



Review

Toxicological effects of pyrethroids on non-target aquatic insects



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ABSTRACT

The toxicological effects of pyrethroids on non-target aquatic insects are mediated by several modes of entry of pyrethroids into aquatic ecosystems, as well as the toxicological characteristics of particular pyrethroids under field conditions. Toxicokinetics, movement across the integument of aquatic insects, and the toxicodynamics of pyrethroids are discussed, and their physiological, symptomatic and ecological effects evaluated. The relationship between pyrethroid toxicity and insecticide uptake is not fully defined. Based on laboratory and field data, it is likely that the susceptibility of aquatic insects (vector and non-vector) is related to biochemical and physiological constraints associated with life in aquatic ecosystems. Understanding factors that influence aquatic insects susceptibility to pyrethroids is critical for the effective and safe use of these compounds in areas adjacent to aquatic environments.

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1. Introduction

Pyrethroids are insecticides with high biological activity and low dose application rates, characterized by low water solubility and strong sorptive properties, which reduce their bioavailability

in natural environments (Davies, 1985). They are also relatively photolabile (Leahey, 1985). Because of increased use of these compounds, concern over their possible ecological non-target effects has increased (Antwi and Peterson, 2009; Elliott et al., 1978; Hill, 1989; Merivee et al., 2015; Palmquist et al., 2011; Weston and Lydy, 2010). Aquatic insects are inherently susceptible to pyrethroids, but the mechanism behind their extreme sensitivity to these compounds is not completely clear (Tang and Siegfried, 1995). The extreme toxicity of pyrethroids to aquatic organisms hinders their wider use in agriculture (Coats et al., 1989; Mugni et al., 2013).

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Aquatic insects are highly sensitive to insecticide poisoning from even extremely low concentrations (often less than 1 ppb) (Coats et al., 1989; Anderson, 1982, 1989; Mian and Mulla, 1992). The high acute toxicity of pyrethroids to aquatic invertebrates and fish restricts their use in areas near aquatic habitats and has raised concerns over the registration of new pyrethroids by the U. S. Environmental Protection Agency (Anonymous, 1990).

Aquatic organisms are exposed to toxicants dissolved in water or compounds bound to food, particulate or dissolved organic matter. Even though most contamination sources are from runoff (Khan, 1983) or aerial drift (Crossland, 1982), pyrethroid contamination levels in surface water in general are within the range that produces toxic effects in aquatic invertebrates (McLeese et al., 1980; Stehle and Schulz, 2015; Weston and Lydy, 2010; Zitko et al., 1977, 1979). In the aquatic environment, a large number of non-target organisms (including predators of pests) are mixed with target pests and disease vectors (such as mosquitoes, midges, and black flies).

Toxicological tests on aquatic organisms are limited by a lack of information on the toxicant concentration at the biological response end point in question (Friant and Henry, 1985), and it is therefore difficult to estimate the dose to which the animal is actually exposed. In view of the problems in determining the lethal dose for particular insecticides to aquatic insects and of standardizing bioassay conditions, it is difficult to compare tests results from different laboratories. Moreover, different aquatic insects vary considerably in their response to insecticides in static exposure tests (Anderson, 1989). Here, we summarize the available data on the impacts of pyrethroids on non-target aquatic insects.

2. Ecological effects

The understanding of physical, chemical, and physiological processes, including the toxicity of mixtures, varying bioavailability, the impact of intermittent exposures and chemical residues in field-collected organisms are critical in addressing aquatic toxicity problems. Spray-drift or run-off may cause minor effects on some aquatic organisms (Hill, 1989; Weston et al., 2011). According to Hill (1989), for realistic field studies with pyrethroids the effects are mostly transient, and they are not likely to cause adverse changes in aquatic ecosystems with respect to population or productivity.

Esfenvalerate sprayed directly on water boatmen (Corixidae) in the laboratory at low levels intended to simulate spray drift from field applications caused observable effects (knockdown) at doses well below the lowest recommended field dose. Moreover, the use of formulated product was more toxic than the technical grade material, suggesting that the additives, like surfactants, increased the toxicity (Samsoe-Petersen et al., 2001). These findings correlate well with the results of several pond studies in which dead, surface-living beetles were collected after pyrethroids were applied to the water surface (Crossland, 1982) or injected into the water column (Woin, 1998) to assess biological effects.

Picket® (a permethrin product) was found to cause a significant drop in larval densities and emergence of adult midges, *Chironomus riparius* (Meigen) (Diptera: Chironomidae) in ponds treated at $>10 \mu\text{g/L}$. Older larvae (third and fourth instars) survived to emergence, but younger larvae did not (Conrad et al., 1999). The recovery of midge population levels observed in this study may be owing to the short life cycle of midges, the close proximity of the study site to untreated ponds that likely acted as sources of midge adults and the reduction of permethrin toxicity within the pond ecosystems as a result of rapid degradation or reduction in bioavailability from the water column. Conrad et al. (1999) observed that emergence of adult midges from treated

ponds resumed within four weeks and that emergence levels were comparable to that in the control pond within two months, a finding consistent with the work of Mulla et al. (1982), who found that synthetic pyrethroids caused 50–100% mortality of non-target arthropods in experimental field ponds and that recovery to pre-treatment levels took place within 2–4 weeks after treatment. Similarly, permethrin applications to lakes, streams and ponds affected aquatic insect populations (Ephemeroptera and Odonata) for only brief periods, with recovery occurring a few weeks to a few months after treatment (Mian and Mulla, 1992). Based on intrinsic sensitivity, biological traits, mode of action, and on invertebrate vulnerability index rankings Ephemeroptera, Plecoptera, Trichoptera, and Odonata genera were potentially most vulnerable to pyrethroids in aquatic ecosystems (Rico and Van den Brink, 2015). Prior studies also support this pattern of the impact of synthetic pyrethroids on aquatic insects (Leahey, 1985; Smith and Stratton, 1986; Hill, 1989; Coats et al., 1989; Mian and Mulla, 1992).

