Chapter

Detailed Review on Pesticidal Toxicity to Honey Bees and Its Management

Gaurava Kumar, Swoyam Singh
and Rukesh Pramod Kodigenahalli Nagarajaiah

Abstract

This chapter deals with the effects of different pesticides used in agro-ecosystem on honey bees and other pollinators and probable measures to manage this escalating problem of global decline of managed as well as the wild insect pollinators. This chapter describes different routes from which pollinators, especially honey bees get exposed to the different toxicants, followed by poisoning symptoms in honey bees. Further, this chapter focuses on the classification of different toxicants in different classes as per their nature. Finally, the management of these different toxicants and their toxicity to avoid bee poisoning has been considered in the later portion of the chapter.

Keywords: pesticide, toxicity, honey bees, pollinator, management

1. Introduction

Honey bees contribute more than 90% of the global pollination of more than approximately 85% of the total cross-pollinated plant species in the world, the blessing of being able to hover around and pollinate this much diverse array of floral plant species comes with a curse to these bees, of being in unremitting contact with a wide array of stresses like, parasites, predators, diseases, chemical, etc. present in the environment [1–3]. As being the most successful and commercially exploited pollinators in agro-ecosystems not just for their pollination duties but for commercially valuable by-products such as, honey, wax, propolis, etc. as well, honey bees faces more diverse stresses in nature. Honeybees (Apis mellifera) are exposed to an ever changing array of xenobiotics from both natural and synthetic sources. Thousands of older foraging worker honey bees travel as far as 10 km from the hive in the course of collecting the nectar, pollen, water, and propolis needed to sustain a colony of tens of thousands of young adult workers, immature bees, and male reproductive or drones [4]. While foraging over this large area for collecting pollen and nectar to satisfy the carbohydrate needs of the colony, bees forage in various flowering plants with different nature, but these food sources are not always entirely pure every time, having either different plant derived chemicals or the widely used toxic agro-chemicals mixed with them. With the ever increasing use of synthetic chemical pesticides in agriculture honey bees and other wild pollinators have faced a serious threat to their global biodiversity in recent decades [5–7]. Nectar and pollen may contain environmental pollutants or
systemic pesticides drawn from the soil, or they can be contaminated from topical pesticide applications or drift from such applications. Different agro-chemicals like, herbicides, fungicides and most importantly, the insecticides, alone and in combination with other factors such as elevated temperature, production of hybrid varieties with lesser quantity of pollen and nectar in their flowers, have caused a devastating effect on honey bees at a global level [2, 8, 9]. Bee foragers may bring such contaminated floral rewards back to the colony for feeding and storing as a resource for future generations [10]. Pesticides which are being used in agriculture crops are highly toxic to bees as they kill the bees through many ways such as, direct killing of foraging workers with their acute toxicity, drifting out from agricultural land to nearby apiaries, thus, making the whole colony more susceptible to different pathogens and to some point reduce their possibility to thrive in the nature by getting accumulated in the pollen inside the colony. Nectars produced by some flowering plant species also contain plant-synthesized chemicals which are toxic to different pollinators [11].

The introduction of chemical pesticides and further increase in its demand in the market is not actually the basic requirements of the farmer; rather it is their mere ignorance. The farmers discriminately use these agro-chemicals with a purpose to manage the pests; instead, they end up with killing their own beneficial insects, i.e., the pollinators. Honey bees and other pollinators get exposed to different toxic agro-chemicals in nature through different paths and these different pesticides affect honey bee colonies to different levels thus; to minimize the losses to pollinators from the adverse effect of pesticide poisoning is a burning topic of interest for human to protect the pollinators.

2. Routes of exposures to different pesticides

The different types of pesticidal formulations travel across the plant through different ways in order to protect the plant or part of it from different factors such as weeds, pathogen, insect pests or rodents, etc. According to the nature of the different pesticides, three principal application methods that are often used to treat crops are: direct spray, which is often used around homes and gardens; soil applications and seed applications, typically used in larger treatment systems. These different methods of application play a crucial role in the exposure of these chemicals to the insect pollinators, visiting a crop (Figure 1).

Thus, on the basis of different application methods and the persistence of different pesticides in nature, bees get exposed to different pesticides through these major routes:

1. Direct contact with chemical during foraging on a treated plant
2. Pesticide particles of dust formulations sticking to the foraging bees or to whole colony via drift through wind
3. Pesticidal runoff from the treated fields to nearby water reservoirs
4. Pesticidal drift to non-treated foraging plants growing nearby to the treated crop [12]
5. Pesticidal residues in pollen through seed treatment [12]

These different routes for exposure of various pesticides to honey bees facilitate their entry into a honey bee colony system, but still the mode by which, these
chemicals are pulled out by the forager bees from the fields are quite different being either by oral, respiratory or dermal intake. These different modes of intake of such chemicals are described here.

3. Mode of intake of toxicants

3.1 Oral intake

Oral intake of chemical pesticides from fields is facilitated through the foraging worker bees. Plants treated with different systemic insecticides, produce nectar and pollen containing these insecticides and thus, worker bees collecting this floral resource carries to the colonies to store it into the colony and further use to feed the young developing brood [13]. Several reports of an extremely high concentration of different pesticidal compounds, including insecticides, fungicides, miticides and herbicides have been reported from pollen samples of several crops [12, 14]. These events, from collecting the pollen in the field to feeding to the developing brood results in to a chain of catastrophic events as: foragers are killed during collecting and transporting such contaminated pollen, nurse bees are killed while storing and feeding pollen and the brood are killed by consuming the toxic pollen, thus, leading to a total collapse of the colony.

3.2 Respiratory intake

Respiration of pure oxygen plays a vital role in an organism’s growth and development since it ensures proper functioning of various organs in the organism. But, respiration of air admixture with toxicants causes various abnormalities such as abrupt behavioral changes and degradation of learning ability [15]. Pesticide formulations like, dust and fumigants travels through the air called ‘drift’ can either be carried out onto the body surface of foraging bees or can be absorbed through trachea (respiratory organs) in sufficient concentrations to be toxic to the bees (Table 1).
Modern Beekeeping

3.3 Dermal intake

This is the major mode of intake of toxicants by the bees since they are exposed to direct contact of pesticides in the fields while foraging on the crops. Honey bee foragers come in direct contact with several pesticides while foraging and such chemicals can be lethal even in small quantities. Dermal toxicity through topical spray has been reported for various insecticides and thorax has widely been regarded as a major route of dermal exposure of pesticides to the honey bees [16, 17]. Other than thorax, insect wings have been reported as a more lethal route of exposure to the bees [18]. Some of the majorly important and frequent ways of dermal intakes are following:

- Majority of bee poisoning is due to application of insecticides to crops during blooming period.
- Bees coming in contact of treated areas.
- Bees coming in contact with insecticides residues on plants and collect insecticide dust with pollen.
- Bees drinking or touching contaminated water or honeydew on the ground or foliage or from nearby water bodies.
- Contamination through treated nectar sources. Dimethoate is the only systemic insecticide known to be excreted in hazardous amount in nectar under field conditions.

