Review article

Methoprene and control of stored-product insects

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ABSTRACT

Estimated direct and indirect losses of grains and grain-based products caused by stored-product insects range from about 10% in temperate regions to almost 50% in humid tropical areas. Pest management strategies in bulk grains include the use of fumigants such as phosphine and sulfuryl fluoride, and grain protectants, which are sprayed directly on commodities as they are loaded into storage. Fumigants, aerosols, and contact sprays are also used as structural treatments in mills, processing plants, and food warehouses. Some older organophosphate protectants and contact sprays have been phased out worldwide and have been replaced by safer insecticides, including pyrethroids and insect growth regulators (IGRs). These IGRs include juvenile hormone analogues (JHAs), ecdysteroids and chitin synthesis inhibitors, and are considered safe due to their insect specificity. Methoprene is the JHA that has been used most extensively in stored-product pest management. The formulations of methoprene originally introduced into the stored-product market in the 1980s contained the racemic mixture with both R- and S- forms, but now only the purified S-methoprene isomer is used. Methoprene has received broad attention and has been tested over decades for its direct lethal effects, but many recent studies focus more on sub-lethal effects. Although methoprene has been used for more than four decades, there has not been a recent and comprehensive synopsis or review of this IGR on stored-product insects. This review addresses the history and present use of methoprene with special emphasis on stored-product protection.

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Contents

1. Stored-product insects

Stored-product insects can be found at many places along the

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post-harvest distribution channel, including warehouses, flour mills, processing plants and stores (Hagstrum and Subramanyam, 2006). These insects damage grains and processed products in a multiplicity of ways: weight loss; nutrient loss: reduced seed viability; contamination with live/dead insects; exuviae or feces; development of hot spots or webbing; and can cause health risks to consumers such as pathogenic microbial infections (Hill, 1990) and allergenic reactions (Larson et al., 2008a,b). These quantitative and qualitative impacts by insects can inevitably lead to reduced market value of stored food products and economic loss (Hagstrum and Subramanyam, 2006). Popular control measures for stored-product insects include the use of contact insecticides such as the pyrethroids cyfluthrin and deltamethrin (Ghimire et al., 2016), application of diatomaceous earth (Golob, 1997; Korunic, 1998, 2013; Dowdy, 1999; Subramanyam and Roesli, 2000), and fumigation with phosphine (Ridley et al., 2011) or sulfuryl fluoride (Reichmuth et al., 2003; Fields, 2012). The use of low temperature (Fields, 1992; Adler, 2010; Arthur et al., 2015; Flinn et al., 2015) and high temperature (Arthur, 2006; Beckett et al., 2007; Subramanyam et al., 2011; Yu et al., 2011) have also been investigated as control strategies. Synthetic neurotoxic insecticides, however, have their limitations, such as the potential presence of chemical residues in food, resistance development by pest species, health risks (Arthur, 1996), escalation of the management costs (Hagstrum and Subramanyam, 2006) and toxicity to non-target organisms (Fields, 1992; Hagstrum and Subramanyam, 2006). To resolve these issues, alternative and safer methods are needed to manage stored-product insects. Insect growth regulators (IGRs) are compounds that could offer many benefits as alternatives to conventional neurotoxins (Mondal and Parween, 2000).

2. Insect growth regulators

The term "insect growth regulators" (IGRs) was first introduced to describe insecticides based on insect juvenile hormone (JH) (Williams, 1967), but the term has since been expanded to refer to other insect hormones or analogues (Oberlander and Silhacek, 2000) that are selective to insects (Mondal and Parween, 2000). IGRs interfere mainly with three physiological processes: growth and development of immature insects; induction of metamorphosis; or chitin synthesis in the integument (Oberlander and Silhacek, 2000). IGRs responsible for the above three modes of action are designated as juvenile hormone agonists, ecdysteroid agonists and chitin synthesis inhibitors, respectively (Oberlander et al., 1997).

