

## CONTENTS

---

<i>Preface</i> .....	(v)
<i>Acknowledgement</i> .....	(vii)
<b>SECTION I</b>	
<b>ESSENTIALS OF DOSAGE FORM DESIGN</b>	
<b>CHAPTER 1</b>	
<b>PREFORMULATION STUDIES</b>	
Introduction .....	3
Organoleptic Properties.....	5
Purity and Impurity .....	5
Particle Size, Shape and Surface Area .....	7
Solubility.....	8
Determination of Solubility.....	9
pH and Solubility .....	9
Particle Size and Solubility .....	11
pK <sub>a</sub> and Solubility .....	11
Salt Formation.....	12
Ionization Constant .....	12
Partition Coefficient .....	14
Permeation through Biological Membrane .....	15
Polymorphism and Crystal Properties..	16
Crystal Characteristics and Bioavailability .....	17
Crystal Characteristics and Chemical Stability.....	18
Crystal Property and Physical Stability.	18
Dissolution.....	19
Factors Affecting Dissolution .....	20
Intrinsic Dissolution.....	21
Biopharmaceutics Classification System (BCS) .....	22
Determination of Solubility	
(Limits of Solubility Term) .....	23
Determination of Permeability	
(Limits of Permeability Term	
Particulate Dissolution .....	23
Stability .....	24
Solid-State Stability .....	24
Effect of Temperature on Stability .....	25
Effect of Humidity on Stability .....	26
Effect of Light .....	26
Effect of Air (Oxygen) .....	27
Solution-State Stability.....	27
Drug-Excipient Compatibility Studies.....	28
Chromatographic Method .....	28
Differential Thermal Analysis.....	28
Diffuse Reflectance Spectroscopy.....	29
Miscellaneous Properties.....	29
Density .....	29
Flowability.....	30
Compactibility or Compressibility.....	31
Wettability .....	32
<b>Model Questions.....</b>	<b>32</b>
<b>References .....</b>	<b>33</b>
<b>SECTION II</b>	
<b>SOLID DOSAGE FORMS</b>	
<b>CHAPTER 2</b>	
<b>TABLETS</b>	
Introduction .....	39
Preformulation/Formulation	
Development Studies .....	40

**(x)      Contents**

---

Systematic Approach to Design	94
A Tablet Dosage Form .....	42
Tablet Components.....	48
Active Ingredient (Drug).....	48
Excipients .....	50
Manufacture of Tablet .....	56
Methods of Manufacture .....	57
Direct Compression.....	57
Excipients .....	59
Water Soluble Diluents (Filler-binders) .....	60
Water Insoluble Fillers .....	63
Co-processed Excipients.....	65
Factors Influencing Direct Compression Formulation.....	67
Compressibility.....	67
Flowability .....	68
Lubrication .....	68
Morphology of Particles.....	69
Co-processed Active Ingredients.....	69
Manufacturing Process .....	69
Granulation .....	70
Characterization of Granules .....	71
Surface Shape Factor .....	72
Granule Density and Packing .....	73
Principle of Wet Granulation .....	77
Excipients .....	81
Diluents .....	82
Binders .....	82
Lubricants.....	85
Glidants .....	87
Disintegrants .....	89
Other Polymers .....	91
Super Disintegrants.....	91
High Shear Granulation .....	92
Flow Process.....	93
Dry Granulation.....	93
Flow Process.....	94
Compression Coated Tablet.....	94
Application of the Method.....	96
Excipients .....	96
Factors affecting Drug Release .....	97
Effect of Core Formulation.....	97
Effect of the Type of Polymer .....	97
Effect of Particle Size of Polymer .....	98
Effect of Porosity of the Coat .....	98
Effect of Core-Coat Ratio .....	99
Effect of Compression Force .....	99
Effect of Position of Core in Coated Layer .....	100
Effect of Compressibility of Materials	100
Effect of Drug-Coat Interaction.....	100
Method of Manufacture .....	101
Equipments .....	102
Effervescent Tablets.....	103
Formulation Ingredients .....	104
Active Ingredient.....	105
Excipients .....	105
Effervescing Components .....	106
Other Effervescent Materials.....	108
Binders .....	108
Diluents .....	108
Lubricants.....	109
Other Ingredients .....	110
Method of Manufacture .....	110
Wet Granulation Method.....	110
Dry Granulation Method.....	112
Fluidized Bed Granulation Method .....	112
Chewable Tablets .....	112
Factors Influencing Formulation.....	113
Excipients .....	114

