

· 专论与综述 ·

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手性农药选择性生物活性与毒性效应研究进展

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摘 要: 手性农药因对映体在生物活性、毒性、环境行为等方面的差异性而备受关注, 充分了解对映体的立体选择性对开发高活性农药及减量使用具有重要意义。本文聚焦手性农药对映体的立体选择性效应, 系统地调研了对映体生物活性和毒性选择性差异, 并进行了分类梳理, 重点综述了手性农药对映体的生物活性及毒性和环境风险的差异性, 阐述了手性农药对非靶标生物造成的氧化应激、内分泌干扰等慢性毒性, 同时关注选择性的规律与机制, 为环境友好型高效手性农药的开发、手性农药的风险评估及管理、手性农药对映体立体选择性机制研究提供参考。

关键词: 手性农药; 对映体; 生物活性; 立体选择性; 毒性效应

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Research progress on the stereoselective bioactivity and toxicity of chiral pesticides

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Abstract: Chiral pesticides have attracted much attention due to enantiomeric differences in biological activity, toxicity and environmental behavior. It is significant to understand the stereoselectivity of enantiomers for developing highly active pesticides and reducing dosage. This review focus on the stereoselective effects of enantiomers of chiral pesticides, thoroughly investigated the enantioselective biological activity and toxicity selectivity, and sort it out, the bioactivity, toxicity and environmental risk of enantiomers of chiral pesticides were reviewed. This review described the chronic toxicity of chiral pesticides to non-target organisms, such as oxidative stress and endocrine disruption, and pay attention to the rules and mechanisms of stereoselectivity, in order to provide reference for the development of environmentally friendly and efficient chiral pesticides, the risk assessment and management of chiral pesticides, and the stereoselectivity mechanism of chiral pesticides.

Keywords: chiral pesticide; enantiomer; bioactivity; stereoselectivity; toxic effect

手性化合物对映体呈镜像关系, 除旋光特性外几乎具有完全相同的物理化学性质, 但与生物体作用时通常差异显著, 因而展现出立体选择性的生物学特性。近年来手性农药的选择性得到了

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广泛关注,如选择性生物活性、毒性毒理、环境行为、不对称合成等。目前我国登记使用的手性农药约 270 种,占比近 40%,并且这一比例一直呈上升的趋势^[1-3]。手性农药对映体通常会具有不同的生物活性,存在高效体、低效体或无效体,所以随着合成工艺的改进,一些手性农药品种以高活性的光学纯单体形式进行生产、登记、销售和使用,如精异丙甲草胺、精甲霜灵、精喹禾灵、精草铵膦和氰氟草酯等^[4-9]。除生物活性外,大量的研究表明,手性农药对映体在环境归趋、毒性毒理方面也广泛存在选择性,如内分泌干扰毒性、生殖毒性和神经毒性等^[10-12]。

前人关于手性农药的综述多集中于手性农药的环境行为、毒性和合成等,而阐述手性农药生物活性和毒性立体选择性差异未见系统报道。本综述调研了近年手性农药的相关研究,拟对目前国内手性农药的选择性生物活性和毒性效应的研究进展展开综述,并且对其进行归类整理,旨在为手性农药选择性环境行为的进一步研究以及手性农药高效、环境友好型光学纯单体农药的开发和应用提供理论依据。

1 手性农药生物活性立体选择性

生物活性是评估农药药效的重要指标之一,研究表明,手性农药对映体之间生物活性的差异主要分为 4 种类型:1) 仅有一个对映体具有活性,其余为无效体或低效体;2) 对映体之间活性差异 10 倍以内;3) 对映体之间活性没有明显差异^[13-14];4) 对映体活性类型不同,以下分别总结手性杀虫剂、杀菌剂和除草剂对靶标生物的对映体活性差异。

1.1 手性杀虫剂生物活性立体选择性

目前我国市售手性杀虫剂约 110 余种^[11],表 1 列举了一些杀虫剂对映体的生物活性信息。拟除虫菊酯类和有机磷类很多品种具有手性,因此有关对映体立体选择性的研究相对较多。如有机磷

农药水胺硫磷,*S* 体对褐飞虱 *Nilaparvata lugens* 和二化螟 *Chilo suppressalis* 的 LC₅₀ 值分别为 341 和 8.63 mg/L,而 *R* 体对这两种害虫的 LC₅₀ 值分别为 1 000 和 500 mg/L,说明 *S*-水胺硫磷对上述害虫的杀虫活性分别是 *R* 体的 2.9 和 57.9 倍^[15];同样,Di 等也发现水胺硫磷 *S* 对映体对朱砂叶螨 *Tetranychus cinnabarinus*、东方黏虫 *Mythimna separata*、豌豆蚜 *Aphis craccivora* 和小菜蛾 *Plutella xylostella* 的杀虫活性约是 *R*-水胺硫磷的 13.2~55.6 倍^[16]; *S*-水胺硫磷对蝗虫 *Locust* 的活性是 *R*-水胺硫磷的 130 倍^[17]。水胺硫磷对于鳞翅目和同翅目害虫有较好防效,其 *S* 体对上述靶标害虫均表现为高效体,具有较大潜力开发为高活性单体农药。拟除虫菊酯类农药中已成功开发高效异构体产品的数量相对较多,如氰戊菊酯, (*S,S*)-氰戊菊酯对德国小蠊 *Blattella germanica* 的杀虫活性是 (*R,S*)-氰戊菊酯的 50 倍^[18],目前以 (*S,S*)-氰戊菊酯光学纯单体进行销售。此外,甲氰菊酯、溴氰菊酯、乙氰菊酯、联苯菊酯、氟丙菊酯、四溴氟菊酯等均以单体形式作为有效成分进行商品化销售和使用^[19]。苯基吡唑类手性杀虫剂有丁虫脒、乙虫脒、氟虫脒等,其选择性生物活性也得到了很好的研究,丁虫脒含一对对映体,其中 *R*-丁虫脒对小菜蛾、东方黏虫、豌豆蚜和褐飞虱的 LC₅₀ 值分别为 0.36、1.37、0.95 和 0.46 mg/L,其杀虫活性是 *S*-丁虫脒的 1.9~5.1 倍^[20];乙虫脒具有一个手性中心, *R*-乙虫脒对豌豆蚜虫 *Macrosiphum pisi* 和褐飞虱的活性分别是 *S*-乙虫脒的 4.26 倍和 2.43 倍^[20]。苯基吡唑类手性杀虫剂多为 *R* 体为高效体,且对映体之间活性差异约在 10 倍以内。其他种类的手性农药杀虫剂如 fluralaner、fluxametamide、乙螨唑、茚虫威等对映体之间生物活性差异在 10 倍以上,其中 *S*-茚虫威作为高效体,其生物活性是 *R*-茚虫威的 1 000 倍以上^[21],目前市售茚虫威原药中 *S*-茚虫威与 *R*-茚虫威的比例约为 3 : 1。

表 1 手性杀虫剂对映体生物活性差异
Table 1 Enantiomer bioactivity difference of chiral insecticides

农药名称 Pesticide name	靶标生物 Target organism	对映体 LC ₅₀ 或 LD ₅₀ 值 Enantiomer LC ₅₀ or LD ₅₀ value/[LC ₅₀ /(mg/L), LD ₅₀ /(mg/kg)]		对映体生物活性 差异倍数 Differential multiple of enantiomer biological activity	参考文献 References
		<i>R</i>	<i>S</i>		
吡丙醚 pyriproxyfen	柑桔矢尖蚧 <i>Unaspis yanonensis</i> (Kuwana)	LC ₅₀ 1.95	6.61	3.33	[22]
	柑橘木虱若虫 <i>Diaphorina citri</i> nymphs	LC ₅₀ 4.82	11.4	2.38	

续表 1
Table 1 (Continued)

农药名称 Pesticide name	靶标生物 Target organism	对映体 LC ₅₀ 或 LD ₅₀ 值 Enantiomer LC ₅₀ or LD ₅₀ value/[LC ₅₀ /(mg/L), LD ₅₀ /(mg/kg)]		对映体生物活性 差异倍数 Differential multiple of enantiomer biological activity	参考文献 References
		R	S		
fluralaner	二化螟 <i>Chilo suppressalis</i>	LD ₅₀ 9.80	0.290	33.8	[23]
	灰飞虱 <i>Laodelphax striatellus</i>	LD ₅₀ 3.20	0.0820	39.0	
仲丁威 fenobucarb	褐飞虱 <i>Nilaparvata lugens</i>	LC ₅₀ 5.84	16.0	2.78	[24]
	淡色库蚊 <i>Culex pipiens pallens</i>	LC ₅₀ 0.540	0.990	1.82	
水胺硫磷 isocarbophos	朱砂叶螨 <i>Tetranychus cinnabarinus</i>	LC ₅₀ >500	16.8	29.7	[16-17]
	黏虫 <i>Mythimna separata</i>	LC ₅₀ >500	9.00	55.6	
	豆蚜 <i>Aphis craccivora</i>	LC ₅₀ >500	13.0	38.5	
	小菜蛾 <i>Plutella xylostella</i>	LC ₅₀ >500	37.8	13.2	
	飞蝗 <i>Locusta migratoria manilensis</i>	LD ₅₀ 79.4	0.609	130	
甲基异柳磷 isofenphos-methyl	褐飞虱 <i>Nilaparvata lugens</i>	LC ₅₀ 22.4	6.09	3.67	[25]
	豆长管蚜 <i>Macrosiphum pisi</i>	LC ₅₀ 50.5	2.27	22.3	
	南方根结线虫 <i>Meloidogyne incognita</i>	LC ₅₀ >200	13.8	14.5	
fluxametamide	小菜蛾 <i>Plutella xylostella</i>	LC ₅₀ 34.2	0.620	55.1	[26]
	甜菜夜蛾 <i>Spodoptera exigua</i>	LC ₅₀ 67.7	0.460	147	
	棉蚜 <i>Aphis gossypii</i>	LC ₅₀ 32.8	0.630	52.1	
	朱砂叶螨 <i>Tetranychus cinnabarinus</i>	LC ₅₀ 104	0.340	304	
丁虫腈 flufiprole	小菜蛾 <i>Plutella xylostella</i>	LC ₅₀ 0.360	0.660	1.82	[18]
	褐飞虱 <i>Nilaparvata lugens</i>	LC ₅₀ 0.460	1.28	2.78	
	黏虫 <i>Mythimna separata</i>	LC ₅₀ 1.37	3.06	2.22	
	豌豆长管蚜 <i>Acyrtosiphon pisum</i>	LC ₅₀ 0.950	4.88	5.26	
呋虫胺 dinotefuran	棉蚜 <i>Aphis gossypii</i>	LC ₅₀ 1.21	0.375	3.20	[27]
	绿盲蝽 <i>Apolygus lucorum</i>	LC ₅₀ 59.7	18.3	3.30	
七氟菊酯 tefluthrin	黏虫 <i>Mythimna separata</i>	LD ₅₀ 0.150	52.6	333	[28]
	甜菜夜蛾 <i>Spodoptera exigua</i>	LD ₅₀ 1.27	3.82	3.01	
	斜纹夜蛾 <i>Spodoptera litura</i> F.	LD ₅₀ 2.99	>200	6.67	
联苯菊酯 bifenthrin	家蝇 <i>Musca domestica</i> L.	LC ₅₀ 1.08	30.7	0.350	[29]
	菜青虫 <i>Pieris rapae</i> L.	LC ₅₀ 0.850	>300	357	
乙螨唑 etoxazole	二斑叶螨 <i>Tetranychus urticae</i>	LC ₅₀ 1.27	0.0760	16.7	[30]
	朱砂叶螨 <i>Tetanychus cinnabarinus</i>	LC ₅₀ 0.837	0.034	24.6	
氟虫腈 fipronil	小菜蛾 <i>Plutella xylostella</i>	LD ₅₀ 2.80	2.00	1.40	[31-32]
	棉红蝽 <i>Dysdercus cingulatus</i>	LD ₅₀ 0.550	0.560	1.02	
	家蝇 <i>Musca domestica</i>	LD ₅₀ 15.0	18.0	1.20	
	谷象 <i>Sitophilus granarius</i>	LD ₅₀ 0.630	0.740	1.18	
茚虫威 indoxacarb	小菜蛾 <i>Plutella xylostella</i>	LC ₅₀ 404	3.52	115	[21]
	中华草蛉 <i>Chrysoperla sinica</i>	LC ₅₀ >2000	1.16	1724	
乙虫腈 ethiprole	豌豆蚜虫 <i>Macrosiphum pisi</i>	LC ₅₀ 0.249	1.06	4.27	[19]
	褐飞虱 <i>Nilaparvata lugens</i>	LC ₅₀ 1.75	4.26	2.43	
苯硫磷 epn	家蝇 <i>Musca domestica</i> L.	LD ₅₀ (+) 1.1	(-) 3.2	2.94	[33]
	二化螟 <i>Chilo suppressalis</i>	LD ₅₀ (+) 2.9	(-) 11.7	4.17	
蔬果磷 salithion	家蝇 <i>Musca domestica</i> L.	LD ₅₀ 0.400	0.050	8.00	[34]
丙溴磷 profenofos	家蝇 <i>Musca domestica</i> L.	LD ₅₀ (+) 23.0	(-) 6.00	3.83	[35]
	粉纹夜蛾 <i>Trichoplusia</i>	LD ₅₀ (+) 56	(-) 13	4.31	
	孑孓 <i>Culicidae</i>	LD ₅₀ (+) 270	(-) 22	12.3	

