Impact of Nematicides on Plant-Parasitic Nematodes: Challenges and Environmental Safety

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ABSTRACT

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Plant Parasitic Nematodes (PPNs) are tiny, pseudocoelomate, unsegmented, bilaterally symmetrical vermiform animals that attack plants. Nematicides are chemically synthesized substances that kill or harm nematodes. Between 1940 and 1950, three chemicals with nematicidal properties were discovered: methyl bromide (bromomethane), D-D mixture, and EDB (1, 2-dibromoethane; as ethylene dibromide) which were fumigants. When fumigant compounds are applied to soil, a gas moves through the open spaces between soil particles or into the water film that surrounds soil particles. Fumigants significantly decrease nematode respiration by oxidizing Fe^{2+} centers and alkylated proteins in the cytochrome-mediated electron transport chain. Despite the efficacy of fumigants in nematode, their use was lowered due to the high environmental risk of these products. A new generation of nematicides was introduced: carbamates and organophosphates that served as contact nematicides, which led to the testing and development of other non-fumigant nematicides such as aldicarb, carbofuran, ethoprop, and fenamiphos. The carbamates and organophosphates acetylcholinesterase inhibitory properties prevent normal nerve impulse transmission in the nematode nervous system. Nematicides are typically non-selective pesticides, and their use impacts non-target organisms, humans, and the environment. Since nematicides are toxic to humans, soil, groundwater, and non-target organisms, cautious nematicide selection and application are vital. New compounds that are less aggressive and more specific for PPNs have been developed, making them safer for the producer, consumer, and environment. Crop rotation, cover crops, organic manuring, use of resistant varieties, and other methods must be integrated with nematicides for increased effectiveness.

Keywords: Human safety, nematicides, organophosphates, plant parasitic nematodes, poisoning

INTRODUCTION

Plant Parasitic Nematodes (PPNs) are tiny, transparent, pseudo-coelomate micro-organisms that resemble microscopic worms and can live either free or as parasites. They can be predatory, aquatic, terrestrial, entomopathogenic, ectoparasitic, endoparasitic, semi-endoparasitic (such as *Tylenchulus semipenetrans*), or stationary (Shah and Mahamood 2017). Nearly 4100 PPN species have been identified, and they are considered a significant threat to world food security (Nicol et al. 2011). While lacking circulatory function, their body has recognizable organs for the digestive, nervous, and excretory systems and a

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well-developed reproductive system (Souza 2008). The majority of the species are referred to as "farmers’ close friends" because many of them kill insects (Shah and Mahamood 2017). Nematode damage to crops is typically difficult to detect because there are so many other variables that impede plant growth (Mitik 2018). Today, the main plant parasitic nematodes in economic terms are root-knot nematodes (*Meloidogyne* spp.), followed by cyst nematodes (*Heterodera* and *Globodera* spp.), root lesion nematodes (*Pratylenchus* spp.), burrowing nematode (*Radopholus similis*), and the stem nematode (*Ditylenchus dipsaci*) (Jones et al. 2013). Since eradication of nematodes is not possible, the goal is to manage their population and reduce their numbers below damaging levels (Mitiku 2018). Planting resistant varieties, rotating crops, adding soil nutrients, and using pesticides are a few common control strategies. The discovery that particular compounds had nematicidal qualities and their subsequent application in agriculture had a significant impact on crop production by raising crop yield and quality globally. These compounds were initially administered to the soil to sterilize it and eliminate any pests and PPNs. As a result, the employment of such chemical agents in agriculture significantly impacted agricultural productivity, increasing crop yield and quality globally (Antônio et al. 2019).

HISTORY OF NEMATICIDES

Chemical control is an important tool in nematode control. It is considered one of the most effective and reliable control techniques within integrated management (Kim et al. 2016). Chemical agents were first used in 1881, with carbon disulfide being the first product discovered as having nematicidal qualities. At the time, it was utilized to treat soil to prevent the spread of *Phylloxera* spp. in grapevines (*Vitis vinifera*). Since chloropicrin has nematicidal properties, it was also utilized to treat nematodes (trichloro-nitromethane). Although nematicidal activity in a synthetic chemical was discovered as a result of the use of carbon disulfide as a soil fumigant in the second half of the nineteenth century, research on the use of nematicides stalled until surplus nerve gas (chloropicrin) became widely accessible after World War I (Brown 1987).

The decade between 1940 and 1950 was profoundly important for the Science of Nematology. Nematicidal properties were discovered for three chemicals: methyl bromide (bromomethane), D-D mixture (1,3-dichloropropene, 1,2-dichloropropane), and EDB (1,2-dibromoethane; commonly called ethylene dibromide). Beginning in the early 1940s, methyl bromide was once the most widely used nematicide in the USA. The Montreal Protocol classified methyl bromide as a Class I ozone-depleting agent, and as a result, the manufacturing and use of the chemical were banned internationally in industrialized nations in 2005 (Fourie et al. 2017). In the 1940s, the discovery that D-D mixture controlled the soil populations of PPNs and led to substantial increases in crop yield provided a great impetus to the development of other nematicides, as well as the development of the science of nematology. Both D-D and EDB, unlike previously identified fumigants, were primarily nematicidal chemicals, easier to apply, and more economical to use. In later years, the 1,3-dichloropropene (1,3-D) component of the D-D mixture was shown to represent approximately 98% of the nematicidal activity of the mixture (Youngson and Goring 1970). As a result of these findings and the presence of 1,2-dichloropropane (1,2-D) contaminants in drinking water, 1,2-D was subsequently removed from the mixture. Subsequently, other halogenated hydrocarbons and other volatile compounds were developed as nematicidal soil fumigants. Metham (sodium N-methyl dithiocarbamate dihydrate) was the last fumigant nematicide introduced and has been shown to control various nematodes, weeds, some fungi, and insects. This material hydrolyzes in soil to form a volatile gas, methyl isothiocyanate (MIT), which is a toxic entity. Metham can be applied as a drench, in irrigation water, or injected into the soil (Rich et al. 2009).