Organoleptic Agents (Sweetner, Flavor, and Color) .....	116	Direct Compression (DC) .....	144
Manufacturing Considerations .....	118	Effervescent Agents .....	145
Buccal Tablets .....	119	Cotton Candy Process .....	147
Advantages of Buccal Drug Delivery.....	121	Spray-Drying.....	148
Manufacturing Considerations .....	122	Sublimation .....	148
Sublingual Tablets .....	123	Mass-Extrusion.....	149
Manufacturing Considerations .....	124	Nanonization.....	149
Vaginal Tablets .....	124	Fast Dissolving Films .....	149
Manufacturing Considerations .....	125	<b>Model Questions.....</b>	<b>150</b>
Rectal Tablets .....	126	<b>References .....</b>	<b>151</b>
Advantages of Rectal Drug Delivery.....	126	<b>CHAPTER 3</b>	
Dispensing Tablets .....	127	<b>CAPSULES</b>	
Tablet Coating .....	128	Introduction .....	158
Characteristics of Tablets .....	129	Advantages.....	159
Types of Coating.....	129	Disadvantages .....	159
Sugar Coating .....	130	Gelatin Capsule .....	160
Film Coating .....	130	Physical Property of Gelatin.....	160
Coating Process.....	132	Preparation of Gelatin.....	161
Defects in Coating .....	134	Hard Gelatin Capsules .....	162
Evaluation of Tablets.....	135	Manufacture of Hard Gelatin Capsule Shells.....	162
Physical Characteristics .....	136	Filling of Powders in Capsules .....	164
Mouth Dissolving Tablets .....	139	Excipients used in the Formulation....	165
Introduction .....	139	Formulation Parameters .....	165
Advantages.....	140	Compatibility with Gelatin .....	166
Ideal Characteristics of MDTs .....	140	Doses .....	166
Disadvantages .....	141	Solubility.....	166
Characteristics of Drugs		Shape of the Particle .....	166
Suitable for MDT .....	141	Particle Size .....	167
Principles Involved in MDT Formulation .....	141	Hygroscopic Compounds .....	167
Techniques/Methods used for MDT Formulation .....	142	Adhesion .....	167
Freeze-Drying or Lyophilization .....	142	Wetting Properties.....	168
Molding .....	143	Moisture Sensitivity of the Drug .....	168
		Lubrication .....	168
		Formulation.....	169

**(xii)    Contents**

---

Hard Gelatin Capsule for Multiple-Units .....	169	Physiological Factors .....	185
Hard Gelatin Capsule for Semi-Solid and Liquid Preparation .....	170	Formulation Considerations.....	185
Excipients .....	171	Drug.....	185
Filling and Sealing.....	172	Physical State .....	186
Modification of Capsule Shell Property .....	172	Bulk Density and Surface Properties..	186
Soft Gelatin Capsule .....	174	Solubility and Partition Coefficient ....	186
Advantages.....	174	pK <sub>a</sub> .....	187
Disadvantages .....	175	Amount of the Drug .....	187
Size and Shape of Soft Gelatin Capsule .....	175	Additives.....	187
Manufacture of Soft Gelatin Capsule.	175	Suppository Base.....	190
Preparation of Gelatin Melt .....	175	Desired Characteristics of Suppository Base.....	190
Composition of Soft Gel Shell .....	176	Classification of Suppository Base.....	190
Preparation of Fill Material .....	176	Natural Bases .....	190
Encapsulation .....	177	Synthetic Bases .....	191
Drying .....	178	Semisynthetic Bases.....	192
Inspection.....	179	Hydrogels .....	192
In-process Control.....	179	Criteria for Selection of Bases .....	192
Finished Product Testing.....	179	Melting Temperature Range .....	192
Polishing .....	180	Iodine Value .....	193
Packaging .....	180	Hydroxyl Index .....	193
<b>Model Questions .....</b>	<b>180</b>	Method of Manufacture .....	193
<b>References.....</b>	<b>181</b>	Fusion Method .....	193
		Compression Method .....	194
		Injection Molding .....	195
		Calibration of Moulds.....	195
		Use of Displacement Value .....	196
		In-process Quality Control .....	196
		Evaluation of Suppositories .....	197
		Physical Tests .....	197
		Chemical Tests .....	200
		Some Manufacturing Problems and their Solutions .....	202

**CHAPTER 4**

**SUPPOSITORIES**

Rectal and Vaginal Drug Delivery System.....	183
Introduction .....	183
Anatomy and Physiology of the Rectum.....	184
Absorption of Drugs from the Rectum ..	184

