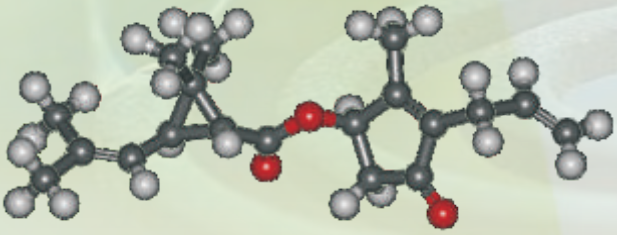
ISSN No. : 0972-1266

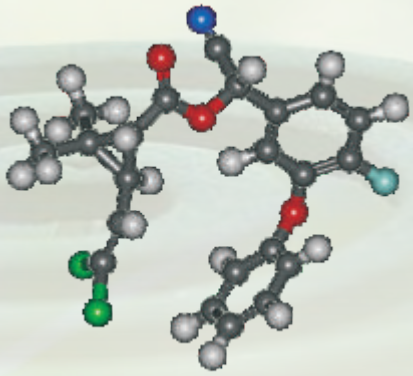
ENVIS Newsletter

Vol. 18 | No. 4 | November 2011

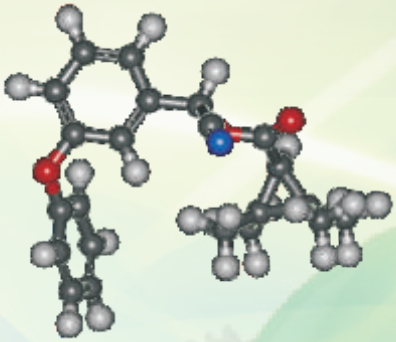
Special issue on Pyrethroid



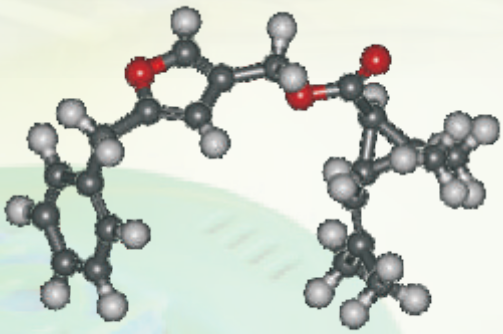
Allethrin



Cyfluthrin



Fenpropathrin



Resmethrin

CSIR-Indian Institute of Toxicology Research
Lucknow, India

IN THIS ISSUE

EDITORIAL

Pyrethroids are organic compounds, collectively obtained from the flowers of *Chrysanthemum cinerariaefolium* and *C. Coccineum which* are known as pyrethrums. Pyrethroids constitute a major commercial household insecticides, they are widely used in home insect-control products, including flea bombs, roach sprays, ant bait, flea-and-tick pet shampoos, and lice shampoos. The chemicals are also sprayed on crops. They have insect repellent properties and are considered harmless to human beings at low doses. In one or two days they breakdown in presence of sunlight .Hence do not affect ground water quality. Pyrethroids are considered safe because most vertebrates have sufficient enzymes required for rapid breakdown. Although toxicity occurs at extremely high concentrations but repeated exposure may increase health risks at even lower concentration as well. Pyrethroids are popular insecticide due to their property of porosity towards exoskeletons of insects. They are poisons and can cause paralysis in an organism. The pyrethroid represents a major advancement in insecticidal activity, fast bio degradation, low mammalian toxicity and negligible persistence. Hence, this property is good for the environment but gives poor efficacy in field application.

1st generation pyrethroids, developed in the 1960s, include bioallethrin, tetramethrin, resmethrin and bioresmethrin. By 1974, the Rothamsted team had discovered a 2nd generation of more persistent compounds like: permethrin, cypermethrin and deltamethrin. The second generation pyrethroids have few less desirable properties like irritant to the skin and eyes, to overcome this drawback special formulations were developed. It is a fact that they are toxic to beneficial insects (bees and dragonflies), pyrethroids are toxic to aquatic organisms like fish. At extremely small levels, such as 2 parts per trillion, pyrethroids are lethal to mayflies, gadflies, and invertebrates that constitute the base of many aquatic and terrestrial food webs. Some of the common pyrethroids are Allethrin stereoisomers, Bifenthrin, Beta-Cyfluthrin, Cyfluthrin, Cypermethrin, Cyphenothrin, Deltamethrin, Esfenvalerate, Fenpropathrin, Tau-Fluvalinate, Lambda-Cyhalothrin, Gamma Cyhalothrin, Imiprothrin, 1RS cis-Permethrin, Permethrin, Prallethrin, Resmethrin, Sumithrin (d-phenothrin), Tefluthrin, Tetramethrin, Tralomethrin, and Zeta-Cypermethrin. Although little data exist about human health concerns, evidence is growing that pyrethroids might be harming aquatic ecosystems.

"I think it's a good idea to minimize pesticide exposure of any sort, not only because of what we know, but because of what we don't know." -Donald Weston, University of California-Berkeley

Editorial Team
Shailendra K. Gupta, Coordinator
Anvita Shaw, S.H.N. Naqvi, Pritimayee Satapathy
Vidisha Srivastava

Published by :
Distributed Information Centre on Toxic Chemicals
Environmental Information System (ENVIS)
at CSIR-Indian Institute of Toxicology Research
Lucknow, India

ODDS AND ENDS

Deltamethrin, a type II pyrethroid insecticide, has neurotrophic effects on neurons with continuous activation of the Bdnf promoter.