The study by Kingsbury and Kreutzweiser (1980), stated that the diet of brook trout fish (*Salvelinus fontinalis* (Mitchill) (Salmoniformes: Salmonidae) was made up of 75% total volume of aquatic insects before permethrin application. Just after spraying permethrin (8.8, 17.5, 35.0, and 70.0 g a.i./ha) to streams the trout consumed large numbers of mayflies, stoneflies, and caddisflies and that this demonstrates the utilization of post spray drift organisms (Kingsbury and Kreutzweiser, 1980). According to Kingsbury and Kreutzweiser (1980) after 11 and 58 days post treatment more than 80% of the trout feeding was mainly on terrestrial arthropods for its diet with the use of chironomid larvae and other aquatic invertebrates accounting for the rest. Moreover this feeding trend continued at the end of the season after 112 days post treatment indicating continued dependence on terrestrial arthropods. Brook trout and slimy sculpins (*Cottus cognatus* (Richardson) Scorpaeniformes: Cottidae) utilize alternate food sources when aquatic insects became unavailable (Kingsbury and Kreutzweiser, 1980). These series of field trials carried out in Canada to examine the side-effects of aerial application of permethrin used to control forest pests also found that two applications at 17.5 g a.i./ha resulted in substantial reductions of invertebrate (ephemeroptera, heptageniidae, plecoptera, and chironomid) populations (Kingsbury and Kreutzweiser, 1980). Recovery in some invertebrate abundance began six weeks after the second treatment. Measured permethrin residue levels never exceeded $2.6 \mu\text{g/L}$ in the treated streams and ponds, and were below $0.25 \mu\text{g/L}$ two days after treatment. The ability of an aquatic ecosystem to recover from insecticide contamination is affected by many factors, including the insecticide's persistence, bioavailability, the life-history attributes of the affected organisms and the proximity of recolonization sites (Fairchild et al., 1992).

Mathias and Schulz (1996) observed that larvae, pupae, and adults of the caddisfly *Limnephilus lunatus* Curtis (Trichoptera: Limnephilidae) exposed to pyrethroids showed decreased survival with increasing pesticide concentration, while emergence was reduced and delayed. The acute toxicity (LC_{50}) of fenvalerate for *L. lunatus* over a 24-h observation period after a one hour exposure was $22.6 \mu\text{g/L}$, reflecting the fact that pyrethroids break down much more slowly in fish and aquatic insects than in warm blooded vertebrates (Coats et al., 1989). Direct lethal effects of acute pyrethroid contamination mostly appear immediately after exposure, and chronic elevated lethality following short term contamination is relatively slight. Insects possess a relatively low capacity for the hydrolysis of both *cis* and *trans*-pyrethroids and, consequently, the toxicity of both groups of isomers is high. However, comparing the toxicity of different pyrethroids is complicated due to differences in species, sex, and application methods employed by studies.

