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Pyrethrum and pyrethroids (e.g. allethrin, cyfluthrin, cypermethrin, deltamethrin, permethrin, resmethrin, phenothrin, tetramethrin) – Evaluation of study results in biological material

Assessment Values in Biological Material – Translation of the German version from 2008

Keywords:

pyrethrum, pyrethroids, allethrin, cyfluthrin, cypermethrin, deltamethrin, permethrin, resmethrin, phenothrin, tetramethrin, biological tolerance value, BAT value, biomonitoring

G. Leng[1]

[1] *Currenta GmbH & Co. OHG, CUR-SEL-SER-GS-BLM-Institute for Biomonitoring, 51368 Leverkusen, Germany*

email: MAK Commission (arbeitsstoffkommission@dfg.de)

BAT value (2007)	**not established**
MAK value (2008)	**not established**
Carcinogenicity	–
Prenatal toxicity	–
Germ cell mutagenicity	–

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	Cyfluthrin/ β-Cyfluthrin	Cypermethrin	Deltamethrin	Permethrin	Pyrethrum	Allethrin	Resmethrin	Phenothrin	Tetra-methrin
Synonyms	3-(2,2-dichloro-ethenyl)-2,2′-di-methylcyclopro-panecarboxylic acid [cyano-(4-fluoro-3-phenoxy-phenyl)methyl]ester; [(R)-cyano-[4-fluoro-3-(phenoxy)phenyl]-methyl] (1R,3R)-3-(2,2-dichloroethenyl)-2,2-dimethylcyclopro-pane-1-carboxylate	(RS)-alpha-cyano-3-phenoxybenzyl (1R,1S)-cis,trans-3-(2,2-dichlorovinyl)-2,2-dimethyl-cyclopro-panecarboxylate; alpha-cyano-3-phenoxybenzyl 3-(2,2-dichlorovinyl)-2,2-dimethyl-cyclopropanecarb-oxylate; alphamethrin	alpha-cyano-m-phenoxy-benzyl (1R,3R)-3-(2,2-dibromovinyl)-2,2-dimethyl-cyclopropane-1-carboxylate; alpha-cyano-3-phenoxy-benzyl (1R-1-alpha(S*),3-alpha)-3-(2,2-dibromovinyl)-2,2-dimethyl-cyclopro-panecarboxylate	Ambush; (−/+)-cis,trans-3-(2,2-dichlorovinyl)-2,2-dimethyl cyclopropane-1-carboxylic acid 3-phenoxybenzyl ester; m-phenoxybenzyl 3-(2,2-dichlorovinyl)-2-dimethylcyclo-propanecarboxy-late	–	(RS)-(3-allyl-2-methyl-4-oxocyclopenta-2-enyl) (1RS,3RS,1RS,3SR)-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclo-propanecarboxy-late; (RS)-(3-allyl-2-methyl-4-oxocyclopent-2-enyl) (1RS,3R)-2,2-dimethyl-3-(2-methylprop-1-enyl)-cyclopropane carboxylate; bioallethrin	5-benzyl-3-furylmethyl cis-chrys-anthemate	(3-phenoxy-phenyl)methyl 2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopro-pane-1-carboxy-late	–
CAS number	68359-37-5	52315-07-8	52918-63-5	52645-53-1	8003-34-7	584-79-2	10453-86-8	26002-80-2	7696-12-0
Molecular formula	$C_{22}H_{18}Cl_2FNO_3$	$C_{22}H_{19}Cl_2NO_3$	$C_{22}H_{19}Br_7NO_3$	$C_{21}H_{20}C_{17}O_3$	[a]	$C_{19}H_{26}O_3$	$C_{22}H_{26}O_3$	$C_{23}H_{26}O_3$	$C_{19}H_{25}NO_4$
Molar mass	434.3 g/mol	416.30 g/mol	505.21 g/mol	391.29 g/mol	316–374 g/mol	302.41 g/mol	338.45 g/mol	350.5 g/mol	331.41 g/mol
Melting point	57–102 °C	60–80 °C	100–102 °C	34–35 °C	17–84 °C	4 °C	43–48 °C	no data	60–80 °C
Boiling point	no data	decomposes on heating	no data	< 290 °C	170–200 °C (1.3 mbar)	281.5 °C	169–172 °C (0.01 mbar)	> 290 °C	185–190 °C (0.13 mbar)
MAK value	0.01 mg/m³ I (2003)	n. e.	n. e.	n. e.	not established	n. e.	n. e.	n. e.	n. e.
Absorption through the skin	–	n. e.	n. e.	n. e.	–	n. e.	n. e.	n. e.	n. e.
Carcino-genicity	–	n. e.	n. e.	n. e.	–	n. e.	n. e.	n. e.	n. e.

