CONTENTS

1. Basic Concepts 1

Biopharmaceutics 2
Pharmacokinetics 8
Pharmacodynamics 16
Pharmacogenetics 17
Toxicokinetics 19
Legal Definitions 20

2. Mathematical Concepts 26

Logarithms 26
Graphic Methods 31
Linear Regression Analysis 35

3. Rate Processes 48

Zero-Order Kinetics 49
First-Order Kinetics 55
Semi-Logarithmic Graph Paper 63

4. Drug Absorption 74

Routes of Drug Administration 77
Topical Absorption 79
Oral Administration 81
Absorption Mechanisms 82
Gastrointestinal Tract 89

5. Drug Distribution 101

Role of Proteins in Drug Distribution 104
Perfusion and Drug Distribution 108
Drug Distribution and Body Water Compartments 110
Volume of Distribution 114
Body Composition 119

6. Drug Elimination 124

Elimination of Drug 124
Routes of Drug Excretion 125
Renal Excretion 131
Glomerular Filtration 133
Urine pH and Reabsorption 137
Pharmacokinetics and Renal Excretion 143

7. Clearance 145

Factors Affecting Clearance 145
Renal Clearance 146
Drugs Eliminated Solely by Renal Excretion 155
Creatinine Clearance 157
Renal Function in Adults 159
Renal Function in Infants 164
Hepatic Clearance 168
First-Pass Effect 171
Dosage in Children 172

8. Bioavailability 177

Determination of Bioavailability 179
Relative Bioavailability 185
Determination of Area under the Curve 186
Intravenous Administration 193

9. Bioequivalence 203

Equivalence 204
Bioequivalency of Generic Drugs 216
Therapeutic Equivalence Evaluations 217
Bioequivalence Studies 223
Oral Dosage Forms that should not be Crushed 232

10. Compartment Models 246

Compartment Modeling 247
One-Compartment Model 248

11. Intravenous Bolus Dose 256

One-Compartment Model 256
Multi-Compartment Model 259
Two-Compartment Model 261
Three-Compartment Model 270

12. Extravascular Bolus Dose **287**

Plasma Profile 287
One-Compartment Model 288
Time of Maximum Concentration (T_{max}) 295
Maximum Plasma Concentration 296
Lag-Time 297
Two-Compartment Model 306

13. Multiple Dosing **330**

Intravenous Administration 330
Steady-State Concentrations 342
Extravascular Administration 349

14. Loading Dose **359**

Intravenous Administration 360
Extravascular Administration 367

15. Continuous Intravenous Infusion **376**

Plasma Profile 378
Steady-State Concentration 386
Loading Dose followed by Continuous Infusion 396

16. Renal Impairment **404**

Dosage Adjustment in Renal Impairment 405
Determination of K_{ri} 407
Dosage Regimen in the Renally Impaired 413
Dosage Adjustment in Renal Insufficiency 420

17. Therapeutic Drug Monitoring **426**

Historical Background 427
Candidates for Therapeutic Monitoring 430
Factors Influencing Drug Variability 434
Presence of Other Drugs 435
Process of Therapeutic Drug Monitoring 438
Intravenous Administration 444
Extravascular Administration 453

18. Non-compartmental Methods **462**

Advantages of Compartment Models 462
Disadvantages of Compartment Models 463

Non-compartmental Methods 463
Mean Residence Time 466
Methods of Determining Mean Residence Time 468
Mean Absorption Time 479
Rate Constant of Elimination 482
Rate Constant of Absorption 484
Total Body Clearance 485

Answers *493*

Appendix A: Glossary of Terms *501*

Appendix B: Nomenclature and Symbols *508*

Index *513*