for</u> <u>Disease Treatment</u>

<u>10.5 The Mechanism of Cell-Mediated Delivery</u> <u>Systems for the Cell Therapies</u>

<u>10.6 The Administration Approach of Cell-Assist</u> <u>Drug Delivery System</u>

<u>10.7 Clinical Application of Cell-Based Delivery</u> <u>Systems</u> 10.8 Conclusion and Outlook

**References** 

<u>11 Overcoming the Translational Gap –</u> <u>Nanotechnology in Dermal Drug Delivery</u>

<u>11.1 Nanotechnology – Failure or Future in</u> <u>Drug Delivery?</u>

11.2 Identification of the Clinical Need

<u>11.3 Nanoparticle Design and Physicochemical</u> <u>Characterization</u>

11.4 Biomedical Studies

<u>11.5 Approaches to Fill the Translational Gaps</u> <u>in Nanotechnology</u>

**References** 

<u>12 Theranostic Nanoparticles for Imaging and</u> <u>Targeted Drug Delivery to the Liver</u>

12.1 Introduction

12.2 The Types of Theranostic NPs

<u>12.3 Mechanisms of NPs Targeting the Liver</u>

12.4 NPs in Liver Target Imaging

<u>12.5 NPs for Therapeutic and Drug Delivery in</u> <u>Liver Disease</u>

<u>12.6 Theranostic NPs in Liver Diseases</u>

12.7 Conclusions

<u>References</u>

<u>13 Toxicology and Safety of Nanoparticles in Drug</u> <u>Delivery System</u>

13.1 Introduction

13.2 Lipid-Based Nanocarrier: Liposomes

13.3 Cellular Uptake Mechanism of Liposomes

<u>13.4 Biodistribution, Clearance and Toxicity of Liposomes</u>

13.5 Application of Liposomes in Drug Delivery

13.6 Inorganic Nanocarrier: Carbon Nanotubes

<u>13.7 Cellular Uptake Mechanism of Carbon</u> <u>Nanotubes</u>

<u>13.8 Biodistribution, Clearance, and Toxicity of</u> <u>Carbon Nanotubes</u>

<u>13.9 Application of Carbon Nanotubes in Drug</u> <u>Delivery</u>

13.10 Conclusion

<u>References</u>

Part III: Administrative Routes for Controlled Drug Delivery

14 Controlled Drug Delivery via the Ocular Route

14.1 Introduction

14.2 Physiology of the Eye

14.3 Ocular Disorders

14.4 Controlled Drug Delivery Systems

14.5 Conclusions

<u>References</u>

<u>15 Controlled Drug Delivery via the Otic Route</u>

15.1 Introduction

15.2 Anatomy and Physiology of the Otic Route

15.3 Controlled Drug Delivery Systems

15.4 Conclusions

<u>References</u>

<u>16 Controlled Drug Delivery via the Nasal Route</u> <u>16.1 Introduction</u> 16.2 Anatomy and Physiology of the Nose

16.3 Absorption from the Nasal Cavity

16.4 Mucus and Mucociliary Clearance

16.5 Drug Delivery Systems

16.6 Conclusion

<u>References</u>

<u>17 Controlled Drug Delivery via the Buccal and</u> <u>Sublingual Routes</u>

17.1 Introduction

<u>17.2 Buccal and Sublingual Physiology and</u> <u>Barriers to Drug Delivery</u>

17.3 Controlled Drug Delivery Systems

17.4 Functional Excipients Used in Controlled Release Systems to Enhance Buccal and Sublingual Drug Bioavailability

17.5 Conclusions

Acknowledgments

**References** 

18 Controlled Drug Delivery via the Lung

18.1 Introduction

18.2 The Relevant Physiology of the Route Including the Barriers to Drug Delivery

18.3 Controlled Drug Delivery Systems

18.4 Conclusions

<u>Acknowledgments</u>

<u>References</u>

<u>19 Controlled Drug Delivery via the Vaginal and</u> <u>Rectal Routes</u>

19.1 Introduction

19.2 Biological Features of the Vagina and<br/>Colorectum19.3 Controlled Drug Delivery Systems19.4 ConclusionsAcknowledgmentsReferencesNote20 Controlled Drug Delivery into and Through Skin20.1 Introduction20.2 Controlled Drug Delivery into and ThroughSkin20.3 Combination Approaches20.4 ConclusionsReferences

<u>Index</u>

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# **List of Tables**

Chapter 1

Table 1.1 Properties and indications of nasally delivered drugs.