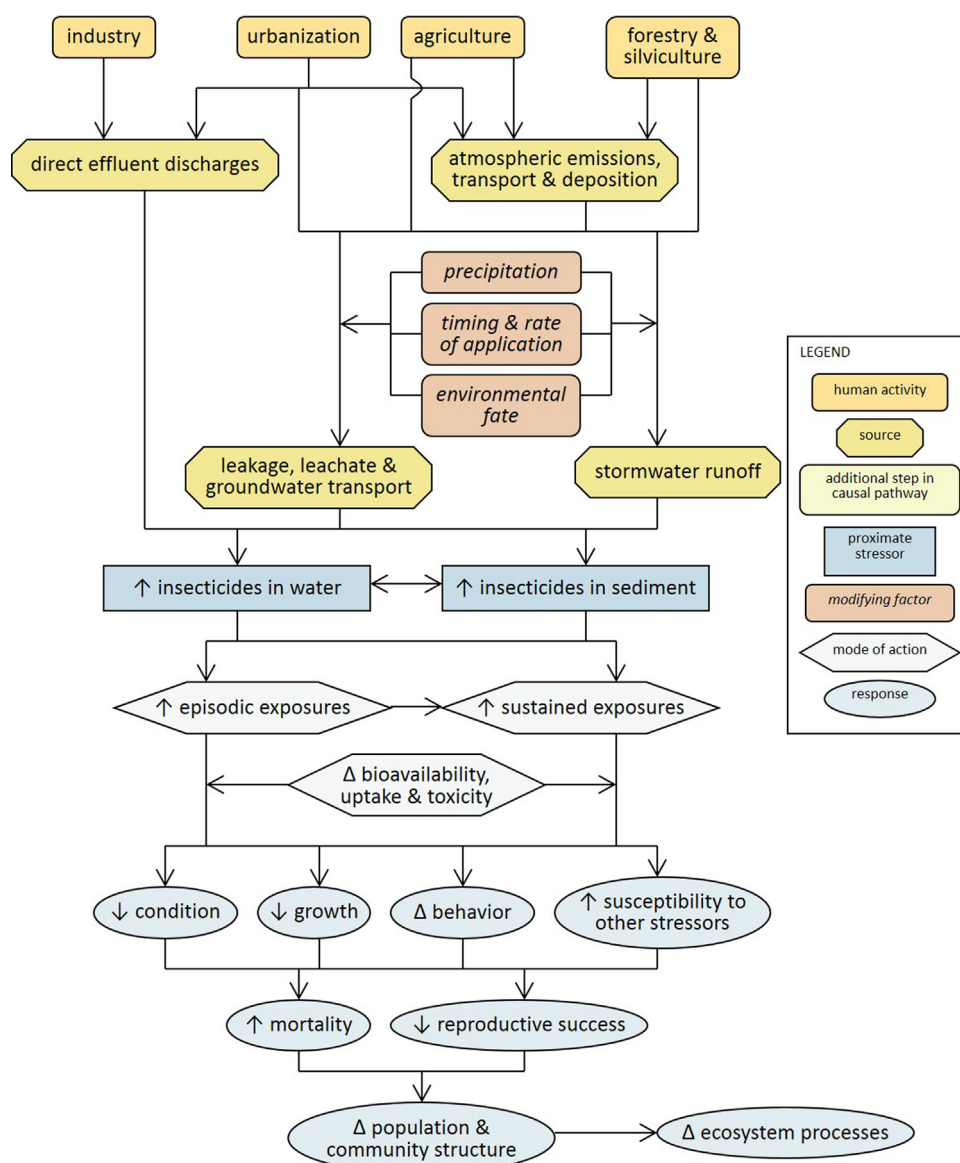


Fig. 1. A conceptual model of mode of entry of insecticide adapted from USEPA (2015).

3. Modes of entry of pyrethroids into aquatic ecosystems

Insecticides enter the environment both directly and indirectly (Fig. 1). Insecticide application for control of pests in agriculture, horticulture, and silviculture (DeBoo, 1980; Herve, 1985) or control of public health pests and disease vectors (Elliott et al., 1978; Mulla et al., 1978, 1979, 1980, 1981; Baldry et al., 1981) are a direct source of contamination. Cypermethrin, deltamethrin, fenpropathrin, fenvalerate, and permethrin have all been used for control of mosquito larvae (Mulla et al., 1978, 1982), and deltamethrin and permethrin for black fly control (Muirhead-Thompson, 1977, 1978, 1981a,b; Mohsen and Mulla, 1981; Bellec et al., 1983). In a spruce forest ecosystem in Canada where permethrin was applied to control spruce budworm, *Choristoneura fumiferana* (Clemens) (Lepidoptera: Tortricidae), streams and ponds were directly exposed to aerial application of the insecticide (DeBoo, 1980). Irrigation water in canals, ditches, and streams around agricultural fields can receive direct spray deposits of cypermethrin, deltamethrin, and permethrin from aerial applications

used to control cotton pests (Davis et al., 1977; Ruscoe, 1979; Herve, 1985).

Pesticides can also enter aquatic systems indirectly, through wind, water, or feed (Westlake and Gunther, 1966). Wind-borne residues ("pesticide drift") and transport of pyrethroid-contaminated sediment through wind or water soil erosion also move chemicals away from application sites. Agricultural ponds are among the aquatic habitats most likely to be exposed to pesticides through spray drift or surface runoff. Water bodies adjacent to cotton, potatoes, sugar beets, and vineyards have been found in field trials to be contaminated by cypemethrin and permethrin (Crossland et al., 1982). Transport of pyrethroids and their residues in runoff depends to a great extent on the solubility of the compound in water, as well as the distance between the point of application and the receiving aquatic habitat. Pyrethroid residues are more readily bioavailable if suspended in water than when they are adsorbed on particulates, resulting in a higher residue uptake by aquatic organisms from water than from food alone (Hill, 1985).

4. Pyrethroid toxicity

4.1. Laboratory studies

Several predaceous and non-target aquatic hexapods have shown similar level of sensitivity to pyrethroids as mosquito larvae (Table 1), including several mayflies (*Baetis* spp., *Cloeon dipterum*, *Ephemerella* spp., and *Hexagenia* spp.), a stonefly (*Pteronarcys dorsata*), a gyrinid beetle (*Gyrinus natator*), caddisflies (*Brachycentrus americanus* and *Hydropsyche* spp.) and a dipteran snipefly, (*Antherix* sp.) (Mian and Mulla, 1992). In contrast, the corixid Hemipteran *Corixa punctata* and notonectid Hemipteran *Notonecta undulata* also have lower sensitivity to some of the pyrethroids (Mian and Mulla, 1992).

