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Review article

Plant protection product residues in plant pollen and nectar: A review of current knowledge

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ABSTRACT

Exposure to Plant Protection Products, PPPs, (fungicides, herbicides and insecticides) is a significant stressor for bees and other pollinators, and has recently been the focus of intensive debate and research. Specifically, exposure through contaminated pollen and nectar is considered pivotal, as it presents the highest risk of PPP exposure across all bee species. However, the actual risk that multiple PPP residues might pose to non-target species is difficult to assess due to the lack of clear evidence of their actual concentrations. To consolidate the existing knowledge of field-realistic residues detected in pollen and nectar directly collected from plants, we performed a systematic literature review of studies over the past 50 years (1968–2018). We found that pollen was the matrix most frequently evaluated and, of the compounds investigated, the majority were detected in pollen samples. Although the overall most studied category of PPPs were the neonicotinoid insecticides, the compounds with the highest median concentrations of residues in pollen were: the broad spectrum carbamate carbofuran (1400 ng/g), the fungicide and nematicide iprodione (524 ng/g), and the organophosphate insecticide dimethoate (500 ng/g). In nectar, the highest median concentration of PPP residues detected were dimethoate (1595 ng/g), chlorothalonil (76 ng/g), and the insecticide phorate (53.5 ng/g). Strong positive correlation was observed between neonicotinoid residues in pollen and nectar of cultivated plant species. The maximum concentrations of several compounds detected in nectar and pollen were estimated to exceed the LD_{50s} for honey bees, bumble bees and four solitary bee species, by several orders of magnitude. However, there is a paucity of information for the biggest part of the world and there is an urgent need to expand the range of compounds evaluated in PPP studies.

1. Introduction

High overwintering losses of honey bee colonies and declines in populations of other insect pollinator species in both Europe and North America (Gierer et al., 2019; Lee et al., 2015; Ollerton, 2017; Potts et al., 2010b; Seitz et al., 2016) have raised public and political concerns about the contribution of Plant Protection Products (PPPs) to bee decline (Cressey, 2015; IPBES et al., 2016).

While there are numerous factors contributing to pollinator decline, the intensification of agriculture over the past six decades, and with it the widespread use of synthetic PPPs, is considered to be a major driver of insect losses (Arena and Sgolastra, 2014; Goulson et al., 2015; Dudley and Alexander, 2017; Rundlöf et al., 2015; Sánchez-Bayo and Wyckhuys, 2019; Williams et al., 2015). PPPs are very widely used (Dudley and Alexander, 2017), and can be very persistent in the environment (Casado et al., 2019; Silva et al., 2019), potentially exposing non-target organisms to mixtures of toxic residues (Botías et al., 2016; Gavrilescu, 2005; Looser et al., 2000). For bees, which have been the focus of widespread concern, PPP exposure routes include particles in the air (dust and spray), nectar, pollen, mud/soil, wax, water, guttation fluid, plant surfaces, and propolis/resin (Boyle et al., 2019). In comparison with other exposure routes (e.g. air particles, soil, guttation fluid etc), dietary exposure through consumption of pollen and nectar is thought to be a significant exposure route, posing highest risk across all bee species (Bireley et al., 2019; Boyle et al., 2019; Cham et al., 2019; Hinarejos et al., 2019; Sgolastra et al., 2019; U.S. Environmental Protection Agency USEPA, 2014).

If plants are flowering at the time of application, nectar and pollen

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can become contaminated with PPPs directly, although most practitioners avoid spraying insect-pollinated crops whilst the crop is in flower (Larson et al., 2013, 2015). Due to the systemic nature of some PPPs, the active ingredient may also be translocated from the soil through the plant tissues, contaminating pollen and nectar (Botías et al., 2015; Cowles and Eitzer, 2017; Stoner and Eitzer, 2012). Since bees bring pollen and nectar back into the nest (Poquet et al., 2016; Sánchez-Bayo and Goka, 2014; Sgolastra et al., 2019), this can create an unintended accumulation of PPP mixtures in stored nectar and pollen (Boyle et al., 2019), and, in the case of honey bees, in other hive materials (e.g. wax etc) (Benuszak et al., 2017). Once this happens, not only the forager bees, but also the brood and, in social species, the rest of the colony (brood, nurse bees, queen, drones) are at risk of exposure to these chemicals (Prado et al., 2019). Recently published analyses of pollen from managed honey bees located near agricultural sites demonstrated that many chemicals (including insecticides, miticides, fungicides and herbicides) were detectable in various hive matrices (Johnson et al., 2012; Lambert et al., 2013; Mullin et al., 2010; Wu et al., 2011). In addition to the active ingredients, bees may also be exposed to additives used in PPP formulations, and these have also been detected in pollen and honey with the potential to interact with PPPs and increase toxic effects (Mullin et al., 2015). Hence, many bee species are likely to be chronically exposed to mixtures of multiple PPPs, throughout their development and adult life, particularly when residing in intensively managed arable and horticultural landscapes (Roszko et al., 2016). The impact of PPP exposure on bees has been tested in numerous lab- and field-based experiments in recent years (Arena and Sgolastra, 2014; Cedergreen, 2014; Goulson et al., 2015; James and Xu, 2012; O' Neill et al., 2018; Sánchez-Bayo and Goka, 2014; Wood and Goulson, 2017), but these experiments can be limited by lack of knowledge of field-realistic doses of these compounds (Lydy et al., 2004; Pohorecka et al., 2012; Siviter et al., 2018).

Field exposure to PPPs from ingesting contaminated nectar and pollen is not only likely to vary across crops and seasons, but also between wild bees and managed social bees (Rundlöf et al., 2015). For example, bumble bees seem to use and benefit similarly from the resources available in a farmland (Wood et al., 2015), while bees from other genera, especially solitary bees, may show more variation in their foraging choices (Wood et al., 2016), and thus, a variable range of levels of exposure to agrochemicals (Botías et al., 2017). Moreover, while honey bees tend to select nectar sources that provide the greatest sugar reward, this may not always be the case with solitary bees (Boyle et al., 2019). Big differences can be also observed in the consistency and constituents of the food mass across bee species, as they may handle their food in different ways (e.g. in social bees pollen is processed by hypopharyngeal glandular secretions before storage) (Nixon and Ribbands, 1952), store for different amounts of time, and some have particular dietary requirements, and thus forage on specific plant species (Benton, 2017).

However, most female adult bees visit flowers to collect pollen to provision their larvae, and consume both nectar and pollen themselves directly from flowers. Thus, it seems that one way to measure the field-realistic exposure of bees to PPP residues is to analyse pollen and nectar directly from plants, and quantify residue concentrations (Stoner and Eitzer, 2012). Determining the quantity, distribution and prevalence of systemic PPP residues present in vegetation is highly relevant for both agricultural management and biodiversity conservation, since establishing the limits of field-realistic exposure is essential to risk assessment for a range of taxa (Botías et al., 2016). Thus, obtaining more information on what constitutes field realistic exposure is vital.

In order to obtain reliable PPP residue data for pollen and nectar, expensive and practically challenging residue studies need to be performed (Gierer et al., 2019). The key limiting factor for evaluating concentrations of PPPs in nectar or pollen is the difficulty in obtaining sufficient quantities to conduct the residue analyses (Cowles and Eitzer, 2017). Since nectar is a much more difficult matrix to collect for many plant species, it is useful to evaluate whether there is a relationship between the two matrices, and whether the values of pollen residues can be used as a predictor for the concentrations found in nectar.

In the present review, we evaluate the current knowledge of field realistic residues of PPPs found in nectar and pollen directly collected from plant species, outline the existing knowledge gaps and highlight the future research needs for residue studies and pollinator risk assessments.

2. Methodology

2.1. Key concepts and research strategy

A systematic review was conducted to address the question: 'What are the field realistic residues of PPPs that bees are exposed to when foraging on nectar and pollen'? The key elements were: (1) bees as main non-target organism of interest, (2) PPPs as the intervention of interest, (3) pollen and nectar directly collected from plant resources as the main matrices evaluated, and (4) the concentrations of the main active ingredients and the plant species evaluated as the outcomes of interest. The reason bees were chosen as a species of interest is because when considering non-target impacts of PPP use for pollinators, regulatory agencies around the world are making decisions using data from mainly bee species as the only model insect pollinator (EFSA, 2013; Franklin and Raine, 2019; Uhl and Brühl, 2019). After initial assessment of publications related to bee PPP exposure, keywords were determined and a systematic literature search was carried out in November 2018 using the databases of Web of Science Core Collection and Scopus. The following search terms to locate potential studies on PPP (pesticide) residues and bees were used: (bee* OR *Apis* OR honey bee* OR bumble bee*) AND (pesticide* OR insecticide* OR fungicide* OR herbicide*) AND (residue* OR exposure) AND (pollen OR nectar)/(pollen) AND (nectar). No limitations of dates or language were applied to the search strategy. To be included in this review, papers must have reported primary research, and detected at least one concentration of PPP in pollen or nectar directly collected from a plant species. Papers referring to PPP residues in pollen and nectar that were processed by bees (e.g. pollen collected from pollen traps, stored pollen or nectar etc.) were not included.