Pyrethroids, widely used insecticides with low acute toxicity in mammals, affect sodium channels in neurons. In a primary culture of rat cortical neurons, deltamethrin (DM), a type II pyrethroid, markedly enhanced the expression of brain-derived neurotrophic factor (BDNF) exon IV-IX (Bdnf eIV-IX) mRNA. In this study, authors found that DM has a neurotrophic effect on cultured neurons and investigated the mechanisms responsible for it. One μM DM increased cell survival, neurite complexity and length. Neurite complexity and length were reduced not only by a blockade of cellular excitation with GABA or Ca(2+) influx via L-type voltage-dependent calcium channels with nicardipine, but also by a blockade of TrkB, a specific receptor for BDNF, with TrkB/Fc. These data indicate DM has neurotrophic actions. DM-induced Bdnf eIV-IX mRNA expression through the calcineurin and ERK/MAPK pathways, the increase of which was reduced by GABA(A) receptor activation. Using a promoter assay, authors found that Ca(2+)-responsive elements including a CRE are involved in the DM-induced activation of the Bdnf promoter IV (Bdnf-pIV). The intracellular concentration of Ca(2+) and activation of Bdnf-pIV remained elevated for, at least, 1 and 24 h, respectively. Moreover, GABA(A) receptor activation or a blockade of Ca(2+) influx even after starting the incubation with DM reduced the elevated activity of Bdnf-pIV. These data demonstrated that the prolonged activation of Bdnf-pIV occurred because of this continuous increase in the intracellular Ca(2+) concentration. Thus, DM has neurotrophic effects on neurons, likely due to prolonged activation of Bdnf promoter in neurons.

[Neuropharmacology. 2011 Nov 7. doi:10.1016/j.neuropharm.2011.10.023 (Epub ahead of print)]

Progress and Future of Pyrethroids.

After the chemical structure of "natural pyrethrins," the insecticidal ingredient of pyrethrum flowers, was elucidated, useful synthetic pyrethroids provided with various characteristics have been developed by organic chemists throughout the world, leading to the advancement of pyrethroid chemistry. Even in pyrethroids with high selective toxicity, a chemical design placing too much importance on efficacy improvements may invite loss of the safety margin. It is strongly hoped that the development of household pyrethroids and their preparations for use in living environments around humans and pets will be achieved in the future by retaining the characteristics of natural pyrethrins.

[Top Curr Chem. 2011 Nov 3. doi:10.1007/128_2011_252 (Epub ahead of print)]

Deep sequencing of pyrethroid-resistant bed bugs reveals multiple mechanisms of resistance within a single population.

A frightening resurgence of bed bug infestations has occurred over the last 10 years in the U.S. and current chemical methods have been inadequate for controlling this pest due to widespread insecticide resistance. Little is known about the mechanisms of resistance present in U.S. bed bug populations, making it extremely difficult to develop intelligent strategies for their control. Authors have identified bed bugs collected in Richmond, VA which exhibit both kdr-type (L925I) and metabolic resistance to pyrethroid insecticides. Using LD(50) bioassays, authors determined that resistance ratios for Richmond strain bed bugs were 5200-fold to the insecticide deltamethrin. To identify metabolic genes potentially involved in the detoxification of pyrethroids, authors performed deep-sequencing of the adult bed bug transcriptome, obtaining more than 2.5 million reads on the 454 titanium platform. Following assembly, analysis of newly identified gene transcripts in both Harlan (susceptible) and Richmond (resistant) bed bugs revealed several candidate cytochrome P450 and carboxylesterase genes which were significantly over-expressed in the resistant strain, consistent with the idea of increased metabolic resistance. These data will accelerate efforts to understand the biochemical basis for insecticide resistance in bed bugs, and provide molecular markers to assist in the surveillance of metabolic resistance.

[PLoS One. 2011;6(10):e26228.]

Advances in the Mode of Action of Pyrethroids.

The ability to clone, express, and electrophysiologically measure currents carried by voltage-gated ion channels has allowed a detailed assessment of the action of pyrethroids on various target proteins. Recently, the heterologous expression of various rat brain voltage-gated sodium channel isoforms in *Xenopus laevis* oocytes has determined a wide range of sensitivities to the pyrethroids, with some channels virtually insensitive and others highly sensitive. Furthermore, some isoforms show selective sensitivity to certain pyrethroids and this selectivity can be altered in a state-dependent manner. Additionally, some rat brain isoforms are apparently more sensitive to pyrethroids than the corresponding human isoform. These finding may have significant relevance in judging the merit and value of assessing the risk of pyrethroid exposures to humans using toxicological studies done in rat. Other target sites for certain pyrethroids include the voltage-gated calcium and chloride channels. Of particular interest is the increased effect of Type II pyrethroids on certain phosphoforms of the N-type Ca(v)2.2 calcium channel following post-translational modification and its relationship to enhanced neurotransmitter release seen *in vivo*. Lastly, parallel

neurobehavioral and mechanistic studies on three target sites suggest that a fundamental difference exists between the action of Types I and II pyrethroids, both on a functional and molecular level. These differences should be considered in any future risk evaluation of the pyrethroids.

[Top Curr Chem. 2011 Oct 25. doi:10.1007/128_2011_268 (Epub ahead of print)]

Systematic review of biomonitoring studies to determine the association between exposure to organophosphorus and pyrethroid insecticides and human health outcomes.

For the appropriate protection of human health it is necessary to accurately estimate the health effects of human exposure to toxic compounds. In the present review, epidemiological studies on the health effects of human exposure to organophosphorus (OP) and pyrethroid (PYR) insecticides have been critically assessed. This review is focused on studies where the exposure assessment was based on quantification of specific biomarkers in urine or plasma. The 49 studies reviewed used different epidemiological approaches and analytical methods as well as different exposure assessment methodologies. With regard to OP pesticides, the studies reviewed suggested negative effects of prenatal exposure to these pesticides on neurodevelopment and male reproduction. Neurologic effects on adults, DNA damage and adverse birth outcomes were also associated with exposure to OP pesticides. With regard to exposure to PYR pesticides, there are currently few studies investigating the adverse health outcomes due to these pesticides. The effects studied in relation to PYR exposure were mainly male reproductive effects (sperm quality, sperm DNA damage and reproductive hormone disorders). Studies' findings provided evidence to support the hypothesis that PYR exposure is adversely associated with effects on the male reproductive system. The validity of these epidemiological studies is strongly enhanced by exposure assessment based on biomarker quantification. However, for valid and reliable results and conclusions, attention should also be focused on the validity of the analytical methods used, study designs and the measured toxicants characteristics.

[Toxicol Lett. 2011 Oct 15. doi:10.1016/j.toxlet.2011.10.007 (Epub ahead of print)]

Efficacy of 10 commercially available household permethrin products against *Culex quinquefasciatus*.

