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From farming to the ecosystem, a review: environmental impacts and using neonicotinoids

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Abstract: *Pesticide use offers disease and pest control in plants assisting in preserving food, leading to enhanced productivity, and ensuring food availability reduced economic losses. Furthermore, pesticides also control vectors that cause human pathogenesis. Among the vast universe of pesticides, neonicotinoids (NEOs) represent 24% of the total insecticide market. Their use is justified by their great efficacy in controlling pests. However, many problems are also related to the extensive use of such substances, such as environmental contamination (water, soil, and air), the presence of residues in food, their persistence in the environment, and the harmful effects caused by their toxicity affecting non-target organisms, among others. Therefore, a literature review was conducted aiming multidisciplinary and contextualized point of view, to compile the most recent and relevant results of their use of NEOs in the agriculture and control of vector-borne diseases in tropical countries and the impacts on environmental and living beings, caused by the large scale use these substances. Our profound literature review evidence these substances have neurotoxic properties and potential bioaccumulation. Moreover, the excessive substances cause resistance in target pests, compromising their efficacy for pest control, and have been linked to the decline of pollinators, such as bees and butterflies. Understanding these problems is crucial for developing sustainable and environmentally friendly pest management practices, ensuring the protection of ecosystems, biodiversity, agricultural productivity, and public health.*

Key Word*: Pesticide pollution; non-target organisms; integrated pest management; vector-borne diseases; sustainable agriculture.*

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I. Introduction

In recent decades, the growing population and industrial increase have directly influenced the number of pollutants, especially in water bodies. These pollutants can be inorganic compounds such as toxic metals or metalloids (Cd, Cr, Pb, As, Hg, and others) or organic compounds such as pesticides (Organochlorines, organophosphates, carbamates, and others [1,2]. Approximately 80% of applied pesticides remain in the soil and pose an environmental threat [3].

When we look only at the agronomic point of view, pesticide molecules have been listed as one of the leading solutions for crop protection, increasing productivity, food availability, food preservation, and reduction of economic losses [4,5]. Pesticides can be classified according to their function: herbicides control weeds, fungicides control phytopathogenic fungi, and insecticides control insect pests [6]. Insecticides are substances used to kill, repel, attract, or disturb insects to reduce or annul the effects of the pest under different crops of economic interests [7].

Currently, four insecticidal modes of action are known: a) insecticides that act on the nervous system and muscles of insects (85% of global sales), b) molecules that act in the midgut of insects (2% of sales), c) insecticides that cause disturbances on cellular respiration (2% of sales), d) insecticides that cause disturbances on the growth and development of insects (8% of sales). As can be seen, insecticides that act directly on the neuromuscular system represent most insecticides used worldwide. Within this mode of action, the group of insecticides neonicotinoids (NEOs) is among the classes of pesticides most widely used in modern agricultural production, representing 24% of the total insecticide market [8].

The use of this class of pesticides is usually justified by the excellent results derived from the molecules in controlling pests, which directly or indirectly help protect crops and maintain high productivity [7]. Several factors contributed to the rapid success of NEOs, such as high efficacy and lower application doses, prolonged and systemic protection, facilitating the control of a wide spectrum of pests, and high application versatility [9].

These molecules act as agonists of acetylcholine, an excitatory neurotransmitter, competing for nicotinic receptors. As a result, such substances persist in the target organism, maintaining the Na+ channels open and preventing the acetylcholinesterase enzyme's natural response. The result is the continuous and uncontrolled transmission of nerve impulses, nervous system collapse, and target death [10].

However, despite its effectiveness, several scientific reports already indicate that this class of pesticides is impacting different ecosystems around the world, significantly harming the population of pollinators. For example, its use has been identified as responsible for the population decline of various bee species [11]. Furthermore, NEOs are also related to problems such as cytotoxicity, causing damage to human cells, affecting non-target aquatic organisms, and reducing the biodiversity of water resources [12]. Recent results indicate that NEOs have a high potential for environmental contamination since they have high solubility and persistence in the aquatic environment and are susceptible to transport, which promotes their movement to adjacent areas and hydrous bodies next to crops [13].