2.2. Data extraction protocol

Each publication was reviewed and data was extracted and recorded in a main dataset, including: location of study (if this information was lacking, the location of the first author's institution was used as a proxy); active substance; time, rate and method of application(s); product name; PPP category (e.g. insecticide, fungicide, herbicide); mode of action (systemic or not); plant taxa (family and scientific name), flowering status during treatment (flowering or not) and state (cultivated or wild); growing and treatment conditions (substrate, indoor/outdoor cultivation); time of collection of matrices (days after treatment); volume of matrices analysed; matrix analysed (pollen, nectar, other); concentration of residues (ng/g); limits of detection (LOD); method of chemical extraction (e.g., QuECheRS etc); analysis method (e.g., UHPLC−MS/MS etc); correlations with other matrices evaluated; and metabolites evaluated (Table S1). In order to facilitate our analysis we used a more simplified form of the main dataset (Table S2). Cultivated plants included (any plant that was part of an actual or artificial cultivation) and wild plants denoted (any plant that was growing naturally in the environment). For each plant species, we recorded its common name, its

synonym according the nomenclature, and its variety (for cultivated plants) (Table S3). The nomenclature of the majority of the plant species was based on Euro + Med PlantBase (2006), and the Plant List database (2013) was used for the varieties of the cultivated plants. As has already been noted by Benuszak et al. (2017), different units are used to express concentrations (i.e. parts per billion, μg/kg and ng/g) in different studies. We used ng/g for all our calculations, and converted other metrics into this unit for analysis. The only exception was the values used for the heatmap, where we converted the PPP residues in pg/g, in order to avoid negative values in the Log_{10} scale. In cases where the residue concentration was given as < LOD/LOQ, we used half of the respective LOD/LOQ values (Dively and Kamel, 2012). The software used for the graph creation was GraphPad Prism 8.

2.3. Statistical analysis

The relationship between the concentrations of insecticide residues in nectar and pollen was assessed using a paired Generalized Linear Mixed Model approach. The aim of this model was primarily to assess whether residue concentrations observed in pollen can be used to predict those observed nectar. As residue measurements may differ based on study specific factors, such as treatments applied and laboratory methods used, we first subsetted the data to include only those plant species where both nectar and pollen had been assessed in the same study. Of the 25 studies in our dataset only seven contained residue estimates for both nectar and pollen. Based on these studies, five compounds had sufficient data to be included in further analysis, namely; clothianidin, dinotefuran, imidacloprid, thiacloprid and thiamethoxam (all of which are neonicotinoid insecticides). This resulted in a dataset of 206 residue measurements from both pollen and nectar across 13 plant families. Prior to model fitting, scatterplots of the relationship between nectar and pollen were visually assessed. These scatterplots showed that both nectar and pollen data were highly skewed, and the variance of both increased with the mean. Furthermore, a linear relationship appeared to exist between the log of these two variables, therefore the natural log of concentration in pollen rather than the raw pollen data was used to predict concentrations in the nectar. The amount of residues in the nectar (ng/g) was fitted as the response variable. The natural log of residue concentrations in pollen (ng/g), the compound type, and the 'Status' of the species (cultivated or wild) were fitted as predictor variables (fixed factors). The interaction between the natural log of residues in pollen and 'Status' was included to test for differences in the relationship between residues in nectar and pollen, between wild and cultivated plants. The model accounted for non-independence of data within 'Study' and 'Plant family', by fitting these as non-nested random factors. Models were initially fitted using a Gaussian error distribution, but the plotted model residuals were non-normal and variance was highly heterogeneous. Therefore, the models were refitted using a Gamma error distribution, and a log link function. GLMM's were fitted using the package *glmmTMB* vr 0.2.3 (Brooks et al., 2017). The amount of variance explained by both fixed and random factors in the model conditional and marginal variance were calculated using the R package *MuMIn vr* 1.43.6 (Barton, 2019). Conditional variance represents the amount of variation in the response explained by the full model (i.e. both random and fixed effects), and marginal variance represents that which is explained by the fixed factors alone (i.e. here pollen measurements, 'Status' (cultivated or wild), and compound type (Nakagawa and Schielzeth, 2013). Analyses were conducted using R version 3.6.1 (R Core Team, 2019).

2.4. Calculation of the pollen and nectar Hazard Quotient and estimated % LD_{50}

In order to put the pesticide residues into a context of risk to bees, we need to have information on both the concentrations of residues detected in pollen and nectar and their respective LD_{50s}. For each compound evaluated in the residue studies reviewed, pollen and nectar Hazard Quotients and Estimated % LD_{50} were calculated using the methods proposed by Stoner and Eitzer (2013), Sgolastra et al. (2017) and Stoner et al. (2019). Estimating these values is an attempt to illustrate a simplified risk to bees from consuming contaminated food (Traynor et al., 2016). The use of these values is in turn a simplified effort to quantify pesticide exposure, encompassing contact and oral risk from the maximum amount of residues detected in pollen and nectar (Stoner and Eitzer, 2013; Traynor et al., 2016). The LD_{50} values represent averaged 24, 48 and 72 h adult acute oral and contact toxicities available from the database of the University of Hertfordshire (2019), except for the compound spinosad, where the respective data were retrieved from Miles et al. (2012). In order to evaluate the PPP residues for bee toxicity, we initially needed to calculate the uptake of each PPP by a bee foraging for pollen and nectar contaminated by the maximum residue of that PPP. Thus, we calculated the Maximum Residue Uptake (MRU) of a certain compound per bee per day (information available for honey bees, bumble bees and solitary bees) (Table S4) and per one foraging bout (information only available for nectar foraging honey bees) (Table S5). The data on the bee daily consumption of nectar and pollen were retrieved from the guidance document on the risk assessment of plant protection products on bees (EFSA, 2013). For the honey bee daily nectar consumption, we used the average consumption value of a forager bee, as they are consuming larger amounts of nectar (Rortais et al., 2005). For the honey bee consumption of nectar per one foraging bout we used the method proposed by Sgolastra et al. (2017). In order to calculate the maximum Hazard Quotient (HQ) for the maximum PPP residues found in pollen and nectar we used the method proposed by Stoner and Eitzer (2013) (Tables S5 and S6):

$$HQ = \frac{Residue\ concentration\ (ng/g)}{LD50\ (\mu g/bee)}$$

In addition, the values of the Estimated % LD_{50} (% LD_{50}) were calculated (Tables S5 and S7) in order to evaluate how much of the LD_{50} of a compound would a bee consume per one foraging bout (only for honey bee nectar forager) (Table S5), and per day (Table S6):

$$\%LD_{50} = \frac{Maximum\ residue\ concentration\ (ng/g)\ x\ Bee\ pollen\ or\ nectar\ consumption\ per\ day\ (mg/bee)}{Oral\ or\ Contact\ LD50\ (\mu g/bee)}$$

For compounds where only a lower limit of LD_{50} was determined, that lower limit was used for calculation (e.g. for $LD_{50} > 100$ μg/bee, the value 100 was used) (Stoner et al., 2019). For a more clear presentation of the results, we chose to report the values of Estimated % LD_{50} in three categories: >100, 50–100 and < 50%, highlighting the values that exceeded 50% of the bee LD_{50s}.

3. Results

3.1. General information

The initial database search yielded a total of 5741 articles (Fig. S1). After the removal of duplicates (1381 articles), titles and abstracts for 4360 papers were screened for relevance. In the end, only 24 articles referred to measurement of PPP residues in pollen and nectar directly collected from plants. At that stage, four papers (Bailey et al., 2005; Lord et al., 1968; Thompson et al., 2015; Waller and Barker, 1979) were added as they were considered very relevant to the present review and they were cited in the 24 primary studies, but did not appear in the initial database search, bringing the total papers to 28. Among the 28 studies, those of Botías et al. (2016) and Thompson et al. (2016) reassessed the results of their previous studies (already included in our sample) and thus were removed. Moreover, the study of Cowles and Eitzer (2017) was also not included in the analyses of the data of the present review, since the exact PPP residues were not clearly articulated. Accordingly, 25 papers were included in our analysis.

The first paper was published in 1968 and the majority of papers appeared in the years 2012 and 2015 (Fig. 1). Seventeen papers evaluated pollen, 16 assessed nectar, while both matrices were evaluated in eight studies (Fig. 1a). Studies were conducted in countries located in North America (48%), Europe (48%) and Asia (4%), while there were no studies from Australia, Africa or South America. The majority of studies were carried out in the United States (n = 11), while the United Kingdom (n = 6), followed by France (n = 4), are the strongest representatives at a European level.