Ten commercial household permethrin products in aerosol formulations were evaluated for knockdown (KD) and mortality of female *Culex quinquefasciatus*. The permethrin concentrations of these products ranged from 0.05% to 0.50%. Eight of the 10 products produced significant KD (%) and mortality (%) post treatment. At 15 min post treatment, 3 household permethrin products provided 100% mortality. At 60 min post treatment, 8 products provided 100% mortality. At 120 min, only 2 products resulted in less than 100% mortality with permethrin concentrations of 0.05% and 0.10%. A linear regression analysis shows a significant relationship between the mortality and times post treatment.

[J Am Mosq Control Assoc. 2011 Sep;27(3):326-9.]

Exposure of flight attendants to pyrethroid insecticides on commercial flights: Urinary metabolite levels and implications.

Pyrethroid insecticides have been used for disinfection of commercial aircrafts. However, little is known about the pyrethroids exposure of flight attendants. The objective of the study was to assess pyrethroids exposure of flight attendants working on commercial aircrafts through monitoring the urinary pyrethroids metabolite levels. Eighty four urine samples were collected from 28 flight attendants, 18-65 years of age, with seventeen working on planes that were non-disinfected, and eleven working on planes that had been disinfected. Five urinary metabolites of pyrethroids were measured using gas chromatographic-mass spectrometric method: 3-phenoxybenzoic acid (3-PBA), cis-/trans-3-(2,2-Dichlorovinyl)-2,2-dimethylcyclopropane carboxylic acid (cis-/trans-Cl2CA), cis-3-(2,2-dibromovinyl)-2,2-dimethylcyclo-propane-1-carboxylic acid (cis-Br2CA) and 4-fluoro-3-phenoxybenzoic acid (4F-3-PBA). Flight attendants working on disinfected planes had significantly higher urinary levels of 3-PBA, cis- and trans-Cl2CA in pre, post- and 24-h-post flight samples than those on planes which did not report having been disinfected. Urinary levels of cis-Br2CA and 4F-3-PBA did not show significant differences between the two groups. Flight attendants working on international flights connected to Australia had higher urinary levels of 3-PBA, cis- and trans-Cl2CA than those on either domestic and other international flights flying among Asia, Europe and North America. Post-disinfection duration (number of days from disinfection date to flight date) was the most significant factor affecting the urinary pyrethroid metabolites levels of 3-PBA, cis- and trans-Cl2CA of the group flying on disinfected aircraft. It was concluded that working on commercial aircraft disinfected by pyrethroids resulted in elevated body burdens of 3-PBA, cis- and trans-Cl2CA.

[Int J Hyg Environ Health. 2011 Sep 19. doi:10.1016/j.ijheh.2011.08.006 (Epub ahead of print)]

Testing the dose addition hypothesis: the impact of pyrethroid insecticide mixtures on neurons.

Pyrethroid insecticides are used extensively in agriculture and in homes to control fleas, cockroaches, bedbugs, and other insects. In a new *in vitro* study researchers tested the hypothesis that mixtures of pyrethroids have a dose-additive effect—that is, that pyrethroids as a chemical group produce toxicity in mammals via a common mode of action and that the combined toxicity of a pyrethroid mixture reflects the sum of its constituents' toxicities [EHP 119(9) :1239–1246; Cao et al.]. Using increased sodium ion influx as a

specific functional measure of toxicity, the researchers found that effects of a mixture of commonly used pyrethroids were consistent with a dose-additive effect on mammalian neurons. Pyrethroids act on the nervous system by disrupting the normal function of voltage-gated sodium channels (VGSCs), which control the influx of sodium ions into neurons to transmit nerve signals. When VGSCs open, the influx of sodium generates the nerve signal; when they close, the electrical signal halts abruptly. Pyrethroids bind to VGSCs and delay their closing, which causes repetitive nerve stimulation that can lead to muscle tremors as well as interfere with the ability of the channels to respond to stimulation. Previous research demonstrated that a mixture of 11 pyrethroids had a dose-additive effect on the rat nervous system, decreasing the animals' motor activity at doses below the threshold dose of each constituent compound. The authors of the current study exposed neurons cultured from the cerebral cortices of embryonic mice to the same 11 pyrethroids, and then examined how VGSCs responded. To measure sodium influx without disrupting cell function, neurons were treated with a sodium-sensitive dye that fluoresced when VGSCs were open. Seven of the pyrethroids tested increased sodium influx in a dose-dependent manner (from highest to lowest potency: deltamethrin, S-bioallethrin, β-cyfluthrin, λ-cyhalothrin, esfenvalerate, telfluthrin, fenpropathrin). Cypermethrin and bifenthrin had only a marginal effect on sodium influx, whereas permethrin and resmethrin had no effect. Despite these variations in activity, the results when neurons were exposed to all 11 compounds together were consistent with a cumulative, dose-additive effect on neuronal sodium influx. People are commonly exposed to low doses of pyrethroid mixtures, which tend to persist as residues on treated surfaces and in household dust. Currently the U.S. Environmental Protection Agency is determining whether a cumulative dose-additive model is appropriate to evaluate potential human health effects of pyrethroid mixtures. This model shows that simultaneous exposure to multiple compounds will produce an effect that is consistent with additivity at the VGSC molecular target.

[Environ Health Perspect. 2011 Sep;119(9):a399.]

Residual pyrethroids in fresh horticultural products in Sonora, Mexico.

This study was conducted to evaluate the presence of cyhialothrin, cyfluthrin, cypermethrin, fenvalerate, and deltamethrin in vegetables produced and consumed in Sonora, Mexico. A total of 345 samples were collected from cluster sampling of markets and fields. Approximately 9% of the samples tested positive for pyrethroids (residue range 0.004-0.573 mg kg(-1)). Based on the results, the potential toxicological risk of human exposure to the pyrethroid insecticides measured in vegetables appears to be minimal, with the estimated exposure being 1,000 times lower than admissible levels.

[Bull Environ Contam Toxicol. 2011 Oct;87(4):436-9.]

Autosomal interactions and mechanisms of pyrethroid resistance in house flies, *Musca domestica*.