续表 1					
Table 1 (Continued)					
农药名称 Pesticide name	靶标生物 Target organism	对映体 LC ₅₀ 或 LD ₅₀ 值 Enantiomer LC ₅₀ or LD ₅₀ value/[LC ₅₀ /(mg/L), LD ₅₀ /(mg/kg)]		对映体生物活性 差异倍数 Differential multiple of enantiomer biological activity	参考文献 References
		R	S		
氰戊菊酯 fenvalerate	德国小蠊 <i>Blattella germanica</i>	(RS) LD ₅₀ 0.300	(SS) 0.006	50	[20]
氯菊酯 permethrin	家蝇 <i>Musca domestica</i> L.	LD ₅₀ 1R <i>cis</i> 8.2	1S <i>cis</i> 155.9	18.9	[36]
		LD ₅₀ 1R <i>trans</i> 16.7	1S <i>trans</i> 161	9.71	
苯醚菊酯 phenothrin epno	家蝇 <i>Musca domestica</i> L.	LD ₅₀ 1R <i>cis</i> 41.6	1S <i>cis</i> 496.2	11.9	[36]
		LD ₅₀ 1R <i>trans</i> 29.2	1S <i>trans</i> 424	14.5	
	家蝇 <i>Musca domestica</i> L.	LD ₅₀ (+) 0.097	(-) 0.16	1.64	[37]
苯腈磷 cyanofenphos	家蝇 <i>Musca domestica</i> L.	LD ₅₀ (+) 1.32	(-) 3.61	2.70	[38]
	二化螟 <i>Chilo suppressalis</i>	LD ₅₀ (+) 2.92	(-) >73	25.0	
甲胺磷 methamidophos	家蝇 <i>Musca domestica</i> L.	LD ₅₀ (+) 2.40	(-) 15.0	6.25	[39]
	德国小蠊 <i>Blattella germanica</i>	LD ₅₀ (+) 2.40	(-) 2.30	1.04	
乙酰甲胺磷 acephate	家蝇 <i>Musca domestica</i> L.	LD ₅₀ (+) 3.00	(-) 15.0	5.00	[39]
	德国小蠊 <i>Blattella germanica</i>	LD ₅₀ (+) 4.2	(-) 4.5	11.08	
苯线磷 fenamiphos	乙酰胆碱酯酶 Acetylcholin esterase	LC ₅₀ (+) 0.008	(-) 0.15	18.9	[40]
地虫硫磷 fonofos	乙酰胆碱酯酶 Acetylcholin esterase	IC ₅₀ (+) >0.406	(-) 0.176	2.31	[41]
地虫磷 chlorethoxyfos	家蝇 <i>Musca domestica</i> L.	LD ₅₀ 6.30	25.0	3.97	[42]
	蚊子 <i>Culicidae</i>	LD ₅₀ 25.0	45.0	1.79	
巴毒磷 crotoxyphos	乙酰胆碱酯酶 Acetylcholin esterase	IC ₅₀ (+) 0.0290	(-) >0.318	11.0	[41]
稻丰散 phenthoate	家蝇 <i>Musca domestica</i> L.	LD ₅₀ D: 0.0540	L: 0.0280	1.93	[42]
	蚊子 <i>Culicidae</i>	LD ₅₀ D: 0.0760	L: 0.0300	2.53	
	二化螟 <i>Chilo suppressalis</i>	LD ₅₀ D: 0.0220	L: 0.109	4.98	
	小菜蛾 <i>Plutella xylostella</i>	LD ₅₀ D: 37.0	L: 66.0	1.79	
烯虫酯 methoprene	烟草天蛾 <i>Manduca sexta</i>	S 体防效为 96%, R 体防效为 8% The control effect of S body was 96%, and that of R body was 8%			[43]

注: 表格中 (+) 代表该化合物旋光性为右旋体, (-) 代表该化合物旋光性为左旋体。
Note: In the table, (+) means that the optical activity of the compound is dextro isomer, and (-) means that the optical activity of the compound is laevo isomer.

1.2 手性杀菌剂生物活性立体选择性

我国已登记使用的杀菌剂中手性杀菌剂约有 60 种, 表 2 中列举了部分手性杀菌剂对映体选择性生物活性的差异情况。目前以光学纯单体登记的手性杀菌剂仅有精甲霜灵和精苯霜灵, 均以 R 体为高效体进行销售和使用。部分杀菌剂对映体生物活性差异在 100 倍以上, 如丙硫菌唑、氯氟醚菌唑、灭菌唑、双炔酰菌胺和氟唑菌酰羟胺等, 其中 R-双炔酰菌胺的杀菌活性是 S 体的 232~592 倍^[7], 此类杀菌剂对映体中只有一个对映体具有杀菌活性, 另一对映体为低效体或无效体, 其高活性单体具有较大潜力开发为光学纯单体农药。此外, 噁唑菌酮对映体对不同靶标的生物活性差异较大, 如防治立枯丝核菌时, 其 R 体活性是 S 体的 178 倍, 而防治尖孢镰刀菌时其差异仅

为不到 4 倍, 但 R 体依旧为高效体^[44]。丙环唑具有两个手性中心, 两对对映体, Tang 等测定了丙环唑 4 个对映体分别对新月弯孢菌 *Curvularia lunata* 和果香地霉 *Colletotrichum musae* 的杀菌活性, 对于新月弯孢菌, 其活性顺序为 (2R,4S)-丙环唑 > (2S,4R)-丙环唑 > (2S,4S)-丙环唑 > (2R,4R)-丙环唑, 而对于果香地霉, 其活性顺序为 (2R,4S)-丙环唑 > (2R,4R)-丙环唑 > (2S,4S)-丙环唑 > (2S,4R)-丙环唑^[45]。

1.3 手性除草剂生物活性立体选择性

我国目前已登记的手性除草剂中约有 70 种具有手性结构, 且多具有一个手性中心^[62]。表 3 列举了部分手性除草剂对映体间的除草活性差异, 多数除草剂高效体为 R 体, 如芳氧苯氧丙酸类除草剂: 吡氟禾草灵、禾草灵、氟吡禾草灵、啶禾

表 2 手性杀菌剂对映体生物活性差异

Table 2 Differences in enantiomer bioactivity of chiral fungicides

农药名称 Pesticide name	靶标生物 Target organism	对映体 EC ₅₀ 值 Enantiomer EC ₅₀ value/(mg/L)		对映体差异倍数 Enantiomer difference multiple	参考文献 References
		R	S		
丙硫菌唑 prothioconazole	腐皮镰刀菌 <i>Fusarium solani</i>	1.24	314	250	[46]
	核盘菌 <i>Sclerotinia sclerotiorum</i>	0.65	23.4	33.3	
戊菌唑 penconazole	胶孢炭疽菌 <i>Colletotrichum gloeosporioides</i>	4.91	1.72	2.85	[47]
	尖孢镰刀菌 <i>Fusarium oxysporum</i>	4.52	2.36	1.92	
氯氟醚菌唑 mefentrifluconazole	核盘菌 <i>Sclerotinia sclerotiorum</i>	0.024 0	2.00	100	[48]
	尖孢镰刀菌 <i>Fusarium oxysporum</i>	0.035 0	11.6	333	
	葡萄孢菌 <i>Botrytis cinerea</i>	0.028 0	4.10	146	
抑霉唑 imazalil	番茄叶霉病菌 <i>Fulvia fulva</i>	0.544	0.099 0	5.49	[49]
	番茄早疫病菌 <i>Alternaria solani</i>	0.718	0.109	6.59	
	马铃薯晚疫病病菌 <i>Phytophthora infestans</i>	2.75	0.915	3.00	
灭菌唑 triticonazole	立枯丝核菌 <i>Rhizoctonia solani</i>	0.006	0.261 9	50.0	[50]
	轮枝镰孢菌 <i>Fusarium verticillioide</i>	0.033 5	2.78	83.0	
	葡萄孢菌 (草莓) <i>Botrytis cinerea</i> (strawberry)	0.119	1.38	11.6	
	禾谷镰刀菌 <i>Fusarium graminearum</i>	19.5	83.3	4.27	
噁唑菌酮 famoxadone	立枯丝核菌 <i>Rhizoctonia solani</i>	0.280	49.9	178	[44]
	尖孢镰刀菌 <i>Fusarium oxysporum</i>	8.78	31.3	3.56	
氟噻唑吡乙酮 oxathiapiprolin	辣椒疫霉菌 <i>Phytophthora capsici</i>	0.170	0.660	3.88	[51]
	黄瓜疫霉菌 <i>Phytophthora melonis</i>	0.450	1.12	2.49	
	荔枝霜疫霉菌 <i>Peronophythora litchi</i>	0.270	1.23	4.56	
双炔酰菌胺 mandipropamid	辣椒疫霉菌 <i>Phytophthora capsici</i>	8.98	0.017 0	528	[7]
	大豆疫霉菌 <i>Phytophthora sojae</i>	1.63	0.007	233	
	黄瓜疫霉菌 <i>Phytophthora melonis</i>	6.52	0.011	592	
氟唑菌酰胺 pydiflumetofen	核盘菌 <i>Sclerotinia sclerotiorum</i>	0.002 9	2.31	797	[52]
	禾谷镰刀菌 <i>Fusarium graminearum</i>	0.025	24.0	960	
粉唑醇 flutriafol	立枯丝核菌 <i>Rhizoctonia solani</i>	0.130	0.810	6.23	[53]
	番茄早疫病菌 <i>Alternaria solani</i>	0.650	3.69	5.68	
氟唑菌苯胺 penflufen	尖孢镰刀菌 <i>Fusarium oxysporum</i>	85.6	46.8	1.83	[54]
	串珠镰刀菌 <i>Fusarium moniliforme</i>	68.5	41.2	1.66	
苯酰胺 zoxamide	辣椒疫霉菌 <i>Phytophthora capsici</i>	0.120	4.14	34.5	[55]
	番茄早疫病菌 <i>Alternaria solani</i>	5.39	64.2	11.9	
	葡萄孢菌 <i>Botrytis cinerea</i>	0.126	17.6	140	
戊唑醇 tebuconazole	葡萄孢菌 <i>Botrytis cinerea</i>	9.10	0.208	43.7	[4]
溴菌腈 bromothalonil	立枯丝核菌 <i>Rhizoctonia solani</i>	4.44	2.92	1.52	[6]
	禾谷镰刀菌 <i>Fusarium graminearum</i>	6.65	5.83	1.14	
	葡萄孢菌 <i>Botrytis cinerea</i>	4.13	3.20	1.29	
氟醚唑 tetraconazole	谷丝核菌 <i>Rhizoctonia cerealis</i>	0.540	0.802	1.49	[56]
	小麦赤霉病菌 <i>Fusarium graminearum</i>	0.382	0.756	1.98	
戊菌唑 penconazole	链格孢菌 <i>Alternaria alternata</i>	1.40	0.780	1.79	[47]
	轮纹病菌 <i>Botryosphaeria berengeriana</i>	1.37	0.310	4.42	
	胶孢炭疽菌 <i>Colletotrichum gloeosporioides</i>	4.91	1.72	2.85	
	尖孢镰刀菌 <i>Fusarium oxysporum</i>	4.52	2.36	1.92	
氟醚唑 tetraconazole	小麦基腐病菌 <i>Pseudocercospora herpotrichoides</i>	0.250	2.00	8.00	[57]
	壳针孢菌 <i>Septoria nodorum</i>	0.100	0.400	4.00	
	白腐小核菌 <i>Sclerotium cepivorum</i>	0.150	1.90	12.7	

续表 2
Table 2 (Continued)

农药名称 Pesticide name	靶标生物 Target organism	对映体 EC ₅₀ 值 Enantiomer EC ₅₀ value/(mg/L)		对映体差异倍数 Enantiomer difference multiple	参考文献 References
		R	S		
腈菌唑 myclobutanil	镰刀菌 <i>Fusarium</i> spp.	(+) 0.425	(-) 0.578	1.36	[58]
甲霜灵 metalaxyl	掘氏疫霉菌 <i>Phytophthora drechsleri</i>	0.129	(<i>Rac</i>) 0.427	—	[59]
己唑醇 hexaconazole	枸杞炭疽病 <i>Colletotrichum gloeosporioides</i> Penz	(+) 3.17	(-) 0.287	11.0	[60]
	轮斑病菌 <i>Alternaria solani</i>	(+) 10.1	(-) 0.751	13.5	
	褐腐病菌 <i>Monilinia fructicola</i>	(+) 0.411	(-) 0.032	12.8	
烯唑醇 diniconazole	柑橘黑点病菌 <i>Diaporthe citri</i>	0.029	1.40	48.3	[61]
	赤霉病菌 <i>Gibberella fujikuroi</i>	0.460	24.0	52.2	
	玉蜀黍赤霉 <i>Gibberella zaeae</i>	0.420	42.0	100	

注: 表格中 (+) 代表该化合物旋光性为右旋体, (-) 代表该化合物旋光性为左旋体。
Note: In the table, (+) means that the optical activity of the compound is dextro isomer, and (-) means that the optical activity of the compound is laevo isomer.

