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# Juvenoids and Its Application in Crop Management

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**Abstract**

Pest management is one of the major growing concerns worldwide. Moreover, these insects are important for natural ecosystem as they perform various functions such as organic matter decomposition and facilitating food for birds, fishes, and reptiles. Juvenoids, the chemical compound which mimics the juvenile hormones and inhibits the metamorphosis process, have gained significant attention among researchers. From the past few decades, intensive research has been done on biochemical and physiological effects of juvenile hormones and their chemical analogs in which they regulate reproduction and metamorphosis of pests. Juvenile hormones are the derivatives of fatty acid which are produced by neurosecretory cells. These juvenoid hormones conserve natural fauna and flora and minimize the chemical pesticide usage. Currently, numerous artificial juvenoids are commercially available and more effective than traditional juvenoids. These artificial juvenoids possess less toxicity and show no teratogenic or mutagenic effects. The juvenoids have inhibition effect on insect morphogenesis as individual specific cells may show an inflexible response and only few cells show

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sensitivity to juvenoids at a particular time. This makes juvenoid usage advantageous over traditional insecticides and a valuable chemical in crop management. In this chapter, we have discussed its various classes, chemistry, mode of action, and application in crop management systems.

**Keywords**
Juvenoids · Analogues · Mode of action · Pest management

## 7.1 Introduction

Insects are one of the most primitive and diverse and living animals on this earth. These insects are found in all habitats like deserts, forest, swamps, and harsh environment except open oceans (Daglish et al. 2018). Undoubtedly, insects are a highly adaptable form of life as there are about five million species of insects, which is very high in comparison to animals. Nearly about 60–70% of stored crops are damaged by pests every year. Pest management is one of the growing concerns worldwide (Clapham et al. 2016). Moreover, these insects are important for natural ecosystem as they perform various functions like organic matter decomposition and facilitate food for birds, fishes, and reptiles. In contrary to that, they also act as herbivores, hosts, parasites, predators, preys, pollinators and saprophages, which shows the ecological importance of these insects in the environment (Losey and Vaughan 2006). Most of the various insect species show negative effect on both the environment and humans. Thus, due to detrimental effect of the insects on the environment, agricultural researchers have started exploring the compatible, eco-friendly, and safer alternative to regulate the growth of these pests (Kenis et al. 2009). Regrettably, various insect species also show negative effect on both the environment and humans (Deroy et al. 2015). Juvenoids, the chemical compound which mimics the juvenile hormones and inhibits the metamorphosis process, have gained significant attention among researchers. Juvenile hormones are the derivatives of fatty acid which are produced by neurosecretory cells. These hormones have methyl ester of epoxy farnesoic acid and have a terpenoid-related structure. This hormone exists in different forms, out of which JH III is the most common and present in species of lepidoptera (Sláma 2014). Some commonly synthesized juvenoids are represented in Fig. 7.1 and natural in Fig. 7.2.

The JH hormones were discovered undoubtedly from ingenious and thoughtful experiments, and the first study was reported by Williams in 1956 in which he synthesized the lipid extracts having juvenoid hormones from the abdomen of *Cecropia moths* and suggested that these extracts could be used as insecticides being nontoxic in nature (Dhadialla et al. 1998). Further experimental findings concluded that these extracts of juvenoid hormones are also present in other invertebrates, plants, and microorganisms (Takatsuka et al. 2017). In the late 1950s, scientists started synthesizing terpenoids and other related compounds to estimate their JH activity (Cherney and Baran 2011). Efforts of Maag Agrochemicals, HLR Sciences, Inc., and Dr.