Five BC $_1$ lines and 16 house fly mass-cross homozygous lines were generated from crosses of the pyrethroid resistant ALHF (wild-type) and susceptible aabys (bearing recessive morphological markers on each of five autosomes) strains. Each of the resulting homozygous lines had different combinations of autosomes from the resistant ALHF strain. Levels of resistance to permethrin were measured for each line to determine the autosomal linkage, interaction and, possibly, regulation in pyrethroid resistance of house flies. Results indicated that factors on autosome 4 are not involved in the development of resistance in house flies, while factors on autosomes 1, 2, 3 and 5 play important roles in pyrethroid resistance. The sodium channel gene has been mapped on autosome 3 and multiple cytochrome P450 genes overexpressed in resistant ALHF house flies have been genetically mapped on autosome 5, suggesting that P450 mediated detoxification and sodium channel-mediated target site insensitivity located on autosomes 3 and 5, respectively, are major factors related to resistance development in house flies. However, neither the factors on autosome 3 or 5 alone, nor the factors from both autosomes 3 and 5 combined could confer high levels of resistance to pyrethroid. In addition, strong synergistic effects on resistance was obtained when autosomes 1 and 2 interact with autosome 3 and/or 5, suggesting that the trans factors on autosomes 1 and 2 may interact with factors on autosomes 3 and 5, therefore, playing regulatory roles in the development of sodium channel insensitivity- and P450 detoxification-mediated resistance.

[Int J Biol Sci. 2011;7(6):902-11.]

Antiplasmodial and antitrypanosomal activity of pyrethrins and pyrethroids.

In a screen of 1800 plant and fungal extracts for antiplasmodial, antitrypanosomal, and leishmanicidal activity, the n-hexane extract of *Chrysanthemum cinerariifolium* (Trevir.) Vis. flowers showed strong activity against *Plasmodium falciparum*. Authors isolated the five pyrethrins [i.e., pyrethrin II (1), jasmolin II (2), cinerin II (3), pyrethrin I (4), and jasmolin I (5)] from this extract. These were tested together with 15 synthetic pyrethroids for their activity against *P. falciparum* and *Trypanosoma brucei* rhodesiense and for cytotoxicity in rat myoblast L6 cells. The natural pyrethrins showed antiplasmodial activity with IC(50)s between 4 and 12 µM, and antitrypanosomal activity with IC(50)s from 7 to 31 µM. The pyrethroids exhibited weaker antiplasmodial and antitrypanosomal activity than the pyrethrins. Both pyrethrins and pyrethroids showed moderate cytotoxicity against L6

cells. Pyrethrin II (1) was the most selective antiplasmodial compound, with a selectivity index of 24.

[J Agric Food Chem. 2011 Sep 14;59(17):9172-6.]

Molecular mechanisms of pyrethroid insecticide neurotoxicity: recent advances.

Synthetic pyrethroid insecticides were introduced into widespread use for the control of insect pests and disease vectors more than three decades ago. In addition to their value in controlling agricultural pests, pyrethroids are at the forefront of efforts to combat malaria and other mosquito-borne diseases and are also common ingredients of household insecticide and companion animal ectoparasite control products. The abundance and variety of pyrethroid uses contribute to the risk of exposure and adverse effects in the general population. The insecticidal actions of pyrethroids depend on their ability to bind to and disrupt voltage-gated sodium channels of insect nerves. Sodium channels are also important targets for the neurotoxic effects of pyrethroids in mammals but other targets, particularly voltage-gated calcium and chloride channels, have been implicated as alternative or secondary sites of action for a subset of pyrethroids. This review summarizes information published during the past decade on the action of pyrethroids on voltage-gated sodium channels as well as on voltage-gated calcium and chloride channels and provides a critical re-evaluation of the role of these three targets in pyrethroid neurotoxicity based on this information.

[Arch Toxicol. 2011 Jun 28. doi:10.1007/s00204-011-0726-x(Epub ahead of print)]

Net risk: a risk assessment of long-lasting insecticide bed nets used for malaria management.

Despite the demonstrated ability of bed nets that have been factory-impregnated with long-lasting insecticides (LLINs) to protect people from malaria and despite the ambitious plans for their widespread use, the health risks from the LLINs themselves have not been adequately investigated and reported in the peer-reviewed science literature. Here, authors use a probabilistic risk assessment approach to estimate the risks to Africans from inhalation, dermal, and oral exposures to the newer LLINs with permethrin, α-cypermethrin, or deltamethrin as the insecticide active ingredient. Authors estimated exposures to LLINs using 17 age groups to incorporate different body weights and sleeping behaviors. Risk quotients (exposure divided by toxic threshold) at the 50th and 90th percentiles for non-cancer risks were < 1.0 for lifetime adjusted risk and all youth and adult age groups. Risk quotients for infants and toddlers (0-3 years) and child groups from 3 to 10 years were ≥1.0 for specific bed nets.

[Am J Trop Med Hyg. 2011 Jun;84(6):951-6.]

Biological monitoring for exposure to deltamethrin: A human oral dosing study and background levels in the UK general population.

An oral dose of the pyrethroid insecticide deltamethrin was administered to five volunteers at the acceptable daily intake (ADI, 0.01mg/kg). Total urine was collected from the volunteers at timed intervals for 60h post-exposure. The metabolites 3-(2,2-dibromovinyl)-2,2-dimethyl-(1-cyclopropane) carboxylic acid (DBVA) and 3-phenoxybenzoic acid (3-PBA) were quantified in hydrolysed urine using GC-MS analysis. Both metabolites exhibited rapid elimination half-lives of 3.6 and 7.1h, respectively. Levels of DBVA quantified in urine were approximately 5 times greater than 3-PBA. Mean metabolite levels found in 24h total urine collections, normalised for a 70kg individual, were 42.8µmol DBVA/mol creatinine (range 34.6-63.2; CV=28%) and 8.7µmol 3-PBA/mol creatinine (range 6.6-12.7; CV=31%). Authors calculate that a 70kg person receiving a dose of deltamethrin at the ADI would be expected to have a 24-h total urine collection level of 32-53µmol DBVA/mol creatinine (95% confidence interval). Analysis of 336 samples from adult UK residents with no known exposure to deltamethrin derives an upper reference value (95th percentile) of 0.5µmol DBVA/mol creatinine (maximum 4.2µmol DBVA/mol creatinine), demonstrating that general population exposure to deltamethrin in the UK is very low and well within levels expected at the ADI.