3.2. PPPs and plant species evaluated

A total of 31 active compounds, two neonicotinoid metabolites and one synergist (a substance that participates in the interaction or cooperation of two or more substances, to produce a combined effect greater than the sum of their separate effects) were identified in pollen and nectar collected directly from plants (Table 1). The majority of the 31 compounds were fungicides (n = 17 compounds) and the rest were insecticides (n = 14 compounds), and they were all systemic compounds except for five (fungicides: chlorothalonil and prochloraz; and insecticides: chlorpyrifos, cypermethrin and lambda-cyhalothrin). In terms of mode of action, the majority of the compounds act as acetylcholinesterase and demethylation inhibitors. No studies evaluated the presence of herbicides in pollen and nectar collected from plants. The maximum number of compounds evaluated in a paper was 20 (two studies), and the mean number of compounds evaluated per study was four. The neonicotinoids have been studied since 2001, but fungicides only started to be evaluated from 2012 (Fig. 1b). The most frequently studied compounds were the insecticides (n = 57 studies), particularly the neonicotinoids (n = 46 studies). Imidacloprid was the most studied compound (n = 17 studies), followed by thiamethoxam (n = 10 studies), and clothianidin (n = 9 studies). The compounds with the highest median levels of residues in pollen were: the carbamate insecticide carbofuran (1400 ng/g), the dicarboximide fungicide iprodione (524 ng/g), the organophosphate insecticides dimethoate (500 ng/g) and chlorpyrifos (100.5 ng/g), the natural product with insecticide properties spinosad, isolated from the bacterial species *Saccharopolyspora spinosa* (320 ng/g), the chloronitrile fungicide chlorothalonil (265.2 ng/g), and in nectar: dimethoate (1595 ng/g), chlorothalonil (76 ng/g), the organophosphate insecticide phorate (53.5 ng/g), and the carbamate insecticide oxamyl (35 ng/g) (Table 2). For the neonicotinoids, median residues were highest for dinotefuran (34.7 ng/g in pollen, 7 ng/g in nectar), and between 0.01 and 0.08 ng/g for the other compounds in both nectar and pollen (Table 2). Metabolites and PPP co-formulants (substances used in commercial formulations in order to optimize the efficacy and the stability of the primary active ingredients), indicated in Fig. 1b as "other compounds", have been evaluated since 2015. The majority of PPP reports for residues in pollen and nectar were a result of application of commercial formulations, rather than application of the

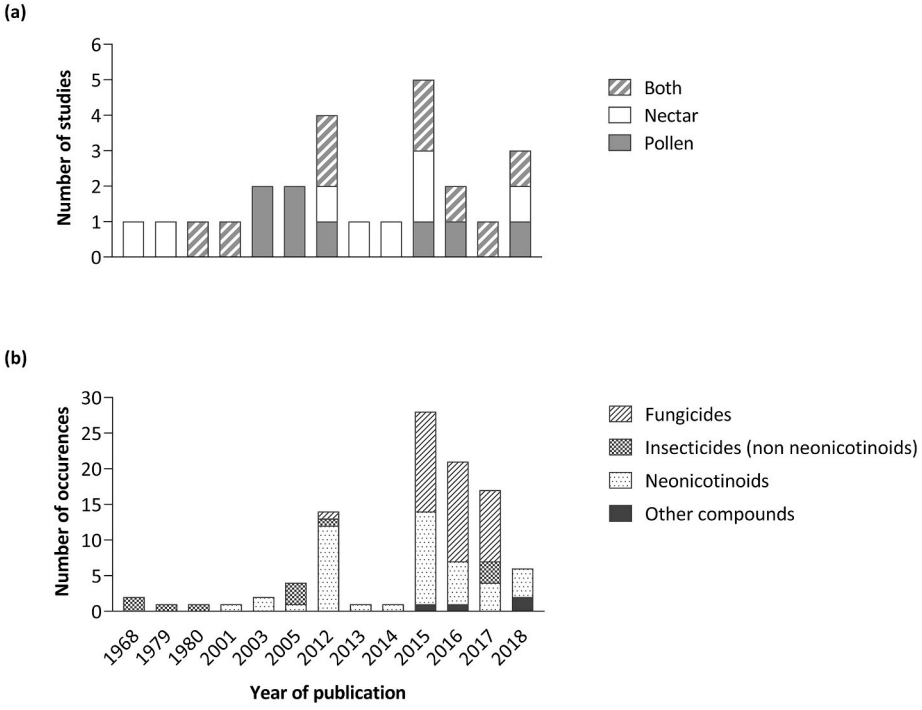

Fig. 1. a) The number of studies and the matrix analysed each publication year, and **b)** The number of times a PPP category (fungicides, non-neonicotinoid insecticides, neonicotinoids and others) was evaluated each publication year.

Table 1
The chemical compounds evaluated for residues in pollen and nectar, their status in Europe and the United States, and the papers they were evaluated in.

Category	Substance group	Compound	Systemic	Current status		Citation [a]
				E.E [b]	U.S [c]	
Insecticides	Neonicotinoids	Acetamiprid	Yes	A[d]	A	11; 16; 20; 22
		Clothianidin	Yes	NA[e]	A	10; 11; 13; 15; 16; 18; 19; 20; 21
		Dinotefuran	Yes	NA	A	9
		Imidacloprid	Yes	RU[f]	–[g]	4; 5; 6; 8; 9; 11; 12; 14; 15; 16; 17; 18; 20; 22; 23; 24; 25
		Thiacloprid	Yes	A	–	11; 16; 20; 22
		Thiamethoxam	Yes	NA	A	9; 10; 11; 12; 15; 16; 19; 20; 22; 24
	Organophosphate	Chlorpyrifos	No	A	A	22
		Dimethoate	Yes	NA	A	1; 2; 3
		Phorate	Yes	NA	A	1
	Carbamate	Carbofuran	Yes	NA	A	7
		Oxamyl	Yes	A	A	9
	Pyrethroid	Cypermethrin	No	A	A	22
		Lambda-cyhalothrin	No	A	A	7; 22
	Natural product	Spinosad	Yes	A	A	7
Fungicides	Benzimidazole	Carbendazim	Yes	NA	A	16; 20; 22
	Carboxamide	Boscalid	Yes	A	A	16; 20; 22
	Chloronitrile	Chlorothalonil	No	NA	A	12
	Dicarboximide	Iprodione	Yes	NA	A	12
	Imidazole	Prochloraz	No	A	–	16; 20; 22
	Morpholine	Spiroxamine	Yes	A	–	16; 20; 22
	Oxathiin	Carboxin	Yes	A	A	16; 20
	Phenylamide	Metalaxyl	Yes	A	A	10
	Strobilurin	Fluoxastrobin	Yes	A	A	16; 20; 22
		Pyraclostrobin	Yes	A	A	16; 20; 22
		Trifloxystrobin	Yes	A	A	10; 16; 20; 22
	Thiophene	Silthiofam	Yes	A	–	16; 20
	Triazole	Epoxiconazole	Yes	A	–	16; 21
		Flusilazole	Yes	NA	–	16; 22
		Metconazole	Yes	A	A	16; 23
		Tebuconazole	Yes	A	A	16; 20; 22
		Triticonazole	Yes	A	A	16; 20
Metabolites		5-Hydroxy-imidacloprid	NA	–	–	25
		Imidacloprid olefin	NA	–	–	25
Synergist		Piperonyl butoxide	NA	–	–	16; 20

[a] The complete citation is given in Supplementary material (Table S1).
[b] European Union.
[c] United States.
[d] Active.
[e] Not active.
[f] Restricted use.
[g] Information could not be acquired for these compounds.

active ingredient itself. In those products, the most usually encountered combinations in the formulations were clothianidin with the compound prothioconazole (fungicide), imidacloprid with beta-cyfluthrin (insecticide), spinosad with 1,2-benzisothiazoline-3-one (preservative with fungicidal properties), thiacloprid with deltamethrin (insecticide), and thiamethoxam with metalaxyl-M and fludioxonil (both fungicides). Out of all these co-formulants, none has been evaluated for plant nectar and pollen residues. Ten of the PPP compounds studied (carbofuran, carbendazim, chlorothalonil, clothianidin, dimethoate, dinotefuran, flusilazole, iprodione, phorate, and thiamethoxam) are not currently approved for use in the European Union - according to Reg. (EC) No 1107/2009.

Information on residues of different compounds is of more value when associated with the plant taxa in which they were detected. In total, 94 plant taxa (41 cultivated and 54 wild, with each variety of cultivated plant considered a different taxon) from 31 plant families were evaluated for pollen and nectar PPP residues (Table 3), and on average, five plant taxa were evaluated in each study. Most taxa evaluated for PPP residues in pollen and/or nectar belonged to Asteraceae (n = 20 taxa). The most studied taxa were cultivated *Zea mays* L. (maize), which was evaluated only for pollen residues (n = 6 studies), and *Brassica napus* L. (oilseed rape), for residues in nectar in five studies and in pollen in three.

In terms of PPP presence, the highest mean numbers of different compounds (reported as > LOD/LOQ) were detected in the families of Poaceae (n = 8), Ericaceae (n = 6), Rosaceae (n = 5) and Brassicaceae/Fabaceae (n = 4). On a species level, in winter *Brassica napus*, 14 different compounds have been detected, in *Fragaria* × *ananassa* (Duchesne ex Weston) Duchesne ex Rozier (strawberry), 12 different compounds have been detected, and in *Vicia faba* L. (field bean), 11 different compounds have been detected (Table 3). In order to obtain a visual indication of the extent to which the compounds were detected in plant taxa, we created a heatmap for the PPP residues, with a Log_{10} scale (Fig. 2). The map depicts the median concentrations of the PPP residues of both nectar and pollen in respective plant families (divided into the categories of cultivated and wild taxa), according to the intensity of a colour scale. The blank squares highlight where specific compounds were not evaluated for certain combinations (compound-family), emphasizing the amount of missing information. The majority of residues were generally below 10 ng/g, and the median concentrations of the compounds found in the cultivated plant families appeared to be higher (1.8 ng/g) than those in the wild plant families (0.04 ng/g).

Table 2
The chemical compounds evaluated for residues in pollen (P) and nectar (N), the number of families and species they were detected, their mean concentrations, the number of times they were detected in pollen and nectar, the mean range of limits of detection, and the number of studies that provided the limits of detection.

