

2688 - 383

Modern Pharmaceutics

Second Edition, Revised and Expanded

edited by

GILBERT S. BANKER

University of Minnesota
Minneapolis, Minnesota

CHRISTOPHER T. RHODES

University of Rhode Island
Kingston, Rhode Island

MARCEL DEKKER, INC.

New York and Basel

Contents

Preface	iii
Contributors	v
Chapter 1. Drug Products: Their Role in the Treatment of Disease, Their Quality, and Their Current and Future Status as Drug Delivery Systems	1
<i>Gilbert S. Banker</i>	
I. Role of Drugs and Drug Products in the Treatment and Prevention of Disease	1
II. Drug and Drug Product Quality and Its Evaluation	6
III. The Drug Product as a Delivery System	15
References	21
Chapter 2. Principles of Drug Absorption	23
<i>Michael Mayersohn</i>	
I. Introduction	23
II. Anatomical and Physiological Considerations of the Gastrointestinal Tract	24
III. Physicochemical Factors Governing Drug Absorption	30
IV. Physiological Factors Governing Drug Absorption	47
V. Complicating Factors in Drug Absorption	62
References	72

Chapter 3.	Pharmacokinetics	91
	<i>David W. A. Bourne and Lewis W. Dittert</i>	
	I. Introduction	91
	II. Principles of First-Order Kinetics	92
	III. First-Order Pharmacokinetics: Drug Elimination Following Rapid Intravenous Injection	100
	IV. Pharmacokinetic Analysis of Urine Data	103
	V. Clearance Rate as an Expression of Drug Elimination Rate	106
	VI. Pharmacokinetics of Drugs Eliminated by Simultaneous Metabolism and Excretion	108
	VII. Kinetics of Drug Absorption	115
	VIII. Bioavailability (Extent of Absorption)	124
	IX. Multiple-Dosing Regimens (Repetitive Dosing)	129
	References	142
Chapter 4.	Factors Influencing Drug Absorption and Drug Availability	143
	<i>Betty-ann Hoener and Leslie Z. Benet</i>	
	I. Introduction	143
	II. Getting the Drug to Its Site of Absorption	144
	III. Getting the Drug into Solution: Factors Affecting the Rate of Dissolution	152
	IV. Gastrointestinal Membrane Transport	174
	V. Moving the Drug Away from the Site of Absorption	174
	VI. Summary	177
	References	177
Chapter 5.	The Effect of Route of Administration and Distribution on Drug Action	181
	<i>Leslie Z. Benet</i>	
	I. Dose-Efficacy Scheme	181
	II. Physiological Considerations for the Various Routes and Pathways of Drug Input	183
	III. Drug Distribution	195
	IV. Summary	204
	References	204
Chapter 6.	Chemical Kinetics and Drug Stability	209
	<i>Ho-Leung Fung</i>	
	I. Introduction	209
	II. Modes of Pharmaceutical Degradation	210
	III. Quantitation of Rate of Degradation	217
	IV. The Arrhenius Equation and Accelerated Stability Testing	224
	V. Environmental Factors That Affect Reaction Rate	226
	References	235

Contents		xi
Chapter 7.	Preformulation	239
	<i>Jens T. Carstensen</i>	
	I. Introduction	239
	II. Timing and Goals of Preformulation	240
	III. Physicochemical Parameters	240
	IV. Compatibility Tests	251
	V. Dissolution of Drug Substance and Dosage Form	258
	References	261
Chapter 8.	Topical Drug Absorption and Topical Pharmaceutical Systems	263
	<i>Gordon L. Flynn</i>	
	I. Introduction	263
	II. Nature of the Skin	264
	III. Mechanistic Analysis of Relevant Skin Functions	273
	IV. Rationale for Topicals	277
	V. Unique Physicochemical Systems Used Topically	298
	VI. Performance Criteria and Performance Evaluation of Topical Therapeutic Systems	310
	References	323
Chapter 9.	Disperse Systems	327
	<i>Christopher T. Rhodes</i>	
	I. Introduction	327
	II. Some Fundamental Properties of Disperse Systems	327
	III. Solubilized Systems	334
	IV. Suspensions	339
	V. Emulsions	347
	References	351
Chapter 10.	Tablet Dosage Forms	355
	<i>Keith Marshall and Edward M. Rudnic</i>	
	I. Introduction	355
	II. Design and Formulation of Compressed Tablets	360
	III. Coated Tablets	388
	IV. The Role of Processing Conditions	400
	V. Molded Tablets (Tablet Triturates)	414
	VI. Evaluation of Tablets	416
	References	421
Chapter 11.	Specialty Tablets and Capsules	427
	<i>Ralph F. Shangraw</i>	
	I. Introduction	427
	II. Buccal and Transmucosal Tablets	427
	III. Sublingual Tablets	428
	IV. Stability and Packaging of Molded Nitroglycerin Tablets	430
	V. Implants	432
	VI. Effervescent Tablets	433

