

Increasing Use of Pyrethroids in Canadian Households: Should We Be Concerned?

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ABSTRACT

Pyrethroids are a class of plant-derived insecticides and their man-made analogues that are increasingly applied in Canada as first choice for pest control in many agricultural and residential settings. Their popularity is partly due to their alleged safety compared to the older organochlorine and organophosphate insecticides. Application of pyrethroids is expanding because of recent increases in the level of pest infestations – such as bed bugs – and the decreased susceptibility of target species to many pest control products. Pyrethroid residues have been documented in homes, child care centres and food. While pyrethroids are considered of low health risk for humans, their increased use is of concern. Our current understanding of the adverse effects of pyrethroids derives mainly from studies of short-term effects in laboratory animals, case reports of self- and accidental poisonings, and high-dose occupational exposures, for which the levels and formulations of pyrethroid products differ from those relevant for long-term exposure in the general population. The available data suggest that the reproductive and nervous systems, endocrine signalling pathways, and early childhood development may be targets for adverse effects in the case of repeated exposure to pyrethroid formulations. Given uncertainty about the existence of long-term health effects of exposure to pyrethroids, particularly under realistic scenarios, we should be cautious when promoting pyrethroid products as safe methods for pest control.

Key words: Pyrethrins; environmental exposure; endocrine disrupting chemicals; toxicology; risk assessment

La traduction du résumé se trouve à la fin de l'article.

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Pyrethroid insecticides and naturally occurring pyrethrins are commonly used for insect control in households and in agriculture.¹ Reasons for this are increasing restrictions in the use of organophosphate and organochlorine insecticides, the greater selectivity of pyrethroids for certain target species,² their moderate acute oral toxicity in vertebrates and humans,³ and relatively low levels of environmental residues due to rapid degradation outdoors.¹ While pyrethroids have received both scientific² and regulatory^{4,5} attention, questions remain as to their safety, especially for residential applications.

What are pyrethroids?

Natural pyrethrins are present in pyrethrum extracts obtained from flowers of some species of chrysanthemum. Because pyrethrins degrade easily under the influence of water and sunlight, more stable alternatives – the synthetic pyrethroids – have been developed, allowing for longer intervals between applications.¹ Pyrethroids and pyrethrins act on the nervous system of flying insects by disrupting the function of sodium channels. They delay the closing of these channels, which results in repetitive firing of neurons, causing paralysis and death.^{1,2} Pyrethroids produce toxicity in non-target species such as mammals in a similar manner.^{1,6,7}

Synthetic pyrethroids are generally classified into two types, based on toxicological and physical-chemical properties. “Type-I”-like pyrethroids include allethrin, bifenthrin, permethrin, phenothrin, resmethrin, tefluthrin and tetramethrin. Examples of “Type-II” pyrethroids are cyfluthrin, cyhalothrin, cypermethrin and

deltamethrin.¹ In Canada, the natural pyrethrins and the synthetic pyrethroids permethrin, allethrin, tetramethrin, phenothrin and resmethrin are registered for residential use.⁸ More than 600 of 2,144 pesticide products currently registered for residential pest control in Canada contain one or more of these substances.⁸

In humans, pyrethroids are rapidly metabolized and excreted in urine. The identification of primary metabolites in urine is of little utility in distinguishing exposure to specific pyrethroids: metabolic pathways for different parent compounds produce the same breakdown products. For example, 3-phenoxybenzoic acid (3-PBA) is a common metabolite of cyhalothrin, cypermethrin, deltamethrin, fenpropathrin, permethrin and tralomethrin. The *cis* and *trans* configurations of 3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylic acid (i.e., *cis*-DCCA and *trans*-DCCA) are the metabolic products of the *cis* and *trans* isomers of cypermethrin, cyfluthrin or permethrin, respectively.¹ Thus, the specific pyrethroid to which an individual was exposed, and its source (e.g., diet or residential use), cannot be readily determined only by analyzing urine.⁹

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To what degree are pyrethroids used?

To the best of our knowledge, there are no Canadian residential use data. In the US, 2 million pounds of permethrin, the most common pyrethroid used, are applied annually in agricultural and residential settings. The majority of permethrin, over 70%, is applied in non-agricultural settings.¹⁰ Again in the US, permethrin residues were found in 89% of homes in a representative sample in 2005-2006.¹¹ In general, pyrethroids registered for home pest control are assumed to degrade rapidly in the environment under the influence of water and sunlight, thus limiting the potential for household exposure. However, when applied indoors, they may not degrade as rapidly and may possibly accumulate in homes, creating a potential for repeated and long-term exposure through contact with floors and other surfaces.

How toxic are pyrethroids?