Pyrethroids dissolved in interstitial water in sediments is another way that benthic invertebrates such as chironomid midges are exposed to pyrethroids. Muir et al. (1985) found that *Chironomus tentans* Fabricius (Diptera: Chironomidae) larvae bio-concentrated *cis* and *trans*-cypermethrin, deltamethrin, fenvalerate, and *cis* and *trans*-permethrin from sand, silt, and clay sediments, as well as from water/sediment suspensions. Details of the test environment affect risk: when larvae of *C. tentans* were exposed for 24 h in sediment or 48 hours in water above different sediments to 12–640 ng/g of C14-labeled cypermethrin or 5–10 ng/g of three other pyrethroids, larvae in water above sand accumulated 5–15 fold more of each pyrethroid than did larvae held in water above silt or clay sediments. The lower availability of these compounds in the water above silt or clay (compared to water above sand) was attributed to a greater adsorption of residues by suspended particulates from silt or clay. The data revealed further that the larvae showed no adverse changes in their behavior when exposed to sediments containing 5 ng/g of each pyrethroid, but at 10 ng/g midge larvae were immobilized. However, a majority of them survived if transferred to pyrethroid-free water.

While various studies (Mugni et al., 2013; Diao et al., 2011; Saha and Kaviraj, 2008; Stephenson, 1982) suggest there is a potential risk from pyrethroids to aquatic invertebrates, these laboratory tests were carried out in a combination of static, flowing or intermittent flow systems. Depending on the physical and chemical properties of the pyrethroid, and the life stage, body size, and weight of exposed organisms, a test organism in a static water system might be exposed to pesticide concentrations for a longer period of time than in intermittent flow and flow-through systems. Therefore it is likely better to study the impact of pyrethroids under field conditions.

4.2. Field studies

In field studies aquatic insects have been observed to exhibit recovery within 6 months. The longer recovery times has been attributed to increased generation times, and restricted recolonization potential (Fairchild et al., 1992). Miura and Takahashi (1976) found that fenvalerate, applied at a rate of 28 g/ha, caused slight mortality in corixids, notonectids, dytiscids and hydrophilid beetle populations, as shown by dead organisms collected in treated ponds. However, there were no significant differences between the numbers of non-target insects trapped in treated and control ponds during the four days following the treatment. Mulla et al. (1969, 1972, 1980, 1982) found Ephemeroptera (mayflies) to be the most sensitive group, with affected populations decreasing by 50–100%. However, recovery to pretreatment or control levels occurred within 2–4 weeks after treatment, suggesting extensive migration of such insects and low persistence of these compounds in aquatic mesocosms at the applied rates. The new insects had to have come from elsewhere in such a short period, unless there was

an invulnerable life table present at the site. Cypermethrin at a rate of 100 g (a.i.)/ha caused 50% mortality in mayflies, with some toxicity to aquatic coleopterans and hemipterans (Smies et al., 1980; Speilberger et al., 1979) and had no adverse effects on odonates, trichopterans, or dipterans. Everts et al. (1983) studied the effects of deltamethrin and permethrin in West African rivers. Deltamethrin applied at 12.5 g/ha in the riverine forest near Bouafle in Ivory Coast caused significant reductions in densities of Ephemeroptera (80–100%), and Trichoptera (26%). Permethrin had effects on shrimps (*Caridina africana* Kingsley (Decapoda: Atyidae) and *Macrobrachium vollenhovenii* (Herklots) (Decapoda: Palaemonidae) and aquatic insects that were similar to deltamethrin. However, recovery of most populations in the deltamethrin-contaminated water of River Marahoue in Ivory Coast was noticed within six months after pesticide application.

Ponds adjacent to cotton fields have frequently been contaminated following applications of permethrin and cypermethrin to cotton fields from a fixed wing aircraft, and follow up studies suggest that the most sensitive organisms were Ephemeroptera, Odonata, Hemiptera (gerrids and notonectids), and Coleoptera (gyrinids) (Crossland, 1982; Hill, 1985). Drift of permethrin from such agricultural applications caused 100% mortality in populations of the affected organisms with some recovery occurring after six months, while cypermethrin caused less mortality and was associated with a shorter recovery period. In trout streams in forest areas in parts of Canada, Ephemeroptera and Trichoptera were the groups most sensitive to permethrin (Kingsbury and Kreutzweiser, 1980).

5. Toxicokinetics

Siegfried (1993) compared the acute toxicity, to aquatic (black fly *Simulium vitatum*, caddisfly *Hydropsyche* and *Cheumatopsyche* spp., mayfly Heptageniidae, damselfly *Enallagma* and *Ishnura* spp., and water scavenger beetle *Hydrophilus* spp.) and terrestrial insects (European corn borer *Ostrinia nubilalis* (Hubner), housefly *Musca domestica* L., and Convergent lady beetle *Hippodamia convergens* Guerin-Meneville), of pyrethroids and organophosphates applied by either topical application or static exposure to aqueous solutions, and found that aquatic insects were inherently more susceptible to these chemicals than terrestrial insects. The author notes, however, that the relationship between LC₅₀ determined by static exposure and the amount of insecticide uptake is unknown and that the toxicity data obtained by topical application is probably irrelevant to natural exposure conditions. In an attempt to clarify the relationship between dose and exposure, the uptake of insecticide by aqueous exposure at the LC₅₀ was determined for permethrin and chlorpyrifos (Tang and Siegfried, 1995). The total uptake for both insecticides expressed as (ng/mg body weight) was less than LD₅₀ (ng/mg body weight) obtained by topical application. These authors were unable to directly compare the uptake of the two insecticides, as the rate of uptake was dependent on concentration, which varied with the LC₅₀ for each insect taxon. They were therefore of the view that the role of insecticide uptake from aqueous solutions in determining insecticide toxicity was uncertain (Tang and Siegfried, 1995).

