Pyrethrins and Pyrethroids

Materials for the July 28-29, 2009 Meeting of the California Environmental Contaminant Biomonitoring Program Scientific Guidance Panel

Agenda Item: "Potential Designated Chemicals: Pesticides"

Overview

At the March 2009 Scientific Guidance Panel (SGP) meeting, Panel members recommended that the pyrethrins and pyrethroids that were designated chemicals in the California Environmental Contaminant Biomonitoring Program (CECBP) be named as priority chemicals. These chemicals have been added to the CECBP priority chemical list.

The Panel expressed interest in considering the addition of the chemical class "Pyrethrins and Pyrethroids" to the designated chemical list. This document provides supporting information for the Panel's discussion of this issue. Additional background information, including summaries of selected exposure and toxicity studies, can be found in documents produced by the Agency for Toxic Substances and Disease Registry (ATSDR, 2003) and the Centers for Disease Control (CDC, 2005). Links to these documents can be found in the reference list.

CECBP status of pyrethrins and pyrethroids

Based on the SGP's recommendation at the March 2009 meeting, the following chemicals were listed as priority chemicals for the CECBP.

- Allethrin
- Cyfluthrin
- cis-Cypermethrin
- trans-Cypermethrin
- Deltamethrin
- Permethrin
  - cis-Permethrin
  - trans-Permethrin
- Pyrethrin I
- Resmethrin

The pyrethrins and pyrethroids listed above are already included in CDC biomonitoring studies. A number of additional pyrethroids are planned for inclusion in future CDC biomonitoring studies.

Table 1 shows the pyrethrins and pyrethroids registered for use in California (see http://www.cdpr.ca.gov/docs/label/labelque.htm). Some of these chemicals are already CECBP priority chemicals, while others are not included in the CECBP as either designated or priority chemicals.

Table 1: Pyrethrins and pyrethroids registered for active use in California

Chemical name	Number of active registered products in California	CECBP status
Allethrin	1	Priority
S-Bioallethrin	16	
D-trans-Allethrin	60	
D-Allethrin	27	
Bifenthrin	163	Not included[1]
Cyfluthrin	44	Priority
Beta-cyfluthrin	21	Priority
Cyhalothrin		Not included
Lambda-cyhalothrin	124	
Gamma-cyhalothrin	13	
Cypermethrin	57	Priority
(S)-Cypermethrin	7	Priority
Cyphenothrin	9	Not included
Deltamethrin	83	Priority
Esbiothrin	6	Not included
Esfenvalerate	89	Not included
Etofenprox	32	Not included
Fenpropathrin	2	Not included
Imiprothrin	15	Not included
Metofluthrin	4	Not included
Permethrin	596	Priority
Phenothrin (sumithrin)	159	Not included
Prallethrin	50	Not included
Pyrethrin[2]	568	Priority (pyrethrin I)
Resmethrin	36	Priority
Tetramethrin	201	Not included
Tralomethrin	9	Not included

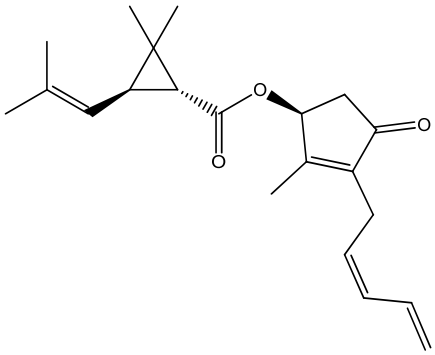
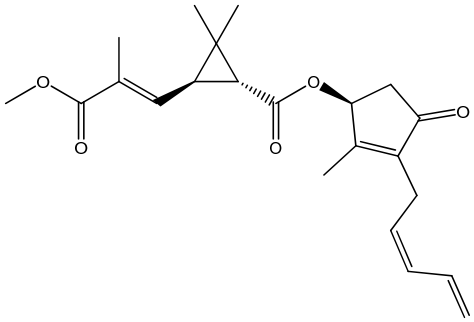
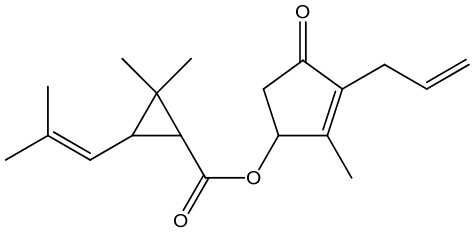
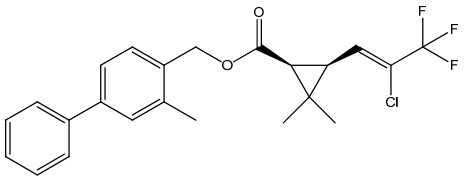
1. Not included in the CECBP as either designated or priority.
2. Isomer not specified by CDPR