Despite the efficiency of fumigants in nematode control, the application difficulties associated with the high costs and high environmental risk of these extremely toxic products resulted in the reduction of their use (Starr et al. 2007). In the 1960s, a new generation of nematicides was introduced, carbamates and organophosphates, that served as contact nematicides, devoid of fumigant activity. The discovery of the nematicidal activity of this chemical led to the testing and development of several other non-fumigant nematicides such as aldicarb, carbofuran, ethoprop, and fenamiphos which are still in production today.

CHEMICAL GROUP OF NEMATICIDES

Nematicides can be divided into groups based on their chemical constitution (for example, isothiocyanates, carbamates, and organophosphates), mode of action (for example, acetylcholinesterase inhibitors), and method of use (e.g., fumigant, non-fumigant) as shown in Fig. 1. The majority of the data used to explain nematicide precise activity in nematodes comes from studies of their recognized effects in insects and mammals, even though there is a wealth of evidence to support the effectiveness of nematicides. The way an active component of a nematicide affects nematodes is known as its mode of action. The mode of action of nematicides can be described at a variety of physiological levels, including morphological alterations, impacted cellular components or biochemical processes, and molecular activity sites.

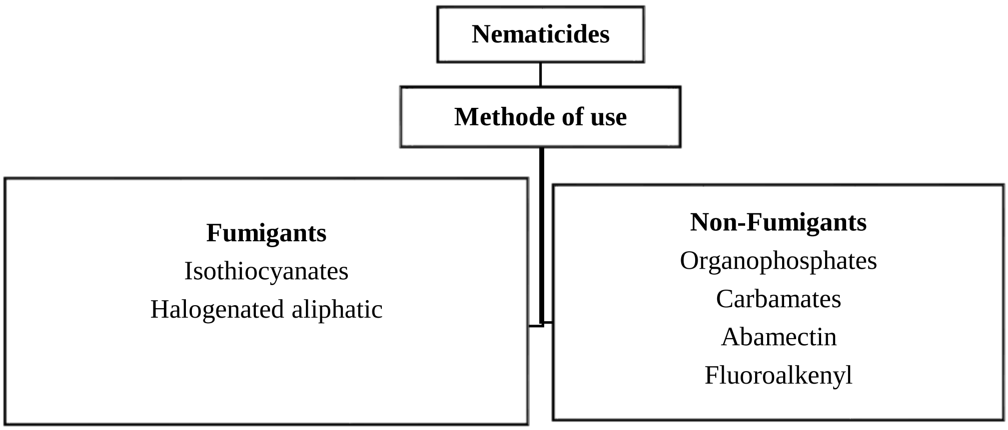

Fig. 1. Groups of nematicides

Fumigant nematicides.

Fumigant nematicides can be divided into two different chemical groups: (1) the halogenated aliphatic hydrocarbons, i.e., ethylene dibromide (EDB), 1,3-dichloropropene mixtures (1,3-D and D-D), l,2-dibromo-3-chloropropane (DBCP) and methyl bromide, and (2) the methyl isothiocyanate (MIT) liberators, i.e., metam sodium, dazomet, and MIT mixtures.

Fumigant nematicides, including methyl bromide, methyl iodide, chloropicrin, 1,3-dichloropene, dimethyl dibromide, and metam sodium and potassium, are formulated in liquids that, when exposed to air, quickly evaporate and flow through open air holes in soil as a gas. They commonly sink deep into the soil due to the detachment of their molecules in the vapor phase, and when exposed to the water in the soil, they disintegrate into chemicals that enter the nematode's cuticle and quickly react with proteins, amino acids, and oxidases to cause metabolic dysfunctions (Galbieri and Belot 2016).

Impact of fumigant nematicides in PPNs.

Broad-spectrum fumigant nematicides do not require ingestion to work because they penetrate the nematode's body wall directly. Since they are drenched in nematicide-containing bodily fluids once they have entered the nematode body cavity, they have an impact on many internal organs (Noling 1997a). Halogenated hydrocarbons have the principal function of acting as alkylating agents. These fumigants are believed to have an immediate impact on respiration and protein synthesis metabolic processes. Protein sulfhydryl groups are more susceptible to methyl bromide-induced methylation (Butler and Rodriguez 1996). According to studies done on nematodes, EDB oxidized Fe^{2+} centers and alkylated proteins in the cytochrome-mediated electron transport chain, limit nematode respiration (Wright 1981).

Metam sodium (Vapam) is a highly soluble compound that activates in water. Decomposition proceeds swiftly in water. Dazomet and sodium N-methyldithiocarbamate, often known as metam sodium, break down in soil to produce methyl isothiocyanate. Cyanide, once within the worm, blocks the use of oxygen, which is likely delivered by oxygen-transporting globins, and so stops respiration. The enzymatic, neurological, and respiratory systems are all affected by a secondary by-product (MITC) that enters through the worm body wall and forms when water is present (Noling 1997a). Unlike D-D, *Rotylenchulus uniformis* eggs and juveniles are equally sensitive to dazomet, although there is limited data on the susceptibility of various nematode species or stages to any of these fumigants (Seinhorst 1973). Beyond a minimal threshold lethal concentration of a fumigant, the susceptibility of a nematode to a fumigant has long been known to be proportional to the product of the concentration of the fumigant and the duration of exposure, i.e., the concentration-time product. Giannakou and Karpouzas (2003) stated that “fumigant nematicides (1,3-dichloro propene, metham sodium) were more effective in the control of root-knot nematodes than non-fumigant nematicides (fenamiphos, cadusafos, and oxamyl)”.

D-D and its nematicidal component 1,3-D are presumably very effective in the field against nematodes of all species, whereas EDB is generally not recommended for cyst nematodes and DBCP is not recommended for *Trichodorus* spp. reported to be inadequate for control (Van Berkum and Hoestra 1979). For EDB, this may be partly due to its relatively low volatility and hence low activity at low temperatures. They showed that juveniles of *Aphelenchus avenae* were able to tolerate EDB exposure for longer periods than juveniles of *Tylenchulus semipenetrans* or *Meloidogyne javanica*, and juvenile stages of *A. avenae* were generally more susceptible to EDB than the adults.

Non-fumigant nematicides.