The environmental problems resulting from the use of these pesticides so that other researchers can assist in the development of new alternative means of insect control, such as biological control. In addition, this work can also influence other researchers in the development of monitoring application areas and in the creation of new technologies and remediation mechanisms for environmental areas contaminated with NEOs [3].

II. Bibliographic Review

2.1 History of neonicotinoids

Until the 1990s, the world insecticide market comprised sales of organophosphates (OPs), carbamates, and pyrethroids [14] NEOs were developed to replace these insecticides, mainly due to the many reports of insect resistance, the concern with the cumulative exposure of workers, and the evidence that impaired neural development in children could be associated with using OPs, carbamates, and pyrethroids [15,16].

The development of NEOs took place in the early 1990s, based on knowledge of the insecticidal effects of nicotine [17] Botanists and farmers have used tobacco leaf infusion as an insecticide since the 19th century [18]. Synthetic molecules with a molecular structure like nicotine began commercializing in the mid-1990s, with imidacloprid being the first NEO registered for use in 1991 [19].

From 1995 to 2002, more NEOs were introduced to the market: nitenpyram and acetamiprid in 1995, thiamethoxam in 1998, thiacloprid and clothianidin in 2001, and dinotefuran in 2002 [20]. However, in 2000 NEOs have become more widely used by farmers, their rapid approval is justified mainly due to the adoption of seed treatment techniques to combat soil pests [19].

In recent years NEOs have been the most used insecticides worldwide, representing 25% of the insecticide market [18]. Its use is authorized in approximately 140 crops and applied to grain crops, fruits, vegetables, cereals, and flowers. Controlling insects such as aphids, thrips, whiteflies, termites, grass insects, and beetles [21], NEOs are, to date, one of the most important groups of pesticides worldwide. However, in 2013 three NEs used as a seed treatment in crops attractive to pollinators were banned in Europe [20].

A review of the risk of NEOs application on bee health was conducted by the European Food Safety Authority (EFSA) in 2012, resulting in a ban of three NEOs use (clothianidin, imidacloprid, and thiamethoxam) in outdoor crops (except winter) and other attractions for bees from the end of 2013. In 2018, EFSA banned the substances mentioned above' use on all outdoor crops. This measure was due to the risk of contamination by insects and pollen, which could mainly compromise the process of pollination and reproduction of plant species [22].

2.2 Chemical structure and mechanism of action

In general, insecticides work through four main modes of action, changing the natural function of 1) growth and development, 2) cellular respiration 3) the midgut, and 4) the nervous system and muscles (Fig1).

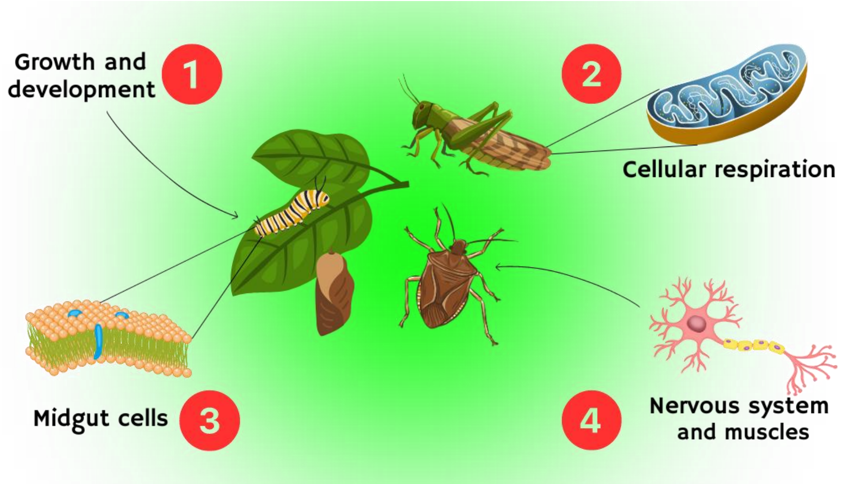

Fig1 Summary of the Mode of Action (MoA) of existent insecticides proposed by the Insecticide Resistance Action Committee. Source: Authors' elaboration.