Indeed, uptake and bio-concentration were generally not correlated with susceptibility, as some of the more tolerant insects were also those that exhibited the highest concentration. According to Siegfried (1993), the discrepancy between uptake and toxicity is due to the fact that the chlorpyrifos uptake rate exceeded permethrin uptake in most taxa despite the fact that permethrin is consistently more toxic than chlorpyrifos. Tang and Siegfried (1995) suggested, therefore, that factors other than the uptake of insecticides from aqueous solutions are responsible for the toxicity of insecticides. The rate of uptake varied considerably among the

Table 1

Acute toxicity of pyrethroids to aquatic insects.

Taxon	Order	Organism	Stage/size	Test condition ^a	Pyrethroid	Toxicity parameter	Toxicity (µg a.i./L)	Footnote references ^b
Insecta	Ephemeroptera	<i>Baetis parvus</i> (Dodds)	Larvae	F	Deltamethrin	24-h LC ₅₀	0.4	5
		<i>Baetis rhodani</i> (Pictet)	Larvae	F	Cypermethrin	96-h LC ₅₀	6.0 ^c	3, 6, 11
					Permethrin	96-h LC ₅₀	12.0 ^c	3, 6, 11
						24-h LC _{90–95} (1 h exposure)	1.0	6
		<i>Cloeon dipterum</i> (L.)	5 mm	S	Cypermethrin	24-h EC ₅₀	0.07	1, 3
						24-h LC ₅₀	0.60	1, 3
			Early Instar	S	Permethrin	72-h EC ₅₀	0.03	1, 3
		<i>Ephemerella</i> sp.	Early Instar	F	Fenvalerate	24-h EC ₅₀	0.31	1, 3
						48-h EC ₅₀	0.07	1, 3
						796-h LC ₅₀	0.93	1, 3
		<i>Hexagenia bilineata</i> (Say)	Nymphs	F	Permethrin	96-h LC ₅₀	0.1	6
		<i>Hexagenia rigida</i> (McDunnough)		-	Permethrin	6-h LC ₅₀	0.6–2.0	2
	Plecoptera	<i>Pteronarcys dorsata</i> (Say)		F	Fenvalerate	72-h EC ₅₀	0.13	1
						72-h LC ₅₀	>1.0	1
				F	Permethrin	72-h EC ₅₀	0.15	1
						72-h LC ₅₀	>0.40	1
						28-d LC ₃₀	0.04	1, 3
		<i>Corixa punctata</i> (Illiger)	Adults	S	Permethrin	24-h EC ₅₀	0.7	1, 3
		<i>Notonecta undulata</i> (Say)	Adults	S	Allethrin	24-h LC ₅₀	>5.0	1, 3
						48-h LC ₅₀	29.0	4
					Dimethrin	48-h LC ₅₀	0.1 ^{c,d}	4
					Tetramethrin	48-h LC ₅₀	33.8 ^d	4
	Hemiptera	<i>Corixa punctata</i> (Illiger)	Adults	S	Resmethrin	48-h LC ₅₀	1.9 ^d	4
		<i>Notonecta undulata</i> (Say)	Adults	S	Bioresmethrin	48-h LC ₅₀	1.2 ^d	4
					Permethrin	24-h EC ₅₀	0.7	1, 3
						24-h LC ₅₀	>5.0	1, 3
			Adults	S	Allethrin	48-h LC ₅₀	29.0	4
					Dimethrin	48-h LC ₅₀	0.1 ^{c,d}	4, 11
					Tetramethrin	48-h LC ₅₀	33.8 ^d	4, 11
					Resmethrin	48-h LC ₅₀	1.9 ^d	4, 11
					Bioresmethrin	48-h LC ₅₀	1.2 ^d	4, 11
		<i>Gyrinus natator</i> (Portevin)	Adults	S	Cypermethrin	24-h EC ₅₀	0.07	1, 3
Trichoptera	Coleoptera					24-h LC ₅₀	0.6	1, 3
						96-h EC ₅₀	0.4	1
						96-h LC ₅₀	>0.5	1
	Diptera	<i>Brachycentrus americanus</i> (Banks)	Larvae	F	Permethrin	24-h EC _{90–95} (1-h exposure)	1.0	6
		<i>Brachycentrus subnubilis</i> (Curtis)	Larvae	F	Permethrin	24-h LC ₅₀	0.4	5
		<i>Hydropsyche californica</i> (Banks)		IF	Deltamethrin	24-h EC _{90–95} (1-h exposure)	0.1	6
		<i>Hydropsyche californica</i> (Banks)			Permethrin	24-h EC _{90–95} (1-h exposure)	0.1	6
		<i>Antherix</i> sp.	Larvae	F	Fenvalerate	3-d LC ₅₀	0.60	1
	Trichoptera					7-d LC ₅₀	0.12	1
		<i>Culex/Aedes</i> spp. ^e	Larvae	S	Cypermethrin	14-d LC ₅₀	0.07	1
					Deltamethrin	28-d LC ₅₀	0.03	1
					Fenvalerate	24-h LC ₅₀	0.07–1.0	7, 8, 9
					Permethrin	24-h LC ₅₀	0.02–0.4	7, 8, 9
					Cypermethrin	24-h LC ₅₀	0.9–2.8	7, 8, 9
					Deltamethrin	24-h LC ₅₀	0.5–3.0	7, 8, 9
					Fenvalerate	24-h LC ₅₀	0.40	7, 8, 9
					Permethrin	24-h LC ₅₀	0.07–0.6	7, 8, 9
					Deltamethrin	24-h LC ₅₀	1.2–5.3	7, 8, 9
					Deltamethrin	24-h LC ₅₀	0.7–6.0	7, 8, 9
						24-h LC ₅₀	0.02	5
					Permethrin	24-h LC ₅₀	0.10	10
						(1-h exposure)		
						24-h LC ₅₀	1.0	6
						(1-h exposure)		

