Permethrin: Uncovering the facts!

C Tech Corporation

INDEX

INTRODUCTION

Pyrethroids: The pre-curser to permethrin

Synthetic pyrethroids are synthesized derivatives of naturally occurring pyrethrins, which are taken from pyrethrum, the oleoresin extract of dried chrysanthemum flowers (the term "pyrethrum" is often used as a generic term to describe either natural pyrethrins or synthetic pyrethroids). The insecticidal properties of pyrethrins are derived from ketoalcoholic esters of chrysanthemic and pyrethroic acids. These acids are strongly lipophilic and rapidly penetrate many insects and paralyze their nervous system (Reigart et al., 1999). Both pyrethrins and synthetic pyrethroids are sold as commercial pesticides used to control pest insects in agriculture, homes, communities, restaurants, hospitals, schools, and as a topical head lice treatment. Various formulations of these pesticides are often

combined with other chemicals, known as synergists, to increase potency and persistence in the environment.

While chemically and toxicologically similar, pyrethrins are extremely sensitive to light, heat and moisture. In direct sunlight, half-lives that can be measured in hours. However, the pyrethroids, the synthetic analogues of naturally occurring pesticides, were developed to capture the effective insecticidal activity of this botanical insecticide, with increased stability in light, yielding longer residence times (Gosselin et al., 1984).

Permethrin: The origin!!!

Permethrin is a common synthetic chemical, widely used as an insecticide, acaricide, and insect repellent. It belongs to the family of synthetic chemicals called pyrethroids and functions as a neurotoxin, affecting neuron membranes by prolonging sodium channel activation.

Permethrin is used:

- as an insecticide
  - in agriculture, to protect crops
  - in agriculture, to kill livestock parasites
  - for industrial/domestic insect control
- as an insect repellent or insect screen
  - in timber treatment
  - as a personal protective measure (cloth impregnant, used primarily for US military uniforms and mosquito nets)
  - in pet flea preventative collars or treatment,
  - Agriculture and forestry
  - In agriculture, permethrin is mainly used on cotton, wheat, maize, and alfalfa crops. Its use is controversial because, as a broad-spectrum chemical, it kills indiscriminately; as well as the intended pests, it can harm beneficial insects including honey bees, and aquatic life.

- Personal insect control
- Permethrin kills ticks on contact with treated clothing. A method of reducing deer tick populations in terms of rodent vectors involves utilizing biodegradable cardboard tubes stuffed with permethrin-treated cotton. Mice collect the cotton for lining their nests. Permethrin on the cotton instantly kills any immature ticks that are feeding on the mice. It is important to put the tubes where mice will find them, such as in dense, dark brush, or at the base of a log; mice are unlikely to gather cotton from an open lawn.
- Permethrin is used in tropical areas to prevent mosquito-borne disease such as dengue fever and malaria. Mosquito nets used to cover beds may be treated with a solution of permethrin. This increases the effectiveness of the bed net by killing parasitic insects before they are able to find gaps or holes in the net. Malaria kills 1–3 million people per year. Military personnel training in malaria-

endemic areas may be instructed to treat their uniforms with permethrin, as well. An application should last several washes.

Permethrin acts as a neurotoxin, slowing down the nervous system through binding to sodium channels. This action is negatively correlated to temperature, thus, in general, showing more acute effects on cold-blooded animals (insects, fish, frogs…) over warm-blooded animals (mammals and birds)

TOXICOLOGICAL ASPECTS

Toxic to Humans:

Pesticide products containing synthetic pyrethroids are often described by pest control operators and community mosquito management bureaus as "safe as chrysanthemum flowers." While pyrethroids are a synthetic version of an extract from the chrysanthemum plant, they were chemically engineered to be more toxic with longer breakdown times, and are often formulated with synergists, increasing potency and compromising the human body's ability to detoxify the pesticide.

Permethrin belongs to a class of chemicals called pyrethroids, described by the Agency for Toxic Substances and Disease Registry (U.S. Department of Health and Human Services) as "manufactured chemicals that are very similar in structure to the [naturally occurring] pyrethrins, but are often more toxic to insects, as well as to mammals, and last longer in the

environment" (ATSDR Public Health Statement, pg. 1). Permethrin is not a natural product. It is one of many synthetic pyrethroids developed for use as an insecticide based on the chemistry of the pyrethrum flowers.

Carcinogenicity:

All pesticides sold or distributed in the Unites States must be registered by the Environmental Protection Agency (EPA), based on scientific studies showing that they can be used without posing unreasonable risks to people or the environment. Because of advances in scientific knowledge, the law requires that pesticides, which were first registered before November 1, 1984, be re-registered to ensure that they meet today's more stringent standards.

In evaluating pesticides for re-registration, EPA obtains and reviews a complete set of studies from pesticide producers, describing the human health and environmental effects of each pesticide. To implement

provisions of the Food Quality Protection Act (FQPA) of 1996, EPA considered the special sensitivity of infants and children to pesticides, as well as aggregate exposure of the public to pesticide residues from all sources, and the cumulative effects of pesticides and other compounds with common mechanisms of toxicity. The Agency develops any mitigation measures or regulatory controls needed to effectively reduce each pesticide's risks. EPA then registers pesticides that meet the safety standard of the FQPA and can be used without posing unreasonable risks to human health or the environment.