The neuromuscular mode of action category insecticide corresponds to 85% of the total volume of globally sold insecticides [8]. According to IRAC classification [23], among insecticides with neuromuscular action, there are different mechanisms of action, such as 1) Acetylcholinesterase (AChE) inhibitors, with groups 1A Carbamates and 1B Organophosphates, 2) Blockers of GABA-controlled chlorine channels, with groups 2A Cyclodiene organochlorines and 2B Phenylpyrazoles (Fiproles), 3) Sodium channel modulators, with groups 3A Pyrethroids, Pyrethrins and 3B DDT and Methoxychlorine, 4) Competitive modulators of nicotinic acetylcholine receptors (nAChR), with groups 4A Neonicotinoids, 4B Nicotine, 4C Sulfoximines, 4D Butenolides, 4E Mosoionics, and 4F Pyridylidenes, 5) Allosteric modulators of nicotinic acetylcholine receptors (nAChR) – site I, from the Spinosyns group (Spinosad), and, finally, 6) allosteric modulators of the glutamate-controlled chloride channel (GluCl), with Avermectins and Milbemycins (Fig2).

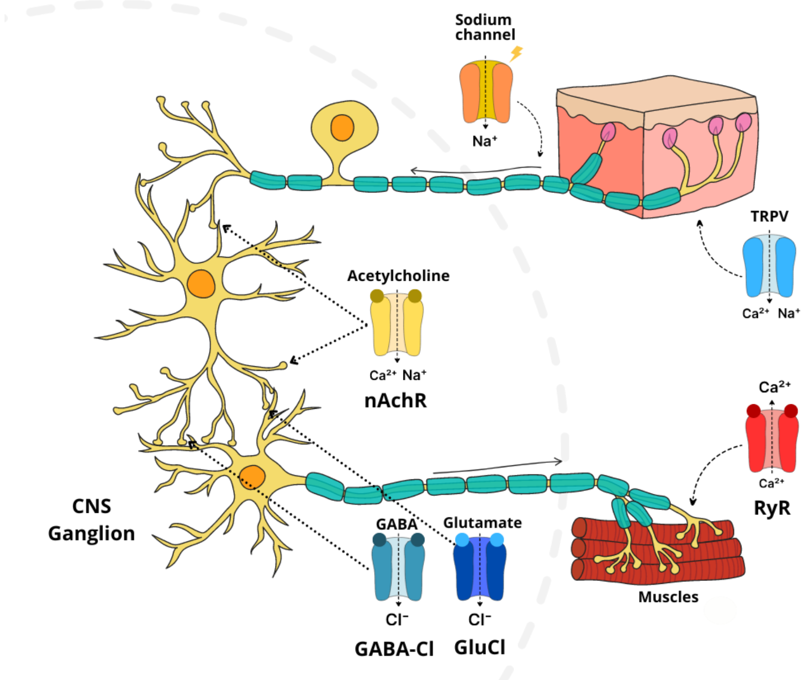

Fig2 The various channels involved in presynaptic and postsynaptic membranes during insecticide action. Source: Authors' elaboration.

Consequently, there are several classes of insecticides that act to control insects in different ways. However, it is essential to highlight that of the products applied in agriculture, those that act directly on the nerves and muscles of insects constitute the most representative class in terms of use [7].

Historically, nicotine was the first insecticide to mimic the neurotransmitter acetylcholine. This botanical insecticide interacts with nicotinic receptors producing initial stimulation followed by prolonged depolarization, which leads to insect paralysis and death [24]. However, the agricultural use of nicotine as an insecticidal agent has declined over time, mainly due to the high cost of production, the strong and unpleasant odor, the high toxicity for mammals, and limited insecticidal action. Nevertheless, it is essential to emphasize that the extract of tobacco leaves, the usual way of obtaining and applying nicotine, can control insect populations through the ingestion of vegetables contaminated with nicotine, by fumigation (through the entry of steam containing nicotine into the spiracles of the insects) and contact (direct: spraying on the insect, or indirect: when the insect becomes contaminated when walking on the applied surface) [25].