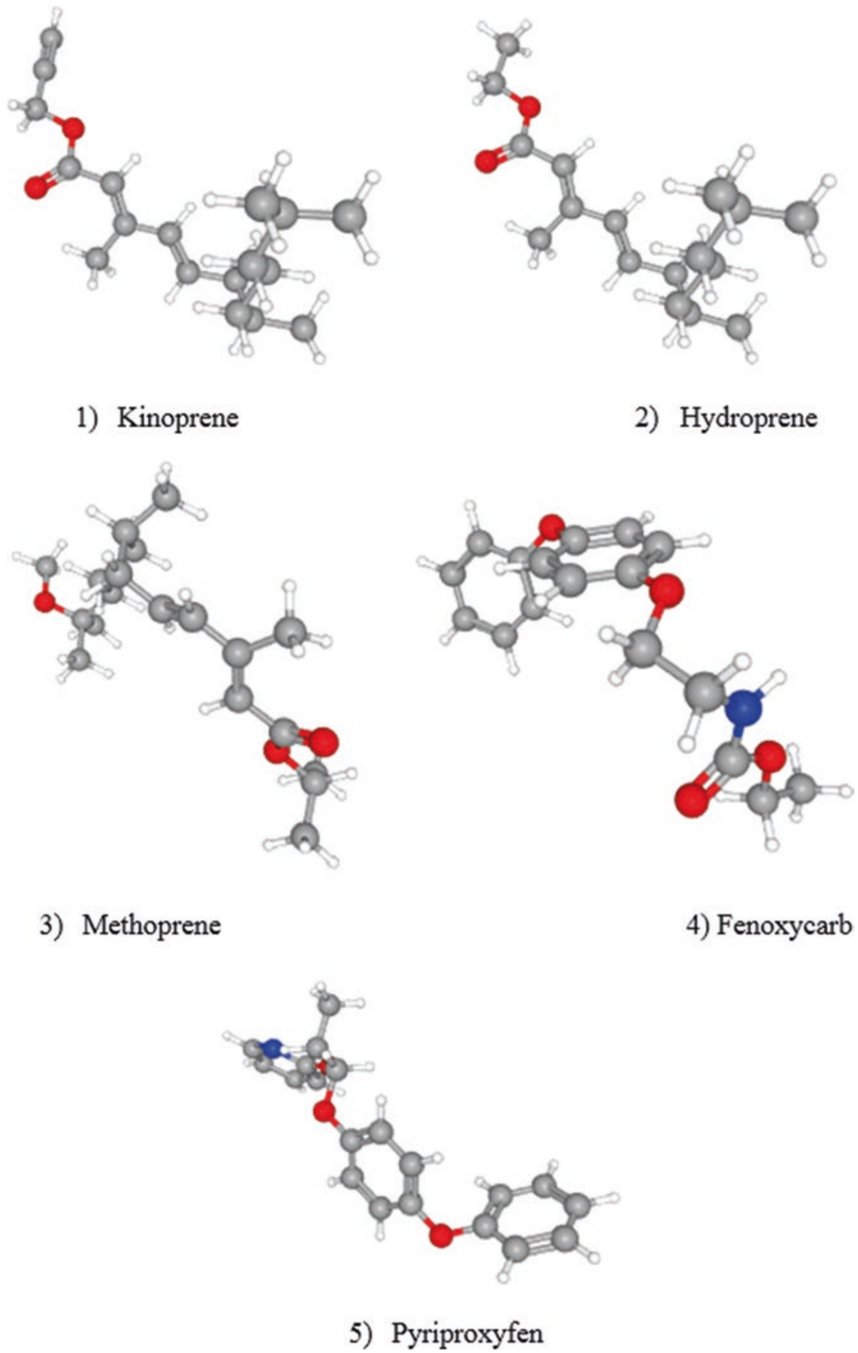


**Fig. 7.1** 3D conformer of few synthesized juvenoids

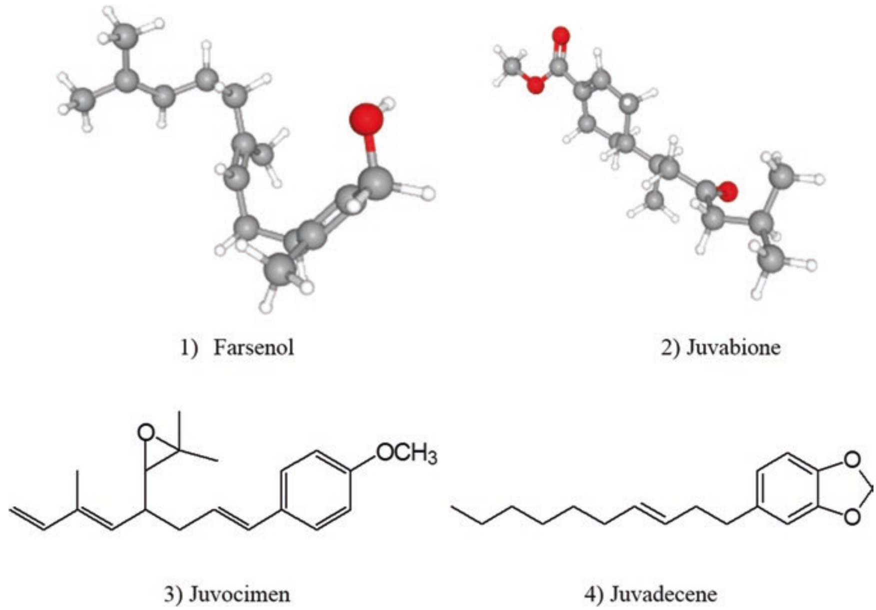


**Fig. 7.2** 2D and 3D conformer of few natural juvenoids

Maag Ltd., Dielsdorf (Switzerland) developed and discovered non-isoprenoid juvenoid which is found to be highly effective, which was further registered for insect control (Mian 2014). The most effective molecule in non-isoprenoid series was ethyl [2-(p-phenoxyphenoxy)ethyl]carbamate (fenoxycarb), which is used to control ants, moths, cockroaches, scale insects, and moths and insects attacking fruit, cotton, olives, etc. (Ramaseshadri et al. 2012). However, though ethyl [2-(p-phenoxyphenoxy)ethyl]carbamate has a carbamate moiety, it has no effect on cholinesterase activity. These juvenoids hormones conserve natural fauna and flora and minimize the chemical pesticide usage (Goncu and Parlak 2012). In this chapter, we will discuss the various classes of juvenoids, chemistry, mode of action, and their application in crop management systems.

## 7.2 Classes and Type of Juvenoids

Depending upon the mode of action, juvenile hormones are of four types: JH 0, JH I, JH II, and JH III. Out of these JH III is the most widely accepted and in use (Noriega 2014). Juvenoid hormones are isolated from various other sources such as dehydro-juvabione and juvabione from *Abies pseudotsuga*; farnesyl-methyl ether from insect excreta, yeast, and plants; sesame from the sesame oil; echinolone from *Echinacea angustifolia*; and juvocimen from *Ocimum basilicium* (Němec 1993). Exogenous use of juvenoid compounds can disrupt and retard the insect growth in various ways (Lee et al. 2015). Juvenoid hormones are sesquiterpenoid compounds which regulate metamorphosis and growth of insects when interacted with ecdysteroids. Juvenoids have well-defined molecular size and certain structural features (Qu et al. 2015). They also have certain properties like lipophilicity, low polarity, less