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REVIEW

The Impact of Pesticides on the Antioxidant System of *Apis mellifera* L. Bees - A Systematic Review

Iloran do Rosário C. Moreira, Guilherme Duarte F. Souza, Aline Astolfi, Isabella Cristina C. Lippi,
Jaine da Luz Scheffer, Renato A. Arruda, Ricardo O. Orsi

Center of Education, Science and Technology in Rational Beekeeping (NECTAR), College of Veterinary Medicine and Animal Sciences, São Paulo State University, Botucatu-SP, Brazil

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Corresponding author
Ricardo de Oliveira Orsi
Faculdade de Medicina Veterinária e
Zootecnia, FMVZ – Campus Botucatu
Distrito de Rubião Junior s/nº
Caixa Postal 560, CEP: 18618-970
Botucatu, São Paulo, Brasil.
E-Mail: ricardo.orsi@unesp.br

Abstract

During foraging, bees come into contact with different pesticides when collecting crop resources, affecting not only the bees but also the entire colony, resulting in damage to the antioxidant and immune system and a reduction in the number of individuals in the colony. An efficient antioxidant system is essential for bees due to their high metabolic rate, which produces significant free radicals under physiological conditions. Antioxidant enzymes such as *superoxide dismutase (SOD), catalase (CAT)*, and *glutathione S-transferase (GST)* are essential for combating oxidative stress. To better understand these effects, we adopted a systematic approach to review existing research on the potential impacts of pesticides on the antioxidant system of honey bees. Therefore, this review aims to list the papers published between 2020-2023 and show the effects of pesticides (insecticides, herbicides, and fungicides) on the antioxidant system of honey bees, focusing on the enzymes *CAT*, *SOD*, and *GST*. A total of 19 articles were found that met the criteria of this review, of which approximately 89% of the experiments were conducted in the laboratory and only 11% in the field. All of the studies assessed the exposure of bees to pesticides through ingestion, highlighting the lack of studies using the contact exposure method and conducting experiments in the field. It was, therefore, possible to suggest several points for future research to improve the current knowledge base on the potential effects of pesticides on honey bees.

Introduction

Modern agriculture is increasingly dependent on the use of pesticides due to the constant increase in pests in the field, which affects crop yields and quality (Todd et al., 2020; Wu et al., 2020). It is estimated that in the coming years, there will be a significant growth in pesticide use, intensifying the risks and negative impacts on non-target organisms, such as bees (Zhao et al., 2022).

While foraging, bees encounter several pesticides, both directly and indirectly, by gathering resources like pollen and nectar from different crops that may have pesticide residues, resulting in contamination through contact and ingestion (Lundin et al., 2015; Jiang et al., 2018; Favaro et al., 2019). The contaminated resource may enter the colony, facilitating the contamination of all members (Johnson, 2015) and leading to both immediate and prolonged issues, including stunted development, damage to the immune and antioxidant systems, and decreased colony population (Al-Dalaen & Al-Qtaitat, 2014; Feazel-Orr et al., 2016; He et al., 2021).

Pesticides are either biological agents or artificially created substances designed to eliminate or limit the growth of organisms (Leska et al., 2021). Herbicides are the most commonly employed pesticides globally, followed by insecticides and fungicides (Barboza et al., 2018). Herbicides are extensively utilized in managing weeds to enhance crop

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quality and production (Ggiglio & Vommaro, 2022). However, they cause direct and indirect effects on non-target organisms (Sharma et al*.,* 2018; Thanomsit et al*.,* 2020).

Studies show that herbicides cause various physiological and behavioral effects in organisms of different species that play important ecological roles in agroecosystems (Freemak & Boutin, 1995; Gusntone et al*.,* 2021), such as nematodes (Sánches-Moreno et al*.,* 2015), earthworms (Stellin et al*.,* 2018), springtails and isopods (Niemeyer et al., 2018), spiders (Michalková & Pekár, 2009; Korenko et al*.,* 2016), insects (Prosser et al*.,* 2016; Sharma et al., 2018) and bees (Alamarsi et al*.,* 2020).