The NEOs family originates from the chemical study of the nicotine molecule and the name means “new nicotine-like insecticides” [26]. These synthetic compounds, like nicotine, are classified as neurotoxic as they can disrupt normal cholinergic signaling [27]. The mechanism of action of NEOs is due to their action as acetylcholine agonists (Fig3.).

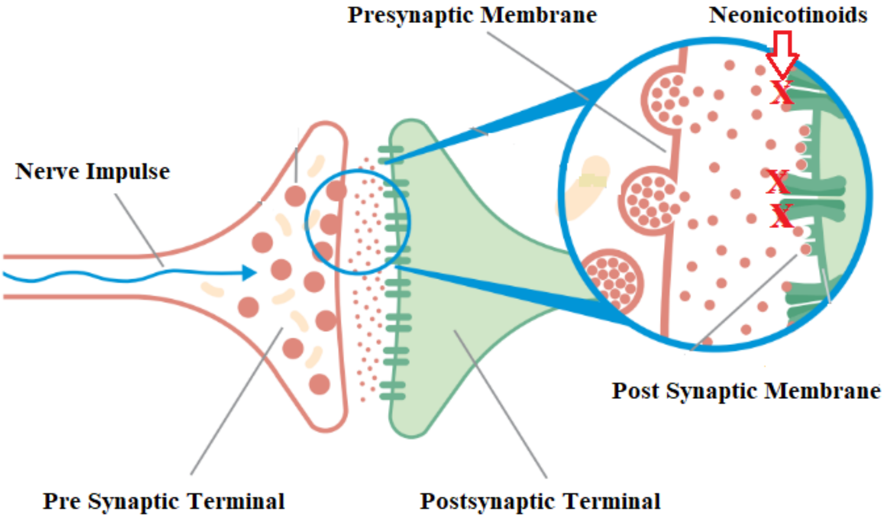

Fig3 Mechanism of action of neonicotinoid insecticides on insects. Source: Authors' elaboration.

After synapsis occurs, insecticidal molecules bind to nicotinic ACh receptors located on the postsynaptic neuron. The result is a constant stimulation of the ACh message in the system, leading to hyper-excitation of the nervous system, causing paralysis and death of insects [24,28].

Although nicotine and NEOs have similar structures, the main difference is in their mechanism of action since nicotine has a protonated region that interacts with biological receptors in mammals at higher levels. However, under the same conditions, NEOs do not have a protonated region depending on the pH condition, which favors the toxicological profile of this class, providing these insecticides with high selectivity and specificity for insects (5 to 10 times more selective for insects versus mammals compared to OPs, carbamates, and organochlorines) [7].

Regarding their physical and chemical properties, NEOs have moderate water solubility or even hydrophobic character and relative photostability. The solubility in water is one of the main characteristics of NEOs, considering this is essential for their proper functioning as systemic pesticides, which need to be absorbed by plants, with the insecticide thiamethoxam being the most soluble (4100 mg L^{-1}) and thiacloprid least soluble (185 mg L^{-1}). Solubility is inversely proportional to the sorption capacity of pesticides in the soil. Due to high water solubility and low octanol-water partition coefficient (log KOW), NEOs have a low tendency to adsorb soil particles [28].

Moreover, NEOs are not readily biodegradable. All insecticides in this class are stable and hydrolyze slowly at acidic or neutral pH [29]. Even in an alkaline medium, they show slow degradation (half-life from 11.5 to 420 days). These characteristics are fundamental concerning the fate of these substances after their insertion into the environment [28].

The Chemical structures of some of the most important NEOs are presented in Fig 4. Regarding the molecular structure, NEOs have a nitromethylene (CH-NO2), nitroimine ($N-NO_2$), or cyanoimine (N-CN) group. An exception is made for sulfoximine, while other NEOs have at least one amine nitrogen. Imidacloprid is the first representative of this class of insecticides (first-generation chloropyridine). Among other NEO molecules are thiacloprid, acetamiprid, nitenpyram (first-generation chloropyridine), thiamethoxam and clothianidin (second-generation chlorothiazoles), dinotefuran (third-generation furanil), and sulfoxaflor (fourth generation sulfoxamines) [30,31].

