Ref. 615.321 EBA 2nd ed.

Contents

Chapter 1 The Pharmacokinetic Basis of Therapeutics 1

Introduction 1
Administration of Drugs 2
Duration of Action 2
Nature of the Drugs 2
Special Circumstances 3
Drug Delivery by Iontophoresis or Phonophoresis 3
Liposomal Drug Delivery System 3
Bioavailability 3
Absorption of Drugs 3
Drug Particle Size 4
Buccal and Sublingual Absorption 4
Intranasal Delivery 4
Rectal Administration 5
Transport Mechanisms 5
Passive Diffusion 5
Carrier-Mediated Transport 5
Facilitated Transport 6
Ion Pair Transport 6
Pinocytosis 6
Receptor-Mediated Endocytosis 6
Other Factors Controlling the Rate of Absorption of Drugs 6
Degree of Ionization 7
Surface Area 8
Blood Flow 8
Gastric Emptying Time 8
Hepatic First-Pass Effect 9
Distribution of Drugs 9
Binding of Various Drugs to Plasma Proteins 10
Albumin 10
Alpha,-Acid Glycoprotein 10
Other Glycoproteins 10
Lipoproteins 11
Tissue Localization of Drugs 11
Apparent Volume of Distribution of Drugs 12
The Blood–Brain Barrier 12
The Placental Barrier 12
Drugs in Pregnancy and the Newborn 13
Drug Therapy in Pregnancy 13
Drug Therapy in the Newborn 13
The Site of Action of Drugs 13
Nature and Type of Pharmacologic Receptor Sites 13
Dose–Response Relationship 14
Potency and Efficacy 14

Physiologic and Pharmacologic Antagonism 16
Enhancement of Drug Action 16
Therapeutic Index 16
Biotransformation 17
Hepatic Drug Metabolism 17
Nonhepatic Metabolism 17
Plasma 17
Lung 18
Intestinal Epithelium 18
Molecular Biology of Multiple Isoenzymes of P-450 18
Scheme of the Mixed-Function Oxidation Reaction Pathway 18
Consequence of Biotransformation Reactions 19
Precursor Activation 19
Metabolic Activation of Drugs 19
Conversion to Metabolites with Dissimilar Actions 19
Conversion to More Active Products 19
Lethal Synthesis 19
Drug Metabolite Kinetics 19
Factors That Modify the Metabolism of Drugs 20
Pharmacogenetics 20
Liver Disease 20
The Influence of Age 20
Enzyme Induction and Inhibition 20
Clinical Implications of Enzyme Induction and Inhibition 21
Renal Excretion of Drugs 21
Rate of Excretion of Drugs by the Kidneys 21
Significance of Blood Flow for Drug Clearance 22
Half-Life of a Drug 23

Chapter 2 Pharmacodynamics 25

Introduction 25
Site of Action 25
Mode of Action 25
Mechanism of Action 25
Structure–Activity Relationship 25
Drug Actions Unrelated to Structures 26
Drug Receptor-Specific Interaction 26
Cellular Sites of Actions of Drugs 27
Drug–Coenzyme Interactions 27
Isoniazid and Pyridoxal Phosphate 27
Folic Acid and **Trimethoprim-Sulfamethoxazole** 27
Drug–Enzyme Interactions 27
Allopurinol, Xanthine Oxidase, and Hyperuremic States 28
Drugs and Bronchial Asthma 28
Drug–Nucleic Acid Interactions 28
The Interactions of Drugs with Neuronal Elements 29
Interaction of Drugs with the Endocrine System 29
Alpha-Methyldopa and Renin 29
Drugs and Prolactin 29

Chapter 3 Adverse Reactions and Drug–Drug Interactions 31

Introduction 31
Definitions 31
Iatrogenic Reactions 31
Allergic Reactions 31
Idiosyncratic Reactions 32
Tolerance and Tachyphylaxis 32
Supersensitivity 33
Pharmacokinetic Interactions 33
Interaction at the Site of Absorption 33
Alteration of Gastric pH 33
Formation of Complex 34
Alteration in Gastric Emptying Time 34
Interactions at the Plasma–Protein Binding Sites 34
Interactions at the Stage of Drug Biotransformation 35
Interactions at the Site of Excretion 36

Chapter 4 Herb–Drug Interactions 37

Herbs and Drug Effects 37
Potential Interactions between Alternative Therapies and Warfarin 38
Anticoagulants and Thrombolytic Agents 38
Aggregin and Platelet Aggregation 42
Vitamin E and Platelet Aggregation 42
Platelet-Activating Factor 42
Platelet-Inhibiting Drugs 42
Fibrinolysis 43
Hirudin and Thrombin 43
Agents that Interfere with Coagulation 43
Oral Anticoagulants 44
Herbs with Coumarin, Salicylate, or Antiplatelet Drugs 44
Feverfew 44
Garlic 45
Ginger 45
Ginkgo 45
Coenzyme Q,,, ... 45
Danshen 45
Devil's Claw 46
Ginseng 46
Green Tea 46
Papain 46
Vitamin E 46

Chapter 5 Natural Products as a Resource for Established and New Drugs 49

The Role of Herbal Medicines in Health Care 49
Drug Therapy in Chinese Traditional Medicine 50
Prescription of Multiple Herbs in CTM 50
Pharmacological Classification of Herbs According to CTM 51
Classic Plant Substances 53
Caffeine 53

Capsaicin 53
β-Carotene 53
Colchicine 53
Nordihydroguaiaretic Acid 53
Pilocarpine 56
Quinine 56
Scopolamine (Hyoscine) 56
Tetrahydrocannabinol 56
Theophylline 56
Antimalarial Agents 56
Cardiovascular Drugs 57
CNS Drugs 57
Antibiotics 58
Antineoplastic Agents 59
Cholesterol-Lowering Agents (Hypolipemics) 60
Immunomodulators 61
Recently Evaluated Herbal Products 61
Aloe Vera Gel (Aloe vera) 61
American Dwarf Palm (Serenoa *repens*) 61
Cranberry juice (Vaccinium spp.) 61
Evening Primrose Oil (Oenothera biennis) 61
Feverfew Leaf (Tanacetum parthenium) 62
Garlic (Allium *sativum*) 62
Ginger Root (Zingiber *officinale*) 62
Ginkgo Leaf (Ginkgo biloba) 62
Hawthorn (*Crataegus* monogyna and C. laevigata) 62
Horse Chestnut (Aesculus hippocastanum) 62
Ipecacuanha (Cephaelis ipecacuanha and C. acuminata) 62
Ispaghula Husk (Plantago *ovato*) 63
Kava-Kava (Piper methysticum) 63
Marijuana (Cannabis *sativa*) 63
St. John's Wort (Hypericum *perforatum*) 63
Tea Tree Oil (Melaleuca *alternifolia*) 63
Wheat Bran (Triticum spp.) 63
New Uses for "Old Drugs 63

Chapter 6 Alternative Therapies 65

Introduction 65
Why Patients Use Alternative Medicine 65
Acupressure 65
Acupuncture 66
Aromatherapy 66
Auricular Therapy 66
Ayurveda 66
Biodynamic Massage 67
Bioenergetic Therapy 67
Chi Kung Medicine 67
Chinese Herbalism 68
Chiropractic Medicine 68
Crystal and Gem Therapies 68

