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REVIEW

Pyrethroid Stereoisomerism: Diastereomeric and Enantiomeric Selectivity in Environmental Matrices – A Review

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Abstract:

Pyrethroids are chiral insecticides characterized by stereoisomerism, which occurs due to the presence of one to three asymmetric (chiral) carbons, generating one or two pairs of *cis/trans* diastereomers, and two or four pairs of enantiomers. Diastereomers have equal chemical properties and different physical properties, while enantiomer pairs, have the same physicochemical properties, with exception by the ability to deviate the plane of polarized light to the right or to the left. However, stereoisomers exhibit different toxicities at the metabolic level, presenting enzyme and receptor selectivity in biological systems. Studies in aquatic organisms have shown that toxic effects are caused by specific enantiomers (1*R-cis* and 1*R-trans*) and that those cause potential estrogenic effects (1*S-cis* and 1*S-trans*). In this context, the same compound can have wide-ranging effects in organisms. Therefore, several studies have highlighted pyrethroid stereochemical selectivity in different environmental matrices. The analytical ability to distinguish the diastereomeric and enantiomeric patterns of these compounds is fundamental for understanding the processes of biotransformation, degradation environmental behavior and ecotoxicological impacts. In this context, a pyrethroid stereochemical approach is recommended and therefore should be included in future risk assessments and regulatory decisions.

Keywords: agrochemicals; chiral pesticides; diastereomers; enantiomers

1. Introduction

Pyrethroid insecticides are synthetic derivatives of pyrethrins, natural compounds found in *Chrysanthemum cinerariaefolium* flowers. The class is characterized by an ester bonding the phenoxybenzoic and cyclopropane moieties and is further differentiated into Type I (absence) and Type II (presence) of the *alpha*-cyano radical, conferring greater photostability and toxicity [1, 2]. Pyrethroids act by prolonging the opening of the voltage-gated sodium channels in axonal membranes, delaying repolarization in the central and peripheral nervous system. In Type II compounds the duration of effects at specific sites is longer, which may explain the differences in toxicity between the two types [3]. Effects of antagonism with gamma-aminobutyric acid (GABA) receptors and action on the calcium and chloride channels have also been previously described [4].

Due to a worldwide trend towards banning more environmentally toxic and persistent target chemicals, such as organochlorines and selected organophosphates, pyrethroids have become the most widely used pesticides in recent decades [5, 6]. In addition to their extensive application in agriculture and livestock production, these chemicals have been also used for vector controls in urban areas and surroundings, especially in households, treatment of lice and scabies, and pet products [7-9]. The range of use becomes more worrisome in countries with large agricultural activity, such as Brazil, where in 2012, around 823,000 tons of pesticides were traded [10].

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According to Garrison [11], 30% of registered pesticides indicate sort of spatial isomerism. Among them, pyrethroids should be highlighted. Pyrethroids are chiral compounds characterized by geometric (*cis* and *trans* diastereomers) and optical isomerism (*R* and *S* enantiomers). Stereoisomers deliver the same molecular formula, but with a different three-dimensional arrangement, which may confer different biological properties. Diastereoisomerism can occur with one or two pairs of *cis*/trans stereoisomers, resulting in different physical properties but with equal chemical properties. The two chiral carbons on the cyclopropane ring produce pairs of diastereomers due to the orientation of the C-1 and C-3 substitutions relative to the cyclopropane ring plane [12]. Optical isomerism can be verified by the ability of the molecule to deviate the plane of polarized light to the right (*R* or +) or to the left (*S* or -). Enantiomeric pairs are non-superimposable molecules, which have the same physicochemical properties. There are other cases that result in molecular asymmetry, but in the case of pyrethroids the chirality is due to the presence of at least one asymmetric (chiral) carbon, with four different ligands. Specifically in this class, spatial isomerism may occur in the acid and alcohol moiety or both. In addition, due to the occurrence of 1 to 3 asymmetric carbons (Figure 1), pyrethroids have four or eight enantiomers [13].