	VII. Vaginal Tablets	436
	VIII. Lozenges	436
	IX. Chewable Tablets	438
	X. Analytical Tablets	438
	References	439
Chapter 12.	Hard and Soft Gelatin Capsules	441
	<i>Larry L. Augsburger</i>	
	I. Historical Development and Role as a Dosage Form	441
	II. Hard Gelatin Capsules	442
	III. Soft Gelatin Capsules	478
	IV. Soft/Liquid-Filled Hard Gelatin Capsules	483
	References	484
	Bibliography	490
Chapter 13.	Parenteral Products	491
	<i>James C. Boylan and Alan L. Fites</i>	
	I. Introduction	491
	II. Routes of Parenteral Administration	493
	III. Specialized Large-Volume Parenteral and Sterile Solutions	500
	IV. Design of Parenteral Products and Methods of Preparation	502
	V. Components of Parenteral Products and Physicochemical Factors Affecting Their Design and Performance	511
	VI. Sterilization Methods	520
	VII. Clinical Considerations in Parenteral Product Design	526
	VIII. Quality Control	531
	References	536
Chapter 14.	Design and Evaluation of Ophthalmic Pharmaceutical Products	539
	<i>Gerald Hecht, Robert E. Roehrs, Eugene R. Cooper, Joseph W. Hiddemen, and Barry F. Van Duzee</i>	
	I. Introduction	539
	II. Historical Background	542
	III. Anatomy of the Eye and Adnexa	543
	IV. Pharmacology and Therapeutics of Ophthalmic Medication	545
	V. General Safety Considerations	547
	VI. Absorption of Drugs in the Eye	554
	VII. Manufacturing Considerations	559
	VIII. Classes of Ophthalmic Products	563
	IX. Contact Lens Care Products	585
	References	598

Contents		xiii
Chapter 15. Pharmaceutical Aerosols		605
	<i>John J. Sciarra and Anthony J. Cutie</i>	
	I. Introduction	605
	II. Definitions	606
	III. Advantages of the Aerosol Dosage Form	606
	IV. Operation of the Aerosol Package	607
	V. Product Formulation	608
	VI. Propellants	616
	VII. Valves	622
	VIII. Aerosol Containers	625
	IX. Oral, Inhalation, and Nasal Aerosols	626
	X. Topical Aerosols	631
	XI. Future Developments	632
	Bibliography	634
Chapter 16. Sustained- and Controlled-Release Drug Delivery Systems		635
	<i>George M. Grass IV and Joseph R. Robinson</i>	
	I. Introduction	635
	II. Terminology	636
	III. Oral Systems	638
	IV. Targeted Delivery Systems	658
	V. Transdermal Systems	663
	VI. Ocular Systems	665
	VII. Intravaginal and Intrauterine Systems	666
	VIII. Injections and Implants	667
	IX. Conclusions	668
	References	668
Chapter 17. Site-Specific Drug Delivery Using Particulate Systems		673
	<i>Eric Tomlinson</i>	
	I. Introduction	673
	II. Site-Specific Drug Delivery	674
	III. Particulate Systems for Site-Specific Drug Delivery and Controlled Release	675
	IV. Properties of Particulate Site-Specific Delivery Systems	679
	V. Uses	691
	References	692
Chapter 18. Packaging of Pharmaceutical Dosage Forms		695
	<i>Donald C. Liebe</i>	
	I. Introduction	695
	II. Packaging of Solid Oral Dosage Forms	699
	III. Packaging of Parenteral and Ophthalmic Dosage Forms	717
	IV. Packaging of Other Dosage Forms	730
	V. Summary and Conclusions	735
	References	736

Chapter 19.	Appraisal of Drug Product Quality and Performance	741
	<i>Stanley L. Hem and Roger G. Stoll</i>	
	I. Introduction	741
	II. Purity and Identity of Active Ingredient	743
	III. Content Uniformity	746
	IV. Chemical Stability	748
	V. Physical Stability	750
	VI. Bioavailability	751
	VII. Inequivalent Bioequivalence	788
	VIII. Relationship Between in Vitro Tests and Bioequivalence	791
	IX. Summary of Factors Influencing Bioavailability Data	795
	X. Quality Control	796
	XI. Manufacturer's Reliability	797
	XII. Manufacturer/Drug Information Profile	799
	References	799
Chapter 20.	Optimization Techniques in Pharmaceutical Formulation and Processing	803
	<i>Joseph B. Schwartz</i>	
	I. Introduction	803
	II. Optimization Parameters	804
	III. Classical Optimization	804
	IV. Statistical Design	806
	V. Applied Optimization Methods	807
	VI. Other Applications	823
	VII. Computers and Systems	826
	VIII. Concluding Remarks	826
	References	827
Chapter 21.	Food and Drug Laws that Affect Drug Product Design, Manufacture, and Distribution	829
	<i>Garnet E. Peck</i>	
	I. Impact of the Food and Drug Laws	829
	II. Laws Governing Evaluation of New Drug Products	834
	III. Laws Governing Preparation and Distribution of Existing Products	841
	IV. Further Considerations	848
	References	849
Chapter 22.	A View to the Future	851
	<i>Gilbert S. Banker and Christopher T. Rhodes</i>	
	I. Introduction	851
	II. The Pharmaceutical Industry	852
	III. Community and Hospital Practice	854
	IV. Advances in the Monitoring of Pharmacotherapeutics and in Drug Delivery System Design	856
	V. Conclusion	869
	References	869
Index		871