When a pesticide is eligible for re-registration, EPA explains the basis for its decision in a Re-registration Eligibility Decision (RED) document. This fact sheet summarizes the information in the RED document for the pesticide permethrin, case 2510.

Permethrin is classified by the United States Environmental Protection Agency (EPA) as a likely human carcinogen, based on reproducible studies in which mice fed permethrin developed liver and lung tumors. Carcinogenic action in nasal mucosal cells due to inhalation exposure is suspected, due to observed genotoxicity in human tissue samples, and in rat livers the evidence of increased pre-neo plastic ions raises concern over oral exposure.

The Agency has classified permethrin as "Likely to be Carcinogenic to Humans" by the oral route. This classification was based on two reproducible benign tumor types (lung and liver) in the mouse, equivocal evidence of carcinogenicity in Long- Evans rats, and supporting structural activity relationship information.

The cancer risk assessment (through diet: food and water) was monitored with reference to a prescribed level adjudged by the EPA which was the 'level of concern'. The aggregate cancer risk estimate exceeded the Agency's LOC for adults exposed to permethrin through food and drinking water, and through post application exposure during high contact activity on lawns and indoor surfaces.

Permethrin has also been linked to disruption of the endocrine system, which can adversely affect reproduction and sexual development, interfere with the immune system and increase chances of breast cancer. Pyrethroids contain human-made, or xenoestrogens, which can increase the amount of estrogen in the body (Garey et al., 1998). When tested, certain pyrethroids demonstrate significant estrogenicity and increase the levels of estrogen in breast cancer cells (Go et al., 1999). Because increased cell division enhances the chances for the formation of a

malignant tumor in the breast, artificial hormones, like those found in pyrethroids, may increase breast cancer risk (PCBR, 1996).

Summary:

Based on studies demonstrating carcinogenicity, EPA ranks permethrin as a class C, or possible human carcinogen (U.S. EPA, 1997). Other studies have shown effects on the immune system, enlarged livers and at high doses, decreased female fertility and endocrine disruption.

Neurotoxicity:

Permethrin is a member of the pyrethroid class of pesticides. Similar to other pyrethroids, permethrin alters nerve function by modifying the normal biochemistry and physiology of nerve membrane sodium channels.

Pyrethroids have irritant and/or sensitizing properties. They are not easily absorbed through the skin, but are absorbed through the gut and pulmonary membrane. Tests of some pyrethroids on laboratory animals reveal striking neurotoxicity when administered by injection or orally. Systemic toxicity by inhalation and dermal absorption is low. The acute toxicity, calculated by LD50's, ranges from low to high, depending on the specific formulation. Low toxicity is attributed to two factors: limited absorption of some pyrethroids, and rapid biodegradation by mammalian liver enzymes (ester hydrolysis and oxidation). Insects, without this liver

function, exhibit greater susceptibility to the chemicals (Reigart et al., 1999).

Pyrethroids interfere with the ionic conductance of nerve membranes by prolonging the sodium current. This stimulates nerves to discharge repeatedly causing hyper-excitability in poisoned animals. The World Health Organization explains that synthetic pyrethroids are neuropoisons acting on the axons in the peripheral and central nervous systems by interacting with sodium channels in mammals and/or insects. The main systems for metabolism include breakage of the ester bond by esterase action and oxidation at various parts of the molecule. Induction of liver microsomal enzymes has also been observed (WHO, 1999).

Permethrin exerts its toxic effects directly on the nervous system. Studies in mice and rats show that sub-lethal intoxication leads to aggression, hypersensitivity to external stimulation, whole-body tremor, convulsions

and paralysis. “If very large amounts of these chemicals were to enter your body, you might experience dizziness, headache, and nausea that might last for several hours. Larger amounts might cause muscle twitching, reduced energy, and changes in awareness. Even larger amounts could cause convulsions and loss of consciousness that could last for several days.” (Toxicological Report, pg. 5).

A report:

Studies by Bloomquist et al., 2002 [suggested a link of permethrin exposure to Parkinson's disease, including very small (per kg.) exposures.

"Our studies have documented low-dose effects of permethrin, doses below one-one thousandth of a lethal dose for a mouse, with effects on those brain pathways [that are] involved in Parkinson's Disease. We have found effects consistent with a pre-parkinsonsian condition”

Endocrine Disruption and pregnancy related disorders:

Permethrin has also been linked to disruption of the endocrine system, which can adversely affect reproduction and sexual development, interfere with the immune system and increase chances of breast cancer.

Endocrine disruptors are chemicals that interfere with the communication system of glands, hormones, and cellular receptors that control the body's internal functions. A relatively unique feature of endocrine disruptors is that they exert their effects at extremely low doses, even when higher doses exhibit no adverse effects. Disorders that have increased in prevalence in recent years such as unusual male gonadal development, infertility, ADHD, autism, intellectual impairment, diabetes, thyroid disorders, and childhood and/or adult cancers are now being linked to prenatal exposure to endocrine disruptors.

In the permethrin studies of health effects on the female reproductive system, excessive cell growth was a common finding. In contrast, cell death and reduced tissue weight of male reproductive organs were among the findings on the male reproductive system. One study suggested that the products permethrin breaks down into may be 100 times more potent with regards to endocrine disruption than permethrin itself. Due to the potential endocrine disrupting effects of permethrin, pregnant women should take extra steps to avoid exposure.

