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NEMATICIDES

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Nematodes are nonsegmented, bilaterally symmetric worm-like invertebrates that possess a body cavity and a complete digestive system but lack respiratory and circulatory systems. The body wall is composed of a multilayered cuticle, a hypodermis with four longitudinal cords, and internal musculature. The most conspicuous feature of the nervous system is the nerve ring near the nematode pharynx. The so-called excretory system has never been associated with removal of metabolic wastes; instead, it functions in osmoregulation or in the secretion of compounds essential to the life history of the nematode, depending on the species and the developmental stage. The digestive and reproductive systems constitute much of the body contents.

Most nematode species are “free-living”; i.e., they feed on microorganisms in water and soil. A smaller number of species are ubiquitous parasites of animals or plants. Indeed, Nathan A. Cobb (1), the father of American nematology, stated in 1914:

> If all the matter in the universe except nematodes were swept away, our world would still be recognizable, and if, as disembodied spirits, we could then investigate it, we should find its mountains, hills, vales, rivers, lakes, and oceans represented by a film of nematodes. The location of towns would be decipherable, since for every massing of human beings there would be a corresponding massing of certain nematodes. Trees would still stand in ghostly rows representing our streets and highways. The location of the various plants and animals would still be decipherable, and had we sufficient knowledge, in many cases even their species could be determined by an examination of their erstwhile nematode parasites.

The development of chemical controls for plant-parasitic nematodes is a formidable challenge. Because most phytoparasitic nematodes spend their lives confined to the soil or within plant roots, delivery of a chemical to the immediate surroundings of a nematode is difficult. The outer surface of nematodes is a poor biochemical target and is impermeable to many organic molecules. Delivery of a toxic compound by an oral route is nearly impossible because most phytoparasitic species ingest material only when feeding on plant roots. Therefore, nematicides have tended to be broad-spectrum toxicants possessing high volatility or other properties promoting migration through the soil. The resulting record of less-than-perfect environmental or human health safety has resulted in the widespread deregistration of several agronomically important nematicides (e.g., ethylene dibromide and dibromochloropropane). The most important remaining fumigant nematicide, methyl bromide, faces immediate severe restrictions and future prohibition because of concerns about atmospheric ozone depletion (2).

This review focuses on the chemical compounds presently used against plant-parasitic nematodes and the compounds with the greatest likelihood to replace some of the current problematic compounds. Chemical control of nematodes of veterinary or medical importance is achieved through use of several compounds useful in management of several types of vermiform parasites besides nematodes. In general, mammalian anthelmintics are poorly suited as agronomic nematicides because of lack of mobility in soil, expense, or other undesirable properties. Readers curious about mammalian anthelmintics should refer to several excellent reviews (3–5). The mode of action of some mammalian nematicides is briefly discussed in this review.

AGRICULTURAL IMPACT OF NEMATODES

As with damage caused by other crop pests and pathogens, the extent of crop losses caused by nematodes is a topic of debate. The most comprehensive estimate was obtained in a 1986 survey incorporating the responses of 371 nematologists in 75 countries (6). Estimates of nematode damage to specific crops ranged from 3.3% to 20.6%, with a mean of 12.3%. Annual production losses at the farm gate (in year 2000 dollars) were \$121 billion globally and \$9.1 billion in the United States. Developing nations reported greater yield loss percentages than did developed countries.

Figures for mean crop losses can be deceptive; yield reduction in specific crops can exceed 75% in some locations (7). More typically, growers are forced to select less profitable crops. In addition to directly causing crop losses, nematodes can vector many plant viruses or create wounds that allow the entry of other root pathogens. Several nematodes are major pests of quarantine importance and interfere with free trade of several agricultural commodities.

SPECIFIC NEMATICIDES: AN INTRODUCTION

Although the discovery of nematicidal activity in a synthetic chemical dates from the use of carbon disulfide as a soil fumigant in the second half of the nineteenth century, research on the use of nematicides languished until surplus nerve gas (chloropicrin) became readily available following World War I (8). In the 1940s, the discovery that D-D (a mixture of 1,3-dichloropropene and 1,2-dichloropropane) controlled soil populations of phytoparasitic nematodes and led to substantial increases in crop yield provided a great impetus to the development of other nematicides, as well as the growth of the science of nematology. Subsequently, other halogenated hydrocarbons and other volatile compounds were developed as nematicidal soil fumigants. In the 1960s, a new generation of nematicides was introduced—carbamates and organophosphates that served as contact nematicides, devoid of fumigant activity. Many of the carbamates and organophosphates are systemic within plants, but only one contact nematicide has registered systemic nematicidal activity. For most systemics, the high concentrations needed to retard nematode development within plant roots is not likely to occur under field conditions (9).

Most soil nematicides are also registered as insecticides or fungicides and are discussed in greater detail elsewhere in this volume. This broad-spectrum activity is a result of the difficulty in discovering or designing compounds capable of movement through the soil. In addition, the small size of the commercial market for nematicides in comparison to other pesticides dictates that nematicide discovery is often an appendage to research programs pursuing controls for other organisms. Compounds included in the following compilation of chemical nematicides are not necessarily registered for usage in the United States or elsewhere, particularly when viewed through their ever-changing regulatory context.

FUMIGANTS

D-D

This mixture of 1,2-dichloropropane and 1,3-dichloropropene had widespread use as an effective nematicide until problems with groundwater contamination resulted in its withdrawal from use in 1984. The 1,2-dichloropropane component was relatively inactive as a nematicide at concentrations used in agricultural fields.