[a] see Hartwig and MAK Commission (2016)
n. e. = not evaluated

Pyrethroids are at present among the most commonly used insecticides. Among other uses, they are applied in agriculture, as fumigants (cyfluthrin, allethrin), as pesticides (cyfluthrin, deltamethrin), in stored product and material protection (permethrin in woollen carpets) as well as in the preservation of wood and structures (cypermethrin, permethrin). These insecticides (against flies, mosquitos, fleas, cockroaches etc.) can be used for example in the form of sprays, gels, insect strips, dustable powders or electric vapourisers ((S)-bioallethrin). They are often also used in combination with other pesticides, for example organophosphates (chlorpyrifos).

A large number of persons are thus exposed to pyrethroids. These include, from an occupational medical viewpoint, farmers, pest control workers and workers in the chemical industry (production and formulation of pyrethroids). From an environmental medical viewpoint, a large number of exposure scenarios for persons not occupationally exposed are to be borne in mind, such as the application of pesticides in private and public interiors (authorised fumigation in accordance with § 10 c *Bundesseuchengesetz* (Federal Law on Contagious Diseases) (BgVV 1998) or private initiative of those affected), applications in gardens and with ornamental plants, in wood preservation as well when dealing with residues in food.

Pyrethroids are synthetically produced derivatives of pyrethrum, which is obtained from chrysanthemum flowers (*Chrysanthemum cinerariaefolium*). The active substances in pyrethrum, pyrethrins, are highly sensitive to atmospheric oxygen, heat and ultraviolet light and are therefore used as short-term insecticides. They belong to the group of contact insecticides, i.e. their effects begin immediately on contact with the insect ("knock-down-effect"). In the case of pyrethrin preparations, piperonyl butoxide is frequently added to enhance the effects. As the increasing worldwide demand for insecticides cannot be covered by the isolation of natural pyrethrins from chrysanthemum plants, the industry started synthesizing compounds similar to pyrethrin, i.e. pyrethroids. Allethrin, today still used in electric vapourizers, has been on the market since 1950 and synthetically produced pyrethroids, which are photostable and therefore effective for a longer time, since the 1960s and 1970s. However, out of the about 1000 synthesized pyrethroids to date, only a few have gained international importance. These include cyfluthrin, cypermethrin, deltamethrin, permethrin, allethrin and bioallethrin as active ingredients.

1 Metabolism and Toxicokinetics

Pyrethrins can be hydrolysed both at the central ester bond as well as oxidized by cytochrome P450. The acute toxicity of the pyrethrins depends on the rate of metabolic detoxification (Hartwig and MAK Commission 2016).

In humans, it was observed that the toxicity of pyrethroids, especially the occurrence of paraesthesias, depends on the individual carboxylesterase activity; the higher the carboxylesterase activities, the more rapid the pyrethroid metabolism and the fewer paraesthesias occur as a result (Leng and Lewalter 1999; Leng et al. 1999 a).

In humans, pyrethroids such as **cyfluthrin, cypermethrin, permethrin** and **deltamethrin** are cleaved by esterases into a large number of metabolites, among others into cis- and trans-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylic acid (DCCA), cis-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxylic acid (DBCA), 3-phenoxybenzoic acid (3-PBA) as well as 4-fluoro-3-phenoxybenzoic acid (FPBA) (see Figure 1). The main site of metabolization is the liver. The detoxified metabolites are excreted mainly with the urine in free or conjugated form (mostly as glucuronides) (Eadsforth and Baldwin 1983; Eadsforth et al. 1988; Woollen et al. 1992). Figure 2 shows the metabolization of cyfluthrin with the corresponding glucuronides as example.