4. Symptoms of bee poisoning

- One of the obvious signs of pesticide poisoning is the presence of a large number of dead or dying bees at the hive entrance. These bees are foragers who have been exposed to pesticides sprayed in the fields.
- Another common symptom includes the presence of a moist and sticky mass of dead bees at the hive entrance. This results from poisoning by some fast-acting pesticides, e.g., organophosphorus pesticides. Dying bees extend their tongues through which nectar is regurgitated resulting in sticky and moist dead bees. Bees that have been exposed to a pesticide may regurgitate a thick and dark fluid.
- Swiftly-acting insecticides kill foraging bees in the field itself, while only some of them manage to return to the hive. Sometimes, while spraying is done in the nearby fields to the apiaries, if such chemicals come in direct contact with colony, the whole colony may also die instantly. Stronger colonies suffer greater

|                | $N_2O$ | $CO_2$ | Ammonium nitrate | Control |
|----------------|--------|--------|------------------|---------|
| With pollen    | 0      | 0      | 0                | 15      |
| Without pollen | 16     | 33     | 25               | 25      |

Source: Data extracted from Mackensen [22].

Table 1. Pollen gathering by bees after anesthetic treatments.
losses from pesticidal poisoning than weaker ones, because they have larger numbers of foraging bees.

- Foraging bees often carry residual pesticides in their pollen loads while returning to the hive. As a result, the behaviour of bees in the hive changes abruptly. Honeybees in such colonies become more aggressive or agitated. When a hive containing pesticide-affected bees is opened, the bees fly out of the hive sometimes straight at the face of the beekeeper handling them.

- Other symptoms include stupefaction, paralysis, aggressiveness and abnormal behaviour, jerky, spinning movements. Slowing down of activity and crawling of bees around the hive entrance. They lose their ability to fly and ultimately die 2 or 3 days after poisoning. Poor egg laying patterns or abnormal supercedure of queens.

- Within the hive, a break in the brood cycle (stages of young bees) or a spotty pattern of the brood could also indicate a pesticide problem.

### 5. Classification of toxicants

Classification of different toxicants to honey bees can be done either on the basis of levels of toxicity or on the basis of sources in the nature. Different toxicants have variable toxicity levels, according to their mode of action on bees and this toxicity level is measured as LD$_{50}$, which is the dose at which 50% of the bee population dies due to the intoxication. On the basis of their LD$_{50}$ levels, toxicants have been classified into four different categories [19].

- highly toxic (acute LD$_{50} < 2 \mu g/bee$)
- moderately toxic (acute LD$_{50} 2–10.99 \mu g/bee$)
- slightly toxic (acute LD$_{50} 11–100 \mu g/bee$)
- nontoxic (acute LD$_{50} > 100 \mu g/bee$) to adult bees

Second type of classification is based on the type of toxicants which are originated from different sources, due to human interventions. These toxicants include:

#### 5.1 Inorganic toxicants

#### 5.1.1 Carbon dioxide

The modern time has become an era of the greenhouse gases and global warming. The ever-increasing concentration of various poisonous gasses in the atmosphere has affected a vast majority of the living beings in this world and honey bees are also not any exception with carbon dioxide being the most important of these gasses. Several scientists have worked on the toxicity of carbon dioxide on honey bees and have found some drastic effect of this gas on honey bee at both the levels including individual bees as well as at the colony level, which includes narcosis in foraging honey bees [11], earlier oviposition of queen [20], reduction in life expectancy [21] and reduction in pollen gathering by foraging bees [1].
5.1.1.1 Narcotic effect of CO$_2$

Bees treated with a mixture of air and CO$_2$ for 5 min have shown to stop their movement and went motionless but regaining their activity, once it was left for 30 min. The same experiment when repeated with only air for comparative study showed that only air did not anesthetize the bee. Thus, it can be concluded that the CO$_2$ at even low concentrations is detrimental to honey bees since they have a narcotic effect \[1\].

5.1.1.2 Effect of CO$_2$ on pollen gathering ability of the forager

The drastic effect of different chemicals used in the apiaries has been shown to decrease the pollen gathering ability of the forager bees. This decrease in the pollen supply during the blooming seasons can cause a severe threat to the reserves of the colony during winter season, where most of the pollen is consumed for the survival of the colony. This decrease in pollen gathering ability in the worker bees have been observed by different workers and such chemicals like, carbon dioxide, nitrous oxide and ammonium nitrate have been found to be decreasing the pollen gathering capacity of as many as 40 treated worker bees with a threatening outcome of no bee being able to gather pollen after the exposure to abovementioned chemicals, which are widely used in apiaries for different purposes \[22\].

5.1.2 Metal toxicity

Continued anthropogenic pressure due to the ever-highest human population, which has no signs to slow down in near future have put an alarming metal and metalloid pollutants pressure over the past century because of anthropogenic emissions into the environment. These pollutants may have negatively impacted the pollinators that reside in the soul of machinery responsible for the food production that sustains this human population. Metal pollutants are discharged into the air, water, and soil through different human activities including mining, agriculture, coal burning, hydraulic fracturing to extract gas and oil, and industrial and municipal waste production. Of all the toxic metals collected cadmium, copper and lead have been proved to be the most toxic to bees \[23\]. These three metals (Cd, Cu and Pb) have also been reported to change the feeding behavior in bees with increased sensitivity towards sucrose.

Once in soil, Cd and Cu is actively absorbed by plant roots, transferred via vascular bundles into the nectar and pollen, and subsequently accumulates in the pollinators and bee products since the pollinators collect the contaminated pollen and nectar. Copper is an essential trace element in plants and is able to accumulate in different plant tissues. Cu co-acts with several essential proteins to enhance growth and development of honey bees but it is toxic when it exceeds the cellular needs.

As lead is not easily trans-located within plants, thus, is also shown to be having a residual effect on forager honey bee. Lead gets trans-located within bees due to transfer through air and dislodgeable residues, resulting from deposition on surface contacted by bees \[23\].

