Exploring neonicotinoids in aquatic ecosystems: A deeper look into their impacts on freshwater fish

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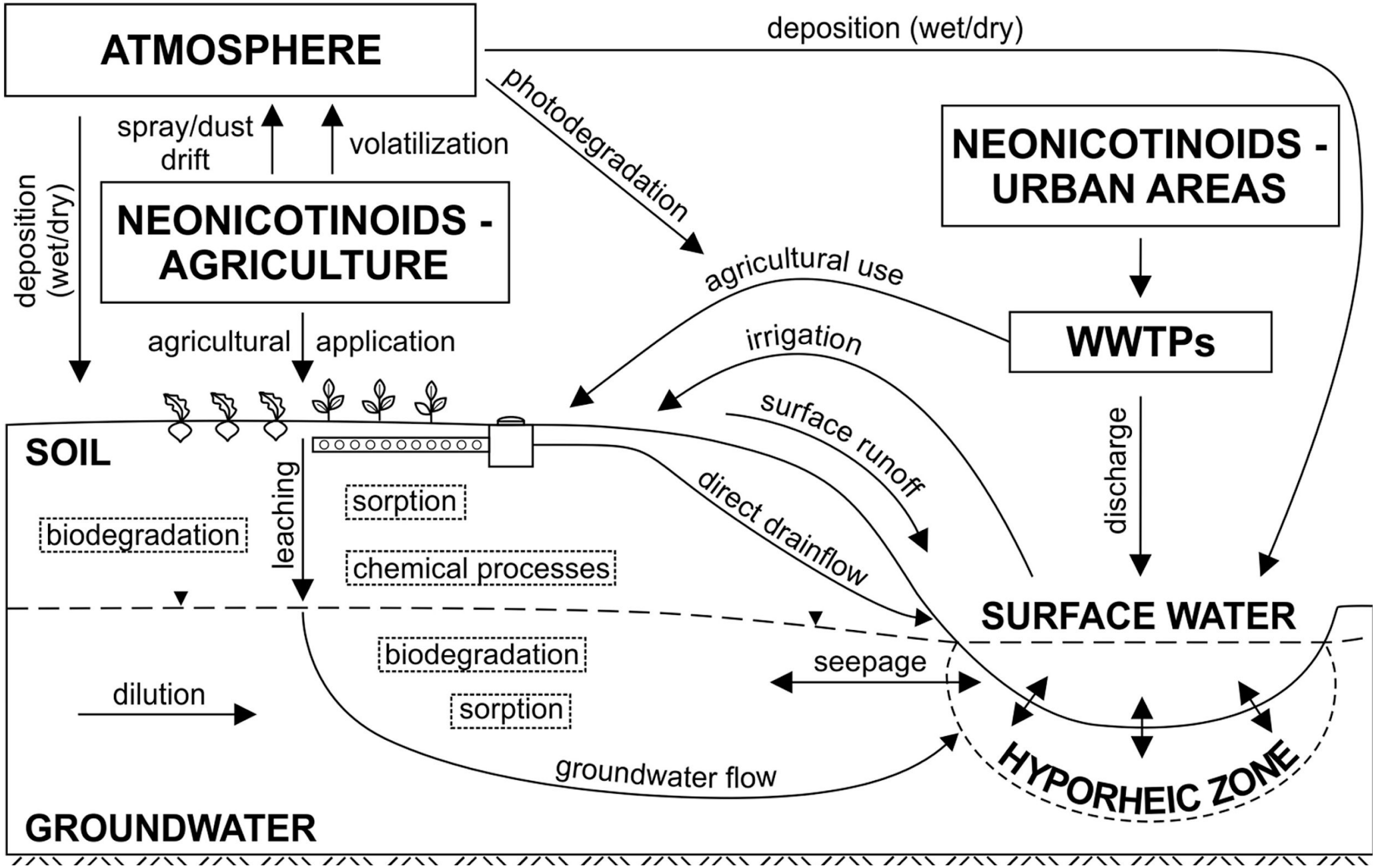
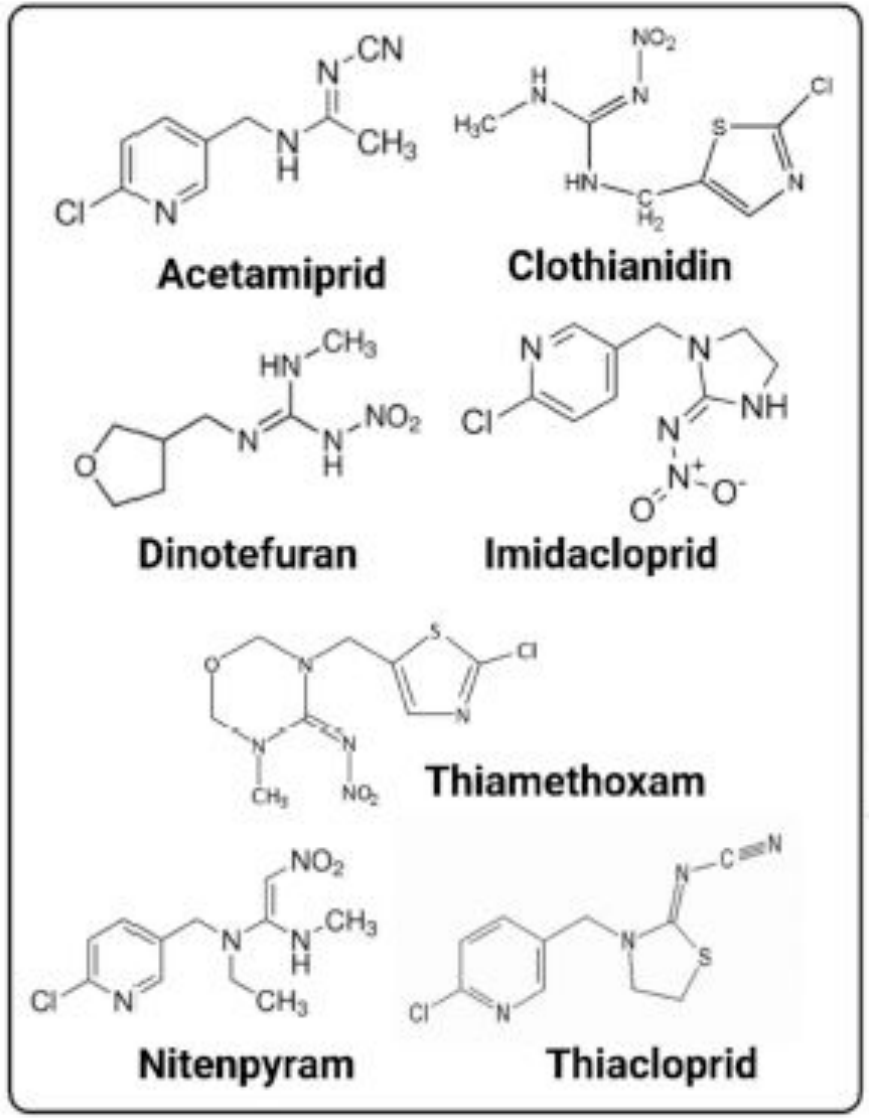
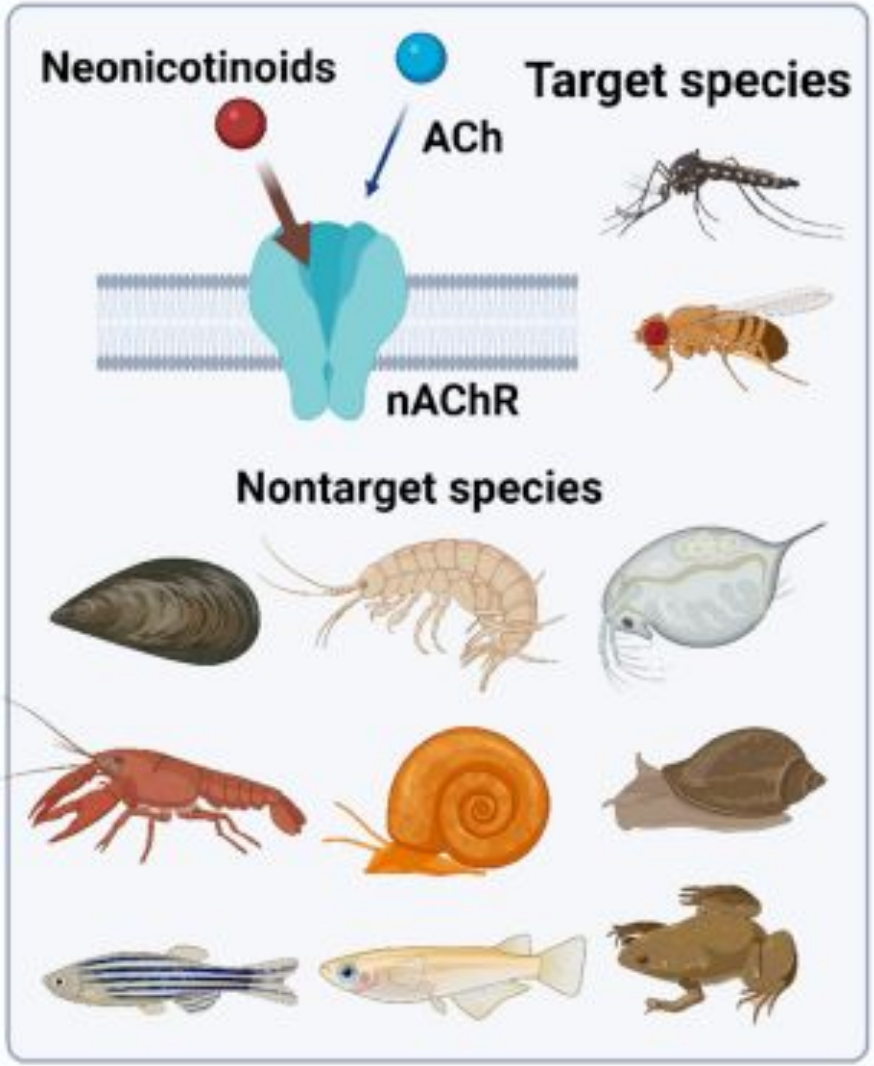


Pietrzak et al.