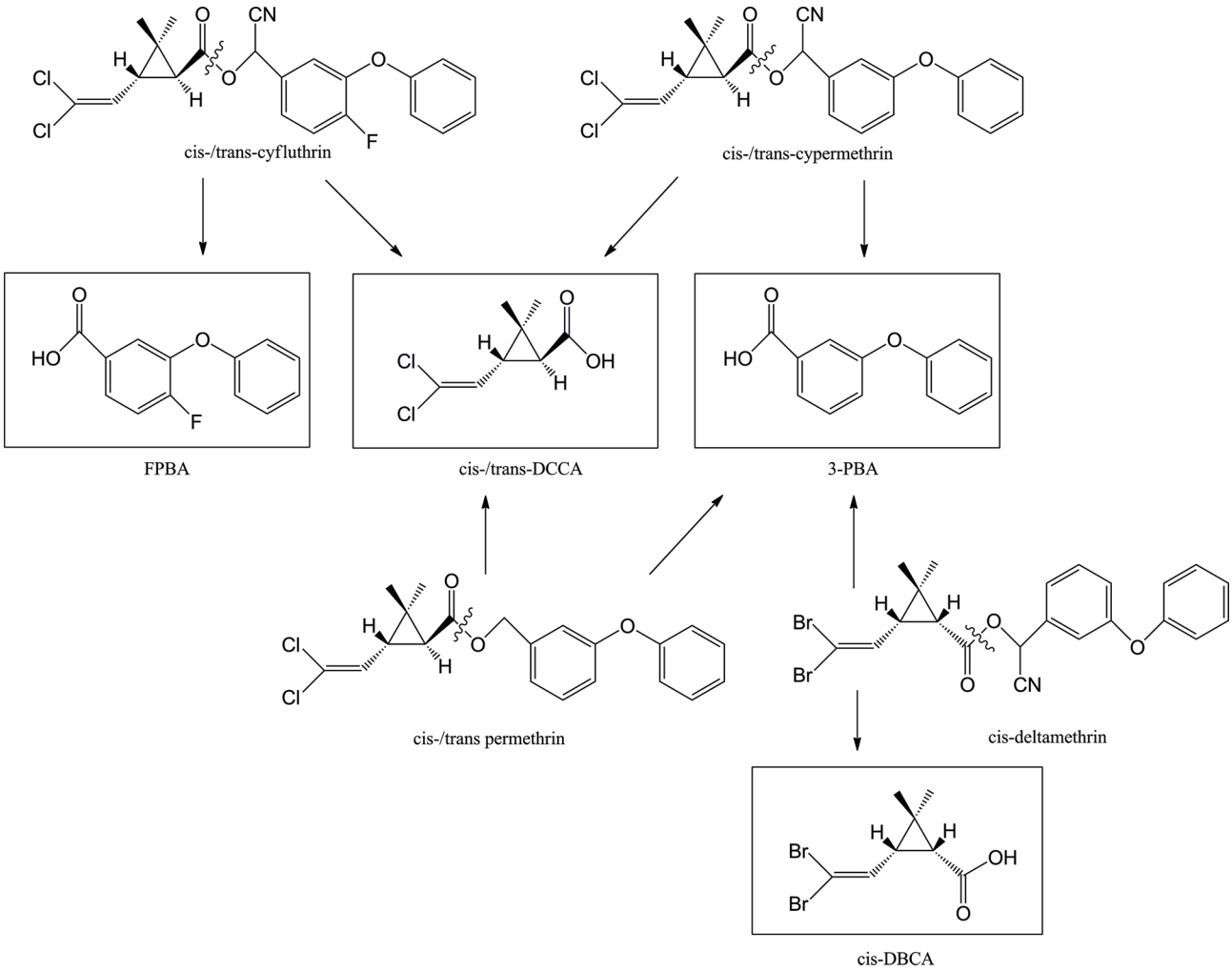

Fig. 1 Metabolism of cyfluthrin, cypermethrin, permethrin and deltamethrin in humans with the corresponding biomarkers

