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Pyrethroid pesticides and their metabolites in vacuum cleaner dust collected from homes and day-care centers ☆

James Starr [a,*], Stephen Graham [b], Daniel Stout II[a], Kim Andrews [c], Marcia Nishioka [c]

[a] US Environmental Protection Agency, National Exposure Research Laboratory, Office of Research and Development, 109 T.W. Alexander Drive, MD D205-05, RTP, NC 27711, USA
[b] US Environmental Protection Agency, Office of Air Quality Planning and Standards, USA
[c] Battelle Memorial Institute, USA

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ABSTRACT

Urinary metabolites of pyrethroid pesticides have been used as biomarkers to estimate human exposure to the parent insecticide. It is important to establish whether these markers are present in environments or media to which humans are exposed routinely. Failure to account for the contribution of pre-existing markers to urinary concentrations could result in risk assessments that overestimate exposure. The purpose of this study was to quantify the concentrations of 13 selected pyrethroid pesticides and their degradation products in samples of indoor dust that had been collected in vacuum cleaner bags during the children's total exposure to persistent pesticides and other persistent organic pollutants (CTEPP) study of homes and day cares in North Carolina and Ohio. Sieved contents of 85 vacuum cleaner bags were analyzed, and permethrin was found in all samples. Sixty-nine samples contained at least one additional pyrethroid, but none contained more than five pyrethroids in detectable concentrations. Resmethrin, prallethrin, and fenpropathrin were not detected in any samples, while 36 contained phenothrin. The median concentration of permethrin in the samples was 1454 ng/g of dust. Excluding permethrin, pyrethroid concentrations were typically less than or equal to 100 ng/g of dust. The majority of degradates were present in more than half of the dust samples, usually at concentrations of less than or equal to 100 ng/g of dust. For those pyrethroids with a characteristic oxydibenzene group, the cyclopropane degradates were present at higher concentrations than the corresponding benzoic acid moieties. Using urinary concentrations of these metabolites to model human exposure to the parent pyrethroids, may over-estimate risk due to the presence of pre-existing degradates in dust.

1. Introduction

Pyrethroid insecticides are an important class of pesticides with extensive commercial and non-commercial usage. Among many other applications, pyrethroids are currently registered for use on edible crops, as veterinary insecticides, and to control household pests (Todd et al., 2003). Due to the widespread use of these pesticides, extensive research has been undertaken to establish relevant environmental and toxicological profiles, including estimates of human exposure. Pyrethroids are synthetic analogs of pyrethrins, the naturally occurring insecticidal compounds that can be extracted from *Chrysanthemum* sp. flowers. Pyrethrins consist of esters of chrysanthemic and pyrethric acid bonded to one of three alcohols via an ester linkage (Vijverberg and Oortgiessn, 1988). Pyrethroids are synthesized using this basic structure, but modified to enhance environmental stability or alter the insecticidal activity. Initial degradation of pyrethroids, whether through metabolic or chemical processes, generally involves hydrolytic cleavage of the ester linkage resulting in dissolution of the parent into alcohol and acid moieties.

In human exposure studies, measurement of these metabolic products (biomarkers) in urine is one technique used to estimate exposure to the parent pyrethroid. Initially, urinary biomarkers of pyrethroids were used to assess occupational exposures (Hardt and Angerer, 2002; Leng et al., 1996; Smith et al., 2002) where there may be relatively high exposures, that presumably occur at specific time points and for defined durations. More recently these biomarkers have been incorporated into studies where the exposure is not known to be occupationally related (Baker et al., 2000; Heudorf et al., 2004; Morgan et al., 2007). Compared to assessment using measurements of the environmental concentrations of the pyrethroids, biomarkers may provide integrated information that is more specific to an individual's dose. However,

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* Corresponding author. Fax: +1 919 541 3527.
E-mail address: starr.james@epa.gov (J. Starr).

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reconciliation of exposure estimated using biomarkers with estimates based on traditional environmental sampling can be difficult (Groopman and Kensler, 1999). This is partially due to extremely varied scenarios that include multiple routes of exposure, inadequate physiological models (Woollen, 1993) and nonspecific markers.

An additional source of error in biomarker-based exposure reconstruction may be introduced if the marker exists exogenously on food or dust and dosing occurs via direct or indirect ingestion. Previous research has demonstrated the presence of such preexisting biomarkers in indoor environments. Rudel et al. (2003) found trichloropyridinol (TCP), a stable metabolic product of chlorpyrifos, in indoor air and dust samples collected in homes. In the Children's Total Exposure to Persistent Pesticides (CTEPP) and Other Persistent Organic Pollutants study of homes and daycares in North Carolina and Ohio, Morgan et al. (2005) measured TCP in hand wipes, food, soil, and floor dust. TCP was present at equal or higher concentrations than chlorpyrifos in all media, except air. Employing simplified exposure estimation methods, aggregate exposure to TCP was four-fold higher than aggregate exposure to the parent compound. When combining the estimated chlorpyrifos and TCP exposures, the relationship between exposure and the eliminated biomarker concentrations improved. However, the authors were only able to account for 40% of the measured urinary levels of TCP. Krieger et al. (2001) used urinary TCP to estimate insecticide exposure before and after residential applications of chlorpyrifos. All nine of the subjects had TCP in their pre-application urine samples with concentrations ranging from 3% to 60% of samples taken post application. No assessment was made of the environmental concentrations of TCP; but the authors' state that the presence of TCP in the pre-application samples may have been partially due to environmental TCP.