Cupping Therapy 68
Dietary and Nutritional Therapies 69
Eastern Herbal Medicine 69
Environmental Therapies 70
Flower and Tree Remedies 70
Food and Diet Therapy 71
Geopathic Therapy 72
Gestalt Therapy 72
Herbal Medicine 72
Homeopathy 74
Hydrotherapy 74
Hypnosis and Hypnotherapy 74
Iridology 74
Japanese Medicine 75
Light Therapy 75
Massage Therapy 75
- Shiatsu 75
- Therapeutic Massage 75
- Reflexology 76
- Sports Massage 76
- Baby Massage 76
- Biodynamic Massage 76

Moxibustion 76
Myotherapy 76
Native American Herbal Medicine 76
Naturopathy (Medicatrix Naturae) 77
Osteopathy 77
Persian Medicine 77
Polarity Therapy 78
Psychic Healing 78
Psychological Therapies 78
- Analytical Therapy 78
- Behavioral Therapy 79
- Humanistic Therapy 79
- Integrative Therapy 79
- Meditation Therapy 79
- Sound Therapy 79

Reflexology (Reflex Zone Therapy) 79
Reiki Therapy 80
Relaxation Therapies 80
- Rolfing Medicine 80

Shamanistic Medicine 80
T'ai Chi Chuan Medicine 81
Therapeutic Diets 81
- Exclusion Diet 81
- Vegetarian Diet 81
- Vegan Diet 81
- Food Combining Diet 81
- Anti-Candida Diet 81
- Liver Diet 81

Low Blood Sugar Diet 81
Macrobiotic Diet 82
Tibetan Medicine 82
Transcendental Meditation (TM) 82
Transpersonal Therapies 83
Visualization Therapy 83
Yoga 83

Chapter 7 Herbal Therapeutics Then and Now 85

Introduction 85
Agnus Castus 85
Agrimony 85
Alfalfa 85
Aloe 85
Aloe Vera 86
Angelica 86
Aniseed 86
Apricot 86
Arnica 86
Artichoke 86
Asafoetida 86
Avens 86
Bayberry 87
Black Cohosh 87
Bloodroot 87
Blue Cohosh 87
Blue Flag 87
Bogbean 87
Boldo 87
Boneset 87
Borage 88
Broom 88
Buchu 88
Burdock 88
Burnet 88
Calamus 88
Calendula 88
Capsicum 89
Cascara 89
Cascara Sagrada 89
Cassia 89
Cat's Claw 89
Celery 89
Centaury 89
Cereus 89
Chamomile 90
Chamomile (German) 90
Chamomile (Roman) 90
Chaparral 90
Cinnamon 90

Clivers....90
Clove....90
Cola....91
Coltsfoot....91
Comfrey....91
Corn Silk....91
Couchgrass....91
Cowslip....91
Cranberry....91
Damiana....92
Dandelion....92
Devil's Claw....92
Dong Quai....92
Drosera....92
Echinacea....92
Elder....92
Elecampane....93
Eucalyptus....93
Euphorbia....93
Evening Primrose....93
Eyebright....93
False Unicorn....93
Fenugreek....93
Feverfew....93
Figwort....94
Frangula....94
Fucus....94
Fumitory....94
Garlic....94
Gentian....94
Ginger....94
Ginkgo....95
Ginkgo biloba....95
Ginseng (Eleutherococcus)....95
Ginseng *(Panax)*....95
Golden Seal....95
Gravel Root....95
Ground Ivy....96
Guaiacum....96
Hawthorn....96
Holy Thistle....96
Hops....96
Horehound (Black)....96
Horehound (White)....96
Horse Chestnut....96
Horseradish....97
Hydrangea....97
Hydrocotyle....97
Ispaghula....97
Jamaica Dogwood....97
Juniper....97

Kava....97
Lady's Slipper....97
Lemon Verbena....97
Licorice....98
Liferoot....98
Lime Flower....98
Lobelia....98
Ma Huang and the Ephedra Alkaloids....98
Marshmallow....98
Mad....99
Meadowsweet....99
Mistletoe....99
Motherwort....99
Myrrh....99
Nettle....99
Panax ginseng....99
Parsley....99
Parsley Piert....100
Passionflower....100
Pennyroyal....100
Pilewort....100
Plantain....100
Pleurisy Root....100
Pokeweed....100
Poplar....100
Prickly Ash (Northern)....101
Prickly Ash (Southern)....101
Pulsatilla....101
Quassia....101
Queen's Delight....101
Raspberry....101
Red Clover....101
Rhubarb....102
Rosemary....102
Sage....102
Sarsaparilla....102
Sassafras....102
Saw Palmetto....102
Senega....102
Senna....103
Shepherd's Purse....103
Skullcap....103
Skunk Cabbage....103
Slippery Elm....103
Squill....103
St. John's Wort....103
Stone Root....104
Tansy....104
Thyme....104
Uva-Ursi....104
Valerian....104

Vervain 104
Wild Carrot 104
Wild Lettuce 105
Willow 105
Witch Hazel 105
Yarrow 105
Yellow Dock 105
Yucca 105

Chapter 8 Dietary Antioxidants 107

Introduction 107
The Role of Diet in Curing and Preventing Diseases 107
Antioxidant Capacity of Vegetables and Fruits 107
Antioxidant Activity in Cereal Grains 108
Antioxidant Actions of Du-Zhong 108
Oxidative Stress and Chemotherapeutic Effectiveness 110
Principle of Cancer Therapy 110
Chemotherapy 110
Alkylating Agents 112
- Nitrogen Mustards 112
- Chlorambucil 112
- Cyclophosphamide 112
- Alkyl Sulfonate 112
- Nitrosoureas 113
- Triazenes 113
- Antimetabolites 113
- Folic Acid Analogs 113
- Pyrimidine Analogs 113
- Deoxycytidine Analogs 114

Purine Antimetabolites 115
Natural Products 115
- Vinca Alkaloids 115
- Dactinomycin 116
- Mithramycin 116
- Daunorubicin and Doxorubicin 116
- Bleomycin 116

Miscellaneous Antineoplastic Agents 116
- Asparaginase 116
- Hydroxyurea 117
- Cis-Platinum 117
- Carboplatin 117
- Procarbazine 117
- Etoposide 117
- Cancer-Chemotherapy-Induced Emesis 117

Oxidative Stress and Interference with the Cytotoxic Effects of Antineoplastic Agents 117
Antioxidant Effects on Antineoplastic Activity and Chemotherapy-Induced Side Effects 118
- Vitamin E 118
- Vitamin C 119
- Coenzyme Q_{10} (Ubiquinonej 119
- β-Carotene 120

Glutathione (GSH) and Glutathione Esters 120
N-Acetylcysteine 121
Glutamine 121
Selenium 121
Genistein and Daidzein 122
Quercetin 122
Conclusions 123

Chapter **9** Herbal Drugs and Their High Demand in Treating Diseases 125

Introduction 125
Laws Regulating Herbs and Dietary Supplements 126
Food, Drug, and Cosmetic Act 126
Nutrition Labeling and Education Act of 1990 126
Dietary Supplement Health and Education Act of 1994 127
Food and Drug Administration Modernization Act 127
Scientists Who Pioneered Herbal Medicine 128

Chapter **10** Algae 139

Introduction 139
Kainic Acid 140
Domoic Acids 141
Toxicity of Caulerpa 142
Toxicity of Gracilaria 142

Chapter **11** Alkaloids 143

Introduction 143
Classification 144
The Group Containing Aliphatic Bases with an Aromatic Nucleus 144
The Pyrrolidine Group 144
The Pyridine Group 144
The Glyoxaline Group 146
Alkaloids with Condensed Pyrrolidine and Piperidine Rings 146
Derivatives of Quinoline 147
Derivatives of Isoquinoline 147
Phenanthrene 147
Indole Derivatives 147
The Purine Bases 148
Alkaloids of Unknown Constitution 149