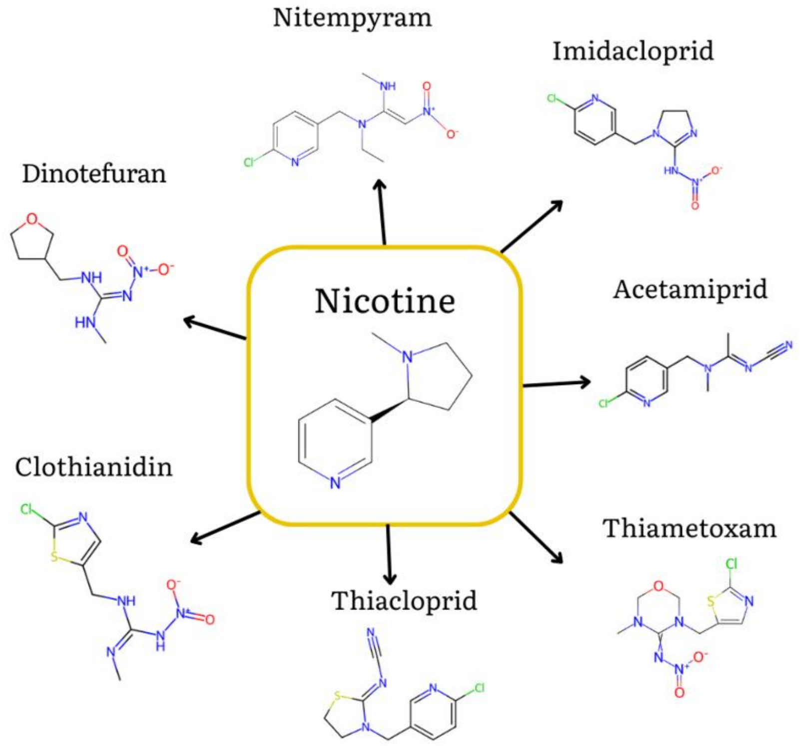

Fig4 Chemical structures of some of the most important neonicotinoid insecticides. Source: Authors' elaboration

2.3 Use and consumption

NEOs are compounds widely used to control and eliminate insects that may cause damage to crops of agricultural interest, but they are also registered globally for non-agricultural uses [32]. In addition, they can also be used in veterinary medicine to control fleas, ticks, and worms in domestic animals or as a pesticide to control domestic pests and disease vectors [33]. These substances have systemic activity in plants, i.e., after application, they are absorbed by the plants and translocated along the roots, leaves, and tissues [32].

Chemical control remains the best way to manage anthropophilic disease vectors during outbreaks [34]. In a study carried out in Africa, NEOs were tested to replace insecticides used to control the population of Anopheles, the mosquito responsible for transmitting malaria, which was resistant to these other pesticides. Lethal concentrations of acetamiprid, imidacloprid, and clothianidin strongly inhibited survival, growth, and emergence in Anopheles. However, according to the study, larvae mosquitoes showed cross-resistance to NEOs [35].

According to Silalahi et al. (2024) [34], the mixture of deltamethrin and clothianidin compounds proved to be efficient in controlling vectors resistant to the mosquito that transmits malaria, which is resistant to pyrethroids, which have long been used to control these insects. In addition, the mixture of insecticides was also investigated in controlling the Taiwanese and Indonesian Aedes Aegypti mosquito population, demonstrating effective results, preventing Aedes mosquitoes from entering residential areas, and reducing the number of mosquito bites [34].

In plants, NEOs can be used through different application methods. Examples are foliar application with aerial or ground spray equipment, soil drenching, chemigation, tree injection, and seed treatment [36,37]. In the United States, for example, more than 1,000 primary and supplemental products containing NEOs are registered on the market. These can be used by oral ingestion in animals to control fleas, in plants of agricultural interest, including cucurbits, fruit, and leguminous plants such as soy, and monocots such as corn, leafy brassicas, walnuts, among others [38].