灵、噁唑禾草灵。氰氟草酯、炔草酯和啶草酯等, *R* 体均为高活性单体^[62, 8]。由于除草剂用量较大, 且手性除草剂光学纯活性单体制备技术突飞猛进, 多种手性除草剂以单一活性单体投入商品化使用, 如精 2 甲 4 氯丙酸、精 2,4-滴丙酸、精禾草灵、精吡氟禾草灵、精喹禾灵、左旋氰氟草酯、炔草酯、精异丙甲草胺和氯氟草醚等^[8]。

笔者综合调研结果, 对上述手性农药对映体活性平均差异倍数进行分类统计, 结果如图 1 所示: 超过 50% 的手性农药生物活性差异在 10 倍以下, 对映体间活性差异不大; 而对映体生物活性超过 10 倍的手性农药占比约为 35.72%~42.86%, 此类农药对映体间活性差异较大, 其中茚虫威、fluxametamide、氟唑菌酰胺、双炔酰菌胺、氯氟醚菌唑、吡氟禾草灵和氟丁酰草胺等对映体间生物活性差异超过 100 倍, 此类手性农药其中一个对映体为低效体或无效体, 具有较大潜力开发手性光学纯单体农药。

多数研究证明手性农药对映体间具有选择性生物活性的主要原因是手性农药对映体与靶标位点结合的差异。分子对接是目前揭示手性农药对映体选择性生物活性的主要手段。例如, 水胺硫磷通过抑制乙酰胆碱酯酶 (acetylcholinesterase, AchE) 来发挥杀虫活性^[83], Kong 等通过同源建模和分子对接分析了水胺硫磷对映体与蝗虫 AchE 之间结合的亲和力, 表明 *S*-水胺硫磷与 AchE 的结合能量高于 *R*-水胺硫磷, 从而解释了 *S*-水胺硫磷对蝗虫杀虫活性更高的原因^[17]。Tian 等模拟果蝇离子型 GABAR 亚基, 使用 *R/S*-丁虫脒进行分子对接, 结果显示, *R*-丁虫脒能更好地阻断 GABAR

中氯离子的通过, 进而使其具有更好的杀虫活性^[18]。苯酰菌胺对映体与病原菌靶标结合位点进行同源建模和分子对接后发现, *R/S*-苯酰菌胺和靶标位点特定受体间范德华力 (van der Waals force) 的差异是导致对映体发挥不同杀菌活性的主要原因, 同样也是 fluxametamide 对映体对小菜蛾产生对映选择性生物活性的主要原因^[7, 26]。尽管手性农药对映体之间拥有极其相似的物化性质, 但进入靶标生物体后, 与氨基酸、蛋白质等手性生物大分子发生对映体选择性结合, 进而产生选择性生物活性。朱欣凯通过体外测定水胺硫磷对映体对东亚飞蝗 *Locusta migratoria* AchE 的活性发现, *S*-水胺硫磷对 AchE 的抑制活性是 *R*-水胺硫磷的 10 倍, 与吡唑硫磷对 AchE 的抑制结果相似^[84], 并且 *S*-水胺硫磷可抑制羧酸脂酶 (carboxylic acid lipase, CarE) 的活性, 而 CarE 作为一种解毒酶, 可缓解杀虫剂分子对其的毒性^[85]。因此, 生物体内解毒酶对手性农药对映体的特异性识别可能也是造成对映体选择性生物活性的原因之一。解析手性农药对映体对靶标生物产生选择性生物活性的机制可为提高手性农药对靶标生物的防效提供新的见解与思路, 也可为新型高效光学纯单体农药的研发提供理论依据。

2 手性农药对非靶标生物的毒性效应立体选择性

近年来大力倡导化学农药“减施增效”, 农药的环境毒理问题受到越来越多研究人员的关注。手性农药进入非靶标生物体后, 其对映体会与氨基酸、蛋白质等生物大分子发生特异性结合, 进

表 3 手性除草剂对映体生物活性

Table 3 Enantioselective bioactivities of chiral herbicides

农药名称 Pesticide name	受试生物 Test organism	对映体生物活性差异 Difference in enantiomer biological activity	参考文献 References
2,4-滴丙酸 dichlorprop- <i>p</i>	藜草 <i>Chenopodium album</i> L. 野生堇菜 <i>Viola arvensis</i>	<i>R</i> 体具有更高除草活性 The <i>R</i> body has higher weed control activity	[63]
2甲4氯丙酸 mecoprop- <i>p</i>	拟南芥 <i>Arabidopsis thaliana</i>	<i>R</i> 体表现出更高的除草活性 The <i>R</i> body has higher weed control activity	[64]
氟吡甲禾灵 haloxyfop	禾本科杂草 Grassy weed	<i>R</i> 体防效是 <i>S</i> 体的 6 倍 The efficacy of <i>R</i> body was 6 times that of <i>S</i> body	[65]
草铵膦 glufosinate	玉米 <i>Zea mays</i> L. 小麦 <i>Triticum aestivum</i> L.	右旋体活性是左旋体的 2.7 倍 The activity of the dextral body was 2.7 times that of the left-handed body	[66-67]
噁唑禾草灵 fenoxaprop-ethyl	野燕麦 <i>Avena fatua</i> L.	<i>R</i> 体高效 <i>R</i> body efficient	[68]
喹禾灵 quizalofop-ethyl	玉米 <i>Zea mays</i> L.	<i>R</i> 体高效 <i>R</i> body efficient	[69-70]
吡氟禾草灵 fusilade	禾本科杂草 Grassy weed	<i>R</i> 体除草活性是 <i>S</i> 体的 1000 倍 The herbicidal activity of <i>R</i> body was 1000 times that of <i>S</i> body	[8]
炔草酯 clodinafop-propargyl	野燕麦 <i>Avena fatua</i> L.	<i>R</i> 体高效 <i>R</i> body efficient	[8]
氰氟草酯 cyhalofop-butyl	马唐 <i>Digitaria sanguinalis</i> L. 稗草 <i>Echinochloa crusgalli</i> L. 狗尾草 <i>Setaria Viridis</i> L.	<i>R</i> 体可达 90% 以上防效 <i>R</i> body can reach more than 90% of the control effect	[8]
禾草灵 diclofop-methyl	燕麦 <i>Avena sativa</i> L.	<i>R</i> 体活性为 <i>S</i> 体的 10 倍 The activity of <i>R</i> bodies was 10 times that of <i>S</i> bodies	[71]
乳氟禾草灵 lactofen	稗草 <i>Echinochloa crusgalli</i> L.	<i>R</i> 体高效 <i>R</i> body efficient	[72]
唑酮草酯 carfentrazone-ethyl	玉米 <i>Zea mays</i> L.	<i>S</i> 体的活性是 <i>R</i> 体的 2 倍 <i>S</i> body are twice as active as <i>R</i> body	[73]
敌草胺 napropamide	苇状羊茅 <i>Festuca arundinacea</i> Schreb.	<i>R</i> 体活性是 <i>S</i> 体的 53 倍 <i>R</i> body were 53 times more active than <i>S</i> body	[74]
乙氧呋草黄 ethofumesate	小麦 <i>Triticum aestivum</i> L. 高粱 <i>Sorghum bicolor</i> L. 黄瓜 <i>Cucumis sativus</i> L.	右旋体活性是左旋体的 3.5 倍 The activity of the dextral body was 3.5 times that of the left-handed body	[75]
氟丁酰草胺 beflubutamid	水芹 <i>Lepidium sativum</i>	右消旋体无活性, 左消旋体 EC ₅₀ 值为 0.5 μmol/L Dextracemic was inactive and levoracemic EC ₅₀ value was 0.5 μmol/L	[76]
异丙甲草胺 metolachlor	稗草 <i>Echinochloa crusgalli</i> L.	除草活性顺序依次为 <i>SS</i> > <i>SR</i> > <i>RS</i> > <i>RR</i> The weeding activity was in the following order: <i>SS</i> > <i>SR</i> > <i>RS</i> > <i>RR</i>	[77]
灭草烟 imazapyr	拟南芥 <i>Arabidopsis thaliana</i>	(+) 灭草烟对乙酰乳酸合成酶(ALS)的抑制效果是 (-) 的 4 倍 The inhibitory effect of (+) imazapyr on acetolactate synthase (ALS) was four times that of (-)imazapyr	[78]
乳氟禾草灵 lactofen	稗草 <i>Echinochloa crusgalli</i> L.	<i>R</i> 体对根抑制率 78.35%, <i>S</i> 体 56.58% The root inhibition rates of <i>R</i> body and <i>S</i> body were 78.35% and 56.58% respectively	[72]
丙酰胺 propionamide	马唐 <i>Digitaria sanguinalis</i> L.	<i>D</i> 体 EC ₅₀ 值为 0.33 mg/L, <i>L</i> 体 EC ₅₀ 值为 2.86 mg/L <i>D</i> body EC ₅₀ value was 0.33 mg/L, <i>L</i> body EC ₅₀ value was 2.86 mg/L	[79]
咪唑乙烟酸 imazethapyr	玉米 <i>Zea mays</i> L.	<i>R</i> 体活性是 <i>S</i> 体的 25 倍 <i>R</i> body was 25 times more active than <i>S</i> body	[80]
甲氧咪草烟 imazamox	玉米 <i>Zea mays</i> L.	<i>R</i> 体 EC ₅₀ 值为 0.229 mg/L, <i>S</i> 体 EC ₅₀ 值为 1.54 mg/L <i>R</i> body EC ₅₀ value was 0.229 mg/L, <i>S</i> body EC ₅₀ value was 1.54 mg/L	[81]
乙草胺 acetochlor	稗草 <i>Echinochloa crusgalli</i> L.	<i>R</i> 体活性约是 <i>S</i> 体的 1.64 倍 The activity of <i>R</i> bodies was about 1.64 times that of <i>S</i> bodies	[82]

注: 表格中 (+) 代表该化合物旋光性为右旋体, (-) 代表该化合物旋光性为左旋体。

Note: In the table, (+) means that the optical activity of the compound is dextro isomer, and (-) means that the optical activity of the compound is laevo isomer.

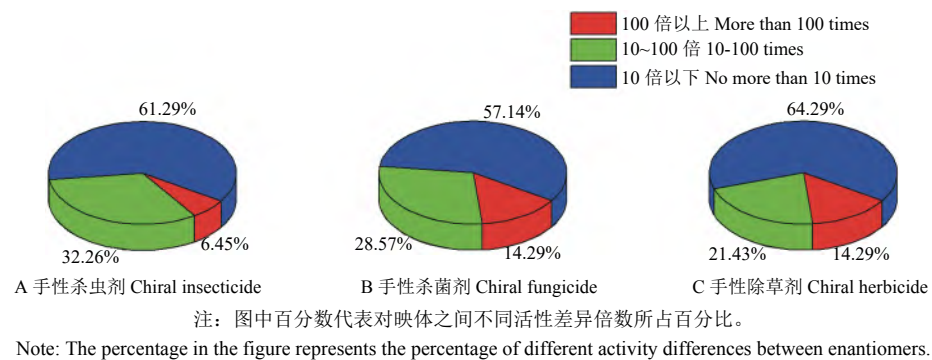


图 1 手性农药对映体生物活性差异倍数分布

Fig. 1 Differential fold distribution of enantiomeric bioactivity of chiral pesticides

而对非靶标生物造成对映体毒性差异^[86]。目前越来越多的研究证明，手性农药对映体对于非靶标生物产生的毒性效应是多方面的，主要包括急性毒性、氧化应激和内分泌干扰等。

2.1 手性农药的急性毒性效应

目前，手性农药对非靶标生物的急性毒性效应的研究主要集中在一些环境模式生物，水生生物如斑马鱼 *D. rerio*、小球藻 *C. vulgaris*、浮萍 *Lemna minor* L.和大型溞 *Daphnia magna* S.等，土壤生物如赤子爱胜蚓 *Eisenia foetida* 等，以及昆虫(如蜜蜂 *Apis mellifera* L.)等。表 4 列举了部分手性农药对于非靶标生物的选择性毒性效应。部分手性农药对靶标生物具有高活性的对映体对于非靶标生物同样具有相对更高的毒性，如水胺硫磷和呋虫胺等，其 *S* 体对靶标生物表现为高活性，对非靶标生物也表现出较高的毒性。部分手性农药对映