Chapter **12** Aloe and Colon Function 151

Introduction 151
Aloe Preparations 151
Chemical Composition of Aloe Plants 152
The Therapeutic Uses of Aloe 152
Aloe and Cancer 152
Aloe and AIDS 153
Aloe and Asthma 153

Aloe and Diabetes 153
Aloe Gel and Skin Ailments 153
Aloe and Constipation 153
Movements of the Colon 154
Mixing Movements: Haustrations 154
Propulsive Movements: "Mass Movements" 154
Initiation of Mass Movements by the Gastrocolic and Duodenocolic Reflexes 155
Defecation 155
The Defecation Reflexes 155
Other Autonomic Reflexes Affecting Bowel Activity 157
Constipation 157
Definition 157
Causes 158
Cathartics 158
Emodin or Anthraquinone Cathartics 159
Cascara Sagrada 160
Senna 160
Rhubarb 160
Aloe 160
Castor Oil 161
Ricin 161
Abrin 161
Croton Oil 161
Resin of Podophyllum 162
Jalap, Scammonium, Ipornea 162
Colocynth, Elaterin, and Bryonia 162

Chapter 13 Banisterine. Selegiline, and Parkinson's Disease 163

Introduction 163
The Actions of Acetylcholine and Dopamine 163
History 164
Selegiline 164
Clinical Pharmacokinetics of Selegiline 165
Lack of Adverse Interaction between Selegiline and Citalopram or between Selegiline and Cabergoline 166
Distribution of Monoamine Oxidases A and B mRNAs in the Rat Brain by In *Situ* Hybridization 167
Inhibition of Monoamine Oxidase B by Banisterine and Selegiline and the Initial Rationale of Using Them in Parkinson's Disease 168
Protection of Dopaminergic Neurons by Rasagiline 169
Protection against MPTP-Induced Neurotoxicity by Selegiline 171
Protection by Selegiline of Dopaminergic Neurons in Culture from Toxic Factors 172
Protection by Selegiline of Dopaminergic Neurons from Glutamate-Induced Excitotoxicity 173
Selegiline: A Calmodulin Antagonist 175
Induction by Selegiline of Dopamine Release through an ATP-Sensitive Potassium Channel 176
Neurotrophic-Like Action of Selegiline: Rescue of Axotomized Motorneurons Independent of Monoamine Oxidase Inhibition 177
Restoration by Selegiline of Serum Insulin-Like Growth Factor-I in Aged Rats 181

Protection by Selegiline of Dopaminergic Neurons from Toxicity Induced by Glutathione Depletion 182
Increase by Selegiline of the Striatal Superoxide Dismutase 185
Protection by Selegiline against Peroxynitrite- and Nitric-Oxide-Induced Apoptosis 186
Antiapoptotic Actions of Selegiline in a Variety of Neurons 187
Stimulation by Selegiline of Biosynthesis of Cytokines Interleukin-1β and Interleukin-6 188
Interleukin 1 189
Interleukin 6 189
Banisterine and Selegiline for the Treatment of Parkinson's Disease 190
Rigidity 191
Hypokinesia 191
Abnormal Gait and Posture 191
Other Clinical Features 191
Summary and Conclusions 193

Chapter 14 Belladonna Alkaloids: Autonomic Drugs 195

Introduction 195
Solanaceae or Nightshade Family 195
Occurrence 196
History 196
Chemistry 197
Botany of Solanaceae 198
Pharmacognosy of Belladonna 198
Preparation of the Leaves 199
Preparations of the Root 199
Atropine and Its Derivatives 199
Belladonna Alkaloids and the Autonomic Nervous System 199
Comparison of the Somatic and Autonomic Nervous Systems 199
Neurochemical Basis of Cholinergic Transmission 200
Division and Functions of the Autonomic Nervous System 200
Classification of Cholinergic Receptors 202
Cholinergic Receptor Blocking Agents 203
Dose-Dependent Effects of Atropine 203
The Historical Uses of Belladonna Alkaloids 203
The Modern Uses of Synthetic Muscarinic Receptor Antagonists 204
Contraindications to Anticholinergic Agents 205
Hyoscyamine 205
Scopolamine 205
Synthetic and Semisynthetic Substitutes for Belladonna Alkaloids 206
Quaternary Ammonium Muscarinic Receptor Antagonists 206
Ipratropium 206
Methoscopolamine 207
Homatropine Methylbromide 207
Methantheline 207
Propantheline 207
Other Compounds 208
Tertiary-Amine Muscarinic Receptor Antagonists 208

Chapter 15 Blueberry *(Vaccinium)* 209

Chapter 16 Botulinum Toxin 213

Introduction 213
Botulinum Toxin Type A (Oculinum) 213
Botulism Antitoxin. Trivalent (ABE) Equine 213
Uses of Botulinum Toxin Injection in Medicine Today 213
Rationale for Treatment with Botulinum Neurotoxin 214
Ophthalmic Disorders 214
Movement Disorders 215
Spasticity 215
Neuromuscular Disorders 215
Pain 216
Ear. Nose. and Throat Disorders 216
Disorders of Pelvic Floor 216
Overactivity of Smooth Muscles 216
Hypersecretion of Glands Supplied by Cholinergic Sympathetic or Parasympathetic Neurons 216

Chapter 17 Brussels Sprouts 217

Introduction 217
Effects of Brussels Sprouts on Oxidative DNA Damage 217

Chapter 18 Cannabis 221

Introduction 221
The Psychoactive Effects of Cannabis 221
Marijuana in History 223
Botanical Properties of *Cannabis indica* or Indian Cannabis (Indian Hemp) 224
Marijuana-Induced Inebriation 225
Cannabinoid Receptor Subtypes 226
Cannabinoid Receptor (CB_1) 227
Cannabinoid Receptor (CB_2) 227
Cannabinoid Receptors and Their Endogenous Agonist. Anandamide 227
Central Nervous System Cannabinoid Receptors 228
Therapeutic Potential of Cannabinoid Ligands 228
Movement Disorders 228
Multiple Sclerosis 229
Huntington's Chorea 229
Neuroprotection 229
Cannabis for Migraine 230
Antiemetic Effects of Cannabis 230
The Physiology of Vomiting 230
The Central Control of Vomiting 230
Drugs to Control the Vomiting Caused by Cancer Therapy 231
Ondansetron 231
Dexamethasone 231
Metoclopramide 232
Phenothiazines 233
Cannabinoids 233
Benzodiazepines 233
Anticipatory Nausea and Vomiting 233

Delayed Emesis 233
Multiple-Day Cisplatin Chemotherapy 233
Summary 233
Cannabis for Dyskinesia 234
Conclusion 236

Chapter **19** Capsicum, Rosemary, and Turmeric 237

Chapter **20** Carotenoids 239

Introduction 239
Prostate Cancer 240
Breast Cancer 240
Cancer of the Head and Neck 240
Cardiovascular Disease 240
Age-Related Macular Degeneration 241

Chapter **21** Chocolate 243

Chapter **22** Cinchona Tree 245

Introduction 245
Cinchona: A Peruvian Bark 245
Varieties of Cinchona 245
Composition of Cinchona 245
Quinine for Treatment of Malaria 247
Blood Schizonticides 248
Quinine Sulfate: A Classic Drug 248
Other Actions of Quinine 250
Colloids and Surface Phenomena 250
Local Actions 251
Lllcers 251
Sunburn Prophylaxis 251
Quinine as Anesthetic 251
Antiseptic Action 251
Effect on Digestion 251
Antipyretic Action 251
Use of Quinine in Colds, Headaches, and Neuralgias 252
Skeletal Muscle 252
Cinchonism 252
Skin Eruptions and Idiosyncrasy 252

