
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	1 3
	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	Diaphenhiuron	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 *Bacillus thuringiensis* and its toxins.....67

4.1	The mechanism of action of 6-endotoxins.....	68
4.2	Biotechnology	70
4.3	Engineered plants	70
4.4	Biology	70
4.5	Commercial products.....	71

Chapter 5 Specific enzyme inhibitors73

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

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

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.....	2 3 4
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?.....	2 4 6
10.7	Conclusions.....	246
	Literature.....	249
	Index.....	265