Structural differences between pyrethroid compounds result in large variations in toxicity (as expressed in acute toxicity experimentation in small rodents).^{1,6,7} There are also other determinants of toxicity in mammals. For instance, formulated commercial products may differ in toxicity from technical grade products, and the toxicological profile of the formulated product is not necessarily identical to that of the pure active ingredient. The ratio of *cis* and *trans* configurations in commercial products is also an important determinant of pyrethroid toxicity in mammals, with *cis* isomers generally being more potent.^{1,12} Finally, commercial pest control products are up to 99% composed of "inert" ingredients, such as synergists (piperonyl butoxide, sulfoxide, sesamex) and solvents. These are relatively non-toxic chemicals, but co-administered in sufficient amounts with active ingredients, they can decrease the threshold doses for pyrethroid toxicity in humans.¹

We have little knowledge of long-term effects

Effects of acute exposure to high levels of pyrethroids are well-known and documented. In general, chemicals are tested at high-effective doses and safe levels are established based on downward extrapolation of the lowest observed adverse effect level (LOAEL) or the no observed adverse effect level (NOAEL) obtained from examining a few endpoints in a limited number of animals. However, this approach may not be appropriate, as post-marketing surveillance has shown adverse effects at levels of exposure considered non-toxic at the time of chemical registration. Further, current assumptions of the safety of long-term exposures in humans are not based on empirical assessments using realistic scenarios of repeated low-dose uptake of multiple pyrethroid compounds. Concerns for effects of long-term exposure include endocrine disruption,^{2,13} functional alterations in reproductive organs,^{2,13} and effects on neurologic development.^{7,14}

In its Endocrine Disruptor Screening Program (EDSP), the U.S. Environmental Protection Agency will be testing a number of pesticide active ingredients and high production volume chemicals for their effects on the endocrine system. Permethrin is on the list of chemicals that will be screened first because of its occurrence in three of four exposure pathways as defined by the EPA: drinking water, food, residential use and occupational exposure.¹⁵ Endocrine disruption is of great importance because chemicals targeting endocrinological domains can have effects at low doses that are not predicted by effects at higher doses.¹⁶

Both animal studies and studies in non-occupationally exposed humans indicate that pyrethroid exposure can affect sperm concentration, motility and morphology. For example, significant positive associations were found between pyrethroid metabolites in urine and FSH (follicle-stimulating hormone) and LH (luteinizing hormone) levels in serum in non-occupationally exposed men.² Elevated levels of FSH are highly predictive of poor semen quality. Associations were also found between sperm quality parameters (concentration, motility, sperm DNA damage and DNA fragmentation) and pyrethroid metabolites in urine.^{2,13} Although most study subjects were recruited from infertility clinics, men with the highest levels of pyrethroid metabolites in their urine had lower semen quality, higher levels of sperm DNA damage and higher levels of DNA fragmentation.²

Since pyrethroids primarily act on the nervous system of insects and mammals,¹⁴ there is also concern for neurological and neuropsychological effects of pyrethroid exposure, such as effects on behaviour, learning and motor performance.⁷ So far, this has only been studied in small rodents. Preliminary evidence indicates that there are age-related differences in neurotoxicity, with neonatal rats being up to one order of magnitude more sensitive to the acute effects of deltamethrin, cypermethrin and permethrin than adult animals when middle-to-high effective doses are administered by the oral route:¹⁴ this may have important implications for the safety of pyrethroids in babies and small children.

Combined exposure to pyrethroids and other chemicals is relevant to realistic exposure scenarios. The effects of repeated exposure to multiple pyrethroids at environmentally relevant levels may differ qualitatively and quantitatively from the acute or subacute effects of clinically effective doses of single compounds. For example, oral administration of a combination of 11 pyrethroids to rats resulted in locomotor effects at levels that were well below the threshold levels for the individual test compounds.¹⁷ Also, there is limited evidence that combined administration of pyrethroids with insect repellents such as DEET and some organophosphates might have additive or synergistic effects on the nervous system.¹

Why should we be concerned?

There are several reasons to be concerned about pyrethroids. First, household use of pyrethroid appears to be common: 89% of US homes had detectable levels of permethrin.¹¹ Although 15% of Canadian households are reported to use pesticide products indoors,¹⁸ no Canadian data are available on the presence of pyrethroid residues in homes. Pyrethroids are the active ingredients of many insecticidal products, including sprays, pet shampoos against ticks and lice, foams, mosquito coils, and powders that appear to be ubiquitous in households. For example, permethrin is used to control bed bugs; its widespread use has likely contributed to the recently documented greater resistance of bed bugs and subsequent increase in infestation rates.¹⁹ Pyrethroids may be applied excessively, which may result in health effects: in a recent US study, pyrethroids, pyrethrins, or both were implicated in 89% of illnesses from insecticides used to control bed bugs.²⁰