In an endeavour to examine the effects of these pyrethroid compounds on humans and the first evaluation of their potential toxicity to the developing fetal brain, scientists of the Columbia Center for Children's Environmental Health at Columbia University's Mailman School of Public Health undertook one such study.

The study was conducted with a subset of 725 pregnant women participating in a prospective longitudinal study of black and Dominican women living in upper Manhattan and the South Bronx underway at the Columbia Center for Children's Environmental Health (CCCEH). The insecticide **permethrin** was selected for the evaluation because it is one of the most common pyrethroid insecticides used in U.S. homes, as well as the most commonly sold pesticide, according to a nationally representative sample.

In all, 342 women were studied for permethrin exposure in personal air during pregnancy; 272 for permethrin in maternal and umbilical cord plasma; and 230 were evaluated for exposure to PBO. To collect the air samples, mothers from the CCCEH Mothers and Newborns cohort wore a small backpack holding a personal ambient air monitor for 48 hours *during the third trimester of pregnancy*.

The children of these mothers were evaluated for cognitive and motor development at age three. CCCEH researchers used the Bayley Scales of Infant Development. In evaluating the results, researchers controlled for gender, gestational age, ethnicity, maternal education and intelligence, quality of the home environment, and prenatal exposure to environmental tobacco smoke and chlorpyrifos. PBO was injected as a marker.

PBO was detected in the majority of personal air samples (75 percent). While the results demonstrate that a significant prenatal exposure to permethrin in personal air and/or plasma was not associated with performance scores for the Bayley Mental Developmental Index or the Psychomotor Developmental Index at 36 months, children who were more highly exposed to PBO in personal air samples (≥4.34 ng/m3) scored 3.9 points lower on the **Mental Developmental Index** than those with lower exposures.

"This drop in IQ points is similar to that observed in response to lead exposure," said Megan Horton of the Mailman School of Public Health and lead researcher. "While perhaps not impacting an individual's overall function, it is educationally meaningful and could shift the distribution of children in the society who would be in need of early intervention services."

The researchers point out that environmental and biological monitoring of pyrethroid insecticides present certain challenges. "We know most pyrethroid insecticides are difficult to measure in the air because they are not volatile and are difficult to measure in bodily fluids because they are rapidly metabolized, and these difficulties may prevent us from seeing significant associations with neurodevelopment outcomes," noted Dr. Horton.

As this is the first study of these compounds, the results should be considered preliminary but, Dr. Horton notes, they do - raise a cautionary red flag about the use of these chemicals during pregnancy. And, she adds, research at the Columbia Center for Children's Environmental Health, indicates that "integrated pest management and the non-spray application of lower toxicity pesticides are viable alternatives to the use of these spray pesticides for pest control."

"This is an important study with potentially broad public health implications," according to Dr. Robin Whyatt, Mailman School professor of clinical environmental health sciences and a co-deputy director at the CCCEH. "Further, it identifies a critical need for additional research."

Summary:

One of the primary concerns is recent research demonstrating that permethrin exhibits the characteristics of an endocrine disruptor.

More research is required to better understand any possible link between permethrin and endocrine function.

Permethrin is included in the draft list of initial chemicals for screening under the U.S. EPA Endocrine Disruptor Screening.

Associated disorders:

Pesticide products containing synthetic pyrethroids are often described by pest control operators and community mosquito management bureaus as "safe as chrysanthemum flowers." While pyrethroids are a synthetic version of an extract from the chrysanthemum plant, they were chemically engineered to be more toxic with longer breakdown times, and are often formulated with synergists, increasing potency and compromising the human body's ability to detoxify the pesticide.

Signs and symptoms of poisoning by permethrin may take several forms. Because of the similarities to crude pyrethrum, permethrin may act as a dermal and respiratory allergen. Exposure can result in contact dermatitis and asthma-like reactions. Persons, especially children, with a history of allergies or asthma are particularly sensitive, and a strong cross-reactivity

with ragweed pollen has been recognized. Severe anaphylactic (allergic) reactions with peripheral vascular collapse and respiratory difficulty are rare. Other symptoms of acute toxicity due to inhalation include sneezing, nasal stuffiness, headache, nausea, in-coordination, tremors, convulsions, facial flushing and swelling, and burning and itching sensations. The most severe poisonings have been reported in infants, who are not able to efficiently break down permethrin (ETN, Pyrethroids, 1994). With orally ingested doses, nervous symptoms may occur, which include excitation and convulsions leading to paralysis, accompanied by muscular fibrillation and diarrhea (ETN, Pyrethroids, 1994). Death in these cases is due to respiratory failure. Symptoms of acute exposure last about 2 days.

To summarize concisely some of the symptoms and areas that are affected with permethrin toxicity include the following:

- Convulsions and tremors of the nervous system
- Asthmatic attacks, breathing difficulties, sneezing, etc.

