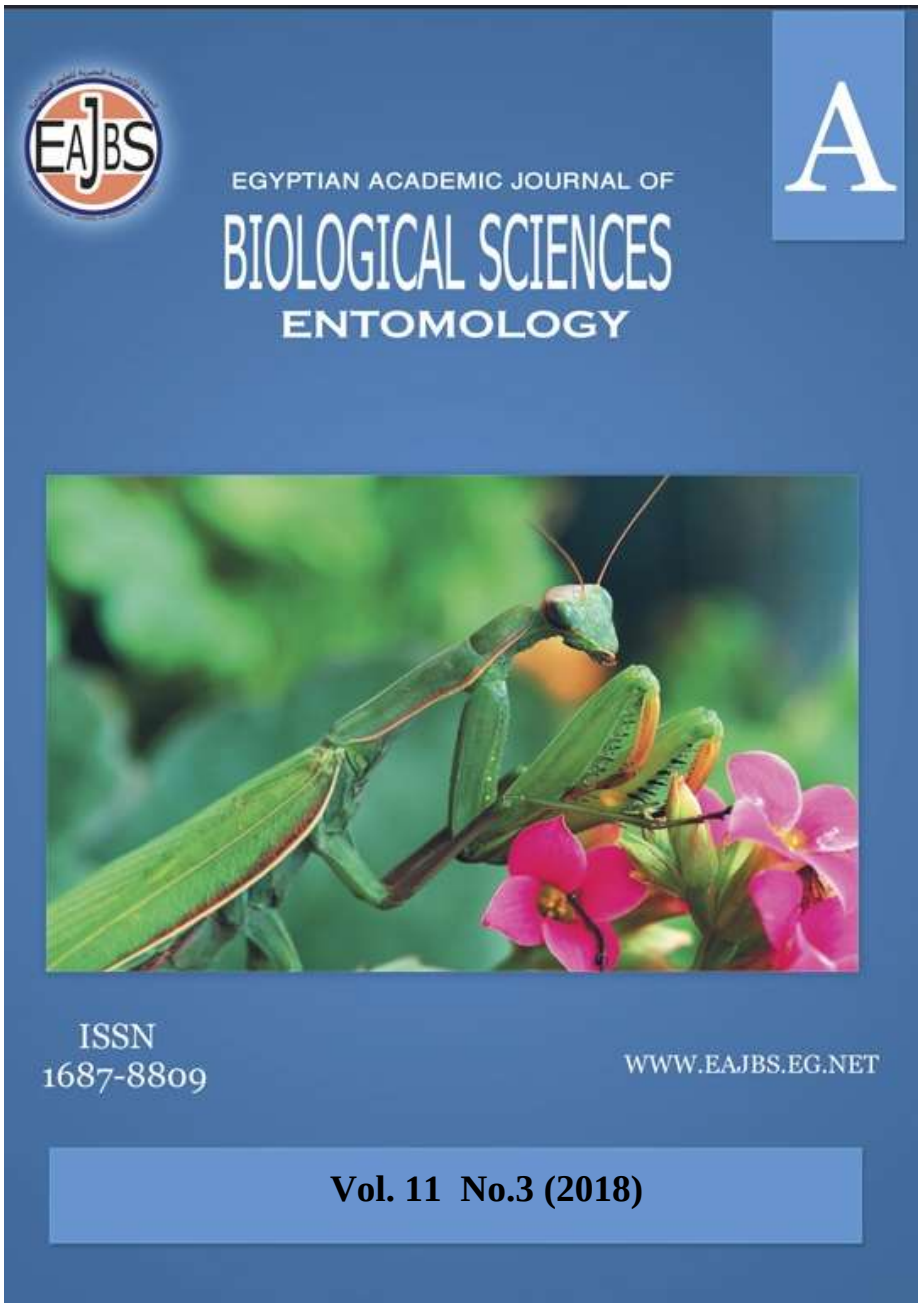

Egyptian Academic Journal of Biological Sciences is the official English language journal of the Egyptian Society for Biological Sciences, Department of Entomology, Faculty of Sciences Ain Shams University.

Entomology Journal publishes original research papers and reviews from any entomological discipline or from directly allied fields in ecology, behavioral biology, physiology, biochemistry, development, genetics, systematics, morphology, evolution, control of insects, arachnids, and general entomology.

www.eajbs.eg.net

Egypt. Acad. J. Biolog. Sci., 11(3): 45-138 (2018)

Egyptian Academic Journal of Biological Sciences
A.Entomology

ISSN 1687- 8809
www.eajbs.eg.net

Physiological Activities of Anti-Juvenile Hormone Agents Against Insects and Their Role For Devising Fourth Generation Insecticides: A Comprehensive Review

Karem Ghoneim[*1] and Reda F. Bakr [2, 3]
1-Department of Zoology and Entomology, Faculty of Science, Al-Azhar University, Cairo, Egypt.
2-Department of Entomology, Faculty of Science, Ain Shams University, Cairo, Egypt.
3-Biology Dept- Faculty of Sciences –University of Bisha- Bisha- KSA
E.Mail : karemghoneim@gmail.com

REVIEW INFO
Review History
Received:20/5/2018
Accepted:21/6/2018

***Keywords*:**
AAntifeedant, behavior, development, diapause, metabolism, metamorphosis, polyphenism, reproduction, sericulture, toxicity.
.

ABSTRACT

To overcome those problems caused by repeated and indiscriminate uses of conventional insecticides, it is necessary to seek environmentally safe and low-cost alternatives for pest control. Among the effective alternatives are anti-JH compounds. The present article was prepared aiming to present an updated overview of different categories of compounds possessing anti-JH activity and their effects on survival, growth, development, metamorphosis, and reproduction of several insects of different orders. This article focused, also, on the effects of these compounds of other physiological processes in insects, such as polyphenism, behavior, diapause, metabolism, enzymatic activities, chemoreceptors and pheromone production, as well as their antifeedant effects against some insect pests. Compounds with anti-JH activity are considered as new representatives of IGRs lacking some disadvantages of juvenoid-type chemicals. In this review we described some advantageous uses of some anti-JH compounds, imidazoles in particular, in the sericulture and silk research fields. In addition, it shed some light on the action mechanisms of anti-JH agents and described the fate of them in the insect body. It is obvious from the present review that the practical use of anti-JH compounds in the pest management has been challenged by some limitations and restrictions. These compounds should be assessed against different insect pests under field conditions. However, these anti-JH agents can be considered as new leads for devising fourth generation insecticides. On the other hand, some of the anti-JH analogues of imidazoles have been successfully used in the practical production of natural silk in the world.

Contents:

1. Introduction:

For fighting against insect pests, conventional insecticides have a major contribution to agriculture and health. As a result of indiscriminate and intensive uses, these insecticides usually exhibit various detrimental impacts on the human health and beneficial animals as well as cause serious toxicological problems to the ecosystems because these chemicals have a long half-life (Van Der Gaag, 2000; Tiryaki and Temur, 2010). Furthermore, the conventional insecticides have a tendency to accumulate in several trophic levels of the food net (Damalas and Eleftherohorinos, 2011; Chowański *et al*., 2014). In addition, the excessive and repeated uses of many conventional insecticides have enhanced resistant insect strains to emerge (Mosallanejad and Smagghe, 2009). Therefore, eco-friendly insecticides have received global attention in recent years as alternative for these conventional insecticides. These alternative compounds should be characterized by shorter half-life and lower toxicity to non-target organisms than conventional insecticides, as well as they should be effective at low concentrations (Gade and Goldsworthy, 2003). Also, they are biodegradable into harmless compounds, which allows for avoiding the problems of environmental pollution (Tiryaki and Temur, 2010; Walkowiak *et al*., 2015; Li *et al*., 2017).

It is important to point out that the moulting, growth, development and metamorphosis of insects are regulated by prothoracicotropic hormone (PTTH), produced by neurosecretory cells of brain and some other parts in central nervous system, ecdysone or moulting hormone (MH), produced by prothoracic gland (PG) and juvenile hormone (JH), produced by the corpora allata (CA) (Nijhout, 1994; Xiang *et al*., 2005). In some insects, PG, ovary and testis produce ecdysteroids but PG is the principal organ responsible for ecdysone production and secretion. Also, the secretory action of PG is regulated by PTTH and JH (Xu and Xu, 2001). The balance in levels of

MH and JH defines the outcome of each developmental transition. During the larval development, MH causes larval-larval molts in the presence of JH in haemolymph. After the CA stop secreting JH in the last larval instar, insect tissues change their commitment, and MH enhances the larval-pupal and pupal-adult molts (Riddiford *et al*., 2003; Dubrovsky, 2005). In some insects, JH controls the ovarian development and maturation in adult females through some aspects, such as the promotion of vitellogenin synthesis. Thus, JH is usually known as 'gonadotropic hormone' (Nijhout, 1994). In addition, JHs play important roles in several other physiological processes, such as reproduction, diapause, behaviour, polymorphism, migration, metabolism and innate immunity (for detail, see Riddiford, 1994; Gilbert *et al*., 2000; Mitsuoka *et al*., 2001; Tatar *et al*., 2001a,b; Truman and Riddiford, 2007; Riddiford, 2008; Flatt *et al*., 2008; Denlinger *et al*., 2012; Amsalem *et al*., 2014a).

On the other hand, the use of JH or JH-based compounds for pest control was early suggested by some authors (Williams, 1967; Sláma, 1971; Staal, 1982) as "third generation insecticides". Screening new targets involving JH-biosynthesis within the CA had been a subject of investigation during the past four decades (Bede *et al*., 2001). Therefore, compounds that interact with the JH, stimulate or inhibit JH-biosynthesis and/or interfere with its catabolism, can be utilized as new effective agents for controlling the insect pests (Nandi and Chakravarty, 2011). These compounds have been collectively known as 'insect growth regulators' (IGRs). Thus, IGRs belong to a group of compounds which are not directly toxic, but act selectively on normal growth, development, metamorphosis and/or reproduction in insects *via* disrupting the hormonally regulated physiological processes (Wang and Liu, 2016). Because of their desirable characteristics, such as high selectivity, low toxicity, less environmental pollution and low impact on natural enemies and human health, IGRs are used to control various insect pests (Wang and Wang, 2007; Resmitha and Meethal, 2016). Depending on the available literature, IGRs are classified according to several parameters. On the basis of mode of action, IGRs had been clssified in three categories: (i) Juvenile hormone analogues (JHAs) (also called as Juvenoids), (ii) Ecdysteroid agonists and (iii) Chitin synthesis inhibitors (CSIs) or moult inhibitors (Oberlander and Silhacek, 2000**)**. Also, they had been grouped in CSIs and substances interfering with the insect hormones (i.e. JHAs and ecdysteroids)(Tunaz and Uygun, 2004).

From the early research works on JHs and JHAs, disruption of the JH activity, at a critical stage in an insect's development, would offer a promising approach to selective insect control (for reviews, see: Staal *et al*., 1981; Kramer and Staal, 1981; Staal, 1982). There are different ways to remove JHs. Removal operation of the CA (allatectomy) is possible in some insects when there is a conjunction of skilled microsurgery with favorable size and anatomy of the glands. This microsurgerical operation consumes time and effort as well as it is not applicable for pest control. Thus, discovery of Ageratochromes (precocenes), plant compounds causing precocious metamorphosis in insects, can be called "chemical allatectomy"(Bowers *et al*., 1976).

An extensive review of the effects of precocenes on pests belonging to various insect orders was provided by Staal (1986). However, Precocene-I (7 methoxy-2,2-dimethylchromene, PI) and Precocene-II (6,7-dimethoxy-2,2-dimethylchromene, PII) have been used as insect regulators by inducing symptoms of JH-deficiency in insects (Ghosh *et al*., 2012). Consequently, this inhibition can disrupt the embryonic development, induce premature metamorphosis, and disturb the insect behavior including aggression, mating behavior, flight behavior, maternal defensive behavior and sexual behavior, beside their effects as antifeedants and repellents (Rankin, 1980;

Srivastava and Kumar, 1997; Kight, 1998; Khan and Kumar, 2000; Pathak and Bhandari, 2002; Khan and Kumar, 2005; Chen et al., 2005a; Ringo *et al*., 2005; Gaur and Kumar, 2009; Lu *et al*., 2014).

PI and PII have been shown to impair the reproductive potential in adults of many insects by prevention of the normal vitellogenesis of the oocytes, leading to sterility (Kumar and Khan, 2004; Ringo *et al*., 2005; Amiri *et al.*, 2010). As reported by some authors (Staal, 1986; Singh and Bhathal, 1994; Hoffmann and Lorenz, 1998), precocenes either inhibit JH biosynthesis or are inhibitors of the enzyme action. In most cases the physiological, but not all the behavioral effects, were reversible by JH replacement therapy (Pathak and Bhandari, 2002; Chen *et al*., 2005a). With a view to promoting the bioactivity profile of precocenes, it was proposed to discover growth regulatory activity of some compounds related to precocenes. Keeping this in mind, synthetic strategies for 2, 2-dimethyl chromenes were developed (Banerji and Goomer, 1984; Banerji and Kalena, 1989) and used for the preparation of precocene analogues (precocenoids). On the other hand, these synthetic analogues acted as stimulators or inhibitors of JH degradation or acted in an antagonistic manner at the target tissue level, i.e. JH receptor levels (Tunaz and Uygun, 2004; Minakuchi and Riddiford, 2006). Thus, discovery of precocenes paved the way for the development of several new compounds with anti-JH activity based on natural/synthetic products which inhibit JH-biosynthesis of insect pests (Bowers, 1985; Kuwano *et al.*, 1985; Barton *et al*., 1989). Moreover, precocenes and their synthetic analogues received a great attention by entomologists due to their twin advantage; using as a physiological probe in the former avoiding surgical allatectomy and as an effective agent in devising 'fourth generation insecticides' in future (Staal, 1986; Muraleedharan *et al*., 1986; Sariaslani *et al*., 1987; Moya *et al*., 1997; Szczcpanik *et al*., 2005; Singh and Kumar, 2011).

From the terminology view of point, the term "anti-allatotropins", originally suggested to describe the precocenes (Bowers, 1976; Bowers *et al.*, 1976), has become no longer valid and precocenes may be more appropriately classified as anti-allatogenic and/or allatotoxic agents. The term "proallatocidins" may possess a wide acceptance if one wishes to emphasize the necessary need for intensive tissue-specific bioactivation to the ultimate allatocidin (Pratt *et al*., 1981). In the present article, we prefer to use the term "anti-JH agents" or "JH-antagonists" to designate those chemicals which induce JH deficiency syndrome, including precocious metamorphosis in principal. It is conceivable that these compounds should function, in one way or another, to impede JH regulatory mechanisms leading eventually to a deficiency in JH.

It is interesting to refer that the design of JH mimics or anti-JH agents is an effective strategy for insecticide discovery (Bede *et al*., 2001) but the chemicals having anti-JH activity are potentially superior to JH mimics for control many insect pests where most of the damage is caused by the harmful feeding immature stages (El-Ibrashy, 1982). In other words, compounds with anti-JH activity are considered as new representatives of IGRs lacking some disadvantages of juvenoid-type compounds (Bowers, 1982; Staal, 1982).

The present article was prepared for some objectives. Primarily, it aimed to comprehensively review and update several aspects of the insect biology and physiology being affected by anti-JH compounds. This article focused, also, on the modes of action of these compounds and their metabolic fates. Insights into the practical uses of these compounds for pest control had been taken into consideration. Secondarily, this article described some advantages of the anti-JH compounds, imidazoles in particular, in the sericulture and silk research fields.

2. Botanical Origin of the Anti-JH Compounds:

In an attempt to compensate their immobility, plants produce diverse chemicals known as 'allelochemicals' which make them suitable for utilization by phytophagous insects and other herbivores by imparting repellency, toxicity, unpalatibility or biochemical alienation of necessary biochemical or physiological functions (Koul and Smirle, 1994; Banerji, 1994; Agrawal, 1998; Arimura, *et al*., 2000). All insects appear to have determinant receptors which interact with certain kind of allelochemicals which deter the insects from ingesting possible toxins (Banerjee *et al*., 2008). As for example, *Ageratum* plant (Asteraceae) has an ingenious measure for protecting itself from insect attacks (for review, see Kumar, 2014).

In this respect, it is important to point out that there are many plant species contain allelochemicals exhibiting anti-JH activities against some insect species. Early, Bowers (1976) and Bowers *et al*. (1976) isolated two ageratochromenes from the common bedding plant *Ageratum houstonianum* and then coined the compounds as precocene I (PI) and precocene II **(**PII) because of their anti-JH activity leading to precocious metamorphosis in some insects (Bowers, 1992). Recently, 35 active constituents had been identified in the essential oil of *A. houstonianum*, among which PII was found in 62.68% and PI was found in 13.21% (Lu *et al*., 2014). The discovery of these active constituents opened a wide gate for searching and isolation of precocenes from other plant species. The plant *Ageratum conyzoides* is another species in the genus *Ageratum* from which Singh and Rao (1999, 2000) isolated PI and PII. Also, the same precocenes, among the main constituents in the essential oil of *A. conyzoides*, were identified in different percentages (Nogueira *et al*., 2010; Abdelkader and Lockwood, 2011; Bayala *et al*., 2014). In addition, *Ageratum vulgaris* contains precocenes, as active principles (Renuga and Sahayaraj, 2009).

Apart from *Ageratum* spp., PI had been isolated from the essential oil of *Plastostoma africanum* (Lamiaceae)(Onayade *et al*., 1989). PI and PII had been isolated from the plants of genus *Nama* (Hydrophyllaceae), such as *N. lobbii*, *N. sandwicens* and *N. hispidum* (Binder *et al*., 1991). Among the major components of essential oil of *Hyptis suaveolens* (Lamiaceae), PI represented 23.02% (Jaya *et al*., 2011). Bowers and Aregullin **(**1987) isolated an anti-JH compound, polyacetylenic sulfoxide, from *Chrysanthemum coronarium* (Asteraceae) which produced sterile adults in the large milkweed bug *Oncopeltus fasciatus*. Arborine is a quinazoline alkaloid compound isolated from *Glycosmis pentaphylla* (Rutaceae) leaves. This compound inhibited the JH-biosynthesis in the CA of adult females of the field cricket *Gryllus maculates in vitro* (Muthukrishnan *et al*., 1999). Adfa *et al*. (2010, 2011) isolated the Scopoletin (7-hydroxy-6-methoxycoumarin) from *Protium javanicum* (Burseraceae) and synthesized some derivatives which are structurally similar to precocenes. Arivoli and Tennyson (2011) reported an anti-JH activity of the crude leaf extracts of *Abutilon indicum* (Malvaceae) against the vector mosquitoes, *viz*., *Aedes aegypti*, *Anopheles stephensi* and *Culex quinquefasciatus* but the active ingredients could not be isolated.

Outside the higher plants, organic extracts of mycelium and culture broth of 21 *Penicillium* isolates had been assessed against *O. fasciatus*. A strong *in vivo* anti-JH activity was detected in the culture broth extracts from *P. brevicompactum* P79 and P88 isolates (Castillo *et al*., 1999).

3. Categorization of Anti-JH Agents:

As previously mentioned, the anti-JH agents inhibit the JH biosynthesis in CA of many insects. The disturbance of this hormone leads to some abnormalities in those biological processes which are already controlled by JH (Staal, 1986; Darvas *et al*.,

1990; Goodman and Granger, 2005). Since Bowers et al. (1976) discovered the insect anti-JHs (PI and PII), several precocenoids have been synthesized and some anti-JH compounds have been so far reported to exhibit activities interfering with JH in insects. According to the available literature, these compounds include Fluoromevalonate (Quistad *et al*., 1981); ETB (Staal *et al*., 1981); EMD (Staal *et al*., 1981; Staal, 1986); J-2710 (Jurd *et al*., 1979; Farag and Varjas, 1983); compactin (Monger et al., 1982; Hiruma et al., 1983); dichloroallyl hexanoate (Quistad *et al*., 1985); several terpenoid imidazoles (Kuwano *et al*., 1983) and 1,5-disubstituted imidazoles (Castillo *et al*., 1998), such as KK-22 (Kuwano *et al*., 1983), KK-42 (Kuwano *et al*., 1985) and KK-110 (Kuwano *et al*., 1988); and brevioxime (Moya *et al*., 1997; Castillo *et al*., 1998). The majority of these compounds had been found to induce precocious metamorphosis in a number of insects (Darvas *et al*., 1990). Also, certain compounds, such as piperonyl butoxide and thiolcarbamates, induce black pigmentation (a symptom of JH deficiency) in the larvae of tobacco hornworm *Manduca sexta* (Kramer *et al*., 1983). However, other anti-JH compounds should be reviewed in the present section.

3.1. Precocenes:

As previously described, precocenes are plant-derived chromenes (2H-1-benzopyran)(Bowers, 1976; Proksch *et al*., 1983; Isman et al., 1986). Bowers et al. (1976) isolated two ageratochromes from *A. houstonianum* and coined them as PI (7-methoxy-2,2-dimethylchromene) and PII (6,7- dimethoxy-2, 2-dimethylchromene)(Bowers, 1992). The discovery of the precocenes provided an interesting alternative to microsurgical removal of the CA, since they have been shown to be cytotoxic to CA in insects, thus prohibiting the biosynthesis or preventing the production of JH (Pratt *et al*., 1980; Schrankel *et al*., 1982).

3.1.1. Insect Sensitivity to Precocenes:

A pertinent point of this context is to shed some light on the insect sensitivity to precocenes. A vast range of biological, physiological and behavioral changes have been caused by precocenes (Bowers, 1983). Of the major insect taxa, paurometabolous insects appear to be the most sensitive to precocenes, such as grasshoppers and cockroaches (Chênevert *et al*., 1980; Kiss *et al*., 1988). However, it has been reported that the phytophagous Sunn pest *Eurygaster integriceps* (Hemiptera) was an insensitive target for PII (Polivanova *et al*., 1983) but sensitive to PI (Amiri *et al*., 2010).

On the other hand, larvae of some holometabolous insects are less susceptible to the action of precocenes (Burt *et al*., 1979). As for example, the mealworm beetle *Tenebrio rnolitor* (Coleoptera) is insensitive to precocene *in vivo* but was found to be intrinsically sensitive *in vitro*. Its CA had been inactivated by exposure to a precocene analogue in a time- and dose-dependent course. These observations indicated that sequestration and detoxification could be the main reason for the apparent insensitivity of holometabolous insects (Haunerland and Bowers, 1985). However, holometabolous insects, such as the lawn armyworm *Spodoptera mauritia* and the Egyptian cotton leafworm *Spodoptera littoralis* (Lepidoptera), have been reported to be sensitive to precocenes (Mathai and Nair, 1984; Khafagi and Hegazi, 2001).