For a subpopulation of the CTEPP study, Morgan et al. (2007) reported urinary excretion levels of 3-phenoxybenzoic acid (3PBA) a common metabolite of several pyrethroids. For these subjects, urinary 3PBA levels were also higher than could be accounted for in the environmental measurement of the parent compounds, although this relationship was not true for the more highly exposed individuals.

Neurotoxicity is generally considered to be the significant human health endpoint resulting from exposure to pyrethroids and is the basis for current risk assessments. While Gaughan et al. (1977) reported lower LD_{50} values for the metabolites relative to permethrin, pyrethroid degradants are not known neurotoxicants (White et al., 1976). Therefore, in risk assessment the importance of exogenous pyrethroid degradation products is their potential to cause an overestimation of exposure when urinary metabolites are used to estimate dose.

Paired measurement of pyrethroid pesticides and their metabolites in indoor dust samples will help establish whether environmental levels of pyrethroid degradates exist, at concentrations sufficient to cause an overestimation of risk. This research describes the first systematic evaluation of the relative proportions of parents and metabolites in indoor dust, an environmental matrix that constitutes an important route of pyrethroid exposure for children. The results of this work will decrease the uncertainty in risk assessments where urinary metabolites are used to reconstruct exposure.

We used a subset of residential dust samples that were collected in vacuum cleaner bags during the CTEPP study to accomplish this. These samples were analyzed for pyrethroid pesticides (allethrin, cyfluthrin, cyhalothrin, cypermethrin, deltamethrin, esfenvalerate, fenpropathrin, imiprothrin, *cis*/*trans*-permethrin, prallethrin, resmethrin, phenothrin, and tetramethrin) as well as their associated metabolic/degradation products (*cis*-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane-1-carboxylic acid (*cis* DCCA), *trans*-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane-1-carboxylic acid (*trans* DCCA), 4-fluoro-3-phenoxybenzoic acid (4F3PBA), *cis*-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane-1-carboxylic acid (DBCA), 3-(2,2-dimethylvinyl)-2,2-dimethylcyclopropane-1-carboxylic acid (CA), and 3PBA). A simplified illustration showing the relationship of the pyrethroids and their degradation products assayed in this study is presented in Fig. 1. Selection of the pyrethroids and degradants was based upon information in government reports and the peer reviewed literature (US Department of Agriculture, 2001; US Department of Health and Human Services, 2005; Tulve et al., 2006). Although this list is not exhaustive, it includes the metabolites commonly used as biomarkers and their pyrethroid precursors most frequently applied in the United States.

The concentrations measured in the samples were used to determine the relative proportion of measured metabolite to total possible metabolic product and whether the presence of the metabolite in this exposure medium could result in an overestimation of exposure when using urinary metabolites as biomarkers of parent pesticides.

2. Materials and methods

2.1. Sample collection

As part of the CTEPP sampling protocol, participant houses and day care centers were vacuumed by the field teams. The vacuuming was performed on the same day that dust samples were taken from small sections of carpeted flooring using a high-volume small surface sampler (HVS3). Samples collected by HVS3 were analyzed and reported as part of the CTEPP study (Morgan et al., 2004) and included *cis*- and *trans*-permethrin and cyfluthrin among a list of more than 50 compounds. The vacuum cleaner samples, however, were not analyzed in the original study but rather shipped to a central facility where they were stored, in the original bags, at room temperature and humidity. A total of 219 vacuum cleaner bags were collected and stored during the CTEPP study, and each bag had an identification number linking it to an HVS3 sample.

The intact vacuum cleaner bags were sterilized by gamma radiation prior to removal of the contents. Where sufficient bulk was available, the dust and other materials in each bag were sieved, first to 1500 μm, then to 150 μm. Both fractions were stored in sealed glass jars but only the 150 μm component was used for this study. Of the 219 available samples, 112 had both significant quantities of dust after sieving and corresponding HVS3 results containing measurable concentrations of permethrin. A subset of 85 of these vacuum cleaner bag samples was used in this study, 5 samples were collected from day care centers and the remainder from residences. In addition to permethrin, 53 of the samples in the selected subset also had corresponding HVS3 results with measurable concentrations of cyfluthrin. The vacuum cleaner bag samples were selected to include a wide range of concentrations of permethrin and cyfluthrin (as indicated by the HVS3 results). Permethrin was present in all samples and ranged in concentration from ng/g to μg/g. Excluding permethrin and cyfluthrin, the other pyrethroids and metabolites evaluated in this study were not assessed in the CTEPP study.

2.2. Preparation of dust extracts (pyrethroid pesticides)

One-half gram aliquots of dust from each sample were weighed and placed individually into 50 mL centrifuge tubes. Subsequently, each was spiked with 250 ng of isotopically labeled *trans*-permethrin, serving as a surrogate recovery standard (SRS). Methylene chloride (12 mL) was added to each tube and vortexed to wet the dust. The samples were sonicated for ten minutes to extract the pyrethroids then centrifuged at 3000 rpm for 10 min to pellet out suspended solids. Extracts were decanted, volume reduced, and solvent exchanged into acetonitrile. The extracts were cleaned by passing them through a solid-phase extraction (SPE) system consisting of a C18 cartridge on top of an aminopropyl cartridge. Prior to analysis, the volume was reduced to 1 mL and 100 ng dibromobiphenyl was added as an internal standard (IS).

2.3. Preparation of dust extracts (pyrethroid pesticide metabolites)

One-half gram aliquots of dust from each sample were also used to determine the concentrations of the pyrethroid degradation products. The SRS used for metabolite analysis included isotopically labeled 3PBA, DCCA, and 3,5-dibromobenzoic