5.2 Toxins used in bee keeping

A proper maintenance of an apiary depends upon the sanitation aspect of beekeeping but a proper and timely application of different synthetically formulated chemicals is also important for avoidance or management of severe health
problems. Different health problems like infestation of *Varroa destructor*, wax moth (*Galleria mellonella*), tracheal mite and other pathogenic diseases along with the long debated CCD of U.S. apiaries exerts a severe pressure and a serious threat of total loss of millions of honey bee colonies throughout the world and have been successfully managed by the use of various chemical treatments known to be less harmful to the honey bees. These chemicals have been shown to be far more successful than the other treatments, but at the same time, their toxicity towards bees has been highly neglected or has been less explored. One of the best examples for this has been the introduction of formic acid and oxalic acid, for the better management of honey bee parasitic mite, *Varroa destructor*. Medicated strips impregnated with synthetic acaricides such as, fluvalinate-tau and coumaphos have been used for many years for the management of this pest but both the coumaphos and fluvalinate are known to be highly toxic to older bees then young bees [24–26]. Workers that were subjected to less stress appear to be more resistant to fluvalinate and coumaphos poisoning [27, 28]. However, the appearance of resistant mite populations has resulted into a sharp rise in the practice to use formic acid (FA) and oxalic acid (OA). Both of the two organic acids, are varroacides in nature and serve as an attractive natural options for chemicals like coumaphos and fluvalinate as both of them have been reported to be naturally present in *A. mellifera* honey [29, 30].

These pesticides have lower efficacy against the *Varroa* mite but when used in an integrated pest management strategy, they have known to provide an efficient way to control *Varroa* populations. FA is most effective by evaporation of an impregnated substrate with 65% FA inside the hive and OA is most effective when applied in honey bee colonies either by dripping or spraying or through fumigation [9].

Both FA and OA have been proved to be effective to control *Varroa* mite but very less work has been done to establish its negative effect on honey bees. Schneider et al. [31] highlighted the detrimental effects of FA and OA on honey bees which include:

1. Increased mortality
2. Negative effects on brood development
3. Reduced fitness of treated colony
4. Decreased division of labour
5. Reduced hive cleaning and increased self-grooming

### 5.2.1 Formic acid toxicity

The mode of action of FA against *Varroa* is by inhibition of electron transport into the mitochondria via binding to the last enzyme of electron transport chain, cytochrome c oxidase [32]. Formic acid may produce different toxicity symptoms in honey bees, including reduced longevity of the worker bees [33] and reduced rate of brood survival [34]. Other negative effects of formic acid treatments to honey bee colony mainly includes, increased number of dead bees in front of colonies during the FA treatment period, rejection of queen, worker bees may repel from the colony and a comparatively lower honey yield from the FA treated colony [9].

### 5.2.2 Oxalic acid (OA) toxicity

As OA is generally provided to the honey bee colony in sugar syrup, in order to increase its efficacy against the *Varroa* mite by increasing its stickiness on to the
mite body, thus, its repeated application to a colony can be proved as lethal to the honey bees as well. A high queen mortality and reduced number of sealed brood have been reported in the colonies treated with OA [35]. The OA treatment has also been reported to be associated with an increased apoptosis in bee midgut [36]. Worker bees have been reported to be showing an abnormal age-related pattern problem while treated with oxalic acid during their early life stages. A dose of 3.5% oxalic acid dehydrates at after 24 h of emergence have been reported to have a disturbance in the normal age-related patterns of worker honey bees. All the age-related patterns of the workers appear in the natural chronology: they shows first events of behavioral patterns for nursing, followed by, honey or pollen manipulation, wax manipulation and patrolling at the same time but in different intensity. The bees start showing all age-related patterns somewhat earlier than the normal. Treated bees show an increased self-grooming, a superior tendency to inactivity and decreased nursing behavior. For all other behavioral patterns, including trophallactic interactions, house-cleaning, honey manipulation and patrolling, bees show no significant changes than the normal chronology [27].

5.3 Agrochemicals

5.3.1 Insecticides

Chemical control for insect pest management contributes as the major part of insect pest management strategies used all over the world [37]. Insecticides have been used since early 1940s for the effective pest management and have been a successful tool for the pest management as saving serious crop losses through insect pest infestations [38]. But, at the same time, the negative effects of these synthetic chemicals have created havoc throughout the world by suppressing the overwhelming populations of several non-target insect species, mainly including the biological control agents and the pollinators. Honey bees are susceptible to many insecticides and different harmful effects of these insecticides are believed to be the prime most reason for the decline in global honey bee populations [9, 39, 40]. The different insecticides have been highly criticized for their possible role in widely discussed and seriously concerning worldwide losses of honey bee colonies [41, 42]. Since the first detailed report and description of the term ‘colony collapse disorder’ (CCD) in 2006 [43] in America and followed by Europe, had again initiated the long term agitation of banning the use of insecticides, posing a serious threat to the billion dollar industry. Since the CCD, possible role of insecticidal residues in weakening the honey bee colonies for an increased susceptibility towards different environmental and pathogenic pressure on different colony levels has widely been discussed in scientific community [7, 44–50].

Lethality of any pesticide to honey bee is measured during toxicological tests of lethality by observing the mortality of bees after the application of pesticides either by oral administration or by topical application. The bee is usually considered dead when it exhibits “no movements after prodding”. Investigation on lethality of any insecticide includes the use of correlation metrics to link the lethality and dose of a toxic chemical or substance to the bees [51, 52]. List of lethality of different class of insecticides was compiled from supporting information from Hardstone and Scott [53], and for the same information regarding fungicides and herbicides was compiled through ECOTOX database [54].

The different class of chemical insecticides poses variable threat to the individual honey bee and a colony level health, thus, the toxic effects and toxicity symptoms of different insecticides can be discussed under one umbrella of major classes of insecticide causing toxicity to the honey bees which is described here.
5.3.1.1 Acetyl cholinesterase Inhibitors

The two widely used groups of insecticides, organophosphates and carbamates, act on insects in a similar way as acetyl cholinesterase (AChE) inhibitors which in normal conditions, inhibits the activity of neurotransmitter acetylcholine in the insect nervous system [53]. These two groups of insecticides have deeply investigated for their toxic effects on honeybees and have been reported to have high larval as well as chronic toxicity to the adult bees causing toxicity symptoms like memory loss and behavioral agitations [55–60]. These two classes of insecticides have a variable amount of topical toxicity to the bees with LD$_{50}$ ranging between 0.018 and 31.2 µg/bee [61, 62], with some of the widely used insecticides enlisted in Tables 2 and 3.

| Insecticide (organophosphate) | LD$_{50}$ (µg/bee) | Risk ranking |
|-------------------------------|-------------------|--------------|
|                              | Mean | Range   |
| Chlorpyrifos                 | 0.01 | —       | High        |
| Coumaphos                    | 31.2 | —       | Low         |
| Diazinon                     | 0.2  | —       | High        |
| Dicrotophos                  | 1.62 | 0.410–3.05 | High |
| Dichlorvos                   | 2.73 | 0.290–5.01 | High |
| Fenitrothion                 | 1.66 | 0.180–3.83 | High |
| Malathion                    | 0.2  | —       | High        |
| Methidathion                 | 0.236 | —       | High        |
| Methyl parathion             | 1.66 | 0.610–3.24 | High |
| Paraoxon                     | 0.600 | —       | High        |
| Parathion                    | 1.36 | 0.100–3.50 | High |
| Phorate                      | 2.45 | 0.910–3.20 | High |
| Phosmet                      | 1.06 | —       | High        |
| Phosphamidon                 | 4.89 | 0.020–14.5 | High |
| TEPP                         | 0.410 | 0.010–1.20 | High |

Source: Data compiled in Hardstone and Scott [53].