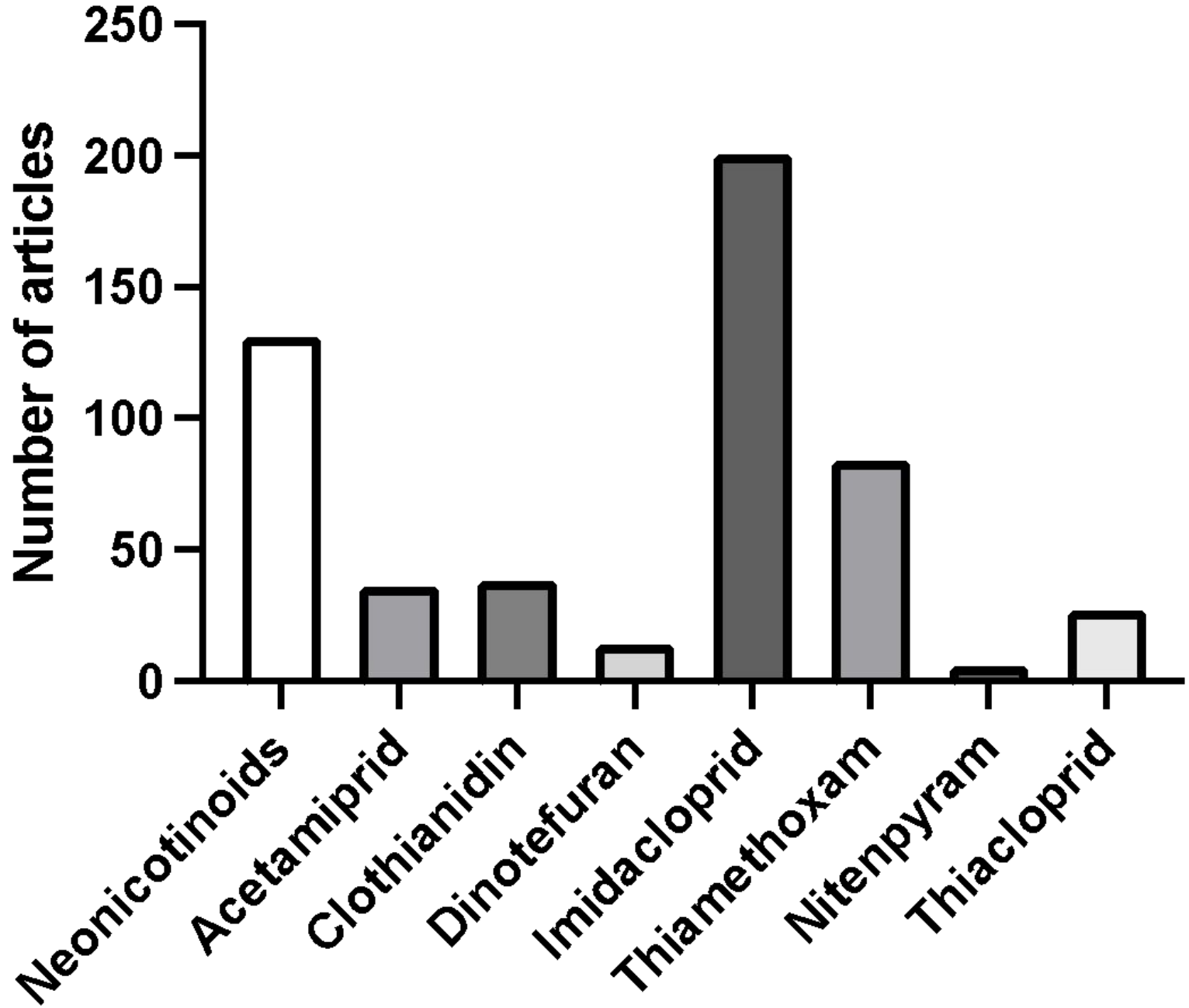
Common neonicotinoids



Malhotra et al. 2021



Malhotra et al. 2021


Number of articles
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200
150
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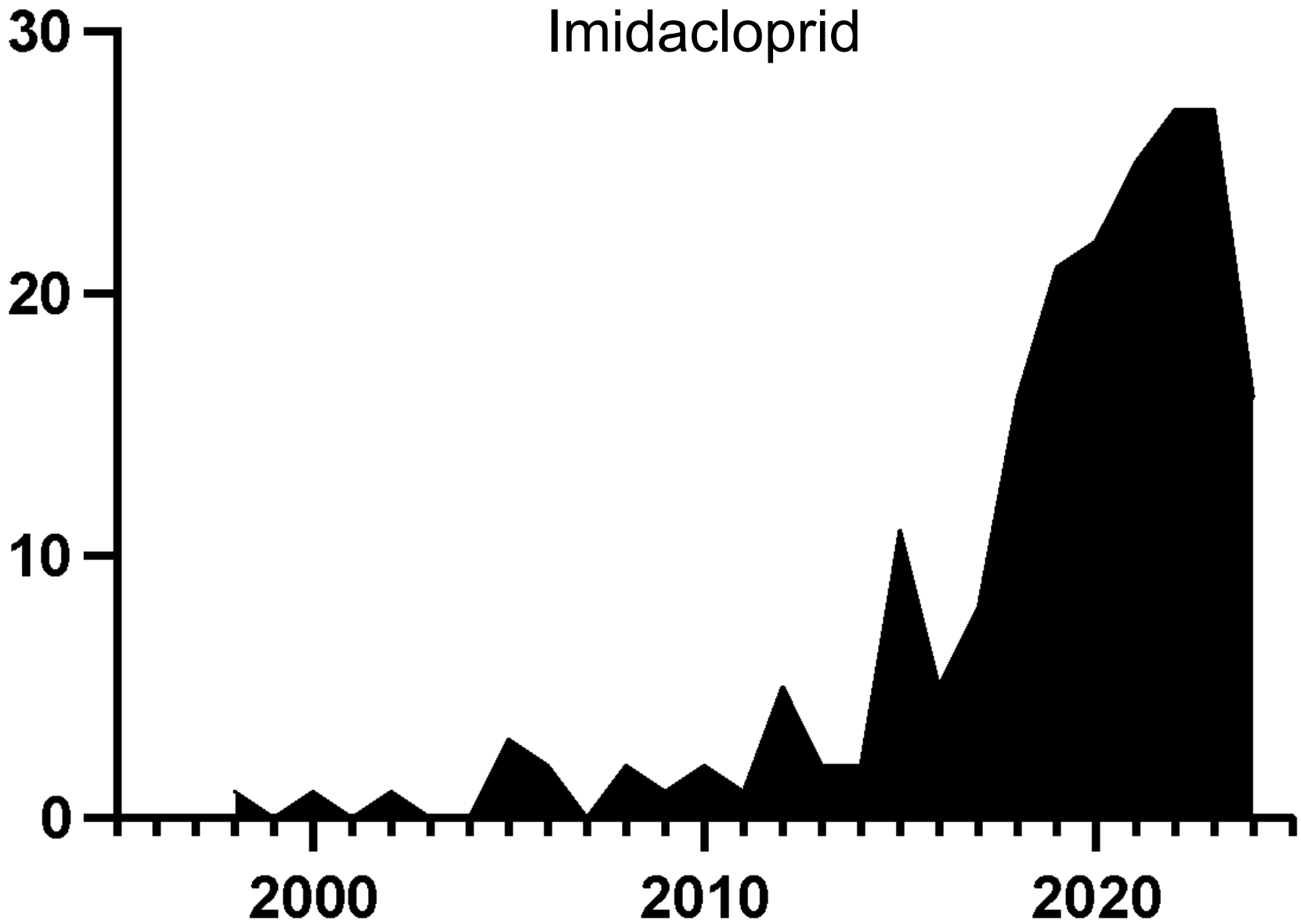
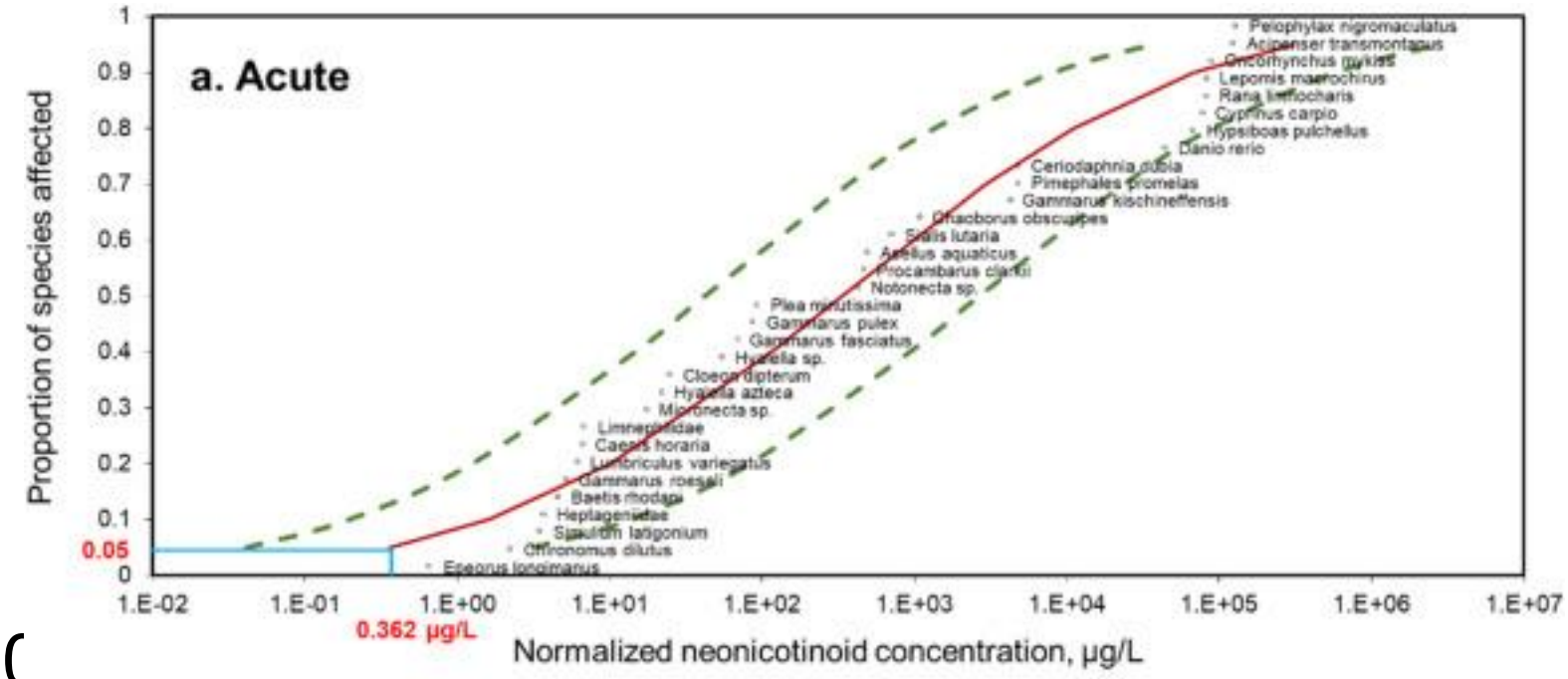
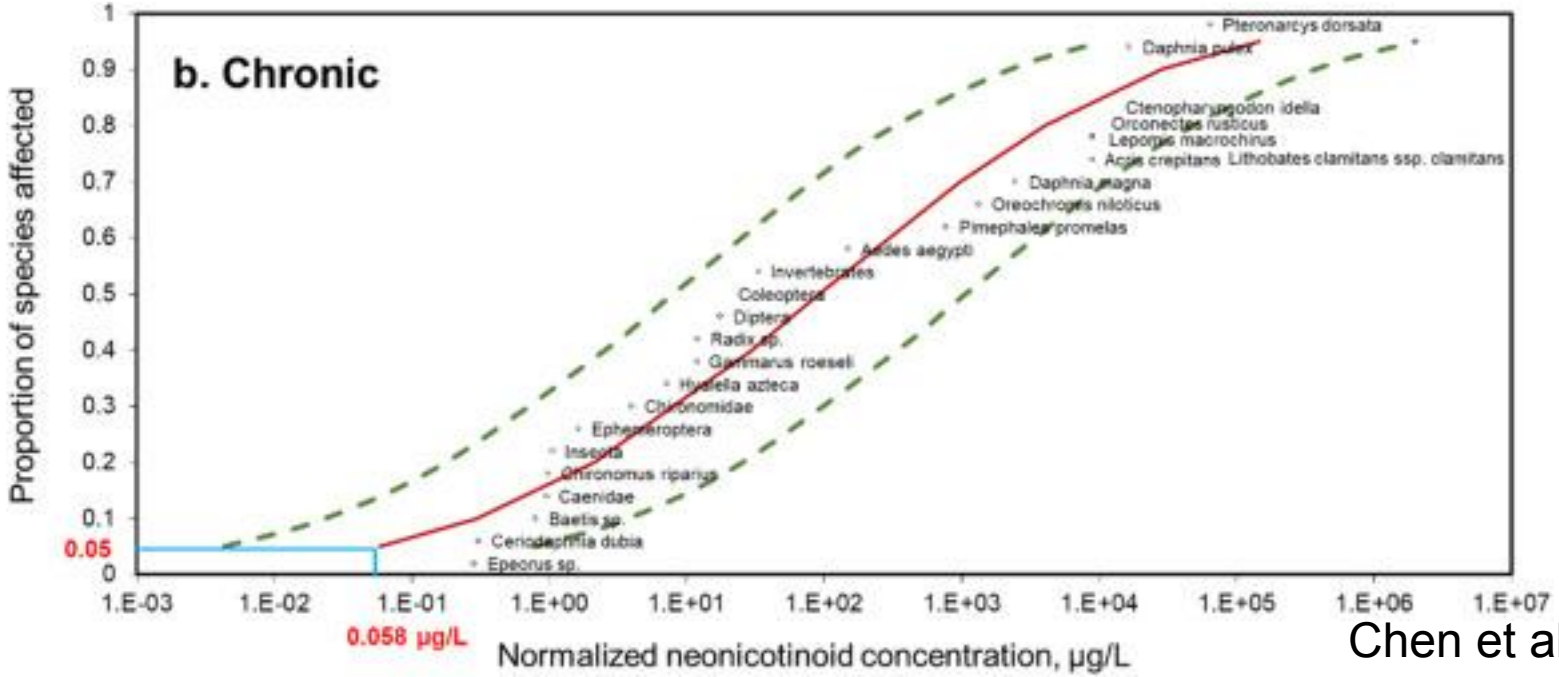
Neonicotinoids
Acetamiprid
Clothianidin
Dinotefuran
Imidacloprid
Thiamethoxam
Nitenpyram
Thiacloprid