Non-fumigant nematicides are nonvolatile poisonous chemicals that can be applied previous to planting, at planting, or after planting through soil drenching, drip irrigation, or scattering onto the crop leafage to reduce population consistency of nematodes and cover crops from damage. From the 1960s, new classes of nematicidal products were developed: organophosphates and carbamates, classified as non-fumigant nematicides.

A major advantage of organophosphates and carbamates is their low persistence as toxic molecules compared to chlorinated hydrocarbon nematicides (Galbieri and Belot 2016). These substances can either be created as liquids, granules, or both. An organophosphorus insecticide called Caudusafos is manufactured as granules (Rugby 200 CS) and liquid (Apache 100 GR). These nematicides are more potent than fumigants even at low concentrations because they have a systemic effect on PPNs. They are highly harmful to mammals and insects despite having little to no phytotoxic action, which causes environmental issues (Jr 1985).

Nematicides are classified into one of two categories: systemic (which kills nematodes after they feed from plant roots) or contact (which kills nematodes in soil by direct exposure). Nematicide non-fumigant compounds spread throughout the soil after being applied by the water in the soil. Non-fumigants effectiveness is independent of soil temperature, unlike fumigant nematicides. The main organismal mode of action may be temporary paralysis, interference with host seeking, suppression of hatching, or disruption of some other process because contact nematicide concentration in agricultural soils after application is typically not high enough to kill nematodes. Inhibition of hatching occurred at concentrations not expected to take place in the field, but the three carbamates aldicarb, carbofuran, and cloethocarb hindered *H. schachtii* juvenile mobility at concentrations of nematicide that occur in field circumstances (Hartwig and Sikora 1991). Because soil is a heterogeneous combination, it is doubtful that a chemical nematicide, even a fumigant, will entirely eliminate a nematode population. Furthermore, contact nematicides are applied in amounts too low to result in instantaneous death. However, the restriction on movement and penetration is typically significant enough to prevent damage to the economy. For perennials or crops with prolonged growth seasons, the reduction in nematode populations may not always last long enough to eliminate the requirement for post-plant reapplication of nematicides. However, higher initial nematicide application rates are usually not economical and may be linked to increasing hazards to the environment or other factors.

As soon as systemic nematicides are applied to plant foliage or the soil, they may be quickly absorbed and disseminated inside the root tissues of plants. Plant uptake, translocation, and ultimate nematicide content in roots are all influenced by a wide range of variables. If there are significant leaching losses, pesticides that are very soluble and mobile in soil may limit the ability of plants to concentrate systemic nematicides in roots. The size of the entire plant or root system also seems to be significant. Systemic nematicides (Temik, Vydate, Nemacur) appear to have toxic qualities that are more protective than directly harmful to the worm. Instead of killing nematodes as the term implies, systemic nematicides that are absorbed and translocated into roots appear to only prevent them from eating, render them temporarily inactive, or drive them away from the roots and their surroundings. In these cases, death occurs as a result of disorientation and starvation.

Impact of non-fumigant nematicides in PPNs.

Non-fumigant nematicides can also directly pierce nematodes body walls. Contrary to fumigants, these substances offer little to no protection against bacterial or fungal infections, but depending on the nematicide employed, they may be insecticidal. The acetylcholinesterase inhibitory properties of the carbamates (Temik, Vydate) and organophosphates (Mocap, Nemacur) used as pesticides prevent normal nerve impulse transmission in insect central nervous systems. This has a history of causing strange behavior, paralysis, and even death. Information on non-fumigant nematicides indicates that nematodes more basic nervous systems may also be impacted. These substances are not typically regarded as real nematicides since they are not as harmful to nematodes as they are to insects. Instead of being killed, nematode death frequently results from a "narcotic" impact and behavioral change. Nematode behavior and development in soil are predominantly impacted by nerve impulse disruption, which can ultimately be fatal at high concentrations over an extended period. For instance, root penetration, nutrition, mobility in the soil, and body movement are all affected. There may also be impaired development inside plant tissues, delayed egg hatch, and molting. The observed decreases in nematode population increase after non-fumigant nematicide treatment are principally attributable to decreased worm infection, development, and reproduction in the plant (Vale and Lotti 2015).

Organophosphate and carbamate nematicides have a more reliable mode of action than fumigant nematicides. It is accepted that the latter compounds act principally by inhibition of acetylcholinesterase at cholinergic synapses in the nematode nervous system (Le Patourel and Wright 1974), which is the same mode of action as in vertebrates and arthropods (Corbett 1974). Suppression of general cholinesterase activity by both organophosphate and carbamate pesticides has been conducted in vitro using extracts from several nematode species (Hart and Lee, 1966; Knowles and Casida 1966) and cholinesterase activity in the region of the nematode nerve ring inhibited by the organophosphate pesticide phorate (Rohde 1960) and by the carbamate oxamyl (Hogger et al. 1978).

NEW SYNTHETIC NEMATICIDES

The newly developed synthetic nematicides listed in Table 1 have distinct effect and regulatory requirements concerning human and environmental safety compared to their predecessors. The registration of these new nematicides is largely based on their behavior in soil, including factors such as leaching potential, soil persistence, selectivity, effects on beneficial soil organisms, degradation, and metabolism pathways (Desaeger et al. 2020). Most oldgeneration nematicides have been banned due to environmental pollution and human toxicity. Out of the 20 key nematicides used in the twentieth century, only 4 (fluopyram, oxamyl, fenamiphos, and ethoprop) are approved for use in the European Union, and only 3 (fluopyram, oxamyl, and 1,3-D) are unrestricted for use in the United States. Additionally, the new generation nematicide, iprodione, has been banned in Europe due to its potential carcinogenicity and high toxicity to aquatic animals (Jiang et al. 2024).

Despite these challenges, several new compounds with very promising efficacy have been developed and released in recent years or are in the process of being registered for use, namely fluensulfone, fluopyram, and fluazaindolizine (Jiang et al. 2024). Overall, all the 3-F nematicides have much lower water solubility, but longer soil half-lives than oxamyl. These nematicides exhibit a significantly safer toxicity profile compared to older classes of nematicides, such as fumigants, organophosphates, carbamates (Table 1). Despite their shared 3-F group, these nematicides differ considerably in their chemical and physical properties, as well as in their modes of action.