- Elevated body temperatures
- Headaches, nausea and dizziness
- Allergic reactions, especially in people sensitive to ragweed
- Skin irritation such as burning and itching, particularly around the mucus membranes
- Tearing and redness of the eyes, and blurred vision
- Reproductive organ compromise (in experiment with rabbits and rats permethrin caused reduced testes and miscarriage)
- Immune cell activity reduction by about 40 percent
- Enlarged adrenal glands
- Attacks on the liver
- Tumor growth by means of carcinogens

Individuals who already have compromised immune systems, such as people with multiple sclerosis or respiratory issues, can be more adversely affected by contact with permethrin based products. Please be on the lookout for this dangerous substance in your home.

- Dermal exposure to permethrin may cause irritation, itching, or paresthesia (a tingly, prickly sensation) at the site of contact.
- Ocular exposures may result in pain, redness, or a burning sensation.
- Ingestion of permethrin may cause sore throat, abdominal pain, nausea, and vomiting.
- Inhalation of permethrin may cause headache, nasal and respiratory irritation, difficulty breathing, dizziness, nausea or vomiting.

Reports:

The Agency for Toxic Substances and Disease Registry (ATSDR) determined Minimum Risk Levels (MRLs) for oral exposures to technical grade permethrin of 0.3 mg/kg/day for acute oral exposures (up to 14 dayn 2007, by fogging the town of Paonia with a well known insecticide formulation, of which the primary active ingredient is permethrin. In an

effort to gather information on the potential impact of permethrin on human health, we conducted an extensive search of the scientific literature published in reviewed academic journals. The following is an overview and summary of our findings.

Permethrin belongs to a class of chemicals called pyrethroids, described by the Agency for Toxic Substances and Disease Registry (U.S. Department of Health and Human Services) as "manufactured chemicals that are very similar in structure to the [naturally occurring] pyrethrins, but are often more toxic to insects, as well as to mammals, and last longer in the environment" (ATSDR Public Health Statement, pg. 1). Permethrin is not a natural product. It is one of many synthetic pyrethroids developed for use as an insecticide based on the chemistry of the pyrethrum flowers. It is used in household insect foggers and sprays, flea dips and sprays for cats and dogs, ornamental garden and turf products, repellent/insecticide for clothing, mosquito abatement products, termite treatments,

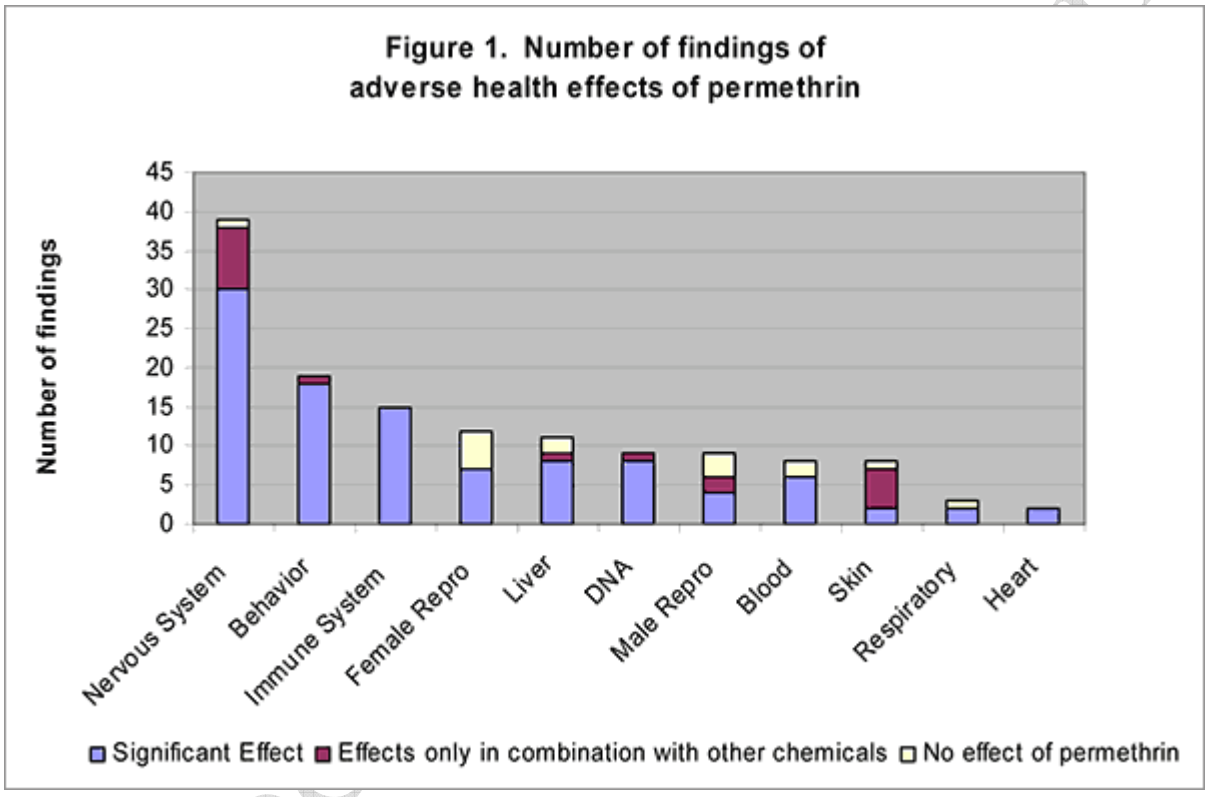
agricultural products, lice shampoos, and body lotions for scabies control. Pyrethroid insecticides are some of the most widely used pesticides in the world because they are believed to be less harmful to humans than other pesticides.