or more pronounced volatility, etc. The common action of juvenoids is inhibition of metamorphosis by preventing adult and pupal emergence (Wheeler and Nijhout 1982). More than 4000 man-made juvenoid analogs have been discovered so far. Juvenoids cause malformation, prolongation of larval stage, disturbance in organ formation, gametogenesis, etc. (Srivastava and Srivastava 1983). Various commercially available juvenoids are well represented in Table 7.1.

**Table 7.1** List of commercially available juvenoids (Wheeler and Nijhout 1982)

| Juvenoids | Dosage | Active substance | Application |
|---|---|---|---|
| Altosid | 280 g/ha or more | Methoprene | Regulate the growth of horn fly and mosquitoes |
| Apex | 1 g/$m^3$ | Methoprene | Regulate the growth of sciarid flies during mushroom culturing |
| Diacon | 1.12 g a.i./100kg (spray) | Methoprene | Regulates the growth of pest affecting the stored products like peanuts |
| Dianex | 0.0207 g a.i./$m^3$ (aerosol) | Methoprene | Regulates the growth of pest affecting the stored products like peanuts |
| Enstar 5E | 0.5% or 0.1 g /$m^2$ (spray) | Kinoprene | Regulates the growth of homopterans in greenhouse |
| Gencor | 0.03 g a.i./$m^2$ | Hydroprene | Regulates the growth of cockroaches |
| Gencor Plus | 0.03 g a.i./$m^2$ | Hydroprene (0.6%) + permethrin (0.25%) | Regulates the growth of cockroaches |
| Kabat | 100 ppm a.i. (spray) | Methoprene | Regulates the growth of *Ephestia elutella* and *Lasioderma serricorne* |
| Manta | 2.5 ppm a.i. (spray) | Methoprene | Enhances the production of silk |
| Precor | – | Methoprene | Regulates the growth of fleas |
| Raid Flea Killer II Plus | – | Methoprene + pyrethroid | Regulates the growth of fleas |
| Ro 13–5223 | 250 g/ha per 2–3 applications; 4–110 ppm; 0.03–0.1 ppm and 5–10 mg/colony | Fenoxycarb | Regulates the growth of fire ants, Homoptera, mosquitos, and Tortricidae |
| S-71639 | 100 g/ha | Pyriproxyfen | Regulates the growth of mosquitos |

