# Investigating the mechanistic basis for species specific sensitivity towards insecticides

## Project

Industrialized civilizations depend on a large number of synthesized chemical compounds which can come into contact with the environment. Among these compounds, plant protection products (PPP) are designed to control pest organisms in agricultural settings but have the potential to cause unintentional adverse effects in non-target species. However, non-target species drastically differ in their sensitivity to PPPs which makes it challenging to estimate the potential risk communities face following PPP exposure. In order to better understand the potential risk for non-target species it is important to identify the underlying mechanisms driving species sensitivity differences. Such knowledge can be used to better understand the potential of PPPs to cause adverse effects in non-target species (Haas and Nauen 2021, Haas, Zaworra et al. 2021) and guide the development of novel PPPs with reduced environmental impact following a safety by design philosophy.

In recent years it has been discovered that detoxifying enzymes (P450s) can explain large differences in pollinator sensitivity to some classes of insecticides (Manjon, Troczka et al. 2018, Beadle, Singh et al. 2019, Hayward, Beadle et al. 2019, Haas, Zaworra et al. 2021). However, similarly large differences in species level sensitivity can also be observed in aquatic organism such as the water fleas *Daphnia magna* and the non-biting midge *Chironomus riparius.* In the case of two neonicotinoids (Clothianidin and Thiacloprid) *D. magna* exhibits high resilience (both LC50 > 40mg/L) while *C. riparius* is moresusceptible(both LC50 < 0.01 mg/L).However, the opposite is true for theorganophosphate Phosphamidon with *C. riparius* being comparatively resilient (LC50 = 1 mg/L) and *D. magna* being more sensitive (LC50 = 0.008 mg/L).

In this project we will investigate if, similarly to pollinators, P450 detoxification enzymes are responsible for the observed differences in species specific sensitivity after PPP exposure. We will use chemical inhibition of P450 enzymes to block their activity and directly test if such inhibition will result in:

1. An overall increase in susceptibility to PPPs if P450s play a role in shaping test species sensitivity to the tested PPPs
2. Assuming that similarly to bees differences in P450 efficiency are responsible for the observed intra species variation in susceptibility we expect a more pronounced increase in susceptibility for the PPP which the species was more tolerant for to begin with (i.e. *D. magna* x neonicotinoids & *C. riparius* x Phosphamidon).

## Planned experiments

Experiment 1: Confirm or establish the LC50 values (*D. magna* and *C. riparius*) for a nitro-neonicotinoid (Clothianidin), a cyano-neonicotinoid (Thiacloprid) and the organophosphate (Phosphamidon). In addition, we will investigate the potential toxic side effects of two P450 inhibitors (LC50 prochloraz & 1-aminobenzotriazole (ABT)) for both *D. magna* and *C. riparius* using a 48-well plate set up.

Experiment 2: Establish IC50 values for both P450 inhibitors (prochloraz & ABT) for *D. magna* and *C. riparius* using full body extracts to confirm the expected inhibition. the results of this experiment will determine the dose setting in experiment E3 (e.g. highest concentration not causing adverse effect).

Experiment 3: Measure the effects of co-exposure of insecticides used in E1 and a suitable P450 inhibitor on the insecticide LC50 (Compare E1 and E3).

## Location and Training

The training & practical work will be based in Monheim am Rhein Germany and include:

1. Culture maintenance of two model organism
2. Fluorescence (coumarin) based P450 enzyme activity assays
3. Plate based (48-well plates) acute toxicity tests for two model species
4. Data management practice
5. Statistical evaluation and presentation of the results

## Compensation

In order to support the project Bayer will provide a monetary compensation for the duration of the practical work.

## Contact

If you are interested in this position, please contact:

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## References

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