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SDHI pesticides (Succinate DeHydrogenase Inhibitors) are widely used as fungicides in agriculture or as nematicides or acaricides. These substances are toxic to mitochondria by disrupting cellular respiration and energy production in the cells of all living organisms, except bacteria. However, the regulatory assessment of SDHIs suffers from shortcomings, since mitotoxicity is not considered, nor are the effects at low doses, the presence of co-formulants, long-term impacts or potential synergies and cocktail effects when combined with other biotic and abiotic stressors.

Holimitox (<https://holimitox.fr/en/home/>) is a research network that has tackled this interdisciplinary issue to improve protection of bees, biodiversity and public health. First, we present a comprehensive review of the scientific literature on the contamination of honeybee matrices (pollen, nectar, wax, etc.) by SDHIs. Next, we introduce 21-day bee co-exposure tests with some SDHIs and the intestinal parasite *N. ceranae*, conducted with both active substances and their corresponding commercial formulations. Finally, using new, highly sensitive analytical methods, we present the results of the contamination of fruits and vegetables sold in France in comparison with data found in the world academic literature. Since these fruits and vegetables came from crops often pollinated by bees, these latter results offer insights into potential risks for bees and consumers.

Results show that SDHIs pose a significant threat to pollinators, biodiversity and public health. Given that mitochondrial dysfunction at the level of succinate dehydrogenase can lead to serious diseases such as neurodevelopmental disorders and cancer, it is imperative to better assess the toxicity of SDHIs at low doses and over the long term. Our findings also show that maximum residue limits (MRLs) should be reduced to offer better protection. As SDHIs are frequently used in combination with other fungicides, such as triazoles and strobilurins (e.g., straw cereals), it is necessary to promote alternative methods to reduce the use of SDHIs.

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Why are SDHI* pesticides of concern to beekeepers and scientists?