Compound	No. Families [a]	No. Species [b]	Median residues (ng/g)		Range (ng/g)				Counts [c]		LOD range (ng/g)	
			P	N	P		N		P	N	P	N
					Minimum	Maximum	Minimum	Maximum				
5-Hydroxy-imidacloprid	2	2	–	17.0	–	–	2.00	69.0	–	10	–	0.50
Acetamiprid	11	18	0.01	0.1	0.002	0.82	0.05	7.60	38	3	0.02–0.84	0.08–0.42
Boscalid	13	23	0.90	0.4	0.06	38.0	0.41	2.05	39	5	0.12–8.20	0.82–4.10
Carbendazim	11	17	2.50	1.3	0.01	204.0	1.25	1.25	37	1	0.08–24.00	2.40–12.00
Carbofuran	1	1	1400	–	1400	1400	–	–	2	–	20.00	–
Carboxin	8	13	0.06	–	0.01	0.06	–	–	33	–	0.12	–
Chlorothalonil	2	2	265.3	76.0	130.5	422	76.0	76.0	2	1	84.00–1521.00	152.00–760.00
Chlorpyrifos	2	2	100.5	–	38.00	163	–	–	2	–	21.00–377.00	–
Clothianidin	21	60	0.03	0.1	0.01	11.0	0.01	2992	214	64	0.12–0.72	0.17–1.00
Cypermethrin	1	1	58.5	–	58.5	58.50	–	–	1	–	24.00–430.00	–
Dimethoate	5	5	500	1595	500	500	100	22940	1	40	0.50	0.10
Dinotefuran	1	1	34.7	7.0	11.20	88.30	2.10	9.20	5	5	0.20	0.20
Epoxiconazole	8	13	0.42	–	0.10	31.0	–	–	33	–	0.84	–
Fluoxastrobin	10	15	0.01	0.01	0.001	0.15	0.01	0.01	35	1	0.01–0.27	0.03–0.13
Flusilazole	8	13	0.12	–	0.03	16.0	–	–	33	–	0.24	–
Imidacloprid	26	78	0.08	0.08	0.01	150	0.01	6588	240	111	0.05–10.00	0.05–3.60
Imidacloprid olefin	2	2	–	30.0	–	–	1.00	55.0	–	10	–	0.50
Iprodione	2	2	524	18.5	53.0	995.0	18.5	18.5	2	1	4.10–75.00	7.50–37.00
Lambda-cyhalothrin	2	2	30.0	–	30.0	57.5	–	–	3	–	11.00–202.00	–
Metalaxyl	1	1	3.10	–	3.10	3.10	–	–	1	–	0.50	–
Metconazole	8	13	0.15	–	0.04	19.00	–	–	33	–	0.30	–
Oxamyl	1	1	35.0	35.0	35.0	35.0	35.0	35.0	1	1	7.00	7.00
Phorate	2	2	–	53.5	–	–	7.00	100	–	2	–	–
Piperonyl butoxide	8	13	0.36	–	0.09	0.36	–	–	33	–	0.72	–
Prochloraz	13	20	0.18	0.30	0.04	46.00	0.30	0.30	40	2	0.33–6.00	0.60–3.00
Pyraclostrobin	11	17	0.12	0.60	0.03	19.60	0.60	0.60	35	2	0.24–12.00	1.20–6.00
Silthiofam	8	13	0.12	–	0.03	0.12	–	–	33	–	0.24	–
Spinosad	1	1	320	–	320	320	–	–	2	–	1.00	–
Spiroxamine	11	22	5.80	0.03	0.002	328	0.03	0.15	41	4	0.02–0.65	0.12–2.20
Tebuconazole	9	14	2.80	0.18	0.12	34.0	0.18	0.18	34	1	0.19–3.50	0.35–1.70
Thiacloprid	24	69	0.01	0.01	0.003	78.0	0.004	65.6	220	65	0.04–0.91	0.03–0.46
Thiamethoxam	21	68	0.06	0.05	0.01	95.2	0.01	11.0	230	74	0.10–1.80	0.10–2.00
Trifloxystrobin	10	15	0.12	1.20	0.03	104	1.20	1.20	35	1	0.24–4.80	0.48–2.40
Triticonazole	8	13	0.12	–	0.03	0.12	–	–	33	–	0.24	–
TOTAL									**1491**	**404**		

[a] The number of families.
[b] The number of species.
[c] The number of records for reported residues.

However, there is a lot of information missing, and in particular for the wild species, which are under-studied compared to the cultivated taxa.

3.3. Extent of PPP residues in pollen and nectar

The majority of studies evaluated pollen as a matrix for detecting PPP residues (Fig. 1a), both overall and when evaluating across the various plant taxa, with 1491 reports for PPP residues present in pollen (compared with 404 reports for residues present in nectar) (Tables 3 and S2). For both pollen and nectar, the majority of residue values were reported as < LOD/LOQ (78% for pollen and 64% for nectar). Pollen was the matrix in which the majority of the different PPPs were detected ($n_{pollen} = 31$ and $n_{nectar} = 21$). However, the individual studies differed in their application rates and types, and rarely if ever included control treatments. This made it difficult to compare between studies and hence, we were restricted to using only the studies with paired residue concentrations for pollen and nectar. Therefore, out of all the studies we were limited to seven for statistical analysis, and out of all the residue reports, we could only use the 206 reports that referred to both pollen and nectar residues. In these studies, research was performed on five compounds that belonged to the category of insecticides (clothianidin, dinotefuran, imidacloprid, thiacloprid and thiamethoxam) and on 13 plant families. Our model results indicated a positive correlation between the natural log of residues in nectar and pollen for these five insecticides ($\beta = 0.593 \pm 0.084$, $p < 0.001$ in cultivated plants). The slope of this relationship was less steep in wild than cultivated species, ($\beta = -0.469 \pm 0.092$, $p < 0.001$). However, the estimate of this slope for wild species may be influenced by the high proportion of measurements of both pollen and nectar that were below the limits of detection in wild plant species. For this dataset comprised of paired data, concentrations of residues were generally lower in wild than cultivated plants (Fig. 3). Concentrations observed in nectar also differed significantly between compounds (Table S7). This difference was primarily driven by the lower concentrations of the insecticide thiacloprid, but this may be due to application rate or other confounding factors rather than the properties of the compound itself. The amount of variation in log concentrations in nectar explained in the full model was 88%, with 78% of this variation being explained by the fixed factors (pollen, compound type, and status (cultivated/wild)). Differences between studies and plant families, explained 5.4% and 4.5% of the model variance respectively.

Table 3
The plant taxa evaluated for PPP residues in pollen (P) and nectar (N), their status (cultivated or wild), the number of compounds that were detected on them, the mean concentration of residues, the number of studies that evaluated pollen and nectar, and the studies they were evaluated in.