^a F, flow-through system; IF, intermittent flow system, S, static.^b 1. Anderson (1982), 2. Friesen et al. (1983), 3. Hill (1985), 4. Mills et al. (1969), 5. Mohsen and Mulla (1981), 6. Muirhead-Thompson (1978), 7. Mulla et al. (1978), 8. Mulla et al. (1980), 9. Mulla et al. (1982), 10. Muirhead-Thompson (1981a), and 11. Mian and Mulla (1992).^c Emulsifiable concentrate (EC) material.^d LC₅₀ was determined from dosage-mortality data (Mian and Mulla, 1992).^e Target pest species.

insects tested, and the highest rates were observed for caddisflies and black flies. Estimates of the elimination half-life of these insecticides reflect accumulation in the target site(s) of target action and the dynamics of the toxicological responses as well as variability

from variety of sources. Pharmacokinetic models are well accepted for quantifying bio-concentration in aquatic organisms, but their use in aquatic toxicology testing is limited by the lack of information on the body toxicant concentration at the biological response

end point in question (Mancini, 1983; Connolly, 1985; Friant and Henry, 1985; Lassiter, 1986).

6. Movement across integument

In any ecosystem insecticide concentrations will induce some response in populations of some animals or plant species. The difference in response between any two species is a measure of the selectivity of the insecticidal action in relation to those species (Winteringham, 1969). Factors such as differences in exposure or behavior of the fauna, and differences in physiological sensitivity after contact between the organism and insecticide account for this selectivity (Winteringham, 1969). Insecticide selectivity depends on the insect's relatively high surface to volume ratio because of its small size and complexity of appendages, and the high accessibility of the insect central nervous system to contact lipophilic insecticides.

Pyrethroid concentration at the primary site of action is influenced by many factors after topical application (Fig. 2). These include penetration, distribution, selective accumulation in insect tissues, biotransformation, and excretion (Brooks, 1976; Kasai et al., 2014; Lin et al., 2012; Narahashi, 1971b; O'Brien, 1967; Tak and Isman, 2015). The pyrethroids which are lipophilic dissolve in the outer wax layer and partition into the inner polar layers of the cuticle. Penetration of the cuticle by pyrethroids takes place due to the network of the wax canals which penetrates the cuticle, through intersegmental areas or lipophilic tracheal lining accessed through the spiracles (Noble-Nesbitt, 1970). There are conflicting view points as to how insecticides arrive at their target following the studies by Gerolt (Gerolt, 1969, 1970). These are penetration through the cuticle and transport by the hemolymph as one viewpoint, and the other viewpoint is lateral transport in the cuticular wax layer and tracheal lining followed by penetration through the glial cells into the central nervous system.

Tang and Siegfried (1996), in tracking insecticide exposure for aquatic insects, separated movement across the insect integument from ingested insecticide. Initial rapid uptake seems to be due to the movement of the insecticide solution across the lipophilic exocuticle. The subsequent movement is due to the steady-state inward diffusion through more polar layers of the integument. The rapid initial movement of insecticide into the exocuticle results in saturation of the outermost layer so that further uptake is governed by the movement of the insecticide across the more polar, inner layers of integument. In the view of Tang and Siegfried (1996), the uptake of insecticides by aquatic insects cannot be predicted simply by the lipophilic nature of the compound, and they suggest instead that insecticide toxicity to aquatic insects is dependent on factors other than high rates of uptake from aqueous solutions, and that differences in toxicity between insecticides are independent of uptake rate. In an earlier studies Siegfried (1993) compared acute toxicities of permethrin, cypermethrin, bifenthrin, and chlorpyrifos by topical and static exposure to a variety of terrestrial and aquatic insects. The author observed that mayflies and damselflies were the most susceptible taxa and that aquatic insects on a dose per body weight were generally more susceptible than terrestrial insects.