1,3-Dichloropropene

Because of the relative lack of nematicidal activity in 1,2-dichloropropane and the desire to eliminate groundwater contamination by a compound not useful for nematode control, 1,3-D became a highly successful nematicide. Although it also has fungicidal activity and insecticidal activity against wireworms in particular, the primary use of the compound is as a nematicide. On a weight basis, 1,3-D is the sixth most abundantly used pesticide in the United States (11); 1,3-D is classified as a possible or probable human carcinogen. Commercial formulations are liquids and contain two isomers. In one series of experiments, aqueous *trans*-1,3-D was 60% as toxic as the *cis* isomer, whereas in the vapor phase, *trans*-1,3-D was 90% as toxic as *cis*-1,3-D (12). In laboratory experiments simulating field situations, the *trans* isomer was completely ineffective against the potato cyst nematode *Globodera rostochiensis* (13).

Ethylene Dibromide

Once the most abundantly used nematicides in the world, use of EDB was prohibited in the United States in 1983 because of groundwater contamination (8,10). It was available in liquid formulations and is regarded as a probable human carcinogen.

1,2-Dibromo-3-Chloropropane

Liquid formulations of this fumigant with substantial nematode-specific activity were once popular. The compound was notable because of its usefulness in postplant applications. The discovery that over one-third of the male workers at a DBCP manufacturing plant in California were sterile led to the immediate 1977 prohibition of its use in the United States, except for usage in pineapple production (14). Sterility problems were also reported among some DBCP applicators (14). All uses were prohibited in the late 1980s. DBCP is classified as a possible or probable human carcinogen.

Methyl Bromide

Methyl bromide is a broad-spectrum fumigant toxic to nematodes. In 1997, methyl bromide was the fourth most commonly used pesticide in the United States (11). It is agronomically useful against soil fungi, nematodes, insects, and weeds. The Montreal Protocol, an international treaty regulating the use of ozone-depleting substances, mandates the elimination of methyl bromide use in developed countries by 2005. Under a 1999 amendment to the Clean Air Act, the United States phaseout of usage will not be more restrictive than that mandated by the Montreal Protocol. Research pursuing the development of nematicidal methyl bromide alternatives has been intensive, but no single compound appears likely to substitute for it. Methyl bromide is used as a gas; because of its lack of odor, small amounts of chloropicrin are often added as an indicator of exposure to applicators and are often required by specific governmental agencies, such as the state of Florida. Methyl bromide is the fastest moving fumigant in soils, followed by chloropicrin, 1,3-D, EDB, methyl isothiocyanate, and DBCP (15).

Chloropicrin

One of the oldest soil fumigants, chloropicrin's primary agricultural use in soils is as a fungicide, although it does have herbicidal and nematicidal activity. It is often added to 1,3-D formulations in order to increase their fungicidal activity. The compound is acutely toxic and is used in liquid formulations. In 1997, it was the 25th most abundantly used U.S. pesticide (11).

Metam Sodium, Dazomet, and Methyl Isothiocyanate (MITC)

Metam sodium is a soil fumigant used to control nematodes, fungi, insects, and weeds; it is the third most commonly used U.S. pesticide (11). When applied to soils, metam sodium is converted to MITC, which is the active biocidal agent. MITC is no longer registered for use as a soil pesticide in the United States, except as a wood preservative. Metam sodium and related compounds have provided excellent control of nematodes in some circumstances but not in others (8,16,17). Dazomet is one of the few compounds with activity as a fumigant that is supplied as a granular formulation. Research on the use of isothiocyanates as nematicides began in the 1930s (18). Several brassicaceous plants contain nematicidal isothiocyanates or glucosinolates that release isothiocyanates when incorporated into soils (19).

Sodium Tetrathiocarbonate

Sodium tetrathiocarbonate is more recently registered preplant soil fumigant active against fungi, insects, and nematodes. It is supplied as a liquid formulation and may be applied via drip or surface irrigation. Sodium tetrathiocarbonate rapidly degrades in soil into carbon disulfide, sodium hydroxide, hydrogen sulfide, and sulfur. Carbon disulfide is the active principle. Although carbon disulfide has a long history as a fumigant, its flammability is legendary. Carbonates and sulfates are the terminal degradation products. Unlike other commonly used fumigants, sodium tetrathiocarbonate does not readily move through soil air and requires a high level of soil moisture when applied in order to be distributed throughout the soil.

CARBAMATES

Aldicarb

Like most other carbamate nematicides, aldicarb was introduced in the 1960s. It is active against a wide variety of nematodes (as well as insects and mites) and is useful in a variety of soil types throughout the world (8). Aldicarb is available in granular formulations and possesses systemic activity. Aldicarb, carbofuran, and oxamyl are highly toxic but have not been shown to be carcinogens.

Aldoxycarb

Aldicarb is oxidized in soils to aldicarb sulfone, which is available in some parts of the world as the insecticide/nematicide aldoxycarb. A flowable formulation is available.

Carbofuran

Carbofuran is another systemic insecticidal/nematicidal carbamate available in granular and liquid formulations. Because use of carbofuran granules was associated with bird kills, the U.S. Environmental Protection Agency (EPA) prohibited the use of carbofuran granules in 1994.

Oxamyl

Like carbofuran, oxamyl is a carbamate that is manufactured in liquid and granular form, but the latter is no longer registered in the United States because of concerns about its consumption by birds. Oxamyl is the only nematicide with downward-moving systemic activity and thus has registered foliar nematicidal applications; foliar applications did reduce *Pratylenchus penetrans* on lily (20). Oxamyl is widely used throughout the world and is less persistent in soil than is aldicarb (8).

ORGANOPHOSPHATES

While this review is being written, the U.S. EPA is actively reviewing the uses of all organophosphates. It is possible that several of the following compounds will face mandatory or voluntary withdrawals from use in the United States.

Ethoprop

Introduced in the 1960s, ethoprop is a nonsystemic insecticide/nematicide. The mobility of ethoprop in soil and its half-life are strongly dependent on soil organic matter (21). It is not known to be carcinogenic and is available as granules or emulsifiable concentrates.