## 7.3 Methods of Juvenoid Application

### 7.3.1 Direct Application

Considering the chemical nature of the juvenoids (i.e., lipophilic), they can be dissolved in wax, acetone, or oil. Then, this can be either directly applied on the surface of insects or injected in the body cavity (Baker et al. 1986). Since a large number of insects have smaller size, both processes require precision to transferring 0.1–1.0 μl solution of juvenoids with <5% (standard error). These approaches are usually used in in vitro analysis for assessing the juvenoid activity on the insects (Žďárek and Denlinger 1975).

### 7.3.2 Indirect Application

This approach is designed in such a way to check out the responses of growing insects at given dose of juvenoids. While applying juvenoids using indirect method, special equipment is used for spraying juvenoid solution per square unit area (Kamya et al. 2017). This method includes dipping and spraying of plants in solution of juvenoids, etc. To increase the stability of juvenoids, they are linked to certain substrates (sugar, fatty acids). The resultant compounds are called juvenogens which when enter the target body, are broken down by enzymes, releasing the juvenoid hormones and triggering its action (Walker 1976).

### 7.3.3 Pest Management by Juvenoids

Various reports have documented the potent role of juvenoids in pest management of lepidopterous pests of forestry and field crops. From the past few decades, intensive research has been done on biochemical and physiological effects of juvenile hormones and their chemical analogs in which they regulate reproduction and metamorphosis of pests (Deb and Chakravorty 1981).

Juvenoid hormones are divided into two main groups: first one is the phenoxy juvenoids like pyriproxyfen and fenoxycarb, and the second one is terpenoid compounds which include kinoprene, hydroprene, and methoprene (Palma et al. 1993). All these hormones are highly effective against the homopteran and dipteran insects but ineffective against lepidopteran pests (Horowitz and Ishaaya 2004). Terpenoid juvenoid hormones such as kinoprene and methoprene have been used against mealybugs, scales, and mosquito larvae. Phenoxy juvenoid hormones cause ovicidal action, infertility, and morphogenic effects (Boina et al. 2010). Fenoxycarb, the first commercially registered juvenoid, is used against sucking insects, fleas, fire ants, apple wooly aphid, etc. Pyriproxyfen offers to be effective against whiteflies, psyllids, and aphids which cause damage to crops (El-Kareim et al. 1988).

All the three juvenile hormones are found in most of the insects; JH I and JH II are the two hormones which regulate metamorphosis, whereas JH III plays gonadotropic role. In adults, juvenile hormones act to induce ovarian development, spermatogenesis, accessory gland, and vitellinogenesis development in males. Insects which produce cyclic batches are more affected by action of juvenile hormones (Hartfelder 2000).

Juvenile hormones also play an important role in color polymorphism, caste and phase determination, pigmentation, diapause, pheromone production, etc. They are also reported to influence good range of physiological process both on mature and developing insects (Riddiford 2012).

Juvenile hormones and their chemically synthesized structures have various effects when sprayed on insects during their developmental stage. Applications of juvenoids result in disruption or developmental retardation and inhibition of function or formation of reproductive system (Elvira et al. 2010). Figure 7.3 describe the effects of juvenoid hormones on pests.

Juvenile hormones are also involved in the regulation or programming of post-embryonic development. Lower doses of juvenile hormones result in successful pupation leading to deformities in pupal adult intermediates (Daimon et al. 2012). Most of the insects are highly sensitive to juvenoids during early pupal and final larval stages. Morphogenetic effects are also seen in penultimate larval instar in hemipteran groups which are found to be sensitive (Truman and Riddiford 2019). Juvenoid biosynthesis hormones are controlled by various neuronal and neuroendocrine in species and complex stage-specific ways. Juvenoid hormones show action via two receptors, that is, nuclear and membrane receptors. SRC and Met, two bHLH PAS transcription factors which form nuclear receptor, interact with juvenoid hormone response element in the promoter of Kruppel homolog 1 and trypsin that activate the transcription of these genes (Miyakawa et al. 2014; Li et al. 2019).