<u>Table 1.2 Physicochemical, pharmacokinetic</u> <u>properties and indications of cur...</u>

Chapter 2

Table 2.1 Physicochemical properties influencing product development.

Table 2.2 BCS classification of drugs.

<u>Table 2.3 Biopharmaceutical properties influencing</u> <u>product development.</u>

Table 2.4 Biopharmaceutical drug disposition classification system (BDDCS).

Chapter 3

Table 3.1 The top 10 drugs (by global sales) in 2007, 2012, and 2017, illust...

Chapter 4

<u>Table 4.1 Example of percentage of dose crossing</u> <u>the skin.</u>

Table 4.2 Link in between flux and free concentration in the different skin ...

Table 4.3 Success rate of oral drug developed topically and first in their c...

Table 4.4 Barrier condition of skin diseases and success rate of topical dru...

Table 4.5*In vitro* potency of some anesthetics, corticosteroids, and immunosuppre...

<u>Table 4.6 Clinical efficacy comparison of some</u> <u>anesthetics, corticosteroids,...</u>

Table 4.7*In vitro* potency vs. clinical efficacy ranking of some anesthetics, cor...

<u>Table 4.8 List of reasons of possible failures during</u> <u>a topical drug develop...</u>

Table 4.9 Example of calculated therapeutic index evaluation.

Chapter 5

<u>Table 5.1 Target sites of enteric-coated marketed</u> <u>mesalazine drugs.</u> Table 5.2 List of common preformulation activities.

Table 5.3 Factors influencing feasibility of CDD systems development.

Table 5.4 Solubility predictions using different*in silico* methods.

Table 5.5 Forced degradation studies.

Table 5.6 Bulk powder test results.

Chapter 6

Table 6.1Type A models: well-stirred vehicle onone membrane.

Table 6.2Type B models: unstirred semi-infinitevehicle on one membrane.a)

Table 6.3Type C models: well-stirred vehicle ontwo membranes in series.a)

Table 6.4Estimates of the timeτ required toapproach steady state for...

Table 6.5First 10 eigenvalues ( $\lambda_n$ ) defined byEq. (A9.1) for selected...

Table 6.6 First 10 eigenvalues ( $\lambda_n$ ) defined by Eq. (C1.1) for  $G_{1,2} = 10...$ 

Table 6.7 Common integrals in separation of variable problems generating sin...

Chapter 7

<u>Table 7.1 Typical "bricks-and-mortar"</u> <u>microstructure parameters of human SC.</u>

Chapter 8

Table 8.1 Drug transporters recommended by the International Transporter Con...

Table 8.2 Expression of drug transporters in different intestinal regions.

Table 8.3 Role of major drug transporters in drug disposition (selected data...

Chapter 9

<u>Table 9.1 Overview of drug delivery systems (DDSs)</u> <u>incorporating growth fact...</u>

Table 9.2 Advanced drug delivery systems investigated for vaginal administra...

Chapter 10

Table 10.1 Summary of cell types and their application for drug delivery.

Chapter 12

<u>Table 12.1 Theranostic NP applications in liver</u> <u>diseases.</u>

Chapter 13

Table 13.1 Approved liposomal and lipid-based products.

Table 13.2 Pharmacokinetic and pharmacodynamic profiles of functionalized ca...

Chapter 15

Table 15.1 Examples of controlled drug delivery systems via the otic route.

Chapter 16

Table 16.1 Factors affecting nasal drug absorption.Table 16.2 Examples of nasal absorption enhancers.Table 16.3 Polymers used for *in situ* forming nasalgels.

Table 16.4 Summary of temperature- and ionresponsive*in situ* gelling systems...

Table 16.5 Pharmacokinetic parameters in adult subjects receiving PecFent an...

Table 16.6 Selected studies on utilization of hydrogel nanoparticles for nas...

<u>Table 16.7 Nanoemulsions employed in intranasal</u> <u>drug delivery.</u>

<u>Table 16.8 Drugs and their formulations reported</u> <u>for nose-to-brain delivery.</u>

Chapter 18

Table 18.1 Examples of controlled drug delivery formulations.

# List of Illustrations

Chapter 1

Figure 1.1 Routes of drug administration and associated dosage forms.