[Toxicol Lett. 2011 Apr 25. doi:10.1016/j.toxlet.2011.04.014 (Epub ahead of print)]

Desorption of pyrethroids from suspended solids.

Pyrethroid insecticides have been widely detected in sediments at concentrations that can cause toxicity to aquatic organisms. Desorption rates play an important role in determining the bioavailability of hydrophobic organic compounds, such as pyrethroids, because these compounds are more likely to be sorbed to solids in the environment, and times to reach sorptive equilibrium can be long. In the present study, sequential Tenax desorption experiments were performed with three sorbents, three aging times, and four pyrethroids. A biphasic rate model was fit to the desorption data with r(2) >0.99, and the rapid and slow compartment desorption rate constants and compartment fractions are reported. Suspended solids from irrigation runoff water collected from a field that had been sprayed with permethrin 1 d before were used in the experiments to compare desorption rates for field-applied pyrethroids with those for laboratory-spiked materials. Suspended solids were used in desorption experiments because suspended solids can be a key source of hydrophobic compounds in surface waters. The rapid desorption rate parameters of field-applied permethrin were not statistically different from those of laboratory spiked permethrin, indicating that desorption of the spiked pyrethroids is comparable to desorption of the pyrethroids added and aged in the field. Sorbent characteristics had the greatest effect on desorption rate parameters; as organic carbon content of the solids increased, the rapid desorption fractions and rapid

desorption rate constants both decreased. The desorption rate constant of the slow compartment for sediment containing permethrin aged for 28 d was significantly different compared to aging for 1 d and 7 d, whereas desorption in the rapid and slow compartments did not differ between these treatments.

[Environ Toxicol Chem. 2011 Aug;30(8):1760-6.]

Runoff transport of pyrethroids from a residential lawn in central California.

An irrigation runoff study on a residential lawn was conducted in California, northeast of Sacramento, during the summer and fall of 2008 to investigate the contribution of turf uses of pyrethroids to residues in Californian urban creek sediments. This study examined how over irrigation (i.e., irrigation that produces runoff) in the summer season may transport recently applied pyrethroids. The study included liquid and granular applications of both bifenthrin [(2-methyl-3-phenyl-phenyl) methyl 3-(2-chloro-3,3,3-trifluoro-prop-1-enyl) -2, 2-dimethyl-cyclopropane-1-carboxylate] and beta-cyfluthrin [Cyano(4-fluoro-3-phenoxy-phenyl)methyl 3-(2, 2-dichloroethenyl)-2,2-dimethyl-cyclopropane-carboxylate]. Gene-rally, runoff did not occur at irrigation rates of 2.03 cm/h (0.8 in/h) but did occur when the irrigation rates were increased to about 3.81 cm/h (1.5 in/h), generating chemical losses in the first runoff event of up to 0.58 and 0.08% of applied for beta-cyfluthrin and bifenthrin, respectively. Chemical runoff losses dropped significantly between over-irrigation events with the third over-irrigation event chemical runoff losses representing 0.026 and 0.015% of applied for beta-cyfluthrin and bifenthrin, respectively. Runoff losses were generally less for liquid formulations than granular formulations but within a factor of three. Additionally, the study included a simulated winter rainstorm 8 wk after application. The low runoff losses from turf seen in this study suggest that other sources could be contributing to observed residues in urban streams. Other sources could include pyrethroids ending up on impervious surfaces, such as concrete driveways from off-target applications to turf, spills, and other poor handling practices, or pyrethroids applied directly to impervious surfaces for insect control.

[J Environ Qual. 2011 Mar-Apr;40(2):587-97.]

Oxidative stress in the blood of farm workers following intensive pesticide exposure.

The aim of this study was to evaluate oxidative stress in workers who formulate organophosphate, synthetic pyrethroid and carbamate pesticides. In this survey, blood erythrocytes from a group of 94 pesticide-formulating workers (at least 5-years experience in pest-control in apple and cherry production) and 45 control subjects were examined for oxidative stress parameters. The control group was composed of 45 healthy people living in the same region with no exposure to pesticides. Lipid peroxidation level, catalase, superoxide dismutase and glutathione peroxidase activities in erythrocytes were analysed as biomarkers of oxidative stress. In addition, the acetylcholinesterase activity was measured as a biomarker of toxicity. Results indicated that chronic exposure to organophosphate, synthetic pyrethroid and carbamate pesticides were associated with increased activities of catalase, SOD and lipid peroxidation in erythrocytes ($p < 0.05$). Acetylcholinesterase activity did not show any significant differences between the two groups ($p > 0.05$). It is concluded that human chronic exposure to pesticides may result in stimulated antioxidant enzymes.

[Toxicol Ind Health. 2011 Oct;27(9):820-5.]

Can piperonyl butoxide enhance the efficacy of pyrethroids against pyrethroid-resistant *Aedes aegypti?*

Pyrethroid resistance can be considered the main threat to the continued control of many mosquito vectors of disease. Piperonyl butoxide (PBO) has been used as a synergist to help increase the efficacy of certain insecticides. This enhancement stems from its ability to inhibit two major metabolic enzyme systems, P450s and non-specific esterases, and to enhance cuticular penetration of the insecticide. To compare the mortality of a characterized resistant *Aedes aegypti* strain, Nha Trang, from Vietnam and the susceptible laboratory strain Bora Bora on netting with the pyrethroid deltamethrin (DM) alone and in combination with PBO. Resistance mechanisms were characterized using molecular and bioassay techniques; standard PCR was used to test for the kdr target site mutation. Potential genes conferring metabolic resistance to DM were identified with microarray analysis using the Ae. aegypti 'detox chip'. These data were analysed alongside results from WHO susceptibility tests. P450, CYP9J32, was significantly over expressed in the DM-resistant strain compared with the susceptible Bora Bora strain. Another five genes involved with oxidative stress responses in mosquitoes were also significantly over expressed. The Nha Trang strain was homozygous for two kdr mutations. WHO cone bioassays were used to investigate mortality with incorporated DM-treated nets with and without PBO. PBO used in combination with DM resulted in higher mortality than DM alone. Synergists may have an important role to play in the future design of vector control products in an era when alternatives to pyrethroids are scarce.