Table 2.
List of organophosphate insecticides with respective toxicity to the bees.

| Insecticide (carbamates) | LD$_{50}$ (µg/bee) | Risk ranking |
|--------------------------|-------------------|--------------|
|                          | Mean | Range   |
| Oxamyl                   | 0.094 | —       | High        |
| Methomyl                 | 0.16  | —       | High        |
| Carbaryl                 | 1.1   | —       | High        |
| Carbofuran               | 1.55  | 1.49–1.60 | High |
| Aldicarb                 | 2.36  | 1.52–2.85 | High        |
| Bendiocarb               | 2.64  | 1.00–4.28 | High        |
| Aminocarb                | 4.40  | 0.85–11.2 | High        |

Source: Data compiled in Hardstone and Scott [53].

Table 3.
List of carbamates insecticides with respective toxicity to the bees.
5.3.1.1 Toxic symptoms of organophosphates

- Regurgitation of ingested food
- Disoriented movements
- Distended abdomens
- Erratic movement of the bees
- Wings hooked together, held away from body
- Extended tongues
- Death of the bee

5.3.1.2 Toxic symptoms of carbamates

- Erratic movement of the bees
- Stupefaction (numb)
- Paralysis
- Break in brood cycle
- Queen ceases egg laying
- Development of supersedure queen bees
- Most bees die at colony

5.3.1.2 Nicotinic acetylcholine receptor agonists

Leaves of *Nicotiana tabacum*, the plant producing the nicotine which mimics the neurotransmitter acetylcholine, activates the nicotinic acetylcholine receptor (nAChR), and promotes the generation of action potentials in postsynaptic nerve cells, contain up to 90,000 ppm of the nicotine, its pollen may contain up to 23 ppm and nectar 0.1–5 ppm alkaloid content [21, 46]. Adult bees have been proven to be successfully detoxifying nicotine in nectar with a median lethal concentration of 2000 ppm for nicotine [21], whereas the larva are sensitive to nicotine and usually die at the third or fourth larval instar at 5 ppm [46].

The neonicotinoids which are synthetic analogs of nicotine insecticides have a greater affinity to nAChR in the insect nervous system, including bees as well. In recent years, several studies and workers have portrayed these insecticides as the most serious cause of well discussed CCD [63–66]. However, these studies have been criticized for using unrealistic doses and duration of exposure [67]. The nitroguanidine neonicotinoids, including imidacloprid, clothianidin and thiamethoxam have been reported to be highly toxic to bees [68], with toxicity levels ranging from 0.004 to 0.075 μg/bee [69, 70] (Table 4). The insecticides like, thiacloprid and acetamiprid which are the member chemicals of cyanoguanidine neonicotinoid group, were much less toxic to the bees with topical or contact LD50 in a range of
7.1–14.6 μg/bee [70]. This relatively lesser toxicity of cyanoguanidines to the bees is probably due to rapid cytochrome P450 detoxification.

The nitroguanidine insecticides also show their toxic effect through impairing the ability of foraging honey bees to return to the hive [28, 71, 72].

5.3.1.3 Voltage-gated Na+ channel agonists

Pyrethrin insecticides, produced by pyrethrum flowers (Chrysanthemum cinerariaefolium) are again a widely used group of insecticidal compounds. Even though, the pyrethrin has a natural origin, still these chemicals are known to be highly toxic to the bees (LD$_{50}$ = 0.05–0.21 μg/bee) [73] (Table 5).

Other than pyrethrins, the pyrethroids, and organochlorine insecticides, show their action on the voltage-gated Na$^+$ channel in the axons of nerve cells, by delaying the closing of the Na$^+$ channel and prolonging the recovery period of the nerve cells, following the transmission of an action potential [74]. Bees show more tolerance towards some of the pyrethroids because of their rapid detoxification by cytochrome P450s. Being a pyrethroid, tau-fluvalinate a widely used miticide also

| Insecticide (neonicotinoids) | LD50 (μg/bee) | Risk ranking |
|-----------------------------|---------------|--------------|
|                            | Mean | Range |       |
| Acetamiprid                | 8.1  |       | Moderate |
| Imidacloprid               | 0.0039 | — | High |
| Thiacloprid                | 17.32 |       | Low |
| Thiamethoxam               | 0.0005 | — | High |
| Clothianidin               | 0.00368 | — | High |
| Dinotefuran                | 0.0023 | — | High |

*Source: Data compiled in Hardstone and Scott [53].

Table 4.
List of neonicotinoid insecticides with respective toxicity to the bees.

| Insecticide (organophosphate) | LD50 (μg/bee) | Risk ranking |
|-----------------------------|---------------|--------------|
|                            | Mean | Range |       |
| Bifenthrin                  | 0.0146 | —  | High |
| Cyfluthrin                  | 0.037 | —  | High |
| Esfenvalerate               | 0.017 | —  | High |
| Fenpropathrin               | 0.05  | —  | High |
| Gamma-Cyhalothrin           | 0.0061 | —  | High |
| Lambda-cyhalothrin          | 0.038 | —  | High |
| Permethrin                  | 0.024 | —  | High |
| Pyrethrin + PBO             | 0.002 | —  | High |
| Pyrethrin                   | 0.022 | —  | High |
| Zeta-cypermethrin           | 0.181 | —  | High |

*Source: Data compiled in Hardstone and Scott [53].

Table 5.
List of pyrethroid insecticides with respective toxicity to the bees.
appears to be less toxic or safer to the honey bees but in higher concentrations this chemical has been reported to affect the health of different castes of honey bee colony. Colonies exposed to high doses of tau-fluvalinate had smaller queen bees [75]. Drones exposed to tau-fluvalinate during development were also reported to be affected with lesser chances of attaining sexual maturity [14].

5.3.1.3.1 Toxic symptoms of synthetic pyrethroids

- Regurgitation of ingested food
- Erratic movement of the bees
- Paralysis
- Many bees die between foraging area and colony

5.3.2 Fungicides

“A fungicide is a specific type of pesticide that controls fungal disease by specifically inhibiting or killing the fungus causing the disease.”