*Succinate DeHydrogenase Inhibitors

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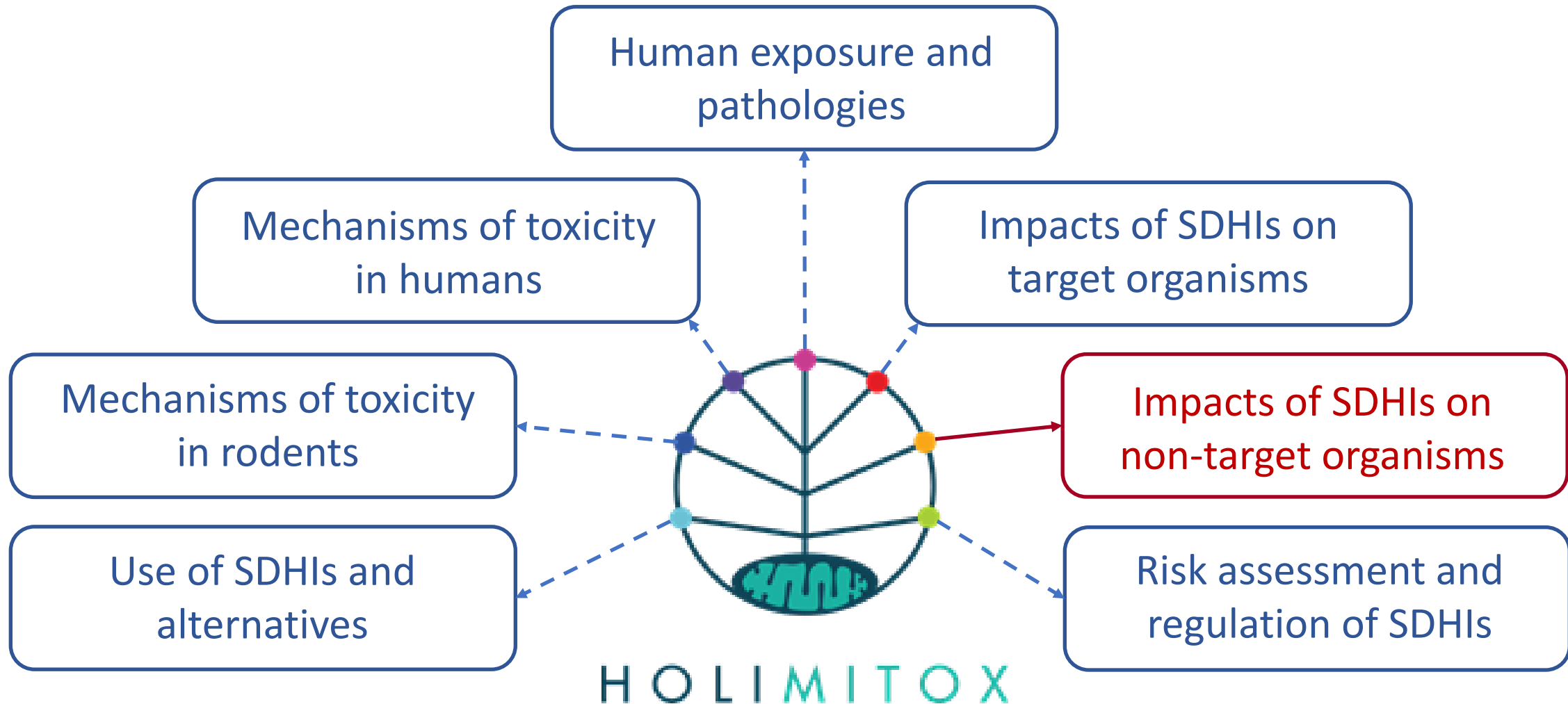
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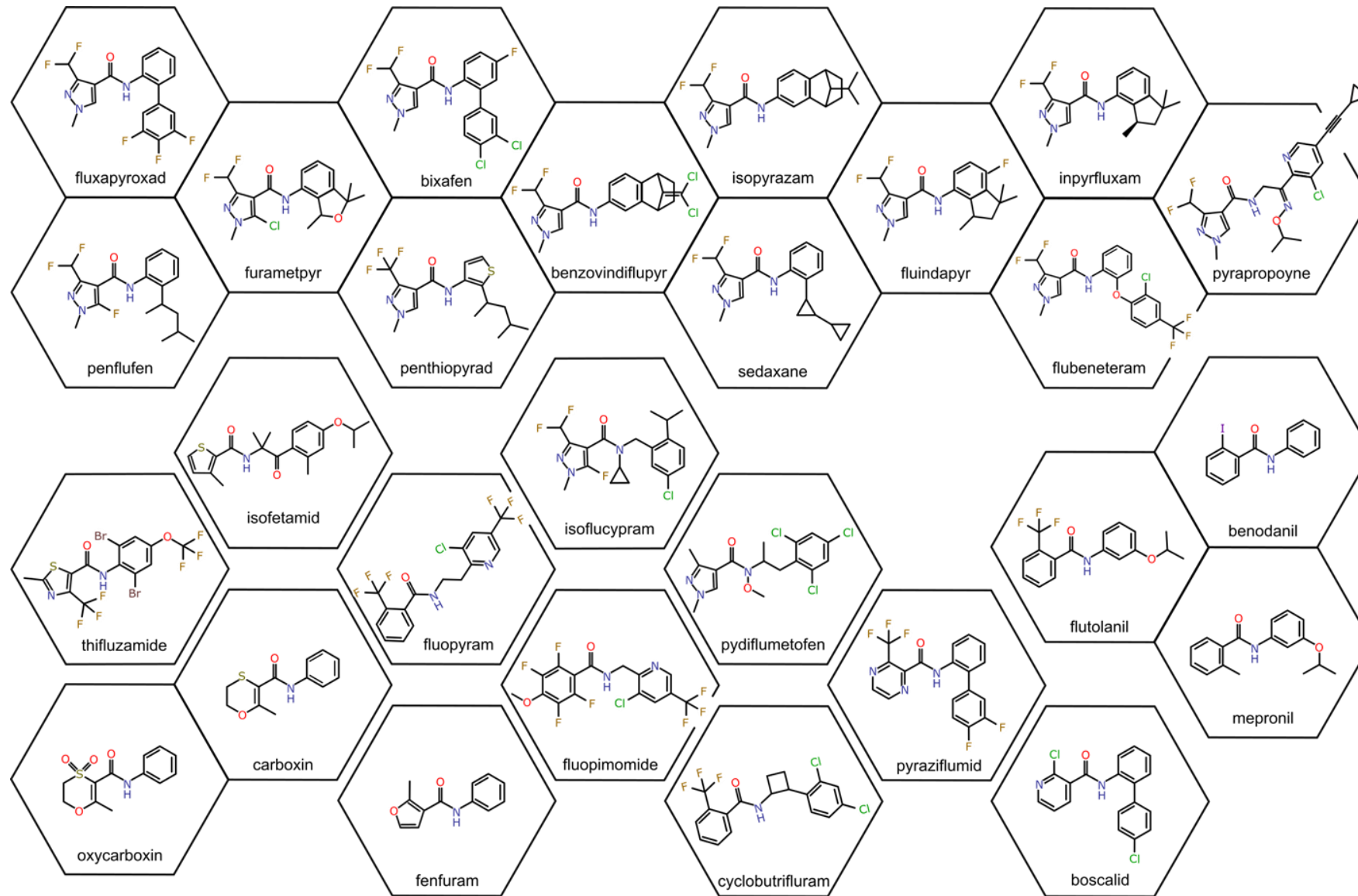
HOLIMITOX : Scientific network (16 laboratories) for the integrated assessment of mitochondrial toxic pesticides (<https://holimitox.fr/en/home/>)



SDHIs : 27 molecules, 16 are registered in USA (11 in Europe)



