RESERVE THIS SPACE

Effects of pyrethroid insecticides on aquatic organisms.

I. Werner[1] and K. Moran[2]

[1]University of California, Davis, Aquatic Toxicology Program, School of Veterinary Medicine, Dept. of Anatomy, Physiology and Cell Biology, Davis CA 95616, *iwerner@ucdavis.edu*
[2]TDC Environmental, LLC, San Mateo CA 94403, *kmoran@tdcenvironmental.com*

Introduction

Most aquatic invertebrates and fish are highly susceptible to synthetic pyrethroid insecticides (*1*, *2*). All pyrethroids are potent neurotoxicants that interfere with nerve cell function by interacting with voltage-dependent sodium channels as well as other ion channels, resulting in repetitive firing of neurons and eventually causing paralysis (*3*, *4*). Exposed organisms may exhibit symptoms of hyperexcitation, tremors, convulsions, followed by lethargy and paralysis. Pyrethroids occur mostly as mixtures of stereoisomeric forms, and the toxicity of individual isomers can vary (*5*). There are two groups of pyrethroids with distinctive poisoning symptoms, type I and type II. Type II pyrethroids are distinguished from type I pyrethroids by an alpha-cyano group in their structure. While type I pyrethroids (e.g. permethrin, cismethrin) exert their neurotoxicity primarily through interference with sodium channel function in the central nervous system, type II pyrethroids (e.g. deltamethrin, esfenvalerate, cypermethrin, bifenthrin) can affect additional ion-channel targets such as chloride and calcium channels (*6*). Pyrethroids also modulate the release of acetylcholinesterase in the brain's hippocampus region (*7*), and can inhibit ATPases (*8*). In addition, these compounds can disrupt hormone-related

RESERVE THIS SPACE

functions (*9, 10*). In mammals, pyrethroids decrease progesterone and estradiol production (*11*), eliciting estrogenic effects in females and anti-androgenic effects in males (*12, 13*). Breakdown products of pyrethroids have been shown to be more potent endocrine disruptors than their parent compounds (*13, 14*). Furthermore, pyrethroids have been shown to inhibit cell cycle progress (*15*), cause cell stress (*16*), and have immunosuppressive effects (*17, 18*). Additional long-term effects may be caused by damage to respiratory surfaces, and interference with renal ion regulation (*3*).

Acute Toxicity

Acute toxicity is defined as a significant reduction in survival of the exposed organisms within a relatively short time (minutes to days), and is expressed as the species-specific median lethal concentration (LC50). For pyrethroid insecticides, most known 96-h LC50s for fish, aquatic insects and crustaceans are well below 1 µg/L (Table I), whereas molluscs are relatively insensitive to these chemicals and can bioaccumulate them (*2*). Crustaceans such as amphipods are among the most sensitive taxa. Little is known about oligochaetes, but available data indicate that this group is much less sensitive than crustaceans or insects (*19, 20*). In a hazard assessment performed by the California Department of Fish and Game (*21*), water quality criteria for cypermethrin and permethrin were derived according to US EPA guidelines (*22*). The proposed final acute values and criterion maximum concentrations were 0.003 and 0.002 µg/L, respectively, for cypermethrin, and 0.059/0.002 µg/L (freshwater/saltwater) and 0.03/0.001 µg/L (freshwater/saltwater), respectively, for permethrin.

Sublethal Toxicity

Sublethal toxic effects can occur at exposure levels far below the concentrations that cause lethality (Table II), and can have severe consequences for the fitness, reproductive success and survival of aquatic organisms, ultimately leading to population-level effects (*23*). Sublethal biological responses include altered behavior, reduced growth, immune system effects, reproductive/endocrine effects, histopathological effects as well as biochemical responses. However, direct links of these responses to higher-level effects are often difficult to establish. Nevertheless, sublethal toxic effects can have far-reaching consequences in the aquatic environment, where organisms are often simultaneously exposed to many different stressors (*24*). Effects of sublethal

environmental stress can be evaluated at several levels of biological organization, from molecular processes to growth and reproduction, that may impact overall population size and community interactions. Some physiological endpoints commonly tested include hematological and immunological parameters (e.g., hematocrit, plasma cortisol concentrations), assessments of liver and gill structure and function (e.g., liver somatic index, mixed function oxidases enzyme induction), energetics (e.g., RNA/DNA ratios, swimming performance, feeding and growth rates), and behavioral and nervous system function (e.g., temperature tolerance, swimming performance, altered predator-prey interactions).

Biochemical and Physiological Effects

The use of biochemical and physiological biomarkers is widespread in aquatic toxicology, partly because their induction is more sensitive to stress than traditional indices such as growth inhibition (*25, 26*). Some of these sublethal stress responses divert an organism's energy away from normal metabolic functions and can result in "higher-level" effects such as growth inhibition or reduced reproductive success.

Induction of heat-shock proteins (hsp) occurred in liver of juvenile Chinook salmon (*Oncorhynchus tshawytscha*) following exposure to sublethal concentrations of esfenvalerate (*27, 28, 29*). Werner et al. (*30*) measured elevated levels of hsp in medaka (*Oryzias latipes*) after feeding on a diet containing 21 µg/g esfenvalerate. Hsp indicate the occurrence of significant protein damage in cells and tissues, and increased expression of these proteins has been linked to abnormal development in larval sturgeon (*31*), as well as an increase in energy expenditure in juvenile steelhead trout (*32*).

An eight-week exposure of Korean rockfish (*Sebastes schlegeli*; mean fish wt: 52 g) to cypermethrin had significant effects on a number of blood parameters (*33*). Red blood cell count, hemoglobin and hematocrit were significantly reduced after exposure to 0.041 µg/L cypermethrin. The activity of several enzymes and serum osmolality were also altered. Reduced levels of serum total protein, albumin, cholesterol, lysozyme activity and significantly higher serum concentrations of glucose, bilirubin and malondialdehyde were attributed to an increased demand for energy by fish under stress. Moore and Waring (*34*) demonstrated that the pyrethroid cypermethrin impaired olfactory function in Atlantic salmon after a 5-day exposure to <0.004 µg/L. Fish (*Heteropneustes*

fossilis) chronically exposed to 1.44 µg/L cypermethrin exhibited decreased blood plasma calcium levels, and degeneration of branchial cells (*35*).

Tissue and Organ Damage

Histopathological lesions in the liver were observed in the Sacramento splittail (*Pogonichthys macrolepidotus*, *29*) shortly (1 wk) after 96-h exposure to sublethal concentrations of organophosphate and pyrethroid insecticides. Fish recovered from these lesions, but showed high (delayed) mortality rates, grew slower and showed signs of cellular stress even after a 3 month recovery period. A significant reduction in liver glycogen levels of fathead minnow (*Pimephales promelas, 36*) was observed after 96-h exposure to 0.20 µg/L esfenvalerate. Likewise, Haya and Waiwood (*37*) found a depletion of glycogen stores in liver and muscle for starving juvenile Atlantic salmon exposed to fenvalerate. The loss of glycogen (a secondary stress response) should be regarded as a nonspecific response signifying stress and has been linked to changes in cortisol during exposure to various stressors (*38*).

Swimming Performance and Behavior

Abnormal behaviors produced by contaminants include changes in preference or avoidance, activity level, feeding, performance, learning, predation, competition, reproduction and species-specific social interaction such as aggression. Such changes can have significant consequences for fitness, survival and reproductive success of an individual. For example, many neurotoxic compounds cause abnormal swimming behavior or compromise swimming ability in fish and other aquatic animals (*39, 40, 41*). In the field, such changes can directly translate into increased vulnerability to predation or decreased food intake.

Because pyrethroids are potent neurotoxins, behavioral endpoints may be among the most sensitive and ecologically relevant measurable parameters to assess their sublethal toxicity. Little and Finger (*42*) describe swimming behavior of fish exposed to a variety of contaminants ranging from pesticides (e.g., DDT, carbaryl, methyl parathion) to metals (e.g., zinc, copper, cadmium), and found that changes in swimming behavior were detected at exposures as low as 0.7 to 5% of the chemical's LC50 values.