Imidacloprid
30
20
10
0
2000
2010
2020

Lethal and Sublethal Impacts

- Lethal Concentration for 50% death or LC50
- Growth and development – wet mass and length





Chen et al.

Lethal Impacts

TABLE 3 Toxicological profiles of the neonicotinoids and nicotine[a]

Compound	Mammal[b]			Bird[f]	Fish[g]
	Acute oral[c] LD_{50} (mg/kg)	NOAEL[d] (mg/kg/day)	Carcinogen[e]	Acute oral LD_{50} (mg/kg)	LC_{50} (ppm)
Neonicotinoids					
Acetamiprid	182	7.1	No	180	>100
Clothianidin	>5000	9.8	No	>2000	>100
(±)-Dinotefuran	2400	127	No	>2000	>40
Imidacloprid	450	5.7	No	31	211
Nitenpyram	1628	—	—	>2250	>1000
Nithiazine	300	—	—	—	150
Thiacloprid	640	1.2	Yes	49	31
Thiamethoxam	1563	0.6	Yes	1552	>100
Nicotinoid					
(−)-Nicotine	50–60	—	—	Toxic	4

[a]Data from References 9, 15, 25–30.

[b]Dermal LD_{50} values of neonicotinoids are >2000 to >5000 mg/kg (rat) except for (−)-nicotine 50 mg/kg (rabbit).

[c]Average data for male and female rats with sex difference less than twofold.

[d]No-observed-adverse-effect-level (NOAEL) for chronic toxicity studies in rats. This value also applies to all adverse effects in chronic toxicity studies with mice and dogs.

[e]Thiacloprid gives thyroid and uterine tumors in rats and ovary tumors in mice. Thiamethoxam gives hepatocellular adenomas and carcinomas in male and female mice. They are considered to be likely human carcinogens.

[f]Japanese or bobwhite quail.

[g]Rainbow trout or carp.

Tomizawa and Casida 2005

Acute Studies fish

Fish	African catfish	*Clarias gariepinus*	acetamiprid	juveniles	96h LC50	265.7	–	Houndji et al. (2020)
	Nile tilapia	*Oreochromis niloticus*	Telfast 20 SP (acetamiprid 20%)	juveniles	96h LC50	195.813	–	El-Garawani et al. (2022)
			Telfast 20 SP (acetamiprid 20%)	juveniles	96h LC50	202.35	–	Hathout et al. (2021)
	Rainbow trout	*Oncorhynchus mykiss*	acetamiprid	2.05 g	96h LC50	> 100	–	EPA (2023)
			flupyradifurone	0.79 g	96h LC50	> 74.2	–	
			thiacloprid	1.2 g	96h LC50	30.2	–	
	Eastern mosquitofish	*Gambusia holbrooki*	RastT 20SP (acetamiprid 20%)	3.5 ± 0.07 cm; 0.54 ± 0.16 g	96h LC50	42.2	significant changes in GST; GR	Demirci and Gungordu (2020)
	Major South Asian carp	*Catla catla*	acetamiprid	10–15 g	96h LC50	–	↓CAT, SOD, GST, GSH in gill; ↓LPO increase	Veedu et al. (2022)
	Grass carp	*Ctenopharyngodon idela*	Telfast 20 SP (acetamiprid 20%)	30 ± 2 g	96h LC50	121.146	–	Azadikhah et al. (2023)

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Acute Studies fish age

			acetamiprid	larvae (5 dpf)	96h LC50	58.39	–	Hu et al. (2023)
			acetamiprid	embryo	96h LC50	143.9	–	
			acetamiprid	adults	96h LC50	10.36	↑GST in brain and liver	
			acetamiprid	juvenile	96h LC50	36.91	–	Wang et al. (2018b)
			acetamiprid	larvae	96h LC50	15.52	–	
			acetamiprid	embryo	96h LC50	13.33	–	
Fish (to be continued)	Zebrafish	*Danio rerio*	flupyradifurone	5.5 hpf	96h LC50	210	↓heart rate, body length, survival rate; abnormalities in cardiac development (elongated pericardium, pericardial edema aggravation, increased atrial ventricular spacing, increased degree of the unlooped heart; ↓CAT, SOD	Zhong et al. (2021)
	Fathead minnow	*Pimephales promelas*	flupyradifurone	0.85 g	96h LC50	> 70.5	–	EPA (2023)
			thiacloprid	0.24	96h LC50	> 104	–	
	Common carp	*Cyprinus carpio*	flupyradifurone	1.7 g	96h LC50	> 80	–	EPA (2023)
	Sheepshead minnow	*Cyprinodon variegatus*	acetamiprid	0.53 g	96h LC50	100	–	EPA (2023)
			flupyradifurone	0.24 g	96h LC50	> 83.9	–	
			thiacloprid	0.23 g	96h LC50	19.7	–	

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Acute studies amphibians

Amphibians	Western clawed frog	*Silurana tropicalis*	acetamiprid	tadpole	96h LC50	> 100	–	Sala and Tada (2021)
	African clawed frog	*Xenopus laevis*	acetamiprid	tadpole	96h LC50	64.48	–	Jiao et al. (2023)
			Calypso OD240 (thiacloprid 240 g/l)	tadpole	96h LC50	13.41	–	Uckun and Ozmen (2021)
	Dark-spotted frog	*Rana nigromaculata*	acetamiprid	tadpole	LC50	18.49	–	Guo et al. (2022)