Fluensulfone, developed by ADAMA and first registered in the USA in 2014 for certain vegetables, is a nematicides with a unique mode of action as a fatty acid beta-oxidation inhibitor, although this mode of action remains unpublished. Unlike older generations of nematicides, fluensulfone poses significantly lower toxicity risks to humans and non-target organisms. Research by Kearn et al. (2017) demonstrated that when second-stage juveniles (J2) of *Globodera pallida* were exposed to fluensulfone, they exhibited increased lipid content, cell viability loss, and tissue degeneration, and these symptoms were not observed in adult of *C. elegans* (Kearn et al. 2017). In soil, fluensulfone degrades into three primary metabolites: methyl sulfone, thiazole sulfonic acid, and butene sulfonic acid, with the latter two being the major metabolites absorbed by plants (APVMA, 2015). Fluensulfone exhibits specific nematicidal activity, which makes it especially effective against *Meloidogyne* species. It is currently registered for use on various crops, including tomato, cucumber, bell pepper, squash, potato, cabbage, broccoli, melon, lettuce, strawberry, and turf, targeting important nematode genera and species such as *Belonolaimus*, *Globodera*, *Hoplolaimus*, *Meloidogyne*, and *Pratylenchus*, depending on the crop and country of registration.

Fluopyram developed by Bayer CropScience (Fought et al. 2009) and introduced in 2009, a member of pyridinyl-ethyl-benzamide group, was initially developed as a fungicide against several fungal pathogens, such as *Botrytis*, *Sclerotinia*, *Erysiphe*, and *Pyrenophora* spp. Its nematicidal activity was discovered later. Fluopyram is regarded as the first SDHI (Succinate Dehydrogenase Inhibitor) nematicide, specifically targeting complex II of the mitochondrial respiratory chain. This inhibition results in a rapid depletion of energy within nematode cells, ultimately causing nematode death (Chen et al. 2020). Fluopyram is recognized for its fast action and high potency as a nematicide. Unlike other 3-F nematicides, it has an exceptionally long soil half-life, lasting up to 746 days. Fluopyram can be considered a "true nematicide," as it causes irreversible immobilization and leads to nematode death even after brief exposure at relatively low concentrations (Oka and Saroya 2019).

Fluazaindolizine, the most recent of the new chemical nematicides, was expected to be registered in 2020 (Lahm et al., 2017). Similar to fluensulfone, fluazaindolizine specifically targets nematodes, with no reported fungicidal or insecticidal activity. It belongs to the carboxamide class, and while its mode of action remains unknown, it is distinct from that of carbamates, organophosphates, or any other known nematicides (Lahm et al., 2017). A study examining the behavior of fluazaindolizine in a tomato field analyzed the metabolites present in soil and plants, revealing that fluazaindolizine is a readily degradable nematicide (Chen et al 2018).

Additionally, other new-generation nematicides, such as spirotetramat, a tetramic acid derivative and systemic insecticide, exhibit distinctive translocation properties, moving throughout the entire vascular system of plants. This nematicide functions by inhibiting acetyl-CoA carboxylase activity, altering lipid storage and fatty acid composition, and disrupting surface coat synthesis in *Caenorhabditis elegans* (Gutbrod et al. 2018). Unlike many other nematicides, spirotetramat is a relatively recent systemic option that can be applied through foliar spraying. Similarly, tioxazafen, a systemic nematicide from the oxadiazole class, acts by disrupting the ribosomal activity of PPNs. This nematicide is primarily used as a seed treatment, offering consistent broad-spectrum control of nematodes in crops such as corn, soy, and cotton (Slomczynska et al. 2015).

Table 1. Characteristics of new synthetic nematicides and their mode of action

Chemical name	First use	Product type	Mode of action	Signal words
Spirotetramat	2008	Tetramic acid	ACC inhibitor	Caution
Dimethyl disulfide	2010	Fumigant	Multi-site	Danger
Allyl ITC	2013	Fumigant	Multi-site	Danger
Fluopyram	2013	Benzamide	SDHI inhibition	Caution
Fluensulfone	2014	Thizaole	Beta oxidation inhibitor	Caution
Tioxazafen	2017	Oxadiazole	Disrupts ribosomal activity	Caution
Fluazindolizine	2020	Carboxamide	unknown	Caution

Note: ACC = acetyl-CoA carboxylase; SDHI = succinate dehydrogenase inhibition (Desaeger et al. 2020).

EFFECT OF NEMATICIDES IN HUMAN AND ENVIRONMENT

Nematicides are intended to control nematodes, but some pesticides can have harmful impacts on ecosystems and human health. Acute and chronic poisoning can result from ingesting, inhaling, or coming into touch with pesticide residues on the skin. Such toxicity levels depend on nematicide types, entrance points, dose, metabolism, accumulation, and other factors. Chronic toxicity is caused by repeated or long-term exposure and occurs over a longer length of time than acute toxicity, which is caused by short-term exposure and occurs in a relatively short amount of time. It mostly interferes with the body's metabolic and systemic processes. The pesticide's chemical component interferes with neurological activity. Additionally, it harms the immunological and endocrine systems (Wesseling et al. 1997).

Human safety.

Exposure during application.

Nematicides are extremely hazardous substances with very low lethal concentrations (LC_{50}, the level at which 50% of animals die). This is crucial for workers who operate application equipment and are at danger of chemical exposure during application. Some of the non-fumigant nematicides have liquid formulations that are emulsifiable concentrates. Therefore, only trained users who take appropriate safety measures should utilize them. This might not always be the case if operators cannot comprehend the product labels instructions or if fundamental educational levels are low. Another concern that pesticide residue monitoring may not be able to adequately prevent is the use of nematicides to crops too soon before harvest.

Remnants in foodstuffs.