Since most enzymes present stereoselectivity, some studies cite different patterns of biochemical transformation of chiral compounds, which directly influence the persistence and preferential bioaccumulation of stereoisomers [11]. This specificity is a determining factor for the occurrence of different bioaccumulation rates in species that live in the same ecosystem [14]. Furthermore, most formulations of chiral pesticides are composed of racemic mixtures, and it is, therefore, essential to define their stereoselectivity patterns to better estimate risk assessment. Another factor to be considered is that, in the racemic formulations, only some enantiomers present insecticidal action. For example, only two enantiomers (1*R*, *cis*, *αS* and 1*R*, *trans*, *αS*) of the cypermethrin racemic formulation have insecticidal activity, the remaining six of them lack specific activity. This represents a greater environmental burden and risk to human and environmental health [15, 16].

In this context, the aim of this review is to highlight the importance of pyrethroid stereoisomers analyses and their evaluation of (bio) degradation and bioaccumulation pathways, as well as the environmental behavior of these target chemicals. This approach can be a relevant tool for more accurate risk assessments of pyrethroid contamination in environmental and biological matrices.

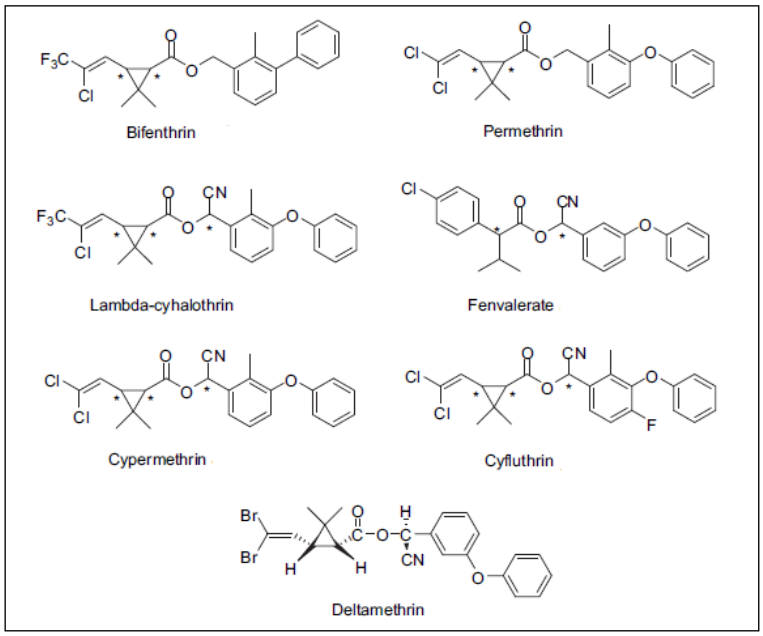

Figure 1. Pyrethroids Type I and II (with CN bonded). Asterisks highlight chiral centers**.** Adapted from Ye et al. [17].

2. Pyrethroid Achiral (Diastereomers) and Chiral (Enantiomers) Analysis

Pyrethroids are chiral insecticides which, through chromatographic techniques, can have their stereochemical forms (diastereomers and enantiomers) separated. However, it is important to consider that pyrethroids act at the molecular level as enantiomeric units. From this perspective, the pattern observed for each diastereomer in samples contaminated with pyrethroids results in only the sum of a pair of enantiomers. The main techniques used for the chromatographic separation of pyrethroid diastereomers and enantiomers are gas chromatography (GC), high pressure liquid chromatography (HPLC) and capillary electrophoresis (CE) [15, 16]. Current methods use different achiral stationary phases for diastereomer separation, while chiral columns are used for enantiomer separation [14, 15, 18]. Figure 2A describes permethrin diastereomer analysis, using high-pressure liquid chromatography (HPLC) with achiral silica-gel column and a mobile phase of hexane/isopropanol. In Figure 2B, an efficient permethrin enantiomer separation can be observed through a Chiralcel OJ-H column (cellulose tris 4-methylbenzoate coated on 5µm silica-gel) with hexane/isopropanol 100:2 (v/v) as a mobile phase [18].