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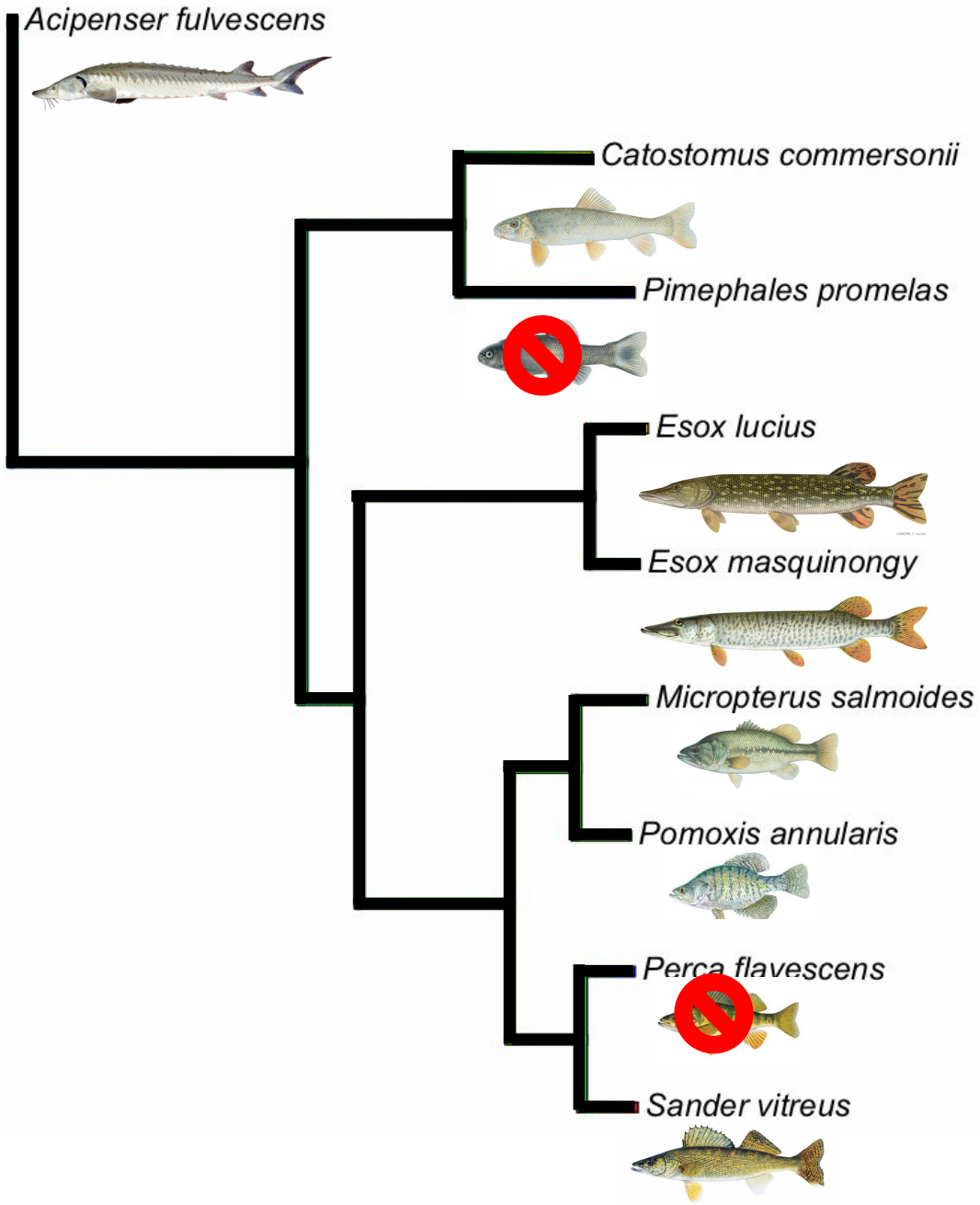
Missing species

- Majority of studies on rainbow trout, carp, zebrafish, fathead minnows.
- Missing game species (walleye, northern pike, etc.)
- One aquaculture species of yellow perch
- Limited studies on amphibians

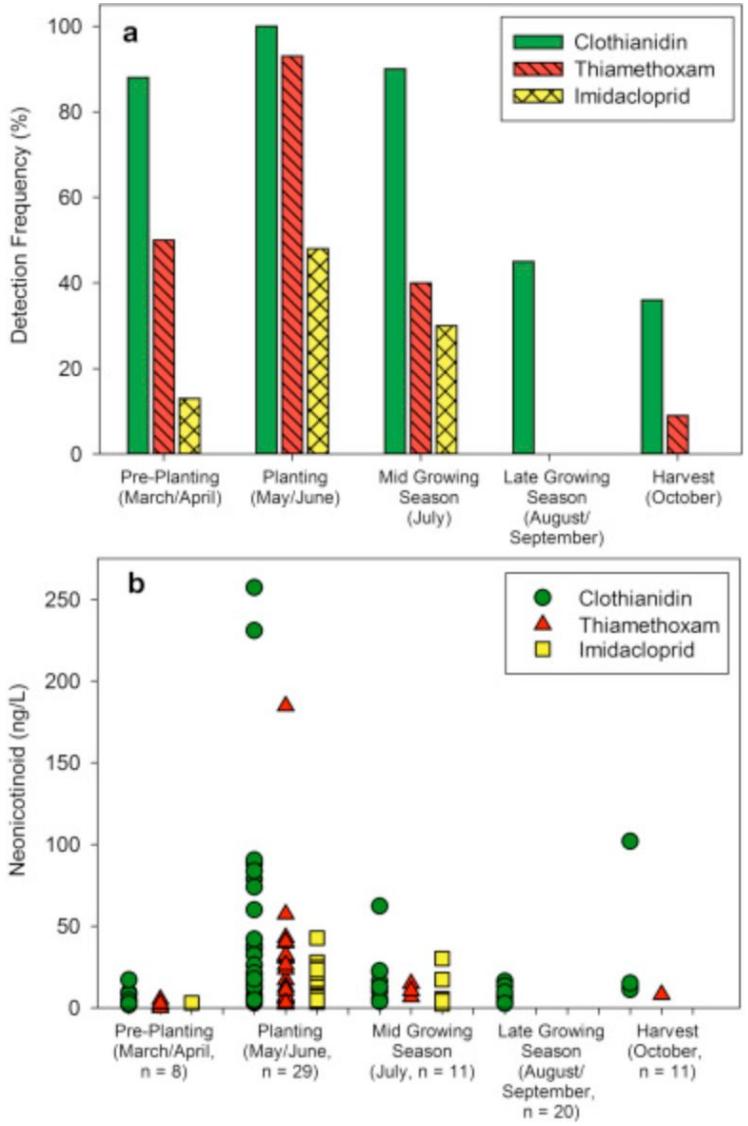

Acipenser fulvescens
Catostomus commersonii
Pimephales promelas
Esox lucius
Esox masquinongy
Micropterus salmoides
Pomoxis annularis
Perca flavescens
Sander vitreus

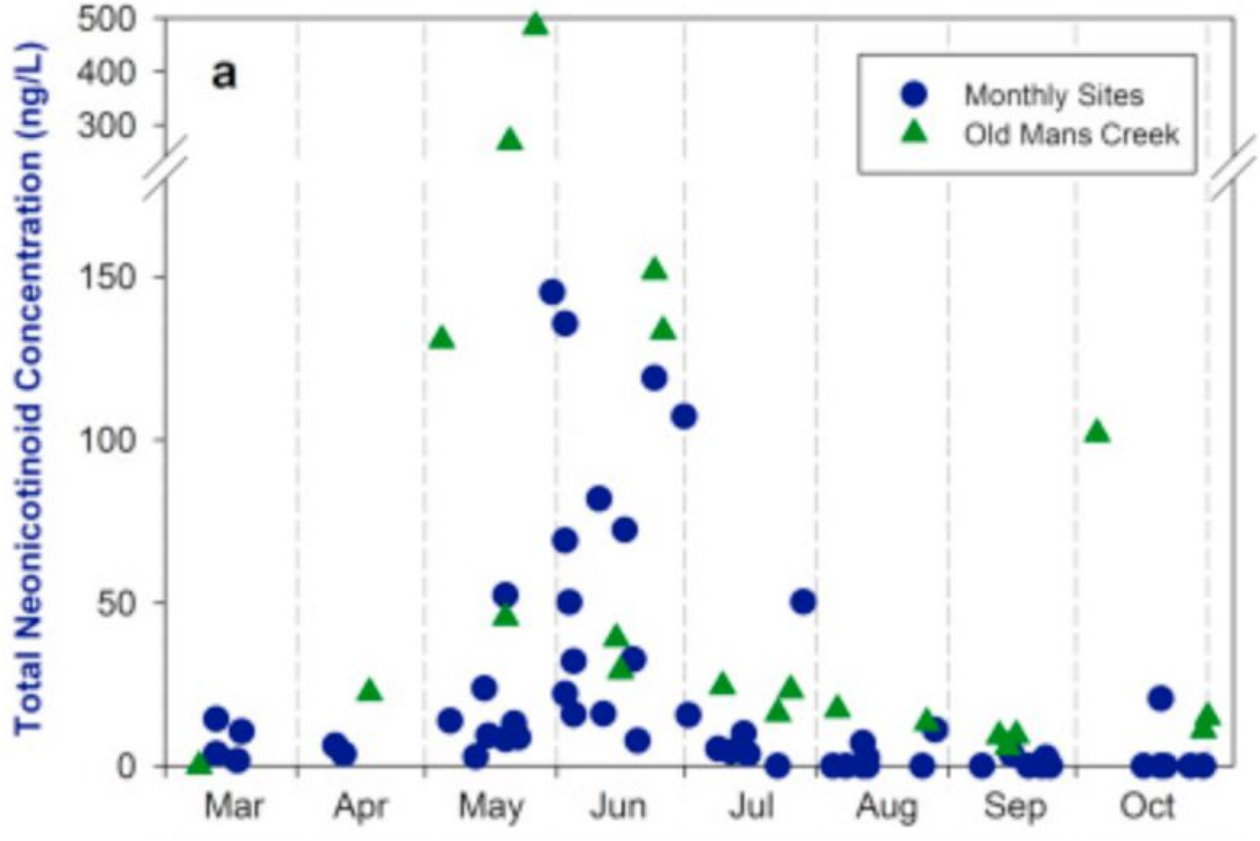
Commercial formulations vs active ingredients

Commercial Name	Active ingredient	Concentration	Formulation	Toxicological classification
Actara	Tiametoxam	250 $g \cdot kg^{-1}$	WG	III
Provado	Imidacloprid	200 $g \cdot L^{-1}$	SC	III
Mospilan	Acetamiprid	725 $g \cdot kg^{-1}$	WG	III
Dinno	Dinotefuran	200 $g \cdot kg^{-1}$	SG	V

WG: dispersible granules; SC: concentrated suspension; SG: Soluble granules; III: Moderately toxic; V: Unlikely to cause acute damage.