It is believed to be nontoxic to bees by farmers and hence it is mostly applied during the flowering of plant coinciding with maximum bee activity. Thus, fungicides often account for most of the pesticide content of pollen [9]. An alarming concentration of fungicide chlorothalonil (99 ppm) has been reported from the honey bee pollen [76]. Other than chlorothalonil, in other studies, fungicides like vinclozolin (32 ppm) and iprodione (5.5 ppm) captan (contact) and difenoconazole [77] have also been reported from beebread. While fungicides are considered to be fairly safe for use around adult honey bees, beekeepers have reported losses of brood in larval and pupal stages coinciding with fungicide use during bloom. Fungicide applications also have been determined to trigger hypothermia in adult honey bees [78]. Fungicide was causing toxic effects to honey bee brood based on finding malformed, and frequently wingless, pupae and recently emerged adult bees. The affected bees accumulated on the bottom boards and at the entrance so hives about 2 week after applications. The toxicity levels for different fungicides lies in the range of LD$_{50}$ > 200 to as small as 0.2 μg/bee (Table 6).

| Active ingredient | Trade name   | LD50 (μg/bee) |
|-------------------|--------------|---------------|
| Dicloran          | Botran       | 0.2           |
| Captan            | Captan       | 10            |
| Dodine            | Sylit FL     | 12.5          |
| Propiconazole     | Bumper       | 25            |
| Ziram             | Ziram        | 46.6          |
| Thiram            | Thiram       | 74            |
| Sulfur            | Disperss     | >100          |
| Mancozeb          | Dithane      | 178.9         |
| Trifloxystrobin   | Flint        | >200          |

Source: Data compiled from ECOTOX database [54].

Table 6.
List of fungicides toxic to bees.
5.3.3 Herbicides

Even though the main purpose of using different herbicides is to control the unwanted weed populations in the fields and there is no such objective to kill insects through them. The toxicity level of herbicides is known to be very less to most of the insects and due to this these pesticides are applied without any restrictions regarding insects. Bees usually come across these chemicals in higher concentrations [79] and toxic effects of these have also been reported on honey bees. Toxicity levels in LD50 values differ from one chemical to another with a range of 14.5–100 μg/bee (Table 7). A widely used herbicide, paraquat has been reported to be toxic to the bees in laboratory conditions, causing median life of worker ten times reduced than the normal, on injecting at the rate of 15 μg per worker and death within a span of 3 days’ time, when sprayed at the rate of 4.5 kg Al/ha [79]. These pesticides may harm the bees in other way around as well as they reduce the number of plants offering floral resources to the bees.

6. Management of pesticidal toxicity to the honey bees

- **Use pesticides only when needed:** insect pests, pathogen or any environmental factor infest or infect the particular crops during specific growth stages of the plant and pesticide application should be done only after surveying the crop fields for the presence of weeds, pest population or disease incidence for threshold levels. This helps in safeguarding the population of insect pollinators, beneficial insects.

- **Do not apply pesticides while crops are in bloom:** use of different pesticides should only be performed only when the crop concerned is not in flowering stages.

- **Apply pesticide when bees are not flying:** the most pollinators are active during 8 a.m. to 5 p.m. and in such favorable conditions pesticides should not be sprayed to help in protecting the forager bees from coming in the direct contact

| Herbicide                             | LD50 (μg/bee) |
|---------------------------------------|--------------|
| 2,4-DB acid                           | 14.5         |
| 2,4-DP-P, dimethylamines              | 25           |
| Triflorysulfuron-sodium               | 25           |
| Pendimethalin                         | 49.5         |
| Triclopyr, butoxyethyl ester          | 62.5         |
| Alachlor                              | 68.1         |
| Simazine                              | 96.7         |
| Atrazine                              | 97           |
| Picloram, potassium salt              | 100          |
| Glyphosate, isopropylamine            | 100          |
| 2,4-D, 2-ethylhexyl ester             | 100          |

*Source: Data compiled from ECOTOX database [54].*

Table 7. List of herbicide toxic to bees.
with pesticide applied. To avoid such condition of direct contact of the pollinators with the pesticides, the application can be mostly in the early evening hours. This late application of the pesticides allows time for these chemicals to partially or totally decompose during the night.

- **Do not contaminate water:** contamination of nearby standing water through pesticides run off should be avoided to prevent the bee losses, as the bees collect water from these water sources to cool down the temperature of the colony during the summer season.

- **Use less toxic compounds:** if the situation allows, then the compounds which are less toxic to the bees should be given preference over the highly toxic chemicals. The pesticide labels should notify the possible hazards to honey bees. If no other alternate option remains then the variations in dosages can be applied.

- **Use less toxic formulations:** many pesticides work equally, when prepared in different formulations.

- **Microencapsulated insecticides** are found to be more toxic to honey bees than any other formulation. As the size of these capsules is similar to that of pollen, thus, it facilitates their transport directly into the colony, where these compounds remain poisonous for long time and can also be fed to the developing brood. Use of this formulation should strictly be prohibited if; there is any chance of collection of pollen by a foraging bee from the treated crop.

- Dusts are more hazardous than the liquid formulations as these chemicals can reach and enter a honey bee colony through drifting along with the air current. Ultra-low-volume (ULV) formulations are also more hazardous than the other liquid formulations as they can enter or reach a colony in the same manner as well.

- Emulsifiable concentrates are less hazardous than wettable powders.

- Granular formulation is also safer for the bees as these chemicals are provided to the lower parts of the plant canopy, which minimizes their direct contact with any flower visiting pollinator.

- **Identify attractive blooms:** attractive blooms in and around the field to be sprayed should be check before the application as most of the times such blooms of weed flora attracts the foraging bees and the pesticidal drift to such blooms can be hazardous to the visiting pollinators. In order to avoid such incidents the blooms of weed plants can be removed before the application.

- **Notify beekeepers:** beekeepers should be notified well before the application, as this time period will allow them to move their colonies to a distance where, pesticidal drift is minimal. Colonies can also be covered with the cloth to confine bees into the box itself to avoid any foraging for 1 or 2 days.

7. **Conclusion**

Pollinators in general, either insects or the handful of other animal species are of utmost importance for their continuous support to most of the cross pollinated plant species for their reproduction. The honey bees, which is considered as the
most important among all the pollinators is responsible for achieving of global food production demand every year. With ever increasing population, human have constantly been searching for a way to maintain this demand of global food production and in order to achieve this goal, the conventional agriculture has evolved over the centuries. In this sequence, for the proper management of insect, plant pathogens and weed plants in agro-ecosystem various chemical pesticides were discovered in the nineteenth century. Ever since the introduction of these chemical pesticides, the serious debate on their effects on non-target insects and other organisms have also started. Thus, this chapter focuses on the different routes, modes and effects of interaction between various pesticidal applications and their toxic effects on honey bees, at both individual and colony level. Agrochemicals used in fields focusing mainly on minimize the crop losses are harmful for non-target organisms and hundreds of pollinator species, including honey bees are also no exception to this. Being the worker caste of the colony honey bee foragers visit various fields and gather pollen and nectar from different plant sources, which makes them in a phase of constant exposure to various chemicals, either natural or synthetic in nature. These foraging workers collect provisions from floral resources from chemically treated plants and carry them to their colony and thus, unknowingly with each visit they carry with them, a serious threat to their own life as well as to their colony as well. The different kinds of agrochemicals may be a fungicide residue, remaining in a plant after the seed treatment; a herbicide molecule, sprayed directly over the weed plants; an insecticide residue either coming through a direct spray or reaching the colony via air current (drift). Other than these agrochemicals, a serious threat for honey bee colonies has also been imposed by the various synthetic chemicals applied to the bees in apiaries itself for the proper management of honey bee health. Several such chemicals, used for the management of honey bee pests have also been reported to be toxic to the bees.

