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Is glyphosate toxic to bees? A meta-analytical review

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Highlights

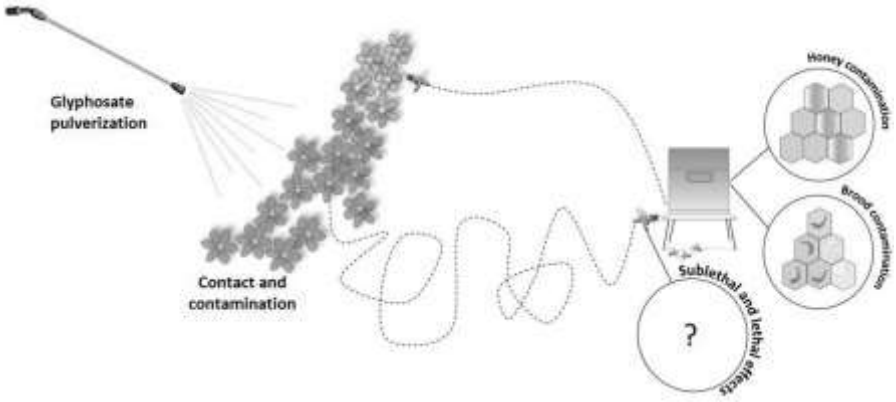
- Meta-analytical review correlating glyphosate (GLY) exposure with bee mortality.
- Significant differences between bees exposed to GLY and control group.
- Ingestion and contact of bees with GLY had a significant effect.
- Most bee species used as a study model were negatively affected by glyphosate.
- Further studies are suggested about sublethal effects of GLY on bees

Abstract

Glyphosate (GLY) is an herbicide widely used in agriculture. First considered as non-toxic or slightly toxic to bees, GLY and its different formulations have shown, more recently, to affect negatively the survival, development and behavior of these insects, even when used in doses and concentrations recommended by the manufacturer. Thus, the results of research on the toxicity of GLY to bees are often conflicting, which makes a meta-analysis interesting for data integration, generating a statistically reliable result. Therefore, this study aimed to evaluate the GLY effects on mortality of bees through a meta-analysis. For this, a search was carried out in the databases Web of Science, CAPES (Coordination for the Improvement of Higher Education Personnel - Brazil), Scopus, and PubMed. Papers that evaluated the effect of GLY on bee mortality published between 1945 and October 2020, were considered. After obtaining the data, R software was used to perform the meta-analytical tests. Sixteen papers on mortality were selected with 34 data sets. Most of the sets demonstrated differences between the control and experimental

groups, showing that the treatments with GLY caused higher mortality of bees. The results considering the methodology used (ingestion or contact), the phase of the biological cycle (adults or larvae), and the dose (ecologically relevant dose and recommended by the manufacturer) were different when compared with their respective control groups. Therefore, GLY can be considered toxic to bees. It is important to emphasize that this meta-analysis identified that papers assessing the toxicity of GLY to bees are still scarce, for both lethal and sublethal effects, mainly for stingless and solitary bee species.

Graphical abstract



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Introduction

Glyphosate (GLY) is the best-selling pesticide in the world, accounting for 71.6% of the active ingredients marketed (Benbrook, 2016). Its use stands out in Brazil, where it represents approximately 31.45% of the chemical products sold per year (IBAMA, 2020). GLY is an herbicide from the chemical group [N-(phosphonomethyl) glycine], with the molecular formula $C_3H_8NO_5P$ (Molecular weight = 169.1 $g.mol^{-1}$), used in the control of several weed species (Dill et al., 2010; Richmond, 2018).

This active principle acts by inhibiting the growth of plants and some microorganisms, as it interferes with the functioning of the enzyme 5-enolypruvylshikimate-3-phosphate synthase (EPSPS). This enzyme acts on the metabolic pathway of “shikimic acid”, important in the formation of the amino acids phenylalanine, tyrosine, and tryptophan, used in protein synthesis (Amarante Junior et al., 2002; Ledoux et al., 2020).

Glyphosate is commonly formulated in its form of isopropylamine salt (IPA salt), though several other related chemical forms are also commercialized. In the 1970s, glyphosate was introduced in the market as Roundup™, which also includes the surfactant polyoxyethyleneamine (POEA) in the commercial product formulation (Pérez et al., 2011). Following the introduction of Roundup™, the use of glyphosate and several other glyphosate-based products increased significantly (Benbrook, 2016; Pérez et al., 2011; Richmond, 2018). Nowadays, agricultural activities are highly dependent on the use of glyphosate-based herbicides, and the global consumption of these products has increased hundreds-fold since the development of genetically modified plants in the mid-1990s (Richmond, 2018). Despite the benefits of using pesticides in agricultural activities (Lewis et al., 2016), including GLY, if not properly used they can cause negative impacts on ecosystems through contamination of water, air, food, fauna, and flora (Giesy et al., 2000; IARC, 2017; WHO, 2017).

While several studies have acknowledged GLY and glyphosate-based herbicide as products practically non-toxic or slightly toxic to animals (Blake and Pallett, 2018; Dill et al., 2010; Giesy et al., 2000; Rolando et al., 2017), other researches have shown negative effects on non-target organisms (Pérez et al., 2011; Gill et al., 2018; Richmond, 2018), including *Apis mellifera* (Balbuena et al., 2015; Gill et al., 2018; Motta et al., 2020; Richmond, 2018) and several other bee species. Regarding bees, they are indubitably among the most exposed organisms to glyphosate-based products, since these insects depend on resources produced by angiosperms, such as pollen and nectar (Michener, 2007).