Sublethal effects of acute cypermethrin exposure on swimming behavior were assessed in studies in rainbow trout and bluegill sunfish (*39*) The sublethal signs of toxicity included rapid and erratic swimming, partial/complete loss of equilibrium, jaw spasms, gulping respiration, lethargy, and darkened pigmentation. For the two studies, the acute NOEC (no observed effect concentration) values for swimming behavior were only slightly lower than the LC50 value; in rainbow trout, the acute NOEC and LC50 values were 0. 68 µg/L and 0.8 µg/L, respectively, and in bluegill sunfish, the acute NOEC and LC50 values were <2.2 µg/L and 2.2 µg/L, respectively. This indicates that toxic effects occur and progress rapidly once a certain pyrethroid concentration is exceeded. However, mortality may be delayed when exposure times are very short, on the order of several hours. For example, Floyd et al. (*43*) report significant effects on swimming ability of fathead minor larvae after 4-h exposures to 0.7 µg/L esfenvalerate, while no mortality occurred during this time at exposure concentrations up to 20 µg/L esfenvalerate. When delayed survival was measured after a 4-h exposure plus a 20-h recovery period in control water, the LC50 was 2.04 µg/L esfenvalerate.

In waterflea, the sublethal signs of pyrethroid toxicity include immobilization and decreased movement in response to stimulation. Acute NOEC values for the sublethal effects of cypermethrin range from 0.085 µg/L to 0.14 µg/L. Christensen et al. (*40*) showed that environmentally relevant, brief (6 h) exposures to 0.1 µg/L cypermethrin decreased feeding efficiency and swimming ability of *Daphnia magna*. Animals recovered after 3 days in clean water. A 30-min pulse exposure of *Gammarus pulex* to lambda-cyhalothrin (*41*) significantly impaired pair formation (pre-copula), with EC10 (30 min) and EC50 (30 min) values of 0.04 and 0.2 µg/L. Significant mortality was observed at 0.3 µg/L, with an LC50 (30 min) of 5.69 µg/L. Sublethal effects (lethargy, erratic swimming behavior, loss of equilibrium, and surfacing) of cypermethrin in estuarine/marine invertebrates were also reported in two studies of mysid shrimp (*39*): Acute NOEC values for sublethal effects range from 1.7 to 2.3 ng/L and are approximately 2 to 3-fold lower than the corresponding LC_{50} values of 5.5 and 5.9 ng/L, respectively.

Reproductive Toxicity and Endocrine Disruption

Pyrethroids were shown to have steroid receptor-binding activity *in vitro* (*14*). Their effects on the endocrine system are not uniform. While Fenpropathrin and permethrin act as weak estrogen agonists, allethrin and cypermethrin have antiestrogenic as well as antiandrogenic activity. Cyfluthrin and fenvalerate

showed very weak antiestrogenic activity, but several metabolites and products of environmental degradation of permethrin and cypermethrin had up to more than 100-fold greater potencies than the parent compound (*13, 14, 44*). In mammals, pyrethroids affect sperm concentration, motility and morphology (*10*).

In fish, Moore and Waring (*35*) demonstrated that the pyrethroid cypermethrin reduced the fertilization success in Atlantic salmon after a 5-day exposure to concentrations of 0.1 µg/L. In a study on bluegill sunfish, Tanner and Knuth (*45*) found delayed spawning and reduced larval survival after two applications of 1 µg/L esfenvalerate.

Day (*46*) showed that concentrations of <0.01 µg/L permethrin and other pyrethroids reduced reproduction and rates of filtration of food by daphnids. A concentration of 0.05 µg/L esfenvalerate also led to a significant decrease in reproductive success (number of neonates) of *Daphnia carinata* (*47*). Reynaldi and Liess (*48*) demonstrated that fenvalerate delayed the age at first reproduction in *Daphnia magna*, and reduced fecundity at a LOEC (lowest observed effect concentration) of 0.1 µg/L (complete mortality occurred at 1 µg/L). Population growth rate was inhibited at 0.6 µg/L (24 h), and recovery occurred after 21 d. Results of chronic toxicity studies in mysid shrimp show that exposure to cypermethrin had adverse effects on reproductive parameters: For a decrease in the number of young, a chronic NOEC value of 1.5 ng/L was reported in two studies (*39*).

Growth

Growth integrates a suite of biochemical and physiological effects into one endpoint that can often be associated with individual fitness. Results of chronic toxicity studies in mysid shrimp show that exposure to technical grade cypermethrin had adverse effects on growth parameters. For decreased growth and length, the chronic NOEC value reported was 0.78 ng/L. In a mesocosm study on bluegill sunfish, Tanner and Knuth (*45*) found that young-of-the-year growth was reduced by 57, 62 and 86% after two applications of 0.08, 0.2 and 1 µg/L esfenvalerate, respectively. Floyd et al. (*43*) showed that feeding and growth was significantly reduced in fathead minnow larvae exposed for 4 h to 0.7 µg/L esfenvalerate.

Immune System Effects

The immune response of fish and invertebrates plays a key role in the control of aquatic diseases, fitness and reproductive success. Pesticides are among those contaminants identified to cause immunosuppressive effects on fish (*49, 50*), but few studies have established the correlation between pyrethroids and disease resistance. Zelikoff et al. (*51*) found reduced disease resistance in fish exposed to the pyrethroid permethrin. Clifford et al. (*18*) demonstrated that the susceptibility of juvenile Chinook salmon to Infectious Hematopoietic Necrosis Virus (IHNV) was dramatically increased in fish exposed to 0.08 µg/L esfenvalerate. Eder et al. (*27*) found that exposure to 0.08 ppb esfenvalerate for 96 h altered the transcription of immune-system messenger molecules (cytokines) in juvenile Chinook salmon (*Oncorhynchus tshawytscha*). Cytokines regulate the innate and adaptive immune systems and are produced in response to infection or an inflammatory insult. Activation of interleukin-6, a key inflammatory cytokine, by cyfluthrin was also reported in human astrocytes (*52*).

Population Level Effects

Pyrethroids are generally of very low water solubility and high lipophilicity, and therefore are rapidly adsorbed to particulate material and other surfaces. Adsorption occurs on the order of hours in sediment-laden solutions under ideal laboratory mixing conditions (*53*) or in systems like farm ponds that contain relatively large amounts of organic matter (*54*); however, in typical streams, where less ideal mixing conditions exist, adsorption may occur over a period of days rather than hours (*55*). In the adsorbed state their bioavailability to aquatic organisms is reduced (*56, 57*). Therefore, for water column exposures field experiments of short duration or pulse exposure experiments are believed to be more environmentally realistic than LC50 data. Below we summarize the results of such field and pulse studies.

Field Studies

Studies on the effects of cypermethrin on fish in streams and ponds, where pyrethroid application rates ranged from 0.011 lb a.i./A (*58*) to 0.0623 lb a.i./A (*59, 60*), found no acute toxicity (expressed as mortality) on fish populations, but sublethal effects including loss of equilibrium, lethargy, and muscle tetany were reported following a single application of 0.011 lb a.i./A. Sublethal pathological

changes in fish were observed for 26 days following the application and were attributed to direct exposure to cypermethrin as well as to dietary exposure from ingestion of dead and dying invertebrates.

In field studies assessing the effects of cypermethrin on aquatic invertebrates and benthic populations, results show that exposure to cypermethrin at application rates to water surfaces ranging from 0.00025 lb a.i./A (*61*) to 0.125 lb a.i./A (*39*) caused significant decreases is abundance and diversity of aquatic invertebrate populations. Effects include catastrophic drift within 0-90 minutes after application of cypermethrin (*59, 62, 63*), and decreased abundance and diversity of macroinvertebrates over several weeks to several months (*61, 62, 64, 65, 66*). Plecoptera and ephemeroptera comprised 89-92% of the invertebrate drift immediately after spraying (*58*). Soon after treatment, concentrations of cypermethrin associated with the surface layer of the water column and emergent vegetation were much greater than those associated with deeper water and benthic sediment. Downward dispersion of cypermethrin was relatively limited. Only 8-16% of cypermethrin applied to the water surface was subsequently found in the water column (*59*).