体对靶标生物高活性，而对于非靶标生物却具有相对更低的毒性，如氟唑菌酰胺、仲丁威、灭菌唑等，此类农药有较大的潜力开发为环境友好型光学纯单体农药；部分手性农药对映体对于非靶标生物毒性差异不大(5 倍以内)，如氟虫腈、烯效唑、敌草胺、苯霜灵、乙虫腈、戊唑醇、吡唑磷等；而诸如氟噻唑酰胺、灭菌唑、乳氟禾草灵、噁唑菌酮和七氟菊酯等手性农药对部分非靶标生物所表现出的对映体间的毒性差异则在 20 倍以上，其中噁唑菌酮对映体对斑马鱼和赤子爱胜蚓的对映体间急性毒性差异倍数分别为 95 和 167 倍。从对映体的水平探究手性农药对映体间的环境行为和毒性毒理，了解手性农药对映体对环境生物的风险对于研发环境友好型光学纯单体农药至关重要。

表 4 部分手性农药对非靶标生物对映体选择性急性毒性

Table 4 Enantioselective acute toxicity of some chiral pesticides on nontarget organisms

农药名称 Pesticide name	受试生物 Test organism	对映体毒性数据 Enantiomer toxicity data/(mg/L)		对映体毒性差异倍数 Enantiomer toxicity differential multiple	参考文献 References
		R	S		
氟唑菌酰胺 pydiflumetofen	斑马鱼胚胎 Zebrafish embryos	LC ₅₀ 0.34	3.63	10.7	[10]
	斑马鱼幼鱼 Zebrafish larvae	LC ₅₀ 0.47	6.92	14.7	
	斑马鱼 <i>D. rerio</i>	LC ₅₀ 0.72	8.23	11.4	
噁唑菌吡乙酮 oxathiapiprolin	蛋白核小球藻 <i>Chlorella pyrenoidosa</i>	EC ₅₀ 2.04	4.27	2.09	[87]
	紫萍 <i>Spirodela polyrrhiza</i> L.	EC ₅₀ 5.49	9.66	1.76	
	斑马鱼胚胎 Zebrafish embryos	LC ₅₀ 6.27	10.3	1.64	
	斑马鱼幼鱼 Zebrafish larvae	LC ₅₀ 6.51	12.5	1.93	
	斑马鱼 <i>D. rerio</i>	LC ₅₀ 7.13	15.1	2.11	
	小球藻 <i>Chlorella vulgaris</i>	EC ₅₀ 27.48	20.9	1.32	
仲丁威 fenobucarb	Hepg2细胞 Hepg2 cell	EC ₅₀ 399.16	231	1.73	[24]
	斑马鱼胚胎 Zebrafish embryos	LC ₅₀ 12.22	8.87	1.38	
	斑马鱼 <i>D. rerio</i>	LC ₅₀ 14.95	5.00	2.99	

续表 4
Table 4 (Continued)

农药名称 Pesticide name	受试生物 Test organism	对映体毒性数据 Enantiomer toxicity data/(mg/L)		对映体毒性差异倍数 Enantiomer toxicity differential multiple	参考文献 References
		R	S		
氟虫腈 fipronil	四尾栅藻 <i>Scenedesmus quadricauda</i>	EC ₅₀ 3.27	7.24	2.21	[11, 88]
	小球藻 <i>Chlorella vulgaris</i>	EC ₅₀ 4.58	5.99	1.31	
	蜜蜂 <i>Apis mellifera</i> L.	LC ₅₀ 3.45	3.38	1.02	
	浮萍 <i>Lemna minor</i> L.	EC ₅₀ 8.51	10.1	1.19	
	背角无齿蚌 <i>Anodonta woodiana</i>	LC ₅₀ 3.27	0.63	5.19	
	赤子爱胜蚓 <i>Eisenia foetida</i>	LC ₅₀ 29 µg/cm ²	50 µg/cm ²	1.72	
氟环唑 epoxiconazole	小球藻 <i>Chlorella vulgaris</i>	EC ₅₀ (R,S) 19.24	(S,R) 15.4	1.24	[86]
氟噁唑酰胺 fluxametamide	蜜蜂 <i>Apis mellifera</i> L.	LC ₅₀ >200	6.47	30.9	[26]
氯氟醚菌唑 mefentrifluconazole	斑马鱼胚胎 Zebrafish embryos	LC ₅₀ 0.753	1.55	2.06	[89]
	斑马鱼幼鱼 Zebrafish larvae	LC ₅₀ 0.553	1.19	2.15	
	赤子爱胜蚓 <i>Eisenia foetida</i>	LC ₅₀ 4.1 µg/cm ²	11.4 µg/cm ²	2.78	
双炔酰菌胺 mandipropamid	斑马鱼胚胎 Zebrafish embryos	LC ₅₀ 13.53	12.61	1.07	[7]
	斑马鱼幼鱼 Zebrafish larvae	LC ₅₀ 6.61	3.5	1.89	
	斑马鱼成鱼 <i>D. rerio</i>	LC ₅₀ 4.58	5.04	1.10	
	紫萍 <i>Spirodela polyrrhiza</i> L.	EC ₅₀ 5.18	14.86	2.87	
苯酰菌胺 zoxamide	羊角月牙藻 <i>Selenastrum carpicornutum</i>	EC ₅₀ 0.02	0.217	10.8	[55]
	大型溞 <i>Daphnia magna</i> S.	LC ₅₀ 0.246	1.19	5.48	
灭菌唑 triticonazole	浮萍 <i>Lemna minor</i> L.	EC ₅₀ 5.86	1.13	5.19	[90]
	大型溞 <i>Daphnia magna</i> S.	LC ₅₀ 1.43	0.061 1	23.4	
	斑马鱼 <i>Danio rerio</i>	LC ₅₀ 18.1	5.06	3.58	
	爪蟾蝌蚪 <i>Xenopus laevis</i>	LC ₅₀ >20.0	8.06	>2.48	
	赤子爱胜蚓 <i>Eisenia foetida</i>	LC ₅₀ 0.116 µg/cm ²	0.067 1 µg/cm ²	1.73	
	蛋白核小球藻 <i>Chlorella pyrenoidosa</i>	EC ₅₀ 0.853	22.002	25.8	
烯效唑 uniconazole	斑马鱼 <i>Danio rerio</i>	LC ₅₀ 10.03	11.63	1.16	[91]
敌草胺 napropamide	小球藻 <i>Chlorella vulgaris</i>	EC ₅₀ 9.72	8.74	1.11	[69]
乳氟禾草灵 lactofen	赤子爱胜蚓 <i>Eisenia foetida</i>	LC ₅₀ 0.378 µg/cm ²	17.7 µg/cm ²	46.8	[92]
噁唑菌酮 famoxadone	月牙藻 <i>Selenastrum bibraianum</i>	EC ₅₀ 0.222	0.394	1.77	[44, 93]
	大型溞 <i>Daphnia magna</i> S.	LC ₅₀ 0.043	0.276	6.42	
	斑马鱼 <i>Danio rerio</i>	LC ₅₀ 0.105	>10	>95.2	
	赤子爱胜蚓 <i>Eisenia foetida</i>	LC ₅₀ 0.3 µg/cm ²	50 µg/cm ²	167	
苯霜灵 benalaxyl	赤子爱胜蚓 <i>Eisenia foetida</i>	LC ₅₀ 4.99 µg/cm ²	6.66 µg/cm ²	1.33	[94]
水胺硫磷 isocarbophos	斑马鱼 <i>Danio rerio</i>	LC ₅₀ 38.6	1.58	24.4	[15]
	青鳉 <i>Oryzias latipes</i>	LC ₅₀ 37.2	1.62	23.0	
	鮡 <i>Gobiocypris rarus</i>	LC ₅₀ 31.1	1.29	24.1	
吡唑硫磷 pyraclofos	斑马鱼 <i>Danio rerio</i>	LC ₅₀ 2.23	3.99	1.79	[95]
甲氧咪草烟 imazamox	浮萍 <i>Lemna minor</i> L.	EC ₅₀ 0.035	0.203	5.8	[96]
乙虫腈 ethiprole	小球藻 <i>Chlorella vulgaris</i>	EC ₅₀ 7.5	8.07	1.076	[97]

续表 4					
Table 4 (Continued)					
农药名称 Pesticide name	受试生物 Test organism	对映体毒性数据 Enantiomer toxicity data/(mg/L)		对映体毒性差异倍数 Enantiomer toxicity differential multiple	参考文献 References
		R	S		
丁虫腈 flufiprole	蛋白核小球藻 <i>Chlorella pyrenoidosa</i>	EC ₅₀ 8.7	15.8	1.82	[98]
	泥鳅 <i>Misgurnus anguillicaudatus</i>	LC ₅₀ 0.13	0.16	1.23	
	银鲫 <i>Silver prussian carp</i>	LC ₅₀ 0.09	0.08	1.13	
	黑斑侧褶蛙 <i>Pelophylax nigromaculatus</i>	LC ₅₀ 1.07	1.56	1.46	
	大型溞 <i>Daphnia magna</i> S.	LC ₅₀ 0.74	0.83	1.12	
乙草胺 acetochlor	Hepg2细胞 Hepg2 cell	EC ₅₀ 68.81	49.14	1.40	[99]
	赤子爱胜蚓 <i>Eisenia foetida</i>	LC ₅₀ 12.28 μg/cm ²	23.32 μg/cm ²	1.90	
丙硫菌唑 prothioconazole	大型溞 <i>Daphnia magna</i> S.	LC ₅₀ 2.65	5.91	2.23	[100]
	小球藻 <i>Chlorella vulgaris</i>	EC ₅₀ 119.1	89.4	1.33	
	浮萍 <i>Lemna minor</i> L.	EC ₅₀ 0.53	0.49	1.08	
己唑醇 hexaconazole	赤子爱胜蚓 <i>Eisenia foetida</i>	LC ₅₀ 22.35 μg/cm ²	8.62 μg/cm ²	2.59	[101]
多效唑 paclobutrazol	小球藻 <i>Chlorella vulgaris</i>	EC ₅₀ 2.4	8.97	3.73	[102]
顺式联苯菊酯 cis-bifenthrin	非洲爪蟾蝌蚪 <i>Xenopus laevis</i>	LC ₅₀ 0.041	0.219	5.34	[103]
七氟菊酯 tefluthrin	赤子爱胜蚓 <i>Eisenia foetida</i>	LC ₅₀ 5.55 μg/cm ²	1 192.1 μg/cm ²	215	[104]
戊唑醇 tebuconazole	赤子爱胜蚓 <i>Eisenia foetida</i>	LC ₅₀ 10.48 μg/cm ²	10.84 μg/cm ²	1.03	[4]
戊菌唑 penconazole	大型溞 <i>Daphnia magna</i> S.	LC ₅₀ 5.96	0.91	6.55	[47]
吡丙醚 pyriproxyfen	蜜蜂 <i>Apis mellifera</i> L.	LC ₅₀ >100	26.32	>3.80	[22]
	斑马鱼 <i>Danio rerio</i>	LC ₅₀ 2.81	1.65	1.70	
溴菌腈 bromothalonil	赤子爱胜蚓 <i>Eisenia foetida</i>	LC ₅₀ 17.53 μg/cm ²	11.99 μg/cm ²	1.46	[6]
茚虫威 indoxacarb	斑马鱼胚胎 Zebrafish embryos	LC ₅₀ 8.67	11.3	1.30	[105]
呋虫胺 dinotefuran	赤子爱胜蚓 <i>Eisenia foetida</i>	LC ₅₀ 0.698 μg/cm ²	0.05 μg/cm ²	14.0	[106-107]
	蜜蜂 <i>Apis mellifera</i> L.	LC ₅₀ 6.42	0.28	22.9	
呋霜灵 furalaxyl	赤子爱胜蚓 <i>Eisenia foetida</i>	LC ₅₀ 1.9 μg/cm ²	1.0 μg/cm ²	1.90	[108]
	斜生栅藻 <i>Tetrademus obliquus</i>	EC ₅₀ 15.26	13.59	1.12	
唑酮草酯 carfentrazone-ethyl	斑马鱼 <i>Danio rerio</i>	LC ₅₀ 4.60	3.66	1.25	[109]
	大型溞 <i>Daphnia magna</i> S.	LC ₅₀ 15.24	16.27	1.07	
	羊角月芽藻 <i>Selenastrum carpicornutum</i>	EC ₅₀ 0.44	0.09	4.89	
	玉米 <i>Zea mays</i> L.	EC ₅₀ 3.93	1.94	2.03	

2.2 手性农药对非靶标生物氧化应激效应

当生物受胁迫时, 细胞内会积聚大量活性氧 (reactive oxygen species, ROS), 如 O₂⁻, 会破坏细胞分子结构并干扰生物正常的生理过程。生物体内具有多种复杂的酶和非酶抗氧化系统来抵御氧化胁迫^[110]。氧化应激是指氧化与抗氧化失衡的一种状态, 是造成细胞凋亡的重要因素, 因此常被用来作为评估外源污染物对环境模式生物安全性的重要指标^[111]。已经有大量文献表明农药会对非靶标