3.1.2. Multiple Effects of Precocenes:

The second pertinent point is to shed some light on the multiple effects of precocenes on insects. These compounds exhibit multiple effects on metamorphosis (precocious metamorphosis) during the pre-adult stages of different non-social insect species (Khan and Kumar, 2000; Khan and Kumar, 2005; Gaur and Kumar, 2009) and on reproduction in adults of several insect orders since they prevent normal

vitellogenic development of the oocytes or disturb the embryonic development (Staal, 1986) leading to sterility (Kumar and Khan, 2004; Ringo *et al*., 2005; Amiri *et al*., 2010). Precocenes, also, act on the induction of diapause (Bowers, 1983). However, the effects of PII, in particular, on different aspects of insect physiology had been studied by several researchers (Khan and Kumar, 2000; Ergen, 2001; Kumar and Khan, 2004; Chen *et al*., 2005b; Mathai and Nair, 2005; Ringo et al., 2005). Moreover, PII was found to be a more potent analog and selectively destroys the CA of insects (Adebayo *et al*., 2010).

In addition, precocenes affect several aspects of behavior in the non-social insect species, such as aggression (Chen *et al*., 2005a), mating behavior (Walker, 1978), flight behavior (Rankin, 1980), maternal defensive behavior (Kight, 1998) and sexual behavior (Pathak and Bhandari, 2002; Ringo *et al*., 2005). They inhibit the production of sex pheromone (Bowers, 1983). Also, they have potential as antifeedants and repellents against several insect species (Khafagi, 2004; Lu *et al*., 2014). In most cases the physiological, but not all the behavioral effects, were reversible by JH replacement therapy (Kight, 1998; Pathak and Bhandari, 2002; Chen *et al*., 2005a).

Apart from anti-JH effects, precocenes, also, exerted some JH-like actions on green stink bug *Nezara viridula* (Mukhopadhyay *et al*., 1988) and brown plant hopper *Nilaparvata lugens* (Pradeep and Nair, 1989). This dual effect will be discussed later in the present article. Outside the insect world, PII had been reported to completely inhibit two species of fungi, *Rhizoctonia solani* and *Sclerotium rolfsii* (Iqbal *et al*., 2004).

3.1.3. Precocenes and Beneficial Insects:

In the precocene context, it is important to shed some light on the precocene effects on natural enemies and beneficial insects. De Loof *et al*. (1979) recorded a failure of precocene to induce diapause in larvae of the parasitoid wasp *Nasonia vitripennis*, whatever the topical application was conducted on the maternal generation, or eggs. PII demonstrated compatibility with *Diaeretiella rapae*, the endoparasite of the green cabbage aphid *Brevicoryne brassicae* (Faraq *et al*., 1985). PII did not interfere with the growth of developing larvae or adults of the honey bee *Apis mellifera* (Dietz *et al*., 1979). Also, Fluri (1983) reported that PII has no anti-JH activity against the adults of honey bees.

On the contrary, only at doses of 50µg/larva and more, PII exhibited toxic effect on the 1- and 2-day-old worker larvae of honey bee (Rembold *et al*., 1979). PII appears to be toxic to the parasitoid *Nasonia vitripennis* (De Loof *et al*., 1979). Hegazi *et al*. (1998) and Khafagi (2004) studied the effects of both PI and PII on *M. rufiventris*, administered *via* its host *S. littoralis*. These precocenes were found to reduce the parasitoid production.

3.1.4. Synthetic Precocenoids:

With a view to enhance the bioactivity profile of precocenes or to optimize allatocidal activity of the natural precocenes, it was proposed to explore some functionally related compounds. Several precocene derivatives, such as azaprecocenes, fluorinated precocenes, and crown-ether precocenes, had already been synthesized (Brooks *et al*., 1979; Camps *et al*., 1980). Rational synthetic strategies for 2, 2-dimethyl chromenes were developed for the preparation of precocene analogues. As for example, PII and 3,4-Epoxyprecocene 2 deuterated analogues were prepared by Camps *et al*. **(**1985). The sulfur analogs of precocenes (2,2-Dimethyl-2H-thiochromenes) were synthesized by Tércio *et al*. (1987). Also, PII was synthesized (Timar and Jaszberenyi, 1988). Precocene-III (7-ethoxy-precocene 2) was synthesized and assessed against the grasshopper *Aiolopus thalassinus* (Osman, 1988). Precocenes

and related analoges were synthesised in good yields using hydrogen peroxide (Kulkarni and Paradkar, 1992). Starting from PI and PII, Szczepanik *et al*. (2005) synthesized four of their derivatives with a lactone moiety. Banerjee *et al*. (2008) synthesized a number of precocenoids and tested them for their toxicity and growth regulating activity against the cotton stainer bug *Dysdercus koenigii*. The precocenoids 6-hydroxy-DMC and 6-bromo-DMC had been synthesized and bioassayed on the 5th instar nymphs of *D. koenigii* (Banerjee et al., 2008). However, the synthetic analogues of precocenes are stimulators or inhibitors of JH degradation or acted in an antagonistic manner at the target tissue level, i.e. JH receptor levels (Singh and Bhathal, 1994; Hoffmann and Lorenz, 1998).

3.2. Terpenoid Imidazoles (Phenylimidazoles):

In the intensive research attention to anti-JH compounds, a new class of compounds with anti-JH activity against the mulberry silkworm *Bombyx mori* has been classified in a group of terpenoid imidazoles (KK compounds) (Kuwano and Eto, 1983; Kuwano *et al*., 1983, 1984). The most active compounds of this group were KK-22, KK-42 and SSP11 (Akai *et al*., 1984).

KK-22 (1-citronellyl-5-phenylimidazole) was reported to be effective, in a dose-dependent course, for inducing precocious metamorphosis in 3rd instar of *B. mori*. This effect was always accompanied by prolongation of the larval instar (Asano *et al*., 1984a). Asano *et al*. (1984 b) demonstrated that the action of this compound was different from that of precocenes in its rate of precocious induction and influence on larval feeding and growth. The anti-JH activity of KK-22 was vanished when the JHA methoprene was applied immediately after KK-22 treatment (Asano *et al*., 1986).

KK-42 (1-benzyl-5-[(E)-2,6-dimethyl-1,5-heptadienyl]imidazole is a synthetic IGR since it was found to affect the normal growth and development of several insect species (Kuwano *et al*., 1992; Kadano-Okuda *et al*., 1994). Additionally, it caused precocious metamorphosis in *B. mori* when applied to the penultimate instar larvae (Kuwano *et al*., 1985; Akai and Mauchamp, 1989). KK-42 was found, also, to inhibit JH biosynthesis and ecdysone synthesis *in vitro*, retarded ovarian growth and adult emergence when applied to the newly ecdysed pupae of *B. mori* (Kadono-Okuda *et al*., 1987). It was reported to delay/inhibit the ecdysteroid production in European corn borer *Ostrinia nubilalis* (Gelman *et al*., 1995) and desert locust *Schistocerca gregaria* (Wang and Schnal, 2001). It has been shown by Hirai *et al*. (2002) that KK-42 acts as an JH-esterase antagonist in *B. mori*. In the study of Soltani-Mazouni *et al.* (2000), when KK-42 was applied onto the newly emerged adult females of *T. molitor*, the hormonal amounts in ovaries had been reduced. However, when its lowest dose was applied later, i.e. on 2-day old females corresponding to the beginning of the vitellogenesis, no significant effect on the ovarian ecdysteroids was observed.

In addition to KK-22 and KK-42, other imidazoles had been synthesized and bioassayed on some insects, such as KK-110 [5-(2-ethoxyphenyl)-l-neopentylimidazole] and KK-135 [1-neopentyl-5-(4-chlorophenyl) imidazole] (Kuwano *et al*., 1988). Anti-JH activities of these imidazoles were evaluated against *B. mori* and their activities could be abolished by simultaneous administration of methoprene (Kuwano *et al*., 1990). Also, other imidazole compounds had been synthezied, such as SSP11 (E-4-chloro-a, a, a-trifluoro-N-[(C1H-imidazole-1- yl)-2-propryethy-lidene]-O-toluidine) (Kiuchi *et al*., 1985) and SM1 (Lu and Li, 1987). The compound SDIII had been reported to exert strong anti-JH and anti-ecdysteroid actions on silkworms (Tan *et al*., 1992). The imidazole compound triflumizole (E)-4-chloro-alpha,alpha,alpha-trifluoro-N-[1(1H-imidazole-1yl)-2-propoxyethylidene] -o-toluidine was found to possess anti-JH activity against *B. mori* (Miyajima *et al*., 2001).

3.3. Fluoromevalonates:

According to the available literature, one of the major groups of anti-JH compounds is Fluoromevalonate or Fluoromevalonolactone, FMev (tetrahydro-4-fluoromethyl-4-hydroxy-2H-pyran-2-one). This group was known for its hypocholesteremic activity in mammals (Nave *et al*., 1985). As reported by Sánchez *et al*. (2015), FMev is a competitive inhibitor of mevalonate diphosphate decarboxylase and exhibits inhibitory effect on cholesterol biosynthesis, cell proliferation and cell cycle progression in human leukaemic HL-60 and MOLT-4 cells.

In insects, FMev was reported to exhibit anti-juvenile hormone activity against seven lepidopterous species: *M. sexta* (Sphingidae), *Samia cynthia* (Saturniidae), *Phryganidia californica* (Dioptidae), *Galleria mellonella* (Pyralidae), *Spodoptera exigua*, *Heliothis virescens* (Noctuidae), and *Hyphantria cunea* (Arctiidae) (Quistad *et al*., 1981). Anti-JH activity of FMev was expressed by the precocious metamorphosis or prepupal behavior (Quistad et al., 1981; Farag and Varjas, 1983). Edwards *et al*. (1985) adverted the anti-JH activity of FMev in the American cockroach *Periplaneta americana* which was mediated through *in vivo* inhibition of JHIII-biosynthesis, so they suggested that FMev could have a much wider range of insect species than was previously expected. The anti-JH activity (precocious metamorphosis) of FMev could be, completely or partially, deleted *in vivo* by concurrent application of a JHA, like hydroprene (Quistad *et al*., 1981; Farag and Varjas, 1983; Staal, 1986) or farnesoic acid *in vitro* (Cusson *et al*., 2013).

On the other hand, no anti-JH activity was recorded for FMev in the non-lepidopterous species, such as those belong to orders Diptera, Coleoptera, Heteroptera, and Orthoptera (Menn, 1985). Therefore, FMev might be a useful compound for "chemical allatectomy" in Lepidoptera (Benz and Ren, 1986). Synthetic efforts to optimize the anti-JH activity of FMev have only resulted in a number of compounds with anti-JH activity inferior to that of FMev (Quistad *et al*. 1982).

3.4. Benzoate and methy dodecanoate compounds:

The benzoate compound ETB (ethyl-4-[2-(tert-butyl carbonyloxy)butoxy] benzoate) was originally developed in 1975 (Kondo *et al*., 1977) as a juvenoid. Edwards *et al*. (1983) reported that the application of ETB on larvae of *M. sexta* resulted in a reduction of endogenous JH titer. It is active on larvae of *B. mori*, causing precocious metamorphosis at lower concentrations, which is partially rescued by the administration of JHA (Kiguchi *et al*., 1984). For preparing effective ETB analogues, Ishiguro *et al*. (2003) found that the 4- ethoxycarbonyl group on the benzene ring was apparently essential for activity. Among ETB analogues, Fujita *et al*. (2005) prepared a series of ethyl 4-[2-(6-methyl-3-pyridyloxy)alkyloxy]benzoates and tested their activities on larvae of *B. mori*. Among the tested compounds, ethyl 4-[4-methyl-2-(6-methyl-3-pyridyloxy)pentyloxy]benzoate was the most effective to induce precocious metamorphosis after topical application onto 1-day old 3rd instar larvae. Furuta *et al*. (2006) synthesized a number of alkyl 4–(2–phenoxyhexyloxy)benzoates and related compounds and evaluated their activities to induce precocious metamorphosis in larvae of *B. mori*. Of these compounds, only the methyl and ethyl esters showed precocious metamorphosis–inducing activity. Fujita *et al*. (2007) synthesized two ETB analogues: Ethyl 4-[2-(6-methyl-3-pyridyloxy)hexyloxy]benzoate and ethyl 4-(2-phenoxyhexyloxy)benzoate which induced precocious metamorphosis in larvae of *B. mori*. Recently, Yamada *et al*. (2016) synthesized a series of ethyl 4-[(7-substituted 1,4-benzodioxan-6-yl) methyl]benzoates and evaluated their anti-JH activities on *B. mori*. The compound Ethyl 4-[(7-benzyloxy-1,4-benzodioxan-6-yl) methyl]benzoate

showed the most potent activity, since JH I and JH II titers of 3rd instar larvae decreased within 24 hr of treatment.

KF compounds are structurally derived from ETB. Some KF compounds had been prepared and bioassyed against *B. mori*. KF-13S and KF-13 induced precocious metamorphosis in *B. mori* (Furuta *et al*., 2007; Fujita *et al*., 2008).

Although EMD (ethyl-[E]-3-methyl-2-dodecanoate) had been reported to exhibit an anti-JH activity on the tobacco budworm *Heliothis virescens* and *M. sexta* (Staal *et al*., 1982), no precocious metamorphosis was induced by it in the 3rd and 4th instar larvae of *B. mori* (Kuwano *et al*., 1988). On the other hand, Balamani and Nair (1989) conducted a study on the activity of EMD against *S. mauritia*. Neck-ligated post-feeding last instar larvae were topically treated with lower doses of EMD. It induced the formation of larval-pupal intermediates whereas those treated with higher dose moulted into either pupae or larval-pupal intermediates. Co-application of JHA with different doses of EMD induced pupation in majority of the ligated larvae and thus appears to a certain extent to counteract the effects of treatments of same doses of EMD alone. Thus, EMD failed to exhibit an anti-JH activity but JH-like activity.

3.5. FGL-amide Allatostatins:

A great deal of effort has nowadays been directed towards the Allatostatins (ASTs) which constitute a class of regulatory neuropeptide hormones in insects. As reported by Hult *et al*. (2008), these compounds occur, also, in diverse invertebrate phyla. By using their consensus sequences, Stay and Tobe (2007) classified ASTs, in insects, in three families: the cockroach type representing the FGL-amide-AST family, the cricket type representing the $W(X)_6$ Wamide-ASTs family and the PISCF/ASTs family.

In the present article, our attention will be paid to FGL-amide-AST family and little types of ASTs. These FGL-amides represent a family of insect neuropeptides originally isolated from the viviparous cockroach *Diploptera punctata* (Pratt *et al*., 1991; Stay *et al.*, 1994), crickets (Lorenz *et al*., 1995) and termites (Yagi *et al*., 2005, 2008). As reported in the available literature, H17 (FGL-amide AST neuropeptidemimic) was quite potent as an inhibitor of JH biosynthesis (anti-JH activity) and was able to inhibit the basal oocyte growth in *D. punctata* (Bendena and Tobe, 2012). Lehmann *et al*. (2015) studied the population dependent differences in diapause induction of the Colorado potato beetle *Leptinotarsa decemlineata* (Coleoptera) in response to negative and positive manipulation of JH III levels. In their study, application of H17 did not induce overwintering related burrowing. Using the H17, as the lead compound, Xie *et al*. **(**2016) designed new AST analogues which exhibited strong potency to inhibit JH production by CA of *D. punctata*. Recently, Wu *et al*. (2017) designed and synthesized 30 analogues, modified with various substituents on the benzene ring at the N-terminus of the lead compound H17. Depending on their results, all analogues exhibited various effects on JH biosynthesis by CA of *D. punctata*. For detail, see Kai *et al*. (2009, 2010, 2011); Xie *et al*. (2011, 2015) and Wu *et al*. (2016).

Ketomethylene and methyleneamino pseudopeptide analogues of ASTs, were designed by Piulachs *et al*. (1997) and had been found to inhibit the JH biosynthesis *in vitro* by CA of virgin German cockroach *Blattella germanica*. Also, synthesized Dippu-AST analogues had been reported to inhibit JH biosynthesis (Nachman *et al*., 1999; Garside *et al*., 2000).

3.6. Benzodioxoles and Benzylphenols:

As a group of compounds with anti-JH activity, Benzodioxoles and benzylphenols were studied by Van Mellaert *et al*. (1983). According to these authors,

these compounds displayed anti-JH activity against the greater wax moth *Galleria mellonella* (Lepidoptera) but less active on Lepidoptera than FMev. It should be mebtioned that Benzyl-l,3-benzodioxoles had been previously known as chemosterilants against several Diptera (Jurd *et al*., 1979). Van Mellaert *et al*. (1983) theorized that the known chemosterilant action of these compounds in the house fly *Musca domestica* and the flesh fly *Sarcophaga bullata* (Diptera) is associated with anti-JH effects. However, blocking of the JH receptor would result in disruption of events leading to egg maturation (Menn, 1985). However, the suggestion that these compounds have a JH antagonist action is controversial (Staal, 1986; Langley and Pimley, 1986). For examples, the compound J-2581 (5-ethoxy-6-[4-methoxyphenyl]methyl-1,3-benzodioxole) was found a relative chemosterilant against the Mediterranean fruit fly *Ceratitis capitata* (Hsu *et al*., 1989) and the oriental fruit fly *Dacus dorsalis* (Hsu *et al*., 1990), but no information is available in the current literature concerning its anti-JH activity against insects.

The compound J-2710 (5-methoxy-6-[l-(4-methoxyphenyl)ethyl]-l,3-benzodi-oxole) was first synthesized by Jurd *et at*. (1979) and described as a fly chemosterilant. This compound has been reported to exhibit anti-JH activity against *G. mellonella*, but there is no evidence of similar activity against larvae of other insect species (Kuwano *et al*., 1988). Thereafter, Darwas *et al*. (1990) assessed J-2710 on *S. bullata*, the treatment resulted in the precocious pupation indicating an anti-JH activity of this compound. In contrast, Readio *et al*. (1987) assessed the anti-JH activities of six benzyl-1,3-benzodioxole derivatives against 4th instar larvae of the mosquito *Culex pipiens* (Diptera) and did not observe clear anti-JH effects.

3.7. Bisthiolcarbamate:

In the context of anti-JH compounds, bisthiolcarbamate (N-ethyl-l,2-bis(S-isobutylthiocarbamoyl)ethane) should be gained some attention. This compound was initially described as an unusual example of non-terpenoid compounds exhibiting JH activity against several insect species (for detail, see Pallos *et al*., 1976; Menn, 1980; Brooks, 1987). Treatment of 3rd instar larvae of *M. sexta* with 50-250 µg bisthiolcarbamate/animal resulted in suppression of JH titer in the subsequent instar. The *in vivo* effects were only manifested by black pigmentation of larvae treated topically (25 µg/ larva) or by feeding (10 ppm); no precocious pupation was observed following treatment with this compound. At higher doses, however, typical JH effects (paleness) were observed. However, the weak activity of bisthiolcarbamate may be due to its rapid degradation *in vivo* (Kramer *et al*., 1983).

3.8. Sulfoxides:

It is well known that thiolcarbamates are rapidly metabolized *in vivo* and *in vitro* to reactive sulfoxides and possibly very short-lived sulfones (DeBaun *et al*., 1978). Some years later, a study of Bowers and Aregullin (1987) was the first to reveal the anti-JH activity of the compound polyacetylenic sulfoxide and inducing the sterility in adults of *O. fasciatus*. Nevertheless, this may be an interesting model for possible additional synthesis of more active and stable analogues (Menn, 1985).

A series of fluorinated vinyl sulfoxides had been developed in the late 1980s. These sulfoxides showed promise as potent and selective anti-JHs against Lepidoptera (Carney and Brown, 1989). The design of these compounds was based on the weakly active EMD and on analogues of dimethylallyl diphosphate (Quistad *et al*., 1985). Topical application of fluorinated vinyl sulfoxides onto lepidopterous larvae caused premature pupation that was recoverable by co-administration of farnesol (Cusson *et al*., 2013).

3.9. Fungi- and Bacteria-derived Compounds with Anti-JH Activity:

Depending on the available literature, a little research attention had been paid to the anti-JH agents from fungi and bacteria. In this respect, it is important to focus on three fungi-derived compounds: Brevioxime, Compactin, Fluvastatin and one of the bacteria-derived compounds, Cycloheximide. Activities of these compounds have been assessed against different insect species. Thereafter, these compounds had been chemically synthesized.

Brevioxime has been isolated from the entomopathogenic fungus *Penicillium brevicompactum.* It was reported to possess anti-JH activity against insects, since it showed a strong *in vitro* inhibition of JH III biosynthesis in CA of the migratory locust *Locusta migratoria* (Moya *et al*., 1997; Castillo *et al*., 1998). This compound shows a sesquiterpene-like structure, corresponding to an empirical formula of $C_{15}H_{22}N_2O_3$. Two natural products were isolated from *P. brevicompactum* P79: N-(2-methyl-3-oxodec-8-enoyl)-2-pyrroline and 2-hept-5-enyl-3-methyl-4-oxo-6,7,8,8a-tetrahydro-4H-pyrrolo[2,1-b]-1,3-oxazine. They were found to possess strong anti-JH activities against *O. fasciatus* (Castillo *et al*., 1999). Synthesis of racemic Brevioxime and related model compounds had been conducted (Clark, 2000; Clive and Hisaindee, 2000; Karadogan and Parsons, 2001). Structures related to brevioxime, and possessing anti-JH activity, have been identified (Cantín *et al*., 1999).

Compactin is a fungal metabolite which had been reported as a potent inhibitor of HMG-CoA R enzyme invertebrates (Monger *et al*., 1982) and also causes hypocholesteremia in mammals (Polivanova *et al*., 1983). In insects, compactin was found to be more potent inhibitor of JH biosynthesis in *M. sexta* (Monger *et al*., 1982**)**, the cabbage moth *Mamestra brassicae* (Hiruma *et al*., 1983) and *P. americana* (Edwards and Price, 1983). Only repeated injection of compactin into *M. sexta* larvae induced the black pigmentation characteristic of JH deficiency (Monger *et al*., 1982). A study on the *in vitro* and *in vivo* effects of compactin, either free or encapsulated into liposomes, on virgin females of *B. germanica* was conducted by Belles *et al*. (1988). Depending on their results, neither compactin nor liposomes were able to inhibit the formation of the first ootheca, although the encapsulated compactin **(**at certain doses) induced a significant delay in the gonotrophic cycle. Sparks *et al*. (1987) observed deformed pupae after treatment of the last instar larvae of cabbage looper *Trichplusia ni* with compactin analogues L-643, 049-01K01 and DPH (3,3-dichloro-2-propenyl hexanoate).