[Trop Med Int Health. 2011 Apr;16(4):492-500.]

Estimation of the percutaneous absorption of permethrin in humans using the parallelogram method.

The objective of this study was to develop an estimate of the percent dermal absorption of permethrin in humans to provide more accurate estimates of potential systemically absorbed dose associated with dermal exposure scenarios. Piperonyl butoxide (PBO) was used as a reference compound. The human percutaneous absorption estimate was based on the assumption that the

ratio of *in vivo* dermal absorption (expressed as a percentage during a given time period) of permethrin through rat skin to *in vitro* dermal absorption through rat skin was the same as the ratio of *in vivo* dermal absorption in humans to *in vitro* dermal absorption with human skin, known as the parallelogram method. The ratio of dermal absorption by *in vitro* rat skin to absorption by *in vitro* human skin ranged from 6.7 to 15.4 (for a 24-h exposure period) with an average of 11. Data suggest *in vivo* human dermal absorption values for permethrin ranging from 1.4 to 3.3% when estimated based on 24-h *in vivo* rat values, and 2.5 to 5.7% based on 5-d *in vivo* rat values. The parallelogram method used to estimate dermal absorption of permethrin and PBO is supported by results from several other compo-unds for which *in vivo* and *in vitro* rat and human dermal absorption data exist. Collectively, these data indicate that estimating human dermal absorption from *in vitro* human and rat plus *in vivo* rat data are typically accurate within ±3-fold of the values measured in human subjects.

[J Toxicol Environ Health A. 2011;74(6):351-63.]

Pyrethroids: mammalian metabolism and toxicity.

Synthetic pyrethroids, a major insecticide group, are used worldwide to control agricultural and household pests. Mammalian metabolism of pyrethroids was substantially launched in the 1960s and 1970s by the research groups of Professor Casida and Sumitomo Chemical Co., which made great contributions to the elucidation of their metabolic fates. They showed that ester hydrolysis and oxidation play predominant roles in mammalian metabolism of pyrethroids and that rapid metabolism leads to low mammalian toxicity. These metabolic reactions are mediated by carboxylesterases and CYP isoforms, the resultant metabolites then undergoing various conjugation reactions. In general, there are substantially neither significant species differences in metabolic reactions of pyrethoids nor metabolic differences among their chiral isomers except with fenvalerate, one isomer of which yields a lipophilic conjugate causing toxicity.

[J Agric Food Chem. 2011 Apr 13;59(7):2786-91.]

Abnormal glucose regulation in pyrethroid pesticide factory workers.

The purpose of this study was to investigate associations between pyrethroids occupational exposures, and risk of abnormal glucose regulation. Data from total of 3080 subjects in two pesticide factories were used. This was a population-based case-controlled study in China. In total, 18.3% of subjects with impaired glucose regulation (IGR) and 6.5% of subjects with diabetes, and the prevalence of abnormal glucose regulation was 24.8%, 86 subjects had known type 2 diabetes and 114 had newly diagnosed diabetes. The prevalence of subjects with abnormal glucose regulation increased from 21.3% in the controls to 29.3% in the exposures (χ^2 = 33.182, P < 0.001). Multivariate logistic regression was used to control potential confounders and calculate odd ratios as the estimate of effect. An indication of increased risk for abnormal glucose regulation was noted for exposure to pyrethroids (OR = 1.482, 95%CI = 1.238-1.774). Abnormal glucose regulation is common in subjects exposed to pyrethroids. The present investigation indicates the adverse health effects of pyrethroids are underestimated.

[Chemosphere. 2011 Feb;82 (7):1080-2.]

Anaphylaxis in an airplane after insecticide spraying.

Flights departing from malarious areas are sprayed with pyrethroids. They are presumed to be safe since reports of adverse responses among passengers or crew were only anecdotal. However, asthmatic reactions after domestic and occupational exposure have been published. Authors present the first case description of pyrethroid allergy in an airplane.

[J Travel Med. 2010 Nov-Dec;17(6):427-9

Effects of non-occupational environmental exposure to pyrethroids on semen quality and sperm DNA integrity in Chinese men.

Observations in several western and Asiatic countries point toward a decline in semen quality which may be associated with environmental exposures. To investigate the effect of environmental exposure to pyrethroids on sperm DNA integrity and semen quality, 240 men were recruited from an infertility clinic through the clinic following strict eligibility screening. Urinary 3-phenoxybenzoic acid (3-PBA) concentration, semen quality, and sperm DNA integrity were evaluated. After adjustment for potential confounders, a significant inverse correlation was observed between the urinary 3-PBA level and the sperm concentration (β=-0.27, 95%CI: -0.41 to -0.12, P<0.001). Moreover, authors also found a significant positive correlation between urinary 3-PBA level and sperm DNA fragmentation (β=0.27, 95%CI: 0.15-0.39, P<0.001). The results suggest that non-occupational environmental pyrethroids exposure may have a negative impact on sperm DNA integrity and semen quality in Chinese males.

[Reprod Toxicol. 2011 Feb;31(2):171-6.]

Simultaneous determination of 16 pyrethroid residues in tea samples using gas chromatography and ion trap mass spectrometry.

Pyrethroids are widely used in tea production, and pesticide residues in brewed tea are becoming a major issue. Thus, an appropriate control method of pyrethroid residues in tea samples has to be developed and used to reduce the potential health hazard from consumption of pyrethroids. A method is described here for the simultaneous determination of 16 pyrethroid residues in tea samples. The insecticides were extracted using acetone and then underwent cleanup through a florisil column. Analysis was performed by gas chromat-ography with ion trap mass spectrometry (GC IT-MS) in MS MS mode. Retention time and

specific ions were used for identification. Recoveries at spiked levels (0.001-0.2 µg/g) for the 16 pyrethroids ranged from 71.3% to 106.3%, and the coefficient of variation was less than 17% in each case. The limits of detection were from 0.001 to 0.05 µg/g. The proposed method was successfully applied to determine pyrethroid residues in 25 brewed made tea samples. It was found that there were bifenthrin, cyfluthrin, lamda-cyhalothrin, cypermethrin, dicofol, fenpropathrin, fenvalerate, fluvalinate, and tetramethrin residues in different samples with levels ranging from 1.18-3071.29 µg/kg.