生物造成氧化应激效应^[112], 手性农药对映体对非靶标生物造成的氧化应激甚至氧化损伤也得到了广泛研究, 其中手性杀虫剂和杀菌剂的毒性效应研究多选用动物作为受试生物, 如 Li 等测试了三氯杀虫酯对映体对大鼠 PC12 细胞的毒性作用, 结果显示 *S*-三氯杀虫酯可显著诱导细胞产生 ROS, 并且降低了超氧化物歧化酶 (superoxide dismutase, SOD) 和过氧化氢酶 (catalase, CAT) 的活性, 使 ROS 难以清除, 造成了严重的氧化损伤, 具有细

胞毒性^[113]。相比于 *R*-呋虫胺, *S*-呋虫胺可诱导蚯蚓产生更强的氧化应激效应, 显著提高了赤子爱胜蚓体内丙二醛 (malondialdehyde, MDA) 的含量以及严重的 DNA 损伤, 抑制了蚯蚓的生长和繁殖^[106], 且当环境中存在其他外源污染物时, 呋虫胺对映体对非靶标生物的氧化应激毒性也会受到影响。当与低剂量的镉共暴露时会加剧 *R*-呋虫胺对斑马鱼氧化应激毒性^[114]。手性杀菌剂己唑醇对赤子爱胜蚓表现出选择性毒性效应, 其中 *S*-己唑醇对赤子爱胜蚓的毒性高于 *R*-己唑醇, 并且诱导出对映体特异性氧化应激, *S*-己唑醇对 MDA、细胞色素 P450 和 8-羟基-2-脱氧鸟苷含量的影响大于 *R*-己唑醇^[101]。*S*-氟唑菌苯胺对斑马鱼毒性是 *R*-氟唑菌苯胺的 54 倍, 且诱导的氧化应激效应更为严重^[115]。Ren 等研究表明, 吡噻菌胺对斑马鱼具有选择性毒性效应, 其中 *S*-吡噻菌胺可引起斑马鱼肝脏产生氧化应激, 并且显著干扰了基因表达, 对斑马鱼表现出较高的毒性^[116]。此外, 除草剂与植物生长调节剂也可对实验动物造成毒性效应, 如 *S*-乙草胺对蚯蚓的急性毒性是 *R*-乙草胺的 1.9 倍, 并且 *S*-乙草胺可显著提高羟基自由基 (hydroxyl radical, OH•) 含量以及 SOD、CAT、细胞色素 P450 的活性^[117]。氧化平衡被破坏后可对生物体产生诸多不利影响, 如 *R*-多效唑对斑马鱼造成的氧化应激比 *S*-多效唑强, 并且过量的 ROS 会进攻细胞膜, 进而干扰斑马鱼 AchE 的活性, 对斑马鱼造成神经毒性^[118]。暴露于 *R*-烯效唑的斑马鱼氧化应激指标的变化是 *S*-烯效唑的 1.27~1.53 倍, 表明 *R*-烯效唑会导致更显著的不良反应^[91]。

手性农药对植物造成的毒性效应研究多集中于除草剂和植物生长调节剂, 如小球藻对于维持水生生态系统稳态十分重要, Liu 等研究了多效唑对映体对小球藻的毒性, 结果表明多效唑可显著诱导小球藻产生氧化应激效应, *R*-多效唑对小球藻细胞结构的破坏作用要强于 *S*-多效唑, 严重抑制了小球藻生长激素的含量, 抑制其生长^[102]。手性农药对陆生植物具有同样的选择性毒性效应, 如 *S*-异丙甲草胺处理后, 小麦植株内 O₂ 含量和 MDA 含量要显著高于空白处理, 其产生的氧化应激效应要强于 *Rac*-异丙甲草胺, 且抑制小麦植株生长^[119]。*R*-咪唑乙烟酸显著增加了小麦植株中 ROS 含量, 干扰了 Fe²⁺ 的释放, 并且 *R*-咪唑乙烟酸可破坏小麦细胞结构, 干扰光合作用, 造成植

物细胞毒性^[120]。手性农药灭菌唑, *R* 体杀菌活性是 *S* 体的 100 倍, 但 *S*-灭菌唑可对小麦幼苗造成氧化损伤, 抑制小麦幼苗生长, 并且干扰了赤霉素和乙烯的合成^[121]。

2.3 手性农药对非靶标生物的内分泌干扰效应

近年来, 一些研究发现某些农药具有内分泌干扰毒性, 干扰生物正常的激素分泌并导致非靶标生物生理功能紊乱。手性农药对于生物内分泌干扰具有选择性毒性效应。基于报告基因分析方法, 能快速通过体外试验的方法, 筛选出农药对映体中具有潜在内分泌干扰作用的单体^[122-123]。顺式联苯菊酯对映体对 H295R 细胞肾上腺皮质激素分泌的选择性干扰效应研究表明, *S*-顺式联苯菊酯和 *R*-顺式联苯菊酯均不同程度地抑制 H295R 细胞肾上腺皮质激素的分泌, 且 *S*-顺式联苯菊酯抑制效应更强^[124]。Hu 等利用体外实验和计算机模拟考察苯基吡唑类杀虫剂氟虫腈、乙虫腈、丁虫腈对映体对牛血清的干扰效应, 结果表明 *S*-乙虫腈和 *S*-丁虫腈可诱导甲状腺功能紊乱, 而 *R*-氟虫腈、*R*-乙虫腈和 *R*-丁虫腈可诱导雌激素分泌异常, 产生这种毒性差异的原因之一是对映体与受体结合亲和力存在差异^[125]。叶菌唑对映体对斑马鱼的甲状腺干扰同样存在选择性效应, (1*R*,5*S*)-叶菌唑对斑马鱼的甲状腺破坏能力强于其它对映体, 利用计算机模拟证明 (1*R*,5*S*)-叶菌唑与甲状腺激素受体之间的结合能力比其他对映体更强^[126]。乙草胺对映体对斑马鱼甲状腺激素干扰实验表明 *S*-乙草胺对甲状腺激素受体和促甲状腺激素基因表达表现出显著促进作用, 相比于 *R*-乙草胺, *S*-乙草胺对斑马鱼甲状腺有更强的破坏效应^[127]。氯氰菊酯 4 个对映体对 H295R 细胞的干扰实验表明, 1*R*-*cis*- α *S*-氯氰菊酯可抑制糖皮质激素受体、盐皮质激素受体和甲状腺受体活性, 1*R*-*trans*- α *S*-氯氰菊酯可抑制雄激素受体和雌激素受体活性, 其余 2 个对映体也可造成类固醇激素相关基因的表达和激素分泌, 表明氯氰菊酯对映体分别可通过不同的通路造成内分泌紊乱^[122]。

随着研究的深入, 越来越多的证据表明农药对非靶标生物存在多方面的干扰效应, 其中对性腺的影响也是近年来的研究热点。Chang 等研究了高效氯氟氰菊酯对映体对丽斑麻蜥 *Eremias argus* 性腺的影响, 结果表明, (+)-高效氯氟氰菊酯处理使得生精小管直径增加, 且性腺的发育基因的相

对表达量显著高于(-)-高效氯氟氰菊酯暴露组^[128]。丽斑麻蜴 *Eremias argus* 经口暴露腈菌唑对映体 28 d, *S*-腈菌唑降低了蜥蜴体重, 且雌二醇 (E2) 含量降低, 并且干扰了性腺发育相关基因的表达, 证明 *S*-腈菌唑对蜥蜴性腺系统发育可能具有干扰效应^[129]。异丙甲草胺对斑马鱼性腺的干扰研究表明 *S*-异丙甲草胺可干扰斑马鱼性腺发育相关基因: *fsh β* 、*cyp17*、*17 β hsd* 和 *cyp19a* 的表达, 导致雌性斑马鱼 E2 含量水平增加, 并且异丙甲草胺和 *S*-异丙甲草胺对斑马鱼内分泌干扰作用的机制不同, 具有生殖毒性^[130]。

2.4 组学分析在手性农药研究中的作用

组学分析技术迅速发展, 为多学科交叉研究提供了更多的可能。目前农药环境毒理学领域有大量研究使用代谢组、转录组、蛋白组等手段深度挖掘农药对环境生物的安全性影响。在手性农药环境毒理学方面, 也有研究借助该方法深层次剖析手性农药对非靶标生物的影响以及产生选择性毒性效应的机制。Zhang 等利用代谢组学研究甲霜灵对映体对乳腺癌细胞的影响, 发现其对映体可通过不同的通路来干扰细胞稳态, 包括能量代谢、氨基酸代谢、脂质代谢和抗氧化防御等^[131]。*S*-甲霜灵为低效体, 但 *S*-甲霜灵饲喂大鼠后检测大鼠尿液代谢谱发现, *S*-甲霜灵可干扰大鼠糖酵解、缬氨酸、亮氨酸和异亮氨酸的代谢水平, 且这些紊乱的代谢途径可能导致遗传疾病并影响肝功能^[131-133]。Qiu 等利用代谢组学研究了 2,4-滴丙酸对映体对拟南芥的影响, 发现其 *R* 体可干扰拟南芥乳糖代谢、淀粉和蔗糖代谢、三羧酸循环、脂肪酸生物合成途径和磷酸戊糖途径等^[134]。在莴苣上分别施用戊唑醇对映体后进行代谢组学分析, *R*-戊唑醇可导致可溶性糖、氨基酸和有机酸的含量下调, 进而影响莴苣的营养品质^[135]。

转录组测序技术同样在手性农药环境毒理学方面得到了很好的应用。通过转录组测序表明, *S*-呋虫胺与赤子爱胜蚓生物大分子的相互作用和对内质网的影响比 *R*-呋虫胺更强, 这可能是对映体之间产生选择性毒性的主要原因^[106]。当斑马鱼暴露于 *S*-呋虫胺时, 苯丙氨酸、酪氨酸和色氨酸的生物合成和视黄醇代谢受到显著干扰, 进而对斑马鱼的能量代谢产生影响; 而仅当暴露于高浓度的 *R*-呋虫胺时, 斑马鱼中与磷脂酰胆碱相关的代谢物才会产生变化, 表明 *S*-呋虫胺对非靶标生物斑马鱼的影响会更强^[136]。更多的组学研究显

示, 暴露于 *S*-呋虫胺会对蜜蜂的解毒相关代谢产生更严重的损害^[137]。结合呋虫胺对映体毒性的相关研究表明: *S*-呋虫胺的环境风险要显著强于 *R*-呋虫胺。

乙草胺对映体处理蚯蚓后, 发现其转录组水平出现对映体选择性差异, *R*-乙草胺可导致蚯蚓部分信号通路功能障碍以及细胞凋亡, 这可能是造成其毒性强于 *S*-乙草胺的原因^[117]。蚯蚓暴露于双炔酰菌胺对映体后, *S*-双炔酰菌胺诱导了更多的差异表达基因, 主要集中于胆汁分泌和甲状腺激素信号通路, 并且其对蚯蚓的毒性要比 *R*-双炔酰菌胺更强^[138]。氯氟醚菌唑可引起斑马鱼对映体选择性的肝毒性, 该效应可能主要与能量代谢、脂质代谢和氨基酸代谢有关^[139]。顺式联苯菊酯对斑马鱼的选择性毒性研究表明, 1*S* 顺式联苯菊酯的毒理学效应大于 1*R*-顺式联苯菊酯, 其中包括生长抑制、神经毒性、脂肪酸合成以及胚胎发育^[140]。Li 等利用转录组学揭示了甲氧咪草烟对映体对浮萍产生对映体选择性毒性的机制, 其中 *R*-甲氧咪草烟干扰了浮萍光合途径、谷胱甘肽代谢途径、戊糖磷酸途径、玉米素生物合成以及卟啉和叶绿素代谢途径中的基因表达, *S*-甲氧咪草烟影响苯丙氨酸代谢、苯丙烷生物合成、玉米素生物合成和次级代谢产物生物合成等通路的基因表达^[96]。

利用组学测序技术可获取大量关于手性农药对映体对非靶标生物的毒理学信息, 该手段可用来深层次解析手性农药对非靶标生物产生选择性效应的原因和机制, 进而发现更多的毒理学数据, 方便更加精准地评估手性农药对映体的毒理学效应以及健康风险, 显示出交叉学科的研究优势, 随着多组学技术的发展以及组学分析成本的降低, 手性农药环境毒理学评估有望得到进一步研究。

3 小结与展望

目前, 手性农药对映体对靶标生物活性差异的研究已经越来越广泛, 多数手性农药对映体之间存在选择性生物活性, 部分对映体活性差异高达 500 倍以上^[5, 121], 这可为手性农药单体的研发提供数据, 但由于光学纯单体制备的成本以及技术等原因, 有大量手性农药的对映体活性差异未见报道; 现阶段关于对映体活性差异机制的研究多采用计算化学辅助的分子对接模型, 并且关于手性农药对靶标生物活性差异机制的研究仍然缺乏。

