
Contents

Chapter 1 Introduction	1
1.1 Motivation	1
1.2 Pesticides and opinion	2
1.2.1 The fly in the soup	2
1.2.2 Low-tech food production	3
1.2.3 Conclusion	3
1.3 A great market	4
1.3.1 The number of chemicals used as pesticides	4
1.3.2 Amounts of pesticides produced	4
1.3.3 Marketing	6
1.3.4 Dirty dozens	7
1.4 Nomenclature, definitions, and terminology	9
1.4.1 Toxicology, ecotoxicology, and environmental toxicology	9
1.4.2 Pesticides, biocides, common names, chemical names, and trade names	10
1.4.3 Chemical structures are versatile	12
Helpful reading	13
Biochemistry and cell biology	13
General toxicology	13
Insect biochemistry, plant physiology, and neurophysiology	13
Pesticides	14
Side effects of pesticides	14
Chapter 2 Why is a toxicant poisonous?	15
2.1 Seven routes to death	15
2.1.1 Enzyme inhibitors	16
2.1.2 Disturbance of the chemical signal systems	16
2.1.3 Toxicants that generate very reactive molecules that destroy cellular components	17
2.1.4 Weak organic bases or acids that degrade the pH gradients across membranes	17
2.1.5 Toxicants that dissolve in lipophilic membranes and disturb their physical structure	18
2.1.6 Toxicants that disturb the electrolytic or osmotic balance or the pH	18

2.1.7	Strong electrophiles, alkalis, acids, oxidants, or reductants that destroy tissue, DNA, or proteins	18
2.2	How to measure toxicity	18
2.2.1	Endpoints.....	18
2.2.1.1	Endpoints in ecotoxicology and pest control	19
2.2.1.2	Endpoints in human toxicology.....	19
2.2.2	Dose and effect	20
2.2.3	Dose and response	21
2.2.3.1	Dose–response curves for the stable fly	24
2.2.3.2	Scatter in dose–response data	25
2.2.4	LD50 and related parameters.....	26
2.2.5	Acute and chronic toxicity.....	27
2.3	Interactions.....	27
2.3.1	Definitions	28
2.3.2	Isoboles.....	29
2.3.3	Mechanisms of interactions.....	30
2.3.4	Examples.....	30
2.3.4.1	Piperonyl butoxide.....	30
2.3.4.2	Deltamethrin and fenitrothion	32
2.3.4.3	Atrazine and organophosphate insecticides.....	32

Chapter 3 Pesticides interfering with processes important to all organisms..... 35

3.1	Pesticides that disturb energy production.....	35
3.1.1	Anabolic and catabolic processes	35
3.1.2	Synthesis of acetyl coenzyme A and the toxic mechanism of arsenic.....	36
3.1.3	The citric acid cycle and its inhibitors.....	36
3.1.3.1	Fluoroacetate	36
3.1.3.2	Inhibitors of succinic dehydrogenase	37
3.1.4	The electron transport chain and production of ATP	38
3.1.4.1	Rotenone	38
3.1.4.2	Inhibitors of electron transfer from cytochrome b to c_1	40
3.1.4.3	Inhibitors of cytochrome oxidase.....	41
3.1.4.4	Uncouplers.....	41
3.1.5	Inhibition of ATP production.....	42
3.1.5.1	Organotin compounds.....	43
3.1.5.2	Diafenthiuron	44
3.1.5.3	Summary.....	45
3.2	Herbicides that inhibit photosynthesis	45
3.2.1	Weak organic acids	49
3.2.2	Free radical generators.....	49
3.2.3	D ₁ blockers.....	51
3.2.3.1	Urea derivatives.....	51
3.2.3.2	Triazines	52

3.2.4	Inhibitors of carotene synthesis	53
3.2.4.1	Amitrole	53
3.2.4.2	Aclonifen	53
3.2.4.3	Beflubutamid	53
3.2.5	Protoporphyrinogen oxidase inhibitors	54
3.3	General SH reagents and free radical generators.....	54
3.3.1	Mercury.....	54
3.3.2	Other multisite fungicides	56
3.3.2.1	Perhalogenmercaptans.....	56
3.3.2.2	Alkylenebis(dithiocarbamate)s and dimethyldithiocarbamates.....	57
3.3.2.3	Fungicides with copper	58
3.4	Pesticides interfering with cell division.....	59
3.4.1	Fungicides.....	61
3.4.1.1	Benomyl	61
3.4.1.2	Thiofanate-methyl	61
3.4.1.3	Carbendazim	62
3.4.1.4	Thiabendazole	62
3.4.1.5	Diethofencarb	62
3.4.2	Herbicides.....	62
3.4.2.1	Trifluralin	62
3.4.2.2	Carbetamide	63
3.5	Pesticides inhibiting enzymes in nucleic acid synthesis.....	63
3.5.1	Sporulation-inhibiting fungicides.....	63
3.5.2	Inhibition of incorporation of uridine into RNA.....	64
Chapter 4 <i>Bacillus thuringiensis</i> and its toxins		67
4.1	The mechanism of action of δ -endotoxins.....	68
4.2	Biotechnology	70
4.3	Engineered plants	70
4.4	Biology	70
4.5	Commercial products	71
Chapter 5 Specific enzyme inhibitors		73
5.1	Inhibitors of ergosterol synthesis	73
5.1.1	Inhibition of HMG-CoA reductase.....	74
5.1.2	Inhibition of squalene epoxidase.....	75
5.1.3	DMI fungicides	76
5.1.4	Examples of DMI fungicides from each group.....	78
5.1.4.1	Azoles and triazoles.....	78
5.1.4.2	Pyridines and pyrimidines	78
5.1.4.3	Piperazines.....	79
5.1.4.4	Amines.....	79
5.1.4.5	Morpholines.....	80
5.1.5	Conclusions	81