Field studies on the effects of esfenvalerate also demonstrated detrimental effects on aquatic systems (2 ha pond) by reduction or elimination of many crustaceans, chironomids, juvenile bluegills and larval cyprinids at exposure levels of 1 µg/L (*45, 67*). Esfenvalerate exposures of 1 and 5 µg/L resulted in drastic reductions or elimination of most crustaceans, chironomids, juvenile bluegills (*Lepomis macrochirus*), and larval cyprinids. Abundance of some copepod and insect genera declined at esfenvalerate concentrations of 0.08 to 0.2 µg/L, and these effects were apparent up to 53 d. Some invertebrate communities were able to recover by day 25 in enclosures containing concentrations of less than or equal to 0.2 µg/L esfenvalerate (*67*).

Roessink et al. (*68*) compared the fate and effects of the pyrethroid insecticide lambda-cyhalothrin in mesotrophic (macrophyte-dominated) and eutrophic (phytoplankton-dominated) ditch microcosms (0.5 m^3). Lambda-cyhalothrin was applied three times at one-week intervals at concentrations of 10, 25, 50, 100, and 250 ng/L. The highest concentration was selected based on a 5% drift emission from a field application of 0.015 kg/ha of lambda-cyhalothrin (as "Karate" formulation) into a ditch with a depth of 0.3 m. The rate of dissipation of lambda-cyhalothrin in the water column of the two types of test systems was similar. After 24 h, 30% of the amount applied remained in the water phase. Initial, direct effects were observed primarily on arthropod taxa. Threshold levels for transient direct toxic effects were similar (10 ng/L) between the two mesotropohic and eutrophic test systems. At treatment levels of 25 ng/L and

higher, apparent population and community responses occurred. At treatments of 100 and 250 ng/L, the rate of recovery of the macroinvertebrate community was lower in the macrophyte-dominated systems, primarily because of a prolonged decline of the amphipod *Gammarus pulex*. This species occurred at high densities only in the macrophyte-dominated enclosures. Indirect effects (e.g., increase of rotifers and microcrustaceans) were more pronounced in the plankton-dominated test systems, particularly at treatment levels of 25 ng/L and higher.

Hill et al. (*69*) reviewed approximately 75 freshwater field studies with pyrethroid insecticides. The studies were carried out in natural/farm ponds, streams or rivers (bifenthrin, cyfluthrin, cypermethrin, deltamethrin, fenvalerate and permethrin), rice paddies (cypermethrin, lambda-cyhalothrin and permethrin), ponds for farming fish and crayfish (fenvalerate and permethrin), lake limnocorral enclosures (fenvalerate and permethrin), pond littoral enclosures (cypermethrin, esfenvalerate and permethrin) and outdoor pond microcosms or mesocosms (bifenthrin, cyfluthrin, cypermethrin, deltamethrin, esfenvalerate, lambda-cyhalothrin, permethrin and tralomethrin). The authors concluded that the spectrum of acute biological effects of these products in bodies of water, at application rates equivalent to a single "drift-entry" of 1-5% of the USA labeled maximum use-rate (applied as multiple treatments), is limited to the zooplankton and macroinvertebrate crustaceans and to some of the aquatic insects.

Van Wijngaarden et al. (*70*) reviewed 18 microcosm and mesocosm studies on eight pyrethroids (cyfluthrin, cypermethrin, deltamethrin, esfenvalerate, fenvalerate, lambda-cyhalothrin, permethrin and tralomethrin). The exposures included single and multiple applications; all except one were performed in stagnant systems. The authors concluded that recovery of sensitive endpoints usually occurs within 2 months of the last application when peak pyrethroid concentrations remain lower than (0.1 x EC50) of the most sensitive standard test species. Amphipoda and Hydacarina were the taxa most sensitive to pyrethroid insecticides, followed by Trichoptera, Copepoda, Ephemeroptera and Hemiptera (Table III).

Organism-Specific Factors Affecting Pyrethroid Toxicity

Critical Life Stages

Gender and reproductive stage will notably influence the effects of substances that interact with the endocrine system, such as synthetic pyrethroids and their breakdown products. An organism's trophic level will determine its susceptibility to predation after being negatively affected by contaminants. Behavioral characteristics (e.g. complex reproductive strategies) can modify the effects of toxic chemicals on the individual. However, information on life-stage or gender-specific susceptibility to pyrethroids is scarce. The available data suggests that toxicity is dose-related and that, in general, smaller organisms and earlier life-stages are more sensitive than larger and adult organisms. For example, <24-h old *Daphnia magna* (Cladocera) were about 10 times more sensitive to cypermethrin than 6-d old adult cladocerans (*19*). Calanoid copepod nauplii (*Acartia tonsa*) were 28 times more sensitive to cypermethrin than adults, with 96-h LC50s of 0.005 µg/L and 0.142 µg/L (measured concentrations) for nauplii and adults, respectively (*71*). In this study, gender differences were also observed: During the first 24 h of exposure, male adult copepods were about twice as sensitive as females.

Fish embryos appear to be less sensitive to pyrethroids than larvae. A study on the toxicity of lambda-cyhalothrin to Chinook salmon (*Onchorhynchus tsahwytscha*) showed no detectable effects on mortality, hatching success, or larval survival when embryos were exposed to nominal concentrations ranging from 0.3-5.0 µg/L during development. The estimated 96-h LC50 for Chinook salmon fry, on the other hand, was 0.15 µg/L (*72*); thus, Chinook salmon fry were at least 33 times more sensitive to lambda-cyhalothrin than embryos.The 48-h LC50 of deltamethrin for carp (*Cyprinus carpio*) embryos was 0.21 µg/L, while the respective LC50 for carp larvae was 0.074 µg/L (*73*). Similarly, topsmelt (*Atherinops affinis*) embryos survived 30-d exposure to 3.2 µg/L fenvalerate, while 0.82 µg/L fenvalerate caused complete mortality of exposed topsmelt fry (*74*). Later-stage (stage 34) medaka embryos were the most sensitive embryonal stage to cypermethrin, probably due to partial degradation of the chorion at this time in development (*75*).

Nutritional Status

Low nutritional status may result in increased susceptibility of organisms to pyrethroids. Barry et al. (*47*) showed that esfenvalerate toxicity to *Daphnia carinata* increased significantly with decreasing food concentration. Fenvalerate decreased survival and growth of *Daphnia magna* in the week following a 24-h

pulse exposure at 1.0 µg/L (*76*). Age at first reproduction increased, with adverse effects on fecundity. Low food conditions exacerbated the effects of fenvalerate exposure on juvenile survival and growth during the first week, and reduced the significant effect concentration from 0.6 µg/L (high food availability) to 0.3 µg/L. No mortality occurred during the 24-h fenvalerate exposure, but complete mortality was observed at 3.2 µg/L after a 6-d recovery period in control water.

Environmental Conditions and Pyrethroid Toxicity Relationship

Temperature

Water temperature is perhaps the most important factor affecting biochemical and physiological processes of individual organisms. It affects contaminant transformation and excretion rates. Temperature is inversely related to pyrethroid toxicity (*77*). This negative temperature dependence of pyrethroid action has in the past been ascribed to the slow metabolism of pyrethroids at low temperature. Recent studies showed that this effect is mostly due to the increased sodium current flow through (i.e., increased sensitivity of) nerve cell membranes at low temperature (*78*).

In natural aquatic systems, surface water temperature is often lower than standard laboratory toxicity testing temperatures. For example, the standard temperature for aquatic toxicity testing of sediment-dwelling invertebrates is 23^{o}C (*79*). This is well above temperatures in creeks that can serve as habitat for salmonids and other cold water fish species, for which preferred creek average temperatures are commonly below 20^{o}C (e.g., 14-17 ^{o}C for coho salmon, *80*).

Suspended Sediment

In their dissolved state, pyrethroids are readily bioavailable to aquatic organisms. In the adsorbed state their bioavailability to aquatic organisms is reduced. Yang et al. (*56*) showed that the presence of suspended sediment (200 mg/L) reduced toxicity of pyrethroids to *Ceriodaphnia dubia* by a factor of 2.5-13. However,

the degradation of pyrethroids bound to sediment particles is considerably slower than in soil. For example, the half-life of bifenthrin is reported to be 8-17 months (20°C) in sediments (*81*), and 42-96 days in soil (*82*).