Fenamiphos

Also introduced in the 1960s, fenamiphos does have some systemic insecticidal activity. It is widely used as a nematicide. Like ethoprop, it is strongly adsorbed onto organic matter. It is acutely toxic but not shown to be a carcinogen.

Cadusafos

This nonsystemic organophosphate not registered for U.S. usage is used to control nematodes and soil insects on bananas and other crops in several countries. The U.S. EPA has granted tolerances for cadusafos in imported bananas, where it provides excellent control of the burrowing nematode, *Radopholus similis* (22). Cadusafos reportedly possesses reduced risk for contaminating groundwater and provided good control of the citrus nematode, *Tylenchulus semipenetrans* (23). Cadusafos is commercially available in granular and microencapsulated formulations.

Fosthiazate

Fosthiazate is a somewhat recently developed (1992) systemic organophosphorus nematicide with broad-spectrum activity (24). A clay-based microgranule formulation is available. Fosthiazate provided control of the lesion nematode *Pratylenchus penetrans* on potato (25) and root knot nematodes (*Meloidogyne* spp.) on tobacco (26) and *M. arenaria* on peanut (27), but it failed to control *M. javanica* on tobacco and *Rotylenchulus reniformis* on pineapple as well as fumigation with 1,3-D (28,29). It is not registered for U.S. usage.

Other Organophosphates

Terbufos is a less widely used organophosphate with insecticidal and a few nematicidal uses. It is available in granular formulations. Fensulfothion is a systemic previously but not currently registered for insecticidal and nematicidal activity in the United States. Granular and emulsifiable concentrate formulations were available. Phorate is primarily used as a soil insecticide but has nematicidal uses. Its current U.S. reregistration process involves the use of several risk mitigation measures. Organophosphate nematicides with limited worldwide use but not registered in the United States include thionazin, fosthietan, and isazofos.

BIOCHEMICALS

DiTera

The nematode-parasitic fungus *Myrothecium verrucaria* produces a mixture of compounds registered in 1996 as a biologically based nematicide named DiTera. Toxicity apparently results from the synergistic action of low-molecular-weight, water-soluble compounds. DiTera is active against many plant-parasitic nematodes but not the free-living and mammalian-parasitic nematodes studied thus far (30). Toxic effects observed with *G. rostochiensis* include disruption of hatching, movement, and response to potato root diffusate; toxicity to *M. incognita* did not involve inhibition of hatching (31,32). DiTera is available as granules, a powder, and an emulsifiable suspension.

ClandoSan

ClandoSan is a granular product made from processed crab and crawfish exoskeletons. The material contains large amounts of chitin and urea and was registered in the United States in 1998 as a nematicide. Its nematicidal activity (33) is believed to result from the stimulation of populations of nematode-antagonistic microorganisms, particularly those that produce chitinase, a major component of nematode eggshells. Proper application is necessary to avoid phytotoxicity (33).

Sincocin

Sincocin is the trade name of the mixture registered in 1997 as "Plant Extract 620" with the U.S. EPA. It consists of a blend of extracts from the prickly pear *Opuntia lindheimeri*, the oak *Quercus falcata*, the sumac *Rhus aromatica*, and the mangrove *Rhizophora mangle*. Sincocin has provided control of the citrus nematode on orange roots (34), the reniform nematode on sunflower (35), and the sugarbeet cyst nematode (36); but control of *M. incognita* on cassava and *R. similis* on anthurium was less successful than that provided by other methods (37,38). Its mode of action has not been fully elucidated.

MODE OF ACTION

In general, nematode developmental stages that are active are more susceptible to nematicides than are resting stages (12,39). The detailed 20-year-old review by Wright (40) on nematicidal mode of action remains relevant because few new nematicides have been introduced since its publication. Moreover, the broad-spectrum activity of most nematicides has resulted in much of their basic biochemical effects being documented in insects or mammals instead of nematodes.

Fumigants

A primary effect of halogenated hydrocarbons is to serve as alkylating agents. The sulfhydryl groups of proteins, in particular, are labile to methyl bromide–induced methylation (41). With respect to research performed with nematodes, EDB alkylated proteins and oxidized Fe^{+2} centers in the cytochrome-mediated electron transport chain, thereby blocking respiration (40). The mode of action of methyl isothiocyanate generators in nematodes is even more poorly understood (42); amino and hydroxyl groups have been speculated as sites of attack (40). 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.

Nonfumigants

Carbamates and organophosphates are well-known reversible inhibitors of acetylcholinesterase activity in insects. Several nonfumigant nematicides have been demonstrated to inhibit cholinesterase in nematodes, e.g., aldicarb, carbofuran, fenamiphos, and oxamyl in *M. incognita* and *M. javanica* (43) and *Aphelenchus avenae* (44). Interestingly, although carbofuran inhibits *Meloidogyne* cholinesterase approximately 10,000 times higher than fenamiphos (43), the latter has greater nematicidal activity against *Meloidogyne*; this discrepancy is correlated with a much quicker metabolism of fenamiphos than carbofuran by root-knot nematodes (45). Chang and Opperman (46) discovered five molecular forms of acetylcholinesterase in *M. arenaria* and *M. incognita*; the forms could be divided into three classes, one of which was highly resistant to aldicarb and fenamiphos.

Given that nonfumigant nematicides inhibit nematode acetylcholinesterase, it is not surprising that many of the symptoms induced in nematodes reflect nervous system dysfunction. These symptoms include stylet thrusting, twitching, trembling, convulsions, soiling and uncoiling, other uncoordinated movements, inhibited penetration, and eventual paralysis if the concentration is sufficiently high (39,47,48). Nematode recovery from acetylcholinesterase inhibitor treatment can occur within a short time, even for the case of the stem and bulb nematode, *Ditylenchus dipsaci*, exposed to 10-mg/ml oxamyl for a day (48). In some cases, however, recovery may not occur, as with *A. avenae* exposed to fenamiphos, but not carbofuran (49). The speed of recovery from acetylcholinesterase inhibition varies among inhibitors, and nematodes that grossly appear fully recovered still can exhibit pronounced acetylcholinesterase inhibition in enzyme assays.