Plant family	Plant species	Status		No. compounds			Median residues (ng/g)		Range (ng/g)				Counts[a]		Citation[b]
		C[c]	W[d]	P	N	>LOD/LOQ[e]	P	N	P		N		P	N	
									Minimum	Maximum	Minimum	Maximum			
Amaryllidaceae	*Allium cepa* L.	1	–	–	1	1	–	1050	–	–	200	6900	–	14	2
Apiaceae	*Aethusa cynapium* L.	–	1	20	–	0	0.10	–	0.005	0.42	–	–	24	–	15; 20
	Anthriscus sylvestris (L.) Hoffm.	–	1	4	–	0	0.02	–	0.004	12.8	–	–	8	–	15
	Heracleum sphondylium L.	–	1	20	–	6	0.06	–	0.001	85.0	–	–	136	–	15; 20
	Pimpinella saxifraga L.	–	1	20	–	5	0.12	–	0.005	5.00	–	–	28	–	15; 20
Aquifoliaceae	*Ilex* x *attenuata*	1	–	–	3	3	–	10.00	–	–	1.00	2.76	–	15	25
Asparagaceae	*Muscari armeniacum* Leichtlin ex Baker	1	–	6	1	1	0.30	0.60	0.01	6.85	0.60	0.60	5	1	22
Asteraceae	*Ageratum houstonianum* Mill.	1	–	6	–	3	3.22	–	0.15	53.0	–	–	6	–	22
	Arctium sp.	–	1	4	4	0	0.01	0.02	0.005	0.04	0.005	0.03	8	4	15
	Carduus sp.	–	1	4	4	1	0.01	0.06	0.004	0.48	0.01	0.08	4	4	15
	Centaurea nigra L.	–	1	4	–	1	0.01	–	0.004	7.60	–	–	4	–	15
	Centaurea scabiosa L.	–	1	4	–	0	0.06	–	0.02	0.08	–	–	4	–	15
	Cirsium arvense (L.) Scop.	–	1	4	4	1	0.02	0.02	0.005	14.8	0.004	0.15	24	16	15
	Cirsium vulgare (Savi) Ten.	–	1	20	4	7	0.03	0.02	0.003	151	0.004	0.15	68	28	15; 20
	Cosmos bipinnatus Cav.	1	–	5	–	2	0.60	–	0.09	0.80	–	–	5	–	22
	Coreopsis grandiflora Sweet	1	–	4	1	0	0.80	0.60	0.06	38.0	0.60	0.60	3	1	22
	Dahlia x *hortensis* Guillaumin	1	–	1	–	1	0.30	–	0.30	0.30	–	–	1	–	22
	Dahlia x *hybrida* (1)[f]	1	–	1	–	0	0.04	–	0.04	0.04	–	–	1	–	22
	Dahlia x *hybrida* (2)	1	–	4	–	3	1.62	–	0.02	2.90	–	–	4	–	22
	Helianthus annuus L.	1	–	1	1	1	3.90	1.90	3.00	18.3	1.90	1.90	3	1	4; 5; 6
	Hieracium sp.	–	1	4	4	0	0.02	0.03	0.005	0.08	0.005	0.25	12	12	15
	Jacobaea vulgaris Gaertn.	–	1	20	–	5	0.06	–	0.003	17.13	–	–	84	–	15; 20
	Matricaria discoidea DC.	–	1	4	–	0	0.13	–	0.02	0.18	–	–	4	–	15
	Matricaria chamomilla L.	–	1	20	–	6	0.06	–	0.001	104	–	–	152	–	15; 20
	Sonchus arvensis L.	–	1	4	4	2	0.02	0.02	0.004	14.8	0.004	0.25	24	20	15
	Sonchus oleraceus L.	–	1	4	4	1	0.01	0.05	0.003	8.11	0.004	1.8	16	12	15
	Unidentified Asteraceae	–	1	4	–	1	0.01	–	0.005	11.7	–	–	4	–	15
Boraginaceae	*Myosotis arvensis* (L.) Hill	–	1	4	–	1	0.07	–	0.02	2.14	–	–	4	–	15
Brassicaceae	*Brassica napus* L. (1)	1	–	–	3	3	–	2.60	–	–	0.10	4.40	–	5	11
	Brassica napus L. (2)	1	–	20	5	14	0.18	0.50	0.005	328	0.05	65.6	226	13	11; 15; 17; 19; 20; 21
	Brassica rapa (L.) L.	–	1	4	–	1	0.03	0.02	0.004	2.70	0.004	0.08	19	8	15
	Cardamine pratensis L.	–	1	4	–	0	0.04	–	0.01	0.06	–	–	4	–	15
	Erysimum linifolium (Pers.) J. Gay	1	–	2	2	0	66.27	38.60	2.05	130.5	1.20	76.0	2	2	22
Campanulaceae	*Campanula portenschlagiana* Schult.	1	–	3	–	1	0.49	–	0.10	0.90	–	–	3	–	22
Caprifoliaceae	*Scabiosa columbaria* L.	1	–	–	2	0	–	0.28	–	–	0.06	0.50	–	2	22
Caryophyllaceae	*Silene dioica* (L.) Clairv.	–	1	4	4	0	0.03	0.06	0.01	0.09	0.01	0.08	4	4	15
	Silene latifolia Poir.	–	1	20	4	8	0.12	0.08	0.005	138	0.01	0.15	88	8	15; 20
	Silene vulgaris (Moench) Garcke	–	1	4	4	1	0.01	0.06	0.004	12.8	0.04	0.25	4	4	15
Clethraceae	*Clethra alnifolia* L.	1	–	–	3	3	–	40.0	–	–	12.0	515	–	15	25
Convolvulaceae	*Calystegia sepium* (L.) R. Br.	–	1	4	4	0	0.02	0.02	0.01	0.04	0.005	0.03	8	4	15
	Calystegia silvatica (Kit.) Griseb.	–	1	4	4	1	0.03	0.01	0.01	6.14	0.004	0.06	12	4	15
	Convolvulus arvensis L.	–	1	4	4	1	0.02	0.02	0.005	17.1	0.004	0.03	16	8	15
Cucurbitaceae	*Bryonia dioica* Jacq.	–	1	4	–	0	0.06	–	0.02	0.08	–	–	4	–	15
	Cucurbita pepo L. (1)	1	–	4	4	3	25.2	6.10	0.1	95.2	0.10	11.20	19	19	9
	Cucurbita pepo L. (2)	1	–	2	2	2	13.0	10.5	12.0	14.0	10.00	11.00	4	4	12
	Cucurbita pepo L. (3)	1	–	2	2	2	13.0	10.5	12.0	14.0	10.00	11.00	4	4	12
	Cucurbita pepo L. (4)	1	–	2	2	2	13.0	10.5	12.0	14.0	10.00	11.00	4	4	12
Dipsacaceae	*Knautia arvensis* (L.) DC.	–	1	4	4	0	0.06	0.02	0.02	0.08	0.005	0.03	4	4	15
Ericaceae	*Erica carnea* L.	1	–	10	–	6	26.5	–	0.49	422	–	–	10	–	22
Fabaceae	*Medicago sativa* L.	1	–	1	1	1	500	1875	500	500	100.00	22940	1	23	3

(*continued on next page*)

Table 3 (*continued*)

Plant family	Plant species	Status		No. compounds			Median residues (ng/g)		Range (ng/g)				Counts[a]		Citation[b]
		C[c]	W[d]	P	N	>LOD/LOQ[e]	P	N	P		N		P	N	
									Minimum	Maximum	Minimum	Maximum			
	Trifolium pratense L.	–	1	4	–	2	0.51	–	0.004	12.6	–	–	4	–	15
	Trifolium repens L.	1	1	4	4	4	0.03	6.20	0.01	0.08	0.004	6588	12	17	13; 15; 18
	Vicia faba L.	1	–	20	2	11	0.28	10503.5	0.01	4.20	7.00	21000	20	2	1; 16
	Vicia sativa L.	–	1	4	–	2	0.51	–	0.004	12.6	–	–	4	–	15
Hypericaceae	*Hypericum hirsutum* L.	–	1	4	–	1	0.07	–	0.02	7.47	–	–	4	–	15
Iridaceae	*Crocus vernus* (L.) Hill	1	–	2	2	0	0.97	0.33	0.39	155	0.30	0.36	2	2	22
	Iris tingitana Boiss. & Reut. × *Iris xiphium* L.	1	–	4	4	2	0.10	0.14	0.01	7.20	0.01	1.25	4	4	22
Lamiaceae	*Ballota nigra* L.	–	1	4	–	1	0.01	–	0.004	17.1	–	–	12	–	15
	Glechoma hederacea L.	–	1	4	4	2	0.03	0.02	0.004	12.6	0.005	0.03	8	4	15
	Lamium album L.	–	1	4	4	2	0.51	0.02	0.004	12.6	0.005	0.03	4	4	15
	Lamium purpureum L.	–	1	4	3	2	0.06	0.02	0.004	12.6	0.005	0.03	11	3	15
	Lavandula stoechas L.	1	–	1	2	1	19.6	0.35	19.6	19.6	0.03	0.41	1	2	22
	Nepeta cataria L. (1)	1	–	–	4	0	–	0.23	–	–	0.03	1.20	–	4	22
	Nepeta cataria L. (2)	1	–	–	3	0	–	0.41	–	–	0.03	1.20	–	3	22
	Salvia longispicata M. Martens & Galeotti x *Salvia farinacea* Benth.	1	–	–	2	0	–	0.10	–	–	0.07	0.14	–	2	22
	Stachys sylvatica L.	–	1	4	–	1	0.01	–	0.004	12.8	–	–	4	–	15
Malvaceae	*Gossypium* sp.	1	–	2	2	2	7.25	0.40	2.9	33.1	0.30	0.90	4	4	24
	Malva moschata L.	–	1	4	4	0	0.07	0.02	0.02	0.18	0.005	0.03	4	4	15
	Malva sylvestris L.	–	1	4	4	1	0.03	0.02	0.01	6.14	0.004	0.06	12	8	15
Oleaceae	*Ligustrum vulgare* L.	–	1	4	–	0	0.03	–	0.01	0.04	–	–	8	–	15
Onagraceae	*Epilobium hirsutum* L.	–	1	4	4	1	0.02	0.04	0.004	7.60	0.005	0.08	24	12	15
	Fuchsia sp.	1	–	–	2	2	–	1495	–	–	100	2890	–	2	1
Papaveraceae	*Fumaria officinalis* L.	–	1	4	–	1	0.03	–	0.004	0.48	–	–	20	–	15
	Papaver rhoeas L.	–	1	20	–	4	0.04	–	0.003	64.1	–	–	56	–	15; 20
Plantaginaceae	*Digitalis purpurea* L.	1	–	2	2	0	1.23	0.44	0.07	2.40	0.03	0.85	2	2	22
	Microrrhinum minus (L.) Fourr.	–	1	4	4	0	0.02	0.02	0.005	0.08	0.005	0.03	8	4	15
	Veronica persica Poir.	–	1	4	–	1	0.01	–	0.003	8.11	–	–	12	–	15
	Veronica spicata L.	1	–	6	6	3	2.87	1.62	0.10	995	0.15	18.5	6	6	22
Poaceae	*Zea mays* L.	1	–	8	–	8	6.60	–	1.7	1400	–	–	15	–	5; 7; 8; 10
Ranunculaceae	*Clematis vitalba* L.	–	1	4	4	2	0.06	0.01	0.005	10.3	0.004	0.02	8	4	15
	Ranunculus repens L.	–	1	20	–	3	0.12	–	0.01	8.50	–	–	24	–	20
Rosaceae	*Agrimonia eupatoria* L.	–	1	4	–	1	0.01	–	0.004	7.60	–	–	4	–	15
	Fragaria x *ananassa* (Duchesne ex Weston) Duchesne ex Rozier	1	–	21	–	12	0.46	–	0.01	58.5	–	–	24	–	16; 22
	Rosa arvensis Huds.	–	1	4	4	2	0.53	0.02	0.005	10.6	0.005	0.03	4	4	15
	Rosa canina L.	–	1	4	4	1	0.04	0.06	0.04	0.32	0.01	0.08	4	4	15
	Rubus fruticosus agg.	–	1	5	4	3	0.02	0.04	0.004	11.7	0.01	0.25	38	12	15; 16
	Rubus sp.	1	–	20	–	10	0.91	–	0.005	23.0	–	–	20	–	16
Rutaceae	*Citrus* × *sinensis* (1)	1	–	–	1	1	–	15.4	–	–	1.79	21.2	–	8	14
	Citrus × *sinensis* (2)	1	–	–	1	1	–	21.2	–	–	0.80	21.2	–	6	14
	Citrus reticulata Blanco	1	–	–	1	1	–	6.82	–	–	6.82	6.82	–	1	14
Solanaceae	*Datura stramonium* L.	–	1	4	–	0	0.01	–	0.005	0.02	–	–	4	–	15
	Solanum dulcamara L.	–	1	4	–	1	0.01	–	0.004	17.1	–	–	8	–	15
Tropaeolaceae	*Tropaeolum* sp.	1	–	–	1	1	–	741	–	–	741	741	–	1	1
Violaceae	*Viola arvensis* Murray	–	1	4	4	2	0.03	0.02	0.005	3.78	0.004	0.03	20	12	15
TOTAL		**41**	**54**										**1491**	**404**	

[a] The number of records for reported residues.
[b] The complete citation is given in Supplementary material (Table S1).
[c] Cultivated.
[d] Wild.
[e] Values of residues above the limits of detection/quantification.
[f] The numbers refer to different varieties or cultivars (e.g. winter or spring), more information in Supplementary material (Table S3).