Pesticides can also reach humans through the ingestion of contaminated food and water. Some pesticide applications do, however, leave residues in the crop that is harvested. The process for approving pesticides includes provisions for the problem of residues in foods and animal feeds. Maximum residue levels (MRLs) are created to track proper pesticide use, and potential residual levels should be toxicologically acceptable. Recent European legislation has undergone significant revisions, imposing stricter regulations on the use of pesticides in agricultural crops, with a strong emphasis on environmental safety as well as human and animal health. The level of chemical residues in food products varies depending on the type of nematicide used. For instance, the MRL for dazomet is 20 µg/kg, while oxamyl is permitted on crops like tomatoes, peppers, eggplants, melons, tobacco, cucumbers, and squash, with an MRL of 10 µg/kg (PPDB 2021). Additionally, in the United States, the MRLs for certain foods, such as tomatoes and cucumbers, are set at 1.0 ppm and 0.6 ppm, respectively (EPA 2016).

Nematicides in the environment.

To guarantee that the control measures chosen can be efficient, ecologically safe, and cost-effective, a well-informed management plan is required. Groundwater contamination is one of the more serious environmental issues sometimes connected to the use of nematicides. Unfortunately, this is rarely the case because the majority of pesticides are general-purpose and may kill organisms that are beneficial to the ecosystem or harmless. The majority of pesticides are thought to poison the environment, with just around 0.1% of them reaching the intended target organisms (Carriger et al. 2006). The repeated use of persistent and non-biodegradable pesticides has contaminated multiple components of water, air and soil ecosystem.

Soil and groundwater.

If nematicides are left in the topsoil, where microbial activity is highest, they will eventually decompose. Nematicides may have a longer persistence after being washed through the upper soil layers or their breakdown products. Nematicides must break down into innocuous substances to stop sticking around in the environment. Nematicides must, however, be sufficiently persistent to successfully manage the target nematode population. Once applied to the soil, there could be direct losses by volatilization to the atmosphere. The majority of the nematicides that is applied, ends up in the soil where it may be physically lost from the soil through leaching or surface runoff or destroyed by microbial or chemical activity. When nematicides are broken down to produce a source of carbon or energy, soil bacteria play a crucial role in the process. However, efficacy can be compromised if the breakdown happens too quickly. Nematicides degrade more quickly in soils that are warm, damp, and alkaline because these are the ideal environmental conditions for microbial activity. Reduced persistence may be the outcome of applying nematicide to the same soil repeatedly. This has been seen for several carbamates and is known as rapid or increased microbial decomposition (Karpouzas and Giannakou 2002). Nematicides may enter groundwater if they are lost from the soil by leaching or surface runoff, both of which are extremely uncommon. Aldicarb and 1,3-D are two nematicides for which this has been recorded (Karpouzas and Giannakou 2002).

Similar to how contact nematicides travel away from their application area, it depends on adsorption onto organic material. Aldicarb and oxamyl are effective in soils with a wide range of organic matter concentrations, whereas ethoprop and fenamiphos are less efficient in soils with high levels of organic matter. Fenamiphos and aldicarb's sulfoxide and sulfone derivatives are more mobile in soils than their parent nematicides and have the potential to contaminate groundwater more easily (Loffredo et al. 1991). The carbamate group is hydrolyzed in oxamyl, not aldicarb. At 10 separate sites, the conversion of oxamyl into harmless oximes was typically accompanied by an increase in pH, warmth, and moisture (Haydock et al. 2012).

Non-target organisms.

Pesticides impact on creatures other than their intended targets has drawn attention and concern on a global scale for many years. Pesticide use has been linked to negative outcomes for non-target arthropods, according to multiple reports (Ware 1980). Unfortunately, pesticides have a particularly negative impact on natural insect adversaries including parasitoids and predators (Vickerman 1988).

Nematicides are usually non-selective pesticides, and their application will generally have an impact on organisms that are not intended targets. The majority of nematicides significantly change soil flora and fauna due to their broad-spectrum actions. Because of the uncontrolled use of nematicides in agricultural systems, the population of soil arthropods is also severely disrupted along with that of their antagonists. When non-target creatures are exposed to lethal or harmful doses of the active ingredient directly by ingestion, contact, or exposure, this has the most visible consequences.

The carbamates oxamyl, aldicarb, and carbofuran (or their metabolites) and the organophosphates fenamiphos, ethoprophos, and cadusafos are all extremely harmful to fish and birds, except oxamyl and ethoprophos, which are only moderately toxic. Van Straalen and Van Rijn (1998) outlined the work that showed carbofuran to be lethal to a wide range of soil organisms including collembola, carabid beetles and earthworms. Stenersen (1979) studied the effect of several chemicals on earthworms and reported that aldicarb was the most toxic, whereas oxamyl was not toxic to any of the species tested. This indicates that even though chemicals may belong to the same family and have related modes of action, they may not all have the same effects on the environment.

Furthermore, a chemical can affect a non-target creature without coming into direct touch with it or exposing it to it directly. For instance, birds may ingest spilled granules and become directly exposed, but they may also consume contaminated earthworms and become indirectly exposed to the chemical. In contrast to non-fumigants, some fumigant nematicides present a further risk to species that are not the intended targets: exposure to the chemical's gaseous state. In this regard, the toxicity classification can be based on inhalation tests on mammals; from these, the EC classification for methyl bromide and chloropicrin is "toxic," while the classification for 1,3-D is "damaging." But, there is no inhalation classification for metam sodium and dazomet. However, dazomet and metam sodium do present significant harm to aquatic creatures and the aquatic environment.

In comparison to untreated soils, potato fields that had received long-term aldicarb treatment had fewer bacterial genera and species, fewer populations of *Rhizobacteria* that promote plant growth, and more total bacterial biomass (Sturz and Kimpinski 1999). Nematicides have the ability to significantly change the structure of nematode communities in soils. For instance, *Helicotylenchus* was replaced by *Pratylenchus* as the main PPNs after pasture soil had been treated with methyl bromide (Yeates and Van Der Meulen 1996).