Dabrowski et al. (*83*) conducted artificial stream microcosm trials by exposing mayfly nymphs (*Baetis harrisoni*) to 1 ppb of cypermethrin. Results demonstrated that exposure to cypermethrin increased mayfly drift significantly under either high turbidity (suspended particles) or high flow conditions, but drift was reduced in the presence of both increased flow and suspended particles.

Organic Matter

Yang et al. (*57*) showed that dissolved organic matter (DOM) at 10 mg/L reduced permethrin toxicity to *Ceriodaphnia dubia* as well as bioaccumulation by *Daphnia magna* by approximately a factor of 2.

Exposure Conditions

The exposure regime (concentration, duration and frequency) is an important factor affecting toxicity. Multiple brief exposures within a given time period to a specific contaminant concentration may not have the same toxic effect as one continuous exposure over the same time period. High magnitude exposures of short duration may be enough to cause population level impacts, while low magnitude, long duration exposures may have no impact at all.

Forbes and Cold (*84*) found that even very brief (1-h) exposures to environmentally realistic concentrations of esfenvalerate during early larval life-stages of the midge *Chironomus riparius* can have measurable population level effects on larval survival and development rates. For surviving organisms, no lasting effects on fecundity or egg viability were observed. Brief (30 min) pulse exposures to lambda-cyhalothrin (nominal conc. 0.05-10 µg/L; *85*) in an in-stream mesocosm study demonstrated that macroinvertebrate drift increased significantly after each exposure. *Gammarus pulex*, Ephemeroptera and Simuliidae were predominantly affected. Structural change in the community was found at 5 and 10 µg/L, and recovery occurred within approximately two weeks.

Joint Interactions with Other Chemicals and Stressors

Pre-exposure or simultaneous exposure to other contaminants, disease or stressful environmental conditions such as salinity and temperature may considerably alter the physiological condition and therefore susceptibility of the organism, as well as modify the toxicity of a given contaminant. Organisms in the environment often experience many stressors simultaneously, including those of a physical, biological, and chemical nature (*24*). Chemical analysis of surface water conducted by the U.S. Geological Survey under the National Water Quality Assessment Program indicates that pesticide mixtures are contaminating surface waters. More than 50% of all stream samples tested contained five or more pesticides (*86*). In addition, many other contaminants such as heavy metals, PAHs and PCBs are often present in aquatic environments. When large numbers of chemicals are included in the mixture experiments, an additive response is typically found (*24*). It is therefore evident that mixtures must be considered to be the most common exposure scenario when evaluating the ecological effects of contaminants.

PBO

The synergist piperonyl butoxide (PBO) is commonly added to pyrethroid and pyrethrin formulations to enhance the toxic effects of the active ingredient. PBO functions by inhibiting a group of enzymes (mixed-function oxidases), which are involved in pyrethroid detoxification. PBO can enhance the toxicity of pyrethroids by 10-150 times (*87*). Recently, 3-4-fold enhancement of pyrethroid toxicity to amphipods has been reported (*88*). The 96-h LC50 of PBO for rainbow trout is 2.4 ppb (*89*). PBO in concentrations less than 1 ppm can reduce fish egg hatchability and growth of juvenile fish**.** Weston et al. (*90*) demonstrated that PBO concentrations in urban creeks after watershed-wide treatment with a pyrethrins/PBO mixture were high enough to enhance toxicity of pyrethroids already existing in creek sediments from general urban pesticide use, effectively "reactivating" pyrethroids already present in the environment. In a study on juvenile (90 d old) striped bass (*Morone saxitalis*), Rebach (*91*) determined 24-h and 96-h LC50s of 32.9 and 16.4 ppb for a 1:1 mixture of PBO and permethrin. No LC50 information for this species is available for permethrin alone.

Pesticide Formulations

Inert ingredients of various pesticide formulations, such as emulsifiers, solvents and surfactants may influence the environmental fate, mobility and the toxicity of pyrethroids. Overall, water-insoluble pesticides applied in emulsion formulations have higher storm- and irrigation runoff potential than water-soluble pesticides (*92, 93*). In a study on stormwater runoff from a stonefruit orchard treated with esfenvalerate in formulation (Asana), runoff from the first storm after application was highly toxic to fathead minnow and rainbow trout larvae, and toxicity to invertebrates was still present in runoff from the third storm after application (*94, 95*). In addition to increasing the risk of exposure, inert ingredients may be biologically active (*96*). For example, a household formulation of bifenthrin reduced the viability of rodent nerve cell cultures, wheres bifenthrin alone did not (*97*). Commercial formulations of bifenthrin (Talstar, Kiros EV) were more toxic to human cell cultures than bifenthrin alone (*98*). In a comparative study on the toxicity of two commercial formulations of permethrin on brook trout (*Salvelinus fontinalis*), Permanone 31-66TM, a permethrin formulation containing 31.28% w/w permethrin and 66% w/w PBO, was almost three times more toxic than Permanone Technical InsecticideTM, which is >92% w/w permethrin (*99*).

Pyrethroid-Other Insecticides

According to the published literature the toxicity of many pesticide combinations is at least additive. In some cases pesticide mixtures, particularly those involving insecticides, have been shown to be synergistic, with reported increases in toxicity of up to 100-fold (*100*). However, these effects are species, time and dose dependent and are therefore difficult to predict routinely. For pyrethroid – organophosphate (OP) mixtures, greater than additive toxicity is to be expected given that P450-activated OPs will inhibit esterases, thus decreasing an organism's ability to detoxify pyrethroids. OPs are increasingly used in combination with pyrethroids because they can synergistically increase the effects of pyrethroids, expecially where pest populations have developed resistance (Perry et al., 2006). Denton et al. (*101*) demonstrated that exposure to the pyrethroid esfenvalerate and the OP diazinon resulted in greater than additive toxicity in fathead minnow larvae. Similarly, mixtures of esfenvalerate and the OP chlorpyrifos resulted in greater than additive toxicity in fathead minnow (*102*). Synergistic toxic effects have also been observed between pyrethroids and

carbamates. Permethrin and the carbamate propoxur elicited greater than additive toxicity in the mosquito *Culex quinquefasciatus* (*103*).

Pyrethroid-Infectious Agents

Clifford et al. (*18*) showed that susceptibility of juvenile Chinook salmon to Infectious Hematopoietic Necrosis Virus (IHNV) was significantly increased when 6-week old fish were exposed to a sublethal concentration of esfenvalerate (0.08 ppb). Of juveniles exposed to both esfenvalerate and to IHNV, 83% experienced highly significant ($p<0.001$) mortality ranging from 20% to 90% at 3 days post-viral exposure. This early mortality was not seen in any other treatment group. In addition, fish exposed to both esfenvalerate and IHNV died 2.4 to 7.7 days sooner than fish exposed to IHNV alone. Results from this study show that accepted levels of pollutants may not cause acute toxicity in fish, but may be acting synergistically with pathogens to compromise survivorship of fish populations through immunologic or physiologic disruption.

Summary

Aquatic organisms, in particular insects, crustaceans and fish, are highly sensitive to pyrethroid insecticides. Acute toxicity to fish and aquatic invertebrates is generally observed at concentrations below 1 µg/L, and sublethal effects have been reported at low ng/L concentrations. Although it is difficult to model sublethal responses to toxicants and predict ecotoxicological impact or risk, measures of sublethal effects are likely to be as important, or more important, than the measures of acute or chronic lethal effects to accurately assess the consequences of contaminant exposure. The primary mechanism of toxic action is often not the only toxic effect a chemical can exert on target and non-target species. For example, neurotoxic pesticides may impair the immune system or exhibit hormonal effects, or can alter behavior with negative effects on predator avoidance or reproductive success. Many of these chemical side effects are poorly understood or unknown.