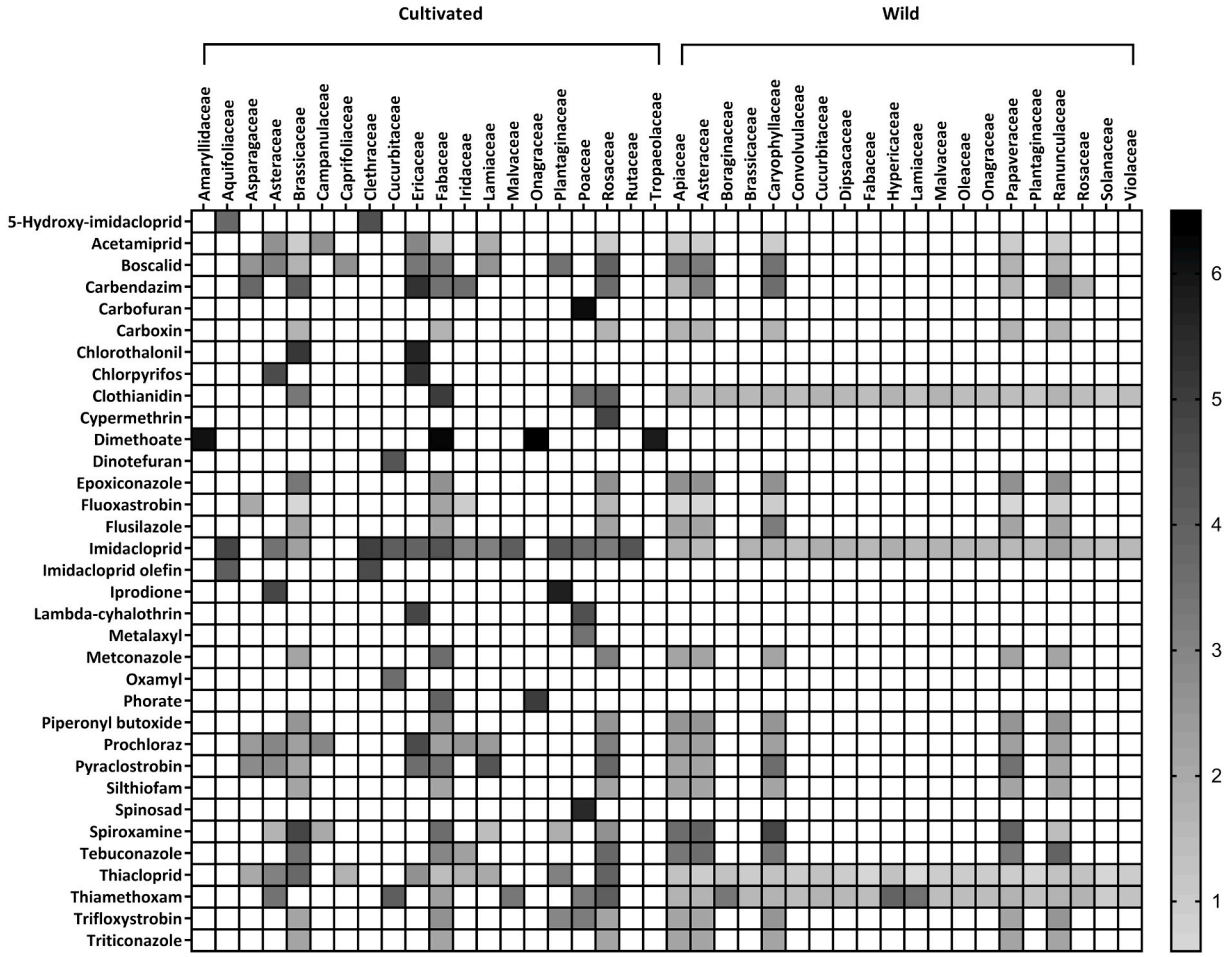

Fig. 2. A heat map on a Log_{10} scale (colour scale on the right), showing the median concentrations of the PPP residues (left y axis) for both nectar and pollen in respective plant families (top x axis). The plant families are separated in two categories: cultivated and wild taxa. The cool colours represent low residue concentrations, while the warmer colours represent higher concentrations. The blank squares highlight the compounds that were not evaluated for certain families, emphasizing the amount of missing information. In order to avoid negative Log_{10} values, and for the purposes of this figure only, we converted the values of the residue concentrations in pg/g instead of ng/g. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

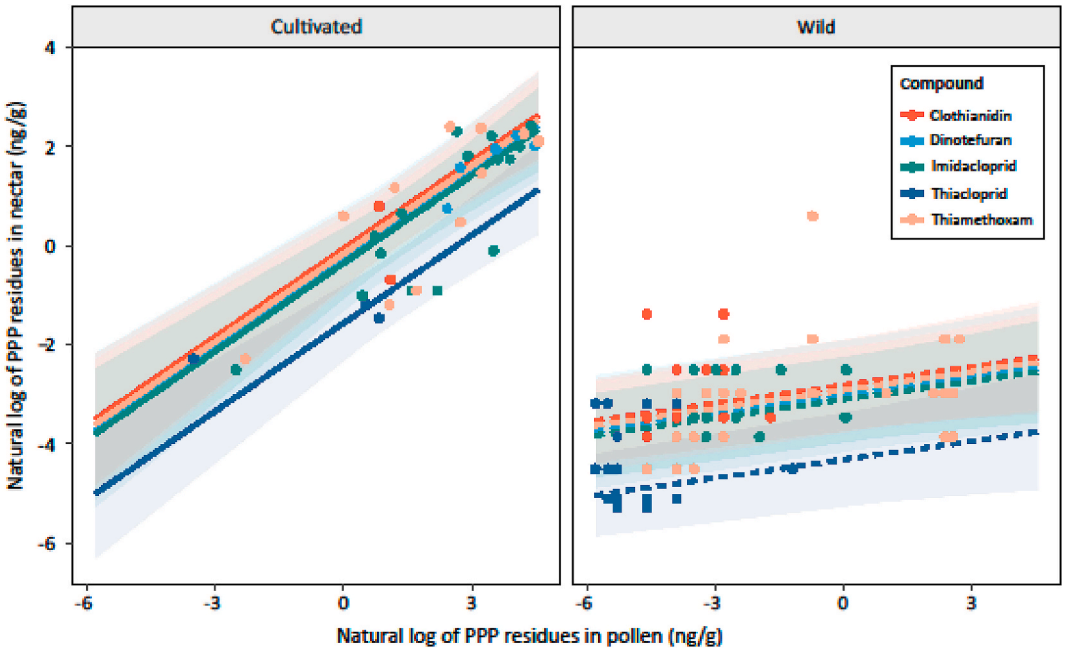

Fig. 3. PPP residues in nectar and pollen for cultivated and wild plant species. Points show data from studies where both nectar and pollen were measured concurrently. Colours indicate PPP compounds investigated. Fitted lines show the relationship between pollen and nectar residues from the Generalized Linear Mixed Model. Shaded areas indicate the 95% confidence intervals on fitted lines. Dashed lines in the wild species plot should be interpreted with caution as the majority of residues were below the limits of detection for wild species (see main text). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

3.4. PPP residues and toxicity to bees

LD_{50s} from toxicity assay data were available for honey bees (*Apis* spp.), bumble bees (*Bombus* spp.) and six species of solitary bees (*Osmia* spp., *Megachile* sp., *Scaptotrigona postica*, *Nannotrigona* sp., *Trigona* sp. and *Nomia* sp.) (University of Hertfordshire, 2019). From this initial assessment, a forager honey bee may daily be exposed to 50–100% (84%) of its LD_{50} for spinosad through both oral and contact exposure to pollen and greater than its LD_{50} for dimethoate, imidacloprid and clothianidin through both oral and contact exposure to nectar (Tables 4 and S6). A bumble bee could daily be exposed to 50–100% (70%) of its LD_{50} for thiamethoxam, and greater than its LD_{50} for the compounds imidacloprid and dimethoate through nectar consumption, and come in contact with greater than its LD_{50s} for the compounds clothianidin, imidacloprid and dimethoate. Our results show that the residues of the compound dimethoate found in pollen can cause contact toxicity to the solitary bee species *Nomia* sp., while having very low % LD_{50} values for other bee species. The same applies for thiacloprid residues found in nectar and the solitary bee species *Nannotrigona* sp. (Tables 4 and S6). A nectar foraging honey bee over a single foraging bout is likely to be exposed to concentrations above its LD_{50s} for the compounds dimethoate, imidacloprid, clothianidin, thiamethoxam, dinotefuran, phorate and oxamyl (Table S5).