Because contact nematicide concentration in agricultural soils following application is usually not sufficiently high to kill nematodes, the primary organismal mode of action may be temporary paralysis, interference with host finding, inhibition of hatching, or disruption of some other process (10). For example, the three carbamates aldicarb, carbofuran, and cloethocarb inhibited *H. schachtii* juvenile mobility at concentrations of nematicide that occur in field situations, whereas inhibition of hatching occurred at concentrations not likely to occur in the field (50).

Because soil is a heterogeneous mixture, complete eradication of a nematode population with a chemical nematicide, even a fumigant, is an unlikely achievement. Moreover, contact nematicides are used at levels insufficient to induce immediate death. Nonetheless, the inhibition of movement and penetration is usually substantial enough to result in lack of economic damage. Sometimes the reduction in nematode populations is not sufficiently long to eliminate the need for postplant reapplication of nematicides, however, especially for perennials or crops with long growing seasons. Nonetheless, higher initial nematicide application rates are often not cost-effective and may be associated with increased environmental or other risks.

The metabolism of nematicides by nematodes has not been extensively studied. In one interesting investigation of the metabolism of carbofuran and fenamiphos by root-knot nematodes, detected metabolites included 3-hydroxycarbofuran, 3-ketocarbofuran, fenamiphos sulfoxide, and various unidentified water-soluble products (45).

Mammalian Anthelmintics

Although the purpose of this review is not to focus on nematicides of veterinary or human medical importance, the modes of action of these compounds have been reviewed (4) and are relevant. Representatives of the most popular classes of compounds include the following: 1) nicotinic agonists such as the imidazothiazole levamisole, the tetrahydropyrimidines pyrantel and morantel, and the pyrimidine methyridine, which act as agonists on muscle acetylcholine receptors and induce paralysis; 2) the GABA agonist piperazine, which induces muscular paralysis, particularly in large nematodes in oxygen-poor environments; 3) macrocyclic lactones such as avermectins and milbemycins, with mode of action as discussed in this review; 4) benzimidazoles such as thiabendazole and mebendazole, which bind to β-tubulin and interfere with nematode microtubule formation; and 5) diethylcarbamazine, which appears to interfere with host and possibly nematode arachidonic acid metabolism.

RESISTANCE TO NEMATICIDES

Resistance of field populations to nematicides has not been well characterized and is remarkably insignificant in comparison to the levels of resistance observed with mammalian parasites. Indeed, a recent National Academy of Sciences monograph stated, “Resistance of nematodes to soil fumigants has yet to be observed but systemic nematocides are relatively new and it is probably only a matter of time until resistance does appear” (51).

In one interesting study, Moens and Hendrickx (52) evaluated populations of *Meloidogyne naasi*, *G. rostochiensis*, and *Pratylenchus crenatus* exposed to aldicarb for 15 years. Although some developmental differences were noticed between treated and control populations when challenged with aldicarb, the differences were species specific and were concluded to be not significant.

In another investigation, the free-living nematode *Rhabditis oxycerca* was bred for 400 generations in order to obtain strains adapted to reproducing on concentrations of 600- and 480-μg/ml aldicarb and oxamyl, respectively. Compared with wild type, the two mutant strains were characterized by decreased size (particularly in the tail region), tolerance of warm temperature, production of offspring, and migration in electric fields, among other characteristics. In nematicide solutions, the wild type exhibited decreased motility, electric field migration, and reproduction (53).

In a third study, genetically selected strains of the insect pathogen *Heterorhabditis bacteriophora* possessed 8–70-fold increased resistance to fenamiphos, avermectin, and oxamyl (54). The enhanced resistance was generally stable in the absence of further nematicide pressure; the strains have obvious potential utility in integrated pest management systems.

APPLICATION METHODS

The methods for treating agricultural soils with nematicides are similar to those used for other pesticides examined in this volume. Nematicide application research is being driven by the need to maximize efficacy while minimizing groundwater and atmospheric contamination.

Fumigation

Soil fumigation requires prior preparation to be effective (55). Prior to fumigant or nonfumigant application, soil is often turned or tilled to increase porosity and uniformity and promote decomposition of residual plant roots, which can serve as hiding places for nematodes or interfere with fumigant movement. Adequate but not excessive soil moisture is critically important to the success of some fumigants. Fumigants are typically injected with chisels or shanks into the upper 15–40 cm of soil, with the actual depth a function of compound, soil structure, and crop. Although deep injection is often required to minimize the escape of fumigant into the surrounding air, inadequate levels of nematicide in the upper soil layers may result in some situations. Following fumigation, the soil surface is often compacted in order to retard fumigant loss from the soil surface.

The design of injection equipment modified for minimization of fumigant escape into the surrounding air is an active research area (56). Because the shallow chisel traces left in treated soils provide a means for fumigant to escape into the atmosphere, some nematicide labels mandate that the traces be covered with soil. Experimental chisels angled to the side 45° in order to eliminate chisel trace formation have provided control of root-knot nematodes on tomato equivalent to conventional chisels (57). Another example of minimizing atmospheric loss is through use of single chisel injections for crops traditionally fumigated with dual chisels (58).