Insecticides control pests but can affect many non-target organisms, such as pollinators, especially *Apis mellifera* bees. Bee colony deaths caused by insecticides have been frequently reported in recent decades (Goulson et al., 2015; Tsvetkov et al., 2017; Zao et al*.,* 2020). This is due to the growing understanding of the harmful effects of these products on bees and other non-target organisms (Tsvetkov et al*.,* 2017; Colin et al., 2019).

Research indicates that contact with agricultural insecticides leads to considerable harm to bee health (Dulin et al., 2014; Tosi & Nieh, 2017; Li et al., 2019; Naiara Gomes et al., 2020), including the suppression of vitellogenin (Christen & Fent, 2017), injury to the optic lobes, a decrease in synapses between the compound eyes and the optic lobes (De Almeida et al., 2013; Fisher et al., 2014), and alterations in the temperature of the flight muscles. Along with inhibiting chemosensory reactions, immunity, and the expression of detoxification-related genes (Tan et al., 2015; Christen et al., 2016), it may also lead to difficulties in learning, muscle growth, movement, flight ability, and disorientation (Zhao et al., 2022). Besides neonicotinoids, bees come into contact with various other insecticides, including pyrethroids, chlorantraniliprole, spinosad, flupyradifurone, and sulfoxaflor (Main et al., 2020).

In addition to insecticides, different chemicals such as acaricides and fungicides, which are often incorporated into seed treatments (coating) and have systemic properties, can also pose risks to bees (Zubrod et al., 2019), as they are highly soluble in water and can be absorbed by plants and translocated by stems, leaves, pollen, nectar and guttation water during plant growth (Sanchez-Bayo; Goka, 2016). In addition, residues from fungicide application on seeds can also be airborne during planting, for example, the planting abrasion of the seed coat as the seed passes through the planter machinery, exposing bees to dust particles by means cuticular contact or inhalation (Krupke et al., 2012; Boyle et al., 2019). Fungicides applied to seeds can persist in low concentrations in plant tissues for several months (Nettles et al., 2016) and in the soil for many years (Lewis et al., 2016), which can result in pollen and nectar contamination of flowers that were open during the fungicide application (Rondeau & Raine, 2022). Bee contact with fungicides can trigger a series of effects, including increased mortality of brood (larvae) and adult bees (Domingues et al., 2017; Fisher et al., 2018; Dai et al., 2018), disorientation (Aartz & Pitts-Singer, 2015), and reduced sperm viability in honey bee drones (Fisher & Rangel, 2018). In addition, when the fungicide is combined with other products, it can have synergic effects, thus increasing its toxicity to bees, which can increase the susceptibility of honey bees to pathogens (Zaluski et al., 2017; Rondeau & Raine, 2022).

The most common active ingredient concentrations used in toxicological studies are environmentally relevant, lethal (LD_{50}), and sublethal. The environmentally relevant dose is determined by averaging the doses found in the field, which can be present in pollen, wax, bees, water, and other resources. This dosage can cause damage to bees, such as altering the regulation of genes in the digestive system (Astolfi et al*.,* 2022).

The LD_{50} or LD_{25} (lethal dose) causes the death of up to 50% or 25% of a population, which is a higher dose when compared to sublethal doses of pesticides. Pesticides that enter the habitats surrounding agricultural land through drift, runoff, and volatilization directly affect the vegetative and reproductive phases of native plants. This results in structural changes in communities and a reduction in species richness and abundance (Florencia et al., 2017; Giglio & Vonmaro, 2022), affecting the ecological dynamics of species associated with crops (primary and secondary consumers, decomposers) (Prosser et al., 2016; Kraus & Stout, 2019), involving species that provide ecosystem services (Pleasants & Oberhauser, 2013), such as pollination (Russo et al., 2020). In bees, it is possible to observe the harmful effects of this dosage related to health, foraging, gene expression, caste differentiation, weight gain, colony growth, and reproductive function (Bernauer et al., 2015; Dos Santos et al., 2016; Lima et al., 2016; Chmiel et al., 2020).

The exposure of bees to pesticides induces oxidative stress, increasing the presence of free radicals in their organisms. Such damage caused by exogenous pollutants is combated by the insects' antioxidant and detoxification systems (Olgun et al*.,* 2020).