<u>Figure 1.2 (a) Approved and under development of</u> <u>transdermal drugs and their...</u>

<u>Figure 1.3 Routes for administration for retinal</u> <u>drug delivery.</u>

<u>Figure 1.4 Overview of drug delivery system</u> <u>development from basic research ...</u>

Chapter 2

<u>Figure 2.1 Plasma concentration profiles of</u> <u>conventional and extended releas...</u>

Chapter 3

<u>Figure 3.1 Assimilating knowledge from various</u> <u>'omic datasets will bring tan...</u>

<u>Figure 3.2 The changing nature of drugs. Lipitor</u> (atorvastatin) was the top-...

<u>Figure 3.3 Schematic representation of the</u> <u>approach taken by Hirsch et al. t...</u>

<u>Figure 3.4 Could nanobots target stem cells to</u> <u>deliver DNA and then trigger ...</u>

Chapter 4

Figure 4.1 Drug discovery process from target selection through to filing of...

<u>Figure 4.2 Example of a screening cascade during</u> <u>the lead optimization phase...</u>

Figure 4.3 Schematic skin concentration in intact and damaged skin.

<u>Figure 4.4 Percutaneous flux of clobetasol</u> <u>propionate from three different f...</u>

<u>Figure 4.5 Clinical efficacy vs. percutaneous flux/in</u> <u>vitro potency.</u>

Chapter 5

<u>Figure 5.1 Decision tree process for selection of a</u> <u>CDD technology.</u>

<u>Figure 5.2 Dissolution profiles for CDD systems. (a)</u> <u>Immediate release, (b) ...</u>

<u>Figure 5.3 Linking patient needs to CDD</u> <u>technology and dosage forms.</u>

Chapter 6

<u>Figure 6.1 Schematic diagrams of the three types</u> <u>of membrane models.</u> <u>Figure 6.2 Distribution of the dimensionless</u> <u>concentration in the membrane</u>

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

<u>Figure 6.3 Dimensionless flux and mass transfer</u> <u>from the vehicle to the memb...</u>

Figure 6.4 Distribution of the dimensionless concentration in the membrane  $\tilde{C}_1$ 

<u>Figure 6.5 Dimensionless average concentration in</u> <u>the membrane</u>  $\tau = \tau_c$  <u>plotted as ...</u>

<u>Figure 6.6 Dimensionless flux and cumulative mass</u> <u>transfer from the membrane...</u>

Figure 6.7 Distribution of the dimensionless concentration in the membrane  $\widetilde{M}_{V,1}$ 

<u>Figure 6.8 Dimensionless average concentration in</u> <u>the membrane</u>  $\tau = \tau_c$  <u>plotted as ...</u>

Figure 6.9 Dimensionless flux from the vehicle to the membrane ( $\langle \tilde{C}_1 \rangle$ ) and from ...

<u>Figure 6.10 Dimensionless cumulative mass</u> <u>transfer from the vehicle to the m...</u>

<u>Figure 6.11 Distribution of the dimensionless</u> <u>concentration in the membrane</u>

Figure 6.12 Dimensionless average concentration in the membrane  $\widetilde{M}_{1,R}/\Lambda_V$  plotted as...

Figure 6.13 Dimensionless flux from the vehicle to the membrane ( $\langle \tilde{C}_1 \rangle$ ) and from...

<u>Figure 6.14 Dimensionless cumulative mass</u> <u>transfer from the vehicle to the m...</u> Figure 6.15 Cumulative mass transfer from the vehicle to the membrane (  $M_{V, 1}$ 

Chapter 7

Figure 7.1 Bricks and mortar microstructure of human SC and permeation pathw...

<u>Figure 7.2 SC lipid-water partition coefficients:</u> <u>experimental data of Rayka...</u>

<u>Figure 7.3 Lateral diffusivity of solute in SC lipid:</u> <u>comparison of differen...</u>

<u>Figure 7.4 Solute binding to corneocyte keratin:</u> <u>comparison of various model...</u>

<u>Figure 7.5 Solute diffusivity in SC corneocytes as a</u> <u>function of molecular w...</u>

<u>Figure 7.6 Sebum-water partition coefficients vs.</u> <u>SC lipid-water partition c...</u>

Chapter 8

<u>Figure 8.1 Subcellular localization of uptake and</u> <u>efflux transport proteins ...</u>

<u>Figure 8.2 Subcellular localization of uptake and</u> <u>efflux transport proteins ...</u>

<u>Figure 8.3 Subcellular localization of uptake and</u> <u>efflux transport proteins ...</u>