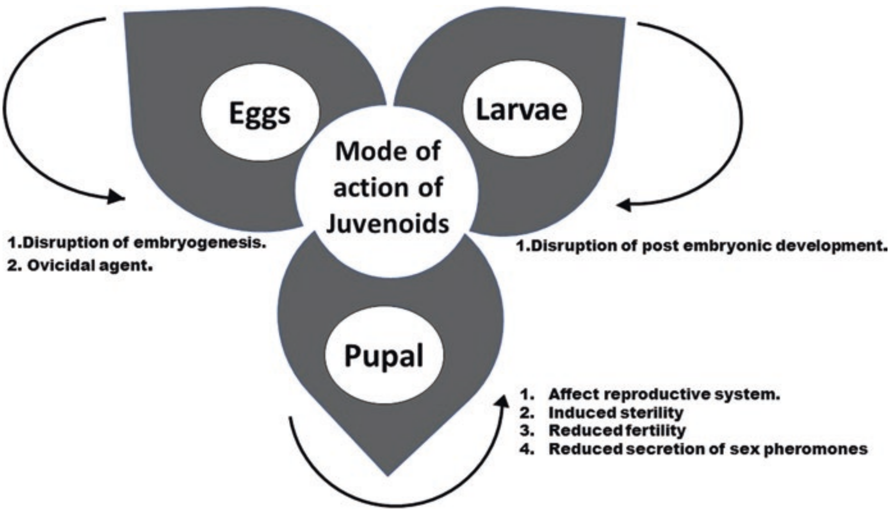


**Fig. 7.3** Mode of action of juvenoids against pests

Mostly juvenoid hormones are reported to affect all the three stages of insect life which include eggs, larval, and adults or pupal. In eggs, usually disruption in embryonic stages of developments was reported along with the ovicidal effects (Oouchi 2005). Juvenile hormones also have a negative effect on disruption of the embryogenesis process which results in ovicidal effects. Juvenoid treatment also leads to disruption of the female reproductive system (Eliahu et al. 2007). Excess of juvenoids on female insects has direct impact on fertility and their physiological processes. Prolonged treatment of juvenoids causes diapause or hemolymph in larvae of insects. However, in adult female of silkworms, juvenoids change the voltinism of larval offsprings. Juvenoids also disrupt the reproduction, general physiology, behavior, and development of treated insects (Mojaver and Bandani 2010).

In larval stages, juvenoid hormones lead to formation with adult features which finally lead to death. Sometimes, it disrupts postembryonic development of larvae. In adults or pupal of insects, the juvenile hormones act to disrupt the diapause. They also reported to affect the reproduction system, induce sterility, affect color polymorphism, reduce fertility, etc. (Ishimaru et al. 2016). Various authors have also reported the applications of juvenoids as pest managements against large number of lepidopterous pests of forestry and field crops. Juvenile hormones are also used to control manure-breeding and water-breeding flies (Singh and Kumar 2015).

Juvenoids were also reported to act on *Lepidopterous* and *Coleopterous* species. Juvenile hormones are also reported to kill the pest in store products. The effect of juvenoid hormones on three pest species *Callosobruchus chinensis*, *Stegobium paniceum* (drugstore beetle), and *Tribolium castaneum* (rust-red flour beetle) were also studied by Thomas and Bhatnagar in which juvenoid hormones have morphogenetic effects at very low doses (Thomas and Bhatnagar-Thomas 1968). These effects include reduction of ovipositions in species of *S. paniceum* and *C. chinensis.* Juvenoid hormones also prevent imaginal differentiation in the *Tenebrio molitor* species of yellow mealworm (Ochoa-Sanabria et al. 2019).

Juvenoid hormones were also reported to enhance the production of silk. When JH I and JH II were injected into the larvae of silkworm, sudden increase in size of larvae was observed with increased spun cocoons (Tan et al. 2005).