Fumigation usually involves the use of plastic tarpaulins to minimize atmospheric losses and deliver nematicide to the target organism. Sometimes, tarpaulins must be in place for 10 days. Even when plastic sheeting is employed, fumigant losses can exceed 50% and approach 80% under extreme conditions (55,59). A variety of injection temperatures and plastic sheeting compositions have been employed to maximize nematicidal activity and reduce atmospheric losses of methyl bromide and other fumigants. Impervious sheeting, warm temperatures, and deep injection often enhance nematicidal activity and permit the use of much smaller quantities of fumigant (41,59). A recovery system involving a double layer of polyethylene sheeting through which air is blown to a methyl bromide collection unit has reduced methyl bromide emissions in a laboratory setting (60). Buffer zones around fumigated areas are often required to reduce the exposure of the general population to airborne fumigants.

Irrigation

Liquid and emulsifiable formulations of nematicides can often be applied through surface or drip irrigation systems. The goal of delivering sufficient nematotoxic materials without excessive leaching is researchable but sometimes difficult to achieve (61). Drip irrigation in particular offers a means of precisely controlling the amount of active ingredient delivered to a field, as well as regulating the amount of water, so that leaching of active ingredient beyond the root zone and into groundwater can be eliminated. Drip irrigation also is useful for postplant applications, and it avoids the use of granular materials that may pose risks to birds. Use of drip irrigation also reduces the amount of personal protective equipment required for field workers. A substantial percentage of pineapple production in Hawaii is drip irrigated, and drip irrigation with ethoprop, fenamiphos, or soluble liquid formulations of 1,3-D have been used to provide control of nematodes in pineapple production in Hawaii (61). In order to minimize leaching of nematicides below the root zone and maximize effectiveness, fields are not irrigated for 2 weeks following application. Successful control of *P. penetrans* on lilies was provided with drip-irrigated ethoprop, fenamiphos, sodium tetrathiocarbonate, 1,3-D, and oxamyl (20); similarly, drip-irrigated emulsifiable 1,3-D provided control of the citrus nematode, *Tylenchulus semipenetrans* (62).

Although less precise than drip irrigation in delivering nematicide to targeted areas, overhead spray irrigation can also effectively convey nematicides (63). However, injection of metam sodium into a center pivot irrigation system was associated with higher airborne concentrations of MITC than that which occurred in fields receiving metam sodium at depths of 5, 15, and 25 cm (64).

Granules and Broadcast Sprays

The most widely practiced method of applying nonfumigant nematicides is with granular formulations. Methods for application of nonfumigants to soil have been thoroughly reviewed (65). In some cases, adequate control can be achieved by band application of nematicides at or before sowing. In band application, plant roots may eventually grow beyond the treated area at a time when the root system will be sufficiently vigorous to not suffer serious damage. In-furrow application sometimes is practiced but may result in lack of delivery to the root zone; in other cases, in-furrow application may be preferable. In some cases, sidedress applications of nematicides are useful replacements or additions to at-plant applications.

In other cases, broadcast application of granules or sprays followed by a thorough mixing of the soil may be effective. Tillage is necessary to distribute nematicide to a broad enough area to provide control, and a thorough mixing is particularly important for nematicides with poor soil mobility characteristics. Use of broadcast sprays instead of granules often promotes greater uniformity in distribution. For many annual crops, incorporating nematicides into the upper 10–15 cm of soil provides the best balance of efficacy, expense, ease, and safety to wildlife. Research on the distribution of granules to soils by various types of tillage equipment can be facilitated via the use of sepiolite granules containing a fluorescent dye (66).

Nematodes are usually distributed unevenly in a given field; nematicide treatment deposits expensive chemical throughout a grower's field, even in areas where it may not be needed. In one interesting study, Baird et al. (67) quantified the numbers of root-knot nematode juveniles at specific locations in experimental cotton fields treated with variable rates of aldicarb or 1,3-D applied with prototype equipment designed to apply nematicide at rates dependent on initial nematode population levels. Although final nematode population levels did not vary among treatments, the variable rate applications of 1,3-D (but not aldicarb) resulted in yield increases and lowered nematicide costs that justified the additional costs of nematode sampling and enumeration.

Seed Dressing and Bare Root Dip

The reasons why few nematicides have been registered as seed coatings include the difficulty in applying a sufficient quantity of nematicide needed to provide control beyond the seedling stage, the expense of registration relative to market size, and the attraction of such products to wildlife (65). Nonetheless, experimental formulations have provided some successes, as with control of *P. penetrans* on corn by seed treatment with oxamyl (68). In addition, seed-transmitted nematodes can be successfully treated with nematicidal treatment of seeds (69). Much experimental research with biocontrol organisms or nematicidal natural products is performed with seed formulations.

The principle behind bare root dips is similar to that for seed dressings; i.e., sufficient nematicide is applied to transplants to protect them at a highly vulnerable time. Root dips have provided nematode control in several situations (8).

NEMATICIDE ECOLOGY

Effects of Temperature on Activity

The effects of temperature on nematicide efficacy are complex and not well studied. Increases in temperature may stimulate the metabolic activity of the target nematode, alter the solubility of the chemical in the aqueous or vapor phases, and alter the rate of microbial or chemical destruction of the nematicide. Because nematicides are often applied at the beginning of a growing season, low soil temperature may be of concern with respect to efficacy in some cases (70). The activity of EDB and 1,3-D against the motility and infectivity of *M. javanica* in fumigation chambers was much less at 5 °C than at 15 °C (12). Similarly, methyl bromide exhibited greater activity against the dagger nematode *Xiphinema index* and *M. incognita* at 30 °C than at 15 °C in soils in sealed cans (71). The enhancement of methyl bromide and 1,3-D activity against *Tylenchulus semipenetrans* by high temperature in controlled-temperature experiments indicated that nematicide efficacy could possibly be improved by soil solarization (72).