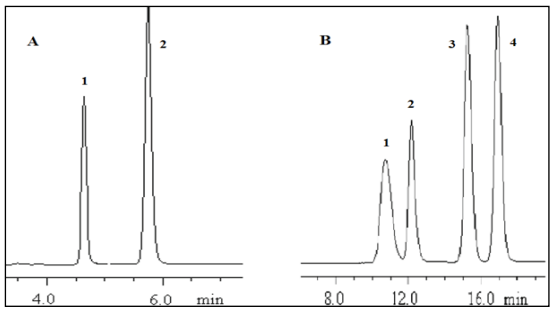

Figure 2. A) Two permethrin diastereomers: (1) *cis*-permethrin; (2) *trans*-permethrin and in B) four permethrin enantiomers: (1) 1*S*-*cis*; (2) 1*R*-*cis*; (3) 1*S*-*trans*; (4) 1*R*-*trans*. Adapted from Li et al. [18].

Some methods still seek to optimize the enantiomers separation, regarding different columns features for two chiral (eg. permethrin, bifenthrin) or three chiral centers (eg. cypermethrin, cyfluthrin) [13, 19]. In Figure 3A-D there can be observed chromatograms of standard enriched cypermethrin formulations eluted in two chiral columns (Chirex 00G-3019-OD) [18].

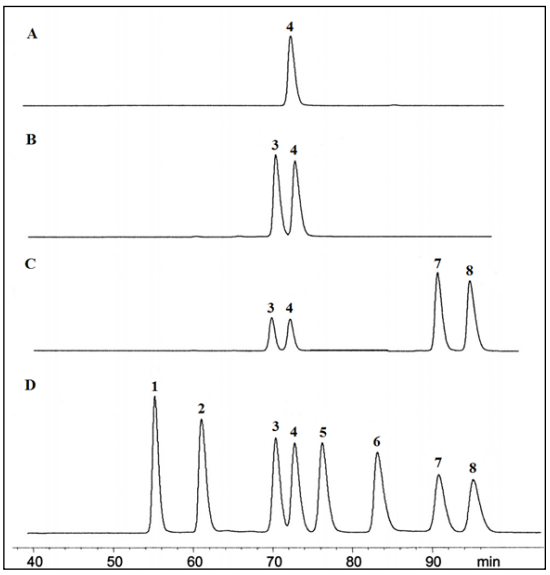

Figure 3. A) *θ*-cypermethrin: (4) enriched in 1*R*-*cis*-*αS*; B) *α*-cypermethrin: (3, 4) enriched in 1*S*-*cis*-*αS* + 1*R*-*cis*-*αR*; C) *β*-cypermethrin: (3, 4, 7, 8) enriched in 1*R*-*cis*-*αS* + 1*S*-*cis*-*αR* and 1*R*-*trans*-*αS* + 1*S*-*trans*-*αR*; D) racemic mixture of cypermethrin: (1, 2, 5, 6) 1*R*-*cis*-*αR* + 1*S*-*cis*-*αS* and 1*S*-*trans*-*αR* + 1*R*-*trans*-*αS* (other peaks described above). Adapted from Li et al. [18].

Epimerization or stereoisomer conversion is another important process that may alter the results of analyses at stereoisomeric levels. Tests with *cis*-bifenthrin and permethrin have demonstrated that organic solvents (hexane, ethyl acetate, dichloromethane and sterile water) did not induce isomer conversions. On the other hand, *β*-cypermethrin and *β*-cyfluthrin in soil may suffer insignificant to low epimerization in the *α*-carbon position, but the phenomenon was attributed to the presence of water in the soil [15, 20]. In addition to the concentration values, authors [7, 8, 14] often present as results the ratio between the total area of the chromatographic peak and the specific area of the diastereomer or enantiomer. The result of the calculation is called the diastereomeric factor (DF) or the enantiomeric factor (EF) [8]. The results can be converted to a percentage for an easier visualization. The diastereomeric calculation consists in DF= (Asd/Atd)*100, where: DF is the diastereomeric factor among isomers; Asd is the area of a specific

diastereomer, and Atd is the total area of the diastereomers. A racemate compound with a pair of cis/trans has DF=0.5 or 50%, while with two pairs, has DF=0.25 or 25% for each diastereomer. The same formula can be applied to calculate EF.