Oxidative stress occurs when oxygen radicals are produced in excess in cells, exceeding the body's normal antioxidant capacity. The stress is characterized by increased production of reactive oxygen species (ROS), which promotes the simultaneous impairment of their elimination systems (Olgun et al., 2020). The increased concentration of ROS can cause oxidative damage to proteins, lipids, and nucleic acids, thus compromising the functions of cells, organs, or even the entire organism, which can lead to death (Kodrík et al., 2015). ROS can be classified into two groups: free radicals and non-radicals. Free radicals arise when molecules have unpaired electrons, making them reactive in the search for stability. In contrast, non-radical forms are generated when two free radicals share their unpaired electrons (Kodrík et al., 2015). The primary sources of ROS are mitochondria (respiratory chain and deamination of biogenic amines), microsomal oxidation of xenobiotics, and phagocytosis (Sagona et al*.,* 2021).

In insects, among the antioxidant enzymes, superoxide dismutase (*SOD*), catalase *(CAT*), and glutathione S-transferase *(GST*) play a crucial role in combating oxidative stress. An efficient antioxidant system is vital for insects, whose high metabolic rate contributes to the production of significant quantities of free radicals under physiological conditions (Candy et al., 1997; Tawfik et al., 2020).

The enzymes *SOD* and *CAT* can remove the excess free radical of superoxide anion (O2-) and hydrogen peroxide in insects to maintain the oxidative balance (Chen et al., 2021). SOD is a metalloenzyme that catalyzes the conversion of superoxide anion into hydrogen peroxide and oxygen. In bees, three types of SOD have been described: the first, cytosolic copper, zinc superoxide dismutase (SOD1 or CuZnSOD); the second, MnSOD, acts as a scavenger of ROS metabolites within the mitochondrial matrix; and the third, extracellular Cu/ZnSOD (SOD3) (Corona & Robinson, 2006; Nikolic et al., 2016; Sagona et al., 2021).

Meanwhile, CAT is a cytoplasmic protein (Corona & Robinson, 2006) that efficiently converts hydrogen peroxide into water and oxygen. GST is a crucial enzyme for detoxification and the antioxidant system in bees, working together with glutathione peroxidase to metabolize toxins and maintain physiological homeostasis (Zou et al., 2017; Wang et al., 2020; Sagona et al., 2021). SOD, CAT, and GST play essential roles in maintaining cellular health and function in honey bees.

This study aims to provide an overview of the known toxicological effects of pesticides on the antioxidant system of honey bees, providing future perspectives for a more accurate assessment of the toxicity and risk of pesticides to honey bees. To this end, a systematic review of the literature was carried out to provide information on the effects of lethal, sublethal, environmentally relevant doses and the association of a wide range of pesticides used and affecting the antioxidant system of honey bees. Specifically, we aim to answer the following questions:

1. In what year and geographical location did the research take place?
2. Which honey bee subspecies was most commonly studied, and how was pesticide exposure carried out?
3. Which pesticides and associations have been most studied, what were the doses, and at what stage of life were the bees most studied?

Materials and Methods

Methods for bibliographical research

The search for scientific articles was based on the methods proposed by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Clarke et al., 2011; Galvão et al., 2015). Keywords were chosen after reviewing publications related to the subject of interest, including *Apis mellifera*, antioxidant system, pesticides, lethal dose, sublethal dose, and stingless bees.

The words were written in English to optimize the search results. Boolean operators (AND, OR, and NOT) were used to make the search more specific. The keywords and Boolean operators were inserted into the search bar: "*Apis mellifera* AND antioxidant system AND pesticides AND lethal dose OR sublethal dose NOT stingless bees". The following databases were used for the research: Scopus, CAPES Journal Portal, and Google Scholar.

Inclusion and exclusion criteria

Experimental studies examining the effects of herbicides, insecticides, and fungicides, as well as their associations with the antioxidant system enzymes CAT, SOD, and GST in honey bees, were included. Only articles published in English were included. Research dealing with native bees, reviews, meta-analyses, articles in other languages, and articles published before 2020 were excluded, and only articles published between 2020 and 2023 were selected. All the articles included were taken from peer-reviewed journals, and the final database query was carried out on October 17, 2023.