<u>Figure 8.4 Subcellular localization of uptake and</u> <u>efflux transport proteins ...</u>

<u>Figure 8.5 Subcellular localization of uptake and</u> <u>efflux transport proteins ...</u>

<u>Figure 8.6 Subcellular localization of uptake and</u> <u>efflux transport proteins ...</u> <u>Figure 8.7 Subcellular localization of uptake and</u> <u>efflux transport proteins ...</u>

Chapter 9

<u>Figure 9.1 The effect of liposomal surface</u> <u>modification on drug delivery to ...</u>

Chapter 10

<u>Figure 10.1 The common cells used for drug</u> <u>delivery. (a) Erythrocytes (red b...</u>

<u>Figure 10.2 The cargo loading into the cells by</u> <u>adsorption (a), internalizat...</u>

<u>Figure 10.3 Covalent conjugation of</u> <u>drugs/nanoparticles on cells.</u>

<u>Figure 10.4 (A) Cell-tracking study protocol of SPIO</u> and <sup>111</sup>In-labeled monoc...

<u>Figure 10.5 (a) Schematic illustration of the 4T1</u> <u>CM-coated gold nanocage (C...</u>

<u>Figure 10.6 (a) Schematic of membrane fusion and</u> <u>coating. Membrane material ...</u>

<u>Figure 10.7 Schematic illustrations of a red blood</u> <u>cell (RBC) membrane-coate...</u>

<u>Figure 10.8 Proposed sequential adhesion model of</u> <u>neutrophil attachment to a...</u>

Chapter 11

Figure 11.1 Limitations of drug transport in extravascular tissue. A drug mu...

<u>Figure 11.2 **Preclinical study design.** Percentage</u> of primary animal studies a...

Figure 11.3 Nanodelivery systems investigated for dermal and transdermal dru... <u>Figure 11.4 Core-multishell (CMS)</u> nanotransporters. (a) Dendritic core...

<u>Figure 11.5 **Triggered drug release.** (a) Change of EPR spectra of DxPCA loade...</u>

Figure 11.6 Several successful applications of machine learning in various s...

<u>Figure 11.7 **Detection of CMS nanotransporters**</u> **in skin.** High resolution X-ray...

Figure 11.8 Circular approach of nanotechnology development. Transition from...

Chapter 12

<u>Figure 12.1 Schematic diagram of theranostic NPs</u> <u>include lipid- and polymer-...</u>

<u>Figure 12.2 Mechanisms of NPs passively and</u> <u>actively targeting the liver. (a...</u>

<u>Figure 12.3 Schematic structure of nanoablation</u> <u>and nanoembolization. (a) In...</u>

<u>Figure 12.4 Schematic illustration of the formation</u> <u>of novel theranostic NPs...</u>

Chapter 13

<u>Figure 13.1 (a) Small unilamellar vesicles (SUV),</u> (b) large unilamellar vesi...

<u>Figure 13.2 Schematic representation of different</u> <u>types of liposomal formula...</u>

<u>Figure 13.3 Cellular uptake mechanism of</u> <u>liposomes: (a) clathrin-mediated en...</u>

<u>Figure 13.4 Types of carbon nanotubes: (a) Single-</u> walled carbon nanotubes, (... <u>Figure 13.5 An energy independent translocated</u> <u>mechanism: (a) hydrophilic CN...</u>

<u>Figure 13.6 Uptake mechanism: (a) non-receptor</u> <u>mediated endocytosis, (b) rec...</u>

Figure 13.7 The mechanism of renal elimination of the nanotubes. (a) Basic s...

<u>Figure 13.8 The mechanism of CNT elimination</u> <u>viabiliary system. (a, b) CNTs ...</u>

Chapter 14

Figure 14.1 Anatomical detail of the human eye.

<u>Figure 14.2 Cross section micrograph of bovine</u> <u>cornea showing the multi-laye...</u>

<u>Figure 14.3 Vascular network within the uveal tract</u> of a healthy individual,...

<u>Figure 14.4 Chemical structure of the prodrug;</u> <u>latanoprost.</u>

<u>Figure 14.5 *In vivo* retention of pluronic</u> <u>formulations containing 1 mg/ml Fl...</u>

<u>Figure 14.6 (a) Guest-host complex of β-CD/drug.</u> (b) Preferential take up of...

<u>Figure 14.7 Scheme for ocular drug delivery via</u> <u>drug eluting contact lenses....</u>

Chapter 15

Figure 15.1 Anatomy of the otic route.