Fluvastatin (3-hydroxy-3-methyl-glutaryl-CoA reductase) contains a disubstituted indole core in place of the hexahydronaphthalene found in the fungal fermentation products. In Medicine, fluvastatin belongs to a class of medications called 'statins' and is used to reduce plasma cholesterol levels and prevent cardiovascular disease (Jokubaitis, 1996). In Entomology, fluvastatin had been assessed against a few numbers of insects. Injection of fluvastatin into the locust *L. migratoria* led to inhibition of JH-regulated metamorphosis. Otherwise, its activity was low *in vitro* (Debernard *et al*., 1994). Fluvastatin inhibited JH acid biosynthesis by CA of the black cutworm *Agrotis ipsilon* when injected in males 4 h before the bioassay (Duportets *et al*., 1996).

Cycloheximide (3-[(2R)-2-[(1S, 3S, 5S)-3,5-dimethyl-2-oxocyclohexyl]-2-hydroxyethyl] glutarimide) is reported as RNA and protein synthesis inhibitor. It was originally isolated from the bacterium *Streptomyces griseus* (Siegel and Sisler, 1963; Baliga *et al*., 1969). Cycloheximide represents the most common laboratory reagent used to block protein synthesis and is widely used in studies regarding trafficking of epidermal growth factor receptor (Wiepz *et al*., 2010). As an antibiotic, cycloheximide

was earlier applied clinically in the treatment of disseminated candidiasis and meningitis (Schmidt and Dikic, 2010).

In the agricultural applications, cycloheximide was found as an inhibitor of protein synthesis and irreversible inhibitor of multiplication nuclear polyhedrosis virus in the fall armyworm *Spodoptera frugiperda* (Kelly and Lescott, 1976). Cycloheximide inhibits the growth, in culture, of many plant pathogenic fungi (MacBean, 2012). With regard to insects, the interference of cycloheximide with the hormonal regulation of developmental process and metamorphosis was studied. Ferkovich *et al*. (1977) reported that cycloheximide inhibited JH-binding protein in the tissue culture of fat body of the Indianmeal moth *Plodia interpunctella*. So, general esterases could degenerate JH causing a deficiency in its level. Cycloheximide induced 60% inhibition of RNA synthesis in 4^{th} and 5^{th} instar nymphs of *L. migratoria* (Phillips and Loughton, 1979).

3.10. Additional Anti-JH Compounds:

In seeking other candidates for pest control, various compounds show anti-JH activities and act as potential inhibitors of the JH-biosynthesis in CA of insects. In the following paragraphs, a variety of these compounds and their functions will be concisely reviewed. Piperonyl butoxide (2-(2-butoxyethoxy)ethyl 6-propylpiperonyl ether) is one of the best known mixed-function oxidase inhibitors and a potent insecticide synergist. It shows moderate anti-JH activity in *M. sexta in vivo* and depression of JH biosynthesis in CA culture assays (Staal, 1982). Quinolones and fluoroquinolones are synthetic bactericidal antibiotics. Quinolone has been reported to cause precocious metamorphosis in *B. mori* (Murakoshi *et al*., 1977). Pyridone has been reported to cause precocious metamorphosis in *B. mori* (Murakoshi *et al*., 1977). The precocious metamorphosis induced by 3-pyridine derivatives was fully counteracted by a simultaneous application of tebufenozide (an ecdysteroid agonist) suggesting that the 3-pyridyl ethers temporarily act as anti-ecdysteroids (Yoshida *et al*., 2000). Lovastatin (known, also, as Mevinolin) was reported to inhibit the JH biosynthesis in insect CA *in vitro* (Feyereisen and Farnsworth, 1987). LC_{50} values of Lovastatin against *M. sexta* and *D. punctata* were estimated in 99.45 and 884.7 µM, respectively (Couillaud, 1991). Arborine is originally a quinazolone alkaloid product of plants (Sreejith *et al*., 2012). It was found to inhibit the JH biosynthesis *in vitro* of CA from 3 day-old females of *G. bimaculatus* (Muthukrishnan *et al*., 1999). Among Allyl alcohols, Quistad *et al*. (1985) synthesized three analogues of 3,3-dimethyl-2-propenol (dimethylallyl alcohol) and evaluated their anti-JH activities against some lepidopterous species. The most active compound (3,3-dichloro-2-propenyl hexanoate) caused precocious metamorphosis in *M. sexta*. The oxathiole is a powerful inhibitor for JH biosynthesis having approximately the same potency of precocenes or better. When applied on the $4^{th}/5^{th}$ instar of *O. fasciatus*, oxathiole induces precocious metamorphosis. This effect can be rescued with JH-agonists, indicating a true anti-JH action of oxathiole (Brooks *et al*., 1984a). Brooks *et al*. (1984 b) reported that 8-methoxynaphth-(1,2-d]-1,3-oxathiole is a potent inhibitor of JH-biosynthesis in CA of *P. americana* and *O. fasciatus in vitro*.

It has been demonstrated that furanyl ethers have potent anti-JH activity in *O. fasciatus* and triatomine bugs, inducing precocious metamorphosis and other modifications in these insects (Bowers *et al*., 1995; Azambuja *et al*., 1996). The synthetic compound 2-(2-ethoxyethoxy) ethyl furfuryl ether was topically applied onto larvae of the reduvid bugs *Rhodnius prolixus, Triatoma infestans* and *Panstrongylus herreri* (Hemiptera). A variety of biomorphological alterations had been observed, including precocious metamorphosis into small adultoids with adult abdominal cuticle,

ocelli and rudimentary adultoid wings (Jurberg *et al.*, 1997). Recently, Li *et al*. (2017) determined the LC_{50} values of Pitavastatin, HMG-CoA) reductase, against *M. sexta* and *D. punctata* as 5.23, and 395.2 µM, respectively.

4. Bioefficacy of Anti-JH Compounds Aagainst Insects:

4.1. Toxicity:

It is well documented that the non-neurotoxic insecticides exhibit their toxicities against insects through different routes other than the central nervous system as performed by the conventional insecticides. Literature sources show various toxic effects of a large number of JHAs on several insect species, such as pyriproxyfen against *L. migratoria* (Hu *et al*., 2012) and *S. mauritia* (Resmitha and Meethal, 2016); kinoprene against *C. pipiens* (Hamaidia and Soltani, 2014); methoprene against *A. ipsilon* (Khatter, 2014); methoxyfenozide against *C. pipiens* (Hamaidia and Soltani, 2016); tebufenozide against the Mediterranean flour moth *Ephestia kuehniella* (Lepidoptera: Pyralidae)(Tazir *et al*., 2016) and cyromazine against the flies *M. domestica, Stomoxys calcitrans* and *Fannia canicularis* (Diptera)(Donahue *et al*., 2017).

However, several anti-JH compounds possess toxic potencies against various insect species as reviewed herein. PII exhibited a nymphicidal effect on the human body louse *Pediculus humanus* (Feldlaufer and Eberle, 1980). Both PI and PII exhibited larvicidal activities against several mosquito species, such as *Aedes aegypti*, *Anopheles sacharovi* and *An. stephensi* (Saxena *et al*., 1994; Yasyukevich and Zvantsov, 1999). When the newly hatched nymphs of white-backed planthopper *Sogatella furcifera* were released on rice plants treated with 500 ppm of PII and continuously contacted with it, about half of the insects died within the first instar (rapid toxicity)(Miyake and Mitsui, 1995). Different doses of PII were topically applied onto the 3rd instar larvae of the grey flesh fly *Parasarcophaga dux* and toxic effects were observed on larvae and pupae, in a dose-dependent course (Nassar *et al*., 1999). PIII was topically applied onto eggs, 5th instar nymphs, and newly hatched adult females of the grasshopper *Aiolopus thalassinus* (Orthoptera). It caused a high mortality in all of the treated stages (Osman, 1988).

As reported in the late two decades, PII exhibited toxic effect on the castor hairy caterpillar *Pericallia ricini* (Lepidoptera)(Khan and Kumar, 2000). PI and PII were topically applied onto the 2nd larval instar of *L. decemlineata* (Coleoptera) in laboratory. Both precocens caused larval mortalities, in a dose-dependent course (Farazmand and Chaika, 2008). A toxicological effect of PII was reported by Abdullah (2009) against larvae of the red palm weevil *Rynchophorus ferrugineus* (Coleoptera). PI had no acute toxicity against *E. integriceps* adults after treatment of 2nd instar nymphs but treatment of the 3rd instar nymphs caused increasing mortality, in a dose-dependent course (Amiri *et al*., 2010). PII exhibited stronger acute toxicity than PI against the booklice *Liposcelis bostrychophila* (Psocoptera)(Lu *et al*., 2014). After exposure of the newly moulted 2nd or 4th (penultimate) instar nymphs of the grasshopper *Euprepocnemis plorans* to some doses of PII, various mortality percentages were recorded among the treated nymphs of different instars and the emerged adults (Ghoneim and Basiouny, 2017). Banerjee et al. (2008) synthesized some precocenoids and tested them against *D. koenigii*. Among different tested compounds, 8-acetyl-7-hydroxy-5-methoxy-dimethylchromene (alloevodinol) was more toxic at very low dose. PII treatment of 0-96 hr-old pupae of the blowfly *Chrysomya megacephala* (Diptera) resulted in mortality during pupation (Singh and Kumar, 2011). PII exhibited larvicidal activity against the 4th instar larvae of the Asian tiger mosquito, *Aedes albopictus* (Diptera)(Liu and Liu, 2014).

Apart from precocenes, Arborine showed larvicidal properties against the the southern house mosquito *Culex quinqeufasciatus* (Hoffmann and Lorenz, 1998). Kuwano *et al*. (1988) synthesized EMD which exhibited acute toxicity on the 3rd instar larvae of *B. mori*. Shuto *et al*. (1988) synthesized some analogues of FMev and assessed their toxicities against *B. mori*. The compound (R)-(-)-FMev was predominantly toxic and the larval mortality increased. Among ten anti-juvenile hormone compounds tested by Connat (1988) against the cattle tick *Boophilus microplus* females, the most toxic compound was FMev, which proved to be lethal at dose 200 µg/female. Basiouny and Ghoneim (2017) topically applied four doses of FMev onto the newly moulted 5th (penultimate) instar larvae and newly moulted 6th (last) instar larvae of *S. littoralis*. FMev exhibited a weak toxicity against larvae, pupae and adults. Lee *et al*. (2015) developed effective *in vitro* anti-JH compounds screening system using yeast cells transformed with the mosquito *Aedes aegypti* JH receptors, (methoprene-tolerant, Met) and FISC. Among 53 compounds with anti-JH activities, penfluridol showed high toxicity against larvae of the mosquito *Aedes albopictus*. Anti-JH activity increased in proportion to the concentration of penfluridol (Lee *et al*., 2018).

In respect of the LD_{50} values of various anti-JH compounds against different insects, LD_{50} of PII against *D. koenigii* has been found to be 85.46 and 82.37 mgl^{-1} for 4th and 5th instar nymphs, respectively (Banerjee *et al*., 2008). After treatment of 4th instar larvae of *A. albopictus* with PI and PII, LC_{50} values were estimated in 41.63 µg/ml and 43.55 µg/ml, respectively (Liu and Liu, 2014). LC_{50} of PII against *L. bostrychophila* was calculated in 30.4$\mu g/cm^2$ but LC_{50} of PI was found as 64.0$\mu g/cm^2$ (Lu *et al*., 2014). LC_{50} of PI against the cat flea *Ctenocephalides felis* was estimated as 10.97 ppm, respectively (Rust and Hemsarth, 2017). LD_{50} values of PII against *E. plorans* were 0.388 and 17.022 $\mu g/cm^2$ after topical treatment of newly moulted 2nd and 4th (penultimate) instar nymphs, respectively (Ghoneim and Basiouny, 2017). Against *S. littoralis*, LD_{50} values of FMev were estimated in 42.03 and 629.20 µg/larva, after treatment of 5th and 6th larval instars, respectively (Basiouny and Ghoneim, 2017). Among the HMG-CoA reductase inhibitors, LC_{50} values of Fluvastatin against *M. sexta*, *A. mellifera* and *D. punctata* were estimated in 5.11, 18.10 and 150.0 µM, respectively (Li *et al*., 2017). LC_{50} values of Lovastatin against *M. sexta* and *D. punctata* were estimated in 99.45 and 884.7 µM, respectively (Li *et al*., 2017). LC_{50} values of Pitavastatin against *M. sexta* and *D. punctata* were estimated in 5.23, and 395.2 µM, respectively (Li *et al*., 2017).

However, LD_{50} (or LC_{50}) value of a compound depends on several factors, such as susceptibility of the insect and its treated stage or instar, lethal potency of the tested compound and its concentration levels, method and time of treatment, as well as the experimental conditions (Ghoneim *et al*., 2017a, b).

4.2. Inhibited Growth and Influenced Development:

4.2.1. Affected Body Weight and Growth:

In insects, the larval growth is usually determined in the growth rate, growth index or coefficient of growth. In addition, the body weight and hence the weight gain can be considered as a valuable indicator to the larval growth of an insect (Armbruster and Hutchinson, 2002; Ghoneim *et al*., 2014a). After topical application of different doses (5-75 µg/larva) of PII onto 1- or 2-day-old worker larvae of *A. mellifera*, the larval weight gain decreased in dose-dependent course (Rembold *et al*., 1979). The larval and pupal weights of *S. bullata* were reduced after treatment with the anti-JH compounds PII, J-2710 and KK-110 (Darwas et. al., 1990). The insect kinins (an insect neuropeptide family) have been isolated from a number of insects. The insect kinins,

and/or analogs, have been reported to inhibit weight gain in larvae of *H. virescens* and corn earworm *Helicoverpa zea* (Seinsche **et al**., 2000; Nachman *et al*., 2002). Yoshida *et al*. (2000) synthesized 3-pyridine derivatives and evaluated their activities against *B. mori*. Among these compounds, the compound 3-(2-methyl-l-phenyl-l-propenyl)pyridine was applied onto 4th instar larvae, body weights of the ecdysed 5th instar larvae increased rapidly reaching to the maximum.

Depending on the available literature, few studies have examined the effects of anti-JH agents on the insect growth as being reviewed herein. Several chromene derivatives inhibited the growth of last instar larvae of *T. molitor* (Roberto *et al*., 1998). PI and PII exhibited growth-inhibiting activities against the mosquitoes *Ae. aegypti*, *An. sacharovi* and *An. stephensi* (Saxena *et al*., 1994; Yasyukevich and Zvantsov, 1999). Treatment of early and late 3rd instar larvae of *C. megacephala* with PII adversely affected the normal growth of larvae (Singh and Kumar, 2011). After exposure of newly moulted 2nd or 4th (penultimate) instar nymphs of *E. plorans* to different doses of PII, the nymphal growth of both 4th and 5th instars had been slightly inhibited after treatment of 2nd instar nymphs, but remarkably reduced after treatment of 4th instar nymphs (Ghoneim and Basiouny, 2017). Four doses of FMev had been topically applied (once) onto the newly moulted 5th (penultimate) instar larvae and newly moulted 6th (last) instar larvae of *S. littoralis*. FMev inhibited the larval growth when applied onto 5th instar larvae but promoted it after treatment of 6th instar larvae (Basiouny and Ghoneim, 2017). Larvae of *M. sexta* were fed on Fluvastatin, Lovastatin or Pitavastatin-treated food, starting with 1st instar. Significantly slow growth rate was recorded for the treated larvae (Li *et al*., 2017).

4.2.2. Influenced Development:

The developmental rate of an insect stage is usually reversely related to the developmental duration, i.e. shorter duration indicates faster rate and *vice versa* (Ghoeneim *et al*., 2014a). In this respect, various anti-JH agents exhibited different effects on the development of some insects, as reported in the present section.

Treatment of 4th instar nymphs of the locust *S. gregaria* with PII resulted in a prolongation of the duration of both 4th and 5th nymphal instars (Eid *et al*., 1982). Treatment of 6th instar larvae of *S. mauritia* with single or repeated daily doses of PII resulted in prolongation of the larval–pupal period (Mathai and Nair, 1984). The nymphal period of the grasshopper *A. thalassinus* was prolonged after topical application of PIII onto 5th instar nymphs (Osman, 1988). Treatment of the tobacco caterpillar *Spodoptera litura* larvae with PI, PII or ethoxyprecocene (a synthetic analog of PII) resulted in prolongation of larval period (Srivastava and Kumar, 1999). After treatment of 4th instar nymphs of *D. koenigii* with PII, duration of the successfully moulted 5th instar nymphs was prolonged (Banerjee *et al*., 2008). Treatment of early and late 3rd instar larvae of the blowfly *C. megacephala* with PII adversely hampered the development (Singh and Kumar, 2011).

Apart from precocenes, Farag and Varjas (1983) recorded a prolongation of larval duration after topical application of FMev doses onto caterpillars of three late instars of the fall webworm *Hyphantria cunea*. Similar results were obtained after treatment of the 3rd instar of *B. mori* with KK-22 (phenylimidazoles)(Asano *et al*., 1984a). Debernard *et al.* (1994) assayed Fluvastatin on the locust *L. migratoria* and recorded a prolongation of the 4th nymphal instar. Yoshida *et al*. (2000) synthesized 3-pyridine derivatives and evaluated their activities against *B. mori*. Among the tested compounds, the compound 3-(2-methyl-l-phenyl-l-propenyl) pyridine prolonged the larval period. Treatment of the 4th instar nymphs of the locust *S. gregaria* with cycloheximide extended the duration of the 4th nymphal instar only (Eid *et al*., 1982).

On the contrary, the larval and/or pupal durations in some insects were significantly shortened after treatment with certain anti-JH compounds, such as the grey flesh fly *P. dux* after treatment of the 3rd instar larvae with different doses of PII (Nassar *et al*., 1999); the flesh fly *S. ruficornis* after treatment of the last instar larvae with PI, II or III (Srivastava and Kumar, 1996); *M. domestica* after treatment of the larvae with PII (Gaur and Kumar, 2009); *B. mori* after treatment of the 3rd and 4th instars with the imidazole compound, SSP-11 (Kiuchi *et al*., 1985). Four doses of FMev had been topically applied (once) onto the newly moulted 5th instar larvae and newly moulted 6th (last) instar larvae of *S. littoralis*. The larval duration was remarkably shortened, but the pupal duration was slightly or remarkably prolonged, depending on the treated larval instar (Basiouny and Ghoneim, 2017).

Moreover, no action was exerted by a number of anti-JH compounds on the developmental (larval and/or pupal) duration of some insects, such as PII after topical application onto the worker larvae of *A. mellifera* (Rembold *et al*., 1979); PI and PII after topical application onto the 2nd larval instar of the beetle *L. decemlineata* (Farazmand and Chaika, 2008). Khafagi and Hegazi (2004) investigated the effects of PI and PII on the parasitoid wasp *M. rufiventris* after topical treatment of the host larvae of *S. littoralis*. The parasitoid developmental duration did not be affected.

4.3. Perturbation of Metamorphosis:

As previously mentioned in the present review, different physiological processes in insects, including embryogenesis, post-embryonic development and metamorphosis have been regulated by JH or JHs which are synthesized and discharged by the CA (Wyatt and Davey, 1996; Flatt *et al*., 2005; Li *et al*., 2007). The most important developmental hormones are 20-hydroxyecdysone (20-E) and JH. Balance in levels of these two hormones defines the outcome of each developmental transition. JH deficiency, in particular, leads to precocious metamorphosis, *viz*., omitting or skipping off the last larval instar and production of dwarf pupae in holometabolous insects and non-viable adultoids in hemimetabolous insects (Minakuchi *et al*., 2008; Triselyova, 2012).

The JH deficiency can be reached by disturbance of its biosynthesis owing to destruction of the CA, microsurgically (allatectomy) or chemically, as well as degradation of JH after release in the haemolymph (Bowers *et al*., 1976; Ohta *et al*., 1977). Therefore, special attention should be paid to the chemical compounds interfering with the JH biosynthesis, such as those known as anti-JH agents, i.e., the effects of some anti-JH compounds inducing precocious metamorphosis in various insects should be discussed in this section.

4.3.1. Precocious Metamorphosis:

In the hemimetabolous insects, precocenes had been reported to induce precocious metamorphosis as expressed in the precocious appearance of adult characteristics in nymphal instars (Pratt *et al*., 1980). The production of such features has been explained by the prevention of JH synthesis in the sensitive insect (Brooks and McCaffery, 1990). On the other hand, larvae of the holometabolous insects, with few exceptions, are less responsive than hemimetabolous insects to the action of PII (Burt *et al*., 1978). In general, anti-JH agents induce precocious metamorphosis in a restricted number of insect species (Darvas *et al*., 1990).

Among Lepidoptera, treatment of *S. litura* larvae with PI, PII or ethoxyprecocene (a synthetic analogue of PII) resulted in formation of adultoids (Srivastava and Kumar, 1999). Treatment of the eri silkworm *Philosamia ricini* with PII resulted in precocious pupation (Khan and Kumar, 2000).

Within Hemiptera/Homoptera, precocious metamorphosis was induced in the kissing bugs *Rhodnius prolixus* and *Triatoma dimidiata* by contact exposure to or fumigation with PII (Tarrant *et al*., 1982); in the lime seed bug *Oxycarenus lavaterae* after application of PII onto 3rd instar nymphs (Belles and Baldellou, 1983); in the brown planthopper, *Nilaparvata lugens* by PII (Ayoade *et al*., 1996). Also, precocious metamorphosis of the green peach aphid *Myzus persicae* (Homoptera), was induced by the precocene analogue 6-methocy-7-ethoxy-2,2-dimethylchromene (Hales and Mittler, 1981).

In Orthoptera, exposure of 4th instar nymphs of the locust *S. gregaria* to 15 µg/cm^2 of PI1 induced precocious adults (Salem *et al*., 1982 a). Different doses of PI or PII (20-100 µg/insect) were topically applied onto the 3rd instar nymphs of Mediterranean splendid grasshopper *Heteracris littoralis*. Different degrees of precocious metamorphosis were irreversible with time, at the subsequent moults (Alrubeai, 1986). Pener *et al.* (1986) treated the late embryos or newly hatched 1st instar nymphs of the locust *L. migratoria* with precocenes and observed precocious appearance of adult features after the second larval molt, but not earlier. Exposure of 2nd instar nymphs of the grasshopper *E. plorans* to a low dose of PII led to precocious moulting into 4th instar, skipping off 3rd instar. Also, exposure of 4th instar nymphs to PII, some treated nymphs precociously metamorphosed into adultoids, omitting the 5th instar (Ghoneim and Basiouny, 2017).

In respect of Coleoptera, topical application of PI or PII onto the 2nd larval instar of *L. decemlineata* led to early formation of pupal characteristic on larvae and formation of adultoids (precocious adults) (Farazmand and Chaika, 2008).