手性农药对非靶标生物的选择性毒性问题目前越来越精细化,可利用手段越来越多,如组学分析、计算机模拟等。现阶段关于手性农药环境毒理学研究多集中于环境模式生物,如斑马鱼、蚯蚓、大型溞、藻类等。手性农药对映体对人体安全性评估数据仍然不足,由于大鼠、小鼠等人体基因型相似的实验动物成本相对较高,试验周期相对较长,且试验所需要的手性农药单体的制备成本高,用量较大,因而只有少数研究进行了手性农药对映体对大鼠的健康风险评估^[113,132,141]。现阶段对手性农药对映体食品安全相关标准的制定仍缺乏对映体水平的毒性数据,完善手性农药对人体的健康风险评估可更加精准的控制手性农药对映体的食品安全风险以及对人体的毒性效应。

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参考文献 (References):

- [1] KATAGI T. Isomerization of chiral pesticides in the environment[J]. *J Pestic Sci*, 2012, 37(1): 1-14.
- [2] YE J, ZHAO M R, LIU J, et al. Enantioselectivity in environmental risk assessment of modern chiral pesticides[J]. *Environ Pollut*, 2010, 158(7): 2371-2383.
- [3] ARMSTRONG D W, REID G L III, HILTON M L, et al. Relevance of enantiomeric separations in environmental science[J]. *Environ Pollut*, 1993, 79(1): 51-58.
- [4] CUI N, XU H Y, YAO S J, et al. Chiral triazole fungicide tebuconazole: enantioselective bioaccumulation, bioactivity, acute toxicity, and dissipation in soils[J]. *Environ Sci Pollut Res*, 2018, 25(25): 25468-25475.
- [5] XU S J, SHEN F, SONG J L, et al. Enantioselectivity of new chiral triazole fungicide mefenfentriazole: bioactivity against phytopathogen, and acute toxicity and bioaccumulation in earthworm (*Eisenia fetida*)[J]. *Sci Total Environ*, 2022, 815: 152937.
- [6] LIANG X Y, XU J B, HUANG X Z, et al. Systemic stereoselectivity study of bromethalonil: stereoselective bioactivity, toxicity, and degradation in vegetables and soil[J]. *Pest Manag Sci*, 2020, 76(5): 1823-1830.
- [7] ZHANG J, WU Q Q, ZHONG Y R, et al. Enantioselective bioactivity, toxicity, and degradation in vegetables and soil of chiral fungicide mandipropamid[J]. *J Agric Food Chem*, 2021, 69(45): 13416-13424.
- [8] 周青燕, 章程, 柴如山, 等. 手性除草剂研究进展[J]. *农药学学报*, 2010, 12(2): 109-118.
- [9] ZHOU Q Y, ZHANG C, CHAI R S, et al. Progress of research on chiral herbicides[J]. *Chin J Pestic Sci*, 2010, 12(2): 109-118.
- [10] WANG C, ZHANG Q, ZHAO M R, et al. Enantioselectivity in estrogenic potential of chiral pesticides[M]//ACS Symposium Series. Washington, DC: American Chemical Society, 2011: 121-134.
- [11] WANG Z, TAN Y T, LI Y H, et al. Comprehensive study of pydiflumetofen in *Danio rerio*: enantioselective insight into the toxic mechanism and fate[J]. *Environ Int*, 2022, 167: 107406.
- [12] QU H, WANG P, MA R X, et al. Enantioselective toxicity, bioaccumulation and degradation of the chiral insecticide fipronil in earthworms (*Eisenia fetida*)[J]. *Sci Total Environ*, 2014, 485-486: 415-420.
- [13] CHENG C, DI S S, CHEN L, et al. Enantioselective bioaccumulation, tissue distribution, and toxic effects of myclobutanil enantiomers in *Pelophylax nigromaculatus* tadpole[J]. *J Agric Food Chem*, 2017, 65(15): 3096-3102.
- [14] WANG X, LIU Y R, XUE M Y, et al. Enantioselective degradation of chiral fungicides triticonazole and prothioconazole in soils and their enantioselective accumulation in earthworms *Eisenia fetida*[J]. *Ecotoxicol Environ Saf*, 2019, 183: 109491.
- [15] TOMBO G M R, BELLUS D. Chirality and crop protection[J]. *Angew Chem Int Ed Engl*, 1991, 30(10): 1193-1215.
- [16] DI S S, CANG T, QI P P, et al. A systemic study of enantioselectivity of isocarboxophos in rice cultivation: enantioselective bioactivity, toxicity, and environmental fate[J]. *J Hazard Mater*, 2019, 375: 305-311.
- [17] DI S S, CANG T, QI P P, et al. Comprehensive study of isocarboxophos to various terrestrial organisms: enantioselective bioactivity, acute toxicity, and environmental behaviors[J]. *J Agric Food Chem*, 2019, 67(40): 10997-11004.
- [18] KONG Y, JI C Y, QU J L, et al. Old pesticide, new use: smart and

- safe enantiomer of isocarbophos in locust control[J]. *Ecotoxicol Environ Saf*, 2021, 225: 112710.
- [18] UMEDA K, YANO T, HIRANO M. Esfenvalerate: its biological activity against German cockroach, *Blattella germanica* (Orthoptera: Blattellidae)[J]. *Jap J Sanit Zool*, 1990, 41(4): 347-351.
- [19] 张青. 手性杀虫剂乙虫腈立体选择性降解、活性、毒性和生态毒理效应研究[D]. 南京: 南京农业大学, 2017
- ZHANG Q. Study on the stereoselectivity degradation, bioactivity, toxicology and ecotoxicology assessment for chiral insecticide ethiprole[D]. Nanjing: Nanjing Agricultural University, 2017.
- [20] TIAN M M, ZHANG Q, HUA X D, et al. Systemic stereoselectivity study of flufiprole: stereoselective bioactivity, acute toxicity and environmental fate[J]. *J Hazard Mater*, 2016, 320: 487-494.
- [21] 于琦童. 茚虫威不同异构体对小菜蛾和中华通草蛉的选择毒力及亚致死效应[D]. 泰安: 山东农业大学, 2021
- YU Q T. Selective toxicity and sublethal effect of different indoxacarb isomers against *Plutella xylostella* and *Chrysoperla sinica*[D]. Taian: Shandong Agricultural University, 2021.
- [22] TONG Z, YANG T M, SUN M N, et al. Systemic assessment of the chiral insecticide pyriproxyfen in a citrus nectar source system: stereoselective degradation, biological effect and exposure risk[J]. *Pest Manag Sci*, 2022, 78(7): 3012-3018.
- [23] ZHANG Z X, ZHOU L L, GAO Y Y, et al. Enantioselective detection, bioactivity, and metabolism of the novel chiral insecticide fluralaner[J]. *J Agric Food Chem*, 2020, 68(25): 6802-6810.
- [24] HE Z Z, LI C L, XIA W T, et al. Comprehensive enantioselectivity evaluation of insecticidal activity and mammalian toxicity of fenobucarb[J]. *J Agric Food Chem*, 2022, 70(17): 5330-5338.
- [25] GAO B B, ZHANG Z X, LI L S, et al. Stereoselective environmental behavior and biological effect of the chiral organophosphorus insecticide isofenphos-methyl[J]. *Sci Total Environ*, 2019, 648: 703-710.
- [26] LI R N, PAN X L, WANG Q Q, et al. Development of *S*-fluxametamide for bioactivity improvement and risk reduction: systemic evaluation of the novel insecticide fluxametamide at the enantiomeric level[J]. *Environ Sci Technol*, 2019, 53(23): 13657-13665.
- [27] CHEN Z L, YAO X M, DONG F S, et al. Ecological toxicity reduction of dinotefuran to honeybee: new perspective from an enantiomeric level[J]. *Environ Int*, 2019, 130: 104854.
- [28] 温勇. 手性杀虫剂七氟菊酯对映体环境行为和生物效应研究[D]. 南京: 南京农业大学, 2020
- WEN Y. Studies on enantioselective environmental behaviours and biological effect of chiral insecticide tefluthrin[D]. Nanjing: Nanjing Agricultural University, 2020.
- [29] 张聪, 刘慧刚, 章晓凤. 联苯菊酯对靶标生物及非靶标生物毒性的对映体差异[J]. *浙江工业大学学报*, 2009, 37(4): 366-371.
- ZHANG C, LIU H G, ZHANG X F. Enantioselective toxicity induced by bifenthrin between target organism and non-target organism[J]. *J Zhejiang Univ Technol*, 2009, 37(4): 366-371.
- [30] 常维霞. 手性农药乙螨唑对映体的果园环境行为及毒性研究[D]. 北京: 中国农业科学院, 2020.
- CHANG W X. Study of etoxazole stereoselective environmental behavior in orchard and toxicology effect[D]. Beijing: Chinese Academy of Agricultural Sciences, 2020.
- [31] 赵琳, 包琛, 杨代斌, 等. 氟虫腈对斑马鱼和小菜蛾毒性的手性选择性研究[J]. *环境科学学报*, 2010, 30(7): 1451-1456.
- ZHAO L, BAO C, YANG D B, et al. Acute toxicities of fipronil enantiomers to zebrafish and diamondback moth[J]. *Acta Sci Circumstantiae*, 2010, 30(7): 1451-1456.
- [32] TEICHER H B, KOFOED-HANSEN B, JACOBSEN N. Insecticidal activity of the enantiomers of fipronil[J]. *Pest Manag Sci*, 2003, 59(12): 1273-1275.
- [33] OHKAWA H, MIKAMI N, OKUNO Y, et al. Stereospecificity in toxicity of the optical isomers of EPN[J]. *Bull Environ Contam Toxicol*, 1977, 18(5): 534-540.
- [34] HIRASHIMA A, ISHAYAYA I, UENO R, et al. Biological activity of optically active salithion and salioxon[J]. *Agric Biol Chem*, 1989, 53(1): 175-178.
- [35] LEADER H, CASIDA J E. Resolution and biological activity of the chiral isomers of *O*-(4-bromo-2-chlorophenyl) *O*-ethyl *S*-propyl phosphorothioate (profenofos insecticide)[J]. *J Agric Food Chem*, 1982, 30(3): 546-551.
- [36] PAP L, KELEMEN M, TÓTH A, et al. The synthetic pyrethroid isomers II. Biological activity[J]. *J Environ Sci Health B*, 1996, 31(3): 527-543.
- [37] NOMEIR A A, DAUTERMAN W C. Studies on the optical isomers of EPN and EPNO[J]. *Pestic Biochem Physiol*, 1979, 10(2): 121-127.
- [38] OHKAWA H, MIKAMI N, MIYAMOTO J. Metabolism of the optical isomers of cyanofenphos in rice stem borer larvae[J]. *Agric Biol Chem*, 1978, 42(2): 445-450.
- [39] MIYAZAKI A, NAKAMURA T, KAWARADANI M, et al. Resolution and biological activity of both enantiomers of methamidophos and acephate[J]. *J Agric Food Chem*, 1988, 36(4): 835-837.
- [40] WANG Y S, TAI K T, YEN J H. Separation, bioactivity, and dissipation of enantiomers of the organophosphorus insecticide fenamiphos[J]. *Ecotoxicol Environ Saf*, 2004, 57(3): 346-353.
- [41] NILLOS M G, RODRIGUEZ-FUENTES G, GAN J, et al. Enantioselective acetylcholinesterase inhibition of the organophosphorous insecticides profenofos, fonofos, and crotoxyphos[J]. *Environ Toxicol Chem*, 2007, 26(9): 1949-1954.
- [42] 周润福. 有机磷旋光异构体与生物活性的关系[J]. *农药*, 1983, 22(3): 41-44.
- ZHOU R F. Relationship between optical isomers of organophosphorus and biological activity[J]. *Agrochemicals*, 1983, 22(3): 41-44.
- [43] FURUTA K, ASHIBE K, SHIRAHASHI H, et al. Synthesis and anti-juvenile hormone activity of ethyl 4-(2-benzylalkyloxy)benzoates and their enantiomers[J]. *J Pestic Sci*, 2007, 32(2): 99-105.
- [44] WANG M, JI Z R, XU J B, et al. Study on stereoselective bioactivity, acute toxicity, and degradation in cucurbits and soil of chiral fungicide famoxadone[J]. *Environ Sci Pollut Res Int*, 2021, 28(13): 15947-15953.
- [45] TANG S Y, MENG X R, WANG F, et al. Four propiconazole stereoisomers: stereoselective bioactivity, separation via liquid chromatography-tandem mass spectrometry, and dissipation in banana leaves[J]. *J Agric Food Chem*, 2022, 70(3): 877-886.
- [46] ZHANG Z X, GAO B B, HE Z Z, et al. Stereoselective bioactivity of the chiral triazole fungicide prothioconazole and its metabolite[J]. *Pestic Biochem Physiol*, 2019, 160: 112-118.
- [47] LI Y, NIE J Y, ZHANG J, et al. Chiral fungicide penconazole: absolute configuration, bioactivity, toxicity, and stereoselective degradation in apples[J]. *Sci Total Environ*, 2022, 808: 152061.
- [48] LI L S, SUN X F, ZHAO X J, et al. Absolute configuration,