HOLIMITOX



benzovindiflupyr
bixafen
Boscalid
carboxin
Cyflumétofen
fluindapyr
fluopyram
flutolanil
Fluxapyroxad
inpyrfluxam
Isofetamid
oxycarboxin
penflufen
Penthiopyrad
pydiflumetofen
sedaxane

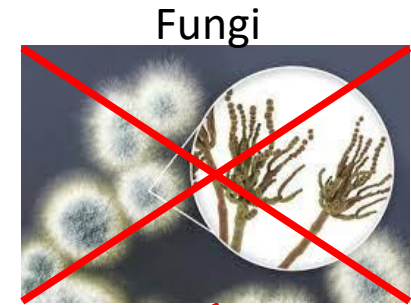
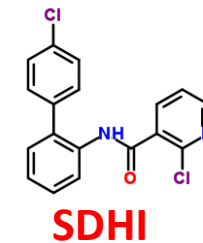
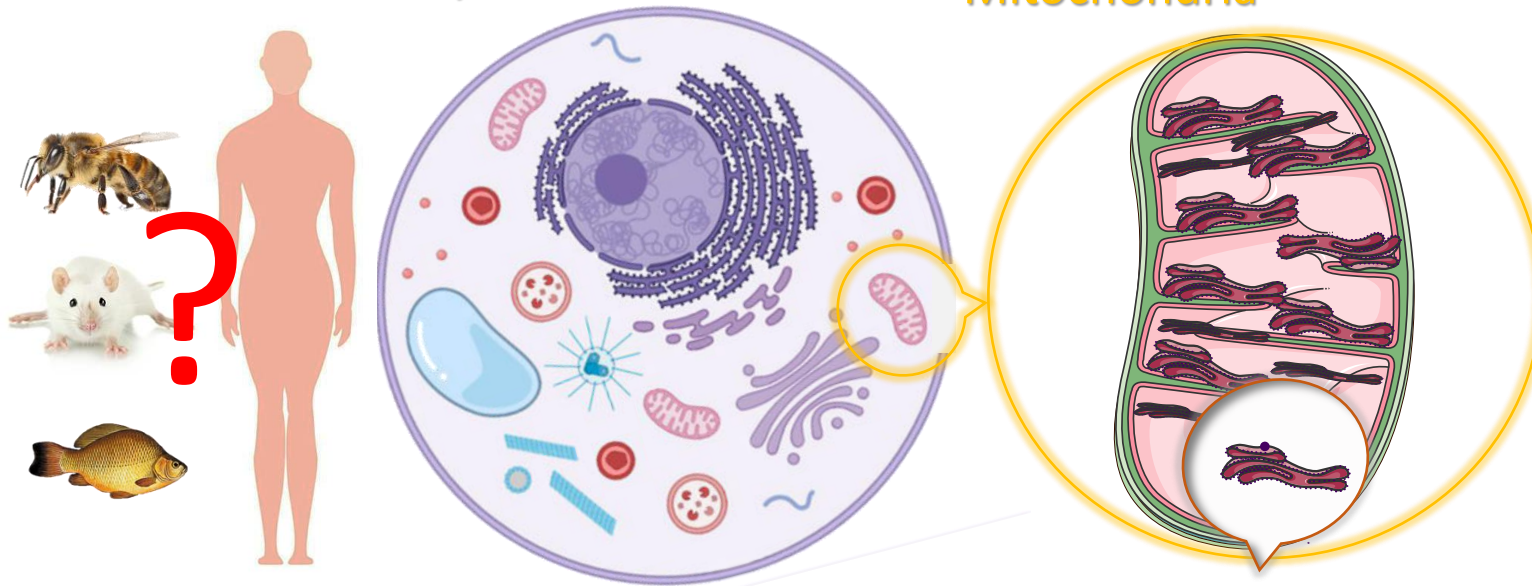
Mode of action of SDHIs (Succinate DeHydrogenase Inhibitors)