Levels found in great lakes region

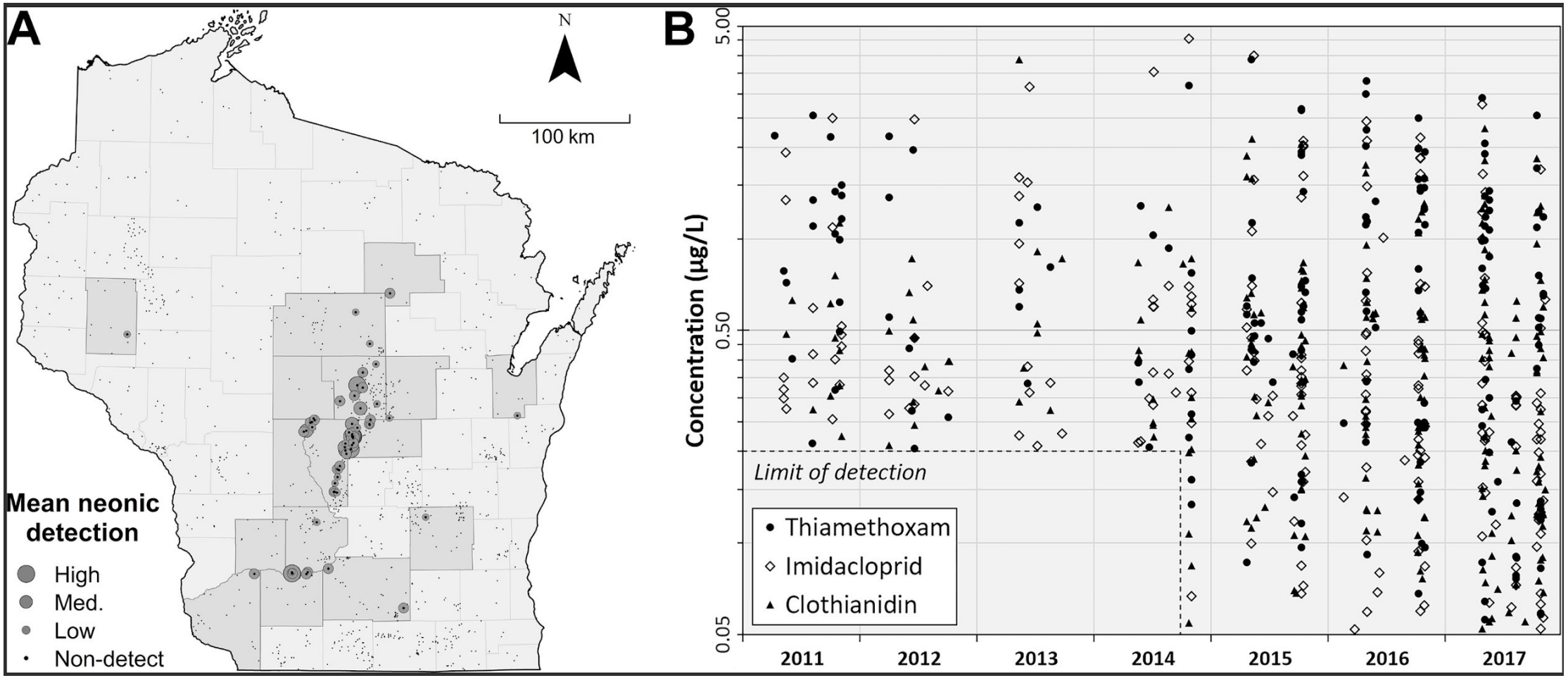




Morrissey et al., 2015

Hladik et al. 2014

Ground Water levels

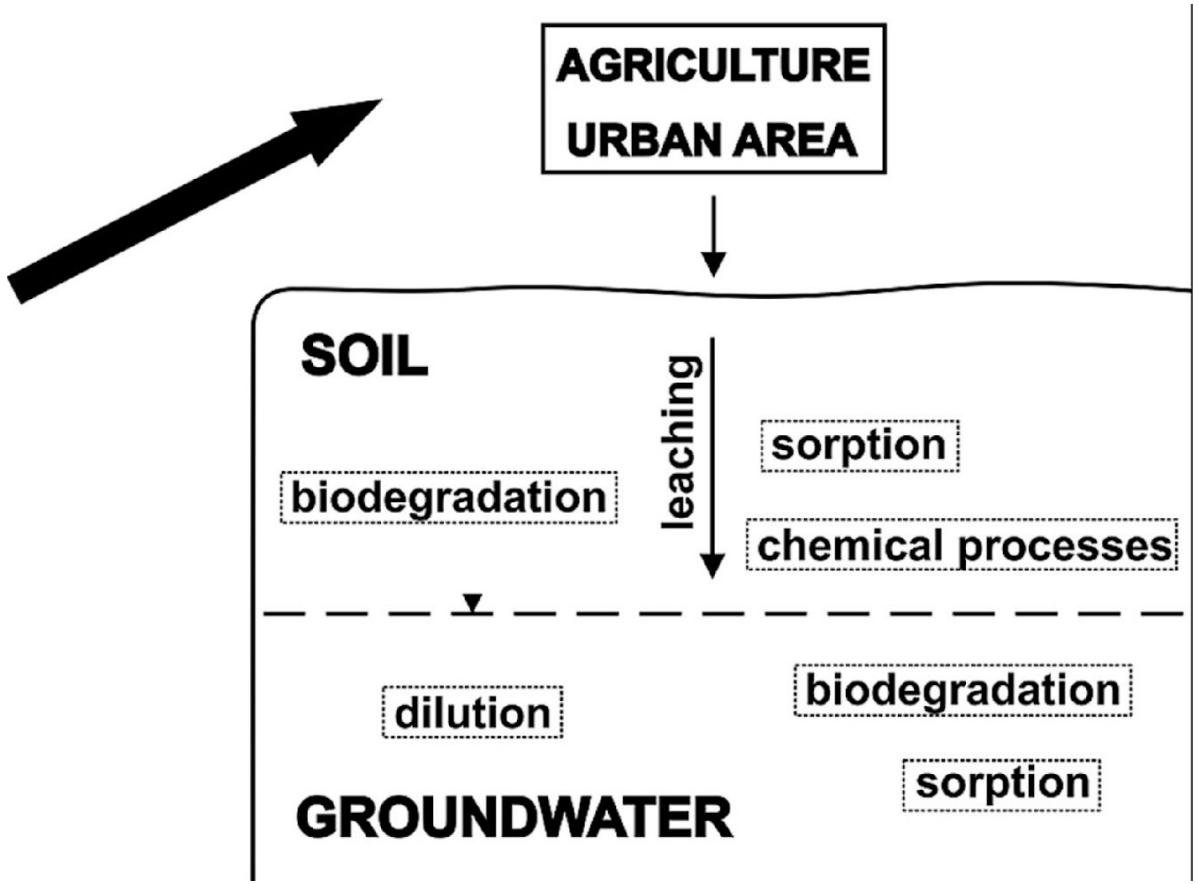


Bradford et al.

Take aways

- Fish and amphibian's similar toxic levels
- No life stage is consistently more or less sensitive
- 100 mg/L or ppm
- Many lethal effects at concentrations higher than environmentally relevant
- Not all neonicotinoids have been studied equally

Half-life



- 28 to 75 + days in water
- 100’s of days in soil

Chronic Studies fish

	Common carp	*Cyprinus carpio*	thiadoprid	35 days	4.5; 45; 225; 450 µg/l	–	–	↓lower weight and length; ↓SOD and GR activity	Velisek and Stara (2018)
	Zebrafish	*Danio rerio*	acetamiprid	154 days	0.19–1 637 µg/l	–	–	feminization and reproductive dysfunction in zebrafish; impaired production and development of offspring	Ma et al. (2022)
Fish	Nile tilapia	*Oreochromis niloticus* (juveniles)	Telfast 20 SP (acetamiprid 20%)	21 days	19.5 mg/l (representing 96h LC50 /10)	–	–	colour darkening; sluggish swimming; raised fins; lethargy; enlarged dark gall bladders	El-Gamawani et al. (2022)
			Telfast 20 SP (acetamiprid 20%)	21 days	10; 20 mg/l	–	–	↓SOD, GPx; production of LPO substances in fish liver	Hathout et al. (2021)
	Rainbow trout	*Oncorhynchus mykiss* (early lyfestages)	thiacloprid	97 days	–	1.91	0.92	–	EPA (2023)
	Fathead minnow	*Pimephales promelas*	flupyradifurone	35 days	–	8.4	4.4	–	EPA (2023)
			acetamiprid	35 days	–	38.4	19.2	–	
			thiadoprid	33 days	–	> 0.170	0.17	–	
				106 days	–	> 0.710	0.71	–	
				260 days	–	–	–	–	