After selecting the articles, the content was read in full to ensure it aligned with the study's initial purpose. Following the reading, the primary information from the articles was tabulated. The selected studies did not consider any restrictions on the use of pesticides.

Results

Using the selected keywords *(Apis mellifera* AND antioxidant system AND pesticides AND lethal dose OR sublethal dose NOT stingless bees), the first search resulted in a primary dataset of 306 publications. To ensure the consistency of the research included in our review, we opted to use only peer-reviewed journal articles reporting primary research; therefore, non-peer-reviewed articles were removed from the dataset. Articles that targeted native bees, systematic reviews, or that did not address the *SOD, CAT,* and *GST* genes being all or at least one of the genes were removed, resulting in 27 remaining articles. These were then examined to determine whether the criteria of this review were met, i.e., whether the article investigated the direct effects on the bees' antioxidant system of at least one herbicide, insecticide, fungicide, and association in any subspecies of the genus *Apis*, resulting in the final set of 19 articles, all of which had their data tabulated.

For each article, the following information was extracted: complete bibliographic reference, country, method of exposure (contact or ingestion), pesticide used, dosage (lethal, sublethal, or environmentally relevant), year of publication, country, whether the authors conducted experiments in the field or laboratory, and genes evaluated (Table 1).

Table 1. Articles selected according to the inclusion criteria.

Papers	Country	Exp.		Pesticides	Products		Exhibition		Genes		
		Field	**Lab.**		**Commercial**	**Pure**	**Cont.**	**Ing.**	***SOD***	***CAT***	***GST***
Zaluski et al., 2020	Brazil	X		Fipronil and pyraclostrobin	X			X	X		X
Li et al., 2021	China		X	Isoclast: 50% sulfoxaflor	X			X	X	X	X
Orčić et al., 2022	Serbia		X	Thiacloprid and clothianidin	N/A			X	X	X	X
Gao et al., 2022	China		X	Acetamiprid and carbaryl		X		X	X	X	X
Wu et al., 2022	China	X		Fluvalinate		X		X	X		X
Pons et al., 2023	Spain		X	Glyphosate		X		X	X	X	X
Cang et al., 2023	China		X	Tetrachlorantraniliprole and tebuconale		X		X	X	X	X
Decio et al., 2021	Brazil		X	Thiametoxam		X		X	X		X
Pal et al., 2022	France		X	Imidacloprid, difenoconazole and glyphosate		X		X	X	X	X
Almasri et al., 2020	France		X	Imidacloprid, difenoconazole and glyphosate		X		X			X
Bartling et al., 2021	Germany		X	Thiacloprid, fludioxonil, dimoxystrobin and pendimenthalin	N/A			X		X	
Li et al., 2022	China		X	Imidacloprid		X		X	X	X	
Whang et al., 2023	China		X	Thiametoxam		X		X	X	X	X
Benito-Murcia et al., 2022	Spain		X	Tau-fluvalinate, coumaphos and dimethoato	N/A			X		X	X
Parkinson et al., 2022	EUA		X	Imidacloprid and sulfoxaflor	N/A			X	X	X	
Paleolog et al., 2021	Poland	X	X	Imidacloprid	N/A			X	X	X	X
Qi et al., 2020	China		X	Flumethrin		X		X	X	X	
Araújo et al., 2023	Brazil		X	Spinosad	N/A			X	X	X	X
Ibrahim et al., 2023	Egypt		X	Sulfoxaflor	N/A			X			X

Exp.= Experiment; Lab.= Laboratory; Cont.= Contact; Ing. = Ingestion; *SOD* (superoxide dismutase); *CAT* (catalase) and *GST* (glutathione S - transferase).
N/A - The information is not available in the study.

In what year and geographical location did the research take place?

The year 2022 had the highest number of articles selected, followed by 2023, 2021, and 2020 (seven, five, four, and three, respectively) (Fig 1). Most of the studies were carried out in China (seven studies) and Brazil (three studies), followed by Spain and France (two studies each), and Serbia, Germany, Poland, Egypt, and the United States (one study each).