With regard to Diptera, treatment of *S. bullata* larvae with PII resulted in precocious pupation (Darwas *et. al*., 1990). In *S. ruficornis*, precocene treatment resulted in precocious metamorphosis due to JH deficiency because the precocene effects could be rescued by application of JH (Srivastava and Kumar, 1996). Precocious abnormal adultoids of *M. domestica* were observed after treatment of larvae with PII (Gaur and Kumar, 2009). Treatment of early and late 3rd instar larvae of the blowfly *C. megacephala* with PII resulted in the precocious metamorphosis (Singh and Kumar, 2011).

Apart from precocenes, many anti-JH compounds had been assessed on various lepidopterous species. With regard to the anti-JH activity of FMev, Farag and Varjas (1983) recorded precocious metamorphosis after topical application of FMev onto caterpillars of three late instars of *H. cunea*, In *M. sexta*, the 3rd instar larvae treated with FMev exhibited visible symptoms of JH deficiency following the moult to 4th instar, such as precocious pupation (Edwards *et al*., 1983). The synthesized (R)-(-)-FMev induced precocious metamorphosis in the 4th instar larvae of *B. mori* by skipping off the 5th instar (Shuto *et al*., 1988). Neck-ligated post-feeding last instar larvae of *S. mauritia* were topically treated with FMev. The treated larvae appeared with complete inhibition of metamorphosis (Balamani and Nair, 1989).

In respect of ETB and some of its analogues, Kuwano *et al*. (1988) synthesized ETB and bioassayed on the 3rd instar larvae of *B. mori*. ETB induced precocious pupation in the treated larvae. After topical application of ETB analogue ethyl 4-[4-methyl-2-(6-methyl-3-pyridyloxy)pentyloxy]benzoate onto 1-day old 3rd instar larvae of *B. mori*, Fujita *et al*. (2005) observed precocious metamorphosis of larvae. Fujita *et al*. (2007) synthesized two ETB analogues: Ethyl 4-[2-(6-methyl-3-pyridyloxy)hexyloxy]benzoate and ethyl 4-(2-phenoxyhexyloxy)benzoate which induced precocious metamorphosis in larvae of *B. mori*. KF compounds are structurally derived from ETB. Furuta *et al*. (2007) reported that KF-13S strongly

induced precocious metamorphosis in *B. mori*. Also, Hexyl (KF-13) and heptyl analogues induced precocious metamorphosis in *B. mori*, at low doses (Fujita *et al*., 2008).

Considering the synthetic imidazole compounds, KK-22 was reported to induce precocious pupation in *B. mori* (Asano *et al*., 1984b). However, there was no significant difference in the induction of precocious pupation in this insect among the administration methods (Asano *et al*., 1986). KK-42 caused precocious metamorphosis in *B. mori* when applied onto the penultimate instar larvae (Akai and Mauchamp, 1989). Treatment of *S. bullata* larvae with KK-110 or the benzodioxole compound J-2710 resulted in precocious pupation (Darwas *et. al.*, 1990). Lu and Li **(**1987) recorded the inducion of tetramolter silkworms into trimolters (precocious metamorphosis in silkworms) after treatment with the imidazole compounds SM1 and SDIII. Yoshida *et al*. (2000) synthesized 3-pyridine derivatives and evaluated their activities against *B. mori*. Among the tested compounds, 3-(2-methyl-l-phenyl-l-propenyl) pyridine induced precocious pupation after treatment of 4th instar larvae. The imidazole compound triflumizole induced the trimolter silkworm. Percentages of trimolter induced by the treatment in the 3rd instar were higher than those in the 4th instar treatment (Miyajima *et al*., 2001). In addition, topical application of fluorinated vinyl sulfoxides onto larvae of some Lepidoptera caused premature pupation that was recoverable by simultaneous application of the JHA farnesol (Cusson *et al*., 2013).

For interpretation of the induction of precocious metamorphosis in insects by anti-JH compounds, it was suggested that the apparent insensitivity of many holometabolous insects to precocene *in vivo* may not be due to the lack of intrinsic sensitivity of their CA to these compounds, but may be due to detoxification in tissues, like fat body (Soderlund *et al*., 1980). To solve the puzzle of molecular basis of JH action, Wilson (2004) reported that the effects of JH may be due to interference with the expression or action of certain genes, particularly the *broad* complex (*br*-C) transcription factor gene, that direct changes during metamorphosis, such as the pupal development. Therefore, JHAs or anti-JH compounds cause misexpression of *br*-C which then leads to improper expression of one or more downstream effector genes controlled by *br*-C gene products. In the hemimetabolous insects (no pupal stage), Erezyilmaz *et al*. (2006) determined the role of *br* in *O. fasciatus*. Induction of a precocious adult molt by application of PII to 3rd instar nymphs of *O. fasciatus* caused a loss of *br* mRNA at the precocious adult molt.

4.3.2. Failure of Some Anti-JH Compounds to Induce Precocious Metamorphosis:

It is important to point out that the induction of precocious metamorphosis in insects by anti-JH compounds have been observed for some but not all tested compounds or all treated insect species. Thus, a pertinent point of this article is to shed some light on the reported cases of failure to induce precocious metamorphosis. No precocious metamorphosis was induced in the sun pest *E. integriceps* after topical application of PI onto the nymphs (Tarrant *et al*., 1982); in the lawn armyworm *S. mauritia* after treatment of 6th instar larvae with single or repeated daily doses of PII (Mathai and Nair, 1984) and in the desert locust *S. gregaria* after topical application of nymphs with PII (Islam, 1995).

Apart from precocenes, no precocious metamorphosis was induced in the silkworm *B. mori* after treatment of 4th instar larvae with the synthesized compound (S)-(+)-FMev (Shuto *et al*., 1988). FMev doses were topically applied (once) onto 1-day-old larvae of the gypsy moth *Lymantria dispar*. All treated larvae on day-2 developed normally, with few exception of incomplete moulting to the last instar (Fescemyer *et al*., 1992). FMev could not induce the precocious metamorphosis in the

codling moth *Cydia pomonella* after treatment of 3rd and 4th instar larvae (Benz and Ren, 1986). Also, no anti-JH activity was exhibited by FMev in the non-lepidopterous species, such as those belong to orders Diptera, Coleoptera, Heteroptera, and Orthoptera (Menn, 1985). After treatment of the 3rd instar larvae of *B. mori* with the synthesized EMD or its analogues, no precocious metamorphosis was induced (Kuwano *et al*., 1988).

4.4. Can Anti-JH Compounds Exhibit a dual Effect (Anti-JH Activity and JH-like Activity)?

In insects, metamorphosis can be impaired after treatment with some IGRs. The major symptoms or features of the impaired metamorphosis have been described as inhibited pupation, blocked adult emergence, production of larval-pupal and/or pupal-adult intermediates, appearance of deformed larvae and/or pupae, production of giant larvae (superlarvae) and supernumerary larval instars (extra moult) as well as appearance of permanent larvae (as expression of suspended development). However, some of these features were observed in various insects as responses to the exogenous JH or treatment with JHAs or other IGRs, such as the green lacewing *Chrysoperla rufilabris* as response to fenoxycarb (Liu and Chen, 2001); *C. pipiens* as response to kinoprene (Hamaidia and Soltani, 2014); the pink bollworm *Pectinophora gossypiella* (Ghoneim *et al*., 2017a) and the olive leaf worm *Palpita unionalis* (Ghoneim *et al*., 2017b) as response to Novaluron.

It is known from the literature sources that few anti-JH agents can exhibit a dual effect on certain insects, i.e., anti-JH activity and JH-like activity, depending on some factors, such as the treated larval instar, the age of larvae and insect sensitivity as well as the time of treatment, the applied dose level, method of application and the proptery of the compound itself. For examples, precocene exhibited some JH-like effects on the brown planthopper *Nilaparvata lugens* (Pradeep and Nair, 1989). Some authors (Sparks *et al*., 1979; Staal, 1986; Riddiford *et al*., 1983; Kiguchi *et al*., 1984) reported a dual effect of ETB on *M. sexta* and *B. mori*, depending on the dose, because at low doses it induced precocious metamorphosis (a clear JH–deficiency symptom), but at higher doses it induced JH-like activity, since larval-pupal intermediates had been observed. Staal *et al*. (1981) and Staal (1986) recorded weaker anti-JH effect of EMD than ETB against the lepidopterous insects *M. sexta* and *H. virescens*. It too shows mixed JH activity and anti-JH activity.

Among the structurally derived compounds from ETB, some KF compounds had been prepared. Furuta *et al*. (2010) designed new anti-JH agents among which KF-38 was found to possess a dual property, strong anti-JH activity and weak JH-like activity. Hexyl (KF-13) and heptyl analogues, which induced precocious metamorphosis in *B. mori* at low doses, had relatively high JH activity (Fujita et al., 2008). In addition to precocenes, some authors (El-Gammal, 1983; Salem *et al*., 1982a; Ghoneim, 1988; El-Gammal *et al*., 2004) recorded a dual effect of cycloheximide on *S. gregaria* nymphs: JH-like activity and anti-JH activity, depending on the applied dose. Recently, Basiouny and Ghoneim (2017) recorded the failure of FMev to exhibit anti-JH activity but a JH-like activity against larvae of *S. littoralis*.

In the context of the JH-like activity of certain anti-JH compounds in some cases, production of larval-pupal intermediates was recorded in *S. litura* after treatment of larvae with PI, PII or ethoxyprecocene (a synthetic analog of PII) (Srivastava and Kumar, 1999); in the wasp *M. rufiventris* parasitizing its host *S. littoralis* after treatment of this host with PI or PII (Khafagi and Hegazi, 1999); and in *S. mauritia* after treatment of last instar ligated larvae with the compound EMD (Balamani and Nair, 1989). Production of pupal-adult intermediates was recorded in *P. ricini* after

treatment of larvae with PII (Khan and Kumar, 2000); in *S. ruficornis* after treatment of larvae with PII (Khan and Kumar, 2005) and in *C. megacephala* after treatment of 0-96 hr-old pupae with PII (Singh and Kumar, 2011). In addition to precocenes, Balamani and Nair (1989) investigated the ability of EMD to prevent the JH dependent phase of larval-pupal transformation of *S. mauritia*. EMD-treatments of the last instar ligated larvae with lower doses induced the formation of larval-pupal intermediates whereas those treated with higher dose moulted into either pupae or larval-pupal intermediates. To understand the production of intermediate forms in insects, the induction of a rapid molt did not provide enough time for the completion of larval-pupal transformation. Thus, the insects molted to non-viable forms between the stages (Tateishi *et al*., 1993). Molts induced during the early phase of the last instar produce larval-like individuals, while those formed in the late phase generate pupal-like individuals (Eizaguirre *et al*., 2007).

In this context, also, the production of extra molt (supernumerary larval instar) depends on some of the aforementioned factors. However, the extra moult and production of supernumerary larval instar evidently indicated a high juvenilizing activity of the tested compound. Induction of supernumerary nymphal instar was reported for some insects as response of JH-like activity of a very few of anti-JH compounds, such as *S. gregaria* after exposure of the 2nd instar nymphs to PII (at 15 µg/cm^2) (Salem *et al*., 1982a) and the white-backed rice planthopper *Sogatella furcifera* after feeding of the newly hatched nymphs on rice plants treated with 500 ppm of PII (Miyake and Mitsui, 1995).

In contrast to the induction of precocious development and production of intermediates and extra moult in insects by certain anti-JH compounds, a feature of the suspended development is known as "permanent larvae". After exposure of the newly moulted 2nd instar nymphs of the grasshopper *Euprepocnemis plorans* to 20 µg/cm^2 of PII, some 'permanent nymphs' were induced in 2nd and 4th instars (Ghoneim and Basiouny, 2017).

4.5. Deranged Morphogenesis:

After treatment of an insect with JHA or IGR, in general, the production of pupal and/or adult deformities usually indicates the interference of this compound with the morphogenesis program. For examples, deranged pupal morphogenesis was reported in some insect species by different IGRs, such as the red flour beetle *Tribolium castaneum* by cyromazine (Kamaruzzaman *et al*., 2006), *S. frugiperda* by methoxyfenozide (Zarate *et al*., 2011), the rice moth *Corcyra cephalonica* by fenoxycarb (Begum and Qamar, 2016), *P. gossypiella* (Ghoneim *et al*., 2017a) and *P. unionalis* (Ghoneim *et al*., 2017b) by Novaluron.

As reported in the current literature, some anti-JH compounds have disrupting the insect morphogenesis, by a mechanism, resulting in malformation of the subsequent stages. For examples, production of abnormal puparia was recorded in *S. ruficornis* after treatment of the last instar larvae with PI, PII or PIII (Srivastava and Kumar, 1996); *P. dux* after treatment of the 3rd instar maggots with highest dose of PII (Nassar *et al*., 1999); and *M. domestica* after treatment of larvae with PII (Gaur and Kumar, 2009). Production of malformed pupae was observed in *S. litura* after treatment of larvae with PI, PII or ethoxyprecocene (a synthetic analog of PII) (Srivastava and Kumar, 1999) and in the parasitic wasp *M. rufiventris* after treatment of its host *S. littoralis* with PI or PII (Khafagi and Hegazi, 1999, 2004). Also, various morphogenic abnormalities and morphological deficiencies had been observed in *A. thalassinus* after topical application of PIII onto eggs or 5th instar nymphs (Osman, 1988); in *T. molitor* after topical application of several chromene derivatives onto

larvae (Roberto *et. al*., 1998); in *E. integriceps* after treatment of larvae with PI (Amiri *et. al*., 2010).

In addition to precocenes, FMev induced various morphogenic abnormalities and death before pupation in *S. mauritia* (Nair and Rajalekshmi, 1988). Application of FMev onto last instar larvae of the cabbage looper moth *Trichoplusia ni* resulted in the formation of abnormal pupae (Newitt and Hammock, 1986; Sparks *et al*., 1987). Its JH deficiency effects, both *in vivo* and *in vitro*, could be fully deleted by co-administration of JHAs *in vivo* and JH biosynthesis is restored by farnesoic acid *in vitro* (Cusson *et al*., 2013). Four doses of FMev had been topically applied onto the newly moulted 5th or 6th (last) instar larvae of *S. littoralis* by Basiouny and Ghoneim (2017). Treatment of 6th instar larvae resulted in the production of morphologically abnormal pupae, at the higher three doses. Sparks *et al*. (1987) observed morphological aberrations in *T. ni* after treatment of last instar larvae with compactin analogues L-643, 049-01K01 and DPH (3,3-dichloro-2-propenyl hexanoate).

5. Disruptive Effects of Anti-JH Compounds on Adult Performance in Insects:

The present article focuses on the most important aspects of the adult performance, *viz*., emergence, survival, morphogenesis and longevity, including the total longevity and its main compartments: pre-oviposition period (ovarian maturation period in many insects), oviposition period (sometimes known as 'reproductive life-time') and post-oviposition period. Disturbances of these parameters of the adult performance by the anti-JH compounds should be discussed in this section.

5.1. Blocked Adult Emergence:

The adult emergence in insects, as a crucial metamorphosis process, is regulated by the eclosion hormone. The disturbance of this hormone results in partial or complete blocking of the adult appearance. It is known from the literature sources that the adult emergence of many insect species was partially or completely blocked after larval treatment with various JHAs, such as the vinegar fly *Drosophila melanogaster* after topical application of 3rd instar larvae with pyriproxyfen (Benseba *et al*., 2015); the mosquitoes *C. quinquefasciatus* and *Ae. albopictus* after larval treatments with pyriproxyfen or methoprene (Khan *et al*., 2016). Moreover, adult emergence was completely prevented in *C. cephalonica* after treatment of 4th instar larvae with fenoxycarb (Singh and Tiwari, 2016).

Depending on the currently available literature, also, few studies have examined the effects of anti-JH compounds on adult emergence in insects. Among these few studies, Khan and Kumar (2005) recorded an inhibition of adult emergence in flesh fly *S. ruficornis* after larval treatment with PII. The adult emergence of the blowfly *C. megacephala* was blocked after treatment of early and late 3rd instar larvae with PII (Singh and Kumar, 2011). Recently, Ghoneim and Bosly (2017) topically applied five sublethal doses of PI (once) onto 1-day old larvae of 5th and 6th (last) larval instars of *S. littoralis*. They recorded a slight or drastic blockage of adult emergence, depending on the dose and larval instar under treatment. Apart from precocenes, the 3rd instar larvae of *B. mori* ingesting diet containing 50-200 ppm of the anti-JH compound KK-22 (a terpenoid imidazole) metamorphosed to pupae but failed in the adult emergence (Asano *et al*., 1984a). Another terpenoid imidazole, KK-42, was reported to inhibit the adult emergence of the same silkworm when applied to newly formed pupae (Kadono-Okuda *et al*., 1987). Four doses of FMev had been topically applied (once) onto the newly moulted 5th or 6th (last) instar larvae of *S. littoralis*. The adult emergence was considerably blocked (Basiouny and Ghoneim, 2017).

As previously mentioned (section of 'precocious metamorphosis'), the effects of JH may be due to interference with the expression or action of the *broad* complex (*br-*

C) transcription factor gene, that direct changes during metamorphosis (Wilson, 2004). Therefore, JHAs or anti-JH compounds cause misexpression of *br*-C which then leads to improper expression of one or more downstream effector genes controlled by *br*-C gene products. On this molecular basis, symptoms of impaired metamorphosis, like blocking of adult emergence, can be explained (Nandi and Chakravarty, 2011).

5.2. Affected Adult Survival:

The available literature has been enriched with many reported results of IGRs' toxicities against adults of several insect species, such as *S. littoralis* after treatment of larvae with novaluron (Hamadah *et al*., 2015); the onion fly *Delia antique* after treatment of larvae with pyriproxyfen (Zhou *et al*., 2016); *P. gossypiella* after treatment of the newly hatched larvae with novaluron (Hassan *et al.*, 2017) and *P. unionalis*, after treatment of newly moulted last instar larvae with 0.10 and 1.00 ppm of novaluron (Hamadah *et al*., 2017). In contrast, very few studies have examined the effects of anti-JH compounds of the adult survival. Different doses of PII were topically applied to the 3rd instar larvae of *P. dux*. Toxic effects were observed on adults, in a dose-dependent course (Nassar *et al*., 1999). Injection of a single dose (50 or 150 µg) of PII into 4-day old adults of *S. gregaria* led to high mortality of adults (Tawfik et al., 2014). Five sublethal doses of PI had been topically applied (once) onto 1-day old larvae of 5th or 6th (last) larval instar of *S. littoralis*. PI exhibited a slightly extended toxic effect on the adult females only with the higher two doses (Ghoneim and Bosly, 2017).

Needless to say the adult life in insects depends on healthy immature stages. Digestive disorders, such as starvation, metabolism disturbance and degeneration of peritrophic membranes, as well as accumulation of faecal materials at the hindgut, may be the cause of adult mortality (Soltani, 1984). Also, the adult mortality, after treatment of larvae with anti-JH agents, can be explained by the retention and distribution of these compounds in the insect body as a result of rapid transport from the gut by direct and rapid transport *via* the haemolymph to other tissues, and/or by lower detoxification capacity of adults against the tested compounds (Osman *et al*., 1984). However, for interpretation of adulticidal effects of IGRs on some insects see Kartal *et al*. (2003).

5.3. Impaired Adult Morphogenesis:

Impaired adult morphogenesis, as expressed in the production of deformed adults after larval treatment of various insects with different JHAs, is widely reported in the available literature, such as *T. castaneum* and *T. confusum* after treatment with cyromazine (Kamaruzzaman et al., 2006); *E. integriceps* after treatment with pyriproxyfen (Mojaver and Bandani, 2010); *C. cephalonica* after treatment with fenoxycarb (Begum and Qamar, 2016); *etc*. With regard to anti-JH compounds, some results of their disruptive effects on adult morphogenesis in different insects can be reported herein. Adult malformations were observed in *P. dux* after topical application of PII onto the 3rd instar larvae (Nassar *et al*., 1999); *P. ricini* after topical application of PII onto larvae (Khan and Kumar, 2000); *S. ruficornis* after topical application of PII onto larvae (Khan and Kumar, 2005); *C. megacephala* after topical application of PII onto the early and late 3rd instar larvae (Singh and Kumar, 2011); *S. littoralis* after larval treatment of with PI and PII (Khafagi and Hegazi, 1999); *L. decemlineata* after topical application of PI and PII onto 2nd instar larvae (Farazmand and Chaika, 2008); *M. domestica* after treatment of larvae with PII (Gaur and Kumar, 2009) and *S. gregaria* after injection of a single dose (50 or 150 µg) of PII into the 4-day old adults (Tawfik *et al*., 2014). Recently, Ghoneim and Bosly (2017) topically applied five sublethal doses of PI onto 1-day old larvae of 5th and 6th (last) larval instars of *S.*

littoralis and observed some adult deformities after treatment of 6th instar larvae. In addition, the development of some adult structures and organs, as affected by anti-JH compounds, had been investigated. After treatment of 4th instar or 5th instar larvae of *D. koenigii* with certain doses of PII or the precocenoid compounds 6-hydroxy-DMC and 6-bromo-DMC, the emerged adults appeared with small pale body and underdeveloped wing pads/wings (Banerjee *et al*., 2008). Treatment of 5th instar larvae or prepupae of large fruit-tree tortrix *Archips podana* with 300, 450, and 600 µg precocene/insect, morphogenesis of the adult antennae was deranged (Triselyova, 2012).

5.4. Disturbed Adult Longevity:

After the attainment of sexual maturity, insects often show degenerative changes in some tissues and organs which can be called 'senility' or 'aging'. The affected adult longevity can be considered as an informative indicator for the adult aging, i.e., prolongation of longevity may denote a delay of aging and *vice versa*, although the death is usually the density of all creatures (Ghoneim *et al*., 2015; Hamadah *et al*., 2017; Tanani and Ghoneim, 2017)

The available literature contains contradictory results of effects of JHAs, or IGRs in general, on the adult longevity in insects. The total adult longevity in some insects was shortened after larval treatment with some IGRs, such as *S. littoralis* by methoxyfenozide (Pineda *et al*., 2009) and novaluron (Hamadah *et al*., 2015); *S. exigua* by methoxyfenozide (Luna *et al*., 2011) and *G. pyloalis* by lufenuron (Aliabadi *et al*., 2016). On the contrary, adult longevity in other insects was prolonged after larval treatment with some IGRs, such as *P. gossypiella* by chromafenozide (Kandil *et al*., 2012) and pyriproxyfen (Sabry and Abdou, 2016) and the mustard aphid *Lipaphis erysimi* by pyriproxyfen (Liu and Chen, 2001).