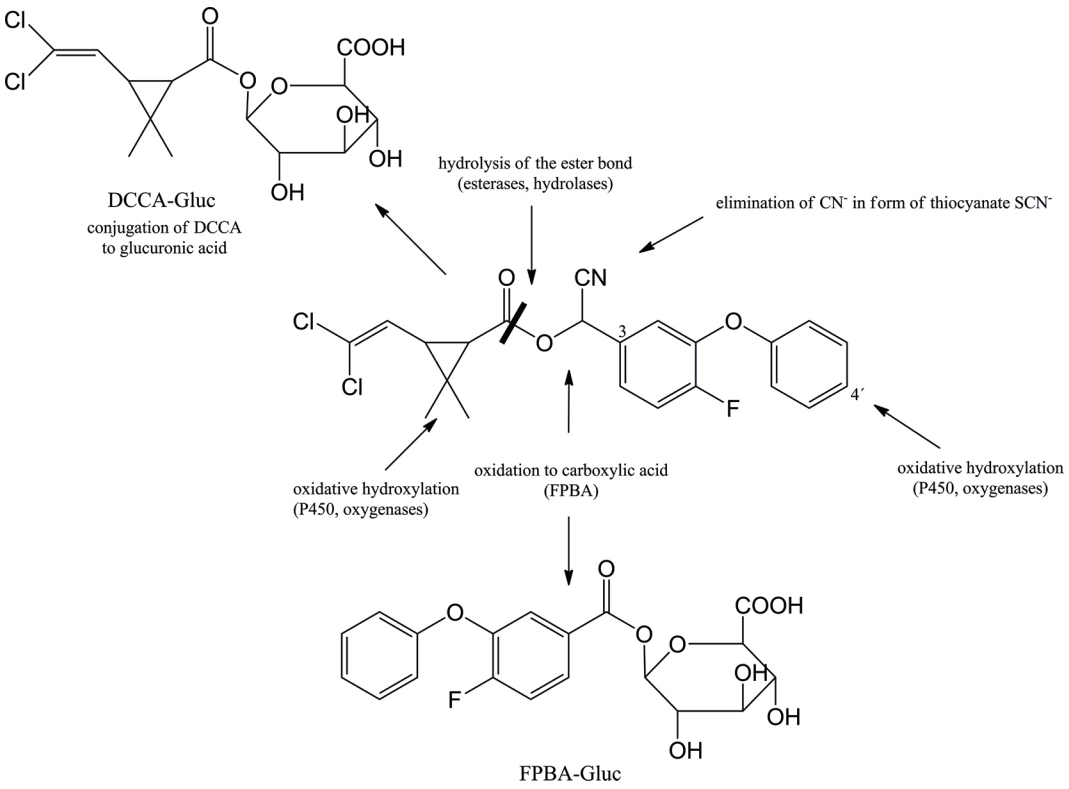

Fig. 2 Metabolism of cyfluthrin with the corresponding biomarkers

The specific biomarker for exposure to **pyrethrum, allethrin, resmethrin, phenothrin** and **tetramethrin** is trans-chrysanthemum dicarboxylic acid (CDCA) (Class et al. 1990; Elflein et al. 2003; Leng and Gries 2005; Leng et al. 1999 b, 2005). The metabolism of these substances is shown in Figure 3 using pyrethrin I as example. Metabolism studies in humans with pyrethrin I are available (Leng et al. 2006). In three test persons, CDCA in urine was determined at timepoints up to 120 hours after the ingestion of 0.3 mg pyrethrin I. The substance was eliminated almost completely within 36 hours, the highest CDCA concentrations were found within the first six hours after ingestion. The elimination half-life can be given as 4.2 hours.

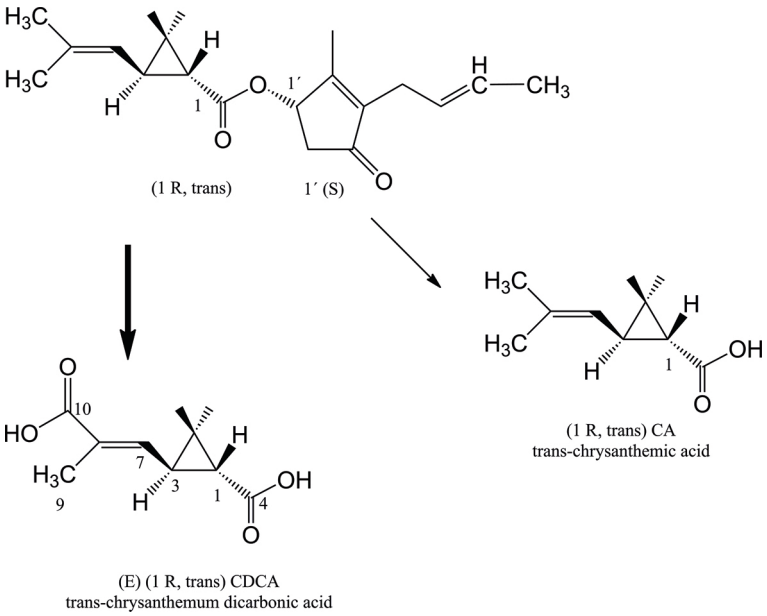

Fig. 3 Metabolism of pyrethrin

The following experimental studies investigating the kinetics of pyrethroid metabolites (inhalation, ingestion, dermal application) are described in the literature:

Inhalation
After inhalation exposure of nine individuals to 160 µg cyfluthrin/m³ for 60 minutes, 93% of the cyfluthrin metabolites were excreted with the urine within 24 hours after exposure. The individual half-lives varied between 3.3–12.2 hours for cis-DCCA, between 2.9–11.6 hours for trans-DCCA, and between 3.1–6.5 hours for FPBA (Leng et al. 1997 a).

Ingestion
In one study, four individuals ingested different quantities of cypermethrin. 78% of the administered dose was excreted with the urine within 24 hours as trans-DCCA and 49% as cis-DCCA (Eadsforth and Baldwin 1983). Repeated daily oral administration of cypermethrin for five days produced no increase in metabolite elimination: 72% of the trans-DCCA and 45% of the cis isomer was excreted within 24 hours (Eadsforth et al. 1988). A further study with α-cypermethrin confirmed these results (Eadsforth 1988). The highest excretion rates for the metabolites 3-PBA and FPBA were found 4 to 24 hours after oral cypermethrin administration to six individuals. 93% of the metabolites were recovered in the urine within 72 hours. The mean elimination half-life of the metabolites was 16.5 hours (11–27 hours) and the ratio between trans-DCCA and cis-DCCA was 2 : 1 (Woollen et al. 1992).

In another investigation, a healthy male individual received an oral cyfluthrin dose of 0.03 mg/kg body weight (total dose: 2.6 mg cyfluthrin). This dose was above the acceptable daily intake (ADI) of 0.02 mg/kg body weight. The urine was collected over two days at 12 hour intervals. The mean half-life of the metabolites was 6.44 ± 0.64 hours (cis-DCCA: 6.66 hours; trans-DCCA: 6.54 hours, FPBA: 6.13 hours). 40% of the administered dose was recovered in the urine. The isomer ratio of trans-DCCA to cis-DCCA was 2.3 : 1. The excreted amount of FPBA was twice as high as the total elimination of cis-DCCA and trans-DCCA (Leng et al. 1997 b).