North America represents the largest market for seed treatments, with clothianidin or thiamethoxam being coated in approximately 80% of corn seeds grown on the continent [39]. In the United States, in the last decade, the increase in the use of treated seeds has tripled, with remarkably rapid growth in use between 2003 and 2011 as a preventive insecticide applied as a seed coating for crops such as maize, cotton, soybeans, and wheat [40].

Nowadays, 50% of soybeans (18.2 million hectares) nearly 100% of corn (>36.4 million hectares), and 95% of cotton (15 million hectares) are treated with NEOs [40]. Moreover, seed treatments also accompany using other substances, such as fungicides, herbicide protectors, nematicides, and plant growth regulators, which are associated with NEOs and can enhance environmental contamination [41].

The massive use of NEOs is also evident concerning the worldwide consumption of these molecules. In 2014, the use of these substances increased global market shares by 25% (revenues of USD 3.7 billion), driven by the expansion to new cultivation areas [42]. Thiamethoxam, imidacloprid, and clothianidin accounted for 85% of all NEO sales worldwide in 2012. Also, imidacloprid is the 12th most widely used pesticide globally and the second insecticide, surpassed only by chlorpyrifos [38].

Even though NEOs are not recent and have been used for more than two decades, due to the positive aspects of using these, this group has expanded its space in the world pesticide market in more than 120 countries, with 17 % of the global market share in 2019, becoming a solid substitute for older groups of pesticides such as OPs and carbamates [43]. Due to that expansion, NEOs are widely used in countries like Brazil, with tropical conditions that favor development or pests in agricultural and urban areas [44].

Brazil is the second-largest world soybean producer and a significant producer and exporter of several other agricultural commodities [45]. The use of pesticides has increased considerably along with the sharp increase in grain production, and Brazil has become one of the four largest consumers of pesticides in the world, along with China (1st), the United States (2nd), and Argentina (4th). Agricultural commodities are one of the mainstays of Brazil's economy, and the benefits of pesticides for crop protection must be appropriately balanced against their potential risks to the environment and human health [46].

Table 1 highlights the main active ingredients of pesticides used in Brazil, where it is observed that glyphosate is the most consumed pesticide. Although it is not an insecticide, it is also an OP widely used in Brazil and worldwide. In the Brazilian territory, the most used insecticides are acephate, malathion, chlorpyrifos (all OPs), and imidacloprid (NEOs). Imidacloprid alone is responsible for consuming approximately 9.4 tons of active ingredients. Other important NEO sold in Brazil did not disclose the amount consumed (acetamiprid, thiamethoxan, clothianidin, dinotefuran) [47].

Table 1 Ranking of Brazil's 10th most used pesticides - Toxicological classification, chemical group, and the amount of active ingredient used in 2020 [29].

Ranking	Active Ingredient	Category/Chemical Class	Toxicological classification*	Sales (ton. a.i.)
1st	Glyphosate	Herbicide/Organophosphate	IV	246,017.51
2nd	2,4-D	Herbicide/Phenoxy	I	57,597.57
3rd	Mancozeb	Fungicide/Dithiocarbamate	III	50,526.87
4th	Atrazine	Herbicide/Triazine-Organochlorine	III	33,321.11
5th	Acephate	Insecticide/ Organophosphate	III	29,982.50
6th	Chlorothalonil	Fungicide/Chlorinated aromatic	III	24,191.03
7th	Malathion	Insecticide/Organophosphate	III	15,702.11
8th	Sulfur	Fungicide/Inorganic	IV	11,390.90
9th	Imidacloprid	Insecticide/Neonicotinoid	II	9,401.65
10th	Chlorpyrifos	Insecticide/Organophosphate	II	8,864.88

*Toxicological classification to mammals (The Brazilian Health Regulatory Agency – ANVISA): (I) Extremely toxic, (II) very toxic, (III) moderately toxic, (IV) slightly toxic; a.i.: Active ingredient of the pesticide.

In the United States, 1.8 million Kg of NEOs were applied to agricultural land in 2017. In Japan, an estimated 703 tons of NEOs were distributed to the market in 2015. The leading consumption regions of NEOs are Latin America, Asia, and North America, with 75% of total use, and Europe, with 11% [43].