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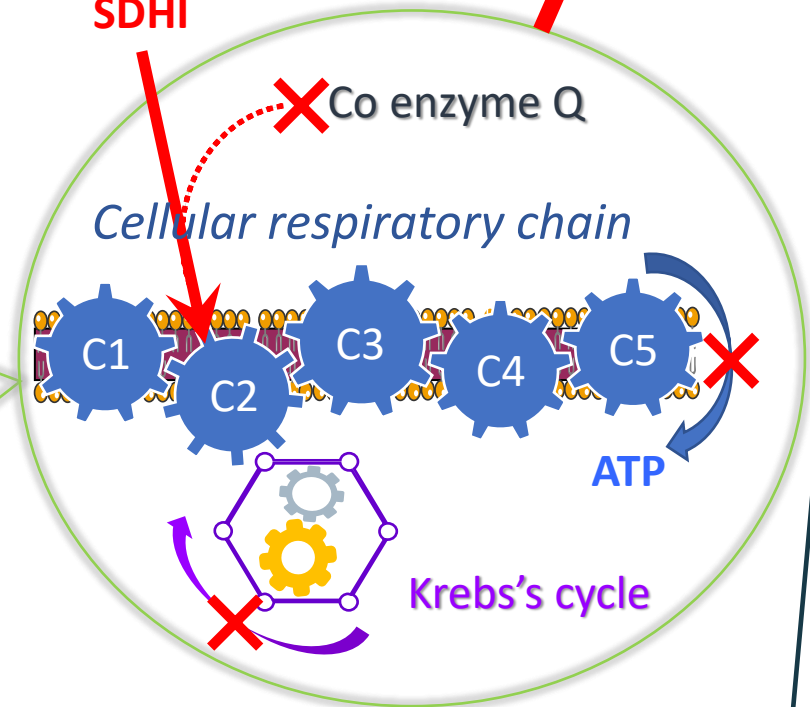
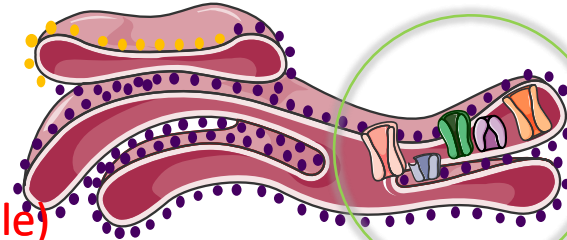
All Eukaryotic cells

Mitochondria



Fungi

Mitochondrial cristae



- Block the cellular respiratory chain
- Inhibit the production of cell energy (ATP)
- Accumulation of succinate & α Kg (Krebs's cycle)
- Conserved mechanism in all animal species
 - => Generation and proliferation of cancers?
 - => Neurotoxicity?
 - => Other effects?

Effects on honeybees (boscalid)

Noa Simon-Delso , Gilles San Martin, Etienne Bruneau & Louis Hautier

DOI: [10.1038/s41598-018-24746-9](https://doi.org/10.1038/s41598-018-24746-9) (2018)

[nature](#) > [scientific reports](#) > [articles](#) > [article](#)

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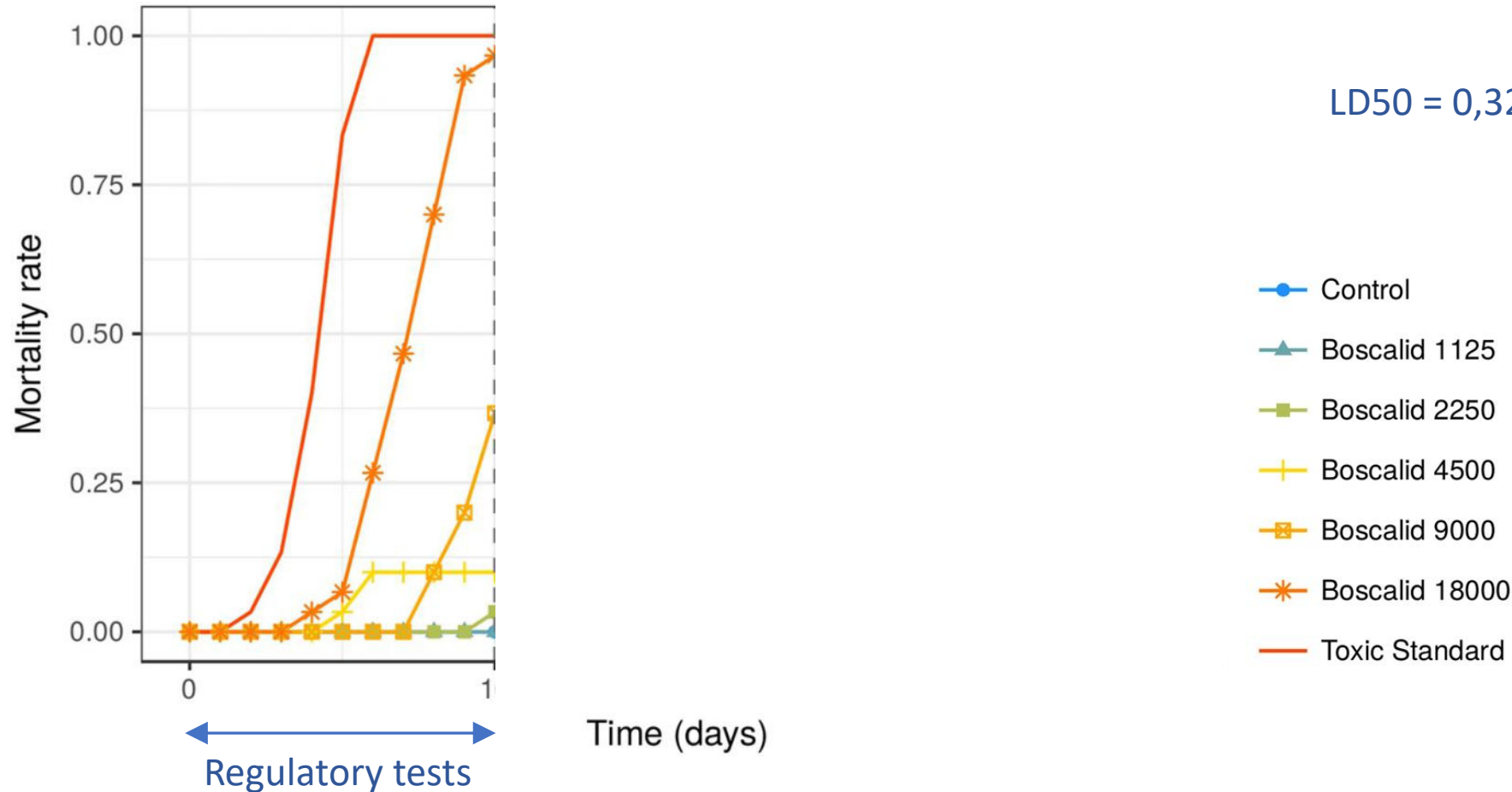
Time-to-death approach to reveal chronic and cumulative toxicity of a fungicide for honeybees not revealed with the standard ten-day test