Absorption through the skin
After dermal application of cypermethrin, elimination was at its highest within the first 12–36 hours. In contrast to oral administration, the trans-DCCA to cis-DCCA ratio was here 1 : 1.2. The absorption of cypermethrin after dermal application was considerably lower than that after oral administration: based on the recovery of 3-PBA

and FPBA, 1.2% was absorbed, compared to 0.3% based on the recovery of DCCA (Woollen et al. 1992). The mean elimination half-life of the metabolites was 13 hours (8–22 hours). Eight hours after application, 41% of the applied dose was recovered after washing the skin with a mild detergent and 24% in the T-shirt which had been worn over the site of application (Woollen et al. 1992). In a dermal cypermethrin study, 0.1% of the applied dose was excreted with the urine in the form of DCCA within 72 hours. After 4-hour duration of contact, the surplus cypermethrin was removed from the treated skin area. Thereby, 71% of the applied cypermethrin was recovered (Eadsforth et al. 1988).

2 Critical Toxicity

2.1 Animals

Compared with other pesticides, pyrethroids have on the one hand a rapid insecticidal effect, but on the other hand a low toxicity in mammals. The LD_{50} values for pyrethroids in insects and rats compared with other classes of insecticides are shown in Table 1.

Tab. 1 Toxicity of insecticide classes for insects and rats (Matsuo 1989)

Insecticide	Topical LD_{50} insect [mg/kg body weight]	Oral LD_{50} rat [mg/kg body weight]	Ratio rat/insect
carbamates	2.8[a] (27[b])	45 (15)	16
organophosphates	2 (50)	67 (83)	34
organochlorine compounds	2.6 (26)	230 (21)	90
pyrethroids	0.45 (35)	2000 (11)	4400

[a] geometric mean
[b] number of animals

Table 2 gives an overview of some toxicity data. The wide range of oral LD_{50} values is due to the different administration forms (for example in oil, water).

Tab. 2 Data on the toxicity of a number of pyrethroids in rats (BGA 1994; WHO 1989 a, b, 1990 a, b)

Active substance	LD_{50}, oral [mg/kg body weight]	LD_{50}, dermal [mg/kg body weight]	NOAEL, oral [mg/kg body weight and day]	ADI[a] [mg/kg body weight and day]
pyrethrum	584–900	1500	10	0.04
bioallethrin	709–1042	> 3000	135	–
cypermethrin	200–800	> 1600	5	0.05
permethrin	450–2800	7200	5	0.05
cyfluthrin	16–1271	> 5000	5	0.02
deltamethrin	50–100	> 2940	2.5	0.01

[a] acceptable daily intake: the quantity a human can ingest daily during a lifetime without adverse health effects, derived from the NOAEL

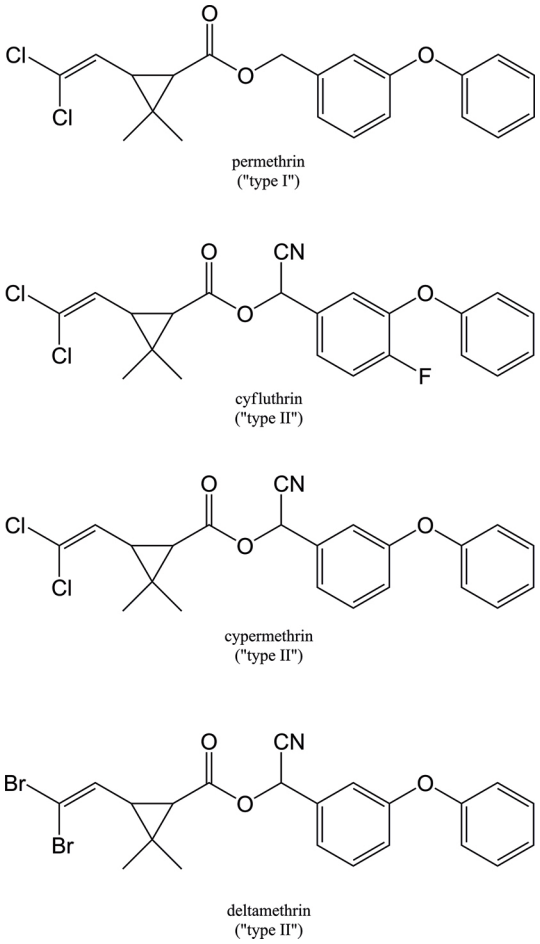

Fig. 4 Chemical structures of type I and II pyrethroids

Based on their effects in the rat, pyrethroids are classified in two groups: type I pyrethroids without the cyano group and type II pyrethroids with the cyano group (see Figure 4). Type I pyrethroids such as pyrethrins, allethrin and permethrin cause the so-called T-syndrome, characterized by tremor, ataxia, increased excitability, and hypersensitivity to external stimuli. Type II pyrethroids such as cyfluthrin, cypermethrin or deltamethrin are the cause of the CS syndrome (choreoathetosis, salivation, clonic seizures).