Effects of Soil Structure on Activity

The physicochemical composition of soil is a critical factor influencing nematicidal efficacy. Nematicides diffuse more slowly through soils with small pore spaces, fine particle size, and low moisture content (73). A high clay content can result in increased adsorption and poorer movement of nematicide (47,61,74). Nematicide adsorption onto organic matter is strongly correlated with lipophilicity (10); organic matter can reduce efficacy, either by increasing moisture content, by acting as an adsorbent, by providing receptors for alkylating agents, or by increasing microbial populations that are capable of degrading the applied nematicide (75). The movement of contact nematicides away from their application zone is similarly a function of adsorption onto organic matter. Fumigants, ethoprop, and fenamiphos are less effective in soils with large amounts of organic matter, but aldicarb and oxamyl are effective in soils with a wide range of organic matter concentrations (65). Riegel et al. (76) noted that 1,3-D applied to microplots supplemented with yard waste compost was less effective in suppressing *M. incognita* reproduction on tomato than in control microplots. Adsorption onto soil organic matter, although undesirable from the perspective of nematicide efficacy, may be negatively correlated with tendency to contaminate groundwater.

Degradation of Nematicides

Once applied to soils, any pesticide is subject to biological and physicochemical transformations. Transformation products may have less or greater toxicity than the parent compound. An analysis of various values reported in the literature indicated half-lives of parent compounds of 2–190 days, depending on the parent compound and the physicochemical properties of the soil (75). Nordmeyer (10) regarded a 14-day half-life as ideal for a balance between efficacy and environmental safety.

In soils, 1,3-D is first biologically or chemically hydrolyzed to 3-chloroallyl alcohol, which is then oxidized to chloroacrylic acid, which in turn is converted to simple short-chain organic acids (77). Chloroallyl alcohol and chloroacrylic acid also are toxic to humans and are of regulatory concern (78). The primary route of chemical degradation of methyl bromide in soil is through hydrolysis to yield methanol and bromide ions and through methylation. Some bacteria, particularly nitrifying bacteria, are capable of oxidizing methyl bromide to form formaldehyde and inorganic bromide (77).

Aldicarb and fenamiphos are initially degraded in soils into sulfone and sulfoxide derivatives with target and nontarget toxicity and with enhanced mobility correlated with increased solubility in water (73,79). Transformation of fenamiphos sulfoxide into sulfone progresses much more rapidly in subsurface soils than in surface soils (80). Aldicarb and fenamiphos sulfoxides may be the major active materials (73,81). Aldicarb is further degraded into oximes and nitriles. The sulfoxide and sulfone derivatives of fenamiphos and aldicarb are more mobile in soils than are the parent nematicides and have the potential to more readily contaminate groundwater (82). Unlike aldicarb, the carbamate group is hydrolyzed in oxamyl. The degradation of oxamyl into nontoxic oximes at 10 different sites was generally associated with increased pH, temperature, and moisture (83).

Microbial transformation of nematicides is an important factor affecting efficacy. As with other types of pesticides, repeated application of nematicides to agricultural soils can result in enhanced microbial degradation and decreased efficacy (77). For example, decreased efficacies of aldicarb, ethoprop, and oxamyl against potato cyst nematodes following multiple applications were associated with increased transformation of the nematicides (75). When previously treated soils were autoclaved, these effects did not occur. Similar phenomena have been observed in fenamiphos-treated soils; the amount of time required for enhanced degradation to disappear has been reported as being from 1 to 5 or more years, depending on the study (79,84,85). Enhanced biological degradation of 1,3-D or methyl isothiocyanate has been described in a number of soils, and various bacteria capable of mineralizing 1,3-D have been isolated (77,86,87). In at least some of these bacteria, a haloalkane dehalogenase gene carried on a plasmid is involved in enhanced degradation (86,87). One such organism (*Pseudomonas cichorii*) can grow on low concentrations of 1,3-D as its sole carbon and energy source (88).

Enhanced microbial degradation of nematicides is a somewhat unpredictable phenomenon, has not been reported with some nematicides, and is generally unpredictable in occurrence (75,77,89). When accelerated transformation exists, the responsible microorganisms generally transform compounds chemically related to the original nematicide (75). Exceptions occur when the enhanced biodegradation occurs as a result of metabolism of a specific part of the nematicide, such as occurred in a situation when enhanced ethoprop degradation resulted from increased hydrolysis of the P–S bond in the *S*-propyl moiety of ethoprop (90). In this case, two strains of *Pseudomonas putida* capable of rapidly degrading ethoprop were isolated from the soil (91).

Effects on Nontarget Organisms

The nontarget effects of nematicide applications are reviewed in this volume and elsewhere; a detailed evaluation is beyond the scope of this review. Because of their broad-spectrum activities, most nematicides radically alter soil flora and fauna. Fumigant usage may result in the absence of nematode competitors, predators, and parasites in soils (92). The elimination of mycorrhizae by methyl bromide can result in poorer plant growth (55). Long-term aldicarb treatment of potato fields decreased the number of bacterial genera and species, decreased the population levels of plant growth-promoting rhizobacteria, and increased total bacterial biomass compared to untreated soils (93).

Nematicides can greatly alter the subsequent structure of nematode communities in soils; for example, *Pratylenchus* recolonized methyl bromide–treated pasture soil, replacing *Helicotylenchus* as the dominant phytoparasitic nematode (94). Nematodes and other organisms play a complex role in agroecosystems (7); use of broad-spectrum biocides makes it difficult to exploit some of these roles.