2.4 Environmental fate of neonicotinoid insecticides

The scenario observed nowadays shows that indiscriminate pesticide use threatens the environment by contaminating soil, plants, and the atmosphere, with the danger of transferring and accumulating pesticide residues in water resources [48,49].

Like other pesticides, insecticides are subject to different transformation, transport, and retention processes after being introduced into the environment. Numerous studies report the occurrence of NEOs in the environment, especially in surface and underground water resources. The combination of environmental conditions and each molecule's physical and chemical properties will influence its destination [50].

A survey based on published studies was performed by Souza in 2020 in Brazilian surface waters (lakes and rivers). Among the main insecticides detected in surface waters, approximately 27% are NEOs, with detection frequency higher than 90% of the samples [51].

Emerging contaminants in surface water, groundwater, and effluents were analyzed in São Paulo, Brazil [52]. A total of 708 samples were analyzed, including raw and treated sewage, surface and groundwater, and drinking water between 2006 and 2015. According to the study, insecticides, imidacloprid, fipronil, and malathion were detected, the first being the most frequent. The average concentrations for insecticides ranged between 10 and 26 ng L^{-1} [53].

Another monitoring study was conducted with pesticide residues and metabolites dissolved in water and surface stream particles from the Cachapoal River basin, in central Chile, in an area of intense agricultural activity. Imidacloprid was detected in all samples of the particulate phase [53].

A recent study investigates for the first time the contamination of water and sediment of the Venice Lagoon by twenty Contaminants of Emerging Concern (CECs), Among them, you five neonicotinoids. The most frequently detected contaminants in water were neonicotinoid insecticides (with a frequency of quantification of single contaminants ranging from 73% to 92%) [54].

The concentration and distribution of pesticides in 147 soil samples at three depths were observed in agricultural areas in Nepal. All study areas were at least seven days without applying any substance before sampling. The highest concentrations and the highest number of pesticides were detected in the superficial layers of the soil. Among the insecticides found are dichlorvos, profenofos, the OPs class, and imidacloprid, the NEOs class, with concentrations much higher than their guideline values for soil samples [55].

Due to their high polarity and good water solubility, plant tissues easily take up neonicotinoids and systemic effect and absorption capacity of 2 to 20% absorption throughout the plant (roots, stem, leaves, flowers, and fruits) [56]. Furthermore, result in long-term residuals, commonly found in fruit and vegetables at concentrations of 0.004 ~ 0.5 mg kg^{-1} [57]. According to the review article carried out by Yang et al. (2024), several NEOs (the most detected being imidacloprid, thiacloprid, clothianidin, thiamethoxam, and acetamiprid) are investigated and determined in a wide variety of foods of plant origin, such as fruits, cereals, vegetables, vegetable oils, seasonings, and teas.

A recent study was conducted on 240 beehive samples and 44 surrounding environmental samples collected from 25 Chinese provinces. The results showed that 83.1% of the samples contained neonicotinoids [58]. Another study collected 160 batches of honey and 26 batches of pollen from different regions and plant sources in China, analyzed the residue patterns of neonicotinoid pesticides, and comprehensively evaluated the exposure risks to non-targeted organisms including bees (adults and larvae) and humans. The findings indicated that 59.4 % of honey samples contained at least one of eight neonicotinoids [59].

The results obtained by the studies prove the massive use and potential for contamination by NEO insecticides under different conditions and in different places worldwide. This fact warns about the consequences that exposure to these substances can bring to living beings.

2.5 Effects of neonicotinoids on living beings

The NEOs can also cause harm to non-target organisms. One of the biggest concerns caused by the indiscriminate use of these compounds is the danger they present to pollinating insects. Bees are the most important pollinators today, 75 to 80% of food production depends on them. The damage caused to bees by NEOs has remained in the spotlight since 1996 when imidacloprid was associated with the death of hives. Studies evaluated the application of three active ingredients were conducted: imidacloprid, clothianidin, and thiacloprid in the central nervous system of insects in non-lethal doses to test their effects on bee navigation. The results state that the treatment with thiacloprid reduced the flight speed of the bees, while the other NEOs did not affect the flight speed [60].