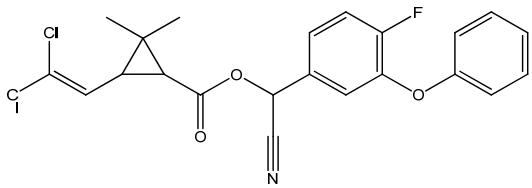
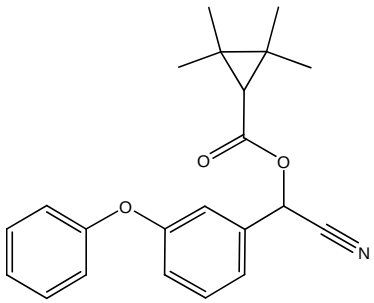
Chemical identification

Pyrethrum is the mixture of chemicals found in chrysanthemum flowers and contains six chemicals with insecticidal properties (pyrethrins) that target the sodium channel of nerve cells and thereby act on insects' central nervous systems. Pyrethroids are synthetic esters derived from pyrethrins and have more stable insecticidal properties. Pyrethroids share a common chemical structure consisting of cyclopropane carboxylic acids, with variations in the alcohol portion of the compounds. Pyrethroids are divided into two different groups: Type I pyrethroids

do not contain a cyano group whereas Type II pyrethroids contain a cyano group added to the benzylic carbon atom (ATSDR 2003). Table 2 shows some example structures for natural pyrethrins as well as Type I and Type II pyrethroids, and the CECBP status for each of these.

Table 2: Chemical structures of selected pyrethrins and pyrethroids

Chemical	Structure	Chemical Class	CECBP status
Pyrethrin I		Pyrethrin	Priority
Pyrethrin II		Pyrethrin	Not included
Allethrin		Pyrethroid, Type I	Priority
Bifenthrin		Pyrethroid, Type I	Not included

Chemical	Structure	Chemical Class	CECBP status
Cyfluthrin		Pyrethroid, Type II	Priority
Fenpropathrin		Pyrethroid, Type II	Not included

Pyrethroid products usually contain a mixture of isomers and do not consist of a single pure compound. They are also usually mixed with synergists, carriers, and inert ingredients to enhance their activity and reduce breakdown in the environment (ATSDR 2003). Major uses include agricultural, structural, and household pest control (including use on pets and for mosquito control) and they are usually applied by spraying. Household use has increased as organophosphate and carbamate use has declined (Barr 2008).

Exposure or potential exposure

In the United States, there are more than 3,500 registered products containing pyrethrins and pyrethroids (U.S. EPA 2009). In California, there are 26 pyrethroids, including isomerically-enriched mixtures, each registered for use in a range of products (Table 1). Two pyrethroids, permethrin and cypermethrin, are on the California Department of Pesticide Regulation (CDPR) list of the top 100 pesticides used statewide in 2007.[1] A total of 413,837 pounds of permethrin were applied in California in 2007, mostly for structural pest control (249,267 pounds) but there were also significant agricultural applications (mostly to pistachios and lettuces). A total of 336,826 pounds of cypermethrin[2] was applied, mostly for structural pest control (194,610 pounds) but also on a number of crops including rappini (137,954 pounds). In 2006, CDPR placed certain pesticide products containing pyrethroids into reevaluation (CDPR 2008). This

[1] CDPR use reporting includes agricultural pesticide applications (to crops, structures, and roadsides) as well as commercial applications (including structural fumigation, pest control, and turf applications). Consumer uses are not reported.

[2] S-cypermethrin (23,594 pounds) is not included in this figure.

was in part due to a statewide investigation revealing increased incidence of toxicity in urban creeks associated with the presence of pyrethroids (CDPR 2009, Holmes et al. 2008).

No reporting is required for household use of pesticides, so volume of household use and subsequent exposure is unknown. Pyrethrins and pyrethroids are used for a number of household purposes including use in gardens, for cockroach and termite control, in pet shampoos, and in flea products. In a recent study conducted by the U.S. Department of Housing and Urban Development and the U.S. Environmental Protection Agency, 17 pyrethroids were detected in floor wipes taken from a nationally representative sample of 1131 homes. *Cis*- and *trans*-permethrin were detected most frequently (89 and 88 percent of the samples, respectively), and at the highest geometric mean concentrations (0.11 and 0.14 ng/cm^2, respectively). Cypermethrin, the next most frequently detected pyrethroid, was detected in 46 percent of the samples at a geometric mean concentration of 0.03 ng/cm^2.

