

# Contents

Preface to the Third Edition .....	xv
Preface to the Second Edition.....	xvii
Preface to the First Edition .....	xviii
Acknowledgments.....	xix
About the Author .....	xx
Glossary of Terms.....	xxi

## Part I

### Basics of Toxicology Related to Food

#### Chapter 1

Introduction to Food Toxicology .....	3
1.1 Introduction.....	3
1.1.1 What Is Toxicology? .....	3
1.2 Food and Environmental Toxicology.....	5
1.3 Short History of Toxicology.....	7
1.4 Toxicity, Dose, and Response.....	9
1.5 Integrated Effect of Toxic Substances.....	16
1.6 Classification of Toxicants .....	17
1.7 Some Principles of Cell Biology and Biochemistry.....	17
1.7.1 Structure of Cell Membranes.....	17
1.7.2 Transport of Substances through Biomembranes .....	19
1.7.3 Cell Receptors.....	21
1.7.4 Ion Channels .....	23
References.....	24

#### Chapter 2

Pathways and Reactions of Xenobiotics in Organisms.....	26
2.1 Entry and Absorption of Foreign Substances .....	26
2.1.1 Digestive Tract.....	27
2.1.2 Respiratory Tract .....	29
2.1.3 Skin .....	29
2.2 Distribution of Xenobiotics in the Organism.....	30
2.2.1 Blood Supply and Membrane Barriers .....	30
2.2.2 Role of Lymph in Absorption and Distribution of Xenobiotics.....	33
2.2.3 Binding of Xenobiotics to Transport Proteins .....	33
2.2.4 Bioaccumulation of Xenobiotics .....	34

2.3	Metabolism of Xenobiotics .....	35
2.3.1	General Principles.....	35
2.3.2	Phase I Reactions .....	37
2.3.3	Phase II Reactions.....	43
2.3.4	Induction and Inhibition of Metabolic Enzymes .....	47
2.3.5	Role of Enteric Microflora in the Metabolism of Xenobiotics .....	50
2.3.6	Influence of Diet on Metabolism .....	51
2.4	Elimination of Xenobiotics and Their Metabolites from the Organism .....	52
2.4.1	Kidneys .....	53
2.4.2	Liver: Enterohepatic (Re)circulation.....	54
2.4.3	Intestines .....	55
2.4.4	Lungs .....	55
2.5	Biomagnification .....	56
2.6	Antidotes .....	57
2.6.1	General Methods.....	57
2.6.2	Specific Methods.....	58
	References.....	59
 Chapter 3		
	Toxic Response .....	62
3.1	Variability in Toxic Response .....	62
3.2	Physiological Classification of Toxic Responses.....	63
3.2.1	General Principles.....	63
3.2.2	Direct Injury to a Cell or Tissue .....	65
3.2.3	Biochemical Damage .....	66
3.2.4	Neurotoxicity .....	68
3.2.5	Immunotoxicity.....	69
3.2.6	Teratogenicity.....	71
3.2.7	Genotoxicity and Mutagenicity.....	73
3.2.8	Carcinogenicity .....	75
3.2.9	Reproductive and Developmental Toxicity .....	82
3.2.10	Multiorgan Toxicity .....	84
3.3	Molecular Mechanisms of Toxicity.....	85
3.3.1	Disturbance of Cell Homeostasis.....	85
3.3.2	Receptor-Mediated Mechanisms .....	86
3.3.3	Other Toxic Effects Mediated by Cell Membranes .....	88
3.3.4	Alteration of Cell Energetics.....	89
3.3.5	Covalent Binding to Important Cell Macromolecules.....	90
3.3.6	Endocrine Disruption.....	91
3.3.7	Oxidative Stress as an Important Part of Mechanism of Various Toxic Effects.....	95

