**Review Article**

**Biological control of plant-parasitic nematode through Avermectin-A review.**

**Abstract:**

Plant-parasitic nematodes cause damage to plants leading to yield losses. Nematode control in plants relies primarily on chemical nematicides. The use of nematicides has led to concern for environmental and worker safety, residue problem and groundwater contamination. One of the new alternative tools for managing plant parasitic nematode is avermectin group. The avermectins are soil microorganisms belongs to actinobacteria, *Streptomyces avermectinius* (formerly, *S. avermitilis*).The Abamectin compounds are important tools in crop protection and are currently registered for use as a nematicide and insecticide. Abamectin acts on nematode in nerve and muscle cells which finally causing death of nematodes and inhibiting egg hatching. This review provides a comprehensive overview of several studies that shown the efficacy of abamectin as a biocontrol method for combating plant-parasitic nematodes.

***Keywords:*** Plant-parasitic nematodes, Biological control, Avermectin, Liquid formulation, Granular formulation, Efficacy.

**Introduction**

Nematodes are non-segmented invertebrates that are thought to be the most prevalent animals on the Earth (Bardgett and Wim, 2014). Nematodes are free-living, obligate parasite and facultative parasite, based on their feeding habit. Obligate parasites feed on plant, invertebrate as well as vertebrate pests. Plant parasitic nematodes that feed on plant are one of the world’s major agricultural pests, causing in excess of $157 billion in worldwide crop damage annually (Elling, 2013). As these nematode attack crop root systems, they suck the growth nutrients and thereby reducing crop yields. The surviving plants are more vulnerable to secondary infections, drought, and other stresses. Nematodes can damage all parts of their host plants, although according to their life style, individual species target the roots, stems, leaves, flowers, or seeds. The vast majority of PPN damage is caused by sedentary endoparasitic forms, the root-knot (*Meloidogyne* spp.), cyst (*Heterodera* spp*.*), and potato cyst (*Globodera* spp.) nematodes, which impact a wide range of crops. However, relatively few measures like crop rotation, use of resistant varieties exist for controlling PPN infestation despite their large damage potential. Nematode control in plants relies primarily on the use of soil applied chemical nematicides. The use of nematicides for control of nematode has led to concern for environmental and worker safety, residue problem and groundwater contamination. Some of the pesticides have been restricted or eliminated because of environmental concerns. Modern agriculture requires a sustainable nematode management approach where environmental factors are prioritized. Therefore, there is a need to analyze the biological activity of biocontrol agents to fulfill the parameters and its performance as nematicides. Biological control of plant parasitic nematodes has assumed great importance after realizing the drawbacks in exclusive usage of chemicals for nematode management. Exploration and exploitation of novel bioactive molecules of microbial origin open a new vista for finding alternative to synthetic chemicals to manage plant parasitic nematodes and other insect pests. One of the new alternative tools for managing plant parasitic nematode is avermectin group. Avermectins has been used extensively as anti-parasites in veterinary medicine and as pesticides in agriculture and horticulture (Putter et al.,1981;Birtle et al.,1982;Khalil, 2013; Cabrera et al., 2013; Seong et al.,2021).

**Avermectin**

Avermectins are one of new alternatives which proved its activity towards different genera of plant parasitic nematodes. Avermectins were discovered in 1976 by scientists of Kitasato Institute at Merck & Co. Inc. which was obtained from soil samples from Kawana, Ito city, Shizuoka Prefecture, Japan. The avermectins are a family of 16- membered macrocyclic lactones produced by the soil microorganisms belongs to actinobacteria, *Streptomyces avermectinius* (formerly, *S. avermitilis*).The major componentof the fermentation, avermectin B1(Abamectin), is a mixture of B1a(≥80%) and B1b(≤ 20%) (Genilloud, 2017). These compounds are important tools in crop protection, and are currently registered for use as a nematicide and insecticide (Dybas and Green, 1984). Abamectin has been shown to have strong activity against a broad spectrum of nematodes yet is generally regarded as safe for mammals because of its inability to pass the blood-brain barrier(Jansson and Dybas, 1998). The stability of abamectin is moderate in environment. The half-life of abamectin under field conditions was about 31 ± 6 days, while the half-life was ranged between 20 and 47 days in soils with pH 5-9. The photo-degradation occurs in thin films (6 hours) and water (12 hours), while it was 21 hours in soil (Wislocki et al., 1989). Despite its rapid decomposition in various systems, abamectin still provides a relatively long residual activity against target pests in field conditions due to its translaminar activity. Most avermectin degradation products have been reported to pose 1-3 times less toxicity than the parent compound. Avermectins degrade in aquatic and terrestrial environments, and are non-phytotoxic, resulting in reduced accumulation and persistence (Bull et al.,1984). It has shown low toxicity to other beneficial and non-target microorganisms (Lasota and Dybas, 1990).

**Mode of action**

Abamectin acts on nematode through direct protein inhibition by binding to the glutamate receptors in nerve and muscle cells which finally causing death of nematodes (Martin et al., 2002), and inhibiting egg hatching of root knot nematode, *M. incognita* (Radwan et al., 2019).