When considering the impact of new-generation nematicides on non-target microorganisms, it is important to note that the manufacturer's recommended application rate for fluopyram is quite low, ranging from 197 to 207 g ha^{-1}, and not exceeding 494 g ha^{-1} per year. This dosage is roughly one-tenth of that recommended for fluensulfone. Such low application rates may help preserve soil microbial ecosystems, including free-living nematodes and beneficial fungi like mycorrhiza, while also minimizing residue levels in crops. However, higher doses might be more effective in controlling PPNs. Research has shown that fluensulfone, while effectively managing *Meloidogyne* spp., did not significantly alter the diversity of free-living nematode populations and had only a minimal suppressive effect on these non-target organisms (Kawanobe et al., 2019).

Fluensulfone, unlike older nematicides, is significantly less toxic to humans and non-target organisms, with an acute LD_{50} of 671 mg/kg in rats, making it considerably safer than older nematicides. However, it is relatively toxic to aquatic organisms, with an EC_{50} of 0.35 mg/L for *Daphnia magna* after 48 h and about 0.04 mg/L for certain green algae species after 72 h. Consequently, its use should be restricted near aquatic environments to prevent harm (APVMA 2019).

Ozone depletion.

Since methyl bromide is poisonous and nonselective when utilized, it also affects species that are not intended targets. This can involve employees working at the application location. The Montréal Protocol on Substances that Deplete the Ozone Layer (1992) establishes a timeline for industrialized and developing countries to reduce and eventually stop using methyl bromide because it is likewise categorized as an ozone-depleting substance. There will be some exceptions for "essential" purposes beyond the phase-out date in 2005, when usage should end in industrialized countries, and after 2015 in developing countries. Penkett et al. (1985) measured concentrations of methyl bromide in the atmosphere and found concentrations were higher in the Northern than in the Southern Hemisphere. These authors speculated that human activity was the primary cause of emissions of methyl bromide into the atmosphere.

CHALLENGES

Since nematodes cannot be completely eradicated, the objective is to control their population and bring it down to harmful levels. Planting resistant varieties, rotating crops, integrating soil amendments, and using pesticides are a few common management techniques. Nematode control cannot be accomplished solely by diagnosing the nematodes and using the proper nematicide. Numerous nematicides made by chemicals are costly, carcinogenic, and hazardous to people, animals, and the environment. Additionally, they are known to eventually degrade the quality of the soil and contaminate the groundwater. Moreover, unfavorable climatic conditions can make the applied nematicide ineffective against nematodes (Jones et al. 2013). Nematicides are a distinctly 20th-century phenomenon since they were first discovered, developed and widely used during that century. With nematicide technology, as in most scientific advances, a large body of knowledge was created which eventually not only showed the many advantages but also the limitations and disadvantages of the technology. As a result, several nematicides were canceled or use restrictions placed upon them to mitigate problems not recognized when they first were used. Wright (1981) alluded to problems of nematicides and many of his comments were prophetic of future events.

Aside from the high toxicity, another problem of nematicide use is the decreased nematicidal activity after repeated applications of the same or a related nematicide to the same field (Davis et al. 1993, Ou et al. 1994, Suett and Jukes 1988). This phenomenon was initially thought to be caused by the development of nematode populations that were resistant to the nematicides. However, in actuality, the decrease in nematicidal activity was found to be caused by the development of soil microorganisms that can use the nematicides as a substrate for their energy generation, termed enhanced or accelerated biodegradation (Cabrera 2010). Nematicides applied to such soil can be degraded more rapidly than in soil with no history of the same nematicide application (Smelt et al., 1987).

With the new nematicides being more selective, and potentially used more frequently, resistance may be more likely to occur. For instance, SDHI compounds like fluopyram, having long soil persistence and similar mode-of-action towards fungi and nematodes, are likely to put significant selection pressure on target nematodes. It is also well-known that many of the older organophosphate and carbamate nematicides can lose efficacy over time due to accelerated degradation in the soil caused by microbial adaptation (Smelt et al., 1987; Johnson, 1998).

Present uses.

Despite product cancellations and use restrictions, and the lesser specter of enhanced biodegradation, nematicides are widely used, particularly in developed countries and on higher value crops. For example, over 80% of flue-cured tobacco hectares in Canada, the USA, and Zimbabwe receive annual nematicide applications (Rich et al. 1989). In Florida, almost 100% of the 16,000 ha of fresh market tomatoes are also treated with multipurpose fumigants, with nematode control as a major element in choosing this treatment (Noling 1997b). Production of these high-value crops is very risky economically, so many growers have used the most effective broad-spectrum fumigants possible to limit even small losses. Multipurpose fumigants have given this assurance to growers in the past and were readily adopted since other management techniques were less reliable.

For many vegetable crops, for example, plant resistance is not available, is limited to only a few potential nematode pests, may be limited by soil temperature, and/or is subject to resistance-breaking biotypes. Crop rotation with less profitable crops often is not an economical option or if possible, only shortened rotations are practical. Thus, agriculture continues to need and demand nematicides.

Farmer's knowledge about nematodes.

A colloquium on tropical nematology was held in 1994 at the 22nd International Symposium of the European Society of Nematologists in Ghent, Belgium. Tropical nematology's shortcomings and needs were summed up as (i) a lack of fundamental knowledge, (ii) a dearth of tropical nematologists engaged in research, (iii) a lack of collaboration, (iv) a communication gap between temperate and tropical nematologists, and (v) a lack of awareness among farmers, agricultural scientists, extension specialists, and decision-makers (Prot and Kermarrec 1995). Nematode awareness by farmers is important not only to implement nematode management strategies, which require that farmers can recognize and understand the pathogen problem in their fields. Farmers in southern Europe have considered soil chemical fumigation, as the most effective method for controlling root knot nematode diseases in intensive horticultural crops, since the efficacy of other nematode control methods has not proven consistent enough when high RKN soil infestations occur (Talavera et al., 2024; Greco et al., 2020). When nematode management was applied, the farmers were able to recognize the effect of the treatment but did not attribute it to the control of the nematodes because of their microscopic size (Speijer et al. 2001).

Proper selection of nematicides.

Managing nematodes in tropical and subtropical environments is a challenge. There are a few effective control measures, and these must be used under conditions in which they will work. For effective management of nematodes, the critical steps are (1) accurate diagnosis, and (2) proper selection of the most effective and environmentally benign control method should be applied.

