Reciprocal interactions between agrochemicals and the commensal gut microbiota impact honeybee health

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Bees are key pollinators suffering sharp population declines due, in part, to agrochemical usage. [1]. While agrochemicals are tested and regulated for their acute toxicity to bees, sub-lethal exposure can depress immunocompetence, pathogen resistance, and foraging behavior. These traits are modulated by the specialized microbial communities in the gut of social bees, who also play an indispensable role in digestion and synthesizing beneficial metabolites [2]. Therefore, investigating the mechanistic interplay between agrochemicals, bees and their microbiota is crucial to understand the full impact of chronic, sub-lethal agrochemical exposure. Limited findings already indicate that the honeybee gut microbiota is perturbed by widely used pesticides [3]. However, practical constraints have prevented widescale investigation of diverse agrochemicals.

We screened reciprocal interactions of chemical toxicity and microbial biotransformation of an agrochemical library against 20 isolate strains representing the species level diversity of the honeybee gut microbiota. We measured in vitro toxicity of 1054 pesticides, antibiotics, and other agrochemical compounds, finding that 13% of the chemicals inhibit bacterial growth at environmentally relevant concentrations. While broad spectrum fungicides such as chlorothalonil, fluazinam, or dodine were more often toxic than herbicides or insecticides, toxicity proved difficult to predict from chemical structure alone. Bacterial susceptibility also diverged sharply across bacterial genera. Many toxic compounds were degraded by the microbiota, though this provided little protective benefit for degrader strains nor cross-protection in microbial communities. We then confirmed that chronic oral exposure to sublethal pesticide doses can perturb microbiota assembly in adult bees, alter gut metabolic function and enhance infection by the opportunistic pathogen *Serratia marcescens*.

In parallel, we found significant biotransformation by at least one strain in 15% of the 656 measurable, non-toxic agrochemicals. Biotransformation was enriched in sulfonylurea and cyclohexanedione oxime herbicides as well as in organothiophosphate insecticides. Well known biotransformation reactions, such as nitroreductase activity, were prevalent. However, we also found numerous instances of unreported degradation and conjugation reactions. Together, our results highlight the gut importance of the gut microbiota in modulating agrochemical impacts on bees.

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