Chapter **23** Coca 253

Introduction 253
Coca 253
Habitat 253
Synonym 253
Er-y-throx'y-Ion L. 253
Co'ca 253
History 253

Plant....254
Commercial Properties....255
Botanical Properties....255
Chemical Composition....256
Cocaine as a Local Anesthetic....256
General Pharmacology of Local Anesthesia....257
Vascular Supply at the Site of Injection....257
Systemic Reactions....258
Cardiovascular Effects....258
Central Nervous System Effects....258
Allergic Reactions....258
Effect of Cocaine....259
Mechanism of Local Anesthetic Action of Cocaine....259
Detailed Pharmacology of Cocaine as a Local Anesthetic....259
Selective Action on Motor and Sensory Fiber....260
Peripheral Paralysis of Special Sense Nerves....261
Site of Action....261
Combination of Anesthetics....261
Potassium Synergism....261
Alkalinization....261
Other Synergisms....262
Epinephrine Anesthetic Combinations....262
Local Vascular Action....262
Practical Application of Local Anesthetics....262
Local Ischemia....263
Surface Anesthesia....263
Ophthalmic Anesthesia....263
Actions of Cocaine on the Eye....263
Insoluble Anesthetics for Open Wounds and Ulcers....263
Conduction and Infiltration Anesthesia....264
Spastic Rigidity of Skeletal Muscles....264
Spinal Anesthesia....264
Sympathetic Stimulation....264
Circulation....265
Cerebral Stimulation....265
Incoordination, Narcosis, and Convulsions....265
Emesis....265
Temperature....265
Examples of Currently Used Local Anesthetics....265
Procaine....265
Chloroprocaine....265
Tetracaine....266
Lidocaine....266
Mepivacaine....266
Prilocaine....266
Bupivacaine....266
Etidocaine....266
Clinical Uses of Local Anesthetics....266
Infiltration Anesthesia....266
Field Block Anesthesia....266
Nerve Block Anesthesia....267

Intravenous Regional Anesthesia (Bier's Block) 267
Spinal Anesthesia 267
Epidural Anesthesia 268
Epidural and Intrathecal Opiate Analgesia 268
Safe and Toxic Dosage of Local Anesthetics 268
Destruction of Cocaine In *Vitro*: Sterilization 269
Cocaine, A "Nerve Stimulant" 269
Cocaine Addiction 270
Uses of Cocaine in the 18th Century 270
Cocaine: A Psychostimulant 270
Cocaine Blocks Dopamine Transporter 271
Biosynthesis of Dopamine 271
Cocaine Withdrawal Symptoms and Signs 272
Pharmacological Interventions 272

Chapter 24 Colchicine and Gout 275

Introduction 275
History 275
Gout and Hyperuricemia 275
Allopurinol 276
Uricosuric Agents 276
Treatment with Colchicine for Gout 277
Pharmacological Properties 277
Effect in Gout 277
Effect on Cell Division 277
Other Effects 277
Pharrnacokinetics and Metabolism 278
Toxic Effects 278
Therapeutic Uses 278
Acute Attacks 278
Prophylactic Uses 279
Other Uses of Colchicine 279

Chapter 25 Compositae 281

Introduction 281
Sesquiterpene Lactones 281
Sesquiterpene-Induced Neurotoxicity 282
Tanacetum Parthenium (Feverfew) 282
Other Asteraceae Groups 283
Achillea 283
Artemisia 283
Baccharis 284
Elephantopus 285
Helenium 285
Montanoa 285
Packera 285
Parthenium 285
Tithonia 285

Chapter 26 Curare and Neuromuscular Blockade 287

Introduction 287
Curare 287
Skeletal Muscle Relaxants 288
The Neuromuscular Junction 289
Nicotinic Cholinergic Receptors 289
Mechanism of Action of Neuromuscular Blocking Agents 289
Phase I: Blockade (Depolarization) 289
Phase II: Blockade (Desensitization) 290
Sequence and Onset of Neuromuscular Blockade 290
Factors Affecting Neuromuscular Blockade 292
Drug Interactions 292
Electrolytes 293
Acid–Base Balance 293
Hypothermia 293
Disease States 294
Age 294
Side Effects of Neuromuscular Blocking Agents 294
Cardiovascular Effects 294
Ocular and Muscular Effects 294
Histamine Release 294
Erythrina Alkaloids 294
Methonium Compounds 295

Chapter 27 Daffodil and Alzheimer's Disease 297

Introduction 297
History and General Effects 297
Compounds Found in Daffodils 297
Lycorine (Formerly Narcissine) 299
Galanthamine 299
Chemistry of Galanthamine 299
Pharmacological Mechanisms of Galanthamine Activity 299
Pharmacokinetics of Galanthamine 299
Use of Galanthamine to Treat Depression 300
Specific Studies Showing Antinociceptive Effects of Galanthamine 300
Summary 300
The Treatment of Cognitive Impairment in Alzheimer's Disease 301
Therapeutic Objectives in Alzheimer's Disease 301
The Cholinergic Hypothesis of Alzheimer's Disease and Cholinergic Enhancement Strategies 301
Acetylcholinesterase Inhibitors 302
Tetrahydroaminoacridine 302
Pharmacology 302
Pharmacokinetics 303
Clinical Applications 303
Side Effects 303
Drug–Drug Interactions 303
Overdosage 303

Physostigmine and Its Derivatives 303
Limitations of AChE-Inhibitor Therapy in Alzheimer's Disease 303
Cholinergic Agonists 305
Acetylcholine Precursors 305
Acetylcholine-Releasing Agent 305
Noncholinergic Neurotransmitter Replacement Strategies 305
Monoaminergic Drugs 305
Neuropeptides 305
Drugs Affecting Glutamate Receptor Sites 305
Nootropics 305
Antioxidants 305
Desferrioxamine: An Iron-Chelating Agent 306
Nerve Growth Factor 306
Anti-Inflammatory Agents 306

Chapter **28** Eggplant 309

Chapter **29** Ephedrine (Ma Huang): A Decongestant and Vasopressor 311

The Actions of Ephedrine 311
History 311
Ephedra 312
Ephedrine 312
Pharmacological Properties of Ephedrine 313
Effect on Organ Systems 313
Cardiovascular 313
Bronchi 314
Eye 314
Other Smooth Muscle 314
Glands 314
Central Nervous System 315
Skeletal Muscle 315
Routes of Administration 315
Absorption, Fate, and Excretion 315
Therapeutic Uses of Ephedrine 315
Bronchial Asthma 315
Allergic Disorders 316
Spinal Anesthesia 316
Heart Block 316
Mydriasis 316
Enuresis 317
Myasthenia Gravis 317
Miscellaneous Actions of Ephedrine 317
Signs and Symptoms of Ephedrine Toxicity 317

Chapter **30** Ergot, Its Alkaloids, and Headache 319

Introduction 319
Ergot and the Ergot Alkaloids 319
Source 319
Constituents of Ergot 319

History 320
Chemistry 321
The Efficacy of Ergotamine in Headache 321
Introduction 322
Classification of Headaches 323
Precipitating Factors of Headache Symptoms 323
Migraine: The Involvement of Serotonin and the Effectiveness of Sumatriptan in Migraine Headache 324
Metabolism of Serotonin 324
Actions of Serotonin 324
Serotonergic Abnormalities 325
Other Hypotheses 325
Serotonin Receptors and Their Subtypes 325
Serotonin Receptor Antagonists 325
Clinical Efficacy of Sumatriptan 325
Side Effects of Sumatriptan 326
Mechanisms of Antimigraine Action of Sumatriptan 326
Prevention and Treatment of Migraine 326
Methysergide 326
Calcium and Calcium-Channel Blockers 328
Calcium Antagonists 328
Other Preventative Agents 328
Cranial Neuralgias 328
Trigeminal and Glossopharyngeal Neuralgias 328
Ergoloid Mesylates (Dihydrogenated Ergot Alkaloids; Dihydroergotoxine) 329