Which honey bee subspecies was most commonly studied, and how was pesticide exposure carried out?

All the papers used a similar method of exposure for the bees, either through the provision of contaminated food or not, and none of the selected papers evaluated contamination by contact. After being challenged with pesticides, 73.68% of the authors chose to analyze the bee's head or entire body, and only 26.32% used the abdomen. Ninety-nine percent of the studies were conducted in the laboratory, while only 1% were conducted in the field. The lethal dose (LD_{50}) was used in most of the selected articles (nine studies), followed by the environmentally relevant dose (seven studies) and the sublethal dose (three studies).

Which pesticides and associations have been most studied, what were the doses, and at what stage of life were the bees most studied?

Of the pesticides investigated, 18 studies evaluated the effects of insecticides, followed by fungicides (six studies) and herbicides (four studies) (Fig 2), with some articles evaluating the effects of one or more pesticides in the same study. The effects were measured as a result of exposure to individual compounds or different combinations of pesticides. Most of the studies analyzed the effects of pesticides on adult bees (16 studies).

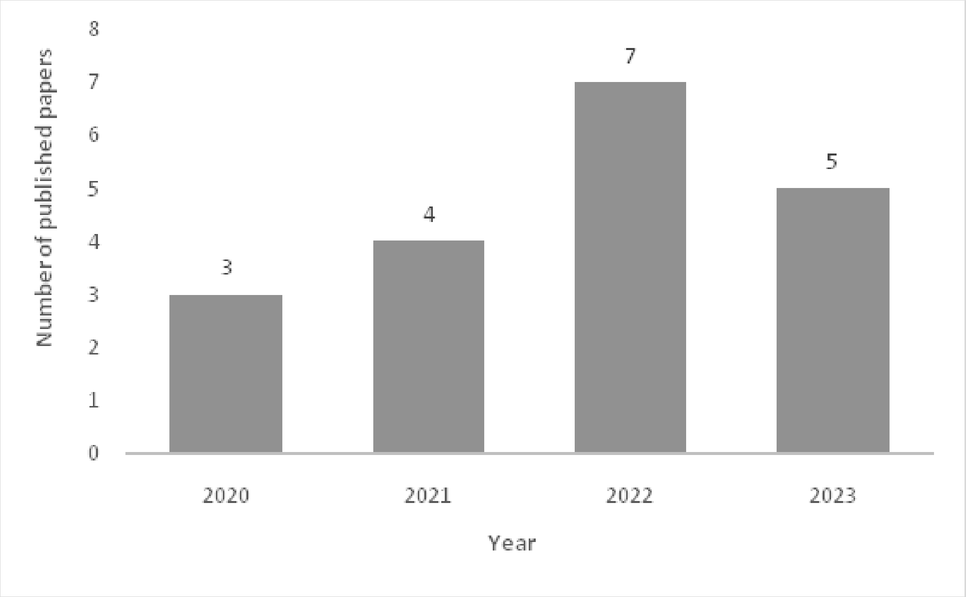

Fig 1. Number of studies meeting the inclusion criteria, distributed by year of publication.