4. Discussion

In the present study, we performed a literature review of the PPP residues detected in nectar and pollen from plants. Most publications originate from North America (mainly United States) and Europe (mainly United Kingdom), while there is complete absence of studies from South America, most of Asia, Africa and Australia, creating a restricted view of the field realistic exposure to PPPs and leading to big knowledge gaps. Hence, there is an urgent need for reporting the field realistic residues from countries of the southern hemisphere and Asia since their particular climatic conditions along with the different agricultural practices and bee species may produce different conclusions from the ones that have been drawn for the Northern hemisphere (Benuszak et al., 2017).

The first reports of PPP residues in nectar date back in the ‘60s (Lord et al., 1968), and until the ‘80s they were mainly focused on the organophosphate compound dimethoate. A significant amount of time passed (20 years) without any additional reports. After the introduction of the neonicotinoid compound imidacloprid to the market (Bonmatin et al., 2003), and the intense concerns associating its wide-spread use with honey bee deaths (Bonmatin et al., 2005a,b), imidacloprid residues were reported in nectar and pollen for the first time in 2001. However, the majority of studies of residues in nectar and pollen were published the years 2012 and 2015, emphasizing the recent concerns regarding the environmental fate and the effects of the chemicals to pollinators (Benuszak et al., 2017). Fungicides were evaluated in nectar and pollen for the first time in 2012, but gained more attention after 2015. This is because until 2015, the acute toxicity of fungicides to adult bees was assumed to generally be low (Johnson, 2015), although it was suspected that they may act synergistically with systemic insecticides, increasing their toxicity by as much as a factor of 1000 (Iwasa et al., 2004; Schmuck et al., 2003). Despite the fact that herbicides have been detected when analysing mixed matrices containing nectar from flowers, nectar stored in the comb, and honey or pollen from pollen traps (Pohorecka et al., 2012; Prado et al., 2019), the presence of herbicides in raw pollen or nectar collected from plants has neither been verified nor evaluated, highlighting that future research needs to address this issue. Insecticides require higher tier risk assessments since they are more toxic to insects (Kyriakopoulou et al., 2017; Sánchez-Bayo and Goka, 2014). However, evidence is emerging that compounds belonging to the category of herbicides were found to implicate sublethal effects on pollinators (Bohnenblust et al., 2016; Cousin et al., 2013; Dai et al., 2018; Faita et al., 2018; Farina et al., 2019; Goñalons et al., 2018; Helmer et al., 2014; Jumarie et al., 2017; Motta et al., 2018; Seide et al., 2018; Vázquez et al., 2018), thus they should also be evaluated for field realistic residues.

We found 31 fungicides and insecticides identified in pollen and nectar collected directly from plants. Even though more fungicide

compounds were examined for PPP residues overall, insecticides were more commonly evaluated, particularly, neonicotinoids. Exposure to neonicotinoids has been cited as an exceptional cause for concern for pollinating insects, because they are widely used systemic agrochemicals that have been shown to contaminate pollen and nectar of crop plants and nearby wildflowers (Bonmatin et al., 2015; Botías et al., 2015, 2016; Chen et al., 2013; Choudhary and Sharma, 2008; Cowles and Eitzer, 2017; Cutler and Scott-Dupree, 2014; Fairbrother et al., 2014; Goulson et al., 2015; Hoffmann and Castle, 2012; Pilling et al., 2013; Tosi et al., 2018; Xu et al., 2016). However, as identified here, none of the compounds with the highest median levels of residues in pollen and nectar (carbofuran, iprodione, dimethoate, spinosad, chlorothalonil, phorate and oxamyl) belongs to the neonicotinoid category. Moreover, for a risk assessment it is very important to collect extended data on various chemical compounds (Benuszak et al., 2017), rather than focusing on just a few. The total number of publications concerning PPP residues in nectar and pollen directly collected from plants (n = 25 studies) and the respective number of PPPs evaluated remains low, given that approximately 1000 active ingredients are globally available (Lewis et al., 2016). However, since it is not possible to test all potential combinations, the mixtures most likely to occur in the agricultural areas of a country should be considered (Sgolastra et al., 2020; Zhu et al., 2017).

Research to date has focused predominantly on parent active ingredients alone, and there is evidence for known concentrations of only two metabolites of the active ingredient imidacloprid (5-Hydroxy-imidacloprid and imidacloprid olefin) and one synergist (piperonyl butoxide), confirming that very few studies evaluate the presence of the main compound degradation products and the ingredients of the commercial formulations (Benuszak et al., 2017). Our review highlights that as the majority of PPP were applied as commercial formulations, co-formulants should therefore be expected to be present, with the most frequent co-formulants found to be three fungicides, two insecticides and one preservative with fungicidal properties. This creates more concerns, since it has been found that co-formulants may have a negative effect on honey bees (Mullin, 2015; Mullin et al., 2015), while it is known that some metabolites of active ingredients may have higher toxicity than the initial compound (Nauen et al., 2001).

Contrary to the limited number of compounds evaluated, a wide range of plant taxa, including both cultivated and wild plants, were studied for PPP residues in nectar and pollen. As illustrated in the heatmap (Fig. 2), it is evident that the concentrations of the compounds found in cultivated plant taxa are higher from those found in the wild. However, there is a lot of information missing as wild species are significantly understudied compared to cultivated. In spite of the fact that, in total, more wild taxa than cultivated have been studied, the cultivated taxa were more often evaluated, while the information about residues found in wild species derives from only two studies (Botías et al., 2015; David et al., 2015, 2016). According to recent research, wild plants growing in close proximity to agricultural land can be a source of higher and more prolonged PPP exposure than the crops (Botías et al., 2015; Wood et al., 2019). Thus, for future residue studies, it is suggested to investigate both cultivated and wild species, preferably in the same study.

In their discussion of determination of PPP residue concentrations in bee relevant matrices in field experiments, it was acknowledged by US regulators that a primary limitation was that both spatial and temporal resolution of the PPP residue profiles in these matrices was low (Heimbach et al., 2017). This is also highlighted in the relevant limited research published. For the chemical analyses of pollen and nectar a minimum of approximately 100 mg (pollen) (Botías et al., 2015) and 10 μL (nectar) (Martel et al., 2013) is required. However, even when these amounts are collected, this may not be sufficient to detect or quantify PPP residues: in the full dataset analysed in our study, the majority of reports for both matrices were reported as below the values of limits of detection or quantification (LOD or LOQ). It is clear therefore that for pollen and nectar analysis in field experiments, significant limitations exist in terms of both sampling requirements and analytical instrumentation capabilities. The low amounts of the acquired matrices are also the reason why a multi residue analysis cannot be easily performed, and the maximum number of PPPs analysed was 20. Moreover, the available studies differed considerably in design, sampling timing, sampling methodology and application scenarios, or lacked data types of active ingredients, meaning residue data were difficult to compare (Gierer et al., 2019). Hence, in order to evaluate if there is a relationship between the two matrices, we chose to perform an analysis with a selected amount of paired data and only for the compounds for which we had enough information. Strong positive correlation was observed between pollen and nectar insecticide residues in cultivated plant species, and this is in accordance with previous findings (Kyriakopoulou et al., 2017). Taking into account the fact that the volume of pollen needed for analysis can be collected more easily than that of nectar, and the fact that there is a correlation between those two matrices - at least for the group of neonicotinoid insecticides, we suggest that pollen could be used as surrogate matrix for the analysis of neonicotinoid residues in cultivated taxa. However, the correlations for wild species were weaker. This may have been influenced by the high proportion of measurements of both pollen and nectar, which were below the limits of detection in wild plant species (82% for pollen and 99% for nectar). For cultivated species with reliable estimates (i.e. above LOD/LOQ values are available), the vast majority (>90%) had higher residues in pollen than in nectar, potentially due to its physical characteristics (i.e. highly sculptured cavities filled with a lipophilic pollen coat) (Mullin et al., 2010). In wild species, the levels of both were mostly below LOD/LOQ, but in pollen more frequently above LOD/LOQ than in nectar. Our analysis suggests that residues in wild plants were generally lower than in cultivated plants (especially in nectar). However, the current data does not permit further assumptions about the relationship between pollen and nectar of wild plants. It should be noted that it is typically much more difficult to collect sufficient pollen and nectar of wild plants for analysis. Pollen resources have been determined to be between 0.0001 μL and 15.9 ± 2 μL per floral unit for pollinator friendly seed mixes (Hicks et al., 2016). Thus, in order to detect and quantify the PPP residues in pollen and nectar, relatively large amounts of the two matrices need to be collected from several plants (~1000 flowers). Given that wild species may not occur at high abundance in agricultural landscapes, reaching the threshold amount of matrix for analysis is challenging, potentially limiting the extent of our knowledge of residues in wild plants. Differences between plant families in terms of residue concentrations explained a relatively low amount of variance in the model (4.5% out of a total of 88% explained by the full model). However, more research should be carried out for other PPP categories (fungicides and herbicides), in order to examine whether the same relationship is applicable. The fact that 'Study' explained a lot of variation in residues measured in nectar emphasises the need for the standardization of protocols for experimental and analytic methods across studies on a global scale. Furthermore, the factor 'Status' was similarly important, and suggests that important differences may exist between wild and cultivated taxa, indicating that studies should examine the same compound on both cultivated (e.g. *B. napus*) and wild (e.g. *Rubus fruticosus* agg.) plant taxa.