Strouhova et al. 2023

Chronic Studies amphibians

Amphibians	African clawed frog	*Xenopus laevis* (tadpole)	acetamiprid	28 days	0.645 and 6.45 mg/l (representing 1/100 and 1/10 96h LC50)	–	–	↑melano-macrophages; obscure liver cords; inflammatory infiltration in liver tissues	Jiao et al. (2023)
		Rana nigromaculata (tadpole)	acetamiprid	28 days	0.185 and 1.85 mg/l	–	–	↑CAT, SOD, GR, GST ↓AChE	Guo et al. (2022)
Amphibians (to be continued)	Egyptian toads	*Sclerophrys regularis* (adults)	Acetamore 20% (acetamiprid 20%)	14 days	40 mg/l	–	–	↑the serum levels of total lipid, cholesterol, triglyceride, AST, ALT; ↓in hepatic GSH and SOD; ↑MDA	Saad et al. (2022)
	Western clawed frog	*Silurana tropicalis* (tadpole)	acetamiprid	26–28 days	0.1 and 1 mg/l (representing 1/10 and 1/100 of 96h LC50)	–	–	no significant differences in any of the endpoints (mortality, malformations and other visually recognisable abnormalities)	Saka and Tada (2021)

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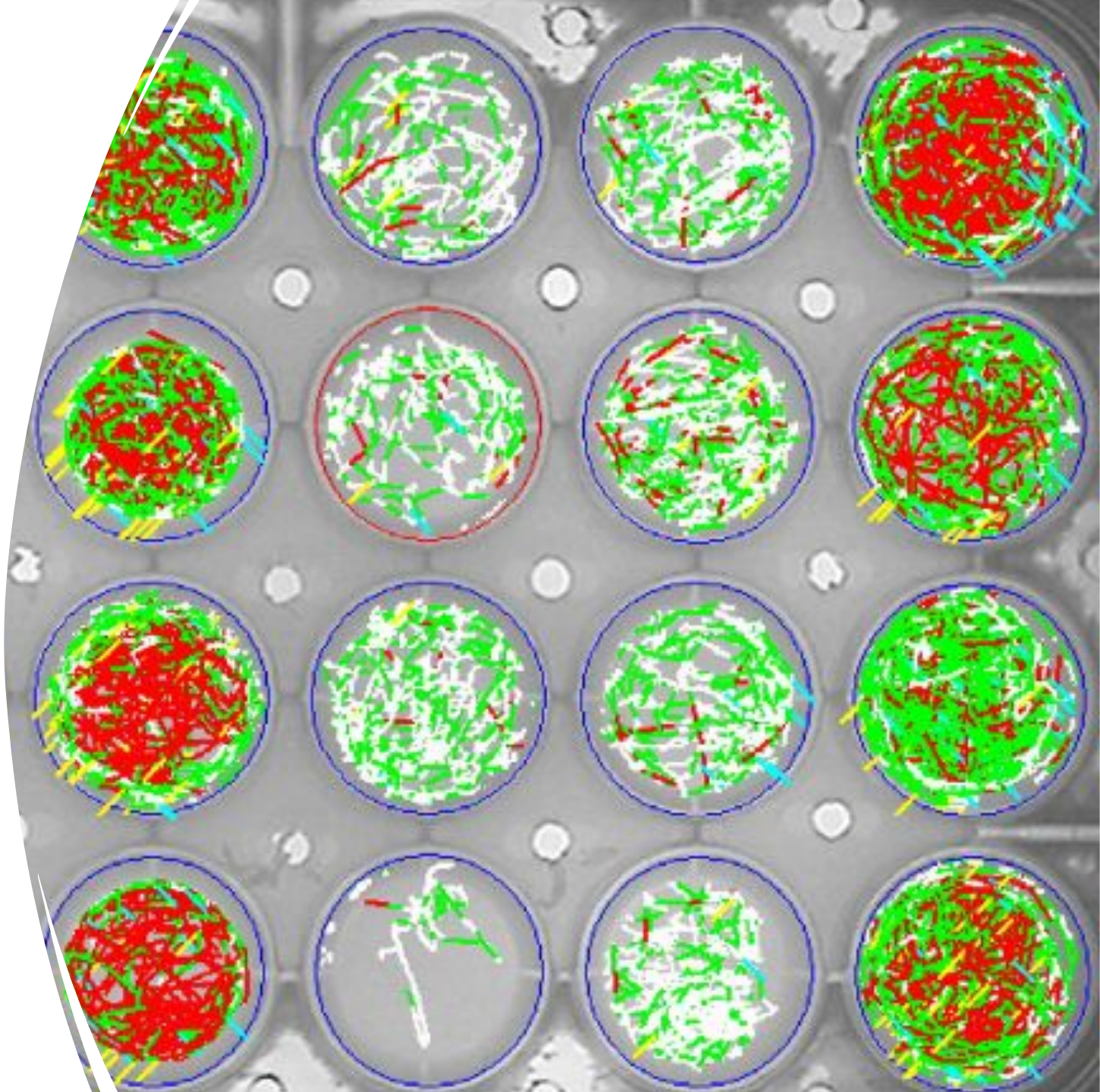
Take aways

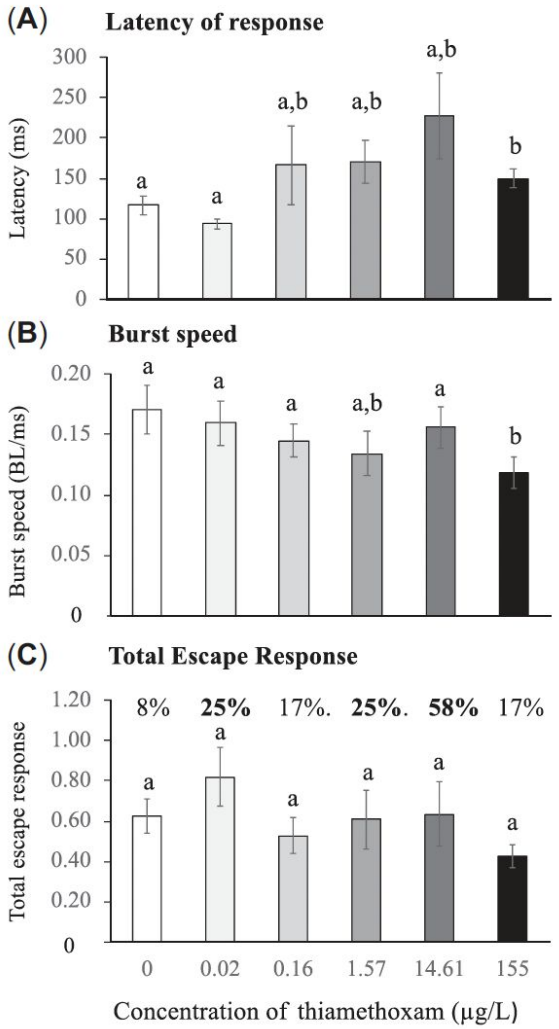
- Chronic exposure more sensitive to impacts
- 0.7 to 10 mg/L or ppm
- Many lethal effects at concentrations higher than environmentally relevant
- Less chronic studies, no transgenerational studies
- Laboratory Studies

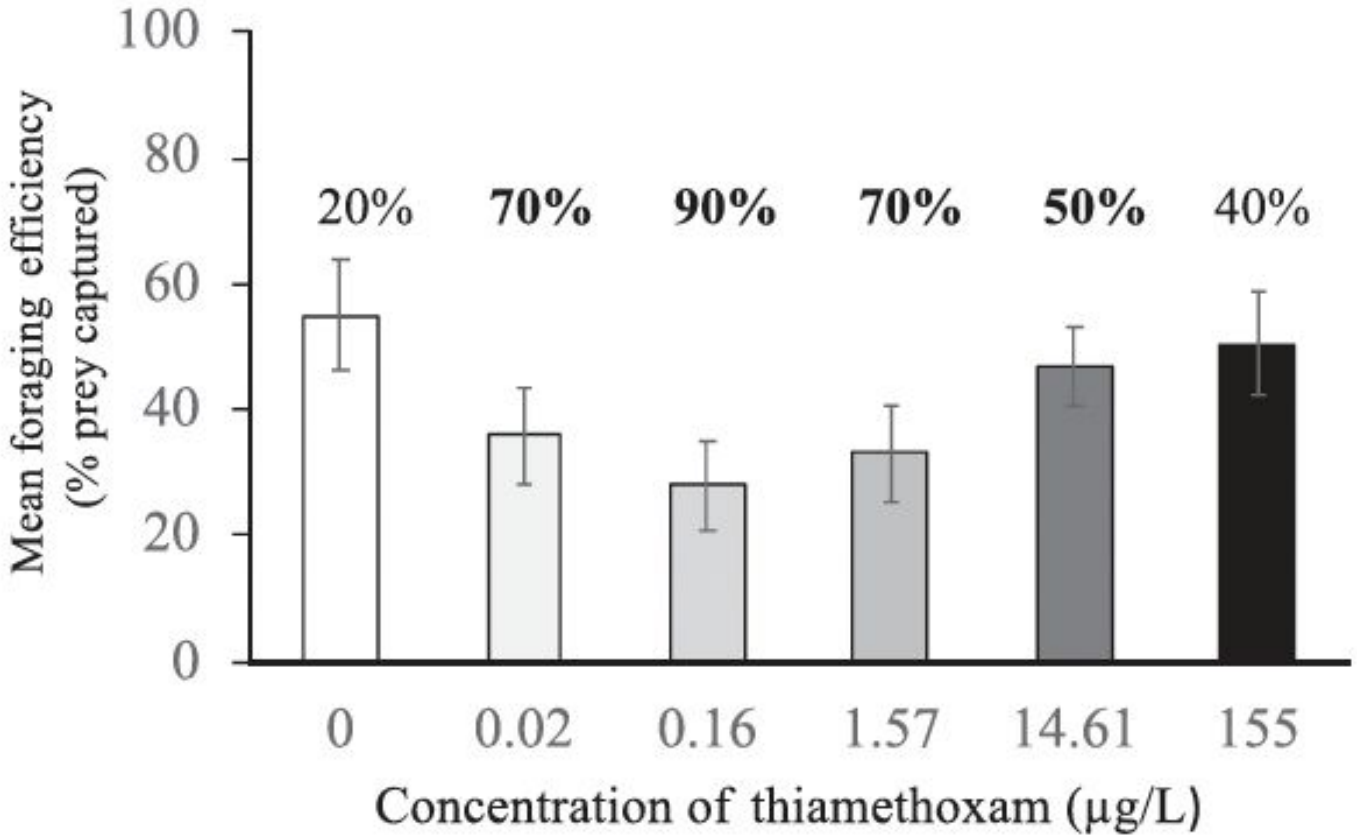
Sublethal Behavioral impacts

- Locomotion
  - Overall movement
- Prey capture
  - Foraging success
  - J - turn
- Predator avoidance
  - C – start
  - Latency response