The main target organ of pyrethrins and pyrethroids in the insect and mammalian organism is the central and peripheral nervous system. The voltage-gated sodium channel in the nerve membrane is the primary site of action. The main effect consists of a stereoselective interaction of the pyrethroids with receptor macromolecules of the activated sodium channels. After a repolarization of the membrane, this effect prevents a rapid closing of the sodium channel. This results in a flow of sodium ions into the nerve cell over a longer time. This increased sodium permeability during the excitation phase results in repeated discharges. This affects the sensory nerve fibres, the sense organs, the motor nerve endings in addition to the fibres of the skeletal muscles (Aldridge 1990).

No accumulation of pyrethroids in the fat has been observed (Appel and Gericke 1993). A study in egg-laying hens (Saleh et al. 1986), where an accumulation of pyrethroids in the brain was found after administration of single doses, could not be reproduced in further investigations (Greim 2007).

2.2 Humans

After contact with pyrethroids, paraesthesias in directly exposed skin areas, irritation of the mucous membranes and respiratory tract as well as negative facial sensations (area innervated by the trigeminal nerve) have been described (Altenkirch et al. 1996; He et al. 1988, 1989; Leng et al. 1998). The duration of symptoms depends on the respective pyrethroid, and varies between 30 minutes and 32 hours (Aldridge 1990). Complaints do not always occur directly after exposure; in some cases not until after a latent period of 30 minutes to eight hours (He et al. 1988). Pathophysiologically, the paraesthesias are explained as repetitive firing of superficial peripheral sensory nerve endings in the skin (Aldridge 1990). Pyrethroids with cyano groups have a more pronounced neuroexcitatory potential than those without, in decreasing order, i.e.: deltamethrin > cypermethrin > permethrin (Aldridge 1990). In cases of severe intoxication with loss of consciousness and muscular fasciculations, the symptoms did not improve again until after two to three weeks (maximum: 55 days) (He et al. 1989).

In addition to the above-mentioned symptoms, general symptoms such as dizziness, nausea, vomiting, weakness, loss of appetite, headache and tiredness are frequently described in literature (Altenkirch et al. 1996; He et al. 1988, 1989; Leng et al. 1998).

3 Exposure and Effects

3.1 Relationship between external and internal exposure

In exposure chamber studies with **cyfluthrin**, a correlation between the cyfluthrin concentration in air and the concentration of metabolites in urine could be demonstrated in test persons. Figure 5 shows the ratio between the cyfluthrin concentration in air and the amount of cyfluthrin equivalents, as derived from the amount of cis-DCCY and trans-DCCA recovered in urine. A four times higher concentration of cyfluthrin in air produced a four times higher amount of cyfluthrin equivalents in urine (Leng et al. 1997 a).

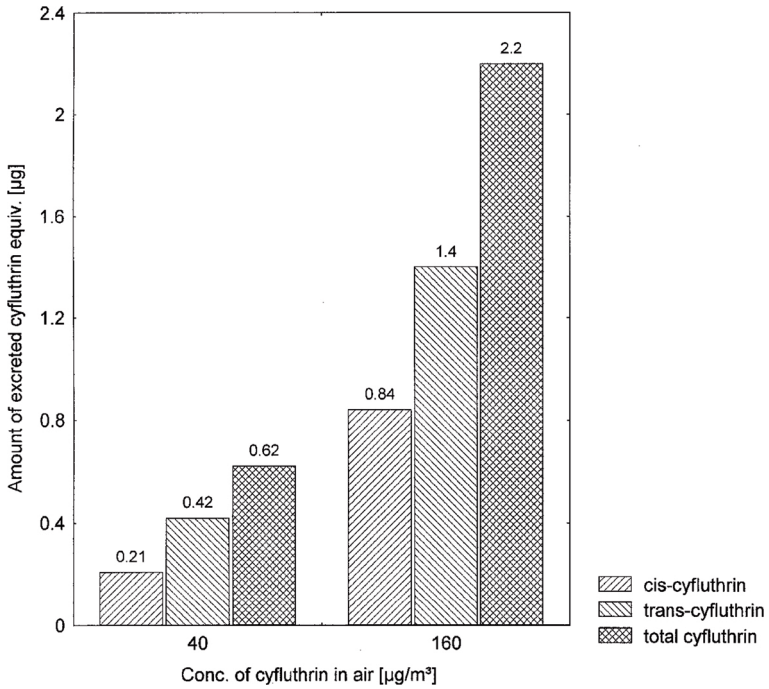

Fig. 5 Dose-dependency of the mean urinary concentrations of cyfluthrin equivalents (µg/l) in five individuals after exposure to 40 µg cyfluthrin/m^3 air and in four individuals after exposure to 160 µg cyfluthrin/m^3 air (Leng et al. 1997 a, reprinted by permission of Taylor & Francis Ltd, https://www.tandfonline.com)

On the other hand, after a pest control measure using various pyrethroids (cyfluthrin, cypermethrin, permethrin and deltamethrin), no correlation between the respective pyrethroid concentration in suspended dust particles and the concentration of metabolites in urine could be found (BMBF 2001).