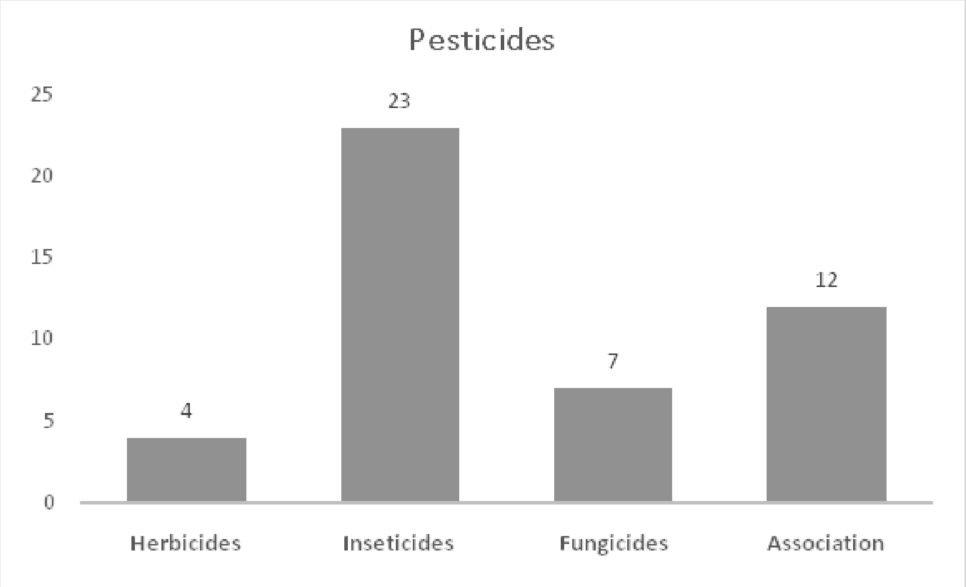

Fig 2. Number of studies, distributed by class of pesticides (herbicides, insecticides, fungicides, and/or association). Articles that examined the association of the effects of one or more pesticides in a single study may include more than one insecticide, herbicide or fungicide in the same work.

At the same time, two studies focused on the larval stage, and one study evaluated the development of the bee from larva to the twentieth day of age. No studies involving bees in the pupal or egg stage were identified.

Of the 19 articles reviewed, six used multiple pesticides, including herbicides, insecticides, and fungicides, or combinations of these, to investigate their effects on the antioxidant system of bees. Generally, in the studies involving fungicides, it was observed that, on average, the doses of these products were higher than those of insecticides and herbicides. In only seven studies were there no significant effects on the regulation of any of the evaluated genes. In contrast, in the other studies, changes in the regulation of the investigated genes were observed.

Herbicides

The main chemical groups of herbicides covered in the studies were bipyridyls (three) and dinitroanilines (one). Glyphosate was the most frequently studied herbicide, analyzed in three studies, followed by pendimethalin in one study. Half of the studies examined focused on the impacts of herbicides alone, while the other half investigated the effects in combination with other pesticides (Table 2).

Table 2. Doses and pesticides used in each study in mg/kg, with the average calculated for multiple doses of the same pesticide.

Papers	Herbicide (mg/kg)	Insecticides (mg/kg)	Fungicide (mg/kg)
Zaluski et al., 2020		Fipronil 0.025	Pyraclostrobin 0.85
Li et al., 2021		Isoclast 1.72	
Orčić et al., 2022		Thiacloprid 1.79 Clothianidin 0.37	
Gao et al., 2022		Acetamiprid 2.00 Carbaryl 5.00	
Wu et al., 2022		Fluvalinate* 18.50	
Pons et al., 2023	Glyphosate* 7.50		
Cang et al., 2023		Tetrachlorantraniliprole* 195.55	Tebuconazole* 288.42
Decio et al., 2021		Thiametoxam 0.02	
Pal et al., 2022	Glyphosate* 0,37	Imidacloprid* 0.37	Difenoconazole* 0.37
Almasri et al., 2020	Glyphosate* 3,01	Imidacloprid* 3.01	Difenoconazole* 3.01
Bartling et al., 2021	Pendimethalin 0,05	Thiacloprid 129.00	Fludioxonil 0.36 Dimoxystrobin 0.09
Li et al., 2022		Imidacloprid 0.04	
Whang et al., 2023		Thiametoxam 0.26	Triazolflusilazol 411.00
Benito-Murcia et al., 2022		Tau-fluvalinate* 0.27 Coumaphos 0.59 Dimethoato 0.01	
Parkinson et al., 2022		Imidacloprid 0.05 Sulfoxaflor 0.05	
Paleolog et al., 2021		Imidacloprid 0.04	
Qi et al., 2020		Flumethrin* 0.37	
Araújo et al., 2023		Spinosad* 18.13	
Ibrahim et al., 2023		Sulfoxaflor* 12.04	

* For studies with multiple dosages of the same pesticide, the average dosage used was calculated.