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LC50 = 14,7 mg/L over 8 days

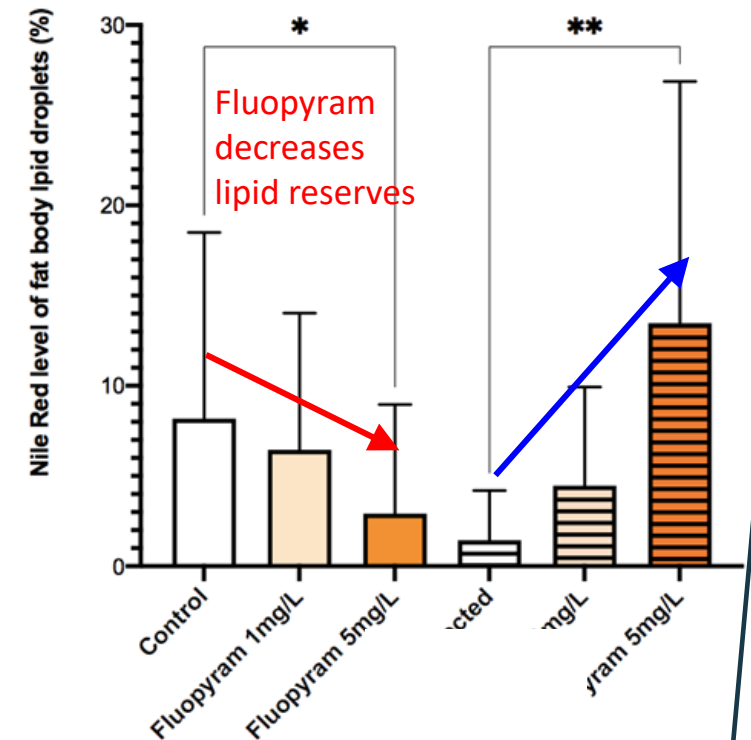
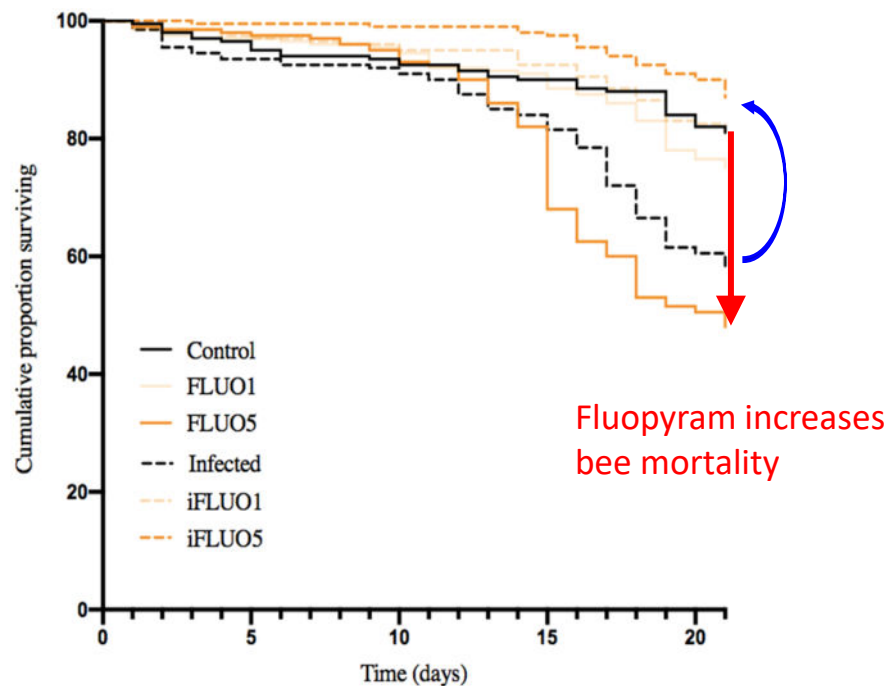
LD50 = 0,32 mg/bee over 8 days