JH is secreted from the corpora allata, a pair of endocrine glands situated in the head of insects (Smith, 1985; Riddiford, 1994). Analogues of JH have been developed, and unlike their natural counterpart JH, these compounds resist degradation by enzymes in the insect body (Riddiford, 1994). Methoprene was the first juvenile hormone analogue (JHA) to be synthesized, and is the JHA closest in structure to the natural JH. Later, hydroprene (Henrick et al., 1973), fenoxycarb and pyriproxyfen were synthesized and developed for use as insecticides (Oberlander and Silhacek, 2000). Methoprene and hydroprene are aliphatic compounds (Fig. 1) that have similar properties such as chemical stability and resistance to degradation within the insect body. Methoprene demonstrates the same effects as the natural juvenile hormone in the endoparasitoid *Apanteles congregatus* (Say) (Hymenoptera: Braconidae) (Beckage and Riddiford, 1982) and male cat flea *Ctenocephalides felis* (Bouché) (Siphonaptera: Pulicidae) (Dean and Meola, 1997) or JH III in *Drosophila melanogaster* (Meigen) (Diptera: Drosophilidae) (Wilson, 2004). In contrast, methoprene is more toxic than JH I to pharate adults and larvae of the parasitoid *Nasonia vitripennis* Ashmead (Hymenoptera: Pteromalidae) (De Loof et al., 1979).
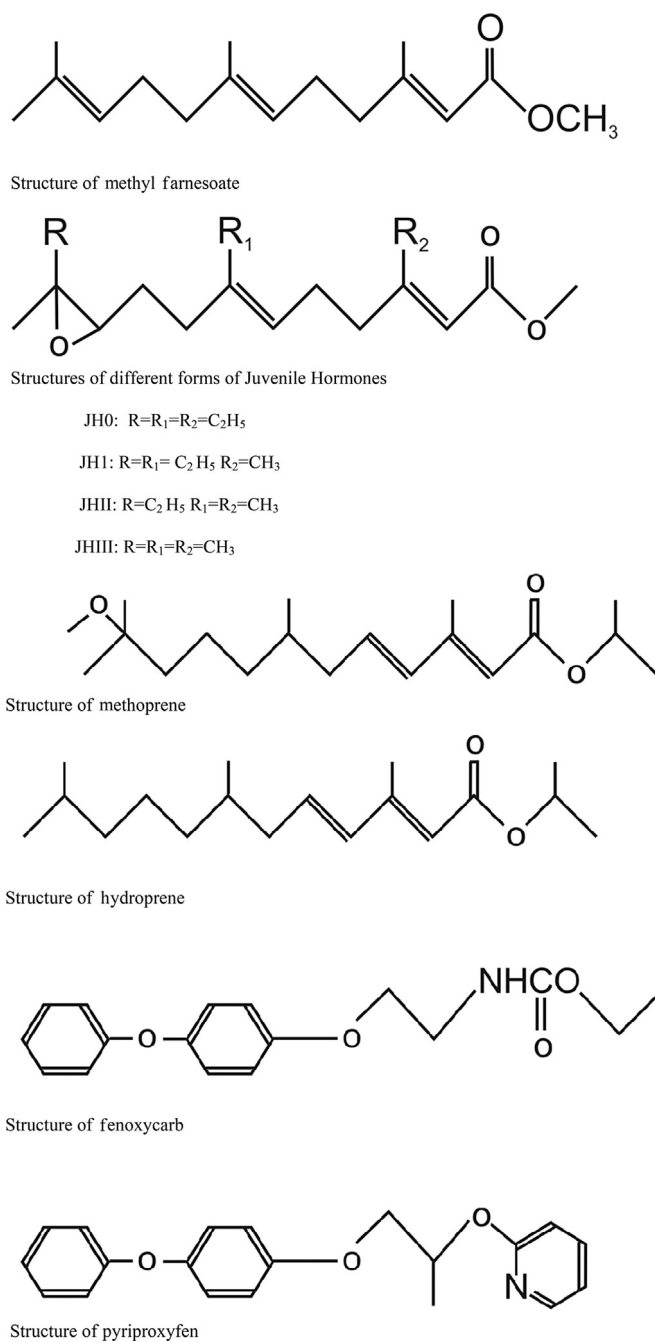

Structure of methyl farnesoate

Structures of different forms of Juvenile Hormones

JH0: R=R1=R2=C2H5

JH1: R=R1= C2 H5 R2=CH3

JHII: R=C2H5 R1=R2=CH3

JHIII: R=R1=R2=CH3

Structure of methoprene

Structure of hydroprene

Structure of fenoxycarb

Structure of pyriproxyfen

Fig. 1. Structure of JH analogues.

Fenoxycarb and pyriproxyfen are aromatic compounds (Fig. 1) (Riddiford, 1994). The structures of various JHAs have been identified: methoprene is isopropyl 11- methoxy (2E, 4E) 3,7,11 trimethyl 2-, 4- dodecadienoate (Wilson and Turner, 1992), hydroprene is ethyl (2E- 4E)-3,7,11 trimethyl-2,4-dodecadienoate (Gupta and Mkhize, 1982), fenoxycarb is ethyl [2-(phenoxy-phenoxy) ethyl] carbamate (Thind and Edwards, 1986) and pyriproxyfen is 4-phenoxyphenyl (R,S)-2-(2-pyridyloxy) propyl ether (Hatakoshi, 1992) or 2-[1-methyl-2-(4-phenoxyphenoxy) ethoxy] pyridine (Ishaaya et al., 1994). Fenoxycarb and pyriproxyfen differ widely from the structure of JH, but still show inhibitory effects on metamorphosis in immature insects similar to those produced by JH (White et al., 1987; Arthur and Phillips, 2009). Toxicity of IGRs varies with the individual IGR, the insect species, and/or specific