[J Chromatogr Sci. 2010 Oct;48(9):771-6.]

Cardiac conduction disturbance due to prallethrin (pyrethroid) poisoning.

Pyrethroids are common household insecticides. Even though they are less toxic to humans, reports of accidental and suicidal poisoning are not uncommon. Cardiotoxicity due to pyrethroid poisoning is rare. Authors report a case of cardiac conduction disturbance due to a pyrethroid, prallethrin. A 28-year-old female presented after a suicidal consumption of prallethrin. Her clinical and laboratory parameters were normal during the first 24 h of hospital stay. On the second hospital day, she developed metabolic acidosis and sinus arrest with escape junctional rhythm. Despite correction of metabolic acidosis, the sinus arrest persisted for 3 days. She reverted back to sinus rhythm with bradycardia after this period and was discharged on the seventh hospital day. Her follow-up was uneventful. Pyrethroid poisoning can affect the gastrointestinal, respiratory, and nervous system. Most serious effects of the toxin in humans are seizures and coma. Mechanism of pyrethroid neurotoxicity is believed to be due to its ability to modify sodium, chloride, and calcium channels of the neurons. This case raises the possibility that cardiac arrhythmia due to pyrethroid poisoning can occur due to its effect on sodium channels in the heart.

[J Med Toxicol. 2010 Mar;6(1):27-30.]

Fatal intoxication with hydrocarbons in deltamethrin preparation.

Pyrethroid insecticides are very widely used in agriculture and household due to high effectiveness and low toxicity to humans. Authors have described a case of a fatal oral intoxication with decis, the insecticide containing pyrethroid (deltamethrin) in a hydrocarbon base. Pyrethroids, including deltamethrin, undergo rapid biotransformation by liver enzymes, which limit their systemic toxicity. Thus, authors assume that in the presented case, fatal outcome of poisoning with decis was rather connected with toxic effects of hydrocarbon base (solvent naphtha) than with deltamethrin action. In the described case, detection of aromatic hydrocarbons in blood and lung tissue and their metabolites in urine confirms that these substances were absorbed from gastrointestinal tract to the systemic circulation. Predominant among the clinical outcomes in the patient was profound depression of CNS with apnea, which could be connected with narcotic action of organic solvents. The cardiac arrest was in mechanism of asystolia with prior non-responsive to catecholamines bradycardia and vascular collapse. Authors connect it with hydrocarbon-induced cardio-toxicity. It is worth remembering that many pyrethroid-containing insecticides are formulated in a hydrocarbon base. Intoxication with such preparations should always be considered not only as poisoning with pyrethroid alone but also as intoxication with hydrocarbons.

[Hum Exp Toxicol. 2009 Dec; 28(12):791-3.]

DID YOU KNOW

- Pyrethroid toxicity is highly dependent on stereochemistry, the three dimensional configuration of the molecule. Each isomer (molecules consisting of the same atoms, but with a different stereochemistry) has its own toxicity.
- Some pyrethroids have as many as 8 different isomers and there are several different types. Acute toxicity of a mixture of 2 isomers depends on the ratio of the amounts of the two isomers in the formulation
- The route of exposure is also critical in assessing the acute toxicity of a synthetic pyrethroid
- Synthetic pyrethroid's principal mechanism of action is believed to be the disruption of the permeability of nerve membranes to sodium atoms.

CURRENT CONCERNS

- Pyrethroids are particularly lethal to cats, bees, and fish and other water-dwelling organisms. The chemicals can harm the nervous system in humans in high doses leading to symptoms like: headache, breathing trouble, nausea, and vomiting. According to Environmental Protection Agency (EPA), permethrin, one among the pyrethroid is "likely to be carcinogenic to humans."
- Pyrethroids are used extensively and are thus present in the environment; they can alter estrogen equilibrium in the body due to their activity on estrogen. Therefore, their effects on the endocrine system in both humans and wildlife is of concern.

REGULATORY TREND

Pyrethrins, pyrethroids and their synergists that were registered after 1984 are currently undergoing registration reviews in the USA to evaluate the effectiveness of recent regulatory decisions and to consider new data. The registration review is focused on developmental neurotoxicity, because recent studies have shown decreases in rat pup weight, pup weight gain, and/or brain weight. In addition, the USEPA has recently updated spray drift regulations for pyrethroids, increasing the buffer between sprayed areas and aquatic environments. Even though pyrethroids are not pest-specific insecticides and have been used for the past 40 years, they continue to be commonly used. This is because they target a wide variety of pests, have low application rates, have low mammalian toxicity and have a favorable environmental fate profile. Provided that they are used appropriately, pest resistance to them is managed effectively and regulations for them are based on scientific evidence, the pyrethrins and pyrethroids will continue to be used well into the foreseeable future.

ON THE LIGHTER SIDE

- A group of organic molecules were having a party, when a group of robbers broke into the room and stole all of the guest's joules. A tall, strong man, armed with a machine gun came into the room and killed the robbers one by one. The guests were very grateful to this man, and they wanted to know who he was. He replied: My name is BOND, Covalent Bond.
- A freshman chemistry student prepared a standard solution and showed it to her professor. The professor gave her a puzzled look, and said: This solution looks a bit WEIRD. Are you sure you used the right set of reagents? The student replied: Absolutely. According to my calculations, this is one NORMAL solution.