With regard to the effects of anti-JH compounds on the adult longevity in insects, the available literature contains rarely reported results. After topical application of PII onto the 3rd instar larvae of *P. dux*, the total adult longevity was significantly shortened (Nassar *et al*., 1999). After topical application of the dose of 25 mg l^{-1} of the precocenoid compound 6-hydroxy-DMC onto the 5th instar nymphs of *D. koenigii*, the emerged adults lived shorter longevity than the control adults (Banerjee *et al*., 2008). Khafagi and Hegazi (2004) investigated the effects of PI and PII on the parasitoid wasp *M. rufiventris* after topical treatment of the host larvae of *S. littoralis*. Longevity of the parasitoid adult females was shortened. In a study conducted by Ghoneim and Bosly (2017), five sublethal doses of PI had been topically applied onto 1-day old larvae of 5th or 6th (last) larval instars of *S. littoralis*. The emerged adult females spent longer longevity than their control congeners. Also, both pre-oviposition and oviposition periods had been slightly, or considerably, shortened.

The affected total longevity of adult females in insects may be attributed to the interference of anti-JH compounds with the hormonal regulation of adult longevity since a close relation between certain hormones and adult longevity was reported in some insects, such as *Drosophila* (Broughton *et al*., 2005; Carbone *et al*., 2006; Chamseddin *et al*., 2012). In insects, it has been reported that the fat body serves many important functions (Arrese and Soulages 2010). Therefore, it is not surprising to suggest the occurrence of a longevity mechanism within the fat body (Hwangbo *et al*. 2004). However, the exact mode of action of anti-JH compounds on the biochemical sites in adults is hitherto unknown.

6. Anti-gonadotropic Activity of Anti-JH Compounds Against Insects:

As previously reported in the present article, JH, produced by CA in insects, is an important regulator of development and physiology in immatures. In adults of many

insect species, JH takes on functions other than development regulation, such as reproductive physiology. JH is responsible for protein metabolism specifically needed for the egg maturation. Yin *et al*. (1990) reported that vitellogenesis in most insects depends on the vitellogenin production by the fat body and/or follicle cells which are promoted by ecdysteroids, JH, or both in addition to other hormones. In their study, Yamamoto *et al*. (2013) reported that the reduced JH limits the reproduction by inhibiting the production of yolk-filled eggs in *D. melanogaster*, and this may arise because JH is required for the post-eclosion development of the vitellogenin-producing adult fat body.

IGRs or JHAs, in particular, have been reported to cause sterility in insects or reduce their fecundity. However, effects of IGRs on the insect reproduction can be grouped into: 1) reproductive behaviour, 2) oviposition, 3) egg hatchability (ovicidal and embryocidal), and 4) sterilization of adults (Mondal and Parween, 2000; Ghoneim *et al*., 2014b).

Shortly, JH functions as gonadotropin in insect adults (Amsalem *et al*., 2014a). Therefore, a JH deficiency, caused by anti-JH compounds, can affect some or all of the reproductive processes. For examples, reproductive potential of the parasitic wasp *M. rufiventris*, reared on its host *S. littoralis*, was reduced after topical application of PII onto larvae of the host (Khafagi, 2000). After application of compactin on virgin females of *B. germanica*, gonotrophic cycle was significantly delayed (Belles *et al*., 1988). The synthetic activity of male accessory reproductive glands of *S. litura* was partially blocked by cycloheximide treatment (Sridevi and Ray, 1988). Topical treatment of the adult females of *P. americana* with FMev led to delay of the production of oöthecae (Edwards *et al*., 1985). In contrast, precocene failed to exhibit specific anti-gonadotropic effect on the mosquito *Ae. aegypti* (Kelly and Fuchs, 1978).

6.1. Oocyte Growth and Ovarian Maturation:

As reported by many authors (Bownes, 2004; Flatt *et al*., 2005; Raikhel *et al*., 2005; Schwedes and Carney, 2012), there is a direct correlation between CA activity and the oocyte growth and ovarian maturation, in part through its regulation of yolk protein uptake while ecdysone, derived from the follicle cells, induces yolk protein synthesis in fat bodies. In adults of various insect species, treatment with an appropriate dose of precocenes prevents the ovarian maturation because it selectively destroys CA resulting in JH deficiency. Meanwhile, replacement therapy of JH or JHA restores, to some extent, the normal ovarian maturation (Woodard and Rankin, 1980; Kumar and Khan, 2004).

There is a large body of literature on the inhibitory activity of different anti-JH compounds against oocyte growth and ovarian maturation in many insects. In hemimetabolous insects, precocene suppressed the development and maturation of ovaries, such as *Diploptera punctata* (Feyereisen *et al*., 1981), *O. fasciatus* (Masner *et al*., 1979) and *Nilaparvata lugens* (Ayoade *et al*., 1996). For some detail, after exposure of the *D. melanogaster* adult females to PI and PII, the number of vitellogenic oöcytes was reduced in a dose-dependent manner at 43 hr after exposure. In addition, precocene directly acts on the CA since it inhibited the oocyte development in decapitated females (Wilson *et al*., 1983). The effects of PII on an apterygote insect were investigated by Bitsch and Bitsch (1984) for the first time in adult females of the firebrat *Thermobia domestica*. Depending on their results, a single application of 10 μg/insect, at the beginning of the post-ecdysial period, onto the non-inseminating adult females caused inhibition of oöcyte maturation. The ovarian maturation in the grasshopper *H. littoralis* was inhibited after topical application of PII (doses of 20-100 μg/insect) onto the 3rd instar nymphs (Alrubeai, 1986). In blow fly

Phormia regina, oocyte development was drastically retarded after treatment with PII and application of a JHA methoprene reversed the the inhibitory effects of precocene on the oocyte development (Yin *et al*., 1989).

Application of two sequential doses of PII onto the young-adults of face fly *Musca autumnalis* led to inhibition of vitellogenesis (Burks *et al*., 1992). The ovarian maturation in *M. domestica* was retarded after topical application of PII (20 μg/fly) onto the newly-emerged females (Li *et al*, 1993). It appeared that precocene caused inhibition of development of vitellogenic oocyte of *Sarcophaga ruficornis* due to deficiency of JH (Srivastava and Kumar, 1996). The oocyte growth and ovarian maturation in *N. lugens* had been inhibited after exposure of 5th instar nymphs to different doses of the PII (Pradeep and Nair, 2000a). To a great extent, similar results had been obtained after topical application of PII onto 0-, 1- and 2-day old eggs of the red cotton stainer bug *Dysdercus cingulatus* (Gayathri-Elayidam and Muraleedharen, 2001). In a wild-type strain of *D. melanogaster*, PI reduced the ovarian maturation (Ringo *et al*., 2005). Also, treatment of the newly emerged adult females of *S. ruficornis* with PII resulted in suppression of different processes in ovaries, such as egg chamber development, oocyte growth and uptake of yolk granules (Kumar and Khan, 2004). Injection of PI restrained the ovarian maturation of short-winged females of the wing dimorphic cricket *Velarifictorus ornatus* when the dosage was over 50 μg, but had no effect when the dosage was lower (Zhao and Zhu, 2013).

Apart from precocenes, the ovarian maturation in *B. mori* was retarded after treatment of the newly formed pupae with the imidazole compound KK-42 (Kadono-Okuda *et al*., 1987). After application of compactin on the virgin females of *B. germanica*, gonotrophic cycle was significantly delayed (Belles *et al*., 1988). The anti-gonadotropic activity of FMev was evaluated against *M. sexta* after injecting only very high dose (2.5 mg/adult) into the adult females 1-2 h after emergence. The oogenesis was inhibited (Quistad *et al*., 1981). The FGL-amide AST neuropeptidemimic, H17, was found quite potent as an anti-JH compound but able to inhibit the basal oocyte growth in *D. punctata* (Bendena and Tobe, 2012).

6.2. Oviposition Efficiency:

In insects, the oviposition rate can be used as an informative indicator for the oviposition efficiency. The oviposition rate of different insect species regressed as a response to various IGRs, such as *S. littoralis* as a response to tebufenozide (Bakr *et al*., 2005) and Novaluron (Ghoneim *et al*., 2014b); *S. gregaria* as a response to tebufenozide (Al-Dali *et al*., 2008); the cowpea seed beetle *Callosobruchas maculates* as a response to cyromazine (Al-Mekhlafi *et al*., 2011); *P. gossypiella* as a response to novaluron (Hassan *et al*., 2017) and *P. unionalis* as a response to methoxyfenozide (Hamadah *et al*., 2017). Effects of anti-JH compounds on this important reproductive parameter had been scarcely reported in the current literature. Exposure of *D. melanogaster* females to 0.14 μmol of PI resulted in remarkably regressed oviposition rate (Ringo *et al*., 2005). Larval treatment of *E. integriceps* with PI led to decreasing egg-laying rate (Amiri *et. al*., 2010). After topical application of PI onto 5th instar larvae of *S. littoralis*, the oviposition rate was drastically regressed only at the lower two doses. After treatment of 6th instar larvae with PI, the oviposition rate was remarkably depressed in a dose-dependent course (Ghoneim and Bosly, 2017). The prohibited oviposition efficiency may be explained as a result of the inhibition of ovarian DNA synthesis or the interference of IGRs or anti-JH compounds with vitellogenesis *via* certain biochemical processes. However, these compounds may exert a reverse action to those exerted by the ecdysteroid agonists which stimulate the neurosecretory cells to release a myotropic ovulation hormone (Parween *et al*., 2001).

6.3. Reproductive Capacity:

The third pertinent point in this context is the reproductive capacity including fecundity (mean number of eggs/female) and fertility (hatching percentage of eggs laid by female). The effects of anti-JH compounds on these reproductive parameters should be reviewed as follows.

6.3.1. Fecundity:

Treatment of immatures of some insects with precocenes or other anti-JH compounds resulted in inhibition of fecundity. On the basis of the available literature, treatment of female crickets *Acheta domesticus* and *Nemobius fasciatus*, beginning 12 hr after adult emergence, with PI or PII resulted in decreasing of egg production, in a dose-dependent course (Bradley and Haynes, 1991). Topical application of PII (doses 0.125 and 0.0625 mg) onto the 3rd instar larvae of *P. dux* inhibited the female natality (Nassar *et al*., 1999). Exposure of 5th instar nymphs and newly ecdysed brachypterous females of *N. lugens* to different doses of the PII resulted in fecundity reduction, in a dose-dependent manner (Pradeep and Nair, 2000a). Repeated daily topical application of PI or PII onto *S. littoralis* larvae led to reduction in fecundity of its parasitic wasp *M. rufiventris* (Khafagi and Hegazi, 2004). After treatment of *E. integriceps* nymphs with PI, fecundity of adult females was reduced (Amiri *et al*., 2010). According to Ghoneim and Bosly (2017), sublethal doses of PI had been topically applied onto 1-day old larvae of 5th or 6th (last) larval instars of *S. littoralis*. The fecundity of adult females was dramatically reduced. On the contrary, precocenes failed to affect the female fecundity of some insects, such as the blood-sucking bug *Panstrongylus megistus* after treatment of males with PII or ethoxyprecocene II (Cavalcante and Regis, 1992).

Apart from precocenes, FMev was reported to exhibit an anti-gonadotropic activity (as recorded in reduced egg production) against different insects, such as *Pieris brassicae* (Pieridae), *Cydia pomonella* (Tortricidae) and *Ephestia kuehniella* (Pyralidae), when these insects were treated in the sensitive period where the JH-dependent vitellogenesis takes place (Benz and Ren, 1986). Among ten anti-JH compounds tested by Connat (1988) against the cattle tick *Boophilus microplus* females, the most active compound was FMev which caused reduction in fecundity at doses as low as 5 μg. The anti-gonadotropic effect of FMev on the tick *Ornithodoros moubata* was studied by Connat and Nepa (1990). Depending on their results, topical application of dose 100 μg onto the mated females 1 day after feeding led to reduction of fecundity in the ovipositing treated females. As found by Lehmann *et al*. (2015), application of the anti-JH compund H17 reduced the fecundity of *L. decemlineata*.

6.3.2. Fertility and Sterility:

As reported in the early literature, sterility was recorded in female offsprings of the tse tse fly *Glossina morsitans* after treatment of parent females with precocenes (Samaranayaka-Ramasamy and Chaudhury, 1982). PIII was topically applied onto eggs, 5th instar nymphs, and newly hatched adult females of the grasshopper *A. thalassinus*. Sterile adult females had been recorded (Osman, 1988). In the late two decades, the phenolic chromene and a hydroxyethyl chromene (isolated from *A. conyzoides*) were found to cause sterility in the bug *Dysdercus flavidus* (Okunade, 2002). The hatching percentage of laid eggs of *E. integriceps* was reduced after treatment nymphs with PI (Amiri *et al*., 2010). PII treatment of 0-96 hr-old pupae of *C. megacephala* resulted in the metamorphosis of sterile adultoids (Singh and Kumar, 2011). Recently, Ghoneim and Bosly (2017) topically applied five sublethal doses of PI onto 1-day old larvae of 5th or 6th (last) larval instars of *S. littoralis*. They recorded complete sterility of adult female moths after treatment of 5th instar larvae with

different doses but complete sterility after treatment of 6th instar larvae only with only 150 and 30 µg/larva. In contrast, precocenrs failed to affect the egg fertility of a few number of insects, such as *P. megistus* in which no effect was observed on the egg hatching after topical application of PII or ethoxyprecocene II onto males (Cavalcante and Regis, 1992). Apart from precocenes, the anti-JH compound, polyacetylenic sulfoxide, was reported to produce sterile adults in *O. fasciatus* (Bowers and Aregullin, 1987). FMev exhibited powerful anti-gonadotropic activity against *S. littoralis*, since complete sterilization was recorded after topical treatment of newly moulted 5th or 6th (last) instar larvae with FMev. It may be considered as chemosterilant against this pest (Basiouny and Ghoneim, 2017). The mode of action of anti-JH compounds on the fertility of some insects could be partially discussed by some authors (Sevela and Davey, 1990; Sevela *et al*., 1995).

7. Roles of Anti-JH Agents in the Insect Polyphenism:

7.1. Hemiptera/Homoptera-wing Dimorphism:

Aphids (Homoptera) live in all climatic regions covering temperate to tropical conditions. They are detrimental pests of grain crops around the world (Hollis and Eastop, 2005). The serious negative economic impacts of aphids are mostly due to their transmission of phytopathogenic viruses and high reproduction rate (Figueroa *et al*., 2007). In nature, life cycle of aphids comprises a range of strategies that allows them to survive the cold winters as overwintering eggs, increase their population when resources are available in spring and autumn (as parthenogens) and migrate to new hosts when food sources are unfavorable (Dixon, 1987). The aphid life cycles can include at least two different forms of polyphenism, (1) cyclic switching between asexual reproduction (viviparous parthenogenesis) and sexual reproduction (associated with the overwintering after fertilization), and (2) switching between a wingless morph (apterae), and a winged morph (alatae) capable of fly and dispersal. The switch from wingless to winged morphs can occur in two different situations in nature (for review, see Hartfelder and Emlen, 2012).

It is worth pointing out that aphids were the predominant model used during several decades to investigate the endocrine control of 'wing dimorphism'. The observation that wingless nymphs and adults are morphologically similar led early some researchers to suggest that high titer of JH induces the wingless nymphs to retain the juvenile characteristics in adults. Attempts to correlate the activity of the organs producing and secreting JH (CA), with the production of wingless morphs have yielded equivocal results. Several studies showed that 3rd - and 4th -instar nymphs without wing buds possess larger CA and subsequently high JH titer (Kennedy and Stroyan, 1959; Elliot, 1975; Hardie *et al*, 1985; Braendle *et al*., 2006).

As plentifully reported in the current literature, precocenes promote the production of alatae in some aphid species (Kambhampati et al., 1984), since exposure to these anti-JH compounds induced the production of winged offspring in *Acyrthosiphon pisum* and *Macrosiphum euphorbiae* (Hardie, 1986), as well as the prenatal PII application could induce the entire suite of characteristics found in the alatae (Hardie *et al*., 1995). On the contrary, the synthetic precocenoid, PIII, was reported to inhibit the production of winged morph, at least in *A. pisum* (Gao and Hardie, 1996).

These contradictory effects of precocenes on the induction of winged morph can be probably understood because their effects are not mediated by JH. Although PII is able to induce alate progeny in several aphid species, the majority of studies suggested that it fails to induce precocious development, the classic JH-mediated hallmark of precocenes (Hardie *et al*., 1996). Moreover, although the inhibition of alate production

caused by PIII is accompanied by precocious metamorphosis and destruction of CA (Hardie *et al*., 1996), the application of JH is capable of rescuing precocious metamorphosis without reversing the inhibition of winged morphs (Gao and Hardie, 1996). In many cases, JH-agonists (JHAs) or JH-antagonists affect on the alate form of aphids as a result of an abnormal disruption of metamorphosis (juvenilization) rather than induction of the apterous morph (apterization). In other cases, JH-agonists or JH-antagonists produce inconsistent effects, or no effects at all (Gao and Hardie, 1996).

In conclusion, results of several research works suggested that the precocenes exert their alate-promoting property on the wing polyphenism independently of JH, and instead depend heavily on the population density. The previously reported results for precocenes, as well as a dearth of clear positive evidence for regulation by JH, leave the issue of hormonal regulation of aphid wing-induction under debate (Hardie *et al*., 1995; Zera and Denno, 1997; Braendle *et al*., 2006).

Another point of interest is the wing dimorphism in planthoppers (Hemiptera). Wing dimorphism in these insects is known to be a common and ecologically important trait. Planthoppers often occur in both winged and wingless forms (Denno and Perfect, 1994). Also, adults of the brown planthopper *Nilaparvata lugens* can be either short-winged (brachypterous) or long-winged (macropterous). Long-winged adults possess long-distance migration ability, and could initiate populations in other new areas, creating difficulties in controlling these pests (Huang *et al.*, 2003). The endocrine regulation of wing polyphenism had been best studied in *N. lugens*. A number of studies indicated that the topical application of JH strongly redirected the development from long-winged to short-winged morph (Ayoade *et al*., 1999; Dai *et al*., 2001; Hartfelder and Emlen, 2012). According to results obtained by Ayoade *et al*. (1996) on two strains of *N. lugens* adults with specific wing form under highly crowded conditions over 70 generations, long-winged adult morph developed from presumptive short-winged morph after treatment with PII. The sensitive periods to PII, affecting wing dimorphism, differed between the two strains. PII induced formation of long-winged individuals in a genetic stock that normally produces short-winged individuals, and the effect of this antagonist could be obviated by simultaneous application of JH (Bertuso *et al*., 2002).

7.2. Orthoptera-phase Transition in Locusts:

Locusts (Acrididae) are among the most dangerous agricultural pests and have long served as a model for insect physiology, neuroscience, and behavior. Phase change in locusts lies at the heart of locust swarming and outbreaks because the migratory swarms are one of the world's most devastating plagues (Lindsey, 2002; Ceccato *et al*., 2007; Ghoneim, 2015). Phase polyphenism is common in several species of locusts, but the best studied locusts are the migratory locust *Locusta migratoria* and the desert locust *Schistocerca gregaria*. As pointed out by many authors (Tawfik *et al*., 1999; Pener and Simpson, 2009; Gordon *et al*., 2012; Harano *et al*., 2012), *S. gregaria* has two phases, solitary and gregarious, which differ considerably in many aspects including morphology, behaviour and physiology.

Gradual phase transition from solitary to gregarious morphs, and *vice versa*, was one of the earliest investigated types of polyphenism (Uvarov, 1921). In order to control the plague of locusts in recent years, many research studies have been devoted for finding the key factor(s) regulating phase transformation in *S. gregaria*. These studies have focused on the changes from gregarious to solitary phase, since only gregarious locusts form large migratory swarms capable of invading and inflicting serious damage to crops (for reviews see Pener and Simpson, 2009; Sword *et al*., 2010). The change in body color in locusts is a remarkable indicator during the phase

transition. Gregarious locusts display a contrasting pattern of black and orange, with little to no variation in pattern among individuals in the same crowd. Solitarious locusts are cryptic and range from green to brown depending on the external environmental factors, such as humidity and temperature (for detail, see Pener, 1991; Tanaka, 2006).

Although the present article was prepared for reviewing the anti-JH agents and their effects on different aspects of insects, it is important to shed some light on the endocrine regulation of phase transition in locusts, with special reference to *S. gregaria*. For some decades, the endocrine system, and in particular the CA (JH-producing organs) was suggested as the main control center (Couillaud *et al*., 1987). Allatectomy (microsurgerical removal of CA) resulted in no gregarious behavior in locusts (Richard *et al*., 2001). Such observation rationally explained the higher activity of CA in solitary *S. gregaria* causing higher titer of JH in haemolymph and a green colouration of the cuticle, but surgical implantation of CA or administration of JH restored yellowing (Uvarov, 1966; Pener and Lazarovici, 1979; Langewald and Schmutterer, 1995), i.e., the solitarious phase is characterized by a higher JH level than the gregarious phase (Dale and Tobe, 1986). This effect was demonstrated, also, in *L. migratoria* (Couillaud *et al*., 1987).

The mechanism(s) by which endocrine organs control the phase color polyphenism in *L. migratoria* and *S. gregaria* had been studied in detail. The JH is a key regulator of the induction of green body color (Applebaum *et al*., 1997). Implantation of extra CA, or injection of synthetic JH (or JHAs), induced the gregarious *L. migratoria* nymphs to turn green in colour. However, green solitarious nymphs lost their green color after being allatectomized or treated with PIII but did not develop the body coloration of gregarious nymphs (Pener *et al*., 1992). Tawfik *et al.*(1999) identified a dark-color-inducing neuropeptide, [His^7]-corazonin, from the corpora cardiaca of *S. gregaria* and *L. migratoria*. However, [His^7]-corazonin did not induce the bright yellow background body color characteristic of last instar gregarious nymphs of *S. gregaria* (Tanaka, 2001). In addition to the interaction between JH and [His^7]-corazonin, the control factors involved in the regulation of yellow coloration are still unknown. Several genes or metabolites have important roles in the regulation of locust phase change. Also, epigenetic mechanisms and non-coding RNAs have been implicated in the regulation of phase change in locusts, but their functional roles have not yet been determined (for review, see Wang and Kang, 2014). However, the involvement of endocrine factors in the regulation of locust phase transformation had been extensively reviewed (Tawfik and Sehnal, 2003; Pener and Simpson, 2009; Tawfik, 2012; Tawfik *et al*., 2014).

On the pheromone basis, the existence of 'gregarization pheromone' was postulated for phase transition in locusts (Nolte, 1963; Gillett and Phillips, 1977). In locusts, pheromone communication may be regulated by the neuroendocrine system (Tawfik and Sehnal, 2003; Pener and Simpson, 2009; Tawfik, 2012). Pheromone production in gregarious adult males of *S. gregaria* was shown to depend on the presence of CA (Loher, 1961; Norris and Pener, 1965; Amerasinghe, 1978). After topical application of JH III onto the gregarious 5th instar nymphs of *S. gregaria*, pheromone production was inhibited and the external colouration changed to the solitary character (Ismail *et al*., 1997). PII was topically applied by Tawfik *et al*. (2014) onto the last (5th) instar nymphs and injected into the newly emerged adults of gregarious phase of *S. gregaria*. Both application methods of PII resulted in fading of the yellow color of crowded adult males instead of the bright yellow color (characteristic of normal gregarious adult males). In conclusion, their results showed

that PII plays a role in the regulation of pheromone production in the desert locust *S. gregaria*.