3.2 Relationship between internal exposure and effects

After a cyfluthrin intoxication, cyfluthrin was determined in plasma as well as the cyfluthrin-specific metabolite FPBA in urine. Table 3 shows the development of the cyfluthrin plasma concentrations and the urinary FPBA concentrations over time. Although the initial concentration of cyfluthrin in plasma was high, no cyfluthrin could be found in plasma any longer after one day. On the other hand, the metabolite could still be found in the urine 3 days after exposure. A correlation factor between the cyfluthrin concentration in plasma and the FPBA concentration in urine could not be observed in the investigations available to date (Leng and Lewalter 1999).

Tab. 3 Time course of cyfluthrin in plasma and urinary FPBA concentrations after cyfluthrin intoxication (Leng and Lewalter 1999)

Time after intoxication [h]	Cyfluthrin in plasma [µg/l]	FPBA in urine [µg/l]
1	180	730
3	105	915
24	< 5	290
72	< 5	70
48	< 5	13
96	< 5	< 0.5

In seven workers accidentally exposed to cyfluthrin, the cyfluthrin concentrations in plasma (1.2 or 1.5 µg/l) and the FPBA concentrations in urine (117 or 146 µg/g creatinine) were increased 30 minutes after the accident (see Table 4). Four of these workers reported paraesthesias, though no paraesthesias occurred in three workers. This could be attributed to individually varying carboxyl esterase activities (see Section 1). Also in workers handling cyfluthrin, paraesthesias were observed only in those with low carboxyl esterase activities (Leng and Lewalter 1999; Leng et al. 1999 a).

Tab. 4 Dependence of the occurrence of paraesthesias on carboxyl esterase (CBE) activity in workers exposed to cyfluthrin (Leng and Lewalter 1999; Leng et al. 1999 a)

Paraesthesias	Exposure by accident	Number of workers	Cyfluthrin [µg/l plasma]	FPBA [µg/g creatinine]	CBE [U/l]
yes	yes	4	1.2	117	313
yes	no	3	0.4	9	320
no	yes	3	1.5	146	713
no	no	135	0.5	14	570

4 Selection of Indicators

4.1 Blood

As the concentration of non-metabolized pyrethroids is responsible for the symptoms – mostly paraesthesias – as well as for the biological effects occurring after exposure to pyrethroids (Aldridge 1990), the pyrethroid con-

centration in the plasma can be determined as effect marker. Nevertheless, due to the rapid metabolization of the pyrethroids, determination of their presence in blood is only useful directly (1–3 hours) after a high exposure.

4.2 Urine

To detect an internal exposure to pyrethroids, determination of the pyrethroid metabolites in urine is recommended for the assessment of total exposure. Due to the rapid metabolization of pyrethroids, it is best to collect the urine directly after exposure, and at all events during the first 24 hours following it. The detection of metabolites in urine is only suitable as an exposure but not as an effect marker, as several studies have shown that there is no correlation between the occurrence of symptoms and the concentration of metabolites in urine in concentration ranges relevant for occupational medicine (BMBF 2000; He et al. 1989; Leng 2000; Leng et al. 1996, 1998).

Tab. 5 Detection of pyrethroid metabolites in workers exposed to pyrethroids

Collective	Pyrethroid	Number of metabolites > LOD	Metabolite concentration [µg/l]	References
pest control workers		n = 14	0.5–277 (range)	Leng et al. 1998
16	cyfluthrin		35 (50^{th} percentile)	
3	permethrin			
2	deltamethrin			
1	cypermethrin			
10 greenhouse workers	deltamethrin	n = 2	4.8–51.7 (range)	Tuomainen et al. 1996
5 forest workers	permethrin	n = 1	0.26	Kolmodin-Hedman et al. 1995
30 pest control workers	pyrethrum	n = 27	< 0.05–54 (range) 0.23 (50^{th} percentile) 9.95 (95^{th} percentile)	Leng et al. 2006

LOD = limit of detection

5 Analytical Methods

5.1 Blood

The presence of the pyrethroids cyfluthrin, cypermethrin, deltamethrin and permethrin in plasma can effectively be demonstrated using gas chromatograph-electron capture detector (GC-ECD) (detection limit 5 µg/l), confirmed by gas chromatographic-negative-ion chemical ionization mass spectrometry (GC/NCIMS) (detection limit 5 ng/l) (Leng 2000; Leng et al. 1997 b).