Source:http://www.coolscience.org/CoolScience/CoolJokes/ChemJokes.htm

CONFERENCES

Florida Pesticide Residue Workshop

July 15-18, 2012

49th Annual Florida Pesticide Residue Workshop (FPRW)

TradeWinds Island Grand, St. Pete Beach, Florida

http://www.flworkshop.com/index.php

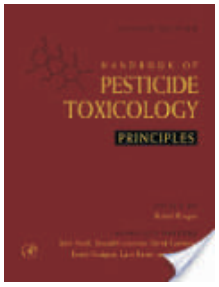
2012 GlobalChem Conference and Exhibition

March 5 - 7, 2012

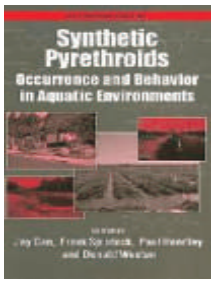
Baltimore, Maryland 21201

http://www.cvent.com/events/2012-globalchem-conference-and-exhibition/event-summary-5024446a5ab54b538fed8d7ef149e93b.aspx

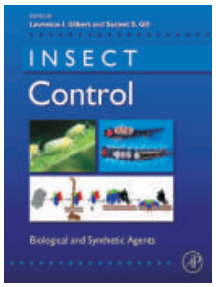
BOOK STOP



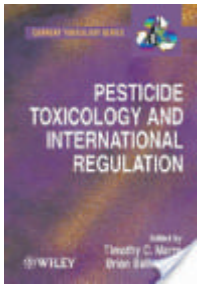
Handbook of pesticide toxicology, Volume 1
Editor: Robert Irving Krieger
Publishers: Academic Press, 2001
ISBN: 0124262619
Length: 1908 Pages



Synthetic Pyrethroids: Occurrence and Behavior in Aquatic Environments
Editors: Jay Gan,Frank, Spurlock, Paul Hendley, Donald P. Weston
Publisher: Oxford University Press
ISBN: 9780841274334
Length: 496 Pages



Insect Control: Biological and Synthetic Agents
Editors: Lawrence I. Gilbert, Kostas Latrou, and Sarjeet S. Gill
Publishers: Academic Press, 2010
ISBN: 9780123814494
Length: 490 Pages



Pesticide toxicology and international regulation
Editors: Timothy C. Marrs, Bryan Ballantyne
Publishers: John Wiley & Sons Ltd., 2004
ISBN: 0471496448
Length: 554 Pages
Length: 554 Pages

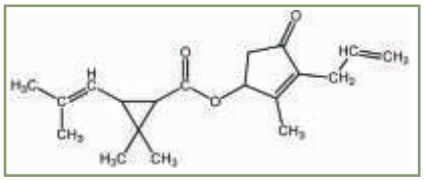
MINI PROFILE

ALLETHRIN

SYNONYM Bioallethrin; allethrine; allethrin; allethrine; esbiothrin; pyrethrin; pynamin; pyresin; pyresyn; trans-allethrin; (+)-Allelrethonyl (+)-cis,trans-chrysanthemate; d-allethrin-; allethrin-i-; allethrolone-ester - of -chrysanthemumm-onocarboxylic-acid-; alleviate-; allyl-cinerin-; allyl-cinerin-i-; 2-allyl-4-hydroxy-3-methyl-2-cyclopenten-1-one-ester-of-chrysanthemummono--carboxylic-acid-; 3-allyl-4-keto-2-methylcyclopentenyl-chrysanthemummonocarboxylate-; 3-allyl-2-methyl-4-oxo-2-cyclopenten-1-yl-chrysanthemate-; allylrethronyl-dl-cis-trans-chrysanthemate-; bioaltrina-; cinerin-i-allyl-homolog-; cyclopropanecarboxylic acid, 2,2-dimethyl-3-(2-methyl-1-propenyl)-, 2-methyl- 4-oxo-3-(2-propenyl)-2-cyclopenten-1-yl ester; depallethrin-; 2,2-dimethyl-3-(2-methyl-1-propenyl)cyclopropanecarboxylic acid 2-methyl-4-oxo-3-(2-propenyl)-2-cyclopenten-1-yl ester; ent-17,510-; ent-16275-; pesticide-code:-004001-; exthrin-.

RTECS NO GZ1476000

CAS NO 584-79-2



MOL FORMULA $C_{19}H_{26}O_3$

MOL WEIGHT 302.39999999999998

PROPERTY

Colour: Pale yellow viscous liquid; BP: 140°C; MP: 4°C ; VP: Pa at 20°C: <10

ANALYTICAL METHOD Gas chromatagraphic method.

USES Flying and crawling insect control for industrial locations and outdoor use .

FORMULATION Aerosol dispenser; emulsifiable concentrate; dispersible powder; wettable powder; Coil.

HAZARD Incompatible with lime & ordinary soaps because acids & alkalies speed up processes of hydrolysis. When heated to decomposition it emits acrid fumes.

HAZARD RATING Moderately hazardous.

TOXICITY DATA

orl-mus LD_{50}: 370 mg/kg

orl-rat LD_{50}: 685 mg/kg

orl-rbt LD_{50}: 4290 mg/kg

Inhalation-Mouse: LC_{50}: >2 gm/m^3

STORAGE Provision to contain effluent from fire extinguishing. Separated from food and feedstuffs. Keep in a well-ventilated room .

DISPOSAL Do not apply directly to water, or to areas where surface water is present, or to inter-tidal areas below the mean high water mark. Do not contaminate water when cleaning equipment or disposing of equipment washwater or rinsate. Recom-mendable methods: Incineration & landfill

Route of exposure	Symptoms	First Aid	Target organs
Inhalation/Ingestion	Cough,nausea, vomiting and abdominal pain	Fresh air, rest. Rinse mouth	Liver and Kidney
Contact	Redness. irritating to the eyes, the skin	Remove contaminated clothes. Rinse and then wash skin with water and soap. Rinse eyes with plenty of water for several minutes (remove contact lenses if easily possible), then take to a doctor.	

MAY WE HELP YOU

To keep abreast with the effects of chemicals on environment and health, the ENVIS Centre of Indian Institute of Toxicology Research, deals with:

Maintenance of toxicology information database on chemicals

Information collection, collation and dissemination

Toxic chemical related query response service

Preparation of monograph on specified chemicals of current concern

Publishing Abstract of Current Literature in Toxicology

for further details do write to

Scientist In-Charge

ENVIS CENTRE

CSIR-INDIAN INSTITUTE OF TOXICOLOGY RESEARCH

Post Box# 80, Mahatma Gandhi Marg, Lucknow-226 001 India.

Phone : (0522) 2284 591, Fax : (0522) 2628227

Email : itrc@envis.nic.in

Website : http://www.itrcenvis.nic.in