5.2	Herbicides that inhibit synthesis of amino acids	81
5.2.1	The mode of action of glyphosate.....	81
5.2.2	Degradation of glyphosate	83
5.2.3	Selectivity.....	84
5.2.4	Mode of action of glufosinate	84
5.2.5	Inhibitors of acetolactate synthase	86
5.3	Inhibitors of chitin synthesis.....	88
5.3.1	Insecticides	88
5.3.2	Fungicides.....	90
5.4	Inhibitors of cholinesterase	90
5.4.1	Acetylcholinesterase	90
5.4.2	Organophosphates	95
	5.4.2.1 Naturally occurring organophosphorus insecticides.....	97
5.4.3	Carbamates.....	97
	5.4.3.1 Molecular structure and potency of inhibition	98
5.4.4	Development of organophosphorus and carbamate insecticides.....	99
	5.4.4.1 Parathion and similar compounds	103
	5.4.4.2 Aliphatic organophosphates.....	107
	5.4.4.3 Examples of carbamates	107
5.5	Other enzymes inhibited by organophosphates and carbamates	109
5.5.1	The butyrylcholinesterases	109
5.5.2	The neurotoxic target enzyme (NTE)	110
5.5.3	Carboxylesterases.....	113
Chapter 6 Interference with signal transduction in the nerves.....		115
6.1	Potency of nerve poisons.....	115
6.2	Selectivity	115
6.3	The nerve and the nerve cell	116
6.4	Pesticides that act on the axon	117
6.4.1	Impulse transmission along the axon.....	117
6.4.2	Pesticides	119
6.4.3	Pyrethroids	119
6.4.4	DDT and its analogues.....	124
6.5	Pesticides acting on synaptic transmission	125
6.5.1	Inhibitory synapses.....	126
6.5.2	Pesticides	127
	6.5.2.1 Lindane.....	127
	6.5.2.2 Fipronil	130
	6.5.2.3 Cyclodiene insecticides.....	130
	6.5.2.4 Avermectins	130
6.5.3	The cholinergic synapses	131
	6.5.3.1 Atropine	133
	6.5.3.2 Nicotinoids and neonicotinoids	134

6.5.3.3	Cartap	136
6.5.4	Calcium channels as possible targets for insecticides	136
6.6	Summary	137
Chapter 7	Pesticides that act as signal molecules.....	139
7.1	Insect hormones	139
7.1.1	Insect endocrinology.....	139
7.1.2	Juvenile hormone	140
7.1.2.1	American paper towels	141
7.1.2.2	Juvenile hormone agonists as pesticides.....	141
7.1.2.3	Antagonists.....	143
7.1.3	Ecdysone.....	143
7.1.3.1	Phyto-ecdysones	144
7.1.3.2	Synthetic ecdysteroids used as insecticides.....	145
7.1.3.3	Azadirachtin.....	145
7.2	Behavior-modifying pesticides	146
7.2.1	Definitions	147
7.2.2	Pheromones.....	148
7.2.3	Structure-activity relationships	148
7.2.3.1	Alarm and trail pheromones	149
7.2.3.2	Aggregation pheromones.....	149
7.2.4	Pheromones used as pesticides and lures.....	151
7.2.4.1	Coleoptera.....	151
7.2.4.2	Lepidoptera.....	152
7.2.4.3	Fruit flies	153
7.2.4.4	Aphid food deterrent.....	154
7.2.4.5	Mosquito repellents.....	154
7.5	Plant hormones	155
Chapter 8	Translocation and degradation of pesticides	161
8.1	The compartment model	161
8.1.1	The bioconcentration factor.....	164
8.1.2	The half-life	164
8.1.3	The area under the curve.....	165
8.1.4	Example	165
8.1.4.1	Disappearance of dieldrin in sheep.....	165
8.1.4.2	Dieldrin uptake in sheep.....	166
8.2	Degradation of pesticides by microorganisms	166
8.2.1	Degradation by adaption.....	166
8.2.2	Degradation by co-metabolism.....	167
8.2.3	Kinetics of degradation	167
8.2.4	Importance of chemical structure for degradation.....	168
8.2.5	Examples.....	169
8.2.5.1	Co-metabolism and adaptation.....	169
8.2.5.2	Parathion and other pesticides with nitro groups....	171