Permethrin can be breathed into the lungs, absorbed through the skin or ingested. The most dangerous route is inhalation through the lungs, as this allows the chemical to move directly to target sites (e.g., the brain) without being metabolized by the liver and other organs. The following recommendation is issued by the U.S. Department of Health and Human Services in their Toxicological Profile for Pyrethrins and Pyrethroids (September 2003). "Remaining indoors and closing your windows while your neighborhood is being sprayed will lessen your exposure." (Toxicological Report, pg. 8). We also recommend turning off air conditioners and swamp coolers and keeping family pets indoors during this time. Because permethrin is odorless and weather conditions vary,

individuals must use their judgment in deciding how long after spraying to keep these precautions in place.

Among the general population, ingestion (usually as residues on food) is the most common way that people are exposed to permethrin. The health department advises "Make sure you wash fruits and vegetables thoroughly before eating them" (Toxicological Report, pg. 8). Absorption through the skin is slow and it appears that only a fraction of the applied chemical penetrates the skin, thus reducing its toxicity via this route. Direct skin exposure may cause itching, tingling or burning sensations that peak within a few hours and resolve within 24 hours. "Pyrethroids might be able to penetrate the skin of infants and young children more easily than the skin of adults. …pyrethroids that penetrate the skin may become more concentrated in internal tissues of the young." (Toxicological Report, pg. 7). Thus, it is important to reduce children's exposure to permethrin as much as possible.

Although it does not accumulate in the body, permethrin (and/or its metabolites) has been detected in human urine, feces, and breast milk. It takes approximately one week to excrete 90% of it, primarily in urine.



Summary and comments

In our literature search we found 108 scientific journal articles on the potential health effects of permethrin. The graph below shows the

number of findings on the most widely researched health-related endpoints. Shaded bars indicate whether or not there were significant effects of permethrin, effects only in combination with other chemicals or no effects.

The bulk of studies on the nervous system demonstrated that permethrin affects the brain in the way that it was designed to behave. That is, it causes repetitive firing of the electronic signals in particular regions of the brain. These effects were found in laboratory animals used for predicting what might happen in humans.

Every one of the 15 studies that we found on the immune system showed significant effects. Results indicated that permethrin led to the death and/or reduced production of blood cells necessary to fight bacteria and

viruses and remove waste products from the blood. Varied physiological changes, including DNA damage, were reported in other systems.

The German tests

Meanwhile, in Germany, the Federal Health Agency, alerted by growing reports of suspected permethrin poisoning cases (around 250 in 1997), commissioned the Fraunhofer Institute to investigate(2). Professor Levsen of the institute points out that inhalation is probably an insignificant route, so their model was designed to test for oral exposure. Rather than using empty boxes, the Institute adopted a model based upon actual living conditions-ten test rooms furnished with carpets, sofas, tables and chairs, and, critically, they provided each test room with a known quantity of house dust.

The dust was circulated within the rooms by fans, with a ventilation rate of 0.8 air changes per hour. The floors were then sprayed with the various permethrin products, and as well as sampling the airborne concentrations, the German team collected and analysed the house dust on tables, chairs and other furniture.

It was found that aerial concentrations died away quite quickly, but wipe tests on the furniture showed that permethrin was being picked up from the floor by the circulating house dust and deposited on the other surfaces. Notably, significant levels of permethrin were still being detected on the coffee tables and dining tables in the test rooms up to two years after initial application. It is fair to assume that in a real home this pick-up and deposition of permethrin would also be occurring on kitchen worktops and other food preparation surfaces.

As a result of the work at the Fraunhofer Institute, it is now recommended in Germany that permethrin is applied in homes as

cautiously as possible, and only on structural timbers known to be subject to active insect attack. Permethrin is not recommended for non-structural timbers such as floorboards. In addition, homes treated with permethrin are now required to be decontaminated by vacuuming and scrubbing with household cleaners before re-occupation.