---

Bioavailability of Drug from Suppositories.....	203	Ointment.....	230
Other Rectal Formulations .....	204	Formulation Consideration .....	230
Vaginal Drug Delivery.....	204	Selection of Ointment Base .....	231
Applications.....	206	Classification of Ointment Bases.....	231
<b>Model Questions .....</b>	<b>206</b>	Oleaginous Base .....	232
<b>References.....</b>	<b>207</b>	Absorption Base .....	232
<b>SECTION III</b>			
<b>SEMISOLID DOSAGE FORMS</b>			
<b>CHAPTER 5</b>			
<b>SEMISOLIDS</b>			
Introduction .....	211	Emulsion Base .....	234
Types of Semisolid Dosage Forms.....	211	Water-soluble Bases .....	235
Advantages.....	212	Manufacture of Ointments .....	236
Disadvantages .....	212	Fusion Method .....	236
Factors Influencing Drug Absorption from Topical Formulation.....	213	Trituration Method .....	238
Permeation through Skin .....	214	Chemical Method.....	238
Skin Microflora .....	215	Emulsification Method.....	239
Skin Temperature.....	215	Packaging .....	240
Penetration/Permeation Enhancers ..	217	Glass Containers.....	241
Formulation Ingredients .....	219	Plastic Containers.....	241
Drugs .....	220	Evaluation of Semisolid Preparations	242
Base.....	220	Rheological Properties .....	242
Preservative .....	220	<b>Model Questions .....</b>	<b>244</b>
Chelating Agent.....	222	<b>References .....</b>	<b>246</b>
Humectants.....	222		
Antioxidants .....	222	<b>CHAPTER 6</b>	
Emulsifying Agents .....	223	<b>GELS</b>	
Perfumes .....	223	Introduction .....	249
Creams .....	223	Characteristics of Gel .....	249
Formulation Considerations.....	224	Uses.....	250
Manufacture of Cream.....	226	Classification of Gels .....	250
Instability of Creams .....	229	Structure .....	252

**(xiv) Contents**

---

Alginates.....	254
Carrageenan.....	255
Xanthan Gum .....	255
Pectin .....	255
Guar Gum.....	255
Gelatin.....	256
Agar .....	256
Chitosan .....	256
Cellulose Derivatives .....	256
Carboxymethyl Cellulose.....	257
Ethyl Cellulose .....	257
Hydroxypropyl Cellulose .....	257
Polyethylene .....	257
Acrylic Polymers .....	257
Dispersible Colloidal Solids .....	258
Microcrystalline Cellulose .....	258
Clays .....	258
Microcrystalline Silica .....	259
Surfactants .....	259
Manufacture of Gel.....	259
Thermal Changes.....	260
Chemical Reaction.....	260
Flocculation .....	261
Stability.....	262
Evaluation of Gel .....	262
pH .....	262
Viscosity .....	262
Homogeneity.....	262
Grittiness .....	262
Spreadability .....	263
Extrudability .....	263
Skin Irritation.....	263
Drug Content.....	263
In-vitro Diffusion .....	263
In vivo Studies .....	264
<b>Model Questions .....</b>	<b>264</b>
<b>References.....</b>	<b>265</b>

**SECTION IV**

**LIQUID DOSAGE FORMS**

**CHAPTER 7**

**SUSPENSIONS**

Introduction .....	269
Types of Suspensions .....	269
Oral Suspensions .....	270
Topical Suspensions .....	270
Parenteral Suspensions.....	271
Ophthalmic Suspensions .....	271
Development of Suspensions.....	272
Characteristics of a well Formulated Suspension .....	272
Formulation Considerations.....	273
Interfacial Properties .....	273
Wetting of Particles.....	274
Zeta Potential.....	276
Crystal Growth .....	277
Aggregation and Caking .....	278
Sedimentation.....	279
Flocculated Suspension.....	280
Prefomulation .....	280
Crystall Properties and Polymorphism	281
Particle Size and Surface Area.....	281
Dissolution .....	282
Rheology (Flow property) .....	282
Drug-Excipient Compatibility .....	283
Formulation Excipients .....	283
Dispersing Agents.....	284
Wetting Agents .....	285
Deflocculating Agents .....	285
Protective Colloids .....	286
Electrolytes.....	286
Suspending Agents .....	287
Cellulose Derivatives .....	287
Polysaccharides and Gums.....	288

---

Synthetic Polymers.....	288	Emulsifiers.....	314
Buffers .....	290	Emulsion Stabilizers .....	318
Humectants and Cosolvents .....	290	Preservatives.....	320
Preservatives.....	290	Antioxidants .....	322
Antioxidants .....	292	Formulation of Emulsions .....	323
Colors .....	292	Optimization of Formulation.....	323
Flavors or Fragrances .....	293	Processing Parameters.....	324
Sweetening Agents.....	293	Methods of Preparation.....	326
Manufacturing Process .....	294	Equipments for Emulsification .....	327
Processing Equipments .....	294	Methods of Manufacture of	
Preparation of Suspension .....	295	Emulsions in the Laboratory .....	332
Dispersion of Drug Particles.....	296	Continental or Dry Gum Method .....	333
Preparation of Structured Vehicle .....	296	Wet Gum Method .....	333
Addition of Formulation Excipients....	296	Forbes Bottle Method .....	334
Incorporation of Drug Dispersion .....	297	In Situ Soap Method.....	334
Deaeration and Volume Make-up.....	297	Pilot Plant Scale-Up.....	334
Homogenization.....	297	Stability of Emulsion.....	335
Stability Studies.....	298	Creaming .....	336
Microbial Stability .....	301	Flocculation.....	336
Kinetics of Drug Degradation .....	301	Coalescence .....	337
Evaluation.....	302	Chemical Stability.....	338
Toxicity (Safety) Test .....	305	Stability Studies and Shelf-Life .....	339
<b>Model Questions .....</b>	<b>305</b>	Physical Parameters .....	339
<b>References.....</b>	<b>306</b>	Visual and Microscopic Examination .	339