As far as our literature survey could ascertain, very few studies examined the effects of anti-JH agents on phase transition in locusts. Injection of cycloheximide into 4th instar nymphs of *L. migratoria* led to the inhibition of JH esterase activity resulting in 5th instar nymphs with a solitary green colour, as a result to the high level of JH (Phillips and Loughton, 1976, 1979). A similar result was recorded in *S. gregaria* (El-Gammal, 1983). Also, El-Gammal et al. (2004) assessed cycloheximide against 4th instar nymphs of *S. gregaria* and obtained results suggesting the anti-JH activity in the 5th nymphal instar, but the lower doses (20, and 10 µg /insect) induced the solitary green colour, that considered as an indicator for the high level of JH in their haemolymph.

From the practical point of view, the elevation of the JH level in gregarious locusts should induce a solitarization tendency, and thus the locust invasion can be avoided, since the gregarious phase is responsible for swarming and subsequently the plague. The exact role(s) of precocenes and other anti-JH agants in the phase transition of locusts is still under debate!!

7.3. Hymenoptera-caste Differentiation in Social Insects:

Prior to the discussion of roles of anti-JH compounds in caste differentiation in social insects, it is important to emphasize that the caste differentiation in social insects has a necessary role in establishment of an effective division of labor. Improper regulation can lead to an over-abundance or disappearance of specific castes, resulting in an inefficient or even impossible colony tasks (Tarver *et al*., 2009). In various species of social insects, it has been found that the queen can help to maintain the reproductive division of labor through the emanation of specific signals, which indicates her greater fertility, and to whom the worker individuals respond by remaining sterile (Le Conte and Hefetz, 2008). It is thought that worker task specialization enhances colony efficiency and therefore, improves colony fitness (Waibel *et al*., 2006).

With regard to the caste polyphenism in ants, experimental results of JH application indicated that the high level of JH stimulates the queen development (Passera and Suzzoni, 1979; Wheeler, 1990; Hartfelder and Emlen, 2012). To regulate the caste of their brood, queens can use the *in situ* JH-III, in their eggs (Wheeler, 1986). Such maternal effect had been reported in the ant *Pheidole pallidula*, where topical application of JH-III onto queens was found to promote sexualization of the female brood, while PII prevented such sexualization (Passera, 1982). Also, PII application prevented the wing shedding in queenless alates of the red imported fire ant *Solenopsis invicta* but JH application rescued the dealation (Burns *et al*., 2002).

In respect of the caste determination in bees, social conditions have a strong impact on the endocrine system, and thus on the switch from worker to queen development in the individual larvae (Cnaani *et al*., 2000). The JH application experiments on bees revealed a prominent role of JH in the caste development (Hartfelder, 1990). As reported by some authors (Rachinsky, 1994; Rachinsky, 1996), a set of peptides, such as Manse- ATS-like peptide, from the brain and subesophageal ganglion as well as biogenic amines, may modulate JH biosynthesis to generate the caste-specific profile. On the other hand, it is difficult to assert that a Manse-ATS-like peptide involved in the regulation of CA activity during the critical stages of caste determination. Depending on the currently available literature, there are no studies revealing the role of anti-JH compounds in cast determination of bees, since PII did not play a role in queen induction in the honey bee *Apis mellifera*, and it also did not

interfere with growth of the developing larvae or adults (Dietz *et al*., 1979). Also, Fluri (1983) reported that PII has no anti-JH activity against adult honey bees.

To shed some light on the role of hormonal compounds, particularly the anti-JH compounds, in the cast determination of termites, termite caste differentiation can proceed along two routes; the imaginal (winged) or the apterous (wingless) route (Lainé and Wright, 2003; Miura, 2004). Caste polyphenism in termites differs from that of the holometabolous Hymenoptera in three important ways (for discussion, see Hartfelder and Emlen, 2012). JH has long been reported to play an important role in the caste differentiation. Nijhout and Wheeler (1982) proposed a model for caste differentiation of termites, in which continuous low JH titers would induce alate adult differentiation, while high JH titers followed by low titers would induce neotenic reproductive differentiation (Cornette et al., 2008). It has been hypothesized that termite soldiers may play a role in regulating worker differentiation to other caste phenotypes (Henderson, 1998).

Reducing effect of precocene on the soldier differentiation in termites was early studied (Krecek *et al*., 1981). Korb *et al*. (2003) investigated the influence of PI on the soldier development in the dry wood termite *Cryptotermes secundus*. Depending on their study, soldierless colonies produced fewer soldiers after treatment with PI. Hence, PI simultaneously promoted the development of adult traits, probably by reducing the JH level. Mao *et al*. (2010) assessed the effects of PI and PII on the soldier caste formation in the Formosan subterranean termite *Coptotermes formosanus*. According to their study, PI (but not PII) significantly delayed the formation of the first soldier and reduced the proportion of soldiers in the colony for 40 days. Their results may reflect the importance of PI in caste control and a reduced importance in biogenic amines to the synthesis or suppression of JH in termites. On the other hand, Gotoh *et al*. (2008) evaluated the effects of precocenes on the CA and the JH titer in the damp-wood termite *Hodotermopsis sjostedti*. They concluded that precocenes were not effective as anti-JH agents in the focal termite species.

8. Roles of Anti-JH Compounds in the Behavioral Patterns of Insects:

8.1. Behavioral Patterns of Non-Social Insects:

In the last few decades, a considerable research interest in the neuroendocrine or hormonal control of insect behavior had been achieved (Truman and Riddiford, 1974; Kimura *et al*., 2005; Cachero *et al*., 2010). Many authors (Walker, 1978; Rankin, 1980; Kight, 1998; Pathak and Bhandari, 2002; Ringo *et al*., 2005; Chen *et al*., 2005a) reported that precocenes affect several aspects of behavior in the non-social insect species, such as aggressive behavior, mating behavior, flight behavior, maternal defensive behavior, sexual behavior, etc. In most cases, not all the behavioral effects were averted by JH replacement therapy (Li *et al*., 1993). Roles of the anti-JH compounds for regulating selected behavioural patterns can be concisely discussed in the following items.

***Sexual Behavior*:**

Effective male ***courtship behavior*** is essential for successful reproduction in most animals and the study of this behavior allows vital insight into the regulation of complex behaviors (for reviews see Greenspan, 1995; Villella and Hall, 2008). Although the CA influence ***sexual receptivity*** in Diptera (Trabalon and Campan, 1984), their regulation of pheromone production had only been implicated through PII treatment of male *C. capitata* (Chang *et al*., 1984). In a wild-type strain of *D. melanogaster*, PI reduced the primary sexual receptivity of virgin females, while PII did not affect this behaviour. Exposure to 70-140 μmol of ethoxyprecocene (synthetic PII analogue) significantly reduced the sexual receptivity (Ringo *et al*.,

2005). A relation between JH and ***sex attractancy*** has been evident for some time. For example, PII was reported to suppress sex attractancy in cockroaches (Bowers *et al*., 1976) and in diamondback moth (Hsu and Chang, 1982). The sex attractancy of virgin male *C. capitata* was reduced by topical application of PII and this effect was recovered by later application of a JHA (Hsu and Chang, 1982). In *C. capitata*, also, anti-JH compounds, such as precocene, had been shown to interfere with JH production and subsequently affected the sex attractancy of males (Chang *et al*., 1994).

Effects of precocenes on ***copulation*** and ***mating*** had been studied in some insects. PII was topically applied to the last (5^{th}) instar nymphs or injected into the newly emerged adults of gregarious phase of *S. gregaria*. The adult males had been delayed, since started sexual behavior and mating between 25-30 days instead of 15-20 days of control congeners (Tawfik *et al*., 2014). Decreased JH in the apterous mutant of *D. melanogaster* (Ringo *et al*., 1991), or treatment of females with precocene led to reduction in the mating of females (Bilen *et al*., 2013). Argue *et al*. (2013) utilized methoprene and precocene to manipulate the JH levels in sexually immature males and females of *D. melanogaster* Treatment of females with precocene increased latency to copulation 5 and 8 days post-eclosion. In males, precocene decreased latency to copulation at the cusp of sexual maturity (3 days post-eclosion), yet the effect did not persist in older animals. In contrast, treatment of *O. fasciatus* adults with PII failed to affect the mating behavioral rhythms (Woodard and Rankin, 1980). Apart from precocenes, injection of Fluvastatin (anti-JH agent) into males of *A. ipsilon* caused a temporary inhibition of male responsiveness (Duportets *et al*., 1996). Injection of Fluvastatin into males of *A. ipsilon*, immediately after mating, disrupted the normal spermatophore transfer during the next mating of the injected males (Duportets *et al*., 1998).

***Feeding behavior*:**

To our knowledge, information concerning the effects of anti-JH agents on feeding behaviour of insects is scarce in the available literature. JH deprivation (by allatectomy) of adult *Culex* mosquitoes, shortly after emergence, was reported to block the initiation of biting behaviour, which was restored by the re-implantation of CA, or injection of exogenous JH. Thus, biting initiation may be a target for inhibition by anti-JH agents (Meola and Petralia, 1980). In contrast, PII failed to affect the feeding behavioral rhythms of *O. fasciatus* adults (Woodard and Rankin, 1980).

***Agonistic behavior*:**

Insect agonistic behaviour is any behaviour related to fighting but the term has been expanded to include threats, kicking, biting, chasing, displays, retreats, placation, and conciliation (for detail, see Sirugue *et al*., 1992; Moore *et al*., 1997). Depending on the currently available literature, the role of JH in the agonistic behavior of the insect adults had been intensively studied but the roles of anti-JH compounds had been rarely examined. However, the role of JH has always been suggested in some insects, such as in the primitive social wasps (Roseler, 1991), bumblebees (Bloch et al., 2000) and the highly social honeybees (Huang and Robinson, 1992). JH titers in the guard honeybees were found higher than those in all other middle-aged bees, and guard individuals exhibited low JH thresholds for the expression of aggression behavior (Breed *et al*., 1992; Huang *et al*.; 1994). Also, Pearce *et al*. (2001) reported that the JH titers were correlated with the aggressive behavior in different seasons. Chen *et al*. (2005a) studied the male conspecific agonistic behavior in the lobster cockroach *Nauphoeta cinereais*. Topical application of JH-III did not affect the determination of dominant

status. In contrast, a tendency for inhibition of a dominant status was induced by PII treatment. PII treatment, also, led to an acceleration of the onset of agonistic behavior.

***Flight activity and migratory behavior*:**

Caldwell and Rankin (1972) reported that JH significantly enhanced the proportion of *O. fasciatus* making long-duration tethered flights (are indicator of tendency to migrate) in a population. Later on, Rankin (1980) examined the effects of precocens on this aspect of behavior in *O. fasciatus*. Treatment of newly emerged adults with PI and PII resulted in an inhibition of long-term flight activity (presumed migratory) in both sexes. In the convergent lady beetle *Hippodamia convergens*, PII prohibited the flight activity for about 10 days but the application of the JHA methoprene onto precocene-treated beetles promoted the migratory behavior (Rankin and Rankin, 1980). In the bark beetle *Dendroctonus rufipennis*, precocene II delayed the flight muscle degeneration and subsequently promoted the flight activity (Sahota and Farris, 1980). Precocene treatment inhibited take-off behavior and suppressed the migratory flight behavior in the grasshopper *E. integriceps* (Polivanova and Triseleva, 1985). Apart from precocenes, Coats *et al*. (1987) investigated the effects of a JH mimic, methoprene and the anti-JH agent FMev on the flight behavior of Western corn rootworm *Diabrotica virgifera virgifera* (Coleoptera). The flight activity of FMev-treated mated, not virgin, females, first decreases and then increases, perhaps by producing intermediate JH levels.

***Aggregation behavior*:**

Depending on the current literature available to us, no research attention had been paid to examine the effects of anti-JH compounds on the aggregating behavior in insects. Whatever, aggregating behavior in the pine bark beetles *Ips* spp. depends on the aggregation pheromone. Biosynthesis of this pheromone is regulated by JH (Tillman *et al*., 2004). The experiments on desert locust *S. gregaria* showed that the aggregation pheromone was JH-dependent and individuals without CA (allatectomy) failed to perform their aggregating behavior (Ignell *et al*., 2001).

***Learning behaviour and memory*:**

Cycloheximide was originally isolated from the bacterium *Streptomyces griseus* (Siegel and Sisler, 1963; Baliga *et al*., 1969). In insects, the interference of cycloheximide with the hormonal regulation of developmental processes and metamorphosis was studied. For examples, Ferkovich *et al*. (1977) reported that cycloheximide inhibited JH-binding protein in the tissue culture of the Indian meal moth, *Plodia interpunctella* fat body. So, general esterases could degenerate JH causing a deficiency in its level. Injection of cycloheximide into adults of the American grasshopper, *Schistocerca americana* resulted in a significant reduction of the grasshopper learning capacity against electric shocks, indicating that avoidance learning was associated with a significant increase in the levels of RNA and protein synthesis (Punzo, 1980). After injection of cycloheximide into the head capsule of adults of the mealworm beetle, *Tenebrio molitor* larvae and the bess beetle *Popilius disjunctus*, the neural protein synthesis was inhibited leading to a significant deterioration of the normal negative phototactic response of these insects (Punzo and Jellies, 1980). When the praying mantis *Stagmatoptera biocellata* was trained to attack a mobile star, memory was disrupted by an injection of cycloheximide shortly after training, but after two hours it becomes irressponsive to this compound (Jaffe, 1980). Wittstock *et al*. (1993) reported that the inhibition of brain protein synthesis by cycloheximide did not affect formation of long-term memory in honeybees after olfactory conditioning.

8.2. Behavioral Patterns of Subsocial Iinsects:

Parental care of offspring is a subsocial behaviour in Arthropoda, including insects. Among insects, order Heteroptera has been the focus of numerous studies, because some of them show maternal care (Smith, 1997). Parental care provides an effective protection of the offspring against the predators, parasites and parasitoids (Tallamy, 2001; Hanelova, 2005). Application of 50 µg JH-III onto adult females of the ring-legged earwig *Euborellia annulipes* (Dermaptera) on the day of oviposition resulted in shortening of the maternal care duration, compared with that of PII-treated females (Rankin *et al*., 1997). Kight (1998) used PII to investigate the relationship of CA activity to subsocial behaviour in the burrower bug *Sehirus cinctus* (Heteroptera). Egg-brooding females treated with PII (at least 70 µg) exhibited reliably depressed maternal defensive behaviour, but attraction to eggs was only depressed at higher dosages. This study provided the first clear evidence that insect parental behaviour can be modified by treatment with anti-JH agents. Tallamy *et al.* (2002) tested the hypothesis that high JH titers promote egg dumping behaviour, while low titers initiate maternal care in the lace bug *Gargaphia solani* (Hemiptera). PII changed the behaviour to egg guarders while egg guarders exposed to methoprene (JHA) became egg dumpers. These results suggest that hormones can trigger the expression of both egg dumping and egg guarding in *G. solani*.

8.3. Behavioral Patterns of Social Insects:

Some studies suggested the involvement of JH in the aggressive behavior of social insects, such as in the primitive social wasp *Polistes gallicus* (Roseler **1991**), buff-tailed bumblebee *Bombus terrestris* (Bloch *et al*. 2000), and the highly social insect *A. mellifera* (Hymenoptera)(Pearce *et al*. 2001). In contrast to the extensive study of precocene effects on different aspects in non-social insects, only very few studies examined its effect on social insects (Bloch *et al*., 2009; Amsalem and Hefetz, 2010). However, an interesting point in this context is to shed some light on anti-JH compounds in relation to some behavioral patterns in honeybees and social wasps.

According to Hartfelder (2000), JH does not function as a gonadotropin in honeybees, but rather regulates behavioral maturation and division of labor. In this honey bee, PII treatment caused atrophy of CA (JH-producing organs) in queen larvae (Goewie *et al*., 1978). In the bumblebee *B. terrestris*, the main effect of **PI** was found to reduce aggression in the most dominant workers and increase pheromone production in the least productive workers, while no specific changes were recorded for the other workers in the dominance hierarchy (Amsalem *et al*., 2014b).

As far as our literature survey could ascertain, no information was available for the effects of anti-JH compounds on the behaviour of social wasps other than the study of Oliveira *et al*. (2017). They found that the application of methoprene (JHA) caused workers of the common wasp *Vespula vulgaris* to acquire queen-like cuticular hydrocarbons, resulting in the excessive production of known queen pheromones as well as some compounds typically linked to worker fertility. In contrast, administration of PI had a tendency to exhibit the opposite effect.

9. Role of Anti-JH Agents in the Regulation of Diapause:

It may be important to give some information about diapause in insects. The ability to pass through adverse periods in diapause helps insects to exploit seasonally changing resources, to diversify in tropical habitats, and allows them to colonize temperate and Polar Regions. Understanding of diapause as a *process*, rather than as a *status*, is now widely accepted by different researchers (Denlinger, 2000; Hodek, 2002; Kostal, 2006).

From the physiological point of view, rapid life history evolution could proceed through changes in the hormonal machinery controlling life-history switches (Flatt and Heyland, 2011; Oostra *et al*., 2014). This is because of hormones coordinate cascades of downstream molecular and physiological changes (Zera, 2007). The diapause hormone (DH) is one of hormones regulating diapause in moths. Among members of the *Helicoverpa*/*Heliothis* complex (Lepidoptera) of agricultural insect pests, DH prompted the termination of pupal diapause. Zhang *et al*. (2011) developed a technique to convert the DH-agonist into a DH-antagonist that blocks the termination of diapause. Diapause induction in larvae of the parasitoid wasp *Nasonia vitripennis* (Hymenoptera) could not be brought about by topical application of precocene onto the maternal generation, or by treating eggs or larvae with this compound (De Loof *et al.*, 1979). The codling moth *Cydia pomonella* (Lepidoptera) exhibits a facultative diapause during the larval stage. Diapause-induced larvae pupated within 10 days of cocoon spinning when the state of induction was changed by injection with 100 µg of PII at the beginning of the last instar (Sieber and Benz, 1980).

In addition, precocene is apparently the only known chemical compound can break both prepupal diapause and pupal diapause in some insects. The pupal diapause in the bollworm *Helicoverpa armigera* (Lepidoptera) was terminated by PII and 20-hydroxyecdysterone, but not by methoprene (JHA), cyclic adenosine monophosphate or 5-hydroxytryptamine (Wang and Gong, 2001). PII was, also, found to induce a precocious termination of diapause in the prepupal stage of two species of aphid parasitoids *Aphidius mutricariae* and *Praon volucre* (Hymenoptera) (Polgar *et a1*. 1991). Apart from precocenes, diapause initiation in species which overwinter as adults, such as *L. decemlineata*, is strongly related to burrowing into the soil. In beetles preparing for diapause, JH-III levels should be low (De Kort, 1990). Thus, after the application of anti-JH agent H17 onto these individuals, declined JH-III level should have negligible additive effect on burrowing (Khan, 1988). On the contrary, increasing JH-III level, by application of a JHA, had strong effect on the same traits (Koopmanshap *et al*., 1989). Thereafter, Lehmann *et al*. (2015) reported that the application of H17 did not induce overwintering related burrowing.

10. Histopathological Effects of Anti-JH Agents on Some Tissues and Organs:

In general, precocenes directly and indirectly influence on tissues, organs and organ systems in some insects, such as *L. migratoria* (Orthoptera), *M. persicae* (Homoptera), *Trialeurodes vaporarium* (Hemiptera) and *A. mellifera* (Hymenoptera)(Triseleva, 2003). In the present article, it is important to review the histopathological effects of precocenes and other anti-JH agents on flight muscles, digestive organs, endocrine organs and reproductive organs in some insects.

***Effects on Flight Muscles*:**

Parts of a flight steering muscle in locusts degenerated shortly after the adult emergence while the JH titer is low (Meuser and Pflüger, 1998). Experimentally elevated JH titers prevent muscle degeneration (Rose, 2004). In contrast, application of PII onto adult females of the spruce bark beetle *Dendroctonus rufipennis* (Coleoptera) caused a temporary inhibition of flight muscle degeneration (Sahota and Farris, 1980). Also, administration of anti-JH agents enhanced the development of flight muscles in the adultiform desert locust *S. gregaria* (Orthoptera) (Wang *et al.*, 1993). On the other hand, effects of PI on flight muscles of the cricket *V. ornatus* (Orthoptera) were examined by Zhao and Zhu (2013). In their study, injection of PI did not influence the development of flight muscles of the short-winged males and long-winged males.

***Effects on Digestive Organs*:**

After feeding of last instar larvae of *Helicoverpa zea* (Lepidoptera) on PII-treated diet, goblet cells in midgut appeared smaller in diameter and had cavities that were elongated when compared to the goblet cells of larvae fed on normal diet (Binder and Bowers, 1994). Farazmand (2009) observed several abnormalities of epithelial cells in different regions of the alimentary canal of the beetle *L. decemlineata* after topical application of different doses of PI and PII onto larvae. In addition, abnormalities in cuticular structure of foregut and hindgut were observed after precocenes treatment.

***Effects on Endocrine Organs*:**

Unnithan *et al*. (1977) reported that treatment of *O. fasciatus* with precocene led to the degeneration of CA. Also precocene showed degenerative effects in CA of the locust *L. migratoria* nymphs (Schooneveld, 1979). In CA of the locust *S. gregaria*, Unnithan *et al*. (1980) observed segregation of various cytoplasmic organelles, vacuoles, residual bodies, pleomorphic mitochondria, irregularly Golgi apparatus, clumping of SER in the treated PII locusts. After exposure of the *D. melanogaster* (Diptera) adult females to PI and PII, CA volume did not increase in precocene-treated females even after 48 hr but increased between 0 and 24 hr after eclosion in control females. When adult females were removed from the precocene medium, CA volume increased within 48 hr to nearly those of control flies (Wilson *et al*., 1983). Topically applied PII onto the young-adults of face fly *Musca autumnalis* (Diptera) reduced the size of the CA (Burks et al., 1992). Santha and Nair (1991) recorded some changes in cerebral neurosecretory cells of *S. mauritia* (Lepidoptera) after treatment with PII. After administration of anti-JH agent, Jinlu to 0-72 hr of 4^{th} (penultimate) instar larvae of *B. mori* (Lepidoptera), Miao et al. (2001) observed some ultrastructural changes in CA and prothoracic glad in early 5^{th} (last) instar larvae. Effects of PII on the fine structure of CA in the adult females of locust *A. aegyptium* (Orthoptera) had been studied by Ergen (2001). He reported that initially CA did not show any atrophy or destruction but 10-20 days after PII treatment changes in nuclei, mitochondria, ER membranes and Golgi complex were produced showing latent effects.