7. Toxicodynamics

7.1. Biochemical effects

The greater sensitivity of aquatic compared to terrestrial insects to pyrethroids may not directly relate to greater uptake or deficiencies in metabolism, as some aquatic insects are known to have well developed detoxification enzyme systems (Siegfried and

Young, 1993). Rather, the greater sensitivity of aquatic insects may be caused by greater sensitivity of physiological sites in aquatic insects. The mode of action of pyrethroids is believed to involve the disruption of the axonal transmission of nerve impulses as a result of altering ion permeability (Clark and Matsumura, 1982). Since freshwater aquatic organisms live in an extremely dilute environment, the processes involved in maintaining ionic balance and osmoregulation are critical to maintenance of homeostasis (Schmidt-Nielsen, 1997). Maintenance of high cellular concentrations of ions against a concentration gradient is regulated by active transport. An insect's ability to maintain ionic balance in water may be affected by exposure to pyrethroids, thereby making them more susceptible. Such effects have also been reported for fish, in which species exposure to pyrethroids disrupts respiratory surfaces and ion regulation (Bradbury and Coats, 1989; Dyer et al., 1989; Symonik et al., 1989). Such effects may generally contribute to the higher sensitivity of aquatic insects and other aquatic organisms.

Pyrethroids have also been shown to inhibit ATPases associated with active transport (Gray and Soderlund, 1985), and may affect ion movement and osmoregulation. Two types of Ca^{2+} stimulated ATPase activities have been recognized. One is $\text{Ca}+\text{Mg}$ -ATPase which is temperature and aging sensitive and requires the simultaneous presence of Mg^{2+} and K^+ for optimal Ca^{2+} stimulation. The second is Ca -ATPase, which is comparatively temperature insensitive, stable and resistant to aging, and requires the presence of Na^+ and K^+ but not Mg^{2+} (Matsumura and Clark, 1980).

Two groups of pyrethroids have been recognized: (1) pyrethrin and allethrin, "natural type" compounds (Elliott et al., 1973) that preferentially affect Ca -ATPase activity and (2) synthetic pyrethroids such as cypermethrin and deltamethrin that preferentially inhibit $\text{Ca}+\text{Mg}$ -ATPase activity (Matsumura and Clark, 1982). The differences, however, may not be due simply to the presence of an α -cyano moiety, as has been postulated (Matsumura and Clark, 1982). Permethrin, for example, lacks this moiety but still exhibits strong inhibition of $\text{Ca}+\text{Mg}$ -ATPase activity (Matsumura and Clark, 1982). Nishimura and Narahashi (1978)'s work on crayfish nerves found that pyrethrin-type compounds induce an immediate excitation that correlates with the compound's insecticidal properties, while pyrethroids do not induce immediate excitation and their insecticidal activities are not directly related to nerve excitation. Vijverberg and van den Bercken (1979) observed that unlike natural pyrethrins, pyrethroids (e.g., cypermethrin and deltamethrin) do not induce the "repetitive discharges" that are characteristic of DDT and pyrethrin insecticides. Rather, pyrethroids suppress the peaks of activity, and that suppression increases with increased stimulation. Hence, the highly modified pyrethroids have different mode of action from the natural-type pyrethrins.

The function of $\text{Ca}+\text{Mg}$ -ATPase is in the sarcoplasmic reticulum of muscle, where it functions to pump Ca^{2+} against a concentration gradient from the intracellular medium into the lumen of the reticulum. Studies with mammalian brain synaptosomes (Blaustein et al., 1978) found ATP-utilizing systems to be active in the endoplasmic reticulum of the presynaptic region, transporting intracellular Ca^{2+} into this reticulum (McGraw et al., 1980). This process is believed to help these cells regulate intracellular free Ca^{2+} levels, leading to an increase in neurotransmitter release as has been shown in heptachlor epoxide poisoning (Yamaguchi et al., 1980).

7.2. Physiological effects

The acute mode of action of pyrethroids is a function of their neuroactivity. Pyrethroids generally act directly on the nervous system, disrupting the normal ion permeability of the nerve