3. Stereoselective Degradation and Bioaccumulation

Pyrethroids may reach different environmental matrices through their extensive application both in urban areas, and especially, in agricultural production areas. In general, due to their semivolatile properties, these chemicals are promptly dispersed into the atmosphere after their use in agriculture and can be found in gaseous and particulate phases. Subsequently, they reach soil surfaces, vegetation and aquatic environments by dry or humid deposition.

Pyrethroid adsorption in soil is high (Log K_{ow} 4.0 - 7.6), which makes them slightly mobile in this environmental matrix. When they reach aquatic ecosystems, due to their high hydrophobicity, they tend to associate with the sediment, the dissolved organic matter and the suspended solids of the water column, which contributes to their sedimentation in these ecosystems and immobilization [3, 5].

Woudneh & Oros [21] found the compounds bifenthrin, cyfluthrin, cypermethrin, delta / tralomethrin, flucythrinate, *λ*-cyhalothrin, permethrin and phenothrin in five affluent sediments from the San Francisco Bay, USA. The same problem was detected in Brazil, where Belluta and co-workers [22], found 4 $ng.mL^{-1}$ of deltamethrin and 110 $ng.mL^{-1}$ of cypermethrin in water samples from a river in an agricultural area from São Paulo state. Moreover, Miranda et al. [23] found permethrin (7.0 $ng.mL^{-1}$), *λ*-cyhalothrin (5.0 $ng.mL^{-1}$) and deltamethrin (20 $ng.mL^{-1}$) in river sediment from the Pantanal wetland. In Argentina (Pampa Ondulada region), cypermethrin was found in river water samples and sediments with maximum concentrations of 194 $ng.L^{-1}$ and 1,075 $ng.kg^{-1}$, respectively [24]. In general, the studies indicate the widespread occurrence of these compounds in the environment, however, many studies do not address the stereochemical characteristics of these compounds.

Feo et al. [5], found cypermethrin in water and sediment samples and deltamethrin in water samples from the Ebro river delta, Spain. In a stereochemical approach in the same ecosystem, Feo and co-authors [25] found total cypermethrin isomers (two *cis* and two *trans* diastereomers) with concentrations ranging from 4.93 to 30.5 $ng.L^{-1}$. The authors observed that the diastereomer ratio values in water samples were similar to those found in commercial products, which suggests recent application, since the stereoisomer degradation in the environment present a different pattern, as observed by Khazri et al. [26].

In the environment, its degradation can occur either through abiotic processes (eg. photodegradation) or biotic means. Biodegradation has been reported in animals, plants and microorganisms [15]. In an experimental study, Liu and co-workers observed that deltamethrin and fenvalerate photodegradation include four main reactions: ester cleavage, photo-oxidation, photoisomerization, and decyanation [27]. According to the authors, the double bonds present in these molecules are unstable to light, and among the possible photodegradation processes, the photo-oxidation reactions are the main ones. Moreover, a study recently highlighted permethrin, cypermethrin and cyfluthrin photolytic isomerization in sunlight assays (wavelength > 250 nm over 7 days) [18]. According to this study, photolytic isomerization may cause enantiomeric inversion, which may alter the bioavailability, toxicity and the ultimate fate of these compounds in the environment.

Enantiomers have different toxicities at the metabolic level, presenting selectivity to enzymes and receptors in biological systems. In this context, the same compound can generate different impacts to organisms in the environment [13]. In addition, these specific interactions in enzymatic levels cause selective isomer degradation through microbiota assembly in soils [16]. For example, a previous study reported faster degradation of *trans*-permethrin and *trans*-cypermethrin diastereomers in soils with acid and alkaline conditions and only the occurrence of *cis*-permethrin in sediment samples [9, 17].