Avermectins have two action sites that differ in their location and pharmacological properties (Stretton et al., 1987). The compound acts at multiple sites depending on the microorganism, different sensitivities of targeted microbes and solubility (Turner and Schaeffer, 1989). In the first mode of action, there is a correlation between abamectin sensitive loci and the presence of δ-aminobutyric acid’s (GABA) sensitive mechanisms involving chloride permeability exchange. In the second mode of action is blocking the transmittance of electrical activity in nerves and muscle cells, by stimulating the release and binding of δ-amino butyric acid (GABA) at nerve ending. This causes an influx of chloride ions into the cells which lead to hyper polarization and subsequent paralysis of the neuromuscular systems, and then death (Kass et al.1984). In nematodes, GABA receptors are found at the neuromuscular junctions and the central ventral cords.

**Action against plant-parasitic nematodes**

Abamectin proved its ability to manage different genera of plant-parasitic nematodes. The mode of action of the avermectins has been studied on plant parasitic nematodes in terms of their gross effects on the movement and infective behavior of the parasites. It is commercially available as a granular or liquid formulation (Avid) and most recently formulated as a seed coating (Avicta) by Syngenta Crop Protection. Abamectin was applied in many different methods such as soil treatment, seed treatment, injection in to plant stem and seedling root dip.

The nematode response to avermectins is triphasic. Nematodes exposed to avermectins for 10 min are inactivated but can partially recover within 30 min of exposure cessation. After 120 min of exposure to avermectins, irreversible loss of movement is obtained (Wright et al.,1984).

Avermectins also reduced egg hatching (Cayrol et al., 1993) and decreased the oxygen consumption of juvenile nematodes (Nordmeyer and Dickson, 1989).

Avermectin affects movement and behavior of *Meloidogyne* spp. Avermectin possesses the capability to kill infective juveniles and reduce egg hatch­ing (Osman et al.,2020).

A pot study demonstrated that Abamecfin injections of 250 and 500 mug a.i./plant were effective at reducing *M.javanica* and *R.similis* infection in banana plant 28 to 56 days after inoculation (Jansson and Rabatin, 1997).

A greenhouse study investigated the efficacy of foliar spray, root dip and pseudostem injection of avermectins in two different crops on *M.incognita*, *M.javanica*, and *Radopholus similis*. This study showed that foliar application was not effective in controlling *M.incognita*, *M.javanica*, and *R. similis*. However, root dips were somewhat effective against *M.incognita* and *R.similis* to tomato and banana, respectively. The highest nematode control efficacy was obtained by pseudostem injection (125-2000 µg / plant) against *M.javanica* and *R.similis* on babana (Jansson and Rabatin, 1998).

Avermectins were also effective in three melon hybrids at concentrations of 27, 36 and 45 µg/ ha against root-knot nematodes under glasshouse conditions (Moreira and Barbosa, 2002).

A laboratory test showed that after a 2 hours exposure time, the avermectins’s lethal dose (LD50) was 1.56 and 32.9 µg a.i. / ml for *M.incognita* and *R.reniformis*, respectfully. In that study, a greenhouse test revealed that sublethal dosages significantly reduced the infectivity of both nematodes to tomato roots and that avermectin’s performance was comparable with that of aldicarb (Faske and Starr,2006).

Avermectins injected to Scot pines paralysed or killed over 80% of the pine-wood nematode, *Bursaphelenchus xylophilus* population. This effect was observed after 48 hr exposure to abamectin concentrations as low as 0.1 μL a.i./L (100 ppb). (James et al.,2006).

According to Corbett et al. (1984), when *M. incognita* were exposed to 20mM aqueous solution of avermectin B2, a 23-ketone, they initially lost movement within 10min partially recovered within 30 min. and irreversibly lost movement after 120 min.

Drenching of avermectin in concentration ranging from 0.125 to 5 ppm reduced the J2 and root gall index of *M.incognita* in tomato. However, in that study, it is suggested that the avermectins were short-lived and had non-systemic activity. Moreover, when the avermectins were applied in soil, it appeared that strong adsorption to soil particles occurred (Lopez-Perez et al., 2011).

Laboratory tests showed that abamectin exhibited rapid knockdown of *M. incognita*, with LC50 and LC90 values that were superior to those of cadusafos and averaged 7.06 and 21.81 mg L−1.In field trials with avermectins applied at 5,7.5 and 10 l/ha substantial control of root-knot nematodes, increased marketable tomato yield compared with untreated plants (Qiao et al.,2012).

Seed treatment with abamectin provided sufficient *M.incognita* control for 3 weeks in cucurbits and tomato. Tomato seeds coated with abamectin at 0.1 or 0.3 mg a.i. / seed significantly reduced *M.incognita* root galling in a greenhouse pot test (Becker et al.2003).

The highest concentration was particularly effective against *Pratylenchus penetrans*. Cotton treated with 100 g of abamectin /100 kg of seed was sufficient for adequate control of *M.incognita* in greenhouse and microplot tests (Monfort et al., 2006).