When silkworm females are treated with methylenedioxyphenyl-substituted juvenoids, increase in egg size and production was observed. The synthetic juvenoid methoprene is the first commercially registered juvenoid used in Japan to increase the yield and production of silkworm. This example makes juvenoid specials to increase the yield of insects rather than to minimize the damage caused from their overproductivity (Nair et al. 2012).

Recent advancement in the field of biochemistry led to increase the stability of juvenoid hormones both in the insect species and adverse environmental conditions. For this purpose, uses of catabolic enzymes are used to improve the hormone's stability. Usually, endogenous enzymes are used to release hormones from long chains of fatty acid esters which acts as pro-juvenoids (Hui et al. 2010).

## 7.4 Factors Influencing the Uses of Juvenoids

Various factors are responsible for influencing the use of juvenoid hormones. It includes choice of target species, resistance, synergism, metabolism, and some biological factors. Biological factors mean the developmental stage of an organism influences the sensitivity of pests when treated with juvenoids (Jindra and Bittova 2019). Timing of application is also a crucial factor which limits the stability of juvenile hormones when used against various pest species. Several other factors such as identification of pests and techniques for spraying the hormones against the pests also play an important role in influencing the effectivity of juvenoid hormones (Ishmuratov et al. 2015). These things should be carefully planned in order to get the desired effect on population of pests which are highly susceptible to both reproductive and morphogenetic effects. Selective management of pest populations also influences the applications of juvenile hormones (Fathpour et al. 2007).

The half-life of most of the juvenile hormones especially JH I is less than 1 h which makes them highly unstable. These juvenoids are highly sensitive to UV radiation and undergo degradation when poured in aqueous media. Juvenoid hormones are usually metabolized in two simple pathways using enzymes JH-esterase and JH-epoxide hydrase in which they form 10-diol derivative, 11-diol derivatives, and 1 molecule of acid derivatives (Bassal et al. 2018).

Sometimes, juvenoid hormones are also reported to bind with certain proteins termed as carrier proteins which protect juvenoid hormones from being metabolized by nonspecific enzymes. These carrier proteins also facilitate the movement of molecules of lipophilic juvenoid hormones to deliver the product into the site of action in stable conditions (Tanaka et al. 2019).

## 7.5 Future Prospects

The juvenile hormones (JH) of insects are involved in various physiological processes like development, morphogenesis, and reproduction in insect pests. Hence, molecules interact with JH or mimic as JH, which either inhibit the biosynthesis of JH or interfere in their catabolism process (Noriega et al. 2006). Since our knowledge related to JH is now significantly expanding, there are chances that some new more target-specific juvenoids will come into existence. The chemical effect in inhibiting the JH biosynthesis can act as persuasive insecticide (El-Ibrashy 1987). Arylpyridyl-thiosemicarbazones and 1,5-dissubtitutedimidazoles are the juvenoid compounds which have been discovered, and they exhibit inhibitory action during JH biosynthesis (Nëmec 1993). Therefore, intense insight about these juvenoids and their action mechanism at gene level as endocrinological level will pave the advance way to develop novel strategies to hinder the life cycle of insect pests. Later, when we will be able to clone the DNA stretches which encode for the receptors that are involved in JH biosynthesis process, they can be used for in vitro assay for JH as it will alleviate the juvenoid exploration process (Ahmad et al. 2018).

## 7.6 Conclusion

In this chapter, we have attempted to compile data on the applications of juvenoids in pest control system. The uniqueness of juvenoid hormones has offered various advancements in the development of effective pesticides which are not having negative effect on animals, plants, and animals. The juvenoids hold the potential by serving as analogs of insect hormones to regulate the insect pests. These juvenoids are analogs of true juvenile hormones, as they have similar distribution of polar functional groups and molecular size as that of juvenile hormones and nowadays are practically used in agricultural fields. Currently, thousands of artificial juvenoids are commercially available and more effective than traditional juvenoids. Moreover, these artificial juvenoids have less toxicity and no teratogenic or mutagenic effect. Primarily, these juvenoids have inhibition effect on insect morphogenesis as individual specific cells may show an inflexible response and only few cells show sensitivity to juvenoids at a particular time. Hence, these advantages of juvenoids over traditional insecticides make it a valuable approach in crop management.

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