Known or suspected health effects

Pyrethrins and pyrethroids have been associated with a range of toxicological effects. For instance, resmethrin is listed as a carcinogen and as a developmental toxicant under California's Proposition 65 (Title 27, California Code of Regulations, Section 27001). Permethrin is classified as "likely to be carcinogenic to humans" by U.S. EPA (2008). Several pyrethroids (bifenthrin, cypermethrin, tetramethrin) are classified as possible human carcinogens by U.S. EPA (2008). Many of these compounds (bifenthrin, bioallethrin, cyhalothrin, cypermethrin, deltamethrin, fenvalerate, permethrin, pyrethrin, resmethrin, and sumithrin) have been identified as having either clear evidence or potential for endocrine disruption (DHI 2007). There is also evidence that low-dose exposure to pyrethrins and pyrethroids, in conjunction with exposure to other chemicals, may be of concern. One study demonstrated that when mice are pretreated with DDT and then exposed to bioallethrin during the "brain growth spurt," adult brain function is disrupted (Eriksson 1997). Of note, not all pyrethrins and pyrethroids have been studied for all of these toxicological endpoints.

Summary

A number of pyrethrins and pyrethroids are already priority chemicals for the CECBP. There are several additional chemicals, registered for use in California, that are not on the designated or priority chemical lists (Table 1).

Table 2 illustrates some of the structural similarities within the pyrethrin/pyrethroid class. Of the chemicals that have been tested for toxicological effects, a number show similar properties. For example, DHI (2007) identified ten pyrethrins/pyrethroids as having evidence of endocrine-disrupting properties.

Many pyrethrins and pyrethroids share common metabolites. For instance, 3-phenoxybenzoic acid (3PBA) is common to approximately 20 pyrethroids (Barr 2008), and c*is* and *trans*- isomers of 2,2-dichlorovinyl-2,2-dimethylcyclopropane-1-carboxylic acid (*cis*- and *trans*-DCCA) are common to permethrin, cypermethrin, and cyfluthrin (Barr 2008). Therefore, even without

specifically listing certain parent compounds, these chemicals will effectively be included in the CECBP if they share the same target metabolites with chemicals that are priority chemicals.

Designating the class of “pyrethrins and pyrethroids” for the CECBP would allow the Program to bring additional members of the class to the Panel for consideration as priority chemicals in an efficient manner. This could be helpful if additional pyrethrins or pyrethroids of unique concern in California are identified.

References

Agency for Toxic Substances and Disease Registry (ATSDR, 2003). Toxicological profile for pyrethrins and pyrethroids. Accessed at http://www.atsdr.cdc.gov/toxprofiles/tp155.html on 6/24/09.

Barr DB (2008). Biomonitoring of exposure to pesticides. Journal of Chemical Health and Safety November/December:20-29.

California Department of Pesticide Regulation (CDPR) (2008). Summary of Pesticide Use Report Data 2007 *Indexed by Chemical*. Accessed at http://www.cdpr.ca.gov/docs/pur/pur07rep/chmrpt07.pdf on 6/24/09.

California Department of Pesticide Regulation (CDPR) (2009). For a list of documents related to the pyrethroid reevaluation, see http://www.cdpr.ca.gov/docs/registration/reevaluation/chemicals/list_pyrethroids.htm, accessed on 6/24/09.

Centers for Disease Control and Prevention (CDC) (2005). Third National Report on Human Exposure to Environmental Chemicals. NCEH Pub. No. 05-0570. Pages 405-415. CDC, Department of Health and Human Services. Accessed at http://www.cdc.gov/exposurereport/pdf/thirdreport.pdf on 6/24/09.

DHI Water and Environment (DHI, 2007). Study on enhancing the endocrine disruptor priority list with a focus on low production volume chemicals. Revised Report to DG Environment. ENV.D.4/ETU/2005/0028r. May 2007. Available at: http://ec.europa.eu/environment/endocrine/documents/final_report_2007.pdf

Eriksson P (1997). Development neurotoxicity of the environmental agents in the neonate. NeuroToxicology 18(3):719-726.

Holmes RW, Anderson BS, Phillips BM, Hunt JW, Crane DB, Mekebri A, Connor V (2008). Statewide investigation of the role of pyrethroid pesticides in sediment toxicity in California's urban waterways. Environ. Sci. Technol. 42:3007-3009.

Stout DM, Bradham KD, Egeghy PP, Jones PA, Croghan CW, Ashley PA, Pinzer E, Friedman W, Brinkman MC, Nishioka MG, Cox DC (2009). American healthy homes survey: A national study of residential pesticides measured from floor wipes. Environ Sci. Technol. 43:4294-4300.

U.S. Environmental Protection Agency (U.S. EPA) (2009). Pyrethrins and Pyrethroids. Accessed at http://www.epa.gov/oppsrrd1/reevaluation/pyrethroids-pyrethrins.html on 6/24/09.

U.S. Environmental Protection Agency (U.S. EPA) (2008). Chemicals Evaluated for Carcinogenic Potential by the Office of Pesticide Programs. September 24, 2008. Accessed at http://envirocancer.cornell.edu/turf/chemseval.pdf on 7/6/09.