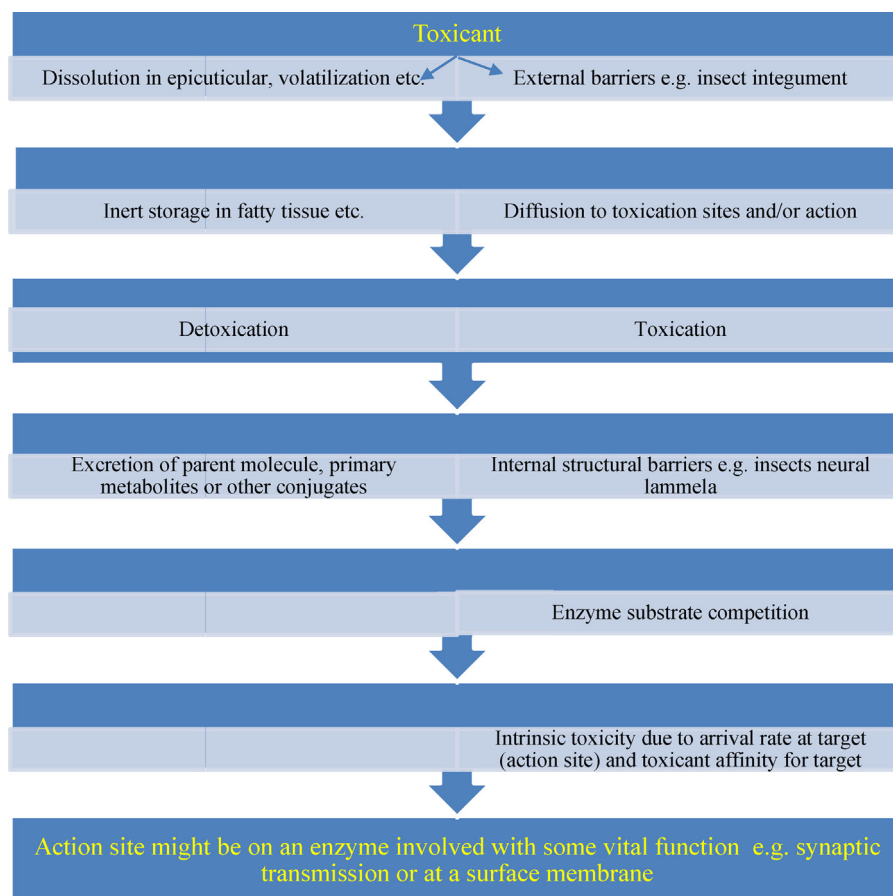


Fig. 2. A model of biochemical and physiological factors influencing the toxicity of an insecticide applied externally. Adapted from Winteringham (1969) and Brooks (1976). Factors on the right represent physical barriers, and other rate limiting steps in the intoxication process. Factors on the left represent processes that reduce effective toxicant amount in the tissues.

membrane responsible for the generation and conduction of nerve impulses (Wang et al., 1972). Narahashi (1976a,b) determined that the permeability of membranes to sodium (Na^+) and to a lesser extent potassium (K^+) ion is affected by pyrethroids. Pyrethroids delay the closing of nerve membrane sodium channels, which may lead to repetitive discharges or to the blockage of nerve conduction (Narahashi, 1979; Vijverberg and van den Bercken, 1982). The α -cyano pyrethroids (e.g., cypermethrin) appear to differ from non-cyano compounds (e.g., permethrin) in their effects. Nerve excitation by pyrethroids has been examined with giant axons of cockroaches, crayfish, and squid (Narahashi, 1971a,b, 1976a,b). Allethrin causes an increased negative after-potential and repetitive firing following electrical stimulation of cockroach preparations, but only above 26°C (Wang et al., 1972; Narahashi, 1962a,b) as the toxicity of pyrethroids increases.

Voltage clamp studies using giant axons of squid show that allethrin shifts the sodium activation curve in the direction of depolarization (Narahashi and Anderson, 1967) and the sodium inactivation curve in the direction of hyperpolarization (Wang et al., 1972). One or both of these effects could account for the prolongation of the transient sodium conductance increase, and are probably also responsible for repetitive firing and nerve blockage. Pyrethroids are believed to increase the frequency of appearance of miniature end plate potentials that represent the action of individual packets of neurotransmitters released from a synaptic vesicle by exocytotic action at the presynaptic release site in a malaria mosquito vector *Anopheles stephensi* (Omer et al., 1980). The neurosecretory cells (NSCs) present on the protocerebral regions of *A. stephensi* were affected by exposure to cyfluthrin through the

endocrine mechanism, in particular the ommatidium (Basker et al., 1999).

7.3. Symptoms

Pyrethroid poisoning symptoms in mammals and terrestrial insects has led to the classification of poisonings as Type I (or T) and Type II (or CS) syndromes (Verschoyle and Aldridge, 1980; Gammon et al., 1981, 1982; Lawrence and Cassida, 1982). Type I effects in mammals (rats and mice) include aggressive sparring behavior, increased sensitivity to external stimuli, fine tremors, prostration, coarse body tremors and increased body temperature. Non-alpha cyano pyrethroids generally elicit Type I symptoms. The symptoms of Type II responses include chewing, profuse salivation, pawing and burrowing, coarse body tremors, increased startle response, abnormal locomotion of the hind limbs, sinuous writhing (chloreoathethosis) and clonic and tonic seizures. Pyrethroids causing Type II symptoms generally contain an S- α -cyano-3-phenoxybenzyl alcohol moiety. In cockroaches, Type I symptoms include restlessness, incoordination, prostration and paralysis, whereas Type II symptoms include incoordination, convulsions and intense hyperactivity.

8. Summary and conclusion

Pyrethroid insecticides are a potent group of chemicals used to control insect pests in agricultural and aquatic systems. The mode of entry of pyrethroids into aquatic habitats is both direct and indirect. Direct sources include purposeful applications of pyrethroids

in vector control as well as agricultural and silvicultural pest control programs. Indirect means through which water bodies could be contaminated with pyrethroid residues include spray drift, runoff and erosion. In field studies, the non-target aquatic groups most affected were the Ephemeroptera, Plecoptera, Odonata, Hemiptera, Coleoptera and Trichoptera. The population of affected organisms, however, generally recovered to pretreatment levels within weeks to months after application. The transient effects of pyrethroids on some non-target species will have a short-term impact on the densities and feeding behavior of some dependent carnivorous fish species in aquatic ecosystems. Fish species like brook trout and slimy sculpins utilize alternate food sources when aquatic insects became unavailable. The susceptibility of aquatic insects may be related to the biochemical and physiological constraints associated with aquatic life. Pesticide bioassays require standardization to allow for more meaningful comparisons between studies. Further understanding of the processes that influence the susceptibility of aquatic organisms to pyrethroid insecticides is critical for the effective and safe use of these compounds in areas adjacent to aquatic environments.

Conflict of interest statement

The authors declare no conflicts of interest.

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