Chapter 31 Flavonoids 331

Introduction 331
The Pharmacodynamics of Flavonoids 332
Protein Kinase C Inhibition 332
Phospholipase A_2 Inhibition 333
Na^+- and K^+-ATPase Inhibition 333
Lipoxygenase and Cyclooxygenase Inhibition 333
Cyclic Nucleotide Phosphodiesterase Inhibition 333
Reverse Transcriptase Inhibition 333
HIV-1 Proteinase Inhibition 334
Omithine Decarboxylase Inhibition 334
Topoisomerase Inhibition 334
Xanthine Oxidase Inhibition 334
Aromatase Inhibition 334
Aldose Reductase Inhibition 335
FAD-Containing Monoamine Oxidase Inhibition 335
Carbonyl Reductase Inhibition (Aldo-Keto-Reductase Family of Enzymes) 335
Hyaluronidase Inhibition 335
Histidine Decarboxylase and DOPA Decarboxylase Inhibition 335
Aldehyde and Alcohol Dehydrogenase Inhibition 335
RNA and DNA Polymerase Inhibition 336
Human DNA Ligase I Inhibition 336
Sialidase Inhibition 337
Antioxidant Properties of Flavonoids 337

Mutagenicity and Genotoxicity of Excessive Flavonoid Intake 337
Characteristics and Content of Flavonoids in Common Foods 338
Safe Flavonoid Intake 339

Chapter 32 Flaxseed 341

Chapter 33 Folate in Fruit 343

Introduction 343
Functions of Vitamin B_{12} 343
Bioavailability of Vitamin B_{12} 343
Food Sources of Vitamin B_{12} for Elderly People 344
Factors Contributing to Declining Vitamin B_{12} Status with Aging 344
Prevalence of Vitamin B_{12} Deficiency in Elderly People 344
Effects of Deficiency 344
Neurological Effects of Deficiency 344
Hematological Effects of Deficiency 344
Gastrointestinal Effects of Deficiency 344
Indicators of Hematological Status 344
Replacement Therapy 345
Function of Folic Acid in Gestation 345
Function in Cardiovascular Disease 345
Antioxidant Vitamins 345
Vitamin B_{12}, Folic Acid, and the Treatment of Megaloblastic Anemias 346
Relationships between Vitamin B_{12} and Folic Acid 346

Chapter 34 Food–Drug Interactions 347

Introduction 347
Biotransformation 347
Hepatic Drug Metabolism 347
Nonhepatic Metabolism 347
Plasma 347
Lung 348
Intestinal Epithelium 348
Molecular Biology of Multiple Isoenzymes of P-450 348
Scheme of the Mixed-Function Oxidation Reaction Pathway 348
Consequence of Biotransformation Reactions 349
Precursor Activation 349
Metabolic Activation of Drugs 349
Conversion to Metabolites with Dissimilar Actions 349
Conversion to More Active Products 350
Lethal Synthesis 350
Drug Metabolite Kinetics 350
Factors That Modify the Metabolism of Drugs 350
Pharmacogenetics 350
Liver Disease 351
The Influence of Age 351
Enzyme Induction and Inhibition 351
Clinical Implications of Enzyme Induction and Inhibition 351
Grapefruit Juice Action on Intestinal Cytochrome P-450 (CYP) Enzymes 352

Chapter 35 Foxglove. Cardiac Glycosides, and Congestive Heart Failure 355

Digitalis 355
The Digitalis Series 355
Chemistry 356
Cardiac Glycosides in the Treatment of Congestive Heart Failure 358
Biochemical Basis of Myocardial Contraction 359
The Positive Inotropic Action of Cardiac Glycosides 360
The Modes of Action of Cardiac Glycosides 360
Electrophysiological Effects of Cardiac Glycosides 360
Digitalis Toxicity 361
Symptoms of Digitalis Toxicity 361
Cardiac Effects 361
Gastrointestinal Effects 362
Visual Effects 362
Neuropsychiatric Symptoms 362
Treatment of Digitalis Toxicity 362
General Treatment 362
Specific Treatment 362
Antidigoxin Antibodies 362
Drugs Acting on Peripheral Dopamine Receptors 362
Dopamine Receptors 362
Drugs Inhibiting Phosphodiesterase 363
Vasodilators and Angiotensin Antagonists 363
Receptor-Dependent Vasodilation 364
Endothelium-Dependent vs. Independent Vasodilators 364

Chapter 36 *Ginkgo biloba* 367

Introduction 367
Ginkgo biloba Extract and Inhibition of Monoamine Oxidase A and B in Living Human Brain 367
Ginkgo biloba and Nitric Oxide 368

Chapter 37 Ginseng and Cholinergic Transmission 371

Introduction 371
Cholinergic Transmission 372
Division and Functions of the Autonomic Nervous System 372
Neurochemical Basis of Cholinergic Transmission 373
Classification of Cholinergic Receptors 373
Cholinergic (Cholinomimetic) Receptor Agonists 374
Anticholinesterase Agents 374
Structure of Acetylcholinesterase 374
Classification of Cholinesterase Inhibitors 374
Antidote to Irreversible Cholinesterase Inhibitors 375
Cholinergic Receptor Blocking Agents 375
Dose-Dependent Effects of Atropine 376
Synthetic Muscarinic Receptor Antagonists 376
Ophthalmology 376
Preoperative Uses 376
Cardiology 376

Gastroenterology....376
Neurology....377
Contraindication to Anticholinergic Agents....377
Other CNS Actions of Ginseng....377
Antineoplastic and Immunomodulatory Effects of Ginseng....377

Chapter 38 Green, White, and Black Teas....379

Introduction....379
Antioxidant Properties....379
The Efficacy of Tea in Attenuating Skin Cancer....380
Anticariogenic Effects of Tea....381
Pathogenesis of Dental Caries....381
Potential Anticariogenic Actions of Tea....381
Benefits of White Tea....381

Chapter 39 Herbal Plants and Tuberculosis....383

Antituberculosis Efficacy of Natural Products....383
Mycobacterial Diseases....384
Tuberculosis....384
Leprosy....384
Other Diseases....385
Antimicrobial Activity of Plants....385

Chapter 40 Herbal Products for the Chemotherapy of Human Immunodeficiency Virus Infection....387

Introduction....387
Herbal Products Used in HIV Therapy....387
Etiological Agent....388
Life Cycle of HIV....388
Immunopharmacology....390
Immune System Components....390
Cyanovirin-N....391
Sulfated Polysaccharides....392
Ingenol Derivatives....392
Flavonoids....392
Glycyrrhizin....393
Mannose-Specific Plant Lectins....393
Siamycins....393
Betulinic Acids....393
Polyphemusins....394
Baicalin....394
Avarol, Avarone, Psychotrine, and Phloroglucinol Derivatives (i.e., Mallotojaponin)....394
Calanolides and Inophyllums....395
Illimaquinone....395
Curcumin, Curcumin Analogs, Dicaffeoylquinic Acid, and L-Chicoric Acid....395
Equisetin....396
Melittin....396
Trichosantin, MAP30, GAP31, DAP31, and DAP32....396