## CHAPTER 8

### EMULSIONS

Introduction .....	309	Electrophoretic Behavior .....	340
Advantages of Emulsions .....	309	Electrical Conductivity.....	340
Theory of Emulsification .....	310	Chemical Parameters .....	341
Surface Tension Theory.....	311	Oxidation and Hydrolysis .....	341
Harkin's Oriented-Wedge Theory .....	311	Adverse Temperature .....	341
Plastic or Interfacial Film Theory.....	312	Centrifugation .....	342
Viscosity Theory .....	313	Agitation.....	342
Formulation Ingredients .....	313	Bioavailability from Oral Emulsions ...	342
Immiscible Phases .....	313	<b>Model Questions.....</b>	<b>343</b>
		<b>References .....</b>	<b>344</b>

## **CHAPTER 9**

### **MICROEMULSIONS**

Introduction .....	348
Advantages.....	349
Disadvantages .....	350
Properties of Microemulsion .....	351
Uses .....	351
Types of Microemulsion.....	352
Phase Inversion Temperature (PIT)....	353
Theory of Microemulsion .....	353
Thermodynamic Theory .....	353
Formulation Consideration .....	354
Conditions Necessary to Produce Microemulsions .....	354
Phase Diagrams.....	354
Dynamic behavior of Microemulsion .	356
Experimental Designing .....	357
Solubilization of Drug Molecules in Microemulsions.....	357
Characteristics of Microemulsion .....	358
Biocompatibility .....	358
Solubility and Stability.....	359
R-ratio.....	359
Methods of Drug Delivery .....	360
Oral Delivery.....	360
Parenteral Delivery .....	361
Topical Delivery.....	362
Preparation of Microemulsion .....	362
Phase Titration Method .....	362
Phase Inversion Method .....	362
Evaluation of Microemulsion .....	363
<i>In-vitro</i> Drug Release Studies .....	364
<b>Model Questions .....</b>	<b>365</b>
<b>References.....</b>	<b>366</b>

## **CHAPTER 10**

### **SOLUTIONS**

Introduction .....	369
Advantages.....	370
Limitations.....	370
Formulation Parameters .....	371
Solubility.....	371
Solubilization.....	375
pH.....	376
Buffer .....	378
Cosolvent .....	379
Dielectric Constant.....	380
Surface Active Agents .....	380
Complexing Agents .....	381
Hydrotropy.....	384
Chemical Modification .....	384
Particle Size Reduction.....	385
Solvents for Aqueous Preparations....	385
Water .....	385
Potable/Drinking Water .....	385
Purified Water.....	385
Reverse Osmosis .....	387
Water for Injections .....	387
Other Grades of Water .....	387
Alcohol .....	387
Diluted Alcohol.....	388
Polyhydric Alcohol.....	388
Solvents for Nonaqueous Preparations.....	388
Oils .....	389
Mineral oil (Liquid paraffin) .....	389
Dimethylsulphoxide (DMSO).....	389
Other Solvents.....	390
Formulation Excipients .....	391
Viscosity Enhancer .....	391
Buffers .....	391

---

**Contents (xvii)**

Preservatives.....	392	Liquefied Gas Propellant.....	421
Density Modifiers .....	394	Coding of Propellants.....	422
Isotonicity Modifiers .....	394	Mixture of Liquefied and Compressed Gases .....	424
Antioxidants .....	395	Two-phase System .....	425
Sweetening Agents.....	395	Three-phase System.....	426
Flavors and Perfumes.....	397	Containers.....	426
Colors .....	398	Tinplate Containers.....	427
Types of Solution Formulations .....	400	Aluminium Containers .....	427
Manufacture of Solution.....	400	Stainless Steel Containers .....	427
Raw Materials .....	400	Glass Containers.....	427
Mixing Equipments .....	401	Plastic Containers.....	428
Clarification/Filtration.....	402	Valves .....	428
Gravity Filtration .....	402	Actuators.....	428
Vacuum Filtration.....	402	Foam Valve.....	430
Pressure Filtration.....	404	Metering Valve.....	430
Meta Filter.....	404	Types of Aerosol System .....	430
Stability Studies.....	405	Water-based System (Aerosol) .....	431
Physical Stability.....	406	Solution System.....	431
Chemical Stability.....	407	Dispersion/Suspension System .....	432
Packaging .....	408	Intranasal Aerosol .....	434
Containers and Closures .....	410	Manufacture of Pharmaceutical Aerosol .....	434
<b>Model Questions .....</b>	<b>410</b>	Preparation of Product Concentrate.	435
<b>References.....</b>	<b>411</b>	Filling of Product Concentrate .....	435