There is generally a correlation between regions that have an increase in NEO use and dead pollinating bee. In the United Kingdom and California, NEOs have contributed to the decline in the population of domestic and wild bees, as well as the butterfly population.

The increasing use of NEOs in recent years has led to increased cases of intoxication by NEs reported worldwide over the past over the past 15. There are also reports on the accumulation of NEOs in plants. As a result, in 2013, the European Union decided to restrict the use of three NEOs, Imidacloprid, clothianidin, and thiamethoxam [61].

Although the direct (acute) toxicity of NEOs is a concern in the environment, the effects of sublethal contamination are also a concern since they can cause changes in behavior, reproduction, mobility, and feeding inhibition. When studying oxidative stress in Australoheros facetus fish exposed to imidacloprid, it concluded that brief exposure to environmentally relevant concentrations of this active ingredient (≥ 10 µg L^{-1}) produces significant levels of oxidative stress in Australoheros facetus [62, 63, 64, 49].

NEOs are widely used in seed treatment. In this way, they may have toxic effects on granivorous birds, which may consume seeds during planting, causing direct lethal or sublethal damage. Sublethal effects may include loss of body mass or flight orientation ability, which is crucial for maintaining the correct migratory trajectory. Even ingesting a few seeds treated with NEOs can be toxic or affect reproductive capacity. Birds can still be harmed due to imbalance in the food academy, especially those with insectivorous characteristics, given that using these compounds can limit their food source [65,66,67,66,69].

A study was carried out to determine Imidacloprid in the urine and hair of animals subjected to long-term subacute chronic exposure to this insecticide. It has been found that Imidacloprid remains for a short period in the urine and a long period in the hair. After tests carried out on animals, the method was applied to hair samples from the urban population of Cretan, where the presence of Imidacloprid was not detected, and in the rural population, detected in 21 people where concentrations varied between 0.03 - 0.27 ng mg^{-1} [70]. However, despite the short degradation period of NEOs in urine samples, several studies have analyzed neonicotinoids in human organisms in this matrix [71].

Children are exposed to an especially higher dose than adults due to their greater food and fluid intake per unit of body weight. Furthermore, because the human nervous system develops rapidly in early childhood, it is predicted that children will be more vulnerable to neurotoxic chemicals from adults [72]. The cumulative exposure of NEOs from 223 young children in Japan was investigated in the summer and winter months. NEO detection rates were 58% for dinotefuran, 25% for thiamethoxam, 21% for nitenpyram, and <16% for all other NEOs. Concentrations varied between 4.7 and 370.2 nmol/g of creatinine, respectively and the children had more exposed NEOs in summer [73].

According to Oya et al. (2021) [70], the toxicity of NEOs in humans has not yet been fully established because existing studies on this issue are insufficient. Some toxic effects induced by NEOs have been described, including hepatotoxicity and nephrotoxicity, toxicity to the respiratory system, hyperglycemia, genotoxicity, endocrine complications, and obesity [74, 72].

III Conclusion

In conclusion, the use of NEOs presents formidable environmental and agricultural obstacles, both in agricultural production and in vector control, particularly in tropical countries. Environmental, farming, and human contamination have been an aggravating result of the excessive use of these substances. Understanding these difficulties is vital for developing sustainable and environmentally friendly pest management practices, ensuring the safeguarding of ecosystems, biodiversity, agricultural productivity, and public health. Therefore, concerted efforts and interdisciplinary collaborations are imperative to mitigate harmful effects and devise effective strategies for the responsible use of this class of pesticides. Furthermore, we highlight the importance of monitoring in application areas and developing new remediation technologies and mechanisms for environmental areas contaminated with NEOs.

Data availability: The data used in this review are from publicly available sources, and there are no restrictions on data access.

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Competing interests: None.

Consent to participate: All the authors listed consent to participate.

Consent for publication: We confirm that this manuscript has not been published elsewhere and is not under consideration by another journal. Furthermore, all authors have approved the final manuscript and agreed with its submission.

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