***Effects on Reproductive Organs*:**

In holometabolous insects, precocene application resulted in various abnormalities in ovaries of the lepidopteran *Spodoptera mauritia* (Mathai *et al*., 1989) and the terminal oocyte development was prohibited in the dipterous flies, *Phormia regina* (Yin *et al*., 1989) and *Drosophila melanogaster* (Wilson *et al*., 1983). Deb and Chakravorty (1982) applied PII, either independently or subsequent to hydroprene (JHA) onto 0-day old last-instar larvae and 0-day and 3-day old pupae of the rice moth *Corcyra cephalonica*. Based on the histomorphology, they recorded considerable abnormalities of female reproductive organs and the most sensitive organs were the ovaries, accessory glands and bursa copulatrix. Exposure of 5^{th} instar nymphs, of different ages, and newly emerged brachypterous females of *N. lugens* (Hemiptera) to different doses of PII inhibited the ovarian growth and severe histopathological alterations were observed in the ovariole and oocytes of insects treated with high doses (Pradeep and Nair, 2000a). Depending on a study of Kumar and Khan (2004), the flesh fly *Sarcophaga ruficornis* appeared susceptible to precocene since the ovaries of precocene-treated flies failed to normally develop but exhibited some morphological abnormalities, like degeneration of follicles and unusual fusion of two ovaries. Also, the growth of follicles was reduced. Ahmed *et al*. (2005) carried out a histopathological study on 5^{th} instar female nymphs of grasshopper *E. plorans* (Orthoptera) after topical treatment with two doses of PI and PII. At the 10^{th} day post-

treatment, several symptoms of deteriorated ovries had been observed, such as degenerated germarium, oogonia and follicular cells.

11. Antifeedant Effects of Anti-JH Agents on Insects:

As previously discussed in the section of 'Categorization of anti-JH compounds', many green plants contain one or more of allelochemicals which are deterrent to some insects. Also, precocenes are ageratochromenes and originally plant-derived products. After few years of discovery of precocenes, researchers synthesized PI and PII and prepared some analogues which have been collectively called 'precocenoids'. These compounds either inhibit JH biosynthesis or inhibit the enzyme action (Bowers *et al*., 1976; Azambuja *et al*., 1982; Staal, 1986; Singh and Bhathal, 1994; Minakuchi and Riddiford, 2006; Banerjee *et al*., 2008; Hiramatsu *et al*., 2013). Although a great research attention has been paid to assess the antifeedant potencies of botanicals and JH mimics against insects, the current literature contains few studies examining the antifeedant activity of anti-JH compounds. Early, Slama (1978) suggested that the inducing action of precocene on insect sterility and/or precocious metamorphosis might be through their antifeedant effects. However, we concisely review the available studies in this section.

With regard to Coleoptera, PII exhibited stronger antifeedant effect than PI on the beetle *T. confusum* (larvae and adults), the weevil *S. granarius* (adults) and the Khapra beetle *Trogoderma granarium* (larvae), while precocene derivatives, especially iodolactones, were the strongest antifeedants against the beetle *L. decemlineata* (adults and larvae) (Szczepanik *et al*., 2005).

Within Hemiptera/Homoptera, PII showed a strong antifeedant effect on 4^{th} instar nymphs of the *R. prolixus*, while other synthetic precocene analogs exhibited no drastic inhibition of feeding. The antifeedant effect of PII on *R. prolixus* may be due to a direct cytotoxic action on the gut tissues which contain activating monooxygenases (Azambuja *et al*., 1982). Pradeep and Nair (2000b) recorded an inducing long-term irreversible antifeedant effect of PII on the brachypterous females of *N. lugens*. As the rate of honey dew excretion is positively correlated with the intake of plant sap, PII prohibited the treated insects to intake of plant sap. According to a study of Szczepanik *et al*. (2005), a dose of 50 mg l^{-1} PII led to lack of appetite of *D. koenigii* nymphs. Moreover, the nymphs did not feed at higher doses of PII. PII showed stronger antifeedant effect than PI against *M. persicae* (Banerjee *et al*., 2008).

Among Isoptera, Adfa *et al*. (2010, 2011) synthesized some derivatives of Scopoletin (7-hydroxy-6-methoxycoumarin) which structurally similar to precocenes and found Scopoletin as a strong antifeedant against *C. formosanus*. Precocenes and synthetic chromene derivatives were able to exhibit antifeedant activities against *C. formosanus*. PII was found stronger antifeedant than PI and other synthetic chromene derivatives (Hiramatsu *et al*., 2013).

In respect of Orthoptera, females of the crickets *Acheta domesticus* and *Nemobius fasciatus* were treated with PI or PII beginning 12 hr after adult emergence. Evidence for decreased feeding of precocene-treated females was observed in both species (Bradley and Haynes, 1991).

In connection with Hymenoptera, worker larvae of *A. mellifera*, of different ages, were removed from the colonies, reared on royal jelly-yeast extract, and after 24 h they were topically treated with different doses of PII. Based on the obtained results, it could be interpreted that precocene acted as an antifeedant at lower doses (Rembold *et al*., 1979). Different single doses of PII were topically applied either on 4^{th} or 5^{th} instar larvae of *A. mellifera*. An antifeedant effect was indicated by lower weight gain and

was only found with doses of 30 myg precocene or more (Czoppelt and Rembold, 1985).

12. Regulatory Roles of Anti-JH Agents in Metabolism and Enzymatic Activities:

Depending on the available literature, precocenes and other anti-JH agents were reported to affect the main metabolites and enzymatic activities in the whole body or certain organs of various insects, as reviewd herein.

12.1. Disturbed Main Metabolites:

***Proteins*:**

Among Orthoptera, adults of the migratory locust *L. migratoria* were treated with PII and the vitellogenin synthesis was prevented, as well as the production of other proteins was inhibited in both sexes (Gellissen and Wyatt, 1981). As recorded by Lange *et al*. (1983), PII-treated *Locusta* males showed a reduced haemolymph protein and in the fat body and accessory reproductive gland. Under crowded conditions, 600 µg PII was topically applied onto the adult females of *L. migratoria*. The fat body of PII-treated females did not synthesise the vitellogenin, owing to the impairement of JH biosynthesis in CA which is necessary of vitellogenin synthesis in fat body (Weers *et al*., 1994; Wyatt, 1988). Cycloheximide almost completely inhibited the protein synthesis in 4th and 5th instar nymphs of *L. migratoria* (Phillips and Loughton, 1979). Within Diptera, exposure of adult females of *D. melanogaster* to PI and PII resulted in a significant decrease of the whole body protein content (Wilson *et al*., 1983). At 48 hours post-treatment of the newly-emerged females of *M. domestica* with high doses of PII (above 100 µg/fly), titers of vitellogenin in hemolymph and total protein in ovaries were obviously declined (Li *et al*, 1993). Also, precocene treatment was found to inhibit the protein synthesis in fat body of banana fruit fly *Zaprionus paravittiger* (Rup and Bangla, 1995; Amiri *et al*., 2010). In Hemiptera, treatment of the newly emerged adult females of *O. fasciatus* with PII prevented the appearance of the female-specific polypeptide bands but induced the accumulation of other proteins in the haemolymph (Martínez and Garcerá, 1987). After treatment of *E. integriceps* nymphs with PI, haemolymph protein level in adult females was lower than the control adults, at first day after treatment. With passage of time, haemolymph protein concentrations remained constant and decreased near oviposition (Amiri *et al*., 2010). Among Lepidoptera, treatment of 3rd and 4th instar larvae of *S. litura* with precocenes (isolated from *A. conyzoides* and *A. vulgaris*) resulted in a significant reduction of total head protein content, after 24, 48 and 72 hrs of both topical application and injection (Renuga and Sahayaraj, 2009). Cycloheximide inhibited the protein synthesis necessary for both the development of EH sensitivity and the appearance of proteins EGPs in *M. sexta* (Morton and Truman, 2008). In respect of Coleoptera, injection of 2.5 µg/insect of cycloheximide into the newly emerged adult females of the beetle *T. molitor* significantly affected both the level of fat body proteins and the incorporation of tritiated leucine into proteins (Soltani-Mazouni and Soltani, 1995).

***Carbohydrates*:**

In general, the total carbohydrate content, or some of the carbohydrate components, in different insect species had been affected by precocenes. For examples, exposure of the newly emerged females of the vinegar fly *D. melanogaster* to PI or PII promoted an increase of carbohydrates (Wilson *et al*., 1983). Garcia et al. (1988) showed that PII treatment led to a declination of glycogen level in the stable fly *S. calcitrans*. Application of PII onto in the banana fruitfly *Z. paravittiger* was found to decrease the contents of glycogen and trehalose in fat body (Rup and Bangla, 1995).

***Lipids*:**

PII treatment was found to block the accumulation of fatty acids in body of the pea aphid *Acyrthosiphon pisum* (Chen *et al*., 2005b). However, it is still unclear whether these effects of precocene are direct, or indirect as consequence of the decreased in JH titers (Amsalem *et al*., 2014b). The eclosion hormone triggers ecdysis behavior at the end of each moult in *M. sexta*. The stimulation of the steroidogenesis in insects was found to be rapidly inhibited by cycloheximide (Keightley *et al*., 1990).

12.2. Influenced Respiratory Metabolism:

Depending on the currently available literature, very few studies examined the effects of precocenes on the respiratory metabolism in insects. PII affected the respiratory metabolism in fat body as well as flight and coxal muscles of the adult females of the desert locust *S. gregaria* (Salem *et al*., 1982b). Precocene treatment was found to increase the oxygen consumption rate in the ovaries of the large milkweed bug *O. fasciatus* that in turn remain inactivated (Garcera *et al*., 1989). Garcera *et al*. (1991) investigated the effects of PII on the metabolic rate in 5^{th} instar nymphs and adult males of the German cockroach *B. germanica*, the soldier bug *Spilostethus pandurus* and the large milkweed bug *O. fasciatus*. PII decreased the oxygen consumption rate in nymphs and adults *B. germanica* and *S. pandurus* 5^{th} instar, whereas *O. fasciatus* oxygen consumption rate was not affected. In addition, Hebbalkar and Sharma (1991) studied the effect of P II on the oxygen consumption of red cotton bug *Dysdercus koenigii*.

12.3. Disturbed Enzymatic Activities:

The available literature contains scarce studies examining the effects of precocenes on enzymatic activities in insects. Depending on Khafagi and Hegazi (2001, 2004), both PI and PII caused a stronger encapsulation reaction in larvae of *S. littoralis* being parasitized by the endoparasitoid *Microplitis rufiventris*. These precocenes, also, enhanced the melanization of capsules, suggesting a possible interaction with phenoloxidase, a key enzyme in the synthesis of melanin. Treatment of the last instar larvae of cabbage looper *Trichplusia ni* with FMev, as well as L-643 (compactin analogue), 049-01K01 and DPH (3,3-dichloro-2-propenyl hexanoate) resulted in a reduction of JH esterase activity (Sparks *et al*., 1987).

13. Effects of Anti-JH Compounds on Chemoreceptors and Pheromone Production:

13.1. Influenced Chemoreceptors:

The chemo-communication and sensory mechanisms have been gained increasing attention of those researchers interested in the feeding behaviour and host-plant selection of the herbivorous insects. Many IGRs affect the development of chemoreceptor organs causing chemical communication disorders in relation to insects' sexual behavior and migratory activities (Dorn, 1982; Polivanova, 1982). Studies on the effects of precocenes on sensory systems have been performed mainly on the hemimetabola insects (with incomplete metamorphosis). In addition, these anti-JH compounds can impair the ability of host-plant searching by larvae of the holometabolous insects (Farazmand and Chaika, 2011).

In respect of the hemimetabolous insects, serious disturbances in the structure of sensory organs have been observed after feeding on plants containg precocenes or after treatment with these anti-JH compounds. For examples, effects of precocenes on the chemoreceptor organs have been studied in *O. fasciatus* (Dorn, 1982) and *E. integriceps* (Hemiptera)(Polivanova, 1982; Polivanova and Triseleva, 1992). Also, precocene treatment of *T. vaporariorum* (Homoptera) led to some disruptions in the

shape of sensilla (Polivanova, 1991). Precocene treatment of *M. persicae* (Homoptera) led to deformity of antenna and reduction of the number of sensilla (Polivanova, 1997).

With regard to holometabolous insects, the available literature contains little information about the effect of precocenes on the development of sensory organs in. In a study on the chemoreceptor apparatus of *A. podana* (Lepidoptera), Triseleva (2007) treated the eggs with PII and observed changes in the basiconic sensilla on the maxillary palp and galea (mouth parts) and on the size of basiconic sensilla on the 2nd and 3rd antennal segments. Farazmand and Chaika (2011) studied the effects of PI and PII on the chemoreceptors on antennae and mouthparts in the 2nd instar larvae of *L. decemlineata* (Coleoptera). Precocene application caused changes in the form, number of sensilla, as well as in the cuticular structure of the antennae and maxilla- labial complex, after the first molt. Also, reduction of both receptor cells and their dendrites were observed.

13.2. Disrupted Pheromone Production:

Hartman and Suda (1973) proposed that the pheromone production is not controlled by JH in the lobster cockroach *Nauphoeta cinerea* and in other cockroach species where the adult male releases a volatile pheromone to attract the female for mating. On the contrary, pheromone production in various insects was reported to depend on the presence of CA (or JH), such as the gregarious adult males of *S. gregaria* (Amerasinghe, 1978). Topical treatment of the bark beetle *Ips paraconfusus* (Coleoptera)(Kiehlmann *et al*. 1982) and *B. germanica* (Dictyoptera)(Schal *et al*., 1990) with PII resulted in the inhibition of pheromone production. Precocene appears to influence pheromone production indirectly by inhibiting JH production, since its effect can be rescued by treatment with Hydroprene (JHA)(Schal *et al*., 1990a, 1991). Depending on the results obtained by Tawfik *et al*. (2014), PII plays a role in the regulation of pheromone production in *S. gregaria*.

14. Miscellaneous of the Anti-JH Compounds' Effects on Insects:

***Effects of Anti-JH Compounds on Insect Haemogram and Immune Responses*:**

Hegazi et al. (2000) investigated the influence of PII on the hemocyte population of *S. littoralis* larvae (Lepidoptera) parasitized by the solitary endoparasitoid *Microplitis rufiventris* (Hymenoptera) and recorded significant decrease in total hemocyte counts (THCs) as well as changes in differential hemocyte counts (DHCs) in *S. littoralis* larvae by the action of PII. Khafagi and Hegazi (2001) found that both PI and PII cause a stronger encapsulation reaction in larvae of *S. littoralis* to the solitary braconid parasitoid wasp *Microplitis rufiventris*. Melanization was larger in either PI- or PII-treated hosts just before the emergence of successful parasitoid larvae. On the basis of considerable increase in encapsulation responses of precocene-treated *S. littoralis* larvae to *M. rufiventris*, it was suggested that the cellular defense reaction may be under inhibitory hormonal action.

***Effects of Anti-JH Compounds on Host-Parasitoid Interactions*:**

In the insect host-parasitoid interactions, the released cells from the parasite egg at hatch into the host's haemolymph are called 'teratocyte' (Vinson, 1970). These cells play important roles in these interactions. Early, Joiner *et al*. (1973) reported the JH activity against the teratocytes of the braconid parasitic wasp *Chelonus nigriceps*. Sixteen years later, Zhang (1989) emphasized the effects of these cells on the hormone-regulating system. Then, teratocytes were suggested to release JH from *Chelonus* species (Grossniklaus-Biirgin and Lanzrein, 1990). In a study of Hegazi and Khafagi (1998), different developmental ages of teratocytes of the solitary endoparasite braconid wasp *Microplitis rufiventris* were topically treated with a dose (70µg/5µl) of PII *via* larvae of its host *S. littoralis*. A dramatic reduction was recorded in both

teratocyte number and size. They concluded that Pll-treatment might has an effect on the absorptive function of the teratocytes.

***Effects Anti-JH Compounds on the Fat Body*:**

Precocene treatment was found to cause hypertrophy of the fat body of female *Oxya japonica* (Orthoptera) (Lee and Tan, 1981).

Inhibition of Cantharidin Biosynthesis:

In blister beetles (Meloidae: Coleoptera) are characterized by producing toxic, vesicant, and purported aphrodisiac product known as cantharidin (Ghoneim, 2014). The anti-JH compound FMev was found to exhibit an inhibitory effect on the cantharidin biosynthesis. It is specifically attributable to the fluorine substituent and not simply to large doses of a substance acting as the metabolic substrate (Carrel *et al*., 1986).

15. Action Mechanisms of Anti-JH Agents:

In the current article, we classified several anti-JH compounds in the section 'categorization of anti-JH agents'. The mechanisms of these anti-JH compounds are yet to be debatable issues among the interested researchers because little is known about either the target sites or the exact modes of the action. At an earlier time, Staal *et al*. (1981) presumed some mechanisms of anti-JH agents, such as: inhibition of the early steps in JH biosynthesis (e.g. FMev) or the final steps in JH biosynthetic (e.g. piperonyl butoxide). Competition of anti-JH agents with the endogenous JH for peripheral JH receptor (e.g. EMD). However, the action mechanisms of different anti-JH agents need to be discussed in some detail.

15.1. Mode(s) of Action of Precocenes:

The depression of JH level below that normally found in immature stages of insects may be due to the selective destruction of CA which are the target organ for precocenes (Leighton *et al*., 1981). To understand the CA destruction, precocenes are presumed to undergo biotransformation into a highly reactive 3,4-epoxide intermediate through the action of monooxygenases within the CA. The reactive epoxide either undergoes hydration to from precocene 3,4-dihydrodiol or alkylation to form alkylates leading to damage of the CA *in vivo* (Pratt et al., 1980; (Hamnett and Pratt, 1983; Camps *et al*., 1985; Brooks and McCaffery, 1990; Kumar and Khan, 2004). Other authors (Haunerland and Bowers, 1985; Sohn *et al*., 1991; Chen *et al*., 2005a) speculated that the reactive epoxide intermediate can easily react with the surrounding nucleophils (eg, proteins), causing the observed parenchymal cell death in CA.

Moreover, it is still unclear whether the effects of precocenes are restricted to CA (Haunerland and Bowers, 1985; Garcera *et al*., 1991; Burks *et al*., 1992) or are more general due to their toxicity (Ergen, 2001), or indirect as consequence of the declination in JH titers (Amsalem *et al*., 2014b) since many studies suggested multiple targets for the effect of precocenes in insects, such as increased oxygen consumption rate by the ovaries (Garcera *et al*., 1989), hypertrophy of the fat body (Lee and Tan, 1981); decreasing glycogen and protein contents in the fat body (Amiri *et al*., 2010); and blocking the accumulation of fatty acids in the aphid *A. pisum* (Chen *et al*., 2005b).

In respect of precocenoids (synthetic analogues of precocenes), it has not been possible to rationalise the activity or inactivity of them, or to explain the considerable specificity of insect species toward these analogues (Pratt *et al*., 1980) because they may act as stimulators or inhibitors of JH degradation or act in an antagonistic manner at the target tissue level, i.e., JH receptor levels (Tunaz and Uygun, 2004; Minakuchi and Riddiford, 2006).

15.2. Mode(s) of Action oOf Imidazoles:

The mode of anti-JH action of imidazoles may be different from that of precocenes. As for example, there are some differences among the imidazole compound KK-22 and precocenes, since KK-22 induced the precocious metamorphosis without lethal activity or larval growth inhibition, but precocenes were reported to show lethal activity and strong inhibition of larval growth (Kuwano *et al*., 1983). Nevertheless, the anti-JH action of KK-22 can be rescued by simultaneous application of methoprene (JHA)(Asano *et al*., 1984 a, b). Another imidazole compound KK-42 was reported to affect both JH and ecdysone because titers of these hormones declined in *B. mori* after treatment with this compound (Kuwano *et al*., 1988; Akai and Rembold, 1989; Wu *et al*., 1991). This was explained by the inhibitory effect of KK-42 on the *cytochrome P*-450-dependent monooxygenases that are involved in the final steps of biosynthesis of both hormones (Feyereisen *et al*., 1981; Kappler *et al*., 1988; Unnithan *et al*., 1995). Depending on the results of Miao *et al*. (2001) on *B. mori*, treatment with the imidazole, Jinlu, led to the inhibition of the CA secretion and initiated the activity of prothoracic gland, leading to precocious metamorphosis (change tetramolters to trimolters in silkworms). Kaneko *et al*. (2011**)** studied the mode of action of the KF-13S (a compound derived from ETB) and concluded that it prevented the transcription of many JH biosynthetic enzymes, so that the JH biosynthesis is suppressed.

15.3. Mode(s) of Action of Fluoromevalonate:

FMev is a potent and selective anti-JH compound for several lepidopterous species (Edwards *et al*., 1983). Although its precise mode of action in insects is unknown, FMev presumably functions as an inhibitor of the early steps in JH biosynthetic pathway, disrupting the metabolism of mevalonate and/or homomevalonate (Quistad *et al*., 1981; Baker *et al*., 1986). In other words, it inhibits one or more steps in JH biosynthesis after the HMG-CoA reductase involvement, presumably on mevalonate kinase and/or pyrophosphomevalonate decarboxylase (Monger *et al*., 1982). Some authors (Kramer and Staal, 1981; Farag and Varjas, 1983) interpreted the precocious pupation, a characteristic response to FMev treatment, by reduced JH titre due to the specific inhibitory action of this compound on JH biosynthesis. For some detail, Granger *et al*. (1995) reported that a JH-related product is biosynthesized *in vitro* by the CA of *M. sexta* and of at least two other Lepidoptera. Its structure appears to be ester-linked JH III acid. Some of the product is stored in the CA, and its synthesis/release is partially inhibited by FMev.

15.4. Modes of Action of Benzoate and Methy Dodecanoate Compounds:

ETB exhibits a dual anti-JH/JH activity and its mode of action is not fully understood until now. For some detail, there are some reasons now to suggest that ETB may exhibit a complex antagonistic activity; as exhibiting inherent JH activity, because it may exert a negative feedback response on titre of the endogenous JH and/or compete for the inter- and intracellular JH receptors. Also, its inhibitory effects on the early steps in JH biosynthesis were strongly argued (Staal *et al*., 1981). More than three decades later, Kaneko *et al*. (2011) reevaluated the mode of action of ETB, since it causes a decrease in JH biosynthesis *in vitro*, as indicated by loss of [^{14}C]labeled JH production by excised CA glands. With regard to the modes of action of ETB-related compounds, KF-13S, as an example, caused reversible inhibition of JH biosynthesis *in vivo* after topical treatment of the *B. mori* 3rd larval instar. Transcript levels of several early JH biosynthetic enzymes declined after the KF-13S treatment. Thus, ETB-related compounds do not work as enzyme inhibitors but as transcriptional regulators of JH

biosynthetic enzymes. In this respect, their overt effect may be seen as being similar to that of allatostatins (Kaneko *et al*., 2011).