8.2.5.3	Ester hydrolysis of carbaryl.....	171
8.2.5.4	Mineralization of dalapon.....	172
8.2.6	The degraders	172
8.3	Soil adsorption	173
8.3.1	Why are chemicals adsorbed?.....	173
8.3.2	Examples.....	173
8.3.2.1	Measurements of adsorption.....	175
8.3.3	Desorption	177
8.4	Evaporation.....	178
8.4.1	Example	179
8.5	Biotransformation in animals	180
8.5.1	Oxidation	181
8.5.2	Epoxide hydrolase.....	184
8.5.3	Glutathione transferase	185
8.5.4	Hydrolases.....	187
8.5.5	Glucoronosyltransferase and sulfotransferase	187
8.5.6	Stereospecific biotransformation.....	188
8.6	Designing pesticides that have low mammalian toxicity	189
8.6.1	Acephate	190
8.6.2	Malathion and dimethoate	191
8.6.3	Nereistoxin	192
Chapter 9 Resistance to pesticides		193
9.1	Definitions	193
9.2	Resistance is an inevitable result of evolution.....	194
9.2.1	Time for resistance development.....	194
9.2.2	Questions about resistance	196
9.2.2.1	Are resistant insects more robust than sensitive ones?.....	196
9.2.2.2	Is resistance caused by one allele in one gene locus?.....	196
9.2.2.3	Do pesticides cause resistance?.....	197
9.3	Biochemical mechanisms	197
9.3.1	Increased detoxication.....	199
9.3.1.1	DDT dehydrochlorinase	199
9.3.1.2	Hydrolases	200
9.3.1.3	CYP enzymes in insects.....	200
9.3.1.4	CYP enzymes in plants.....	201
9.3.2	Insensitive target enzyme or target receptor site	201
9.3.2.1	Acetylcholinesterase.....	201
9.3.2.2	kdr resistance	202
9.3.3	Resistance in fungi.....	203
9.3.3.1	Benzimidazole	203
9.3.3.2	Sterol biosynthesis inhibitors.....	204

9.3.4	Atrazine resistance and plants made resistant by genetic engineering	204
9.3.5	Resistance to glyphosate	205
9.3.5.1	Summary	207
9.3.6	Resistance to older biocides used as pesticides	207
9.3.7	Resistance to third- and fourth-generation pesticides	208
9.4	How to delay development of resistance	208
9.4.1	Refuge strategy	209
9.4.2	Mixing pesticides with different modes of action and different detoxication patterns	210
9.4.3	Switching life-stage target	210
9.4.4	Increased sensitivity in resistant pests	210
9.4.5	Inhibition of detoxication enzymes	210
9.5	Conclusions	211
Chapter 10 Pesticides as environmental hazards		213
10.1	Pesticides are poisons	213
10.1.1	Pesticides are xenobiotics	215
10.1.2	Various types of bias	217
10.1.2.1	Publication bias	217
10.1.2.2	Test bias	218
10.1.2.3	Extrapolation bias	219
10.1.3	Benchmark values	220
10.2	Required toxicological tests for official approval of a pesticide	220
10.3	Analysis of residues in food and the environment	222
10.3.1	Definitions	222
10.3.2	Sampling	223
10.3.3	Sample preparation	223
10.3.4	Analysis	224
10.3.4.1	Chromatographic methods	224
10.3.4.2	Biological methods	225
10.4	Pesticide residues in food	226
10.4.1	Toxicity classification of pesticides	226
10.4.1.1	Classification of carcinogenicity	227
10.4.2	Definitions of ADI and NOEL and tolerance limits	227
10.4.2.1	ADI	227
10.4.2.2	NOEL	228
10.4.2.3	Residue tolerance limits	228
10.4.3	Comparing health hazards of pesticides with other toxicants present in the market basket	229
10.5	Elixirs of death	230
10.5.1	Nomenclature and structure of dioxins	231

10.5.2	Dioxins in pesticides.....	232
10.5.2.1	Vietnam	232
10.5.2.2	Presence of dioxins in pesticides in general	233
10.5.3	Toxicology.....	234
10.5.4	The target.....	234
10.5.4.1	Dioxin and metabolism of caffeine.....	236
10.5.5	Analysis.....	237
10.5.5.1	Saturday, 12:30, July 10, 1976.....	238
10.5.6	Summary.....	239
10.6	Angry bird-watchers, youth criminals, and impotent rats.....	239
10.6.1	Clear Lake.....	240
10.6.2	Peregrine falcons and other birds of prey	242
10.6.2.1	Borlaug's warning	244
10.6.2.2	DDT and impotence?	246
10.7	Conclusions.....	246
	Literature.....	249
	Index	265