By relating the maximum residue values of the PPPs found in nectar and pollen with the contact and oral LD_{50s} from toxicity assays for bees using the Estimated % LD_{50s}, we found that bees could be exposed to a high percentage of a toxic dose of certain compounds. For example, a nectar foraging honey bee over a single foraging bout is likely to be exposed to values that exceed the honey bee LD_{50s} for the compounds dimethoate, imidacloprid, clothianidin, thiamethoxam, dinotefuran, phorate and oxamyl (Table S5). In the present review, we indicate that a mean number of two compounds was detected in each plant species, while a single cultivated (*Brassica napus*) or wild (*Silene latifolia*) plant has been found to be contaminated with up to 14 and 8 different compounds respectively. This implies that a nectar foraging honey bee could be exposed to a poisonous cocktail of PPPs if they forage on multiple

Table 4
The percentages of the Estimated % LD_{50} based on the maximum residues of the PPP detected in pollen (P) and nectar (N) and the respective oral (O) and contact exposure (C) LD_{50s} from toxicity assays.

	Estimated % LD_{50} [a]																							
	Honey bees				Bumble bees				Solitary bees															
	Apis spp.				*Bombus* spp.				*Osmia* spp.				*Megachile* sp.				*Scaptotrigona postica*		*Nannotrigona* sp.		*Trigona* sp.		*Nomia* sp.	
	C [b]		O [b]		C		O		C		O		C		O		O		C		C		C	
Compound	**P**	**N**	**P**	**N**	**P**	**N**	**P**	**N**	**P**	**N**	**P**	**N**	**P**	**N**	**P**	**N**	**P**	**N**	**P**	**N**	**P**	**N**	**P**	**N**
Acetamiprid	<50	<50	<50	<50	<50	<50	<50	<50	<50	<50	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Boscalid	<50	<50	<50	<50	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Carbendazim	<50	<50	<50	<50	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Carbofuran	<50	-	<50	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Carboxin	<50	-	<50	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Chlorothalonil	<50	<50	<50	<50	<50	<50	<50	<50	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Chlorpyrifos	<50	-	<50	-	<50	-	<50	-	<50	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Clothianidin	<50	**>100** [c]	<50	**>100**	<50	**>100**	-	-	<50	**>100**	<50	<50	-	-	<50	<50	-	-	-	-	-	-	-	-
Cypermethrin	<50	-	<50	-	<50	-	<50	-	-	-	-	-	-	-	-	-	-	-	-	-	<50	-	-	-
Dimethoate	<50	**>100**	<50	**>100**	<50	**>100**	<50	**>100**	<50	**>100**	<50	**>100**	**>100**	**>100**	-	-	-	-	-	-	-	-	**>100**	**>100**
Dinotefuran	<50	<50		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Epoxiconazole	<50	-	<50	-	<50	-	<50	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Fluoxastrobin	<50	<50	<50	<50	<50	<50	<50	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Flusilazole	<50	-	<50	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Imidacloprid	<50	**>100**	<50	**>100**	<50	**>100**	<50	**>100**	<50	**>100**	-	-	<50	**>100**	-	-	<50	<50	-	-	-	-	-	-
Iprodione	<50	<50	<50	<50	-	-	-	-	<50	<50	<50	<50	-	-	-	-	-	-	-	-	-	-	-	-
Lambda-cyhalothrin	<50	-	<50	-	<50	-	<50	-	<50	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Metalaxyl	<50	-	<50	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Metconazole	<50	-	<50	-	<50	-	<50	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Oxamyl	<50	<50	<50	<50	<50	<50	<50	<50	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Phorate	-	<50	-	<50	-	<50	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Piperonyl butoxide	<50	-		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Prochloraz	<50	<50	<50	<50	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Pyraclostrobin	<50	<50	<50	<50	<50	<50	<50	<50	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Silthiofam	<50	-	<50	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Spinosad	**50-100** [d]	-	**50-100**	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Spiroxamine	<50	<50	<50	<50	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Tebuconazole	<50	<50	<50	<50	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Thiacloprid	<50	<50	<50	<50	<50	<50	-	-	<50	<50	-	-	-	-	-	-	-	-	<50	**>100**	-	-	-	-
Thiamethoxam	<50	<50	<50	**50-100**	<50	<50	**50-100**	**50-100**	-	-	-	-	-	-	-	-	-	-	<50	<50	<50	<50	-	-
Trifloxystrobin	<50	<50	<50	<50	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Triticonazole	<50	-	<50	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

[a] The Estimated % LD_{50} was calculated using the maximum PPP concentrations and the respective oral and contact exposure LD_{50s} from toxicity assays of the various bee species. More information on the exact values can be found in the text Supplementary material (Tables S4 and S6). [b] The information about the LD_{50s} was retrieved from the Pesticide Properties DataBase, developed by the Agriculture & Environment Research Unit (AERU) at the University of Hertfordshire, [c] The values highlighted in dark blue shading and bold white font (>100) indicate high percentages exceeding the Estimated % LD_{50}, [d] The values highlighted in light blue shading and bold black font (50-100) indicate values exceeding the 50% LD_{50}, but below the 100% LD_{50}.

plant taxa during a single foraging bout. Research has shown that short-term (acute) exposure to insecticides during one foraging bout can significantly impair learning and memory in bees (Siviter et al., 2018). Moreover, this could also mean that a generalist bee (a bee that visits a wide range of plant species) might be exposed to a higher number of PPPs during her lifespan (chronic exposure). This may also occur through repeated foraging on a large PPP-treated food source that flowers over a prolonged period, such as oilseed rape, and may be extended by the presence of PPPs within honey and pollen stores (Mitchell et al., 2017). According to our calculations, all the three bee types (honey bees, bumble bees and solitary bees) are likely to be exposed to values above the respective bee type LD_{50s} for several compounds (Table 4). Exposure to combinations of various types of PPPs, either during a single foraging bout, or throughout their life cycle, can have a variety of negative impacts on their health (Gill et al., 2012; Lentola et al., 2017; Sánchez-Bayo et al., 2016). It has also been reported that many compounds become more toxic with repeated exposure over time, so that even low concentrations can eventually result in death (Rondeau et al., 2014; Sánchez-Bayo and Goka, 2014; Suchail et al., 2001). However, levels of contaminant mixtures can vary widely depending on the location and the type of plants (cultivated or wild), as well as the diet breadth and foraging area of the bee (Botías et al., 2015), and unfortunately there is limited data regarding the exact amount of flowers of a certain plant species that a bee might visit on a single bout, in order to be able to make assumptions on the exact level of exposure.

Our results indicate that residues of compounds found in pollen (such as dimethoate) or nectar (such as thiacloprid), that may have low Estimated % LD_{50} values for honey bees and bumble bees, can have high Estimated % LD_{50} values for solitary bee species (e.g. *Nomia* sp. and *Nannotrigona* sp.). This highlights that we need to expand toxicity assays to more bee species and stresses that using honey bees as a surrogate for PPP risk assessment for all bee species is insufficient (Bireley et al., 2019; Boyle et al., 2019; Cham et al., 2019; Hinarejos et al., 2019; Sgolastra et al., 2019, 2020). It should also be noted that the compounds detected in high concentration levels in pollen and/or nectar (carbofuran, iprodione, dimethoate, spinosad, and chlorothalonil, phorate and oxamyl), did not necessary have high Estimated % LD_{50} values. In fact, it was mainly the neonicotinoid compounds that had high Estimated % LD_{50} values, despite their low concentrations detected in pollen and nectar. This implies that compounds with similar properties to those of neonicotinoids (designed to have high efficacy, long persistence, high systemicity, high mobility, and application versatility) (Sgolastra et al., 2020), are likely to be more toxic to bees than others. The compounds that showed high Estimated % LD_{50s} were all insecticides, systemic and still approved for use in the United States, albeit, only two of them are still approved for use on a European level (oxamyl and spinosad). Since there is not enough available data on other, non-neonicotinoid insecticide groups (e.g. pyrethroids, phosphorothioates, sulfoximines etc.) (Siviter et al., 2018), future studies should start investigating more insecticides both for their effects on bee species and for their residues in nectar and pollen.

5. Conclusions and future research

Based on our findings, major knowledge gaps in this field have been identified: 1. There is paucity of information from extensive geographical areas of the world and thus we have incomplete information on how the same compounds behave in different climates and landscapes. 2. There is an urgent need to expand the range of compounds analysed in these studies. Herbicide and fungicide residues in pollen and nectar should be evaluated, alongside insecticides. Moreover, co-formulants used in PPPs along with the main active ingredients, and certain metabolites that derive from the degradation of the active compounds of those products, should be evaluated too. 3. As important differences may exist between cultivated and wild taxa, we suggest that at least one model wild plant species growing in the margins of the target crop should be evaluated in the same study. From our findings, *Rubus fruticosus* agg. , and *Trifolium repens* are the wild plant taxa most widely evaluated, hence they could act as model taxa. 4. PPP residues in pollen and nectar are affected by plant taxon, application method, physicochemical properties of the active ingredient or the formulation, and environmental conditions. However, very few of the studies reported all this information, which precludes further evaluation of the fate of the compounds in pollen and nectar. We strongly advise that future research include detailed information of all these factors, and especially the study design, sampling points and their spatial and temporal distribution. 5. In cultivated plant species, the residues found in pollen were positively correlated with those found in nectar, hence, risk assessments could be based on the concentrations found in pollen. Overall, given that maximum concentrations of several compounds detected in nectar and pollen were estimated to exceed the LD_{50s} for several species of bee, nectar and pollen residues represent an ongoing risk to flower-feeding insects and need to be better studied before being properly integrated into risk assessment.

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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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2020.109873.

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