Effects on honeybees (fluopyram)

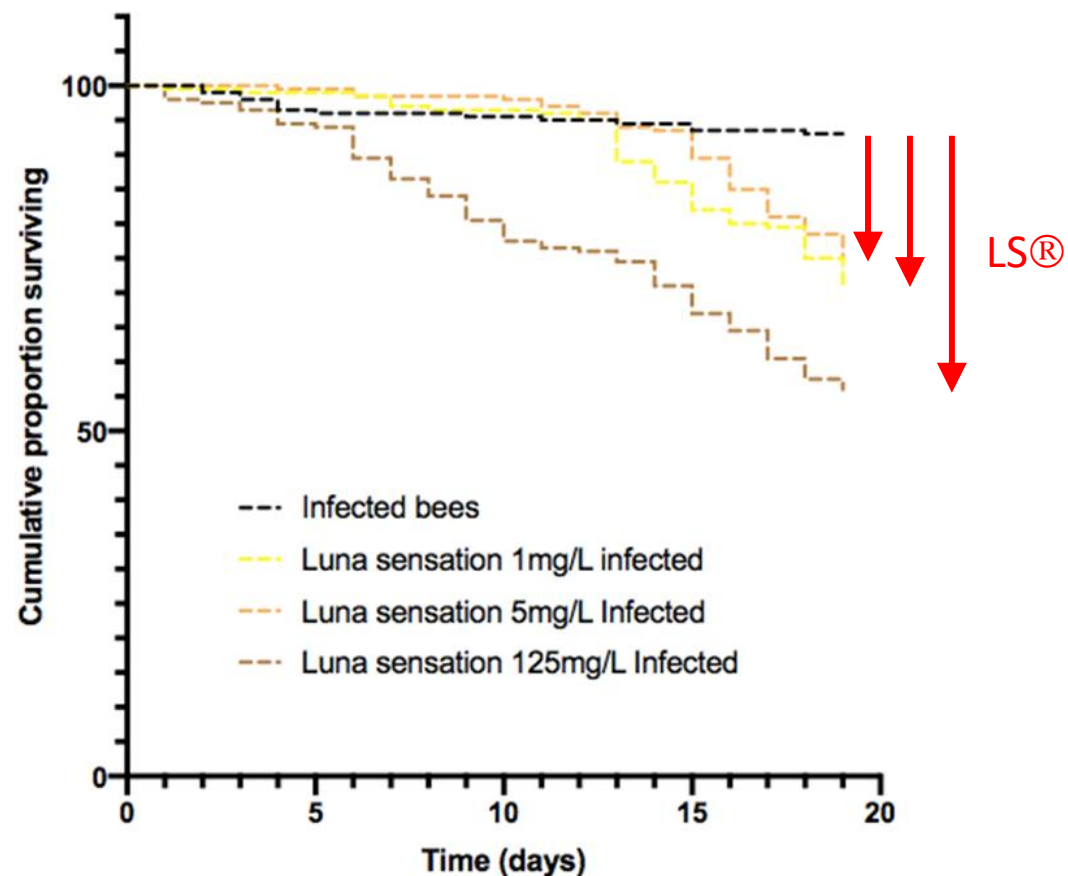


Without/with exposure to *Nosema ceranae* (bee brood frame), then exposure of emerging bees to fluopyram
Tests at 2 doses : Fluo1 : 1 mg/L (LD50/260) & Fluo5 : 5 mg/L (LD50/26)