3.3.8	Inhibition of DNA Repair .....	97
3.3.9	Multiple Organ Effects .....	97
3.4	Biomarkers of Toxic Effects.....	98
	References.....	100
Chapter 4		
	Analytical Toxicology: Determination of Xenobiotics.....	105
4.1	General.....	105
4.2	Hyphenated Chromatographic and Spectrophotometric Methods.....	106
4.3	Immunological Methods for Sample Preparation and Analysis .....	110
4.3.1	Immunoaffinity Columns.....	110
4.3.2	Enzyme-Linked Immunosorbent Assay (ELISA) .....	110
	References.....	110
Chapter 5		
	Evaluation of Toxicity of Substances.....	112
5.1	Epidemiological Studies.....	112
5.1.1	Experimental Studies.....	114
5.2	Animal Tests .....	116
5.2.1	General Principles.....	116
5.2.2	Organism-Depending Factors Influencing the Compound Toxicity.....	120
5.3	Cell Culture Tests.....	125
5.4	Computer Calculations.....	128
5.5	Acute Toxicity Tests .....	128
5.6	Subacute/Subchronic Toxicity Tests.....	130
5.7	Chronic Toxicity Tests: ADI and TDI.....	131
5.8	Specific Toxicity Tests.....	132
	References.....	133
Chapter 6		
	Toxicological Safety and Risk Analysis .....	136
6.1	Toxicological Safety .....	136
6.2	Risk Assessment.....	137
6.2.1	Hazard Identification.....	139
6.2.2	Demonstration of a Dose-Response Relationship.....	140
6.2.3	Assessment of Exposure .....	142
6.2.4	Risk Characterization .....	142
6.3	Risk-Benefit Analysis .....	145
	References.....	147

**Part II****Main Groups of Food Toxicants****Chapter 7**

Endogenous Plant Toxicants .....	151
7.1 Lectins or Hemagglutinins.....	151
7.2 Enzyme Inhibitors.....	153
7.3 Alkaloids .....	154
7.3.1 Pyrrolizidine Alkaloids .....	155
7.3.2 Solanine Group Glycoalkaloids .....	157
7.3.3 Xanthine Alkaloids.....	159
7.3.4 Ephedrine Alkaloids .....	161
7.3.5 Vicine and Convicine – Favism .....	162
7.4 Cyanogenic Glucosides: Toxicity Mechanism of HCN .....	164
7.5 Phytoestrogens .....	167
7.6 Glucosinolates and Bioactive Metabolites .....	168
7.7 Coumarin .....	170
7.8 Cucurbitacins .....	171
7.9 Thujones.....	172
7.10 Toxic Amino Acids .....	173
7.11 Erucic Acids.....	175
7.12 Oxalates.....	175
7.13 Fluoroacetates .....	177
7.14 Bracken Toxins.....	178
7.15 Saponins.....	179
7.16 Grayanotoxins .....	181
7.17 Soybean as a Potential Source of Various Toxicants .....	182
7.18 Plant-Based Meat Alternatives.....	183
7.19 Mushroom Toxins .....	184
7.19.1 General Principles.....	184
7.19.2 Amatoxins.....	185
7.19.3 Muscarine .....	187
7.19.4 Isoxazoles .....	188
7.19.5 Other Mushroom Toxins .....	189
References.....	191
<b>Chapter 8</b>	
Geochemical Elements That Plants Absorb from Soil and Water.....	197
8.1 Arsenic .....	197
8.2 Selenium.....	200
8.3 Fluorine .....	203
References.....	205

## Chapter 9

Environmental Pollutants.....	207
9.1 Toxic Chemical Elements.....	207
9.1.1 Mercury .....	207
9.1.2 Lead .....	210
9.1.3 Cadmium .....	212
9.1.4 Chromium .....	214
9.1.5 Copper .....	215
9.1.6 Nickel.....	216
9.1.7 Iron .....	216
9.2 Polychlorinated Biphenyls (PCBs).....	217
9.3 Polychlorinated Dibenzodioxins and Dibenzofurans .....	220
9.4 Emerging Contaminants .....	225
9.4.1 PFAS, PFOA, and PFOS: Flame Retardants .....	225
9.4.2 Micro- and Nanoplastics in the Environment and Food.....	227
9.4.3 Drug Residues in the Environment.....	229
9.5 Transfer of Environmental Toxicants to Food through Animal Feeds.....	230
References.....	231

## Chapter 10

Mycotoxins.....	237
10.1 Overview .....	237
10.2 Aflatoxins .....	239
10.3 Ochratoxins.....	242
10.4 Sterigmatocystin .....	244
10.5 Zearalenone.....	244
10.6 Fumonisin.....	245
10.7 Trichothecenes .....	246
10.8 Patulin .....	248
10.9 Citrinin and Citreoviridin .....	249
10.10 Ergot Toxins .....	250
10.11 Other Mycotoxins.....	252
10.12 Combined Toxicity of Mycotoxins.....	252
References.....	253

## Chapter 11

Animal Endogenous Poisons .....	257
11.1 Prions .....	257
11.2 Lactose .....	259
11.3 Phytanic Acid.....	260
11.4 Avidin.....	261
References.....	261