Cotton seeds treated with 150µg of abamectin / seed with an insecticide and fungicides provided adequate protection at the tap root length 5 cm but nematode penetration increased as the root developed (Faske and Starr, 2007). This study suggested that abamectin from the seed treatment mainly remains in the seed coat itself and only low amounts on the radial permitting nematode infection.

The abamectin seed treatment effective concentration 80 (EC 80) was 1 and 0.28 mg a.i./seed in maize, cotton against *Pratylenchus zeae* and *M.incognita*, respectively under greenhouse condition (Cabrera et al., 2009). However, the study reported that no EC80 was reached by treating sugarbeets with up to 1 mg a.i./seed against *Heterodera schachtii*, but the EC 50 was 0.026 mg a.i./seed.

Another pot study showed that the maximum EC80 to reduce *M.incognita*, *M.arenaria* and *M.javanica* egg masses in tomato was 0.51 mg a.i./seed. The seed treatment was protecting tomato plants up to 8 weeks (Cabrera et al., 2009).

A pot test and field trials near Tustin, and Riverside, California, demonstrated the potential of granular and liquid formulations of avermectin applied by furrow or drip irrigation in concentration varying from 0.093 to 0.31 kg a.i./ha to reduce root galling of *M.incognita* on tomato (Garabedian and Van Gundy,1983). It was suggested that avermectin’s nematicidal activity is at least 10 times more effective than oxamyl and aldicarb.

Abamectin at 10-20 ppm for 20 min at 18 or 49oC were highly effective in controlling the *Ditylenchus dipsaci*, on garlic seed cloves when compared to the untreated control (Robberts and Matthews,1995).

Abamectin is adsorbed tightly to soil particles which attributed to the immobility of abamectin molecules in the soil (Lopez-Perez et al., 2011; Muzhandu et al., 2014). Therefore, Poly-γ-glutamic acid (γ-PGA) and chitosan (CS) based nanoparticles of avermectins were prepared to control pine wood nematode. The mortality rate of nematodes which were treated with 1 ppm of AVM content of AVM-CS/γ-PGA was 98.6% after 24 h, while one of free AVM was only 69.9% (Liang et al.2018).

Abamectin loaded Red clover necrotic mosaic virus (RCNMV) was prepared to produce a plant virus nanoparticle (PVN) delivery system. PVNAbm enlarged the zone of protection from *Meloidogyne hapla* root knot nematodes in the soil as compared to treating with free Abm molecules. Tomato seedlings treated with PVNAbm had healthier root growth and a reduction in root galling demonstrating the success of this delivery system for the increased efficacy of Abm to control nematode damage in crops (Cao et al.,2015).

*S. avermitilis* MICNEMA2022 demonstrated a suppressive effect against the *M. incognita* infecting tomato plants, as evidenced by the significant reductions in the number of the studied nematode’s reproductive criteria and galls, as well as the average nematode reproduction rate (Radwan et al.,2024).

**Drawback**

One basic problem that compromises Abamectin efficacy is its insolubility in water and its lipophilic nature; hence, a high tendency to bind to organic contents in soil and poor distribution throughout the soil. These traits create a very limited zone of protection around the developing root system. It has been reported that a large portion of the Abamectin dose remains with the seed coat, leaving the seedling radicle unprotected after germination. Abamectin in liquid formulations also demonstrated minimal uptake by the root system with resultant poor efficacy. Another drawback of Abamectin as a PPN nematicide is its lack of persistence over time because of its rapid degradation by photo-oxidation. As a result, although PPN damage reduction is reported by using Abamectin formulations, it is generally minor (±50%) and only marginally economic for lower value crops. The residue of avermectins is rapidly decomposed under sunlight, They are rapidly photodegraded in water with a half-life (t½) of approximately 0.5 days or less in summer. However, emamectin has improved thermal stability, greater water solubility (Cheng et al. 2015). The half-life of emamectin benzoate may reach 7 days in water, but may reduce to one day if the water contained a natural photosensitizer such as humic acid. The half-life of abamectin on water surface was only 4 to 6h (Zhu et al.2011). The residues of abamectin are very low in treated plants because of it is highly degraded readily by soil microorganisms. Moreover, the most avermectin degradation products have been reported to pose 1-3 times less toxicity than the parent compound. The temperature coefficient of abamectinis positive which mean that the toxicity increased with the increment of temperature till 37 °C.

**Conclusion**

Avermectins are valuable compounds which were first isolated from soil.Abamectin concerned biodegradation that often limits their bioaccumulation and translocation in the environment and minimized their exposure to non-target organisms or location. Numerous studies have shown the efficacy of abamectin as a biocontrol method for combating plant-parasitic nematodes. Further research is required to investigate the mechanistic aspects of nematode management with different formulations of abamectin.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that they have no known competing financial interests OR non-financial interests OR personal relationships that could have appeared to influence the work reported in this paper.

**DISCLAIMER (ARTIFICIAL INTELLIGENCE)**

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

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