Insecticides

The most studied chemical groups of insecticides were neonicotinoids (five studies), followed by organophosphates (two studies), and, with one study each, pyrazoles, carbamates, pyrethroids, cyanopyrethroids, and sulfoxamines. Imidacloprid was the insecticide most frequently analyzed (five studies), followed by sulfoxaflor (three studies). Other insecticides examined include thiamethoxam, thiacloprid (two studies each), fipronil, clothianidin, acetamiprid, carbaryl, fluvalinate, tetrachloranthraniliprole, coumaphos, tau-fluvalinate, dimethoate, flumethrin, and spinosad (one study each). Six studies investigated the combined effects with other pesticides (Table 2).

Fungicides

The main chemical groups of fungicides analyzed in the studies were triazines (in three studies), followed by strobilurins (in two studies) and phenylpyrazoles (in one study). Among the most frequently mentioned fungicides in the studies were difenoconazole (in two studies), followed by pyraclostrobin, triazole, flusilazole, fludioxonil, dimoxystrobin, and tebuconazole (each mentioned in one study). In addition, five studies examined the combined effects with other pesticides (Table 2).

Discussion

With the increasing global population, environmental concerns are receiving growing attention in the media, highlighting the urgent need for sustainable management of agricultural systems. Moreover, it is crucial to understand the advantages and drawbacks of pesticide usage for both human health and the environment to inform agricultural management decisions (Cullen et al*.,* 2019). Understanding the studies on pesticides and their chemical groups is fundamental to comprehending the potential impacts on bees.

In the literature, reviews focusing on the effects of specific types of insecticides, such as the influence of neonicotinoids on bees, are already available, resulting in 543 articles during an initial search, with 268 included in the review (Lundin et al., 2015). A separate review addressing all types of fungicides and herbicides found 437 articles, of which 90 were pertinent to the review (Cullen et al., 2019). In this systematic review focused on the effects of pesticides on the antioxidant system, 309 articles were initially found, of which only 19 were included in the review. Although pesticides have not been formulated to target bees, several studies have shown how harmful these products are to bees, being responsible for the decline of these pollinators (Zaluski et al., 2017; Bovi et al., 2018; Camilli et al., 2022; Astolfi et al., 2022).

The majority of studies identified were conducted in China and Brazil, with 2022 witnessing the most significant number of publications on this topic, contrasting with the findings by Cullen et al. (2019), as most of their identified studies took place in North America and Europe. Nevertheless, it is essential to note that pesticide usage varies significantly across regions, influenced by soil and climate conditions, as well as local factors.

However, it is worth noting that the use of pesticides varies significantly from region to region, depending on soil and climate characteristics, as well as regional factors. Brazil is currently one of the countries that consumes the most pesticides in the world (De Oliveira et al., 2023). This excessive use of insecticides is justified by the fact that it is a country with a high level of food production, but on the other hand, it is necessary to use more sustainable alternatives to these products. In some European Union countries, such as Italy, for example, there is already a ban on organophosphate, carbamate, and neonicotinoid insecticides due to their harmful effects on bee health (Zhao et al., 2022).

All the analyzed articles focused on the impact of pesticides on three specific genes (SOD, CAT, and *GST*) of the antioxidant system in honey bees. In nine of the 19 studies, emphasis was placed on the joint evaluation of these three genes, showing that the coordinated action of the immune and antioxidant systems maintains homeostasis in individual bees and colonies. The systems act to mitigate adverse effects originating from external factors, such as exposure to xenobiotics (Dziechciarz et al., 2023). To date, it has been confirmed that the effectiveness of the antioxidant system in worker bees is influenced by external environmental factors such as pesticides (Cullen et al., 2019; Paleolog et al., 2021).

Thus, the exposure of bees to pesticides harms the antioxidant system, leading to oxidative stress, a condition where the antioxidant defense system fails to counteract the harmful effects of free radicals. In this situation, the physiological condition enhances the functionality of enzymes like SOD, CAT, and GST to safeguard the organism from harm inflicted by ROS (Migdal et al., 2020). All nine studies that investigated the three genes reported changes in gene regulation after the bees were exposed to pesticides (Li et al., 2021; Paleolog et al., 2021; Gao et al., 2022; Li et al., 2022; Orcic et al., 2022; Pal et al., 2022; Araújo et al., 2023; Cang et al., 2023; Pons et al., 2023; Whang et al., 2023). These findings emphasize the vulnerability of the bee antioxidant system to pesticides and underscore the necessity of comprehending the impact of these chemicals on colony health.