Indeed, there are specific detoxification pathways for pyrethroid isomers, in which *trans*

stereoisomers are hydrolyzed faster than *cis*, when the oxidation of *cis* stereoisomers is the main metabolic process [28]. Moreover, studies indicate that *cis* diastereomers have a lower metabolization rate, resulting in higher toxicity effects in mice [3, 29]. In mammals, this phenomenon may be because the liver fractions are poor at metabolizing *cis* isomers, while the *trans* isomers are readily metabolized by esterases [12]. According to Schleier III and Peterson, in most pyrethroids the 1*R-cis* isomers are more stable and toxic, while the 1*R-trans* isomers are rapidly metabolized in organisms [12].

Although studies have cited stereoisomeric degradation and bioaccumulation patterns, where the *cis* isomers in general are more persistent, there are also reports of a higher proportion of *trans* isomers in environmental samples, evidencing the complexity of this issue [15, 30]. In the following figure (4A and B), the distinct cypermethrin diastereomeric patterns of a commercial product and a spruce bark extract, which involved exposure to the same technical formulation (exposure after 6 weeks) are presented. The analyses were performed by gas chromathography on a column with lipophilic characteristic (DB5).

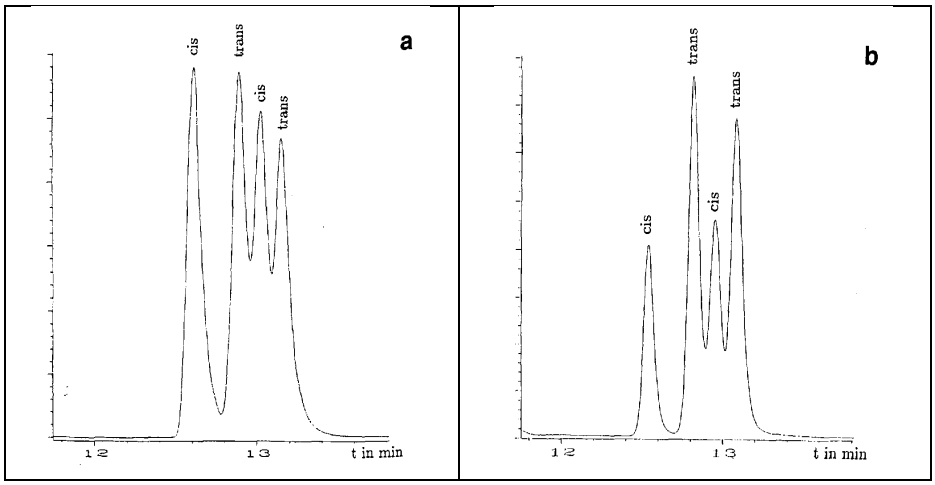

Figure 4. A) Diastereomeric cypermethrin pattern (commercial product); B) Cypermethrin pattern from spruce bark extract after 6 week of product application. Adapted from Kutter and Class [30].

In the interpretation of the isomeric patterns found in environmental samples, intrinsic characteristics of each compound, such as: solubility, vapor pressure, octanol-water partition, among other parameters must be considered. On the other hand, stereoselectivity patterns, as in the case of Fig. 4B, may be influenced by the sampling site, enantioselective biodegradation of microorganisms, and other parameters such as pH and oxidation processes in the matrix [15].

Regarding aquatic environments, pyrethroids can bioconcentrate [3] or bioaccumulate in organisms, presenting enantiomeric and diastereomeric selectivity [26]. Bioconcentration occurs when free dissolved chemicals in the water are concentrated in organisms [31, 32]. Bioaccumulation, in turn, is the enrichment of the contaminant concentration in the organisms due to both the absorption of the chemical dissolved in water and in solids (food, sediment, soil and fine particles in suspension). Unlike bioconcentration, bioaccumulation encompasses the uptake of the contaminant from all available sources, both in the abiotic and in the biotic environment [33, 34].