Bellenamine....396
Hypericin and Pseudohypericin....397

Chapter 41 Honey: The Nectar of Life....399

Introduction....399
Wonder of Honey....399
Curative Properties of Honey....400
Common Kinds of Honey....400
Honey: An Antioxidant....403
Honey Enhances Memory Formation....403
Neurochemical Basis of Cholinergic Transmission....403
Classification of Cholinergic Receptors....403
Honey and the Treatment of Wounds and Bums....404
Honey for the Treatment of Peptic Ulcers....405
Honey for the Treatment of Gastroenteritis....405
Honey in Inflammatory Bowel Disease....406
Honey Protects against Carcinogenesis....406
Honey in the Treatment of Herpes Simplex Lesions....407
Treatment of Bullous Keratopathy with Honey....407

Chapter 42 Horseradish and Antiplatelet Actions....409

Introduction....409
Antiplatelet Drugs....409
Aspirin....409
Dipyridamole....4 1
Ticlopidine....1 1
Therapeutic Uses of Anticoagulant. Thrombolytic. and Antiplatelet Drugs....412
Venous Thromboembolism....412
Myocardial Infarction....412
Unstable Angina....412
Saphenous Vein Bypass Grafts....412
Percutaneous Transluminal Coronary Angioplasty....412
Atrial Fibrillation....412
Prosthetic Heart Valves....412
Valvular Heart Disease....413
Cerebrovascular Disease....413
Peripheral Vascular Disease....413
Primary Prevention of Arterial Thromboembolism....413

Chapter 43 Hypericum (St. John's Wort) and Depression....415

Introduction....415
St. John's Wort....416
Botanical Name....416
Family....416
Synonyms....416
Common Names....416
Commercial Products....416
Active Ingredients....416

Hypericum (St. John's Wort) in Folk Medicine and Traditional Systems of Medicine.....417
Antidepressants.....417
Neurotransmitters and Their Role in Depression.....419
Classification of Antidepressants.....419
Dibenzapine Derivatives.....419
Conversion to Pharmacologically Active Metabolites.....420
Various Properties of the Tricyclic Antidepressants.....420
The Sites of Action of Antidepressants.....420
Side Effects of Antidepressants.....422
Therapeutic Indications.....422
Fatal Overdoses.....423
Monoamine Oxidase Inhibitors.....424
Indications for Monoamine Oxidase Inhibitors.....424
Newer, Novel, or Atypical Antidepressants.....424
Control of Manic Episodes in Manic-Depressive Psychosis Using Lithium.....425
Pharmacokinetics.....425
Side Effects.....425
Pharmacodynamics of Lithium.....426
Therapeutic Uses of Lithium.....426
Regulatory Status of Hypericum.....426

Chapter 44 Ipecac.....427

Ipecacuanha and Emetine.....427
Ipecac.....427
History.....427
Active Principles.....427
Status and Use.....427
Drugs That Produce Vomiting (Emetics).....429
Source, Nature, and Preparations.....429
Nature of Emetic Action of Ipecac.....430
Clinical Effects.....431
Prevention of Further Absorption of Poison.....431
Emesis.....431
Syrup of Ipecac.....432
Monitoring.....432
Amebiasis.....433
Treatment of the Asymptomatic Camer.....433
Treatment of Acute Amebic Dysentery.....433
Treatment of Amebic Hepatitis and Abscess.....433

Chapter 45 Manuka and Fungal Disease.....435

Tea Tree Oils from Australia and New Zealand.....435
Fungal Diseases.....436
Antifungal Agents.....436
Systemic Antifungal Agents.....436
Amphotericin B.....436
Pharmacodynamics.....437
Pharmacokinetics and Proper Usage.....437
Flucytosine.....438

Ketoconazole 438
Fluconazole 438
Griseofulvin 438
Nystatin 439
Topical Antifungal Agents 439
Clotrimazole 439
Econazole 439
Miconazole 439
Terconazole and Butoconazole 439
Ciclopirox Olamine 440
Haloprogin 440
Tolnaftate 440
Naftifine 440
Undecylenic Acid 440
Benzoic Acid and Salicylic Acid 440
Aromatherapy Cautions 440

Chapter 46 Marine Therapeutics 441

Chapter 47 Morphine: *Papaver somniferum* 445

Introduction 445
Opioid Analgesics in History 445
Friedrich Wilhelm Adam Sertürner and Opium 446
Opium 446
Cultivation, Collection, and Commerce 447
Morphine and Other Narcotic Analgesics 448
Multiple Medications to Treat Painful Conditions 448
Endogenous Opioid Peptides 449
Opioid Receptors 449
The Evidence for Multiple Opioid Receptors 449
Distribution of Opioid Receptors 450
Proposed Functions of the Opioid Receptor Subtypes 450
Morphine and Related Compounds 452
Morphine: A Naturally Occurring Analgesic 452
Effects on the Central Nervous System 452
Analgesic Effects 455
Therapeutic Uses of Morphine 456
Sedation and Sleep 458
Side Effects of Morphine 459
Morphine-Induced Addiction 460
Withdrawal Symptoms 462
Antidiarrheal Effects 463
Oliguric Effect 463
Morphine-Induced Tolerance 464
Natural Opium Alkaloids 464
Codeine 464
Papaverine 464
Noscapine 465
Synthetic Derivatives of the Opium Alkaloids 465
Heroin (Diamorphine) 465

Dihydrocodeinone....466
Dihydromorphinone....466
Dextromethorphan Hydrobromide....466
Levorphanol Tartrate....467
Ethylmorphine....467
Apomorphine....467
Symptoms....467
Nonopiate Addicting Analgesics....468
Meperidine (Pethidine)....468
Action....468
Undesirable Side Effects....469
Metabolism....469
Therapeutic Use....469
Methadone....469
Action....470
Mechanism of Action....470
Therapeutic Uses....470
Alphaprodine Hydrochloride....470
Anileridine....471
Phenazocine....471
Piminodine Ethanesulfonate....471
Dextropropoxyphene....471
Opioids with Mixed Actions: Agonists–Antagonists and Partial Agonists....472
Opioid Receptor Antagonists....472
Antitussive Preparations....472

Chapter 48 Oats (**Avena** *sativa* L.) and Their Antioxidant Activity....473

Introduction....473

Chapter 49 Olives and Olive Oil....475

Chapter 50 Onion and Garlic....477

Introduction....477
Active Ingredients in Onion and Garlic....477
Inhibition of Platelet Aggregation by Onion and Garlic....478
Anticoagulants and Thrombolytic Agents....478
Aggregin and Platelet Aggregation....478
Vitamin E and Platelet Aggregation....479
Platelet-Activating Factor....479
Platelet-Inhibiting Drugs....479
Eicosanoids....479
Pharmacokinetic Properties of the Eicosanoids....479
Physiology of the Eicosanoids....479
The Pharmacodynamics of Eicosanoids....480
The Therapeutic Uses of Eicosanoids....481
Agents That Alter Metabolism of Eicosanoids....481
Effect of Garlic and Onions on Eicosanoid Metabolism....482
Cardiovascular and Lipid-Lowering Effects of Garlic....482
Garlic and Cancer Prevention....483