**SECTION V****GASEOUS DOSAGE FORMS****CHAPTER 11****AEROSOLS**

Introduction .....	417	Quality Control of Pharmaceutical Aerosol .....	437
Types of Aerosol Products .....	418	Propellants .....	437
Advantages.....	419	Valve, Actuator and Dip Tube .....	437
Disadvantages .....	419	Method .....	438
Basic Components of Aerosol or Pressure Pack.....	419	Interpretation.....	438
Product Concentrate.....	419	Containers.....	439
Propellants .....	421	Weight Variation .....	439

**(xviii) Contents**

---

Leak Test .....	439	Materials .....	461
Spray Test.....	439	Environmental Control.....	462
Evaluation of Aerosol .....	439	Air-Handling Unit.....	463
Stability Studies.....	442	Ventilation.....	464
Product Concentrate and Propellant.....	442	Filtration of Air .....	466
Container.....	442	Testing of HEPA Filter.....	468
Valve Assembly .....	443	Test for Efficiency (Hot DOP Test).....	468
Advancement in Aerosol Technology .....	443	Integrity Testing .....	468
<b>Model Questions .....</b>	<b>443</b>	Evaluation of Air Filter System .....	469
<b>References.....</b>	<b>444</b>	Evaluation of Airflow Resistance.....	469
		Evaluation of Filter Efficiency.....	469
		Evaluation of Service Life .....	470
		Evaluation of Arrestance.....	470
		Temperature and Humidity Control...	471
		Control of Airborne Contamination ...	471
		Packaging Materials .....	471
		Rubber Components .....	472
		Elastomeric Closures .....	472
		Washing.....	473
		Siliconization .....	473
		Sterilization .....	474
		Glass Components .....	474
		Washing.....	475
		Sterilization of Containers.....	476
		Sterilization of Plastic Containers .....	476
		Moist Heat Sterilization .....	476
		Radiation Sterilization .....	477
		Gas Sterilization .....	478
		<b>Model Questions.....</b>	<b>478</b>
		<b>References .....</b>	<b>479</b>

**SECTION VI**

**STERILE PRODUCTS**

**CHAPTER 12**

**STERILE PRODUCTS**

Introduction .....	449
Preparative Steps .....	450
Planning, Scheduling and Control .....	450
Materials Management.....	451
Personnel Management.....	452
Documentation .....	452
Standard Operating Procedures.....	452
Master File .....	453
Environmental Records .....	453
Validation Records .....	453
Material Records.....	454
Distribution Records .....	454
Complaint File .....	454
Preparation of Facilities and Equipments .....	454
Environment.....	454
Air Control.....	457
Personnel .....	459
Equipments .....	460

Materials .....	461
Environmental Control.....	462
Air-Handling Unit.....	463
Ventilation.....	464
Filtration of Air .....	466
Testing of HEPA Filter.....	468
Test for Efficiency (Hot DOP Test).....	468
Integrity Testing .....	468
Evaluation of Air Filter System .....	469
Evaluation of Airflow Resistance.....	469
Evaluation of Filter Efficiency.....	469
Evaluation of Service Life .....	470
Evaluation of Arrestance.....	470
Temperature and Humidity Control...	471
Control of Airborne Contamination ...	471
Packaging Materials .....	471
Rubber Components .....	472
Elastomeric Closures .....	472
Washing.....	473
Siliconization .....	473
Sterilization .....	474
Glass Components .....	474
Washing.....	475
Sterilization of Containers.....	476
Sterilization of Plastic Containers .....	476
Moist Heat Sterilization .....	476
Radiation Sterilization .....	477
Gas Sterilization .....	478
<b>Model Questions.....</b>	<b>478</b>
<b>References .....</b>	<b>479</b>

**CHAPTER 13**

**STERILIZATION**

Introduction .....	480
Pyrogens.....	481
Microbial Death Kinetics .....	481
Selection of Sterilization Process .....	483