Although toxic concentrations of pyrethroids in sediments of surface waters have been reported, there is presently limited information on their temporal and spatial distribution, as well as concentrations of pyrethroids in the water column. One of the major limitations for obtaining data on the sources and quantities of

pyrethroids in the environment, in particular in water samples, is the sensitivity of the existing analytical chemistry techniques. Because pyrethroids are toxic at extremely low concentrations (low to mid parts per trillion range) monitoring data that are based on insufficiently low detection limits are of little use. In fact, such data can convey a false sense of safety with regard to the potential toxic effects of pyrethroid contamination on aquatic ecosystems, especially if multiple pyrethroids are present simultaneously. Due to their relatively short half-lives and hydrophobic nature, pyrethroid concentrations in larger water bodies are expected to be generally ephemeral, especially in the water column. Higher toxicity and reduced degradation rates at low temperatures may render pyrethroids a greater risk to aquatic life during the winter period, which—along with winter rains and associated stormwater runoff —has the potential to make winter applications of pyrethroids more important environmentally than summer applications.

Critical data gaps on pyrethroids exist. To provide much needed information the following questions should be answered in future work: How do sublethal toxic effects affect the ecological fitness of organisms and populations? - Do pyrethroids interact with other stressors or chemical contaminants to induce toxicity? – What are the effects of inert ingredients in pyrethroid formulations on toxicity and environmental fate and transport?

References

1. Smith, T.M.; Stratton, G.W. *Residue Reviews* 1986, 97:93-120.
2. Clark, J.R.; Goodman, L.R.; Borthwick, P.W.; Patrick, J.M.Jr.; Cripe, G.M.; Moody, P.M.; Moore, J.C.; Lores; E.M. *Environ. Toxicol. Chem*. 1989, 8:393-401.
3. Bradbury, S.P.; Coats, J.R. *Environ. Toxicol. Chem*. 1989, 8:373-380.
4. Shafer, T.J.; Meyer, D.A. *Toxicol. Appl. Pharmacol.* 2004, 196 (2): 303-318.
5. Liu W.P., Gan J.Y., Lee S., Werner I. *Environ. Toxicol. Chem.* 2005, 24(8):1861-1866.
6. Burr, S.A.; Ray, D.E. *Toxicol. Sci.* 2004, 77 (2): 341-346.
7. Hossain, M.M.; Suzuki, T.; Sato, I.,; Takewaki, T.; Suzuki, K.; Kobayashi, H. *Toxicol. Appl. Pharmacol*. 2004, 197 (3): 319-320 729.
8. Litchfield, M.H. In *The Pyrethroid Insecticides;* Leahay, J.P.; Ed.; Taylor & Francis, Philadelphia, PA, USA, 1985; pp 99–150.
9. Go, V.; Garey, J.; Wolff, M.S.; Pogo, B.G.T. *Environ. Health Perspect*. 1999, 107:173-177.

10. Perry, M.J.; Venners, S.A.; Barr, D.B.; Xu, S. 2006. *Reproduct. Toxicol*. 2007, 23(1):113-118.
11. Chen, J.F; Chen, H.Y.; Liu, R.; He, J.; Song, L.; Bian, Q.; Xu, L.C.; Zhou J.W.; Xiao, H.; Dai, G.D.; Wang, X.R. *Biomed. Environ. Sci*. 2005, 18(2):108-116.
12. Kim, S.S.; Lee, R.D.; Lim, K.J.; Kwack, S.J.; Rhee, G.S.; Seok, J.H.; Lee, G.S.; An, B.S.; Jeung, E.B.; Park, K.L. *J. Reprod. Develop*. 2005, 51(2):201-210.
13. Sun, H.; Xu, X.-L.; Xu, L.-C.; Song, L.; Hong, X.; Chen, J.-F.; Cui, L.-B.; Wang, X.-R. *Chemosphere* 2007, 66 (3): 474-479.
14. Tyler, C.R.; Beresford, N.; Van Der Woning, M.; Sumpter, J.P.; Thorpe, K. *Environ. Toxicol. Chem.* 2000, 19(4):801-809.
15. Agarwal, D.K.; Chauhan, L.K.S.; Gupta, S.K.; Sundararaman, V. *Mutation Research* 1994, 311:133-138.
16. Kale, M.; Rathore, N.; John, S.; Bhatnagar, D. 1999. *Toxicol. Lett.* 1999, 105:197-205.
17. Madsen, C.; Claesson, M.H.; Ropke, C. *Toxicol.* 1996, 107:219-227.
18. Clifford, M.A.; Eder, K.J.; Werner, I.; Hedrick, R.P. *Environ. Toxicol. Chem*. 2005, 24:1766-1772.
19. Sherratt, T.N.; Roberts, G.; Willliams, P.; Whitfield, M.; Biggs, J.; Shillabeer, N.; Maund, S.J. *Environ. Toxicol. Chem.* 1999, 18(11):2512-2518.
20. Lozano, S.J.; O'Halloran, S.L.; Sargent, K.W.; Brazner, J.C. *Environ. Toxicol. Chem.* 1992, 11(1):35-47.
21. California Department of Fish and Game (CDFG), Hazard assessment of the synthetic pyrethroid insecticides bifenthrin, cypermethrin, esfenvalerate, and permethrin to aquatic organisms in the Sacramento-San Joaquin River System. Administrative Report 00-06, California Department of Fish and Game, Office of Spill Prevention and Response, Sacramento, California, USA, 2000.
22. U.S. Environmental Protection Agency (USEPA), Guidelines for deriving numerical national water quality criteria for the protection of aquatic organisms and their uses. Office of Research and Development, Washington, D.C., USA, 1985.
23. Carson, R. *Silent Spring*; Houghton Mifflin Publishers, Boston, MS, USA, 1962; 368 pp.
24. Lydy, M.; Belden, J.; Wheelock, C.; Hammock, B.; Denton, D. *Ecol. Soc*. 2004, 9(6): 1.
25. Feder, M.E.; Hofmann, G.E. In *Annual Review of Physiology;* Hoffman, J.F., Ed.; Annual Reviews Inc.: Palo Alto, CA, USA, 1999; Vol. 61, pp 243-282.
26. *Biomarkers: Biochemical, Physiological and Histological Markers of Anthropogenic Stress*; Huggett, R.J.; Kimerle, R.A.; Mehrle, Jr. P.M.;

Bergman, H.L.; Eds.; Lewis Publishers, Boca Raton, FL, USA, 1992; pp. 346.
27. Eder, K.J.; Leutenegger, C.M.; Wilson, B.W.; Werner, I. *Mar. Environ. Res.* 2004, 58:809-813.
28. Eder, K.J.; Koehler, H.-R.; Werner, I. *Environ. Toxicol. Chem.* 26(6):1233-1242.
29. Teh, S.J.; Deng, D.F.; Werner, I.; Teh, F.C.; Hung, S.S.O. 2004. *Mar. Environ. Res.* 2004, 59:203-216.
30. Werner, I.; Geist, J.; Okihiro, M.; Rosenkranz, P.; Hinton D.E. *Environ. Res.* 2002, 54:609-614.
31. Werner, I.; Linares-Casenave, J.; Van Eenennaam, J.P.; Doroshov, S.I. *Environ. Biol. Fish* 2006, DOI 10.1007/s10641-006-9070-z.
32. Viant, M.R.; Werner, I.; Rosenblum, E.S.; Gantner, A.S.; Tjeerdema, R.S.; Johnson, M.L. *Fish Physiol. Biochem.* 2004, 29:159-171.
33. Jee, J.H.; Masroor, F.; Kang, J.C. *Aquaculture Res.* 2005, 36 (9), 898-905
34. Moore, A.; Waring, C.P. *Aquat. Toxicol.* 2001, 52:1-12.
35. Mishra, D.; Srivastav, S.K.; Srivastav, A.K. *Ecotox. Environ. Safety* 2005, 60(2):193-197.
36. Denton, D.L. Ph.D. thesis. University of California, Davis, CA, USA, 2001.
37. Haya, K.; Waiwood, B.A. In *Aquatic Toxicology;* Nriagu, J.O.; Ed; Wiley, New York, NY, USA, 1983; pp 307-333.
38. Wedemeyer, G.A.; Barton, B.A.; McLeay, D.J. In *Methods for Fish Biology ;* Schreck C.B. ; Moyle, P.B, ; Eds. ; American Fisheries Society, Bethesda, MD, USA, 1990 ; pp 451-489.
39. U.S. Environmental Protection Agency (USEPA), 2005. EFED Risk Assessment for the Reregistration Eligibility Decision (RED) on Cypermethrin. (values reflect corrections in June 9 2006 "Addendum to the EFED RED Chapter for Cypermethrin").
40. Christensen, B.T.; Lauridsen, T.L.; Ravn, H.W.; Bayley, M. *Aquat. Toxicol.* 2005, 73(2):210-220.
41. Heckmann, L.H.; Friberg, N.; Ravn, H.W. *Pest Managem. Sci.* 2005, 61(7):627.
42. Little, E.E.; Finger, S.E. *Environ. Toxicol. Chem.* 1990, 9 (1): 13-19.
43. Floyd, E.Y.; Geist, J.P.; Werner, I. *Environ. Toxicol. Chem.* In review.
44. McCarthy, A.R.; Thomson, B.M.; Shaw, I.C.; Abell, A.D. *J. Environ. Monit.* 2005, 8:197-202.
45. Tanner, D.K.; Knuth, M.L. *Arch. Environ. Contam. Toxicol.* 1996, 31:244-251.
46. Day, K. E. 1989. *Environ. Toxicol. Chem.* 1989, 8, 411-416
47. Barry, M.J.; Logan, D.C.; Ahokas, J.T.; Holdway, D.A. *Ecotoxicol. Environ. Safety* 1995, 32( )3, 273-279.
48. Reynaldi, S.; Liess, M. *Environ. Toxicol. Chem.* 2005, 24(5):1160-1164.