Anticlastogenic Effects of Garlic and Onion 483
Antimicrobial Effects of Garlic and Onion 483
The Antioxidant Actions and Other Therapeutic Effects of Garlic 484
Cardioprotective Actions of Wild Garlic ***(Allium ursinum)*** in Ischemia and Reperfusion 484
ACE Inhibitors 484
Myocardial Infarction 485
Progressive Renal Impairment 485
Scleroderma Renal Crisis 486
Antioxidant Activity of Allicin, an Active Principle in Garlic 486
Attenuation of Ischemic Brain Damage by Aged Garlic Extracts 487
Inhibition of Free-Radical Generation and Augmentation of Antioxidant Enzyme Activity in Vascular Endothelial Cells by Garlic 488
Attenuation of Renal Oxidative Stress with Garlic Oil 489
Amelioration of Hyperlipidemia in Chronic Aminonucleoside Nephrosis by Garlic 490
Amelioration of Gentamicin Nephrotoxicity by Garlic: Relation to Antioxidant Enzymes 491

Chapter 51 Immunoenhancing Actions of Plantain 493

Introduction 493
Immunopharmacology 494
Therapies That Enhance or Suppress the Immune System 494
Radioimmunotherapy 494
Cell Transfer Therapy and Cancer 494
Immunosuppressive Agents 494
Corticosteroids 496
Cytotoxic Compounds as Alkylating Agents 496
Antimetabolites 497
Cyclosporin A and Dihydrocyclosporin C 497
Antilymphocyte Globulin 497
Rho (D) Immune Globulin 497
Immunomodulating Agents 498
Summary 498

Chapter 52 Plants and Diabetes 499

Introduction 499
Antidiabetic Agents 499
Effects of Food on Insulin Release 500
Effects of Fasting on Insulin Release 500
Metabolic Consequences of Diabetes Mellitus 500
Diabetes Mellitus and Pregnancy 501
Classes of Diabetes Mellitus 502
Signs and Symptoms of Diabetes 502
Complications of Diabetes 502
Vascular Complications 502
Neuropathy 502
The Insulin Receptor 502
Structure and Function 502
Termination of Insulin Signal 503
Clinical Syndromes Associated with Cellular Defects in Insulin Receptor 503

Treatment of Diabetes Mellitus 503
Dietary Treatment 503
Drug Treatment 504
Insulin 504
Oral Hypoglycemic Agents 505
Receptors for Sulfonylurea and Their Mechanism of Action 506
Treatment of Diabetic Ketoacidosis 506

Chapter 53 Pomegranate 507

Chapter 54 Pycnogenol 509

Introduction 509
Antioxidant Activity of Pycnogenol 509
Vasorelaxant Activity 510
Inhibition of Platelet Aggregation 510
Enhancement of Microcirculation 510
Inhibition of Elastase Activity 511
Regulation of Inflammatory Response 511
Modulation of Macrophage Activity 511
Summary 511

Chapter 55 *Pygeum africanum* and Permixon for the Treatment of Patients with Benign Prostatic Hyperplasia 513

Introduction 513
Urinary Symptoms and Flow Measures 514
Permixon in the Treatment of Symptomatic Benign Prostatic Hyperplasia 514

Chapter 56 Reserpine 515

Introduction 515
The *Rauwolfia* Alkaloids 515
Chemistry 515
Pharmacology 516
Mechanism of Action 517
Prevention of the Storage of Norepinephrine by Reserpine 518
Neurochemical Basis of Adrenergic Transmission 518
Catecholamine Metabolism 519
Adrenergic Neuronal-Blocking Drugs 519
Side Effects 519

Chapter 57 Rhubarb 521

Introduction 521
Rhubarb and Its Laxative Properties 521
Constipation 522
Laxatives and Cathartics 523
Irritants 523
Bulk Saline Laxatives 523
Lubricants 523

Other Uses of Laxatives....524
Antioxidant Properties of Rhubarb....524

Chapter 58 Saffron....525

Introduction....525
Antioxidant Effect of Saffron....525
Effect of Saffron on Learning and Memory....525
Possible Molecular Target of Crocin....526

Chapter 59 Salicylate....529

Introduction....529
Source....529
Official Salicylates Used in the Early 20th Century....529
Analgesics–Antipyretics and Anti-Inflammatory Agents....530
Mechanism of Action of Aspirin....531
Aspirin and Its Uses....531
Aspirin-Induced Analgesia....531
Aspirin-Induced Antipyresis....532
Uricosuric Effects of Aspirin....532
Anti-Inflammatory Effects of Aspirin....532
Aspirin and Cardiovascular Disease....532
Aspirin and the Premenstrual Syndrome....532
Side Effects of Aspirin....532
Effects of Salicylate on Respiration....532
Treatment of Aspirin Poisoning....533
The Gastrointestinal Effect of Aspirin....533
The Hematopoietic Effect of Aspirin....533
New Uses of Aspirin....533
Salicylate Protects against MPTP-Induced Parkinsonism....534
Health Effects of Salicylates in Foods....535
Aspirin-Induced Asthma....535
Aspirin and Other Natural Inhibitors of Tumor Necrosis Factor-a Production, Secretion, and Function....540
Inhibition of TNF Production and Secretion....540
Inhibitors of TNF-Mediated Cytotoxicity....542

Chapter 60 Sex Herbs....545

Introduction....545
Impotence....545
Normal Sexual Function....546
Failure of Erection....547
Therapy....547
Drugs That Stimulate Sexual Behavior....549
Levodopa....549
Amyl Nitrite....549
Vitamin E....550
Sildenafil (Viagra)....550
Emerging Pharmacological Therapies for Erectile Dysfunction....550

Chapter 61 Sponges and Steroids 553

Introduction 553
Examples of Steroids Found in Sponges 553
Polyoxygenated Steroids 553
Steroid Sulfates 553
Steroids with Unconventional Side Chains 554
Adrenal Steroids 554
The Synthesis of Cholesterol 555
Classification of Adrenal Steroids 555
The Glucocorticoids 555
The Mineralocorticoids 556
The Sex Hormones 557
Regulation of Adrenal Steroid Biosynthesis 557
Adrenocorticotropic Hormones 558
Actions and Pharmacological Applications of Glucocorticoids 558
Central Nervous System Effects 559
Calcium Metabolism 560
Contraindications to Glucocorticoid Therapy 561
Adrenal Disorders — Cushing's Syndrome 561
Reproductive Pharmacology 561
Steroid Hormones 561
Receptors 561
Receptor Antagonists 561
Estrogens 562
Progesterone 564
Antifertility Agents 566
Androgens 566

Chapter 62 Taxol (Paclitaxel) and Cancer Chemotherapy 571

Introduction 571
Chemical Groups of Natural Products with Anticancer Properties 571
Cancer Chemotherapy 574
Alkylating Agents 575
Nitrogen Mustards 575
Chlorambucil 576
Cyclophosphamide 576
Alkyl Sulfonate 576
Nitrosoureas 576
Triazenes 576
Antimetabolites 576
Folic Acid Analogues 576
Pyrimidine Analogs 577
Deoxycytidine Analogs 578
Purine Antimetabolites 578
Natural Products 579
Vinca Alkaloids 579
Dactinomycin 579
Mithramycin 579
Daunorubicin and Doxorubicin 580

Bleomycin 580
Paclitaxel and Docetaxel 580
Miscellaneous Antineoplastic Agents 581
Asparaginase 581
Hydroxyurea 581
Cis-Platinum 581
Carboplatin 581
Procarbazine 581
Etoposide 582
Cancer Chemotherapy-Induced Emesis 582

Chapter 63 Tomatoes and Medicine 583

Lycopene and Prostate Cancer 583
History of Carotenoids 584
Physicochemical Nature of Carotenoids 584
Lycopene: An Important Carotenoid in Tumor Suppression 584
Carotenoid Content of Fruits and Vegetables 584
Distribution of Lycopene in Humans 585
Concentrations of Carotenoids in Human Organs 585
Tomatoes. Lycopene. and Cancer Risk 587
Lung and Pleural Cancers 587
Quenching of Reactive Oxygen by Lycopene 588