In a bioaccumulation assay of cypermethrin in the mussel (*Unio gibbus*), the authors observed different bioaccumulation trends: 1) enrichment of the *cis* isomer at low and high concentrations, with ratio *cis*/*trans* equal to 7.19 and 6.39, respectively. 2) ratio (R) between *cis*1/*cis*2 and R *trans*1/*trans*2 were similar; and 3) at low concentrations, the higher accumulation capacity of 1*S*-3*S*-*αR*-cypermethrin enantiomer was observed in relation to 1*S*-3*S*-*αS* [26].

Corcellas and co-workers also observed enantiomeric selectivity bioaccumulation in fish from four rivers in Spain [8]. In this study, the authors reported the presence of nine pyrethroids (bifenthrin, cyhalothrin, cypermethrin, fenvalerate,

tetramethrin, permethrin, cyfluthrin and deltamethrin/tralomethrin). The predominance of *cis*-isomers bioaccumulation was widely observed in all species, with R *cis*/*trans* varying between 0.60 and 29.7. On the other hand, R *cis*1/*cis*2 suggests species-dependent bioaccumulation for cyfluthrin and cypermethrin. However, R *cis*1/*cis*2 cyhalothrin (0.29 to 0.65) suggests *cis* 2 isomer bioaccumulation. Enrichment of *cis* 1 and *cis* 2 enantiomers are also species dependent. However, it should be noted that fish may be in different food chains of these ecosystems, which may determine specific enrichment and not solely from organism physiology.

There are also reports of pyrethroid transfer in birds, through its detection in eggs from both wild birds [14] and chickens from commercial farms and home production [35]. Corcellas and co-authors, in a study carried out with wild bird eggs from Spain, found a high pyrethroid concentration in eggs from birds with anthropogenic food habits, followed by aquatic birds [14]. According to the authors, enantiomer evaluations evidence a high *cis* isomers bioaccumulation. Among the Type II pyrethroids, the ratio (R *cis*1/*cis*2) did not indicate the preference of any isomer, except in the Gadwall, an aquatic species (anseriform), the only herbivore studied, which presented an enrichment of the *cis* 2 isomer. Parente and co-workers [35], have recently observed the selectivity patterns of *cis*-permethrin, *cis*-phenothrin and *cis*-cypermethrin diastereomers in chicken eggs. In Figures 5A and 5B, are presented the pattern of a commercial product with cypermethrin in racemic formulation and in an egg sample. The figures show a clear stereoisomeric selectivity in eggs after product application in chickens. The analyses were performed by gas chromatography coupled to mass spectrometry in a lipophilic column (HP5).

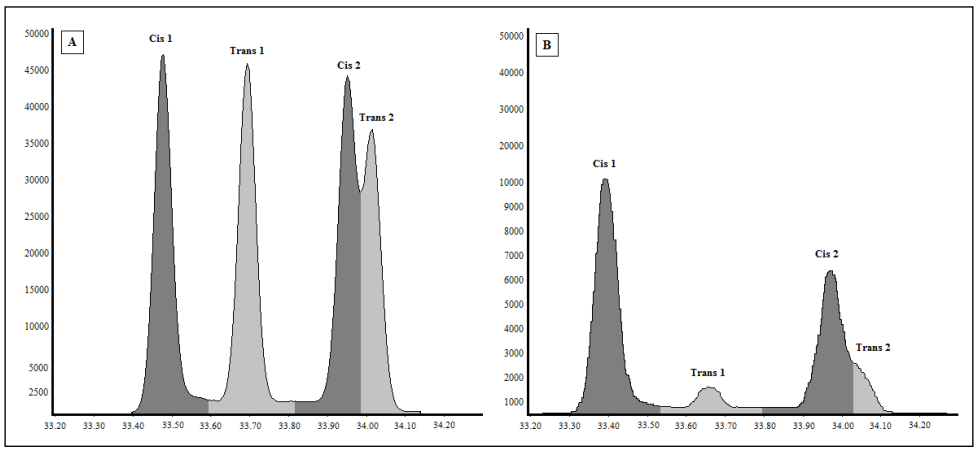

Figure 5. A) Diastereomeric cypermethrin pattern (commercial product); B) Cypermethrin pattern in an egg sample after product application. Adapted from Parente et al. [35].