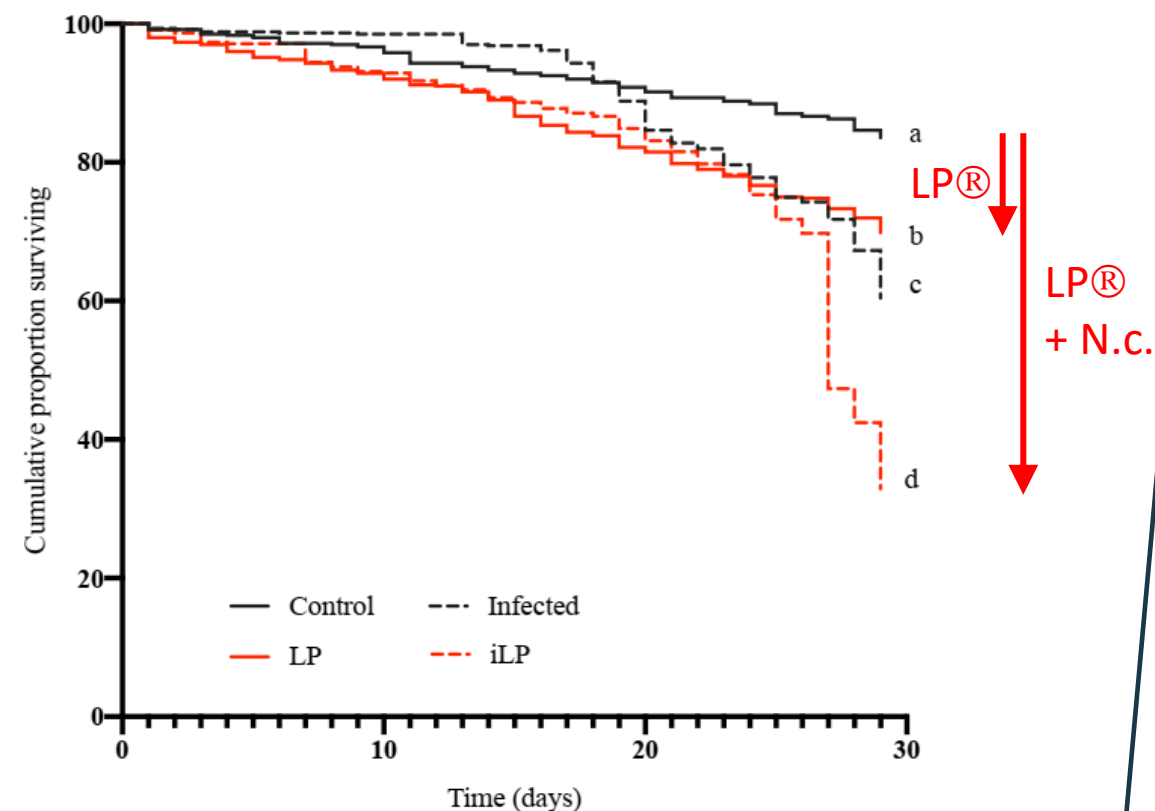
Effects on honeybees (fluopyram formulations)

Luna Sensation® (fluopyram + trifloxystrobin) with *N. ceranae*



⇒ Higher toxicity of the formulation

Luna Privilege® (fluopyram 50 mg/L) without/with *N. ceranae*



⇒ Synergy between formulation and *Nosema ceranae*

Exposure of honeybees to SDHIs



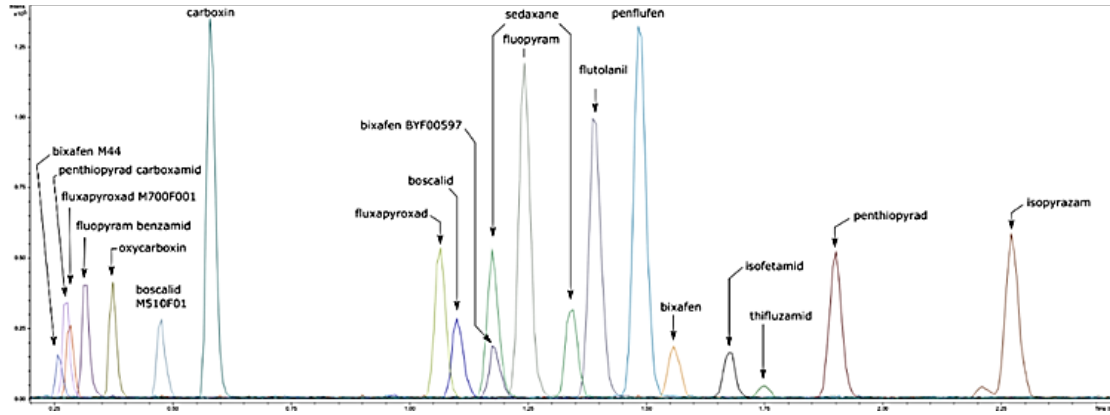
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Development and validation of a highly sensitive method for the analysis of succinate dehydrogenase inhibitors (SDHIs) in plant-based food and beverages

Camille Pasquet^a, Sylvie Guinchard^b, Marie Villier^b, Eléa Guyaz^b, Jean-Marc Bonmatin^a, Gaetan Glauser^{b,*}