In this context, GLY can decrease food resources, reducing the diversity of plants around the crop and, consequently, reducing pollen and nectar. It can also cause the contamination of forage bees when they go in search of resources to maintain the hive (Johnson, 2015). Lethal and sublethal effects of GLY have been observed to larvae and adults of several bee species (Blot et al., 2019; Motta et al., 2018; Nocelli et al., 2019; Pires et al., 2016; Ruiz-Toledo and Sánchez-Guillén, 2014; Tomé et al., 2020; Vázquez et al., 2018). Moreover, it is also shown that GLY impairs the cognitive capacities needed to navigate successfully back to the hive (Balbuena et al., 2015), as well as the sleep in honey bees (Vázquez et al., 2020a), indicating a negative effect of this herbicide on bee behavior. Thus, it is not surprising that GLY is now recognized as moderately toxic to bees (PPDB, 2020).

In the environment, the GLY molecule is degraded and transformed into other compounds by microbial action (Mamy et al., 2016; Gill et al., 2018). The main product of GLY degradation is aminomethylphosphonic acid (AMPA), which can contaminate water, soil, food and living organisms (Blot et al., 2019; Gill et al., 2018; Van Bruggen et al., 2018; Zhang et al., 2015). Recently, metabolites resultant from GLY degradation have also been focus of interest concerning their impacts on bees. Specifically, data on the effect of AMPA exposure to bees have become available (Blot et al., 2019; El Agrebi et al., 2020), revealing that AMPA is neither lethal to *A. mellifera* (El Agrebi et al., 2020) and nor alters its intestinal microbiota (Blot et al., 2019). However, the number of studies is still scarce to draw any definitive conclusion on the effects of these residues on bees.

With more than 20,000 species described (Orr et al., 2020), bees are important pollinators of both natural vegetation and crops, participating in the cross-fertilization of most angiosperms (Michener, 2007). They are involved in the reproduction of approximately 73% of the vegetables grown in the world, increasing the yield of crops and the genetic variability of plants (Beringer, 2019; Calderone, 2012; FAO, 2013). In addition, their products are useful for humans, such as honey and propolis (FAO, 2013; Pires et al., 2016). However, GLY residues in samples of honey have been detected in concentrations above the limit of quantification – LOQ (Rubio et al., 2014). In this context, some species of bees are being used as bioindicators of environmental contaminants (Balayiannis and Balayiannis, 2008; Quigley et al., 2019). Bees have also been used as an animal model for human cell testing (Maleszka, 2014).

Considering the importance of bees, researchers have been working to explain the possible causes of the decline in bee populations and colony collapse disorder (CCD). In this perspective, studies that evaluate the effect of glyphosate-based products on bees are becoming increasingly important for understanding the possible impacts on different species (Cullen et al., 2019; Goulson, 2003; Pires et al., 2016).

However, many papers report conflicting, or even contradictory results regarding the effect of GLY on bees. In this sense, the development of a meta-analysis is useful to compile results from different studies, since it uses mathematical criteria, synthesizing the data and enabling the formation of a statistically reliable conclusion on the subject (Fagard et al., 1996; Hua and Bureau, 2012). In addition, as far as we know, there are no meta-analyses on the impact of GLY on bees. Therefore, the objective of this study was to evaluate the lethal (mortality) effects of the herbicide GLY on several species of bees through a meta-analysis.

Section snippets

Study development, data search and structuring

This is a meta-analytical review conducted in accordance with the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA, 2015). A search was conducted in the electronic databases “Web of Science” (http://www.webofscience.com↗), Periódicos CAPES (Coordination for the Improvement of Higher Education Personnel – Brazil) (https://www.periodicos.capes.gov.br/↗), Scopus (https://www.scopus.com/↗), and PubMed (https://www.ncbi.nlm.nih.gov/pubmed/↗). For the

Selection of items and data sets

After the initial search carried out in the databases, the abstracts were read, and several papers excluded. Subsequently, each paper was evaluated to verify whether it presented the necessary data for the meta-analysis. Finally, papers with numerical data on the mortality of bees exposed to GLY and a control were included. After refinement, 52 papers were found, of which 16 papers were selected because they met all the inclusion criteria, generating 34 data sets (Fig. 1, Table 1).

Some papers

Discussion

In recent decades, several papers have evaluated the lethal and sublethal effects of GLY on non-target organisms, using several animals as models of toxicological evaluation (Desneux et al., 2007; Ghisi et al., 2016; Giesy et al., 2000; Gill et al., 2018). Although many papers have used bees for toxicological evaluation (Abraham et al., 2018; Blot et al., 2019; Dai et al., 2018; Helmer et al., 2015; Motta et al., 2018; Ruiz-Toledo and Sánchez-Guillén, 2014; Tomé et al., 2020), this is the first

Conclusion

The present study supports the hypothesis that the exposure of bees to GLY and glyphosate-based formulations, in ecologically relevant doses or in recommended concentrations used in agricultural settings, might cause lethal effects (mortality) in these insects, since in most categories significant differences were reported between the experimental and control groups. The GLY ingestion (food), spraying and contact with GLY had a significant effect on bees. Adult bees or larvae were shown to be

CRediT authorship contribution statement

Lucas Battisti: Conceptualization, Methodology, Data curation; Formal analysis, Investigation, Writing - original draft. **Michele Potrich**: Conceptualization, Investigation, Resources, Project administration, Supervision. **Amanda Roberta Sampaio** and **Raiza Abati**: Formal analysis, Investigation, Writing - original draft. **Nédia de Castilhos Ghisi**: Methodology, Data curation; Formal analysis, Writing. **Fabiana Martins Costa-Maia**: Formal analysis, Investigation. **Claudia Bueno dos Reis Martinez** and

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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