The risks of these compounds to bees were traditionally assessed using LD_{50} tests. However, sublethal doses can cause effects as harmful as those of higher dosages, including an increase in lipid peroxidation, changes in the expression of genes related to oxidative stress, antioxidant enzyme activities, and oxidative damage in bees (Gao et al., 2022; Pons et al., 2023). The number of studies investigating the potential sublethal effects of pesticides on bees is low (three studies focused only on sublethal effects, nine examined effects of the lethal dose, and seven examined effects of the environmentally relevant dose), making this an area worthy of more attention.

In 89% of the selected studies, the focus was on investigating bee exposure in the laboratory, while only 11% were conducted in the field. Therefore, the scarcity of research that evaluates the effects of pesticides on the colony as a whole rather than just focusing on bees at specific stages is evident. Field studies provide important data on the actual exposure of the bees and how the colony behaves in the face of contamination, and this type of study is critical to understanding the effects of pesticides in the field. The high number of laboratory studies can be attributed to the toxicity of pesticides, which can cause significant damage to bees, such as atrophy of the hypopharyngeal glands, reduction in the area of the acini, death of larvae, and reduction of brood (Zaluski et al., 2017; Traynor & Lamas, 2021). Therefore, the contamination of bees in a controlled environment becomes more feasible for researchers, avoiding significant losses to individuals.

In 100% of the studies evaluated, the method of exposure used was via ingestion of contaminated food, completely ignoring other routes of exposure, such as contact exposure. Zaluski et al. (2015) noted that the insecticide fipronil was more harmful to bees exposed through contact than those that consumed contaminated food, leading to behavioral alterations like agitation, spasms, tremors, and paralysis. Bovi et al. (2018) observed in their research that the insecticides fipronil and imidacloprid affected the movement of bees exposed to contact and consumption. These findings indicate that even minimal doses, like those utilized in the contact exposure experiments, harm bees considerably, underscoring the need for further investigation into this exposure type.

In this analysis, we have focused on the impact of pesticides on the antioxidant system in honey bees. It is important to consider additional effects and consequences not covered in this research, like pollination. This is essential for agricultural output, enhancing the economic worth of produce and elevating the quality of fruits. In several Latin American nations (Argentina, Brazil, Chile, Mexico, and Uruguay), substantial commercial agriculture and family farming support local economies, fulfilling a significant socio-economic function (Basualdo et al*.,* 2022).

More than 20,000 species of bees have been described worldwide. Approximately 12 species play a significant role in crop pollination, including the western honey bee (*Apis mellifera*), the eastern honey bee (*Apis cerana*), melipona (stingless bees), and solitary bees (Feketéné Ferenczi et al*.,* 2023). The services provided by pollinators play a crucial role in guaranteeing and increasing the economic value of agricultural production, and their services are considered essential for food production and for economies at regional and global levels (Feketéné Ferenczi et al*.,* 2023).

Elements such as the application of pesticides, notably the insecticide acetamiprid and ergosterol-inhibiting fungicides, also impact the pollination services bees provide (Han et al., 2019). Traces of these pesticides and artificial substances remain in the nectar and pollen gathered by bees, leading to neurotoxicity, immune system compromise, behavior alterations, and long-term illnesses (Christen et al., 2018). Furthermore, the use of pesticides, including fungicides, insecticides, and herbicides, leads to contamination, toxicity, and a decrease in the quality and quantity of nutrients in pollen and nectar, affecting colony health and jeopardizing the survival of bees (Jiang et al., 2018). These secondary effects of pesticide use on bees and bee pasture could also be a focus for future research.

This review analyzed and summarized the peer-reviewed literature, but we were unable to determine whether all relevant studies to date were identified in our search. Not all the articles found were in peer-reviewed journals, and there may have been a time lag between publication and appearance in the system. Although there is a growing body of scientific literature on the effects of the subject, there remain several important knowledge gaps in our current understanding.

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Author's Contribution

All authors contributed equally to the conception of the subject, writing, and review of the manuscript.

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