---

Thermal Sterilization .....	484
Dry Heat Sterilization .....	485
Types of Sterilizer .....	485
Natural Convection Type (Hot Air Oven) .....	486
Forced-Convection Type Oven .....	486
Dry Heat Tunnels.....	487
Effect of Higher Temperature on Materials .....	489
Moist Heat Sterilization.....	489
Steam Sterilization .....	491
Advantages.....	492
Disadvantages .....	492
Factors Influencing Sterilization Cycle .....	493
Chemical Cold Sterilization.....	494
Ethylene Oxide .....	494
Hydrogen Peroxide.....	495
Hydrogen Peroxide and Steam .....	495
Chlorine Dioxide .....	496
Ozone .....	497
Chlorine Bleach .....	497
Formaldehyde .....	497
Other Sterilizing Agents .....	498
Radiation Sterilization .....	498
Gamma Radiation ( $\gamma$ -radiation).....	498
Electron Accelerators .....	499
Filtration .....	500
Types of Filters and Filtration Mechanism .....	501
Screen Filtration .....	501
Depth Filtration .....	502
Cake Filtration .....	503
Membrane Filtration.....	503
Validation of Sterilization Process.....	504
<b>Model Questions .....</b>	<b>506</b>
<b>References.....</b>	<b>507</b>
 <b>CHAPTER 14</b>	
<b>SMALL VOLUME PARENTERALS</b>	
Introduction .....	509
Formulation Considerations.....	510
Route of Administration.....	510
Vehicle.....	510
Types of Vehicle .....	511
Water for Injection.....	511
Cosolvents.....	511
Nonaqueous solvent .....	512
Solubilization.....	512
Effect of Additives .....	514
Buffers.....	515
Antioxidants .....	517
Preservatives.....	518
Tonicity.....	520
Effect of Containers.....	520
Glass .....	521
Rubber Closures .....	522
Manufacture of the Product .....	524
Preparation of Parenteral Solution ....	524
Preparation of Parenteral Suspension...527	
Preparation of Freeze Dried Powder Injectables .....	529
Preparation of Sterile Dry Fill Powders .....	531
Lyophilization .....	532
Stability Studies.....	533
<b>Model Questions.....</b>	<b>534</b>
<b>References .....</b>	<b>536</b>
 <b>CHAPTER 15</b>	
<b>LARGE VOLUME PARENTERALS</b>	
Introduction .....	538
Formulation Consideration .....	540
Physiological.....	540
Physicochemical.....	541

**(xx)    Contents**

---

Physical.....	542	Method of Manufacturing .....	577
Packaging Materials .....	542	Ophthalmic Solution does not Contain any Gum.....	577
Stabilization.....	543	Ophthalmic Solution Containing a Gum.....	577
Raw Materials .....	543	Ophthalmic Suspensions.....	577
Types of Formulation .....	545	Preservatives.....	578
Solutions.....	546	Method of Manufacturing .....	578
Electrolyte Solutions .....	546	Ophthalmic Ointments.....	580
Carbohydrate Solutions .....	549	Method of Manufacture .....	581
Fat Emulsions .....	549	Ophthalmic Gel .....	581
Total Parenteral Nutrition.....	550	Method of Manufacture .....	582
Nutritional Content .....	551	Irrigating Solutions .....	582
Complications.....	553	Method of Manufacture .....	583
Intravenous Admixture .....	553	<b>Model Questions.....</b>	<b>584</b>
Parenteral Incompatibility .....	554	<b>References .....</b>	<b>585</b>
<b>Model Questions .....</b>	<b>555</b>		
<b>References.....</b>	<b>556</b>		

**CHAPTER 16**

**OPHTHALMIC PRODUCTS**

Introduction .....	557
Anatomy of Eye .....	558
Absorption of Drug from the Eye .....	561
Therapeutic Classification of Ophthalmic Products .....	564
Formulation Consideration .....	566
Development of Ophthalmic Formulation .....	566
Excipients .....	569
Wetting Agents .....	569
Buffer Systems .....	570
Viscosity Enhancing Agent .....	571
Antioxidants .....	572
Preservatives.....	572
Tonicity (Osmolarity)-Adjusting Agent..	575
Ophthalmic Solutions .....	576
Factors Influencing Formulation .....	576

**CHAPTER 17**

**CONTACT LENSES**

Introduction .....	587
Soft Contact Lens .....	587
Advantages of Contact Lens.....	590
Manufacturing Process .....	591
Molding Method .....	591
Lathe Process .....	591
Finishing .....	592
Problems Associated with Contact Lens.....	592
Quality Control.....	593
Contact Lens Care Products .....	593
Wetting Solutions.....	593
Cleaning Solutions.....	594
Soaking Solution.....	594
<b>Model Questions.....</b>	<b>596</b>
<b>References .....</b>	<b>596</b>