Although, several studies have been put forward regarding pesticidal toxicity to honey bees, but still a proper management strategy in order to minimize the honey bees exposure is still lacking. However, all pesticidal applications should be done in a way to minimize their exposure to honey bees, so as to prevent the further decline of honey bee population throughout the world. Furthermore, there exists a need of an extension program, for the farmers and beekeepers to spread the awareness regarding the hazardous effects of different agrochemicals to the honey bees, in order to make the existing management strategies more effective in future.
References

[1] Ollerton J, Winfree R, Tarrant S. How many flowering plants are pollinated by animals? Oikos. 2011;120(3):321-326. DOI: 10.1111/j.1600-0706.2010.18644.x

[2] Ostiguy N, Drummond FA, Aronstein K, Eitzer B, Ellis JD, Spivak M, et al. Honey bee exposure to pesticides: A four-year nationwide study. Insects. 2019;10(1):13. DOI: 10.3390/insects10010013

[3] Wright SI, Kalisz S, Slotte T. Evolutionary consequences of self-fertilization in plants. Proceedings of the Royal Society B: Biological Sciences. 2013;280(1760):20130133. DOI: 10.1098/rspb.2013.0133

[4] Beekman M, Ratnieks FL. Long-range foraging by the honey-bee, Apis mellifera L. Functional Ecology. 2000;14(4):490-496. DOI: 10.1046/j.1365-2435.2000.00443.x

[5] Decourtye A, Mader E, Desneux N. Landscape enhancement of floral resources for honey bees in agro-ecosystems. Apidologie. 2010;41(3):264-277. DOI: 10.1051/apido/20100024

[6] Charrière JD, Neumann P. Surveys to estimate winter losses in Switzerland. Journal of Apicultural Research. 2010;49(1):132-133. DOI: 10.3896/IBRA.1.49.1.08

[7] Henry M, Beguin M, Requier F, Rollin O, Odoux JF, Aupinel P, et al. A common pesticide decreases foraging success and survival in honey bees. Science. 2012;336(6079):348-350. DOI: 10.1126/science.1215039

[8] Malone LA, Pham-Delège MH. Effects of transgene products on honey bees (Apis mellifera) and bumblebees (Bombus sp.). Apidologie. 2001;32(4):287-304. DOI: 10.1051/apido:2001130

[9] Johnson RM, Ellis MD, Mullin CA, Frazier M. Pesticides and honey bee toxicity—USA. Apidologie. 2010;41(3):312-331. DOI: 10.1051/apido/2010018

[10] Pawlikowski T. Pollination activity of bees (Apoidea: Apiformes) visiting the flowers of Tilia cordata Mill. and Tilia tomentosa Moench in an urban environment. Journal of Apicultural Science. 2010;54(2):73-79

[11] Maini S, Medrzycki P, Porrini C. The puzzle of honey bee losses: A brief review. Bulletin of Insectology. 2010;63(1):153-160

[12] Krupke CH, Hunt GJ, Eitzer BD, Andino G, Given K. Multiple routes of pesticide exposure for honey bees living near agricultural fields. PLoS One. 2012;7(1):e29268. DOI: 10.1371/journal.pone.0029268

[13] Wu J, Anelli C, Sheppard W. Sublethal effects of pesticide residues in brood comb on worker honey bee (Apis mellifera) development and longevity. PLoS One. 2011;6:e14720. DOI: 10.1371/journal.pone.0014720

[14] Mullin CA, Frazier M, Frazier JL, Ashcraft S, Simonds R, et al. High levels of miticides and agrochemicals in North American apiaries: Implications for honey bee health. PLoS One. 2010;5:e9754. DOI: 10.1371/journal.pone.0009754

[15] Karise R, Mänd M. Recent insights into sublethal effects of pesticides on insect respiratory physiology. Insect Physiology. 2015;5:31-39

[16] Directive C. Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. Official Journal of the European Communities L. 1991;230:1-32
European and Mediterranean Plant Protection Organization. Efficacy evaluation of plant protection products: Side-effects on honeybees. Bulletin OEPP/EPPO. 2001;170:95-99

Poquet Y, Kairo G, Tchamitchian S, Brunet JL, Belzunce LP. Wings as a new route of exposure to pesticides in the honey bee. Environmental Toxicology and Chemistry. 2015;34(9):1983-1988. DOI: 10.1002/etc.3014

Ebadi R, Gary NE, Lorenzen K. Effects of carbon dioxide and low temperature narcosis on honey bees, *Apis mellifera*. Environmental Entomology. 1980;9(1):144-150. DOI: 10.1093/ee/9.1.144

Simpson J. Effects of some anaesthetics on honeybees: Nitrous oxide, carbon dioxide, ammonium nitrate smoker fumes. Bee World. 1954;35(8):149-155. DOI: 10.1080/0005772X.1954.11096685

Singaravelan N, Inbar M, Ne’eman G, Distl M, Wink M, Izhaki I. The effects of nectar–nicotine on colony fitness of caged honeybees. Journal of Chemical Ecology. 2006;32(1):49-59. DOI: 10.1007/s10886-006-9350-2

Mackensen O. Effect of carbon dioxide on initial oviposition of artificially inseminated and virgin queen bees. Journal of Economic Entomology. 2014;40(3):344-349. DOI: 10.1093/jee/40.3.344

Nikolić TV, Kojić D, Orčić S, Batinić D, Vukašinović E, Blagojević DP, et al. The impact of sublethal concentrations of Cu, Pb and Cd on honey bee redox status, superoxide dismutase and catalase in laboratory conditions. Chemosphere. 2016;164:98-105. DOI: 10.1016/j.chemosphere.2016.08.077

Henderson C. Tests of chemical control agents for *Varroa jacobsoni* in honey-bee packages. In: Needham GR, Page RE, Delfinado-Baker M, Bowman CE, editors. Africanized Honey Bees and Bee Mites. West Sussex, England: Ellis Horwood, Ltd.; 1988. p. 380-386

Currie RW. Fluvinate queen tabs for use against *Varroa jacobsoni* Oud.: Efficacy and impact on honey bee, *Apis mellifera* L., queen and colony performance. American Bee Journal. 1999;139:871-876

Gregorc A. A clinical case of honey bee intoxication after using coumaphos strips against *Varroa destructor*. Journal of Apicultural Research. 2012;51(1):142-143. DOI: 10.3896/IBRA.1.51.1.19