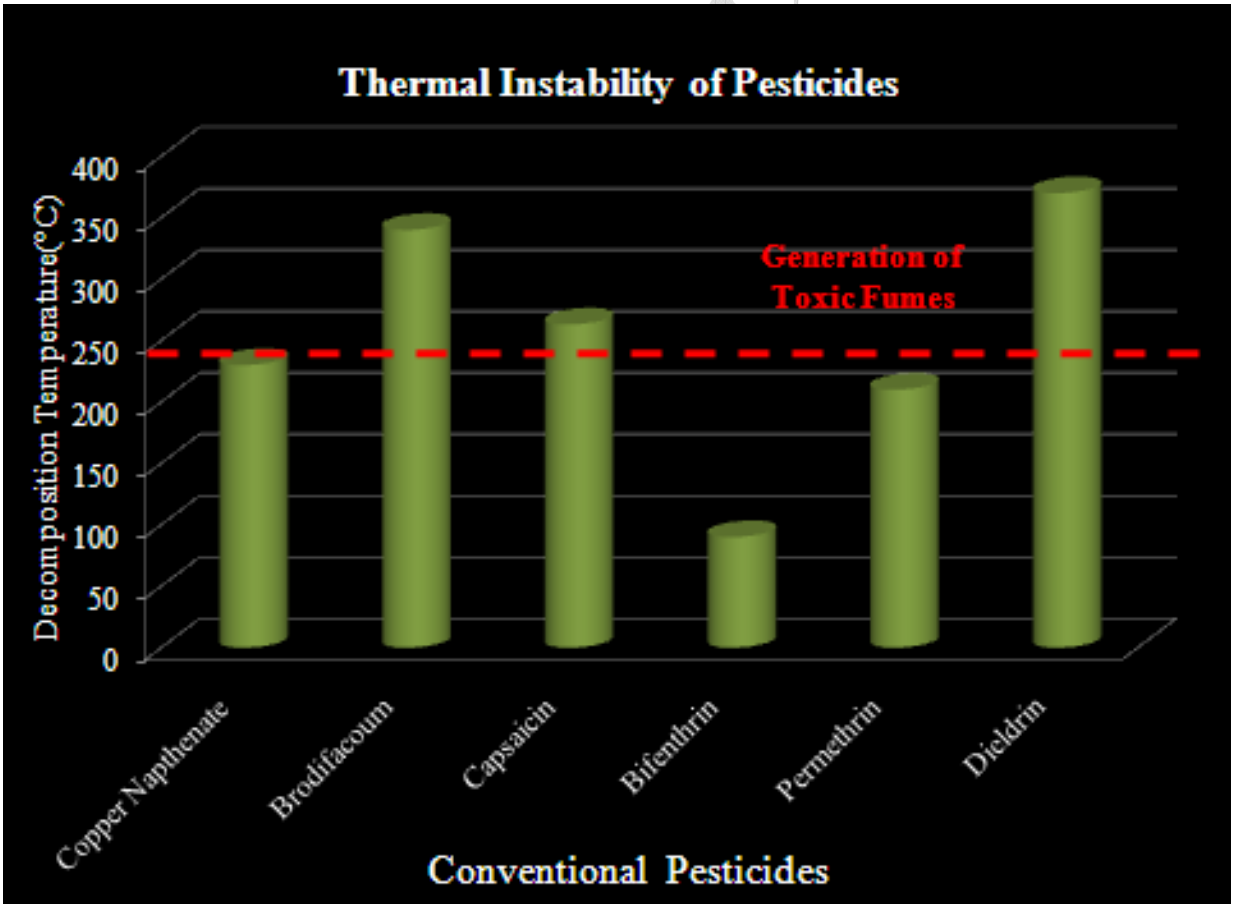
Recently, in South Africa, residues of permethrin were found in breast milk, together with DDT, in an area that experienced DDT treatment for malaria control, as well as the use of pyrethroids in small-scale agriculture.

The problems on the shop-floor:

Excessive exposure to permethrin can cause nausea, headache, muscle weakness, excessive salivation, shortness of breath, and seizures. Worker exposure to the chemical can be monitored by measurement of the urinary metabolites, while severe overdosage may be confirmed by quantitation of permethrin in serum or blood plasma. These harmful insecticide additives volatilize at polymer processing temperatures and release extremely toxic fumes. These toxic fumes are many times more lethal than the original .This poses fatal hazards to workers handling such products at the shop floor. As (air) temperature increases, vapour hazards will increase. The vapours from many pesticides increase three to four times for each 10° C increase in temperature. This is one reason why pesticide should be stayed away from sunlight and why it is typically recommended that pesticides not be applied when air temperatures are above 30° C. Extrusion temperatures are as high as 100-300° C.

Toxic Vapours!!!

Permethrin has a low thermal decomposition temperature **of 240-250°C**. When such chemicals are used in extrusion for manufacturing of wire and cables, pipelines etc, they decompose during the process only. The decomposition leads to the formation of toxic fumes. These fumes are highly toxic especially for the personnel working on the shop floor. The graph below shows the thermal instability of various pesticides currently used worldwide.



The thermal degradation temperature of Permethrin is 243°C which is in the same range as the process of extrusion. Elevated as well as localized temperatures in an extruder can go as high as 400°C and even beyond. This can result in serious problems for workers which will be handling the product. Moreover the temperatures are quite high near the tube exits of the extruder which could be a major source of toxic fumes. In case of insufficient ventilation which is normally the case in case of compact arrangements near the exits, these fumes can accumulate thus increasing the toxicity in general 30° C. Extrusion temperatures are as high as 100-400° C.

The Agency has determined that there is potential exposure to applicators and/or other handlers during typical use patterns associated with these chemicals. Specifically, the Agency is concerned about potential dermal and inhalation exposures to handlers during the loading and application of these chemicals. Based on the use patterns and potential exposures, major handler scenarios were identified such as (l) placing bait packs; (2)

loading bait boxes or bait stations with meal bait, grain bait, bait pellets, or other food-based bait from larger containers; (3) breaking parafinized blocks into pieces and placing the pieces in bait stations; (4) securing large paraffin blocks in bait stations used in sewers; (5) applying bait by hand; and (6) applying bait, e.g. pellets in broadcast treatments using ground and (6) spray

Acute toxicity values!!!

According to **WHO Recommended Classification of Pesticides by Hazard**, this compound falls in **Class II** meaning an "**hazardous substance"**.