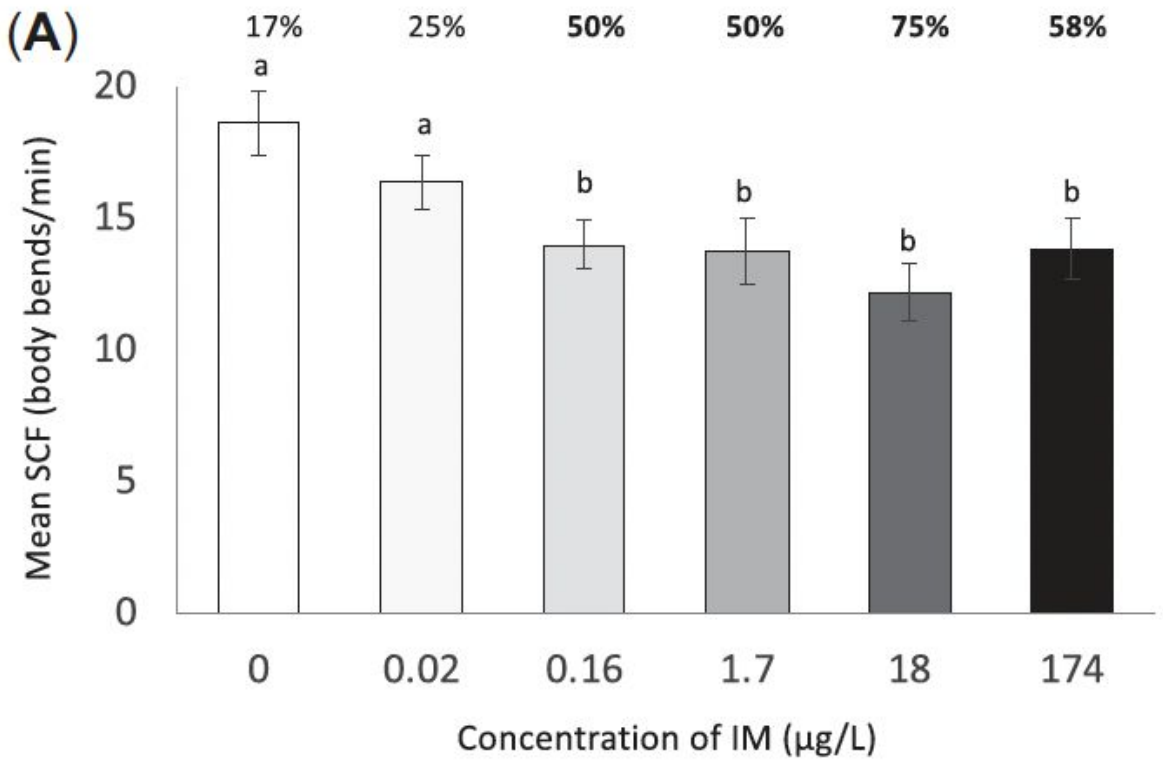
Thiamethoxam Alters Neurobehavior of Fathead Minnows

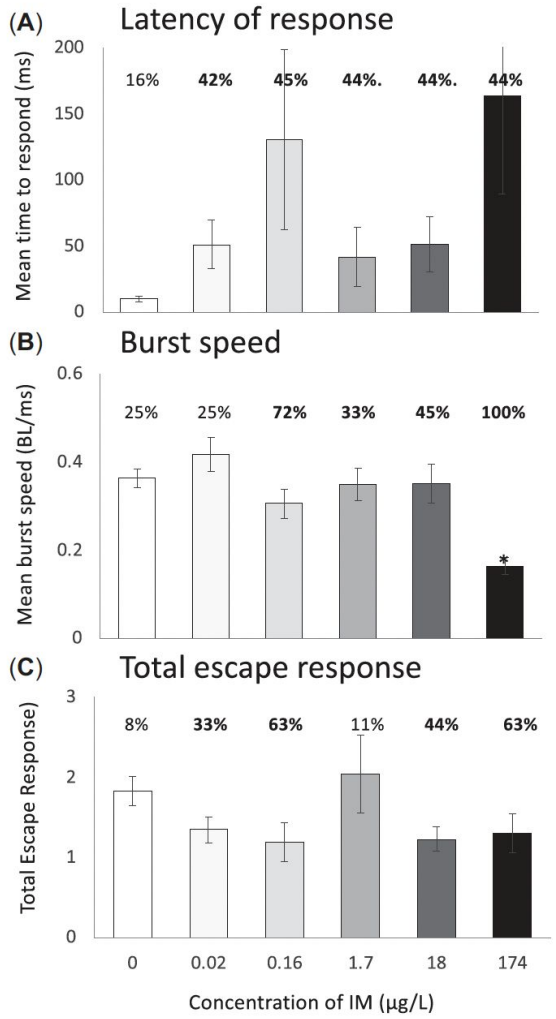




Victoria et al . 2022

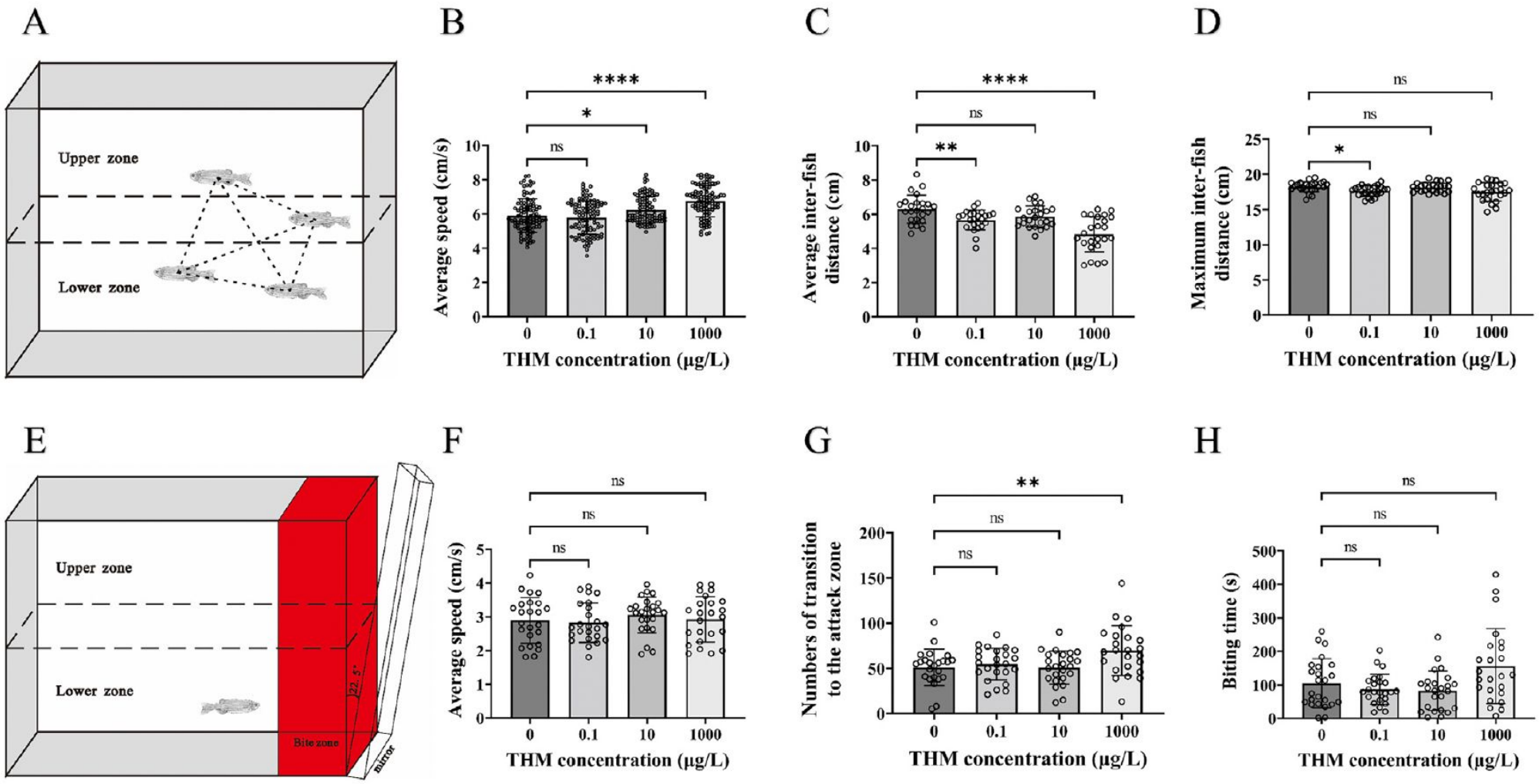
Imidacloprid Impact Ecologically Relevant Behaviors of Fathead Minnow Larvae