Although most of the time, it is not possible to establish the initial pattern of the source of contamination, whenever it is possible this is an important discussion tool for understanding the environmental behavior of pyrethroids. On the other hand, in some cases, the commercial formulation is enriched with certain isomers, which may influence the analysis and discussion of the results regarding the stereoisomeric selectivity patterns. Previous studies found a higher proportion of *trans*-tetramethrin isomers in fish and wild bird eggs samples [8, 14]. In this case, according to the authors, the *trans*-tetramethrin enantiomer (1*R*-3*S*) is enhanced in commercial formulations in order to increase the insecticidal activity.

Pyrethroid bioaccumulation was also observed in the aquatic mammal Franciscana dolphin (*Pontoporia blainvillei*) collected from two locations along the Brazilian Southeastern Coast and from the Southern Coast [36]. The authors observed the highest concentrations in newborns, tending to decrease in adult animals. No differences were observed in the isomeric factor (IF) for esfenvalerate/fenvalerate and cypermethrin over the age of the studied animals. On the other hand, permethrin presented a difference in isomeric factor (*cis*/*trans*), with newborns presenting mean values of 84% to *cis* diastereomers and juveniles and adults of 60%

and 69%, respectively. In addition, the maternal transfer of pyrethroids (permethrin, bifenthrin, tetramethrin, deltamethrin/tralomethrin) was observed both during pregnancy and lactation period [36]. Later, Alonso and colleagues [37] also observed the transfer of pyrethroids, by analyzing mothers and fetuses from the Guiana dolphin (*Sotalia guianensis*) and mothers, fetuses, placenta, umbilical cord and milk from the Franciscana dolphin (*P. blainvillei*) along the Brazilian coast.

The transfer of pyrethroids through milk has also been observed in humans from South Africa for the following compounds: permethrin, cyfluthrin, cypermethrin and deltamethrin [38]. Corcellas and co-workers also highlighted pyrethroids in breast milk from Brazil, Colombia and Spain, which tetramethrin, bifenthrin *λ*-cyhalothrin, deltamethrin/tralomethrin, esfenvalerate/fenvalerate, permethrin and cypermethrin were the main detected chemicals [39]. In the same study, authors observed the following percentage proportion of transference to Type I (with only one *cis* and *trans* diastereomers): permethrin (65% *cis*) and esfenvalerate/fenvalerate (53% *cis*). For Type II pyrethroids, with four different isomers (*cis* 1, *trans* 1, *cis* 2, *trans* 2) the percentages of contribution of the first elution isomer (*cis* 1) were 37%, 29% and 10% respectively, for cyfluthrin, cypermethrin and tetramethrin. Although there is a clear selectivity for *cis*-1-cyfluthrin, the authors did not confirm a selective pattern probably due to non-separation of the remaining diastereomers in the chromatographic analysis. In addition, there is a lack of information that does not permit the comparison between the product pattern and those of the samples and thus is an important factor to consider [39].

4. Pyrethroid Commercial Products and Environmental Impact

The pyrethroid class consists of a complex mixture of stereoisomers with at least one chiral center, which is a mixture of two molecules that can act distinctly at the enzymatic sites of a cell. Thus, the difference between the effects of the stereoisomers in the active sites is one of the reasons for the wide variation in the reported toxicities of these compounds. On the other hand, many pyrethroids are marketed as racemic mixtures, which have in equal enantiomeric proportions. These commercial formulations do not take advantage of enantiomerically pure products, in which the active isomer is the predominant compound. The ineffectiveness of stereoisomers in commercial blends directly influences a higher application volume of the compound, affecting the quality of agricultural products, increasing environmental overload and the possible impacts on the environment and human health [16]. In addition, many ecotoxicological risk assessments of chiral pesticides are based on racemic formulations and are therefore non-specific [19].