<u>Figure 15.2 Anatomy of the inner ear</u> (<u>http://anatomypicture.blogspot.com</u>)....

<u>Figure 15.3 Illustration of Silverstein MicroWick</u> <u>procedure (http://ent-spec...</u> <u>Figure 15.4 A wearable system for microfluidic</u> <u>drug delivery from an integra...</u>

Chapter 16

<u>Figure 16.1 Anatomy of the upper respiratory</u> <u>system.</u>

<u>Figure 16.2 Schematic representation of the</u> <u>respiratory mucosa and the possi...</u>

<u>Figure 16.3 Schematicillustration of the mechanism</u> of *in situ* gelation of a ...

<u>Figure 16.4 The structure of native (a) and low-acyl</u> (b) form of gellan gum....

<u>Figure 16.5 Gradual transformation of gellan gum</u> <u>from aqueous solutions.</u>

<u>Figure 16.6 Shear thinning gellan gum fluid gel</u> <u>containing caffeine.</u>

Figure 16.7 Chitin and chitosan.

<u>Figure 16.8 Cross section of the human nasal cavity</u> <u>with the olfactory regio...</u>

<u>Figure 16.9 Development of cellular and humoral</u> <u>immune responses following m...</u>

<u>Figure 16.10 Effect of different types of formulation</u> (ketoprofen or ketopro...

Chapter 17

<u>Figure 17.1 Diagram of mucosa distribution in the</u> <u>oral cavity showing that b...</u>

<u>Figure 17.2 Representation of the stratified and</u> <u>non-keratinized buccal epit...</u>

<u>Figure 17.3 Diagram showing the two scenarios of</u> <u>controlled release from buc...</u> <u>Figure 17.4 Diagram showing the *in situ* crosslinking observed in thiolated ...</u>

Chapter 19

<u>Figure 19.1 Schematic representation of the</u> <u>interaction of several types of ...</u>

Figure 19.2 Comparison of dissolution profiles of marketed tablets of povido...

<u>Figure 19.3 Schematic of solid body and hollow-</u> <u>type suppositories developed ...</u>

<u>Figure 19.4 *In vitro* release profiles of vaginal</u> <u>mucoadhesive propranolol hy...</u>

<u>Figure 19.5 *In vitro* release of butoconazole from a standard (conventional) ...</u>

<u>Figure 19.6 *In vitro* release of amphotericin B</u> (AmB)-hydroxypropyl-gamma-cyc...

<u>Figure 19.7 Schematic representation of basic</u> <u>vaginal ring designs and typic...</u>

Figure 19.8 Serum concentration-time curve (mean  $\pm$  standard deviation; n = 1...

<u>Figure 19.9 The International Partnership for</u> <u>Microbicides dapivirine matrix...</u>

<u>Figure 19.10 SILCS diaphragm device: (a-c) three-</u> <u>step injection molding manu...</u>

<u>Figure 19.11 Efavirenz release properties in</u> <u>simulated vaginal fluid (pH 4.2...</u>

<u>Figure 19.12 (a) Release profile of rhodamine 6G</u> (used as model drug) from e...

<u>Figure 19.13 Release profiles of acetaminophen</u> <u>from suppositories at 37 °C. ...</u> <u>Figure 19.14 Release profiles of quinine in</u> <u>deionized water (pH 6.9) for the...</u>

<u>Figure 19.15 Distribution of various sizes of</u> <u>mucoadhesive particles (MAP) a...</u>

Chapter 20

<u>Figure 20.1 Diagrammatical representation of the</u> <u>structure of human skin....</u>

<u>Figure 20.2 A representation of human epidermal</u> <u>cell layers and differentiat...</u>

<u>Figure 20.3 Representation of the "brick and</u> <u>mortar" description of the stra...</u>

<u>Figure 20.4 Illustration of the three routes by</u> <u>which a molecule can enter i...</u>

<u>Figure 20.5 Examples of materials shown to have</u> <u>penetration-enhancing effect...</u>

<u>Figure 20.6 Illustration of the potential to generate</u> <u>supersaturated systems...</u>

<u>Figure 20.7 Drug release profiles from Eudragit</u> <u>L100 microparticles containi...</u>

<u>Figure 20.8 Release of hydrocortisone from gelatin</u> <u>particles produced by O/W...</u>

<u>Figure 20.9 Illustration of the principle of</u> <u>iontophoresis.</u>

## 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 cellmediated 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".

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