**SECTION VII****PHARMACEUTICAL PACKAGING****CHAPTER 18****PACKAGING MATERIAL**

Functions of Packaging.....	602
Protective Function.....	602
Physical Protection.....	602
Storage Function .....	602
Loading and Transport Function .....	602
Identification .....	603
Mechanical Protection .....	603
Environmental Protection .....	604
Chemical Protection.....	605
Biological Protection .....	607
Containment .....	608
Transfer of Information.....	608
Marketing.....	608
Convenience.....	608
Security.....	608
Cost .....	608
Aseptic Packaging Systems .....	608
Fill and Seal .....	608
Erect, Fill, and Seal .....	609
Form, Fill, and Seal .....	609
Thermoform, Fill, and Seal .....	609
Blow Mold, Fill, and Seal .....	610
Bulk Storage and Packaging .....	610
Selection of Packaging Materials .....	611
Product.....	611
Distribution System.....	611
Market.....	612
Manufacturing Facility .....	612
Types of Packaging Materials.....	612
Packaging Components.....	614
Paper and Board.....	614
Glass .....	615
Types of Glass.....	617
Type I or Borosilicate Glass .....	617
Type II or Treated Soda-Lime Glass....	617
Type III or Regular Soda-Lime Glass ...	618
Type NP or General Soda-Lime Glass .	618
Manufacture of Glass.....	619
Types of Glass Containers .....	619
Ampoule .....	619
Bottles, Vials, and Syringes .....	620
Plastic Packaging Components.....	620
Polyethylene .....	621
Polypropylene .....	621
Polyvinyl Chloride (PVC).....	622
Polystyrene .....	622
Nylon (Polyamide).....	623
Polycarbonate .....	623
Acrylic Multi-polymers (Nitrile Polymers) .....	623
Polyethylene Terephthalate (PET) .....	624
Plastic Containers.....	624
Interaction between Plastic and Product .....	625
Permeation.....	625
Leaching .....	626
Sorption.....	626
Change in Physicochemical Properties .....	627
Chemical Reaction.....	627
Closures.....	629
Types of Closures .....	629
Threaded Screw Cap .....	630
Continuous Threaded (CT) Closures...	630
CT Plugs Combination Closure .....	630
Crown Cap.....	631
Roll-on Type .....	631
Friction-Fit Closures .....	632
Lug-Style Closures .....	632

**(xxii) Contents**

---

Snap-Fit Closures.....	633	Fin-Seal Wrapping .....	647
Press-on Vacuum Caps.....	633	Shrink Wrapping.....	648
Vial and Bottle Stoppers.....	634	Blister Packing .....	648
Rubber Stoppers .....	634	Bubble Packing.....	649
Performance of Elastomeric Closure .	635	Shrink Banding .....	649
Flanged Plug Elastomeric Stoppers ....	636	Secondary Packaging Materials .....	650
Flanged Hollow Elastomeric Plug with Cutouts .....	637	Boards .....	650
Metal Closure with an Elastomeric Disk .....	637	Evaluation of Packaging Materials .....	652
Tube Closures.....	637	Glass Containers.....	652
Special Closures.....	638	Water Attack Test .....	652
Dispensing Closures and Closure with Applicators .....	638	Powdered Glass Test.....	653
Fitment Closure.....	638	Preparation of Sample .....	653
Spray and Pump Dispensers.....	639	Plastic Containers.....	655
Precise Dose-Dispensing Closure .....	639	Physicochemical Test .....	655
Single-Dose Closures .....	640	Elastomeric Closures .....	657
Liner-less Closures.....	640	Secondary Packaging Materials .....	658
Child-Resistant (CR) Closures .....	640	Coding in Pharmaceutical Packaging .	661
Aerosol Closures.....	641	Symbology.....	662
Closure Liners.....	641	Current Trends in Packaging .....	663
Selection of Closure Liner .....	642	Types of Packaging Machines .....	664
Composition of Closure Liners .....	642	<b>Model Questions.....</b>	<b>664</b>
Non-Reclosable Packages.....	643	<b>References .....</b>	<b>666</b>
Pouches .....	643		
Peelable Seals.....	643		
Collapsible Tubes .....	644		
Metal Tubes .....	644		
Tin.....	644		
Aluminium.....	645		
Lead.....	645		
Plastic Tubes.....	646		
Tamper-Resistant Packaging .....	646		
Film Wrapping .....	647		
End-Folded Wrapping .....	647		

**SECTION VIII**

**VALIDATION OF  
PHARMACEUTICAL PROCESSES**

**CHAPTER 19**

**VALIDATION OF  
PHARMACEUTICAL PROCESSES**

Introduction .....	671
Situations need	
Pharmaceutical Validation .....	673
Advantages of Validation .....	674
Major Phases of Validation .....	675
Protocols of Validation.....	676