Giovenazzo P, Dubreuil P. Evaluation of spring organic treatments against *Varroa destructor* (Acari: Varroidae) in honey bee *Apis mellifera* (Hymenoptera: Apidae) colonies in eastern Canada. Experimental and Applied Acarology. 2011;55(1):65. DOI: 10.1007/s10493-011-9447-3

Schneider CW, Tautz J, Grünwald B, Fuchs S. RFID tracking of sublethal effects of two neonicotinoid insecticides on the foraging behavior of *Apis mellifera*. PLoS One. 2012;7(1):e30023. DOI: 10.1371/journal.pone.0030023

Bogdanov S. Contaminants of bee products. Apidologie. 2006;37(1):1-8. DOI: 10.1051/apido:2005043

Rademacher E, Harz M. Oxalic acid for the control of varroosis in honey bee colonies—A review. Apidologie. 2006;37(1):98-120. DOI: 10.1051/apido:2005063

Schneider S, Eisenhardt D, Rademacher E. Sublethal effects of oxalic acid on *Apis mellifera* (Hymenoptera: Apidae): Changes in behaviour and longevity. Apidologie.
[32] Keyhani J, Keyhani E. EPR study of the effect of formate on cytochrome c oxidase. Biochemical and Biophysical Research Communications. 1980;92(1):327-333. DOI: 10.1016/0006-291X(80)91556-9

[33] Underwood RM, Currie RW. The effects of temperature and dose of formic acid on treatment efficacy against Varroa destructor (Acari: Varroidae), a parasite of Apis mellifera (Hymenoptera: Apidae). Experimental & Applied Acarology. 2003;29(3-4):303. DOI: 10.1023/A:1025892906393

[34] Fries I. Treatment of sealed honey bee brood with formic acid for control of Varroa jacobsoni. American Bee Journal (USA). 1991;131:313-314

[35] Higes M, Meana A, Suárez M, Llorente J. Negative long-term effects on bee colonies treated with oxalic acid against Varroa jacobsoni Oud. Apidologie. 1999;30(4):289-292. DOI: 10.1051/apido:19990404

[36] Gregorc A, Škerl MI. Toxicological and immunohistochemical testing of honeybees after oxalic acid and rotenone treatments. Apidologie. 2007;38(3):296-305. DOI: 10.1051/apido:2007014

[37] Ehler LE. Integrated pest management (IPM): Definition, historical development and implementation, and the other IPM. Pest Management Science. 2006;62(9):787-789. DOI: 10.1002/ps

[38] Oberemok VV, Laikova KV, Gninenko YI, Zaitsev AS, Nyadar PM, Aseyemi TA. A short history of insecticides. Journal of Plant Protection Research. 2015;55(3):221-226. DOI: 10.1515/jppr-2015-0033

[39] Atkins EL. Injury to honey bees by poisoning. In: The Hive and the Honey Bee, Rev. Hamilton, IL: Dadant and Sons; 1992. p. 1324

[40] Moritz RF, Erler S. Lost colonies found in a data mine: Global honey trade but not pests or pesticides as a major cause of regional honeybee colony declines. Agriculture, Ecosystems & Environment. 2016;216:44-50. DOI: 10.1016/j.agee.2015.09.027

[41] Lee KV, Steinhauser N, Rennich K, Wilson ME, Tarpy DR, Caron DM, et al. A national survey of managed honey bee 2013-2014 annual colony losses in the USA. Apidologie. 2015;46(3):292-305. DOI: 10.1007/s13592-015-0356-z

[42] Potts SG, Biesmeijer JC, Kremen C, Neumann P, Schweiger O, Kunin WE. Global pollinator declines: Trends, impacts and drivers. Trends in Ecology & Evolution. 2010;25(6):345-353. DOI: 10.1016/j.tree.2010.01.007

[43] Evans JD, Saegerman C, Mullin C, Haubruge E, Nguyen BK, Frazier M, et al. Colony collapse disorder: A descriptive study. PLoS One. 2009;4(8):e6481. DOI: 10.1371/journal.pone.0006481

[44] van Engelsdorp D, Hayes J, Underwood RM, Caron D, Pettis JS. A survey of managed honey bee colony losses in the USA, fall 2009 to winter 2010. Journal of Apicultural Research. 2011;50:1-10. DOI: 10.3896/IBRA.1.50.1.01

[45] Hayes Jr, Underwood RM, Pettis J. A survey of honey bee colony losses in the US, fall 2007 to spring 2008. PLoS One. 2008;3(12):e4071. DOI: 10.1371/journal.pone.0004071

[46] Cresswell JE. A meta-analysis of experiments testing the effects of a neonicotinoid insecticide (imidacloprid) on honey bees.
Detailed Review on Pesticidal Toxicity to Honey Bees and Its Management
DOI: http://dx.doi.org/10.5772/intechopen.91196

Ecotoxicology. 2011;20(1):149-157. DOI: 10.1007/s10646-010-0566-0

[47] De la Rúa P, Jaffé R, Dall’Olio R, Muñoz I, Serrano J. Biodiversity, conservation and current threats to European honeybees. Apidologie. 2009;40(3):263-284. DOI: 10.1051/apido/2009027

[48] Chauzat MP, Faucon JP, Martel AC, Lachaize J, Cougoule N, Aubert M. A survey of pesticide residues in pollen loads collected by honey bees in France. Journal of Economic Entomology. 2006;99(2):253-262. DOI: 10.1093/jee/99.2.253

[49] Frazier J, Mullin C, Frazier M, Ashcraft S. Pesticides and their involvement in colony collapse disorder. American Bee Journal. 2011;151:779-781

[50] Wade A, Lin CH, Kurkul C, Regan ER, Johnson RM. Combined toxicity of insecticides and fungicides applied to California almond orchards to honey bee larvae and adults. Insects. 2019;10(1):20. DOI: 10.3390/insects10010020

[51] Badawy ME, Nasr HM, Rabea EI. Toxicity and biochemical changes in the honey bee Apis mellifera exposed to four insecticides under laboratory conditions. Apidologie. 2015;46(2):177-193. DOI: 10.1007/s13592-014-0315-0

[52] Medrzycki P, Giffard H, Auipinel P, Belzunces LP, Chauzat MP, Classen C, et al. Standard methods for toxicology research in Apis mellifera. Journal of Apiicultural Research. 2013;52(4):1-60. DOI: 10.3896/IBRA.1.52.4.14

[53] Hardstone MC, Scott JG. Is Apis mellifera more sensitive to insecticides than other insects? Pest Management Science. 2010;66(11):1171-1180. DOI: 10.1002/ps.2001

[54] US EPA Pesticide Ecotoxicity Database of the Office of Pesticide Programs. Ecological Fate and Effects Division. Available from: http://cfpub.epa.gov/ecotox/ [Accessed: 18 September 2019]