Nematicide treatment rates required for effective nematode control can be influenced by nematicide adsorption to soil organic matter, treated soil volume (which is determined by soil type), and soil moisture content. For instance, studies have shown that nematicide treatments are typically more effective once crop debris has started to degrade since there is less nematicide adsorption. Larger treatment rates for fumigant nematicides and perhaps non-fumigant nematicides may be required for efficient nematode control because of the "sink" effects of organic matter in soil pH (Noling 1997a).

As indicated, the mobility of a nematicide relies upon, especially upon its affinity for soil organic matter and the physical characteristics of the soil to which it is applied. In sandy soils for example, both Temik and Vydate are weakly adsorbed to organic matter and consequently potentially very mobile in soil, whereas Nemacur and Mocap are greater strongly absorbed and much less mobile. It is identified at this factor that many nematicides are degraded into byproducts that are toxic to nematodes and which bind and leach in the soil in a different way than the guardian nematicide. For example, Nemacur is degraded into two toxically energetic components in plant life and soil, and these metabolites may also be greater cellular than the mother or father compound itself although still less mobile than Vydate and perchance Temik. So, one of a kind nematicides must be applied in the discipline primarily based on the nature, stage, and type of nematode, kind of soil, and active compound in the nematicide, and through considering these matters proper management of nematode can be done (Noling 1997a).

Alternative of nematicides to control nematodes.

We have already discussed nematicides and their effects on human health, soil, and water, as well as non-target creatures. Because nematodes cannot be eradicated, the goal is to regulate their population and keep it below dangerous levels. Planting resistant crop varieties, rotating crops, integrating soil amendments, and spraying pesticides are all common management techniques. Solarization of the soil may be feasible in some instances. Because there are so few and their nematode resistance is particular, the application of resistant plant cultivars is limited. Because nematode resistance is species- and race-specific, precise identification of the nematode species and race is required before selecting the appropriate cultivar (Schmitt and Sipes 1998)

Thoden et al. (2011) highlighted the application of various organic amendments that have proven successful in mitigating the effects of PPNs in various crop plants. The amendments, such as slurries and their organic acids, had the potential to accumulate/form high concentrations of nematicidal compounds and were able to create anaerobic conditions to directly suppress the PPN population. To control the root-lesion nematode *Pratylenchus penetrans*, Korthals et al. (2014) reported using eight soil health treatments (anaerobic soil disinfestation, biofumigation, chitin, compost, grass-clover, marigold, a physical technique, and a combination of marigold, compost, and chitin). Regarding their positive impact on the physical and chemical qualities of soil, all of the treatments were shown to be superior substitutes for chemical treatments. The overall beneficial effect of organic improvement agents is a result of their role in strengthening the population of free-living nematodes, insects, and bacteria. These organisms go on to play a significant role in promoting plant growth, nutrient supply, and mineralization, making plants resistant to PPN infections. Fallow soil deprives PPNs of a living host, which over time reduces their populations. Green manuring, tilling under a crop that grows rapidly and produces a lot of biomasses that adds organic matter and, depending on the green manure crop used, may add substances that repel or kill nematodes.

In the EU, the following extracts are registered as active ingredients: garlic extract, clove oil, a mixture of oils based on thymol and geraniol, and azadirachtin whose result have been found comprehensive in various research. The persistence of the product is about 14 days; therefore, after the first treatment, the product should be applied at 2-week intervals (Andres 2012). The formulations are effective against *Meloidogyne* spp., *Tylenchus* spp., *Trichodorus* spp., *Longidorus* spp., *Pratylenchus* spp., *Xiphinema* spp. and the cyst nematodes *Globodera* spp. and *Heterodera* spp. (Andres 2012, Jardim 2020). The commercial product is a natural formulation based on clove oil extracted from *Eugenia caryophillata* with high nematostatic and nematicidal action (Meyer 2008).

Another nonchemical approach to controlling nematodes is organic control using other organisms towards the pest organism. An excessive level of herbal organic manipulation is basically existing in the soil. Most organisms determined to be concerned with nematode suppression are nematophagous fungi (e.g *Pochonia chlamydosporia*, *Hirsutella rhossiliensis*, *Dactylella oviparasitica*) and bacteria (e.g *Pasteuria penetrans*) that parasitize their nematode hosts. Microbes that compete for nutrients, produce toxins, or result in host resistance, such as some rhizosphere microorganisms (e.g *Pseudomonas* spp., *Agrobacterium radiobacter*, *Bacillus subtilis*) may also decrease nematode harm, however, can also no longer furnish the long-term manipulate of nematode populations associated with suppressive soils. It is generally difficult to apply biological control agents for the administration of PPNs, and the majority of empirical studies has produced contradictory outcomes. Some products, such as *Paecilomyces* spp., *P. penetrans*, and *Trichoderma* spp., have been commercialized, but some may also be used practically in nematode treatment. The steps for commercialization include resolving the most impressive isolates, producing inoculum, and developing a technique for the microbial agents. The application of organic control retailers must be taken into consideration within the context of various management approaches, notably, their interaction with cultural control methods since biological control is not a substitute for chemical control (Atkinson 1992; Lee 2002).

There is always a need for new nematicidal compound formulations, but there are not any that are close to commercial development at the moment. Microbial-derived avermectins, which are effective anthelmintics, have been produced for veterinary use. The efficiency of compounds against PPNs is well-known; however, their complexity prevents them from being used as effective soil treatments. An ideal nematicide should be highly effective against all PPNs at a low cost and dose, while being non-toxic to non-targets, including crops. Additionally, it should be easily applicable and safe for users, consumers, and the environment. Furthermore, new application methods, such as seed treatment, can reduce the application dose and cost, as well as protect plants at a crucial stage of development, while safeguarding the environment from nematicide pollution. The three nematicides probably have different modes of action, and this can be an advantage in nematode management. Additionally, we must keep in mind that managing nematodes is a difficult task that requires more than just using nematicide; instead, an integrated management approach must be used for cost-effective and environmentally sustainable nematode management.