In a stereochemical approach, Liu and co-workers have shown acute toxic effects by specific enantiomers in aquatic invertebrates (*Ceriodaphnia dubia* and *Daphnia magna*), which were exposed to four commonly used pyrethroids (bifenthrin, permethrin, cyfluthrin and cypermethrin) [13]. According to the authors, the 1*R-cis* isomers of bifenthrin and permethrin, were 15 to 38 fold more active than the 1*S-cis* enantiomers. Besides that, the 1*R-trans* isomer of permethrin was more toxic than the 1*S-trans* enantiomer. The authors also observed that only two (1*R-cis-αS* and 1*R-trans-αS*) of the eight stereoisomers of cypermethrin and cyfluthrin inducted toxic effects, while the other six stereoisomers were nontoxic. Schleier III and Peterson cite in a review that 94 to 97% of acute toxicity of permethrin and resmethrin, pyrethroids Type I with four enantiomers, are related only to the I*R-cis* and I*R-trans* isomers, while the I*S-trans* and I*S-cis* isomers presented insignificant toxicity for the studied specie [12]. The same authors highlight the response of survival and fecundity of *Daphnia magna* exposed to bifenthrin in a chronic test, where the I*R-cis* isomer was 80-fold more toxic than the 1*S-cis* isomer. According to the study, the selective toxicity can be attributed to the high absorption (40-fold higher) of I*R-cis* isomer in relation to the 1*S-cis* isomer.

Mu and co-workers assessed the enantioselective toxicity of *β*-cypermethrin in zebrafish (*Danio rerio*) [40]. According to the study, acute toxicity was more lethal with 1*R-cis-αS* and 1*R-trans-αS* enantiomers than 1*S-cis-αR* and 1*S-trans-αR*. Moreover, no significant oxidative stresses were observed to 1*S-cis-αR* and 1*S-trans-αR* enantiomers. According to

Schleier III and Peterson, only the cyclopropanecarboxylic acid esters that have the *R* configuration at the cyclopropane C-1 and *α*-cyano-3-phenoxybenzyl esters with the *S* configuration at the C-*α* present toxic activity [12]. The authors' statement is in agreement with the results observed in the tests performed with *Ceriodaphnia dubia*, *Daphnia magna* [13] and *Danio rerio* [40], species of different trophic levels, where the authors observed significant toxicity only for the 1*R*-*cis* and 1*R*-*trans* enantiomers.

On the other hand, assays with Japanese fish (*Oryzias latipes*) exposed to 10 ng.mL^{-1} of bifenthrin demonstrate that 1*S*-*cis*-bifenthrin have an endocrine disruption effect 123 fold greater, if compared with the *R*-enantiomer [41]. Jin and co-authors, in tests with zebrafish exposed to 500 ng.L^{-1} of permethrin, observed that the *S*-*trans*-permethrin inducted the greatest estrogenic activity compared to the four enantiomers [42]. Furthermore, the authors highlight that the activity of *S*-*trans*-isomer was 4-fold higher than the estrogen 17*β*-estradiol (50 ng.L^{-1}). The first study used the vitellogenin as a molecular marker of exposure to estrogenic endocrine disruptive compound [41], while the second, assessed the induction of hepatic estrogen-responsive gene transcription [42].

5. Conclusions

Pyrethroid stereoisomerism is an important characteristic that must be considered in the analysis of these compounds in environmental matrices, since they present enantiomeric selectivity in the biogeochemical cycle, toxicokinetic and toxicodynamics. Studies have shown that the induction of toxic effects are derived from distinct enantiomers that those causing potential estrogenic effects. In this context, research on the environmental impacts in a pyrethroid stereochemical approach further extends its relevance. The ability to differentiate the stereochemistry selectivity pattern is fundamental for understanding the biotransformation, degradation and environmental behavior of these compounds. Studies with a stereochemical approach have been more frequent in recent years. However, much remains to be investigated, especially with respect to its isomeric bioaccumulation patterns and its possible toxicological effects on non-target organisms in the environment. In this context, in a less aggressive approach to the environment, pyrethroids should be formulated with enantiomers active only against target organisms, thereby reducing the environmental burden of isomers lacking the desired specific effect and which may act undesirably upon non-target organisms. Moreover, this chemical feature must be considered in future risk assessments and regulatory decisions.

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