[55] Atkins EL, Kellum D. Comparative morphogenic and toxicity studies on the effect of pesticides on honeybee brood. Journal of Apicultural Research. 1986;25(4):242-255. DOI: 10.1080/00218839.1986.11100725

[56] Davis Davis AR. The study of insecticide poisoning of honeybee brood. Bee World. 1989;70(4):163-174. DOI: 10.1080/0005772X.1989.11099013

[57] Fiedler L. Assessment of chronic toxicity of selected insecticides to honeybees. Journal of Apicultural Research. 1987;26(2):115-122. DOI: 10.1080/00218839.1987.11100747

[58] Dulin F, Halm-Lemeille MP, Lozano S, Lepailleur A, Sopkova-de Oliveira Santos J, Rault S, et al. Interpretation of honeybees contact toxicity associated to acetylcholinesterase inhibitors. Ecotoxicology and Environmental Safety. 2012;79:13-21. DOI: 10.1016/j.ecoenv.2012.01.007

[59] Gauthier M, Belzunces LP, Zaoujal A, Colin ME, Richard D. Modulatory effect of learning and memory on honey bee brain acetylcholinesterase activity. Comparative Biochemistry and Physiology Part C: Comparative Pharmacology. 1992;103(1):91-95. DOI: 10.1016/0742-8413(92)90233-W

[60] Gauthier M, Dacher M, Thany SH, Niggebrügge C, Déglise P, Kljucevic P, et al. Involvement of α-bungarotoxin-sensitive nicotinic receptors in long-term memory formation in the honeybee (Apis mellifera). Neurobiology of Learning and Memory. 2006;86(2):164-174. DOI: 10.1016/j.nlm.2006.02.003

[61] Johnson RM, Dahlgren L, Siegfried BD, Ellis MD. Acaricide,
fungicide and drug interactions in honey bees (*Apis mellifera*). PLoS One. 2013;8(1):e54092. DOI: 10.1371/journal.pone.0054092

[62] Detzel A, Wink M. Attraction, deterrence or intoxication of bees (*Apis mellifera*) by plant allelochemicals. Chemoecology. 1993;4(1):8-18. DOI: 10.1007/BF01245891

[63] Chensheng LU, Warchol KM, Callahan RA. Sub-lethal exposure to neonicotinoids impaired honey bees winterization before proceeding to colony collapse disorder. Bulletin of Insectology. 2014;67(1):125-130

[64] Girolami V, Mazzon L, Squartini A, Mori N, Marzaro M, Di Bernardo A, et al. Translocation of neonicotinoid insecticides from coated seeds to seedling guttation drops: A novel way of intoxication for bees. Journal of Economic Entomology. 2009;102(5):1808-1815. DOI: 10.1603/029.102.0511

[65] Hoshi N, Hirano T, Omotehara T, Tokumoto J, Umemura Y, Mantani Y, et al. Insight into the mechanism of reproductive dysfunction caused by neonicotinoid pesticides. Biological and Pharmaceutical Bulletin. 2014;37(9):1439-1443. DOI: 10.1248/bpb.b14-00359

[66] Di Prisco G, Cavaliere V, Annoscia D, Varricchio P, Caprio E, Nazzi F, et al. Neonicotinoid clothianidin adversely affects insect immunity and promotes replication of a viral pathogen in honey bees. Proceedings of the National Academy of Sciences. 2013;110(46):18466-18471. DOI: 10.1073/pnas.1314923110

[67] Carreck NL, Ratnieks FL. The dose makes the poison: Have “field realistic” rates of exposure of bees to neonicotinoid insecticides been overestimated in laboratory studies? Journal of Apicultural Research. 2014;53(5):607-614. DOI: 10.3896/IBRA.1.53.5.08

[68] Tomizawa M, Casida JE. Neonicotinoid insecticide toxicology: Mechanisms of selective action. Annual Review of Pharmacology and Toxicology. 2005;45:247-268. DOI: 10.1146/annurev.pharmtox.45.120403.095930

[69] Iwasa T, Motoyama N, Ambrose JT, Roe RM. Mechanism for the differential toxicity of neonicotinoid insecticides in the honey bee, *Apis mellifera*. Crop Protection. 2004;23(5):371-378. DOI: 10.1016/j.cropro.2003.08.018

[70] Guez D. A common pesticide decreases foraging success and survival in honey bees: Questioning the ecological relevance. Frontiers in Physiology. 2013;4:37. DOI: 10.3389/fphys.2013.00037

[71] Casida JE, Durkin KA. Neuroactive insecticides: Targets, selectivity, resistance, and secondary effects. Annual Review of Entomology. 2013;58:99-117. DOI: 10.1146/annurev-ento-120811-153645

[72] Vandame R, Belzunces LP. Joint actions of deltamethrin and azole fungicides on honey bee thermoregulation. Neuroscience Letters. 1998;251(1):57-60. DOI: 10.1016/S0304-3940(98)00494-7

[73] Pettis JS, Lichtenberg EM, Andree M, Stitzinger J, Rose R. Crop pollination exposes honey bees to pesticides which alters their susceptibility to the gut pathogen *Nosema ceranae*. PLoS One. 2013;8(7):e70182. DOI: 10.1371/journal.pone.0070182

[74] Haarmann T, Spivak M, Weaver D, Weaver B, Glenn T. Effects of fluvalinate and coumaphos on queen honey bees (Hymenoptera: Apidae) in two commercial queen rearing operations. Journal of Economic...
Detailed Review on Pesticidal Toxicity to Honey Bees and Its Management
DOI: http://dx.doi.org/10.5772/intechopen.91196

Entomology. 2002;95(1):28-35. DOI: 10.1603/0022-0493-95.1.28

[75] Rinderer TE, De Guzman LI, Lancaster VA, Delatte GT, Stelzer JA. Varroa in the mating yard. I. The effects of Varroa jacobsoni and apistan on drone honey bees. American Bee Journal (USA). 1999;139:134-139

[76] Kubik M, Nowacki J, Pidek A, Warakomska Z, Michalczuk L, Goszczyński W. Pesticide residues in bee products collected from cherry trees protected during blooming period with contact and systemic fungicides. Apidologie. 1999;30(6):521-532. DOI: 10.1051/apido:19990607

[77] Kubik M, Nowacki J, Pidek A, Warakomska Z, Michalczuk L, Goszczyński W, et al. Residues of captan (contact) and difenoconazole (systemic) fungicides in bee products from an apple orchard. Apidologie. 2000;31(4):531-541. DOI: 10.1051/apido:2000144

[78] Johansen CA. Pesticides and pollinators. Annual Review of Entomology. 1977;22(1):177-192

[79] Moffett JO, Morton HL, MacDonald RH. Toxicity of some herbicidal sprays to honey bees. Journal of Economic Entomology. 1972;65(1):32-36. DOI: 10.1093/jee/65.1.32