CONCLUSION

PPNs are becoming more of a problem, and proper nematode management is required for efficient crop production. There are various types of chemical nematicides, each with its mode of action and effect on nematode physiological levels such as morphological changes, affected cellular components or biochemical processes, and molecular activity sites. Because nematicides are harmful to human health, soil, groundwater, and non-target organisms, proper nematicide selection and application methods are critical. Other control methods must be integrated for improved control. Although chemical control began with more harmful effects, new compounds that are less aggressive and more specific for PPNs have been developed, making this tool safer for the producer, the consumer, and the environment. Because nematodes cannot be eliminated, the goal is to manage their population, reducing their numbers to dangerous levels. The first step in effective nematode management is an accurate diagnosis, followed by the proper selection of the most effective and environmentally friendly control method. Crop rotation, cover crops, and other alternative method can be combined into a cultural method.

RESUME

Tiwari S. 2024. Impact des nématicides sur les nématodes phytoparasites: Défis et sécurité environnementale. Tunisian Journal of Plant Protection 19 (2): 101-120.

Les nématodes parasites des plantes sont de minuscules animaux vermiformes pseudocoelomates, non segmentés, bilatéralement symétriques qui attaquent les plantes. Les nématicides sont des substances synthétisées chimiquement qui tuent ou nuisent aux nématodes. Entre 1940 et 1950, trois produits chimiques aux propriétés nématicides ont été découverts: le bromure de méthyle (bromométhane), le mélange D-D et l'EDB (1,2-dibromoéthane, sous forme de dibromure d'éthylène) qui étaient des fumigants. Lorsque des composés fumigants sont appliqués au sol, un gaz se déplace à travers les espaces ouverts entre les particules du sol ou dans le film d'eau qui entoure les particules du sol. Les fumigants diminuent considérablement la respiration des nématodes en oxydant les centres Fe^{2+} et les protéines alkylées dans la chaîne de transport d'électrons médiée par le cytochrome. Malgré l'efficacité des fumigants contre les nématodes, leur utilisation a été réduite en raison du risque environnemental élevé de ces produits. Une nouvelle génération de nématicides a été introduite: les carbamates et les organophosphates qui ont servi comme nématicides de contact, ce qui a conduit à tester et à développer d'autres nématicides non fumigants tels que l'aldicarbe, le carbofuran, l'éthoprop et le fénamiphos. Les propriétés inhibitrices de l'acétylcholinestérase des carbamates et des organophosphorés empêchent la transmission normale de l'influx nerveux dans le système nerveux des nématodes. Les nématicides sont généralement des pesticides non sélectifs et leur utilisation a un impact sur les organismes non ciblés, l’homme et l'environnement. Puisque les nématicides sont toxiques pour l’homme, le sol, les eaux souterraines et les organismes non ciblés, une sélection et une application prudentes des nématicides sont essentielles. De nouveaux composés moins agressifs et plus spécifiques aux nématodes phytoparasites ont été développés, les rendant plus sûrs pour le producteur, le consommateur et l'environnement. La rotation des cultures, les cultures de couverture, la fumure organique, l'utilisation de variétés résistantes et d'autres méthodes doivent être intégrées aux nématicides pour une efficacité élevée.

Mots clés: Empoisonnement, nématicides, nématodes phytoparasites, oorganophosphorés, sécurité humaine

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ملخص

تيواري، سريجان. 2024. تأثير المبيدات النيماتودية على النيماتودا الطفيلية النباتية: التحديات والسلامة البيئية. Tunisian Journal of Plant Protection 19 (2): 101-120.

النيماتودا الطفيلية النباتية هي حيوانات دودية صغيرة، شبه جوفية، غير مجزأة، ثنائية التناظر تهاجم النباتات. المبيدات النيماتودية هي مواد مصنعة كيميائيًا تقتل أو تضر بالنيماتودا. بين عامي 1940 و1950، تم اكتشاف ثلاث مواد كيميائية ذات خصائص قاتلة للنيماتودا: بروميد الميثيل (برومومیثان)، وخليط D-D، و EDB (1،2- ثنائي برومومیثان؛ مثل ثنائي بروميد الإيثيلين) والتي كانت مبيدات مبخِّرة. عندما يتم تطبيق مبيدات مبخّرة على التربة، يتحرك الغاز عبر المساحات المفتوحة بين جزيئات التربة أو إلى طبقة الماء التي تحيط بجزيئات التربة. تقلل المبيدات المبخّرة بشكل كبير من تنفس النيماتودا عن طريق أكسدة مراكز Fe^{2+} والبروتينات المؤلكلة في سلسلة نقل الإلكترونات بوساطة السيتوكروم. على الرغم من فعالية المبيدات المبخّرة على النيماتودا، انخفض استخدامها بسبب المخاطر البيئية العالية لهذه المواد. تم تطوير جيل جديد من المبيدات النيماتودية: الكارباماتات والفوسفاتات العضوية التي تعمل كمبيدات نيماتودية ملامِسة، مما أدى إلى

اختبار وتطوير مبيدات نيماتودية غير مبخّرة أخرى مثل الألديكارب والكاربوفوران والإيثوبروب والفيناميفوس. تمنع خصائص الكارباماتات والفوسفاتات العضوية المثبطة لأستيل كولينستريز انتقال النبضات العصبية الطبيعية في الجهاز العصبي للنيماتودا. المبيدات النيماتودية هي مبيدات غير انتقائية بشكل عام، واستخدامها يؤثر على الكائنات غير المستهدفة والإنسان والبيئة. وبما أن المبيدات النيماتودية سامة للإنسان والتربة والمياه الجوفية والكائنات غير المستهدفة، فإن اختيار هذه المبيدات وتطبيقها بحذر أمر حيوي. تم تطوير مبيدات نيماتودية جديدة أقل عدوانية وأكثر تخصصا للنيماتودا الطفيلية النباتية، مما يجعلها أكثر أمانًا للمنتج والمستهلك والبيئة. يجب دمج تناوب المحاصيل ومحاصيل التغطية والتسميد العضوي واستخدام الأصناف المقاومة وطرق أخرى في استعمال المبيدات النيماتودية لزيادة فعالية المكافحة.

كلمات مفتاحية: تسمم، سلامة الإنسان، فوسفاتات عضوية، مبيدات نيماتودية، نيماتودا طفيلية نباتية

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