49. Banerjee, B.D. *Toxicol. Lett*. 1999, 107:21-31.
50. Austin, B. *J. Appl. Microbiol*. 1999, 85:234S-242S.
51. Zelikoff, J.T. 1998. *Toxicol.* 1998, 129:63-71.
52. Mense, S.M.; Sengupta, A.; Lan, C.; Zhou, M.; Bentsman, G.; Volsky, D.J.; Whyatt, R.M.; Perera, F.P.; Zhang, L. *Toxicol. Sci*. 2006, 93(1):125-135.
53. Maund, S.J.; Hamer, M.J.; Lane, M.C.G.; Farrelly, E.; Rapley, J.H.; Goggin, U.M.; Gentle, W.E. *Environ. Toxicol. Chem.* 2002, 21 (1): 9-15.
54. *The Pyrethroid Insecticides*; Leahy, J.P.; Ed.; Taylor & Francis, Philadelphia, PA, USA, 1985.
55. Capel, P.D.; Larson, S.J.; Winterstein, T.A. *Hydrological Processes* 2001, 15: 1251-1269.
56. Yang, W.; Spurlock, F.; Liu, W.; Gan, J. *Environ. Toxicol. Chem*. 2006, 25(7):1913-1919.
57. Yang, W.; Spurlock, F.; Liu, W.; Gan, J. 2006b. *J. Agric. Food Chem*. 2006, 54(11):3967-3972.
58. Davies, P. E.; Cook, L. S. J. *Aquat. Toxicol*. 1993, 27(3-4), 201-24.
59. Crossland, N. O. *Aquat. Toxicol*. 1982, 2(4), 205-22.
60. Crossland, N.O.; Shires S.W.; Bennett D. *Aquat. Toxicol*. 1982, 2:253-270.
61. Mulla, M.S.; Navvab-Gojrati, H.A.; Darwazeh, H.A. *Mosquito News* 1978, 38(1):90-96.
62. Farmer, D.; Hill, I.R.; Maund, S.J. *Ecotoxicology* 1995, 4(4):219-244.
63. Mohsen, Z.H.; Mulla, M.S. *Environ. Entomol*. 1982, 11(2):390-398.
64. Kedwards, T.J.; Maund, S.J.; Chapman, P.F. *Environ. Toxicol. Chem.* 1999, 18(2):149-157.
65. Kedwards, T.J.; Maund, S.J.; Chapman, P.F. *Environ. Toxicol. Chem.* 1999, 18(2):158-166.
66. Mulla, M.S.; Darwazeh, H.A.; Ede L. *Mosqito News* 1982, 42(4):583-590.
67. Lozano, S.J.; O'Halloran, S.L.; Sargent, K.W.; Brazner, J.C. *Environ. Toxicol. Chem.* 1992, 11(1):35-47.
68. Roessink, I. G.; Arts, H.P.; Belgers, J. D. M.; Bransen, F.; Maund, S. J.; Brock, T. C. M. *Environ. Toxicol. Chem.* 2005, 24(7):1684–1696.
69. Hill, I.R.; Shaw, J.L.; Maund, S.J. In *Freshwater Field Tests Hazard Assess. Chem., [Proc. Eur. Workshop Freshwater Field Tests];* Hill I.R.; Ed.; Lewis Publisher, Boca Raton, FL, USA, 1994; pp 249-71.
70. Van Wijngaarden, R.P.A.; Brock, T.C.M.; Van den Brink, P.J. *Ecotoxicology* 2005, 14(3):355-380.
71. Medina, M.; Barata, T.; Telfer, C.; Baird, D.J. 2002. *Arch. Environ. Contam. Toxicol*. 2002, 42:17-22.
72. Phillips, J.P. Master's thesis, University of California, Davis, CA, USA, 2005.
73. Koprucu, K.; Aydin, R. *Pestic. Biochem. Physiol.* 2004, 80(1):47-53.

74. Goodman, L.R.; Hemmer, M.J.; Middaugh, D.P.; Moore, J.C. *Environ. Toxicol. Chem.* 1992, 11:409-414.
75. Gonzalez-Doncel, M.; Fernandez-Torija, C.; Hinton, D.E.; Tarazona, J.V. *Arch. Environ. Contam. Toxicol*. 2005, 48(1):87-98.
76. Pieters, B. J.; Paschke, A.; Reynaldi, S.; Kraak, M.H.S.; Admiraal, W.; Liess M. *Environ. Toxicol. Chem.* 2005, 24(9):2254–2259.
77. Motomura, H.; Naharashi, T. *J. Membrane Biol*. 2000, 177:23-39.
78. Narahashi, T.; Ginsburg, K.S.; Nagata, K.; Song, J.H.; Tatebayashi, H. *Neurotoxicol*. 1998, 19(4-5):581-90.
79. U.S. Environmental Protection Agency (USEPA), Methods for Measuring the Toxicity and Bioaccumulation of Sediment-Associated Contaminants with Freshwater Invertebrates. EPA 600/R-99/064. Second Edition, 2000.
80. Sullivan, K.; Martin, D.J.; Cardwell, R.D.; Toll, J.E.; Duke, S. 2000. An analysis of the effects of temperature on salmonids of the Pacific Northwest with implications for selecting temperature criteria. Sustainable Ecosystems Institute, Portland, Oregon, USA; URL http://www.sei.org (June 2007).
81. Gan, J.; Lee, S.; Liu, W.; Haver, D.; Kabashima, J. *J. Environ. Qual.* 2005, 34:836-841.
82. Laskowski, D.A. *Rev. Environ. Contam. Toxicol.*, 2002, 174:49-170.
83. Dabrowski, J.M.; Bollen, A.; Schulz, R. *Environ. Toxicol. Chem.* 2005, 24(6):1395–1402.
84. Forbes, V.E.; Cold, A. *Environ. Toxicol. Chem.* 2005, 24(1):78-86.
85. Heckmann, L.H.; Friberg, N. *Environ. Toxicol. Chem.* 2005, 24(3):582-590.
86. U.S. Geological Survey (USGS). Pesticides in surface and ground water of the United States: summary of the results of the National Water Quality Assessment Program (NAWQA). U.S. Geological Survey, Washington, D.C., USA, 1998.
87. Wheelock, C.E.; Miller, J.L.; Miller, M.J.; Gee, S.J.; Shan, G.; Hammock, B.D.; *Environ. Toxicol. Chem*. 2004, 23(11):2699–2708.
88. Amweg, E.L.; Weston, D.P.; Johnson, C.S.; You, J.; Lydy, M.J. *Environ. Toxicol. Chem*. 2006, 25(7):1817-1825.
89. U.S. Environmental Protection Agency (USEPA), Ecotox (Acquire) database: http://www.epa.gov/ecotox/, accessed October 2005.
90. Weston, D.P.; Amweg, E.L.; Makebri, A.; Ogle, R.S.; Lydy, M .J. *Environ. Sci. Technol.* 2006. 40(18): 5817-5822.
91. Rebach, S. *Bull. Environ. Contam. Toxicol*. 1999, 62:448-454
92. Wauchope, R.D. *J. Environ. Qual*. 1978, 7(4): 459-472.
93. Moran, K. Insecticide Market Trends and Potential Water Quality Implications. Report for the San Francisco Estuary Project. TDC Environmental, San Mateo, CA, USA; URL http://tdcenvironmental.com/Pesticides.html, 2003.