Second, pyrethroids do not remain in the air but deposit onto surfaces and may accumulate in house dust²¹ due to their low vapour pressure.¹ They may not degrade as rapidly in indoor environments as previously thought. It has been stated that household exposure contributes little to the overall uptake of pyrethroids, and

that diet is the most significant source of the body burden.¹ Recent research shows that household use may actually contribute more to overall pyrethroid exposure than diet, especially for small children (who crawl on the floor and practice hand-to-mouth behaviour).^{9,22} Multi-day measurements strongly suggest that the variation in levels of pyrethroid metabolites can be attributed to pest control product applications at home,^{9,23} and that peaks following household use of insecticide products may be more relevant for long-term health risks than food consumption, especially when exaggerated or improper application is practiced.

Pyrethroids are assumed to metabolize rapidly in mammals, but a recent study shows that pyrethroids bioaccumulate in dolphins and are transferred from mother to calf through breast milk.²⁴ A body burden of pyrethroids has also been found in humans: metabolite levels found in urine samples in the Canadian population are similar to those observed in the US population.^{25,26} Although measurable levels of pyrethroid metabolites do not necessarily mean that adverse health effects will occur,³ the fact that they are detected in the general population indicates that the alleged high metabolic capacity for pyrethroids in mammals, including humans, may not be optimal and that exposure is likely to be ongoing.

Implications for public health

No reliable data on use and exposure are available for Canada, but public health professionals should be aware that pyrethroids are almost certainly ubiquitous in Canadian households. Education is needed because occupants may not realize that many of the products they use contain pyrethroids.

Public health practitioners may also help lobby for better labelling of pyrethroid products. For example, information on the ratio of *cis* and *trans* isomers, which greatly affects toxicity, is often not included on Material Safety Data Sheets. Also, it is known that people often do not understand the technical information and application instructions included on pesticide labels,²⁷ which may result in improper use and sometimes higher application rates than those recommended on the label.²⁸

Pyrethroids may be perceived as safe because they are wrongly thought to be “natural”. People may equate natural pyrethrins with synthetic pyrethroids, and deem both natural and safe. Modern synthetic pyrethroids certainly are not natural but rather man-made chemicals that were designed to optimize the insecticidal attributes of natural pyrethrins. Further, natural does not necessarily mean harmless.

A handful of reports unequivocally indicate that exposure to pyrethroids may lead to alterations in the neurological, endocrine and reproductive domains at doses near and below previously proposed toxic thresholds in laboratory animals. At present, it is unclear to what extent these findings can be extrapolated to humans. Few human studies are available, but preliminary results seem to point in the same direction.^{2,13} Currently, empirical evidence is lacking to produce well-informed decisions on health protection from long-term exposure to pyrethroid insecticides.

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RÉSUMÉ

Les pyréthrinoïdes, une catégorie d'insecticides dérivés des plantes et leurs analogues synthétiques, sont de plus en plus utilisés au Canada comme premier choix dans la lutte antiparasitaire dans bien des contextes agricoles et résidentiels. Leur popularité est due en partie à leur innocuité présumée comparativement aux insecticides organochlorés et organophosphorés plus anciens. La demande de pyréthrinoïdes augmente en raison des hausses récentes du niveau d'infestations par des insectes nuisibles (comme les punaises de lit) et de la vulnérabilité réduite des espèces cibles à de nombreux produits de lutte antiparasitaire. Des résidus de pyréthrinoïdes ont été détectés dans des logements, des centres de la petite enfance et des aliments. Bien que l'on considère que les pyréthrinoïdes présentent peu de risques pour la santé humaine, leur utilisation croissante est un problème. Nos connaissances actuelles des effets indésirables des pyréthrinoïdes découlent principalement d'études de leurs effets à court terme sur des animaux de laboratoire, d'études de cas d'empoisonnement volontaire et accidentel, et de cas d'exposition professionnelle à des doses élevées; or, dans ces situations, les niveaux et les formulations des produits aux pyréthrinoïdes diffèrent de ceux qui s'appliqueraient à l'étude de leurs risques à long terme dans la population générale. Selon les données disponibles, l'appareil génital, le système nerveux, les voies de signalisation endocrinienne et le développement du jeune enfant pourraient être la cible d'effets indésirables en cas d'exposition répétée à des formulations à base de pyréthrinoïdes. Étant donné l'incertitude entourant l'existence d'effets à long terme sur la santé à la suite d'une exposition aux pyréthrinoïdes, surtout dans des scénarios réalistes, la prudence est de mise lorsqu'on présente les produits aux pyréthrinoïdes comme des outils de lutte antiparasitaire sans danger.

Mots clés : pyréthrine; exposition environnementale; perturbateurs endocriniens; toxicologie; évaluation du risque