Environmental Contamination

One of the greater environmental problems sometimes associated with nematicide usage is groundwater contamination. Indeed, the initial detection of the nematicides DBCP and aldicarb in groundwater in the United States over 20 years ago led to the stimulation of scientific and regulatory interest in pesticide contamination of groundwater that continues to this day (95). Even though DBCP usage was prohibited in 1977, groundwater contamination persists (96). In 1990, the manufacturer of Temik (aldicarb) announced a voluntary halt on its sale for use on potatoes because of concerns about groundwater contamination. The following year, a train wreck released 72,000 L of metam sodium into the Upper Sacramento River and resulted in soil microbial changes that persisted for at least a year (97). When the special review of 1,3-D by the U.S. EPA was terminated, several measures for reducing potential groundwater contamination were instituted, such as prohibition of usage within 100 feet of drinking-water wells, in areas overlying karst geology, and in several states with certain soil types and where groundwater is 50 feet from the soil surface (78).

As previously indicated, 1,3-D use was suspended in California in 1990 for several years because of its detection in air distant from application sites, specifically in a school. This has resulted in the creation of 300-foot–wide buffer zones around residences for fumigation (100 feet wide if fields are drip irrigated). In addition, "township caps" limit the total amount of 1,3-D that can be used in a given area in California (98).

THE FUTURE

Presently, only a few chemical nematicides remain, and some of these will undoubtedly be withdrawn before the end of the decade, if not before the end of this year. The economic cost of research and registration of new chemicals is an enormous hurdle for a new chemical nematicide to overcome. Of the 497 new active ingredients registered for use as pesticides from 1967 to 1997, only seven were registered as nematicides (11). Nonetheless, the decreasing number of compounds and the enormous economic damage caused by phytoparasitic nematodes continues to maintain the interest of private and public sector researchers in pursuing the development of new chemical nematicides. In some countries, demand for nematicides is high. Although the nematicide market in the United States represents a small fraction of total pesticide usage, in The Netherlands, nematicides represent more than 60% of the total pesticides used in agriculture (13).

Future control of nematodes will increasingly rely on site-specific, sustainable management practices, as well as on integrated pest management involving the judicious use of nematicides. Nonchemical strategies available to growers for some nematode-host combinations include crop rotation, altered planting time, resistant germplasm, solarization, fallow, and nematode-suppressive soil amendments. Many of these strategies are less expensive and sometimes less effective than is traditional chemical control.

The development of new nematicides has been reviewed (8,10,99). Prospective compounds can originate from empirical screening or by rational design of compounds that can exploit biological or biochemical weaknesses of nematodes. The underlying biochemistry of plants and nematodes is similar in many respects; successful transfer of a rationally designed compound from laboratory to the field has not yet been achieved, in no small part because of the previously described difficulties in nematicide design.

It is beyond the scope of this review to list every compound described as possessing nematotoxicity. However, the following compounds are worthy of discussion. Biorationals are listed at the conclusion.

Methyl Iodide and Propargyl Bromide

The immediate demand for methyl bromide replacements makes it likely that the next nematicides to be registered could be compounds similar to methyl bromide; for example, methyl iodide and propargyl bromide. The latter has provided experimental control of *M. incognita* on tomato, although the explosiveness of the compound requires that innovative formulations be developed (100). Methyl iodide exhibits greater toxicity to phytoparasitic nematodes than does methyl bromide, perhaps because of greater reactivity or lower volatility than methyl bromide (101), and it is degraded in the atmosphere before it has the opportunity to react with ozone (102). Because it is a liquid at ambient temperature, methyl iodide is easier than methyl bromide to apply safely. Methyl iodide has provided control of *M. incognita* on carrot (102), but it also eliminated *Rhizobium* nodules (101).

DMDP

One compound moving closer to agricultural utilization is 2,5-dihydroxymethyl-3,4-dihydroxypyrrolidine (DMDP), a naturally occurring sugar analog from the tropical legume *Lonchocarpus felipei*, which inhibited hatching of *G. pallida* and movement of *G. rostochiensis* (103). The compound is downwardly mobile in plant phloem; foliar applications on tomato decreased galling induced by *M. incognita*. Use as a nematicide has been patented, and plans are underway to produce this compound from natural sources in tropical America.

Avermectins

The avermectins are often drugs of choice for treatment of human and veterinary nematode infections. These macrocyclic lactones have experimentally provided successful control of nematodes in the field (104,105) but are not registered for use against phytoparasitic nematodes. *Meloidogyne javanica* and *R. similis* on banana were controlled by injections of abamectin into the pseudostem as well as preplant applications of fenamiphos (106). The effects of avermectin have been best documented in the mammalian intestinal parasite *Ascaris* and the free-living nematode *Caenorhabditis elegans*. Avermectin paralyzes somatic musculature in *Ascaris* and pharyngeal musculature in *C. elegans* by irreversibly opening glutamine-gated chloride channels (5,107).

Sodium Azide

Sodium azide is a potent inhibitor of cytochrome oxidase and disrupts the respiratory electron transport chain. It was registered as a nematicide in the United States in 1974, but its nematicidal use was withdrawn. Preplant applications provided successful control of *M. incognita* and *Helicotylenchus dihystera* on potato (108). Interest in this compound is intensifying because of the urgent need for methyl bromide replacements.

Furfural

Like sodium azide, furfural is being investigated as a replacement for methyl bromide. Furfural has provided control of nematodes on pineapple and cotton (109,110).

Phytochemicals

Several researchers are attempting to develop phytochemical-based strategies for nematode control (19). To some extent, this research has its roots in the complex chemical interactions between plants and nematodes. In addition, there has been a vast body of work involving the application of green manures to or within soils. Moreover, because members of the plant kingdom produce a variety of secondary metabolites, many investigators have ventured beyond allelopathic interactions and looked for nematode-antagonistic substances in plant parts unlikely to be involved in nematode-plant interactions, such as leaves, or in algae or fungi. A rich assortment of over 100 different secondary metabolites has been identified as being responsible for plant- or fungal-mediated nematotoxicity (19).

In recent years, various plant-based products have appeared with putative antinematodal activity. Most of these have not been available long enough to permit satisfactory evaluation by agricultural researchers. A few of these products may curtail nematode damage by stimulating plant growth.