94. Werner, I.; Deanovic, L.A.; Hinton, D. E.; Henderson, J. D.; Oliveira, G.H.; Wilson, B.W.; Osterli, P.; Krueger, W.; Wallender, W. W.; Oliver, M. N.; Zalom, F. G. *Bull. Environ. Contam. Toxicol*. 2002, 68(1):29-36.11.
95. Werner, I.; Zalom, F.G.; Oliver, M.N.; Deanovic, L.A.; Kimball, T.; Henderson, J.D.; Wilson, B.W.; Krueger, W.; Wallender, W.W. *Environ. Toxicol. Chem*. 2004, 23(11):2719-2726.
96. Cox, C.; Surgan, M. *Environ. Health Perspect*. 2006, 114(12):1803-1806.
97. Tran, V.; Hoffman, N.; Mofunanay, A.; Pryor, S.C.; Ojugbele, O.; McLaughlin, A. 2006. *Med. Sci. Monitor* 2006,12:BR57-62.
98. Skandrani, D.; Gaubin, Y.; Vincent, C.; Beau, B.; Murat, J.C.; Soleilhavoup, J.-P.; Croute, F. Relationship between toxicity of selected insecticides and expression of stress proteins (HSP, GRP) in cultured human cells: Effects of commercial formulations versus pure active molecules. *Biochimica et Biophysica Acta* 2006, 1760:95-103.
99. Paul, E.A.; Simonin, H.A.; Tomajer, T.M. *Arch. Environ. Contam. Toxicol.* 2005, 48:251-259.
100. Thompson, H.M. *Ecotoxicology* 1996, 5, 59-81.
101. Denton, D.; Wheelock, C.; Murray, S.; Deanovic, L.; Hammock, B.; Hinton, D. *Environ. Toxicol. Chem.* 2003, 22:336-341.
102. Belden, J.B.; Lydy, M.J. *Environ. Toxicol. Chem*. 2006, 25(2):623-629.
103. Corbel, V.; Raymond, M.; Chandre, F.; Darriet, F.; Hougard, J.M. *Pest Management Science* 2004, 60 (4): 375-380.
104. California Department of Pesticide Regulation (DPR), Ecotox Database; URL http://dpr.ca.gov, 2007.
105. PAN (Pesticide Action Network) Pesticides Database; URL http://www.pesticideinfo.org/Index.html, 2007.
106. Schroer, A.F.W.; Belgers, J.D.M.; Brock, T.C.M.; Matser, A.M.; Maund, S.J.; Van den Brink, P.J. *Arch. Environ. Contam. Toxicol*. 2004, 46 (3): 324-335.
107. Anderson, B.S.; Phillips, B.M.; Hunt, J.W.; Worcester, K.; Adams, M.; Kapellas, N.; Tjeerdema, R.S. *Environ. Toxicol. Chem.* 2006, 25:1160-1170.
108. Paul, E.A.; Simonin, H.A. Toxicity of three mosquito insecticides to crayfish. *Bull. Environ. Contam. Toxicol*. 2006, 76:614-621.
109. Little, E.E.; Dwyer, F.J.; Fairchild, J.F.; DeLonay, A.J.; Zajicek, J.L. *Environ. Toxicol. Chem.* 1993, 12:871-878.
110. Hansen, D.J.; Goodman, L.R.; Moore, J.C.; Higdon, P.K. *Environ. Toxicol. Chem.* 1983, 2:251-258.

Table I. Summary of aquatic toxicity data for selected pyrethroids (lowest values).

Species	Lambda-Cyhalothrin		Bifenthrin		Cyfluthrin		Cypermethrin		Deltamethrin		Esfenvalerate		Permethrin	
	Test	µg/L	Test	µg/L	Test	µg/L	Test	µg/L	Test	µg/L	Test	µg/L	Test	µg/L
Invertebrates														
Waterflea, *Ceriodaphnia dubia*			48-h LC50	0.07	48-h LC50	0.14					96-h LC50[4]	0.3	48-h LC50	0.55
Waterflea, *Daphnia magna*	48-h EC50[7] 21-d NOEC[7]	0.36 0.002	48-h LC50 48-h EC50	0.32 1.6	48-h LC50 48-h EC50	0.17 0.025	24-h LC50 48-h LC50[3] 48-h EC50	0.53 0.13 1.00	24-h LC50 48-h LC50 96-h LC50 96-h EC50	0.11 0.037 0.01 0.003	48-h LC50[1] 48-h LC50 48-h EC50	0.24 0.27 0.15	48-h LC50[1] 72-h LC50 96-h LC50 96-h EC50	0.075 6.8 0.3 0.039
Waterflea, *Daphnia pulex*													3-h LC50 48-h LC50 72-h LC50	9,200 2.75 0.08
Copepod, *Cyclops* sp.	48-h EC50[7]	0.3												
Mayfly, *Hexagenia bilineata*													96-h LC50[3]	0.1
Mayfly, *Procloeon* sp.			48-h LC50[9]	0.084									48-h LC50[9]	0.090
Mayfly, *Cloeon dipterum*	48-h EC50[7]	0.038					72-h EC50[3] 96-h LC50[3]	0.006 0.023 0.03						
Isopod, *Asellus aquaticus*	48-h EC50[7]	0.026					72-h LC50[3]	0.008						
Midge, *Chironimus dilutus*			96-h LC50[9]	26.15									96-h LC50[9]	10.45
Midge, *Chironimus riparius*	48-h EC50[7]	2.4					48-h LC50[3]	0.007						
Midge, *Chironimus plumosus*													48-h EC50[3]	0.56
Grass shrimp, *Palaemonetes pugio*							96-h LC50[3]	0.016						

Oligochaeta							48-h LC50[11]	>100						
Hyalella azteca	48-h EC50[7]	0.0023	96-h LC50[9]	0.009			48-h LC50[3]	0.005			42-D LOEC 96-h LC50[6]	0.05 0.008	96-h LC50[9]	0.021
Gammarus pulex	48-h EC50[7] 0.5-h LC50[8]	0.014 5.69												
Gammarus daiberi											96-h LC50[6]	0.033		
Gammarus pseudolimnaeus													96-h LC50[3]	0.17
Crayfish, *Orconectes immunis*													96-h LC50[10]	0.08
Mysid shrimp (B) *Americamysis bahia*			96-h LC50	0.004	96-h LC50	0.00242	96-h LC50	0.005	96-h LC50	0.0017	96-h LC50[1]	0.038	96-h LC50[3]	0.02
Pink shrimp (S, juv.), *Penaeus duorarum*							96-h LC50[3]	0.036					96-h LC50[3]	0.22
Stone crab (S), *Menippe mercenaria*													96-h EC50[3]	0.018
Fiddler crab (S), *Uca pugilator*													96-h LC50[3]	2.39
Penaeus sp. (S)							96-h LC50	0.036					96-h LC50	0.17
Oyster, *Crassostrea virginica* (S, B)			48-h EC50 (embryo)	285	96-h EC50	2.69	96-h EC50	370	96-h EC50	8.2			48-h EC50 96-h EC50	1000 40.7
Oyster, *Crassostrea gigas* (S, B)	48-h EC50[2] (larvae)	590.00					48-h LC50	2,270					48-h EC50	1,050

Sources: All unmarked values from (*89*); [1] (*104*); [2] (*105*); [3] (*21*); [4] (*94*); [5] (*27*); [6] Werner I., unpublished data; [7] (*106*); [8] (*41*); [9] (*107*); [10](*108*); [11](*19*)
(S) saltwater species
(B) brackish water species

Table 1 (continued). Summary of aquatic toxicity data for selected pyrethroids (lowest values).