Jeninga et al. 2023

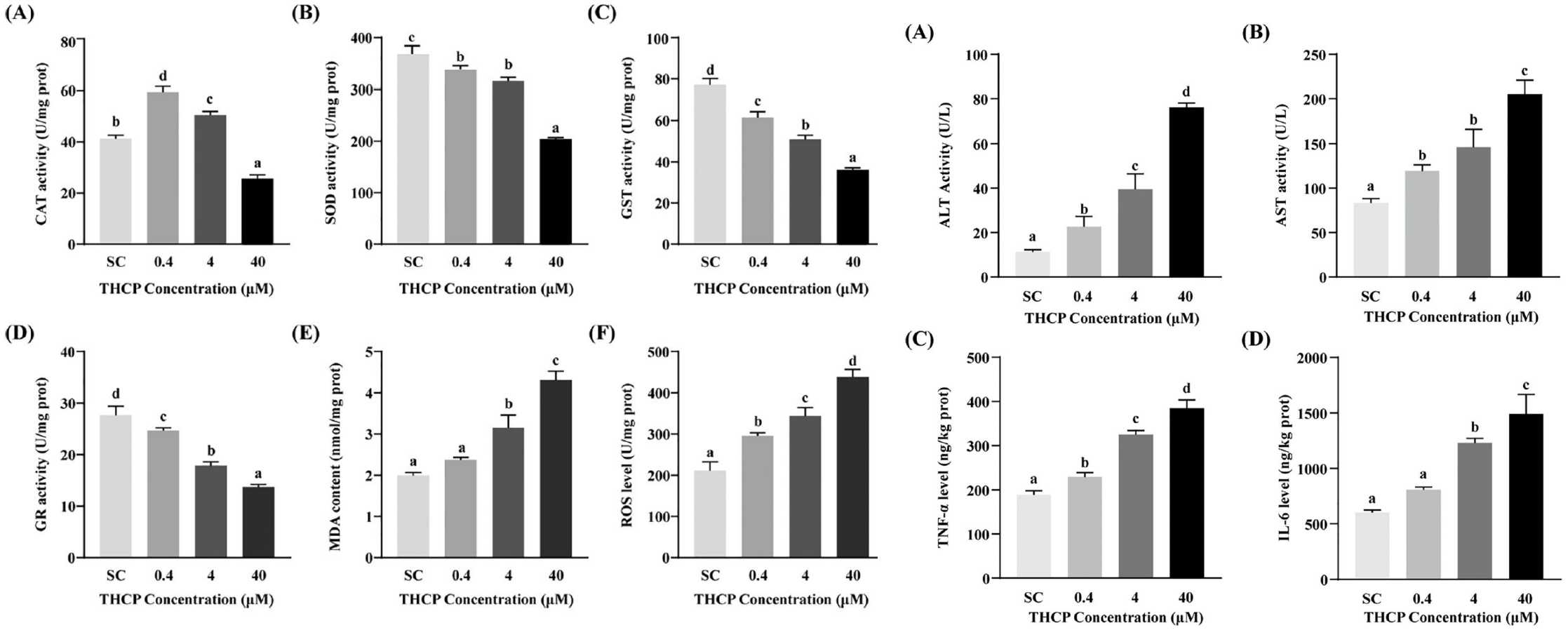
Thiamethoxam on the behavioral profile alteration in zebrafish



Yang et al. 2023

Sublethal physiological effects

THCP exposure induced oxidative stress, liver damage and the increases of inflammation markers



Z. Xie et al. 2022

Sublethal Genetics/DNA impacts

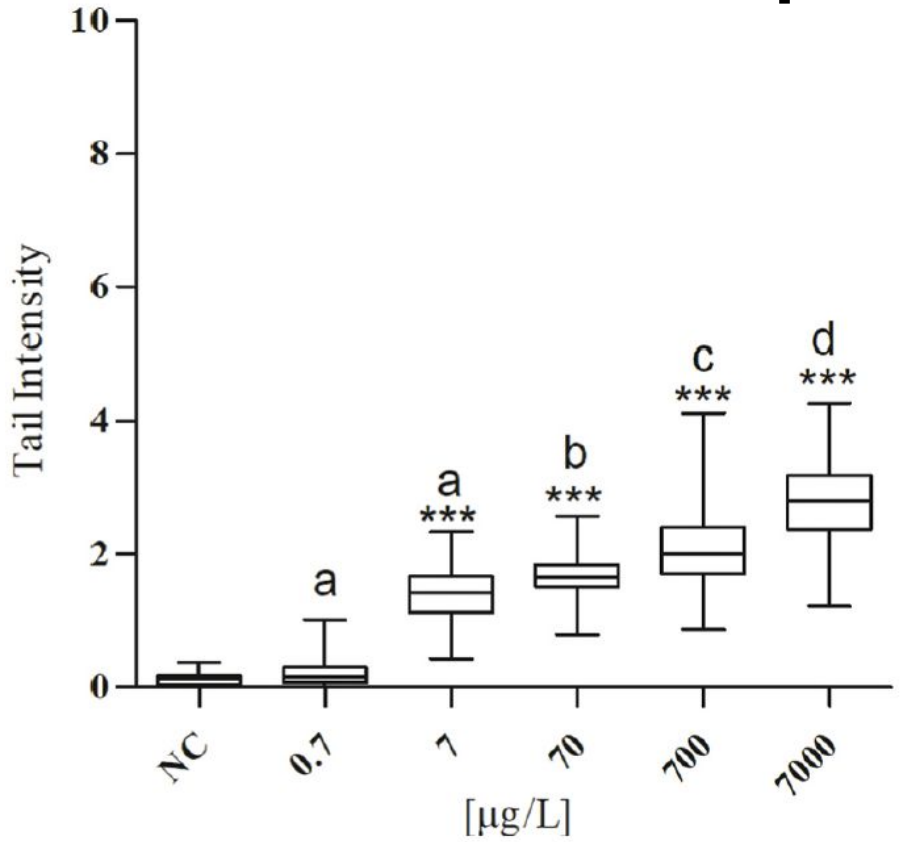


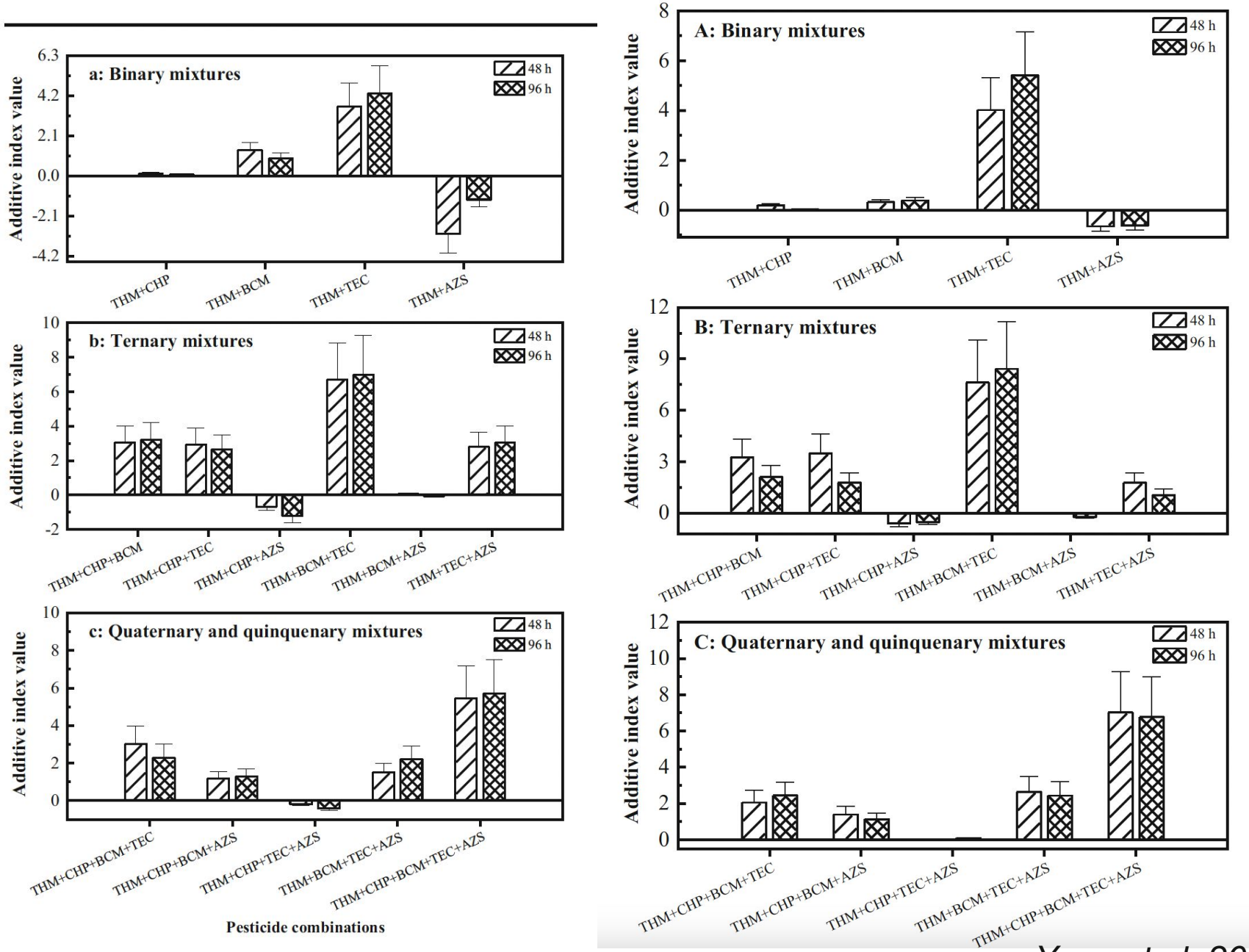
Fig. 2. Effect of imidacloprid on induction of DNA damage in *C. dubia*. Outcomes, expressed as Tail Intensity, are from 400 nuclei for each concentration. Data are presented as quartile box plot. Significant differences from negative control were determined with Dunnett's test (***$p < 0.0001$). Different letters for significant differences ($p < 0.05$) among concentrations (µg/L) were used for Tukey's HSD multiple comparison test.

Nugnes et al. 2023

Sublethal Genetics/DNA impacts

- Imidacloprid induced oxidative stress and genotoxicity revealed by downregulation of the immuno-antioxidant genes (*TNF-α*, *TLR-5*, *TLR-1, LYSC*, *LYSG*, *TGF-β*, *MYE, CXC, HSP90,* and *SOD1.* Rahman et al. 2023
- Imidacloprid altered the fish's genetic integrity through the occurrence of DNA damage. Iturburu et al. (2018) and Alvim and Martinez (2019)
- Down-regulation of immune-related genes was observed in *C. gariepinus* upon exposure to Imidacloprid Abdel Rahman et al., 2022a

Mixtures



Yang et al. 2021

QUESTIONS?

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