R- and S-Phrases:

R-phrases (short for Risk Phrases) are defined in Annex III of European Union Directive 67/548/EEC: Nature of special risks attributed to dangerous

substances and preparations. The list was consolidated and republished in Directive 2001/59/EC, where translations into other EU languages may be found. R-phrases for permethrin are:

R25 Toxic if swallowed;

R37 Irritating to respiratory system;

R38 Irritating to skin;

R42/43 May cause sensitization by inhalation and skin contact.5

S-phrases are defined in Annex IV of European Union Directive 67/548/EEC: Safety advice concerning dangerous substances and preparations. The list was consolidated and republished in Directive 2001/59/EC, where translations into other EU languages may be found. S-phrases for permethrin are:

S22 Do not breathe dust;

S26 In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.

S28- After contact with skin, wash immediately with plenty of water;

S36/37/39 Wear suitable protective clothing, gloves and eye/face protection.

S45 In case of accident or if you feel unwell; seek medical advice immediately (show the label where possible).

Toxicity to animals:

Mode of Action:

Target Organisms

- Permethrin acts on the nervous system of insects. It interferes with sodium channels to disrupt the function of neurons, and causes muscles to spasm, culminating in paralysis and death.

Permethrin can be effective by contact or ingestion and also acts as a mild repellent.

Non-target Organisms

- Permethrin is highly toxic to honeybees, fish, and aquatic invertebrates due to disruption of sodium channels

Permethrin is extremely toxic to fish and aquatic life in general, so extreme care must be taken when using products containing permethrin

near water sources. Permethrin is also highly toxic to cats, and flea and tick-repellent formulas intended and labeled for (the more resistant) dogs may contain permethrin and cause feline permethrin toxicosis in cats. Very high doses will have tangible neurotoxic effects on mammals and birds, including human beings. Due to high toxicity for aquatic life, permethrin and permethrin-contaminated water should be properly disposed of. Degradation is quick and should the chemical be disposed of far from any aquatic life, the negative effects would be minimized.

Toxicity in cats:

Cats can get very ill and even die when inadvertently or inappropriately treated with permethrin spot-on flea and tick treatments developed for dogs. While these dog treatments specifically warn against use on cats, these warnings are sometimes overlooked or ignored by many users. The results can often be fatal causing anguish and heartache to cat owners.

The problem is widespread throughout the world. A 2008 Australian survey revealed more than 500 cases of cats being poisoned with dog tick and flea treatments resulting in 130 deaths.

Toxic effects include behavior changes, drooling, tremors and death. Seek veterinary advice immediately if you suspect toxicity in a cat.

Survey:

Towards the end of 2008, Richard Malik and other members raised their concerns about the number of cases they were seeing, and initiated a national survey to gauge the number of cases presenting to veterinarians in Australia. Stephen Page provided important input into the design and implementation of the survey, which involved the AVA, the Centre for Veterinary Education and the Australian College of Veterinary Scientists in a cooperative venture. The survey results have since been published,1 building on the clinical study by Dymond and Swift published in the *Australian Veterinary Journal* in 2008.2

255 survey responses described 750 individual cases of feline intoxication that had presented for treatment in the previous two years. 166 deaths were reported. While most cases of intoxication were reported to be due to directly treating cats with permethrin spot-on products (primary intoxication), a small number resulted from close contact between cats and recently treated dogs (secondary intoxication).

All high concentration permethrin products are approved only for use in dogs and specifically warn against use in cats, but the warnings appear to be ignored or overlooked by some users. Some reported to the veterinarian that they didn't see the warnings, while others thought the warning was just a sales ploy to get them to purchase a more expensive cat product, so they ignored it.

"It was clear from fairly early on that we were dealing with a significant issue for cat owners in Australia," said Richard Malik.

"It was a case of totally preventable heartache for the owners, and I really wanted to see something done about this problem that exists all over the developed world."

Toxicity in bees:

This product is highly toxic to bees exposed to direct treatment or residues on crops or weeds. Hence it is advisable to not employ the use of this product or allow it to drift to crops or weeds on which bees are actively foraging.

Toxicity to aquatic life:

This product is extremely toxic to fish and aquatic invertebrates. Hence it is advisable to not apply directly to water, or to areas where surface water

is present or to intertidal areas below the mean high water mark. It is advisable to not contaminate water by cleaning of equipment or disposal of equipment wash waters and when weather conditions favor drift from treated areas.

Care needs to be taken when making applications near ponds, lakes, streams, reservoirs and other aquatic environments where fish are present.

Permethrin is highly toxic to both freshwater and estuarine aquatic organisms. Most agricultural, public health, and down-the-drain scenarios modeled resulted in exceedances in the acute risk quotient (RQ) for freshwater and estuarine fish, invertebrates, and sediment organisms. The agricultural and public health scenarios also showed the potential for chronic risks to estuarine and/or freshwater organisms. Further, there is a potential concern for direct effects to a variety of aquatic organisms.

The chronic RQs for mammals exceeded the Agency's LOC. The potential for risk to terrestrial and aquatic plants from exposure to permethrin cannot be assessed because toxicity data are not available. However, any toxicity to plants would occur for reasons other than permethrin's insecticidal mode of action because permethrin works as a neural toxin, and unlike insects, plants do not have neural networks that could be affected.