Systemic Acquired Resistance Inducers

Systemic acquired resistance (SAR) is a phenomenon in which exposure of plants to one pathogen or elicitor can result in resistance to several diverse kinds of pathogens. A few laboratories are currently investigating the use of SAR inducers such as salicylic acid and benzo-(1,2,3)-thiadiazole-7-carbothioic acid *S*-methyl ester as nematode control agents (111–113).

Hatching Stimulants and Inhibitors

Although not nematicidal, hatching stimulants could be used to induce hatch in the absence of host plants, resulting in the death of host-deprived nematodes. Stimulation of potato cyst nematode hatching by potato root diffusate has been investigated for decades and results from a complex mixture of at least 20 distinct compounds (114). A hatching stimulant for the soybean cyst nematode was isolated from 1058 kg of dried kidney bean roots and identified as a complex triterpenoid derivative named glycinoeclepin A (115). Two simpler analogs stimulated hatch, although at higher concentrations than required than for glycinoeclepin A (116). Two other simpler analogs were also synthesized (117); one inhibited hatch but the other stimulated it.

Transgenic Proteins

As with most other classes of plant pests and pathogens, transgenically based plant resistance is expected by many to provide the basis for future management of phytoparasitic nematodes. Although no transgenic system has resulted in commercial success equivalent to that of insect-resistant plants expressing *Bacillus thuringiensis* toxins, substantial progress is being made. For example, transgenic plants expressing a proteinase inhibitor resulted in a 50% decrease in the reproduction of *M. incognita*, compared to control rice plants (118). Strains of *B. thuringiensis* are known that produce toxins to the free-living nematode *Caenorhabditis elegans* (119).

Behavior-Modifying Compounds

A variety of behaviors are involved in host- and mate-finding by nematodes. The only nematode compound with sex attractant activity is vanillic acid, which is produced by soybean cyst nematode females. Several synthetic analogs did lower cyst production in field and microplot experiments (120). The possibility of using specific compounds to attract nematodes to toxic baits was shown in laboratory experiments with *T. semipenetrans*, and three different nematicides whose activity was increased by the attractant sodium acetate (121). When precise molecular interactions between nematodes and their hosts important to parasitism are discovered, these could be exploited.

Steroids and Hormones

Nematodes possess a nutritional requirement for sterols; dietary sterols are converted to sterols typical of nematodes. Several compounds interfere with the conversion of plant sterols to nematode sterols and disrupt the nematode life cycle (122). The identification of a nematode hormone has not been achieved, a necessary first step to permit their exploitation in a manner similar to that of insect juvenile and molting hormones.

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Mention of trade names or commercial products in this publication is solely for the purpose of providing specific information and does not imply recommendation or endorsement by the U.S. Department of Agriculture.

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NITRATE IN GROUNDWATER

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INTRODUCTION

The nitrate ion is one of the more ubiquitous chemical substances on the planet and is nearly always found in water. Most of the water around us contains nitrate, but the water with which we are concerned here is groundwater, which is water accumulated in the saturated zones of certain rock formations, usually at depth. Most of this water has passed through the soil before it accumulates, so that activities at the soil surface, particularly agriculture, can have a strong influence on the concentrations of nitrate and other agrochemicals in groundwater. Despite its commonplace nature, nitrate has for at least two decades been a source of widespread concern because of its perceived effects on our environment and our health. As a result, the "nitrate problem" has been a major influence on agroecological research in the developed world during this period. Environmental concern has centered mainly on the formation of algal blooms and excessive growth of water plants in surface fresh waters and in the coastal areas of the sea. Worries about our health spring from fears that nitrate in potable water might cause stomach cancer in adults or methemoglobinemia ("blue-baby" syndrome) in infants. Recent medical research, however, suggests not only that nitrate is beneficial to our health but also that we produce it within our bodies. Water supplies are drawn from both ground and surface waters according to their availability. This article is concerned with nitrate in groundwater, which has health, rather than environmental, implications, but environmental issues are not ignored.

NOMENCLATURE

"Nitrate" is the chemical name for the NO_3^- ion, and it is not known by any other. The practice of referring to "nitrates" in natural waters and water supplies is incorrect because, as in all dilute electrolyte solutions, the anions and cations are dissociated from each other. The species with which we are concerned is, therefore, the free nitrate ion, which is unique rather than plural.

Structural Formula

The nitrate ion, NO_3^-, has a symmetrical planar trigonal structure in which the nitrogen atom has a formal positive charge. Two negative charges are shared between the three oxygen atoms in a resonance structure comprising three electronic conformations in which each of the oxygen atoms, in turn, is without charge. The uncharged atom has two electron pairs and is attached to the nitrogen atom by a π-bond, and the charged atoms have three electron pairs.

PHYSICAL PROPERTIES

Solubility

The salts formed by the nitrate ion are generally soluble, and calcium nitrate has such a high affinity for water that it is deliquescent, which means that it will pick up moisture from the air and dissolve in it. The main cations in groundwater are likely to be calcium, magnesium, potassium, sodium, iron, and aluminium, and the salts they form with nitrate are all very soluble (Table 1). Ammonium nitrate is also highly soluble. Calcium is usually the dominant cation in groundwater, and the nitrate concentration at the limit of solubility for calcium nitrate is 32,000 times greater than the U.S. limit for nitrate concentration in potable water and 28,000 times greater than the E.C. limit. Solubility cannot, therefore, limit nitrate concentrations in groundwater.

Sorption

Nitrate, being an anion, is attracted to positively charged surfaces. Nearly all agricultural soils in the developed world are usually maintained at pH values that are not acid enough to permit the development of the positive charges that will retain nitrate. However, there are some soils, particularly highly weathered soils in the Tropics,