Species	Lambda-Cyhalothrin		Bifenthrin		Cyfluthrin		Cypermethrin		Deltamethrin		Esfenvalerate		Permethrin	
	Test	µg/L	Test	µg/L	Test	µg/L	Test	µg/L	Test	µg/L	Test	µg/L	Test	µg/L
Vertebrates														
Fathead minnow *Pimephales promelas*	96-h LC50[7]	0.70	96-h LC50[1]	0.26	96-h LC50[1]	2.49					24-h LC50 48-h LC50 96-h LC50	0.24 0.24 0.22	24-h LC50 96-h LC50[1]	5.4 2
Rainbow trout *Oncorhynchus mykiss*	96-h LC50[2] 96-h LC50[2]	0.54 0.24	96-h LC50	0.15	48-h LC50 96-h LC50	0.57 0.3	12-h LC50 24-h LC50 48-h LC50 96-h LC50	2.5 5 5 0.39	24-h LC50 48-h LC50 96-h LC50	0.7 0.5 0.25	96-h LC50[1] 96-h LC50	0.26 0.07	24-h LC50 48-h LC50 96-h LC50	4.3 6 0.62
Carp, *Cyprinus carpio*	96-h LC50[7]	0.50					96-h LC50[3]	0.9						
Mosquitofish, *Gambusia affinis*	24-h LC50[2] 24-h LC50[2]	0.18 0.08												
Atlantic salmon *Salmo salar*													96-h LC50[3]	17
Chinook salmon, *Onchorynchus tshawytscha*											96-h LC50[5]	0.1-1.0		
Coho salmon, *O. kisutch*													96-h LC50[3]	3.2
Brook trout, *Salvenlinus fontinalis*													24-h LC50 96-h LC50[3]	4 3.2
Sacramento splittail, *Pogonichthys macrolepidotus*											96-h LC50[4]	0.50		
Sheepshead minnow (S) *Cyprinodon variegatus*	28-d NOEC[7]	0.25	96-h LC50[3]	17.8	96-h LC50	4.05	96-h LC50	0.73	96-h LC50	0.36	96-h LC50[1]	430	96-h LC50	7.8
Atlantic													96-h LC50[3]	2.2

silverside, (S) *Menidia menidia*														
Inland silverside, (S) *Menidia beryllina*													96-h LC50	27.5
Bluegill (S),	96-h LC50	0.42	144-h LC50[3]	0.35	96-h LC50	0.87	96-h LC50[3]	1.78	96-h LC50	0.36	96-h LC50[1]	0.26	24-h LC50	6.6
Lepomis macrochirus	96-h LC50	0.21											96-h LC50[3]	2.5
Plants														
Selenastrum capricornutum	96-h EC50[7]	>1000												
Skeletonema costatum														

Source: All unmarked values from (*89*); [1] (*104*); [2] (*105*); [3] (*21*); [4] (*94*); [5] (*27*); [6] Werner I., unpublished data; [7] (*106*)
(S) saltwater species
(B) brackish water species

RESERVE THIS SPACE

Table II. Reported sublethal effects of several several pyrethroids on aquatic species.

Pyrethroid	Species	Life-Stage/Test Duration	Effect	Effect Concentration (µg/L)	Source
Lambda-Cyhalothrin	*Gammarus pulex*	Adult/ 30 min	EC10 (Pair formation) EC50 (Pair formation)	0.04 0.20	(*41*) “
Cypermethrin	*Daphnia magna*	Adult/6 h	LOEC (Decrease in feeding efficiency and swimming ability)	0.1	(*40*)
	Mysid shrimp, *Americamysis bahia*	28 d	LOEC (fecundity) NOEC (fecundity) LOEC (growth)	0.0028 0.0015 0.00078	(*39*) “ “
	Fathead minnow, *Pimephales promelas*	Larvae/30 d	LOEC (growth) NOEC (growth)	0.33 0.15	(*21*) “
	Rainbow trout, *O. mykiss*	-	LOEC (behavior)	0. 68	(*39*)
	Bluegill sunfish, *Lepomis macrochirus*	-	LOEC (behavior)	<2.2	(*39*)
	Atlantic salmon, *Salmo salar*	Gamets/5 d Adult/5 d	LOEC (fertilization success) Impaired olfactory function	0.1 <0.004	(*34*) “
	Korean rockfish, *Sebastes schlegeli*	52 g/8 wk	Changes in blood parameters	0.041	(*33*)
Esfenvalerate	*Daphnia carinata*	Adult	Reduced fecundity	0.05	(*47*)
	Midge, *Chironomus tentans*	Larvae/14-16 d	EC10 Mobility EC50 Mobility	0.078 0.21	(*103*) “
	Fathead minnow, *Pimephales promelas*	Larvae/96 h	Reduction in hepatic glycogen NOEC Swimming performance	0.20 0.13	(*36*) “
	Fathead minnow, *Pimephales promelas*	Larvae/4 h	Swimming performance	0.7	(*43*)

RESERVE THIS SPACE

	Bluegill, *Lepomis macrochirus*	Juvenile/90 d Young-of-the-Year Adult Embryos/Larvae	LOEC (behavior) NOEC (behavior) Growth Delayed spawning Reduced larval survival	0.025 0.010 0.08 1.0 1.0	(*109*) “ (*45*) “ “
	Medaka, *Oryzias latipes*	Adult/7 d	Stress protein (hsp) increase	21 µg/g (diet)	(*30*)
	Chinook salmon, *Oncorhynchus tshawytscha*	Juvenile/96 h	Alteration of immune response Stress protein (hsp) increase	0.08 0.01	(*18*) (*28*)
Permethrin	Daphnid	Adult	LOEC (fecundity)	<0.01	(*46*)
	Sheepshead minnow, *Cyprinodon variegatus*	28 d	LOEC (growth) NOEC (growth)	22 10	(*110*) “

Table III. Reported negative effects on various taxonomic groups as a result of repeated application of pyrethroids in aquatic microcosms and mesocosms.

	TU_{mso} 0.001-0.01	0.01-0.1	0.1-1	1-10
Amphipoda	-	100% (1)	100% (11)	100% (7)
Isopoda	-	-	80% 5)	100% (2)
Copepoda	0% (1)	60% (5)	56% (16)	73% (11)
Cladocera	0% (1)	0% (2)	50% 10)	86% (7)
Ostracoda	0% (1)	0% (1)	50% (2)	-
Trichoptera	0% (1)	67% (3)	86% (7)	83% (6)
Ephemeroptera	0% (1)	50% (6)	82% (17)	85% (13)
Diptera	0% (1)	33% (6)	82% (17)	100% (13)
Hemiptera	0% (1)	50% (2)	67% (6)	100% (2)
Odonata	0% (1)	33% (3)	36% (11)	50% (10)
Coleoptera	0% (1)	0% (2)	64% (11)	60% (10)
Hydracarina	0% (1)	100% (1)	100% (1)	-
Fish	0% (1)	0% (5)	33% (6)	83% (6)
Rotifera	0% (1)	0% (3)	0% (13)	0% (11)
Mollusca	0% (1)	0% (3)	0% (12)	0% (10)
Annelida	0% (1)	0% (2)	0% (11)	0% (6)
Turbellaria	0% (1)	0% (1)	0% (7)	0% (3)
Plants	0% (1)	0% (5)	0% (13)	8% (12)

The effects are arranged according to toxic units and expressed as a percentage (%) of the cases (n) in which a reduction in numbers or biomass of one or more taxa within a taxonomic group was reported. Table is reproduced from Van Wijngaarden et al. (2005) with kind permission from Springer Science and Business Media. TU_{mso}=toxic units= pyrethroid concentration divided by the EC50 of the most sensitive standard test species *(Daphnia magna, Pimephales promelas, or Onchorynchus mykiss).*