Chapter 12	
Food Toxicants from Aquatic Animals.....	263
12.1 Introduction.....	263
12.2 Shellfish Toxicants .....	263
12.2.1 Paralytic Shellfish Poisoning .....	264
12.2.2 Diarrhetic Shellfish Poisoning .....	266
12.2.3 Neurotoxic Shellfish Poisoning.....	268
12.2.4 Amnesic Shellfish Poisoning .....	268
12.2.5 Microcystins and Nodularins.....	270
12.3 Fish Toxins .....	271
12.3.1 Tetrodotoxin .....	271
12.3.2 Ciguatoxin .....	273
References.....	275
Chapter 13	
Pesticide Residues.....	277
13.1 Overview: Insecticides .....	277
13.2 Herbicides.....	284
13.3 Fungicides .....	286
References.....	286
Chapter 14	
Veterinary Drugs and Feed Additives .....	289
14.1 Introduction.....	289
14.2 Antibiotics.....	290
14.3 Hormones .....	291
14.4 Other Veterinary Drugs .....	292
14.4.1 Coccidiostats.....	292
14.4.2 Anthelmintics.....	293
14.4.3 $\beta$ -Agonists .....	294
References.....	295
Chapter 15	
Toxicants Formed during Processing, Storage, and Digestion of Food.....	297
15.1 Introduction.....	297
15.2 Products of Maillard Reaction .....	298
15.3 Acrylamide.....	299
15.4 Polycyclic Aromatic Hydrocarbons .....	301
15.5 Heterocyclic Aromatic Amines.....	305
15.6 Oxidation Products of Polyunsaturated Fatty Acids.....	306
15.7 Alcohols .....	307

15.8	Bacterial Toxins .....	310
15.8.1	Exotoxins .....	311
15.8.2	Endotoxins .....	319
15.9	Biogenic Amines.....	321
15.9.1	Scombroid Poisoning .....	323
15.10	Nitrates, Nitrites, and Nitrosamines.....	325
15.11	Trans-Fatty Acids (TFAs) .....	328
15.12	Chlorinated Propanols .....	329
15.13	Food Contact Materials.....	330
15.13.1	Phthalates .....	330
15.13.2	Bisphenols .....	332
	References.....	333

## Chapter 16

	Food Additives.....	340
16.1	General Principles.....	340
16.2	Colorants: Azo-Dyes.....	343
16.3	Artificial Sweeteners.....	345
16.4	Preservatives .....	348
16.5	Antioxidants .....	348
16.6	Glutamates .....	349
	References.....	350

## Chapter 17

	Vitamins.....	353
17.1	General.....	353
17.2	Vitamin A: Phenomenon of Smokers.....	354
17.3	Vitamin D.....	357
17.4	Vitamin E.....	358
17.5	Vitamin K.....	359
17.6	Vitamins of Group B.....	361
17.6.1	Vitamin B <sub>6</sub> .....	362
17.7	Vitamin C.....	363
17.8	Vitamin B <sub>3</sub> .....	364
17.9	Diagnosing and Therapy of Vitamin Intoxications.....	365
	References.....	365

## Chapter 18

	Food Adulteration .....	368
18.1	What Is Food Adulteration? .....	368
18.2	Melamine and Cyanuric Acid.....	368
18.2.1	Combined Toxicity of Triazine Compounds.....	371

18.3 Fish Adulteration..... 372  
 18.4 Anisatin..... 373  
 18.5 Toxic Oil Syndrome ..... 373  
 18.6 Epidemic Dropsy..... 374  
 References..... 375

Index ..... 379

12.11 trans-Fatty Acids (TFAs).....  
 12.12 Chlorinated Paraffins.....  
 12.13 Poly-Cyclic Aromatic Hydrocarbons (PAHs).....  
 12.13.1 Phthalates.....  
 12.13.2 Bisphenols.....  
 References.....

Chapter 16

Food Additives

16.1 General Principles.....  
 16.2 Colorants: Azo-Dyes.....  
 16.3 Artificial Sweeteners.....  
 16.4 Preservatives.....  
 16.5 Antioxidants.....  
 16.6 Chelators.....  
 References.....

Chapter 17

Vitamins

17.1 General.....  
 17.2 Vitamin A: Retinoids.....  
 17.3 Vitamin D.....  
 17.4 Vitamin E.....  
 17.5 Vitamin K.....  
 17.6 Vitamins of Group B.....  
 17.6.1 Vitamin B<sub>1</sub>.....  
 17.7 Vitamin C.....  
 17.8 Vitamin B<sub>12</sub>.....  
 17.9 Diagnostic and Therapeutic Use of Vitamin Intake.....  
 References.....

Chapter 18

Food Adulteration

18.1 What is Food Adulteration?.....  
 18.2 Melamine and Cyanuric Acid.....  
 18.3 Combined Toxicity of Triazine Compounds.....