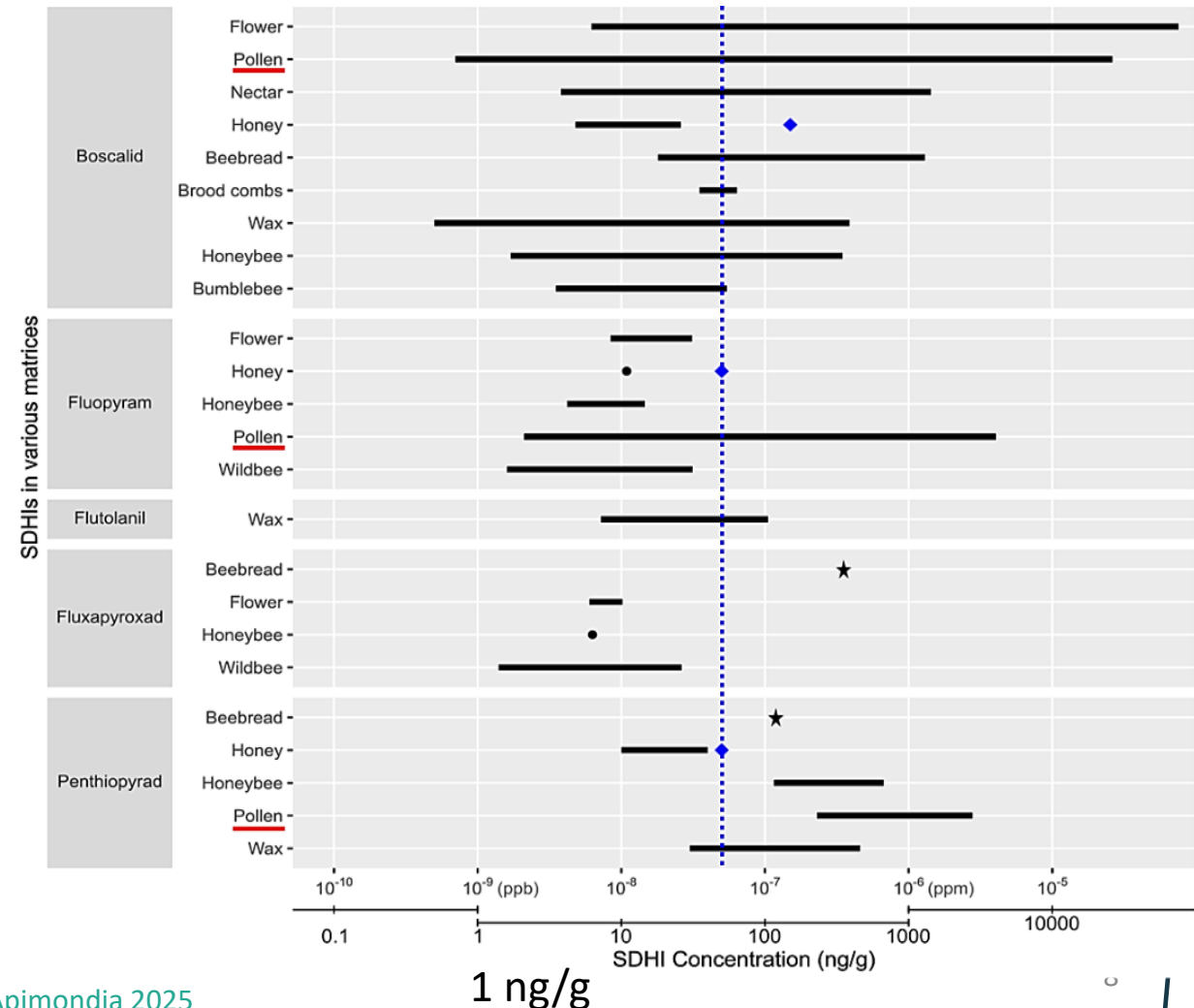
Food Chemistry 485 (2025) 144532 <https://doi.org/10.1016/j.foodchem.2025.144532>

UPLC/MS-MS: Very sensitive method to detect 12 SDHI and 7 metabolites



- Range (min-max)
- One data
- Mean value
- UE MRL (honey)
- Lowest UE MRL (honey: 50 ng/g) (Fluopyram, Penthiopyrad)

5 SDHIs contaminates pollen, nectar & bees, then the beehive (beebread, combs, wax)



Exposure of honeybees to SDHIs

Flowers (up to 30,000 ng/g)



Pollen (up to 3,000 ng/g)

Boscalid
Fluopyram
Flutolanil
Fluxapyroxad
Penthiopyrad



Honey (up to 40 ng/g)



Lowest EU MRL for
honey: 50 ng/g

Exposure of humans to SDHIs



Boscalid
Fluopyram



Boscalid
Fluopyram
Fluxapyroxad



Boscalid
Fluopyram

Conclusions

- The amount of SDHIs for crop production is increasing
 - The number of SDHIs in use is increasing
 - The mode of action of SDHIs is not selective to pest fungi
-
- SDHIs increase the mortality of **honeybees** by chronic exposure
 - SDHI formulations are more toxic than the SDHI alone
 - Antagonist effect of SDHI alone on *Nosema ceranae* development
 - But toxic synergies of SDHI formulations with *Nosema ceranae*
 - Synergy with a strobilurins (e.g., trifloxystrobin) increases toxic effects of SDHI
-
- ❑ Behavioural alterations were found on **fish** at environmental levels
 - ❑ Main effects on **human cells** suggest SDHI to be **mitotoxic, carcinogenic and neurotoxic**
 - ❑ Numerous organ alterations were found on **rodents** at the “acceptable daily intake” (ADI)
-
- ❖ Food and drinks in France contain levels of SDHIs below Maximum Residue Limits (MRLs)
 - ❖ However, EU- and USA-MRLs are not protective enough => set all MRLs at the lowest EU MRL for SDHIs (10 ng/g)



Thank you for your attention