## **Contents (xxiii)**

---

Types of Validation.....	677	The Validation Report .....	697
Validation Master Plan.....	677	Validation of Cleaning Process .....	698
Content of Validation Master Plan.....	678	Type of Contamination .....	698
Validation of Analytical Methods.....	678	Validation of Cleaning Process .....	699
Strategy for Methods Validation.....	679	<b>Model Questions .....</b>	<b>700</b>
Types of Procedures to be Validated .	679	<b>References .....</b>	<b>701</b>
Validation Report .....	682		
Equipment Validation/Qualification ..	682		
The Pharmaceutical Process Equipment.....	682		
Design Qualification (DQ).....	683		
Installation Qualification (IQ).....	683		
Operation Qualification (OQ).....	684		
Performance Qualification (PQ) .....	684		
Environmental Considerations.....	685		
Cleaning and Clean Room Standards .	685		
Process Validation.....	686		
Pre-requisites for Process Validation .	686		
Priority of Process Validation.....	686		
Sterile Products and their Processes..	687		
Nonsterile Products and their Processes .....	687		
Approaches to Validation Process ..	687		
Types of Process Validation .....	688		
Prospective Validation .....	688		
Formulation Development.....	690		
Process Development .....	690		
Retrospective Validation .....	692		
Concurrent Validation.....	693		
Revalidation .....	694		
Stages of Process Validation .....	695		
Process Design (Stage I) .....	695		
Process Qualification (Stage II) .....	695		
Continued Process Verification (Stage III).....	696		
Expert Evaluation .....	697		

**(xxiv) Contents**

---

General Case .....	719
Validation of Analytical Procedures [Q2 (R1)].....	719
Text and Methodology .....	719
Types of Analytical Procedures to be Validated.....	719
Validation of Analytical Methodology	724
Identification .....	725
Assay and Impurity Test(s) .....	725
Impurities in New Drug Substances, [Q3A (R2)].....	726
Classification of Impurities .....	726
Impurities in New Drug Products, Q3B (R2) .....	727
Impurities: Guideline for Residual Solvents, Q3C(R5) .....	728
Classification of Residual Solvents by Risk Assessment.....	728
Pharmaceutical Development, ICH Q8.....	730
Pharmaceutical Quality System, ICH Q10.....	731
Elements of Pharmaceutical Quality System .....	732
Knowledge Management.....	733
Quality Risk Management.....	733
Design and Content Consideration ....	734
Quality Manual.....	734
Quality Policy.....	734
Management Responsibility .....	734
Quality Planning .....	735
Resource Management.....	735
Internal Communication .....	735
Management Review .....	735
<b>Model Questions .....</b>	<b>736</b>
<b>References.....</b>	<b>737</b>

**CHAPTER 21**

**SUSTAINED & CONTROLLED RELEASE FORMULATIONS**

Factors influencing Oral Sustained Release Dosage Forms .....	741
Biological Factors .....	741
Physiological Factors .....	743
Oral Sustained-and Controlled-Release Products .....	745
Advantages.....	745
Disadvantages .....	746
Dissolution-Controlled Systems .....	746
Diffusional Systems .....	749
Reservoir Devices .....	749
Matrix Devices.....	752
Bioerodible and Combination Diffusion and Dissolution System .....	755
Osmotically Controlled System .....	756
Ion-Exchange System .....	758
Targeted Drug Delivery .....	759
<b>References .....</b>	<b>767</b>

**Chapter 22**

**CLINICAL TRIALS**

Developing Clinical Trial Protocols....	770
Purpose of Research Proposal .....	771
Aim .....	771
Components of a Research Protocol..	772
Title of the Study.....	772
Administrative Details.....	772
Project Summary.....	773
Institutional Review Board/	
Independent Ethics Committee .....	773
Formulation and Working Hrs.	
Procedures Informed .....	776
Consent Process and Procedures.....	781

---

**Contents (xxv)**

Complex Information .....	782	Pre-clinical Studies .....	788
Poor Understanding and Comprehension of Consent Forms ....	783	Phase 0 .....	788
Patient Competence .....	783	Phase I .....	788
Informed Consent in India .....	783	Phase III .....	789
Potential Strategies to Enhance Informed Consent Process in India ....	785	Phase IV.....	790
Simplification of Consent Documents	785	Investigational New Drug (IND) / Clinical Trial Exception (CTX) / Clinical Trial Authorization (CTA) Application .....	790
Assessment of Patient Comprehension.....	786	New Drug Application (NDA)/Marketing Authorization Application (MAA).....	791
Printed Brochures and Information Sheets.....	786	Pharmacovigilance Safety Monitoring in Clinical Trials.....	793
Audio-Visual Presentations.....	786	Pharmacovigilance .....	794
Extended Informed Consent Discussions .....	787	Pharmacovigilance in Clinical Trials ...	795
Hipaarequirement to Clinical Study Process .....	788	<b>References .....</b>	<b>797</b>
Introduction .....	788	 	
		<b>Index.....</b>	<b>801</b>