- enantioselective bioactivity, and degradation of the novel chiral triazole fungicide mefenftrifluconazole[J]. *J Agric Food Chem*, 2021, 69(17): 4960-4967.
- [49] LI R N, PAN X L, TAO Y, et al. Systematic evaluation of chiral fungicide imazalil and its major metabolite R14821 (imazalil-M): stability of enantiomers, enantioselective bioactivity, aquatic toxicity, and dissipation in greenhouse vegetables and soil[J]. *J Agric Food Chem*, 2019, 67(41): 11331-11339.
- [50] ZHANG Q, ZHANG Z X, TANG B W, et al. Mechanistic insights into stereospecific bioactivity and dissipation of chiral fungicide triticonazole in agricultural management[J]. *J Agric Food Chem*, 2018, 66(28): 7286-7293.
- [51] GAO Y Y, ZHAO X J, SUN X F, et al. Enantioselective detection, bioactivity, and degradation of the novel chiral fungicide oxathiapiprolin[J]. *J Agric Food Chem*, 2021, 69(11): 3289-3297.
- [52] WANG Z, LI R, ZHANG J, et al. Evaluation of exploitive potential for higher bioactivity and lower residue risk enantiomer of chiral fungicide pydiflumetofen[J]. *Pest Manag Sci*, 2021, 77(7): 3419-3426.
- [53] ZHANG Q, HUA X D, SHI H Y, et al. Enantioselective bioactivity, acute toxicity and dissipation in vegetables of the chiral triazole fungicide flutriafol[J]. *J Hazard Mater*, 2015, 284: 65-72.
- [54] FANG K, FANG J W, HAN L X, et al. Systematic evaluation of chiral fungicide penflufen for the bioactivity improvement and input reduction using alphafold2 models and transcriptome sequencing[J]. *J Hazard Mater*, 2022, 440: 129729.
- [55] PAN X L, WU X M, LIU N, et al. A systematic evaluation of zoxamide at enantiomeric level[J]. *Sci Total Environ*, 2020, 733: 139069.
- [56] TONG Z, DONG X, YANG S S, et al. Enantioselective effects of the chiral fungicide tetraconazole in wheat: fungicidal activity and degradation behavior[J]. *Environ Pollut*, 2019, 247: 1-8.
- [57] GOZZO F, CARELLI A, CARZANIGA R, et al. Stereoselective interaction of tetraconazole with 14 α -demethylase in fungi[J]. *Pestic Biochem Physiol*, 1995, 53(1): 10-22.
- [58] 李纳, 张丽阳, 刁雪, 等. 3种三唑类杀菌剂对映体对镰刀菌的选择性活性[J]. *华南农业大学学报*, 2017, 38(5): 56-60.
- LI N, ZHANG L Y, DIAO X, et al. Selective bioactivity of enantiomers of three triazole fungicides against *Fusarium* spp.[J]. *J South China Agric Univ*, 2017, 38(5): 56-60.
- [59] 刘西莉, 马安捷, 林吉柏, 等. 精甲霜灵与外消旋体甲霜灵对掘氏疫霉菌的抑菌活性比较[J]. *农药学报*, 2003, 5(3): 45-49.
- LIU X L, MA A J, LIN J B, et al. The comparison of inhibitory action between stereoisomers of metalaxyl[J]. *Chin J Pestic Sci*, 2003, 5(3): 45-49.
- [60] HAN J J, JIANG J Z, SU H, et al. Bioactivity, toxicity and dissipation of hexaconazole enantiomers[J]. *Chemosphere*, 2013, 93(10): 2523-2527.
- [61] TAKANO H, OGURI Y, KATO T. Antifungal and plant growth regulating activities of enantiomers of (*E*)-1-(2,4-dichlorophenyl)-4,4-dimethyl-2-(1,2,4-triazol-1-yl)-1-penten-3-ol (*S*-3308L)[J]. *J Pestic Sci*, 1986, 11(3): 373-378.
- [62] BUERGE I J, BÄCHLI A, HELLER W E, et al. Environmental behavior of the chiral herbicide haloxyfop. 2. Unchanged enantiomer composition in blackgrass (*Alopecurus myosuroides*) and garden cress (*Lepidium sativum*)[J]. *J Agric Food Chem*, 2015, 63(10): 2591-2596.
- [63] CHEN S Y, CHEN H, CHEN Z W, et al. Enantioselective phytotoxic disturbances of fatty acids in *Arabidopsis thaliana* by dichlorprop[J]. *Environ Sci Technol*, 2019, 53(15): 9252-9259.
- [64] 常江海, 郭维, 郑姚颖, 等. 手性除草剂 2 甲 4 氯丙酸对映体在拟南芥中吸收转运及亚细胞分布的差异研究[J]. *核农学报*, 2021, 35(3): 681-687.
- CHANG J H, GUO W, ZHENG Y Y, et al. Uptake, translocation and subcellular distribution of mecoprop enantiomers in *Arabidopsis thaliana*[J]. *J Nucl Agric Sci*, 2021, 35(3): 681-687.
- [65] GERWICK B C, JACKSON L A, HANDLY J, et al. Preemergence and postemergence activities of the (*R*) and (*S*) enantiomers of haloxyfop[J]. *Weed Sci*, 1988, 36(4): 453-456.
- [66] ZHANG Q, CUI Q M, YUE S Q, et al. Enantioselective effect of glufosinate on the growth of maize seedlings[J]. *Environ Sci Pollut Res Int*, 2019, 26(1): 171-178.
- [67] KHODADADY M, RAMEZANI M K, MAHDAVI V, et al. Enantioseparation and enantioselective phytotoxicity of glufosinate ammonium on catechin biosynthesis in wheat[J]. *Food Anal Methods*, 2014, 7(4): 747-753.
- [68] 李涛, 袁国徽, 钱振官, 等. 7种茎叶处理除草剂对野燕麦的生物活性评价[J]. *植物保护*, 2018, 44(6): 224-229.
- LI T, YUAN G H, QIAN Z G, et al. Bioactivity evaluation of seven post-emergence herbicides to *Avena fatua*[J]. *Plant Prot*, 2018, 44(6): 224-229.
- [69] CAI X Y, LIU W P, SHENG G Y. Enantioselective degradation and ecotoxicity of the chiral herbicide diclofop in three freshwater alga cultures[J]. *J Agric Food Chem*, 2008, 56(6): 2139-2146.
- [70] 刘祈星, 胡艾希, 王晓光, 等. *N*-杂环甲基-2-(4-杂芳氧基苯氧基)丙酰胺的合成及除草活性[J]. *高等学校化学学报*, 2014, 35(2): 262-269.
- LIU Q X, HU A X, WANG X G, et al. Synthesis and herbicidal activity of *N*-arylmethyl-2-(4-aryloxyphenoxy) propionamide[J]. *Chem J Chin Univ*, 2014, 35(2): 262-269.
- [71] SHIMABUKURO R H, HOFFER B L. Enantiomers of diclofop-methyl and their role in herbicide mechanism of action[J]. *Pestic Biochem Physiol*, 1995, 51(1): 68-82.
- [72] XIE J Q, ZHAO L, LIU K, et al. Enantiomeric characterization of herbicide lactofen: enantioseparation, absolute configuration assignment and enantioselective activity and toxicity[J]. *Chemosphere*, 2018, 193: 351-357.
- [73] 段幼生. 手性除草剂唑啶草酯立体选择性降解、活性和生物毒性研究[D]. 南京: 南京农业大学, 2018.
- DUAN J S. Study on the stereoselectivity degradation, bioactivity and toxicology of chiral herbicide carfentrazone-ethyl[D]. Nanjing: Nanjing Agricultural University, 2018.
- [74] QI Y L, LIU D H, ZHAO W T, et al. Enantioselective phytotoxicity and bioactivity of the enantiomers of the herbicide napropamide[J]. *Pestic Biochem Physiol*, 2015, 125: 38-44.
- [75] 王萍. 手性农药乙氧呋草黄对映体在生物体和环境中的活性及立体选择性行为的研究[D]. 北京: 中国农业大学, 2005.
- WANG P. Studies on enantiomeric activity and stereoselective behavior of chiral pesticide ethofumesate in organism and environment[D]. Beijing: China Agricultural University, 2005.
- [76] BUERGE I J, BÄCHLI A, DE JOFFREY J P, et al. The chiral herbicide beflubutamid (I): isolation of pure enantiomers by HPLC, herbicidal activity of enantiomers, and analysis by enantioselective GC-MS[J]. *Environ Sci Technol*, 2013, 47(13): 6806-6811.
- [77] ZHAO L, GAO Y, XIE J Q, et al. A strategy to reduce the dose of multichiral agricultural chemicals: the herbicidal activity of