No validated method exists to determine carboxylesterase activity.

5.2 Urine

To analyse pyrethroid metabolites in urine, a method tested by the Commission (gass chromatography/mass spectrometry, GC/MS; detection limit 0.5 µg/l) is available (Angerer et al. 1999). In addition, there is also a very sensitive gas chromatography coupled with high resolution mass spectrometry (GC-HRMS) method, with which a detection limit of 0.03 µg/l can be obtained (Leng et al. 1997 c). The method has been tested and approved by the Working Group "Analyses in Biological Material" of the Commission (Berger-Preiss et al. 2013; Elflein et al. 2003; Leng and Gries 2005; Leng et al. 2013).

6 Background Exposure

6.1 Blood

In persons not exposed to cyfluthrin, the cyfluthrin concentration in blood is below 5 ng/l and the FPBA concentration in urine below 0.1 µg/l (Leng et al. 1997 c).

6.2 Urine

The concentration of pyrethroid metabolites in the urine of persons not exposed occupationally has been investigated in a number of studies (see Table 6). In a collective of 254 persons, the 95th percentile was 0.5 µg/l for DCCA and 0.6 µg/l for 3-PBA (Butte et al. 1998). Based on a collective of 45 persons, the 95th percentile was 0.6 µg/l for cis-DCCA, 0.9 µg/l for trans-DCCA and was below the detection limit for DBCA and FPBA (Hardt et al. 1999). In 1177 persons including children the 95th percentile was 0.5 µg/l for cis-DCCA, 1.5 µg/l for trans-DCCA, 0.3 µg/l for DBCA and 0.3 µg/l for FPBA (Heudorf and Angerer 2001). It seems that the background exposure of the general population can be attributed to eating habits (Hardt et al. 1999; Heudorf and Angerer 2001).

Tab. 6 Concentrations of individual pyrethroid metabolites in the urine of occupationally non-exposed persons

Number of persons	Metabolite concentration in urine [µg/l]						References
	cis-DCCA	trans-DCCA	cis-DBCA	trans-CDCA	3-PBA	FPBA	
45	0.6[a]/1.6[b]	0.9/3.8	0.1/0.5	n. d.	n. d.	< 0.2/< 0.2	Hardt et al. 1999
254	0.51[c]/11.6	n. d.	n. d.	n. d.	0.57/15.6	n. d.	Butte et al. 1998
1177	0.51/9.76	1.43/17.82	0.30/9.19	n. d.	n. d.	0.27/5.11	Heudorf and Angerer 2001
61	0.5/1.2	< 0.2/1.2	< 0.2/< 0.2	n. d.	0.2/0.8	< 0.2/< 0.2	Leng et al. 2003
15	0.95/2.33	1.46/3.35	0.11/0.18	0.12/0.13	1.41/3.1	0.02/0.02	Leng and Gries 2005

[a] 95th percentile
[b] maximum value
[c] given as total DCCA
n. d. = no data

The Human Biomonitoring Commission of the *Umweltbundesamt* (Federal Environment Agency) has derived the following reference values: cis-DCCA: 1 µg/l, trans-DCCA: 2 µg/l and 3-PBA: 2 µg/l urine (UBA 2005).

7 Evaluation

At present, a MAK value has only been established for cyfluthrin at 10 µg/m^3 (Greim 2007) to avoid sensory irritation; the former MAK value for pyrethrum of 5 mg/m^3 was withdrawn in 2007 (translated in Hartwig and MAK Commission 2016). No biological tolerance values (BAT values) are available for pyrethroids to date. As the local sensory irritation is the most sensitive endpoint, no correlation exists between the occurrence of symptoms and the urinary metabolite concentration, and the detection of pyrethroids in plasma with the analytical methods available at present is, due to their rapid metabolization, only useful after accidental poisoning, it is not useful from an occupational medical viewpoint, to derive health-based biological limit values to assess exposure to pyrethroids.

No BAT value can therefore be established at present.

8 Interpretation of Data

At present, it is only possible to compare pyrethroid exposure at the workplace with the background exposure in the general population. As reference values for the general population, 1 µg/l urine has been derived for cis-DCCA, 2 µg/l for trans-DCCA and 3 µg/l urine for 3-PBA (UBA 2005).

ADI (acceptable daily intake) values between 0.01 and 0.05 mg/kg body weight and day exist for a large number of pyrethroids (BGA 1994). These ADI values protect from the dose-dependent, central nervous and systemic effects of pyrethroids (Pauluhn 1998), but not from the local sensory irritation of the skin, the mucous membranes, the eyes and the upper respiratory tract already occurring at lower doses or concentrations.

Notes

Competing interests

The established rules and measures of the Commission to avoid conflicts of interest (https://www.dfg.de/en/dfg_profile/statutory_bodies/senate/health_hazards/conflicts_interest/index.html) ensure that the content and conclusions of the publication are strictly science-based.

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