While the development of the synthetic pyrethroids was heralded with claims of selective toxicity to insects, both pyrethroids and pyrethrins are extremely toxic to aquatic organisms, including fish such as the bluegill and lake trout, with LC50 values less than 1.0 parts per billion. These levels are similar to those for mosquito, blackfly and tsetse fly larvae, often the actual target of the pyrethroid application. Lobster, shrimp, mayfly nymphs and zooplankton are the most susceptible non-target aquatic

organisms (Mueller-Beilschmidt, 1990). The nonlethal effects of pyrethroids on fish include damage to the gills and behavioral changes.

Other:

Pyrethroids are moderately toxic to birds, with most LD50 values greater than 1000 mg/kg. Birds can also be indirectly affected by pyrethroids, because of the threat to their food supply. Waterfowl and small insectivorous birds are the most susceptible (Mueller-Beilschmidt, 1990). Because pyrethroids are toxic to all insects, both beneficial insects and pests are affected by pyrethroid applications. In some cases, predator insects may be susceptible to a lower dose than the pest, disrupting the predator-prey relationship.

A brief summary:

Signs of Toxicity - Animals

Dermal exposures to cats and dogs may cause temporary paresthesia and neurological signs as evidenced by paw flicking or ear, tail or skin twitching, or rolling on the ground.

Cats exposed dermally to some permethrin products may experience hyperexcitability, depression, ataxia, vomiting, anorexia, tremors, or convulsions. Symptoms can begin within a few minutes or up to three days after the exposure. Some permethrin products contain high concentrations of the active ingredient and are labeled for use only on dogs. Close physical contact with a recently treated dog may also lead to symptoms in cats. If symptoms are severe and untreated, they may result in death.

A report of 11 cats intentionally treated with products containing 45-65% permethrin described adverse effects including muscle tremors, seizures, incoordination and agitation after exposure. Of the 11 cats that were treated, all were hospitalized, and four died after the exposure. Seizures were found to develop within 24 hours of exposure, with some cats experiencing seizures within two hours. In one additional case, a cat was in proximity of two large dogs treated with a permethrin product 48 hours after treatment. Between 18 and 24 hours after being near the dogs, the cat developed signs including agitation, tremors, seizures, and ataxia. Animals may also display drooling or lip-smacking. This is believed to be a result of licking at the application site and thought to be caused either by the taste or a tingling sensation in the mouth.

Permethrin: A brief summary!

Permethrin has been used as a pesticide since 1977. At that time it was regulated only for use on cotton plants and in head lice ointments. Today, permethrin is also used as a pesticide on a variety of different products, including fruit, meat, and vegetables.

Here are some straightforward answers to the common questions regarding permethrin:

What is Permethrin?

Permethrin is a synthetic product that was approved in 1977 by the Federal Department of Agriculture as an insecticide. However, since that time, head lice resistance to permethrin has become widespread. Certain popular head lice lotions that use permethrin are promoted, as long as they are used in a geographical area that is not already resistant to permethrin.

What is Permethrin Used For?

Permethrin is used in a variety of insecticides, including several head lice lotions and bug sprays. Approximately two million pounds of permethrin are used annually, with about 70 percent being distributed in non-agricultural places. 55 percent of that is used by professionals, 41 percent by homeowners, and four percent is applied on mosquito abatement areas.

What are the Effects of Permethrin Toxicity?

Because permethrin affects the nerves, it has the potential to cause neurological damage in sensitive individuals.

After the Environmental Protection Agency (EPA) evaluated the toxicology and ecological effects of this chemical, it was determined to be

a weak carcinogen, though highly toxic to fish and aquatic invertebrates. While there is some concern over tumors grown in lab mice and how permethrin might affect humans, the EPA determined the risks did not reach a high enough level of concern.

Children are more susceptible to permethrin toxicity than adults. Early experiments discovered that permethrin can target the immune system and cause a variety of illnesses, some of which may occur in the reproductive organs and cause damage to the unborn fetus. Additionally, permethrin is a mutagen, and capable of causing chromosome abnormalities. Potential damage to a breastfeeding infant is not known at this time.

Is Permethrin a Carcinogen?

Yes. But the EPA has determined permethrin to be a weak carcinogen, and classified it as a Pregnancy B Drug. Pregnancy B Drugs are drugs that

show little or no evidence of risk to humans. However, because permethrin is a carcinogen, even a weak one, there still is a chance that a fetus could be harmed by this chemical. Additionally, it is unknown whether it is safe for use during breastfeeding.

Why is Permethrin Still in Use?

Because of its low cost and high efficiency, permethrin is the most widely used mosquito repellent in the United States. Unfortunately, while permethrin is considered a carcinogen, highly toxic to fish and other aquatic vertebrates, and a cancer and reproductive risk, the EPA has decided the health risks to humans fall below their level of concern.

CONCLUSION

The above reported results show how permethrin has been found to be toxic and therefore extensive study of the same is the need of the hour which would then probably reveal in alarming proportions whatever has been found so far to have affected humans and animals alike! What however we can do is stop or reduce the use of such compounds as ultimately it is us the end users who suffer the consequences and not the ones who supply it or market it and develop use of better non toxic and effective alternatives.

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