- metolachlor against *Echinochloa crusgalli*[J]. *Sci Total Environ*, 2019, 690: 181-188.
- [78] HSIAO Y L, WANG Y S, YEN J H. Enantioselective effects of herbicide imazapyr on *Arabidopsis thaliana*[J]. *J Environ Sci Health Part B*, 2014, 49(9): 646-653.
- [79] CHAN J H, WALKER F, TSENG C K, et al. Synthesis and herbicidal activity of *N*, *N*-diethyl-2-(1-naphthoxy) propionamide and its optical isomers[J]. *J Agric Food Chem*, 1975, 23(5): 1008-1010.
- [80] ZHOU Q Y, ZHANG N, ZHANG C, et al. Molecular mechanism of enantioselective inhibition of acetolactate synthase by imazethapyr enantiomers[J]. *J Agric Food Chem*, 2010, 58(7): 4202-4206.
- [81] WEI J, ZHANG X X, LI X S, et al. Enantioselective phytotoxicity of imazamox against maize seedlings[J]. *Bull Environ Contam Toxicol*, 2016, 96(2): 242-247.
- [82] XIE J Q, ZHAO L, LIU K, et al. Enantioselective effects of chiral amide herbicides napropamide, acetochlor and propisochlor: the more efficient *R*-enantiomer and its environmental friendly[J]. *Sci Total Environ*, 2018, 626: 860-866.
- [83] LIU H G, LIU J, XU L H, et al. Enantioselective cytotoxicity of isocarbophos is mediated by oxidative stress-induced JNK activation in human hepatocytes[J]. *Toxicology*, 2010, 276(2): 115-121.
- [84] 钮利喜, 朱欣凯, 王萍, 等. 吡啶硫磷对映体对东亚飞蝗的对映选择毒性及其机制研究[J]. *山西农业大学学报 (自然科学版)*, 2016, 36(5): 357-363.
- NIU L X, ZHU X K, WANG P, et al. Study on the mechanism of the enantioselective toxicity of pyraclofos to *Locusta migratoria manilensis*(meyen)[J]. *J Shanxi Agric Univ(Nat Sci Ed)*, 2016, 36(5): 357-363.
- [85] 廖逊, 万虎, 李建洪. 褐飞虱对杀虫剂抗性研究进展[J]. *农药学报*, 2019, 21(Z1): 718-728.
- LIAO X, WAN H, LI J H. Research progress on insecticides resistance in brown planthopper, *Nilaparvata lugens*(Stål)[J]. *Chin J Pestic Sci*, 2019, 21(Z1): 718-728.
- [86] KAZIEM A E, GAO B B, LI L S, et al. Enantioselective bioactivity, toxicity, and degradation in different environmental mediums of chiral fungicide epoxiconazole[J]. *J Hazard Mater*, 2020, 386: 121951.
- [87] ZHOU L L, WU Q Q, GAO Y Y, et al. Enantioselective aquatic toxicity and degradation in soil of the chiral fungicide oxathiapiprolin[J]. *Sci Total Environ*, 2022, 836: 155632.
- [88] OU Y J, YAN Z Y, SHI G F, et al. Enantioselective toxicity, degradation and transformation of the chiral insecticide fipronil in two algae culture[J]. *Ecotoxicol Environ Saf*, 2022, 235: 113424.
- [89] LI Y H, REN B, ZHAO T T, et al. Enantioselective toxic effects of mefentrifluconazole in the early life stage of zebrafish (*Danio rerio*)[J]. *Environ Toxicol*, 2022, 37(7): 1662-1674.
- [90] LIU R, DENG Y, ZHANG W G, et al. Risk assessment of the chiral fungicide triticonazole: enantioselective effects, toxicity, and fate[J]. *J Agric Food Chem*, 2022, 70(8): 2712-2721.
- [91] GUO D, HE R J, LUO L L, et al. Enantioselective acute toxicity, oxidative stress effects, neurotoxicity, and thyroid disruption of uniconazole in zebrafish (*Danio rerio*)[J]. *Environ Sci Pollut Res Int*, 2022, 29(26): 40157-40168.
- [92] DIAO J L, XU P, WANG P, et al. Enantioselective degradation in sediment and aquatic toxicity to *Daphnia magna* of the herbicide lactofen enantiomers[J]. *J Agric Food Chem*, 2010, 58(4): 2439-2445.
- [93] XU G F, JIA X H, WU C, et al. Chiral fungicide famoxadone: stereoselective bioactivity, aquatic toxicity, and environmental behavior in soils[J]. *J Agric Food Chem*, 2021, 69(30): 8530-8535.
- [94] XU P, LIU D H, DIAO J L, et al. Enantioselective acute toxicity and bioaccumulation of benalaxyl in earthworm (*Eisenia fetida*)[J]. *J Agric Food Chem*, 2009, 57(18): 8545-8549.
- [95] ZHUANG S L, ZHANG Z S, ZHANG W J, et al. Enantioselective developmental toxicity and immunotoxicity of pyraclofos toward zebrafish (*Danio rerio*)[J]. *Aquat Toxicol*, 2015, 159: 119-126.
- [96] LI R, LUO C X, QIU J S, et al. Metabolomic and transcriptomic investigation of the mechanism involved in enantioselective toxicity of imazamox in *Lemna minor*[J]. *J Hazard Mater*, 2022, 425: 127818.
- [97] GAO J, WANG F, WANG P, et al. Enantioselective toxic effects and environmental behavior of ethiprole and its metabolites against *Chlorella pyrenoidosa*[J]. *Environ Pollut*, 2019, 244: 757-765.
- [98] GAO J, WANG F, JIANG W Q, et al. Biodegradation of chiral flupirole in *Chlorella pyrenoidosa*: kinetics, transformation products, and toxicity evaluation[J]. *J Agric Food Chem*, 2020, 68(7): 1966-1973.
- [99] WANG S S, ZHANG Y, GAO J F, et al. The enantioselective study of the toxicity effects of chiral acetochlor in HepG2 cells[J]. *Ecotoxicol Environ Saf*, 2021, 218: 112261.
- [100] ZHAI W J, ZHANG L L, CUI J N, et al. The biological activities of prothioconazole enantiomers and their toxicity assessment on aquatic organisms[J]. *Chirality*, 2019, 31(6): 468-475.
- [101] LIU T, FANG K, LIU Y L, et al. Enantioselective residues and toxicity effects of the chiral triazole fungicide hexaconazole in earthworms (*Eisenia fetida*)[J]. *Environ Pollut*, 2021, 270: 116269.
- [102] LIU C X, LIU S Z, DIAO J L. Enantioselective growth inhibition of the green algae (*Chlorella vulgaris*) induced by two paclobutrazol enantiomers[J]. *Environ Pollut*, 2019, 250: 610-617.
- [103] ZHANG W J, CHEN L, DIAO J L, et al. Effects of *cis*-bifenthrin enantiomers on the growth, behavioral, biomarkers of oxidative damage and bioaccumulation in *Xenopus laevis*[J]. *Aquat Toxicol*, 2019, 214: 105237.
- [104] WEN Y, ZHOU L L, LI D, et al. Ecotoxicological effects of the pyrethroid insecticide tefluthrin to the earthworm *Eisenia fetida*: a chiral view[J]. *Environ Res*, 2020, 190: 109991.
- [105] FAN Y M, FENG Q, LAI K H, et al. Toxic effects of indoxacarb enantiomers on the embryonic development and induction of apoptosis in zebrafish larvae (*Danio rerio*)[J]. *Environ Toxicol*, 2017, 32(1): 7-16.
- [106] LIU T, CHEN D, LI Y Q, et al. Enantioselective bioaccumulation and toxicity of the neonicotinoid insecticide dinotefuran in earthworms (*Eisenia fetida*)[J]. *J Agric Food Chem*, 2018, 66(17): 4531-4540.
- [107] LIU S H, LIU Y M, HE F M, et al. Enantioselective olfactory effects of the neonicotinoid dinotefuran on honey bees (*Apis mellifera* L.)[J]. *J Agric Food Chem*, 2019, 67(43): 12105-12116.
- [108] QIN F, GAO Y X, GUO B Y, et al. Enantioselective acute toxicity effects and bioaccumulation of furalaxyl in the earthworm (*Eisenia foetida*)[J]. *Chirality*, 2014, 26(6): 307-312.
- [109] DUAN J S, SUN M N, SHEN Y, et al. Enantioselective acute toxicity and bioactivity of carfentrazone-ethyl enantiomers[J]. *Bull Environ Contam Toxicol*, 2018, 101(5): 651-656.
- [110] LI D J, SHEN L, ZHANG D, et al. Ammonia-induced oxidative stress triggered proinflammatory response and apoptosis in pig lungs[J]. *J Environ Sci*, 2023, 126: 683-696.

- [111] PANDA P, NATH S, CHANU T T, et al. Cadmium stress-induced oxidative stress and role of nitric oxide in rice (*Oryza sativa* L.)[J]. *Acta Physiol Plant*, 2011, 33(5): 1737-1747.
- [112] LEE K M, PARK S Y, LEE K, et al. Pesticide metabolite and oxidative stress in male farmers exposed to pesticide[J]. *Ann Occup Environ Med*, 2017, 29: 5-5.
- [113] LI L, HU F, WANG C, et al. Enantioselective induction of oxidative stress by acetofenat in rat PC12 cells[J]. *J Environ Sci (China)*, 2010, 22(12): 1980-1986.
- [114] DI S S, QI P P, WU S G, et al. Low-dose cadmium stress increases the bioaccumulation and toxicity of dinotefuran enantiomers in zebrafish (*Danio rerio*)?[J]. *Environ Pollut*, 2021, 269: 116191.
- [115] DI S S, WANG Z W, CANG T, et al. Enantioselective toxicity and mechanism of chiral fungicide penflufen based on experiments and computational chemistry[J]. *Ecotoxicol Environ Saf*, 2021, 222: 112534.
- [116] REN B, ZHAO T T, LI Y H, et al. Enantioselective bioaccumulation and toxicity of the novel chiral antifungal agrochemical penthiopyrad in zebrafish (*Danio rerio*)[J]. *Ecotoxicol Environ Saf*, 2021, 228: 113010.
- [117] LIU Y L, FANG K, ZHANG X L, et al. Enantioselective toxicity and oxidative stress effects of acetochlor on earthworms (*Eisenia fetida*) by mediating the signaling pathway[J]. *Sci Total Environ*, 2021, 766: 142630.
- [118] GUO D, LUO L L, KONG Y, et al. Enantioselective neurotoxicity and oxidative stress effects of paclobutrazol in zebrafish (*Danio rerio*)[J]. *Pestic Biochem Physiol*, 2022, 185: 105136-105136.
- [119] QU Q, KE M J, YE Y Z, et al. Enantioselective oxidative stress induced by *S*- and *rac*-metolachlor in wheat (*Triticum aestivum* L.) seedlings[J]. *Bull Environ Contam Toxicol*, 2019, 102(3): 439-445.
- [120] HUANG J Y, BAO M X, LI J, et al. Enantioselective response of wheat seedlings to imazethapyr: from the perspective of Fe and the secondary metabolite DIMBOA[J]. *J Agric Food Chem*, 2022, 70(18): 5516-5525.
- [121] LIU R, ZHANG H J, DENG Y, et al. Enantioselective fungicidal activity and toxicity to early wheat growth of the chiral pesticide triticonazole[J]. *J Agric Food Chem*, 2021, 69(38): 11154-11162.
- [122] JI C Y, YU C, YUE S Q, et al. Enantioselectivity in endocrine disrupting effects of four cypermethrin enantiomers based on *in vitro* models[J]. *Chemosphere*, 2019, 220: 766-773.
- [123] SONG Q, ZHANG Y, YAN L, et al. Risk assessment of the endocrine-disrupting effects of nine chiral pesticides[J]. *J Hazard Mater*, 2017, 338: 57-65.
- [124] 王春蕾. 顺式联苯菊酯对映体对H295R细胞肾上腺皮质激素分泌的选择性干扰效应[D]. 杭州: 浙江省医学科学院, 2020.
- WANG C L. Selective disruption of *cis*-bifenthrin enantiomers on secretion of adrenocortical hormones in H295R cells[D]. Hangzhou: Zhejiang Academy of Medical Science, 2020.
- [125] HU K M, ZHOU L L, GAO Y Y, et al. Enantioselective endocrine-disrupting effects of the phenylpyrazole chiral insecticides *in vitro* and *in silico*[J]. *Chemosphere*, 2020, 252: 126572.
- [126] HE R J, GUO D, LIN C, et al. Enantioselective bioaccumulation, oxidative stress, and thyroid disruption assessment of *cis*-metconazole enantiomers in zebrafish (*Danio rerio*)[J]. *Aquat Toxicol*, 2022, 248: 106205.
- [127] XU C, SUN X H, NIU L L, et al. Enantioselective thyroid disruption in zebrafish embryo-larvae via exposure to environmental concentrations of the chloroacetamide herbicide acetochlor[J]. *Sci Total Environ*, 2019, 653: 1140-1148.
- [128] CHANG J, XU P, LI W, et al. Enantioselective elimination and gonadal disruption of lambda-cyhalothrin on lizards (*Eremias argus*)[J]. *J Agric Food Chem*, 2019, 67(8): 2183-2189.
- [129] 朱飞龙, 郝伟玉, 尹晶, 等. 腈菌唑不同对映体对丽斑麻蜥性腺系统的影响[J]. *生态毒理学报*, 2018, 13(5): 147-155.
- ZHU F L, HAO W Y, YIN J, et al. Effects of myclobutanil enantiomers on the gonadal system in Mongolia racerunner(*Eremias argus*)[J]. *Asian J Ecotoxicol*, 2018, 13(5): 147-155.
- [130] OU-YANG K, FENG T Q, HAN Y F, et al. Bioaccumulation, metabolism and endocrine-reproductive effects of metolachlor and its *S*-enantiomer in adult zebrafish (*Danio rerio*)[J]. *Sci Total Environ*, 2022, 802: 149826.
- [131] ZHANG P, ZHU W T, WANG D Z, et al. Enantioselective effects of metalaxyl enantiomers on breast cancer cells metabolic profiling using HPLC-QTOF-based metabolomics[J]. *Int J Mol Sci*, 2017, 18(1): 142.
- [132] GU J P, CHENG Y F, JI C Y, et al. Analysis of the different metabolic phenotypes of metalaxyl enantiomers in adolescent rat by using ¹H NMR based urinary metabolomics[J]. *Chem Res Toxicol*, 2020, 33(6): 1449-1457.
- [133] ZHANG P, WANG S, HE Y H, et al. Identifying metabolic perturbations and toxic effects of *rac*-metalaxyl and metalaxyl-M in mice using integrative NMR and UPLC-MS/MS based metabolomics[J]. *Int J Mol Sci*, 2019, 20(21): 5457.
- [134] QIU D Y, YE Y Z, KE M J, et al. Effects of chiral herbicide dichlorprop on *Arabidopsis thaliana* metabolic profile and its implications for microbial communities in the phyllosphere[J]. *Environ Sci Pollut Res Int*, 2022, 29(19): 28256-28266.
- [135] ZHAO L Q, ZHANG Y W, WANG L, et al. Stereoselective metabolomic and lipidomic responses of lettuce (*Lactuca sativa* L.) exposing to chiral triazole fungicide tebuconazole[J]. *Food Chem*, 2022, 371: 131209.
- [136] ZHOU X, YANG Y, MING R Y, et al. Insight into the differences in the toxicity mechanisms of dinotefuran enantiomers in zebrafish by UPLC-Q/TOF-MS[J]. *Environ Sci Pollut Res*, 2022: 1-9.
- [137] ZHANG Y, CHEN D, XU Y Z, et al. Stereoselective toxicity mechanism of neonicotinoid dinotefuran in honeybees: new perspective from a spatial metabolomics study[J]. *Sci Total Environ*, 2022, 809: 151116.
- [138] FANG K, HAN L X, LIU Y L, et al. Enantioselective bioaccumulation and detoxification mechanisms of earthworms (*Eisenia fetida*) exposed to mandipropamid[J]. *Sci Total Environ*, 2021, 796: 149051.
- [139] LI Y H, LIANG H W, REN B, et al. Enantioselective toxic effects of mefentrifluconazole in the liver of adult zebrafish (*Danio rerio*) based on transcription level and metabolomic profile[J]. *Toxicology*, 2022, 467: 153095.
- [140] XIANG D D, QIAO K, SONG Z Y, et al. Enantioselectivity of toxicological responses induced by maternal exposure of *cis*-bifenthrin enantiomers in zebrafish (*Danio rerio*) larvae[J]. *J Hazard Mater*, 2019, 371: 655-665.
- [141] GU J P, JI C Y, YUE S Q, et al. Enantioselective effects of metalaxyl enantiomers in adolescent rat metabolic profiles using NMR-based metabolomics[J]. *Environ Sci Technol*, 2018, 52(9): 5438-5447.

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