Chapter 64 Ulcer Therapy with Herbal Medicine 591

Introduction 591
Acid-Pepsin Disease 591
Pathogenesis of Peptic Ulcer 591
Physiology of Gastric Acid Secretion 591
Drug Therapy 592
Antacids 592
Anticholinergic Drugs 592
Histamine-Receptor Antagonists 593
Inhibitors of H^+K^+-ATPase 593
Active Herbal Products with Antiulcer Activity 593
Flavonoids 593
Quercetin 594
Naringin 595
Anthocyanosides 595
Sophoradin Derivatives 595
Saponins 595
Tannins 596
Gums and Mucilages 597
Herbal Drugs with Antiulcer Activity 597
Licorice 597
Aloe Gel 598
Capsicum (Chili) 598

Chapter 65 Valerian 599

Introduction 599
Valerian in the Management of Insomnia 599
The Use of Valerian in Folk Medicine and Traditional Systems of Medicine 600
Valerian 600
γ-Aminobutyric Acid 600
Basic Mechanisms of Epilepsy 601
The Anxiolytic Agents 602
Pharmacodynamics of Benzodiazepines 602
GABA Receptors 603
Benzodiazepine-Binding Sites 603
Mode of Action of Benzodiazepine Derivatives 604
Antianxiety Effects 604
Muscle Relaxant Activity 604
Sedative Effects 605
Anticonvulsant Activity 605
Mode of Actions of the General Anesthetics 605
Glycine 606
Sedatives and Hypnotics 606
The Barbiturates 606
Classification 606
Pharmacokinetics 607
Acute Toxicity 607
Addiction 608
Selection of Drugs 608
Nonbarbiturate Sedatives and Hypnotics — Benzodiazepine Derivatives 608
Regulatory Status 609

Chapter 66 Vitamins and Diet 611

Introduction 611
Nutritional Actions of Vitamins 611
Part One: Fat-Soluble Vitamins 611
Vitamin A 611
Retinols 611
Beta Carotene 611
Vitamin K 613
Vitamin K Derivatives 613
Vitamin D (Calciferol) 613
Vitamin E (Tocopherols) 614
Part Two: Water-Soluble Vitamins 614
Biotin 614
Folate (Folic Acid, Folacin) 614
Niacin (Vitamin B_3, Nicotinic Acid, Nicotinamide) 614
Pantothenic Acid (Vitamin B_5) 615
Riboflavin (Vitamin B_2) 615
Thiamine (Vitamin B_1) 615
Vitamin B_6 (Pyridoxine, Pyridoxamine, Pyridoxal) 615
Vitamin B_{12} (Cobalamins) 615
Vitamin C (Ascorbic Acid) 615
The Importance of Vitamin A in Human Nutrition 616
Dietary Sources of Vitamin A 616

Action of Vitamin A 617
Vitamin A and Carcinogenesis 617
Vitamin A and Immune Function 617
Symptoms of Deficiency 618
Eye 619
Bronchorespiratory Tract 619
Skin 619
Genitourinary System 619
Gastrointestinal Tract 619
Sweat Glands 619
Bone 619
Miscellaneous 619
Therapeutic Uses 620
Vitamin A Deficiency Diseases 620
Dermatological Diseases 620
Cancer and Other Uses 620
Excessive Vitamin A Intake (Hypervitaminosis A) 620
Vitamin A (Retinol) (Aquasol A) 621
Aging and Diet 621
Basic Dietary Recommendations 621
Antioxidants, Protective Plant Chemicals, Preventing Diseases 621
Essential Trace Minerals 622
Foods That Help 623
Apples 623
Apricots 623
Artichokes 624
Asparagus 624
Avocados 624
Bananas 624
Beans 624
Bean Sprouts 624
Beef and Veal 624
Beer 624
Beets 624
Bioflavonoids 624
Blackberries 625
Blueberries 625
Bread 625
Brussels Sprouts 625
Buckwheat 625
Butter and Margarine 625
Cabbage 625
Caffeine 625
Cakes, Cookies, and Pastries 626
Carrots 626
Cauliflower 626
Celeriac 626
Celery 626
Cereals 626
Cheese 626
Cherries 627

Chestnuts 627
Chilies 627
Chocolate and Candy 627
Coconuts 627
Coffee 627
Corn 627
Cranberries 627
Cucumbers 628
Currants 628
Dates 628
Eggplants 628
Eggs 628
Fennel 628
Fiber 628
Figs 628
Fruits 628
Fish 629
Flours 629
Garlic 629
Ginger 629
Gooseberries 629
Grains 629
Grapefruit 629
Grapes 629
Guavas 630
Honey 630
Ice Cream 630
Kale 630
Kiwi Fruits 630
Kohlrabi 630
Lamb 630
Leeks 630
Legumes 6 1
Lemons 6 1
Limes 631
Malted Milk, Malt Extracts 631
Mangoes 631
Mayonnaise 631
Melons 631
Milk and Milk Products 632
Mushrooms and Truffles 632
Nectarines 632
Nuts and Seeds 632
Oils 632
Okra 632
Olives 633
Onions 633
Oranges 633
Organ Meats 633
Papayas 633
Parsnips 633

Pasta....633
Peaches....633
Pears....634
Peas and Pea Pods....634
Peppers....634
Pickles and Other Condiments....634
Pineapples....634
Plums....634
Pork....634
Poultry....634
Prunes....635
Pumpkins....635
Quinces....635
Quinoa....635
Radishes....635
Raspberries....635
Rhubarb....635
Rice....636
Salad Dressings....636
Salt and Sodium....636
Sauces and Gravies....636
Seaweed....636
Shellfish....636
Smoked, Cured, and Pickled Meats....637
Snacks and Dips....637
Soft Drinks....637
Soups....637
Spinach....637
Squash....638
Strawberries....638
Tangerines....638
Tea....638
Tomatoes....638
Turnips....638
Vinegar....639
Watercress....639
Wine....639
Yams and Sweet Potatoes....639
Yogurt....639
Zucchini....639
Zwieback....639

Chapter 67 Wheat Germ....641

Introduction....641
Mitochondrial Dysfunction in Neurodegeneration....642
Toxin Models of Parkinson's Disease....644
Toxin Models of Huntington's Disease....644
Alzheimer's Disease....644

Increase in Brain Mitochondrial Concentrations and Exertion of Neuroprotective Effects by Coenzyme Q_{10} 645
Neuroprotective and Neurorestorative Strategies for Parkinson's Disease 645
Efficacy of Coenzyme Q_{10} in Parkinson's Disease 645
The Neuroprotective Role of Vitamin E 646

Chapter 68 Wine 647

Introduction 647
Effects of Red Wine 647
Alcohol 647
The Pharmacology of Alcohol 649
Effects of Ethyl Alcohol 649
Central Nervous System 649
Acute Intake of Alcohol 649
Cardiovascular System 649
Gastrointestinal Effects 649
Liver 650
Endocrine Glands 650
Fetal Alcohol Syndrome 651
Pharmacokinetics of Ethanol 651
Poisoning and Toxicity 652
Acute Poisoning 652
Delirium Tremens 652
Chronic Toxicity 652
Treatment of Alcoholism 652
Disulfiram: An Alcohol Sensitizing Agent 653

Chapter 69 Yogurt and the Immune System 655

Introduction 655
Immune System Functions 655
In *Vitro* Indexes of Immune Function 656
Phagocytic Activity 656
Lymphocyte Proliferation Assay 656
Cytokine Production 657
Yogurt Components with Potential Immunostimulatory Effects 658

Specific References 661

General References 669

Index 673