The direct action of EMD on JH receptors has been suggested depending on both *in vitro* and *in vivo* studies (Kramer and Staal, 1981). In contrast to ETB, EMD does not exhibit an inhibitory effect on the whole sequence of JH biosynthesis or considerably affect the whole body JH titre. Therefore, it may compete for JH receptors with a deficient JH activity (Staal *et al*., 1981; Menn, 1985). Based on the currently available literature, there is no further information on the mode of EMD action. Thus, the exact mode of action of EMD is still obscure until now.

15.5. Modes of Action of Bisthiolcarbamate and Benzodioxoles:

It is not clear yet whether bisthiolcarbamate exerts its action *via* JH biosynthesis inhibition or JH-agonist feedback inhibition *via* the insect brain (Kramer *et al*., 1983). Some authors (Jurd *et al*., 1979; Van Mellaert *et al*., 1982, 1983) postulated that benzyl-1,3-benzodioxoles, such as J2710 and J2922 which showed strong anti-JH effects in their *Galleria* assay, either compete for or inactivate JH receptors or prevent binding of JH to the receptor sites. Readio *et al*. (1987) detected no evidence for such effects when the newly emerged adults of *C. pipiens* were injected with six benzyl-1,3-benzodioxole derivatives. Thus, receptor activity in *C. pipiens* was apparently unaffected by the tested compounds in their study.

15.6. Mode of Action of FGL-Amide Allatostatins:

Allatostatins (ASTs) constitute a class of regulatory neuropeptide hormones in insects and some invertebrate phyla (Hult *et al*., 2008). The FGL-amide ASTs represent a family of insect neuropeptides (see section 'Categorization of the anti-JH compounds' in the present article). Although the discovery of the first AST almost forty years ago, the exact mode(s) of action is still unknown or remains poorly understood (Weaver and Audsley, 2009; Stay and Tobe, 2007; Chowański *et al*., 2016). However, the AST compound H17, as well as Ketomethylene, methyleneamino and Dippu-AST (pseudopeptide analogues of ASTs) had been reported as potent inhibitors of JH biosynthesis in some insects (Nachman et al., 1999; Garside *et al*., 2000; Bendena and Tobe, 2012; Wu *et al*., 2017). According to the current literature, Nouzova et al. (2015) carried out a study aiming to understand the mode of AST compounds in *Aedes aegypti*. They investigated the *A. aegypti* allatostatin-C on JH III synthesis by CA and concluded that inhibition of JH III synthesis might be due to the disruption of citrate mitochondrial carrier (that transports citrate from the mitochondria to the cytosol) and subsequently blocking the production of cytoplasmic acetyl-CoA that sustains JH III synthesis in the mosquito CA.

15.7. Anti-JH Compounds with Unknown Modes of Action in Insects:

Cycloheximide is a potent inhibitor of protein biosynthesis in eukaryotic organisms. It is also the DNA damaging agent (for some detail, see section of 'Categorization of the anti-JH compounds' in the present article). As far as our literature survey could ascertain, no information was available on the mode of action cycloheximide in insects as JH-agonist or anti-JH agent. On the other hand, its mode of action was widely examined in organisms other than insects. Early, Baliga *et al*. (1969) used a cell-free system prepared from rat liver for investigating the sites of cycloheximide action on protein synthesis. The cycloheximide action on polysome aggregation differs from its effect on peptide chain elongation. In studies on the ‘programmed cell death’, cycloheximide has been widely employed. The anti-apoptotic mechanism of cycloheximide action was studied by Mattson and Furukawa (1997). Some years later, Vajrala *et al*. (2014) conducted a trial to understand the mode of action of cycloheximide on the inhibition of bacteria-specific protein synthesis in the

bacterium *Nitrosopumilus maritimus*. In conclusion, the exact mode of action of Cycloheximide, as anti-JH compound against insects, is not known until now.

Compactin is one of many fungal metabolites that possess interesting biological activities including anti-JH effects (Hiruma *et al*., 1983). Extracts of the fungus *Penicillium brevicompactum*, which displayed anti-JH effects on the locust *L. migratoria*, were sub-fractionated and characterized to yield the novel sesquiterpene-like structure Brevioxime (Castillo *et al*., 1998). This compound caused a dose-dependent inhibition of JH biosynthesis in cultured CA, which could not be restored by the addition of farnesol, farnesoic acid, or mevanolactone. While these results suggest that brevioxime inhibits the final steps of JH biosynthesis, the exact mode of action of this compound remains unknown (Cusson *et al*., 2013). Mevinolin (known, also, as Lovastatin) was reported to inhibit the JH biosynthesis in insect CA *in vitro* (Feyereisen and Farnsworth, 1987). Arborine is originally a quinazolone alkaloid product of plants (Sreejith *et al*., 2012). It was found to inhibit the JH biosynthesis *in vitro* of CA. The oxathiole is a powerful inhibitor for JH biosynthesis having approximately the same potency of precocenes or better (Brooks *et al*., 1984 b). No information on the modes of action of these compounds is available in the current literature. Also, the modes of action of other compounds having anti-JH activities against insects are still unknown up to the present moment, such as Fluvastatin, Quinolones and fluoroquinolones, Pyridone, Allyl alcohols, furanyl ethers and Pitavastatin.

16. Fate and Metabolism of Precocenes:

As previously discussed (see the section of 'Action mechanisms of anti-JH agents'), precocenes are probably biotransformed into a highly reactive 3,4-epoxide intermediate through the action of monooxygenases in the CA of insects. The eucaryotic metabolism of PI, by the insect and animal enzyme systems, involves oxidation to an unstable compound 3,4-epoxy-7-methoxy-2,2-dimethyl-chromene which produces the corresponding *trans*-5 and *cis*-6-diols (Halpin *et al*., 1982, 1984; Jennings and Ottridge, 1984). Considering the metabolism of PII in several insect species, Ohta *et al*. (1977) reported that its metabolism showed that the 6,7-dimethoxy-2,2-dimethylchromene-3,4-diol (PII diol) was the major organosoluble metabolite while the 6,7-dimethoxy-2,2-dimethylchroman-3-ol (PII 3-oi) was a minor metabolite.

Some researchers (Bergot *et al*., 1980; Haunerland and Bowers, 1985) investigated the pharmacokinetics of PII in a sensitive insect (*O. fasciatus*) and an insensitive insect (the corn earworm *Helicoverpa zea*). PII was segregated by the fat body in *O. fasciatus* and slowly metabolized, but rapidly metabolized and sequestered in *H. zea*. The *in vitro* studies, using inhibitors for cytochrome *P*-450 and for cyt *P*-450-NADPH-reductase, confirmed the expected detoxification of precocene by a mixed-function oxidase *via* 3,4-epoxide.

Apart from insects, precocene metabolism had been studied in rats and parallel views have been described between the bioactivation of precocenes by rats and the production of carcinogenic bay region diol epoxides from polycyclic aromatic hydrocarbons in mammals (Hsia *et al*., 1981; Halpin *et al*., 1982). Also, the precocene metabolism in microorganisms, such as various species of *Streptomyces* and *Aspergillus*, was reported by some authors (Sariaslani *et al*., 1987; Boyd *et al*., 1996). In these microorganisms, PII is transformed to three major metabolites (*cis*- and (+) trans-PII-3,4-dihydrodiols and (+)-3-chromenol).

17. Potential Use of Anti-JH Agents for Pest Control:

Screening new targets involved in JH-biosynthesis within the CA in insects has been a subject of study in recent decades (Bede *et al*., 2001). In this regard, researches in some parts of the world have already made discovery of anti-JH compounds which inhibit JH-biosynthesis of insect pests (Bowers, 1985; Kuwann *et al*., 1985; Barton *et al*., 1989). This discovery heralded a new era in the JH research since these compounds are used to evaluate the role of JH in various JH-regulated physiological processes (Singh and Kumar (2011).

From a practica1 point of view, precocenes have been found to be toxic to the liver and kidneys of vertebrates (Staal, 1986; Okunade, 2002). This is an important limiting factor for the human health in the field application of precocenes as large-scale insecticidal agents (Massuod *et al*., 2014). Moreover, the PII-resistant insect species metabolise it *via* the epoxy-precocene. This finding could be a severe limitation for the practical application of precocene analogues as effective insecticides (Chenevert *et al*., 1980). In addition, precocenes had limited utility, showing anti-JH activity in only a few insect species, representatives of the orders Hemiptera and Orthoptera (Menn, 1985). On the contrary, Dietz *et al*. (1979) reported that the lack of malformations in honey bees treated with PII low doses indicated no detrimental effect on the honey bee larvae of at least 4½-day old. While high doses of precocene quickly killed most 3½-day old larvae. Therefore, the use of low doses of such compound can be applied as a control agent in insect populations.

Although several precocene derivatives have already been synthesized to optimize allatocidal activity of the natural precocenes (Brooks *et al*., 1979; Camps *et al*., 1980), the chemical potential of this area has not yet been fully explored. Only with extending our knowledge of the metabolic mechanisms of precocenes and their analogues to a wide array of insects and by obtaining adequate data on the structure-activity relationships for selectivity, we will find out derivatives or analogues having significant impacts for controlling the major agricultural pests (Cusson *et al*., 2013).

In respect of FMev, it should be emphasized that its biological activity is not sufficiently high even on the lepidopterous pests, in spite of the report of Benz and Ren (1986) that FMev might be a useful tool for "chemical allatectomy" in Lepidoptera. The limited effectiveness of FMev precludes its use as a commercial anti-JH compound. However, it provides encouragement for further search for synthetic active analogues inhibiting JH biosynthesis as new selective insect control agents (Quistad *et al*., 1981; Cusson *et al*., 2013).

With regard to ETB, its dual anti-JH/JH activity was reported and the exact mode of action is uncertain hitherto. These obstacles have precluded its development as an effective insecticidal agent. However, recent work on its mode of action and on the development of novel derivatives has created a renewed interest in ETB and related compounds (Cusson *et al*., 2013).

Although anti-JH compounds are selectively toxic to CA and as such interfering with the biosynthesis and release of JH leading to disturbance of different physiological processes in insects, majority of the research works on these compounds have been conducted in laboratory and no compounds have been used under field conditions. Also, very few developed compounds have been shown to be sufficiently active for the practical purposes in pest management programs as yet (Asano *et al*., 1984; Quistad *et al*., 1985; Yaguchi *et al*., 2009). Nevertheless, those compounds interacting with JH, stimulate or inhibit the JH-biosynthesis, or interfere with its catabolism, can be utilized as new effective insecticides (Nandi and Chakravarty, 2011).

However, when these compounds are poorly applicable control agents, they are at least used as an effective tool in devising 'fourth generation insecticides' (Staal, 1986; Moya *et al*., 1997; Szczcpanik *et al*., 2005). Very recently, Lee *et al*. (2018) reported that anti-JH compounds may be effective for controlling the target pests during their larval stages which have high level of endogenous JH titer.

On the other hand, the situation of anti-JH compounds in sericulture is not as in the field of pest control. In the light of many reported results, the anti-JH compounds are a promising candidate in the research field of sericulture (Liu *et al*., 1987; Yoshida *et al*., 1989; Miao *et al*., 1996; Tsubouchi *et al*., 1997). Up to now, imidazoles and some of other anti-JH compounds have been used in the practical production of natural silk at commercial scale (Miao *et al*., 2001; Niu *et al*., 2013). However, this interesting aspect will be discussed in the following section.

18. Role of Anti-JHs in Sericulture and Silk Research Fields:

Silk is normally produced from cocoons of the mulberry silkworm (= Chinese silkworm) *Bombyx mori* (Lepidoptera: Bombycidae) in Asia and Europe, though other species may be used in different parts of the world, such as Eri silkworm *Philosamia ricini*, Ailanthus silkworm moth *Samia cynthia*, Japanese oak silkworm *Antheraea yamamai*, giant silkworm moth *Eriogyna pyretorum*, tussor silkworm *Antheraea paphia*, muga silk worm *Antheraea assamensis* (Lepidoptera: Saturniidae) and African wild silkworm *Anaphe infracta* (Lepidoptera: Eupterotidae). However, the domesticated *B. mori* is the intensively studied silkworm and the most widely used in sericulture. For history of silk culture, see reviews of Vainker (2004) and Capinera (2008).

The cultivation of silkworms to produce silk, at the commercially large scale, can be called 'Sericulture', i.e., the production of raw silk, or silk farming. It is an agro-based industry that involves cultivation of food plants for silkworms, reeling and spinning of cocoons for production of valuable yarn, added benefits such as processing and weaving. Sericulture is one of the oldest industries in India and Asia. It has become an important cottage industry in different countries of the world. For its economic importance, these studies are collectively known as "Sericology". It was reported that the major silk producing countries in the world are: China, India, Uzbekistan, Brazil, Japan, Republic of Korea, Thailand, Vietnam, DPR Korea, Iran, etc. Few other countries are also engaged in the production of cocoons and raw silk in negligible quantities; Kenya, Botswana, Nigeria, Zambia, Zimbabwe, Bangladesh, Colombia, Egypt, Japan, Nepal, Bulgaria, Turkey, Uganda, Malaysia, Romania, Bolivia, *etc*. For silk industry in the world, see Giridhar *et al*. (2010); Amppiah *et al*. (2014); Jalba (2016); Pallabi and Sharma (2017).

18.1. Hormone Analogues in The Silk Research Fields:

Organochloride insecticides, like Hexachlorocyclohexane, were reported to cause a decrease in fibroin content, pupal weight and fecundity as well as deterioration in quality and quantity of silk thread in *B. mori* (for detail see Bhagyalakshmi *et al*., 1995; Li *et al*., 2010).

In the silk research field, many investigators used juvenoids (JH-analogues, JHAs) in order to enlarge the silk yield. JHAs enhance the silk production when applied with the appropriate dose but not high doses. In India, many workers used some JHAs in the sericulture aiming to improve the silk yield (Trivedy *et al*., 1993, 1997; Nair *et al*., 2000; Nagendraradhya and Jagadeesh Kumar, 2013). Also, ecdysteroids are known to influence the silk producing potential of *B. mori* (Srivastava and Upadhyay, 2013a, b). In contrast, some authors (Gu *et al*., 1995; Mitsuoka et al., 2001) reported that the application of either JHAs (like methoprene) or 20-

hydroxyecdysone can change trimolter (three molts to produce four larval instars) to tetramolter (normal four molts to produce five larval instars) *B. mori* or induce extra larval ecdysis of the 4th (last) larval instar. Because of these problematic findings, many researchers are paying attention toward compounds other than juvenoids and ecdysteroids, such as anti-JH compounds.

18.2. Anti-JH Compounds and Their Potential as Candidate for Sericulture:

For improving characters of the natural silk, as well as shortening of the larval duration, many research institutions have usually focused on the precocious metamorphosis (skipping off the 5th larval instar) in silkworms, i.e., induction of trimolters (three moltings) instead of tetramolters (normal four moltings) in the larval stage. In this context, anti-JH compounds are considered more useful to control the moultinism in silkworm because the action of precocious metamorphosis, induced by anti-JH compounds, can be expected to produce advanced or novel silk materials.

As previously reviewed in section 'categorization of anti-JH agents', several compounds classified in different categories had been reported to exhibit anti-JH activities against various insect species. As far as our literature survey could ascertain, no information was available on the activity of any group of anti-JH compounds to induce the trimolter silkworms but only two groups, imidazoles and benzoates (ETB and its analogues), were widely used for this purpose in sericulture.

Many imidazoles and their analogues had been studied in the recent 30 years for inducing trimolter silkworms (for review see Wu *et al*. (2013). For some detail, many imidazole derivatives, such as KK-22, KK-42, KK-110, have been proved to be promising compounds in sericulture, from the standpoint of producing fine cocoon filament in *B. mori* (Akai *et al*., 1986), increasing efficiency of egg production (Kawaguchi *et al*., 1993) and breaking of diapause in pharate first instar larvae of the wild silk moth *Antheraea yammami* (Suzuki *et al*., 1989). However, some reported research works about the effectiveness of these compounds as trimolter inducers in silkworms, can be reviewed herein.

Imidazoles inhibit ecdysone synthesis in the prothoracic gland (PG) of *B. mori*, since inhibitory action of KK-42 (1-benzle-5 [(E)]2, 6, dimethyl-1, 7 heptadienyl] imidazole) on ecdysteroid level had been recorded (Akai and Rembold, 1989). In *B. mori*, KK-42 treatment led to the declination of both ecdysone and JH titres and subsequently to the induction of precocious metamorphosis (Kuwano *et al*., 1988). With regard to the improvement of silk, treatment of *B. mori* larvae with 0.5 μg/μl of KK-42 induced trimolters with better physical characteristics of the raw silk. The dry and wet strengths and knot strength were high in silk filament of treated cocoons than control congeners. Also, silk fabrics were soft (Kanda *et al*., 1985; Akai *et al*., 1986). Topical application of another imidazole compound, KK-22 (1-citronellyl -5-phenyl imidazole), onto 0 hr-old 3rd and 4th instar larvae of *B. mori* successfully induced 100% precocious pupation without lethal effect (Kuwano *et al*., 1984). The anti-JH activity of this compound vanished when methoprene (a JH analogue) was applied immediately after KK-22 treatment (Asano et al., 1986). In addition, the synthesized imidazole KK-110 (1-neopentyl 5-imidazole) had been found to be highly effective for producing precocious pupation in *B. mori* (Kuwano *et al*., 1990). When penultimate (4th) instar larvae of *B. mori* were topically applied with the imidazole compound KS-175 [1-(4-Phenoxyphenoxypropyl) imidazoles], they did not molt for more than 20 days. When the treated 4th larvae were fed on an artificial diet supplemented with 20-hydroxyecdysone, they molted to the ultimate (5th) instar. Therefore, KS-175 irreversibly impaired the ecdysone biosynthesis in the PG (Shiotsukia *et al*., 1999).

Other imidazoles, such as SM-1, Jinlu, SSP-11, SDIII, Lin II, Kang-20, YA_{20}, had also been synthesized. After administration of some of these compounds, *via* food, to 3rd or 4th instar larvae of *B. mori*, they effectively induced precocious metamorphosis with the production of superfine cocoon (Shen *et al*., 1990; Tan *et al*., 1992; Miao *et al*., 1996). Precocious trimolter *B. mori* was induced by the dietary administration of the imidazole compound SSP-11 (E-4-chloro-a, a, a-trifluoro-N-[(C1H-imidazole-1-yl)-2-propryethy-lidene]-O-toluidine) in the early 3rd or 4th larval instar of *B. mori* (Kiuchi *et al*., 1986). Feeding of the 4th instar larvae of *B. mori* on a diet treated with the anti-JH compound Kang-20, during the first 48 hr, a tetramolter strain was efficiently induced into trimolters (Lin *et al*., 1991). In the 2nd ～4th larval instars of *B. mori*, the anti-JH compound YA_{20} could induce 100% trimolter in anytime of the 24 hr ago for 48 hrs (Zhuang *et al*., 1992). SD-III was reported to exert strong anti-JH activity and anti-ecdysteroid activity on *B. mori*. After body surface spraying with 300 ppm SD-III, trimolter silkworms (95%) were induced (Tan *et al*., 1992). The imidazoles compound SM1 had been reported to induce the tetramolter silkworms into trimolters (Lu and Li, 1987).

As a trimolter inducer, the imidazole derivative Jinlu had received a great rsearch attention in the context of sericulture during the last two decades. Treatment of *B. mori* with Jinlu resulted in improved silk filament size, reliability, neatness and cleanness defect of trimolter cocoons (Lu and Xiao, 1997). In addition, Jinlu could induce the tetramolters into trimolters in the Chinese tasar moth *Antheraea pernyi* treated in early period of 3rd instar (Qin *et al*., 1999), as observed also in the Japanese oak silkworm *Antheraea yamamai* (Jian *et al*., 1999). In a study of Miao *et al*. (2001), the conversion ratio of tetramolters into trimolters was 100% after treatment of the 4th (penultimate) instar larvae of *B. mori* with Jinlu while treatment of 5th (last) instar larvae led to lengthening of the instar by one day. Recently, Niu *et al*. (2013) conducted an investigation using two races of *B. mori* to assess the activity of Jinlu on the improvement of silk quality in the inducted trimolters. These investigators obtained fine filament silk with high quality in the early period of 3rd instar, which was superior to that of tetramolters, and the super fine filament silk can be produced in the 4th instar induced by this compound.

As reported by Miyajima *et al*. (2001), the imidazole compound, triflumizole (E)-4-chloro-alpha,alpha,alpha-trifluoro-N-[1(1H-imidazole-1yl)-2-propoxyethylidene] -o-toluidine, induced the trimolter *B. mori*. After treatment of the 3rd instar, percentage of trimolter was higher than that induced after treatment of the 4th instar. Cocoon form of trimolters became rounder than that of the untreated tetramolters. Alson cocoon filament size of the trimolters, induced by the 3rd instar treatment, was larger than of the untreated tetramolters.

In respect of ETB and its related compounds, ETB analogue ethyl 4-[4-methyl-2-(6-methyl-3-pyridyloxy)pentyloxy]benzoate induced precocious metamorphosis after topical application onto 1-day old 3rd instar larvae of *B. mori* (Fujita *et al*., 2005). Fujita *et al*. (2007) synthesized two ETB analogues which induced precocious metamorphosis in larvae of *B. mori*. KF compounds are structurally derived from ETB. Furuta *et al*. (2007) reported that KF-13S strongly induced precocious metamorphosis in *B. mori*. KF-13 and heptyl analogues induced precocious metamorphosis in *B. mori* at low doses (Fujita *et al*., 2008).

It is important to highlight some points in sericulture. The trimolter cocoons, produced by anti-JH agent-treated caterpillars, have greater tensile strength, stiffness, compressive resilience, and crystallinity of the treated silk than those of the untreated caterpillars (Yoshida *et al*., 1989). In other words, the cocoon of induced trimolter

silkworms has better physical properties, including cocoon weight, filament size and strength than the normal tetramolters (Tsubouchi *et al*., 1997). Moreover, Niu *et al.* (2013) reported that the trimolter silk fiber has special economic value and bright prospect in terms of developing the distinctive silk textile of high quality. It appears that better rearing of *B. mori* larvae on imidazoles or ETB-treated mulberry leaves is possible due to the following reasons: (a) larval duration is shortened by 4-5 days, thus saving labour and leaves. (b) Skipping off the 5^{th} larval instar decreases the diseases incidence, resulting in good pupation rate. (c) Moths of trimolters are more active than those of tetramolters resulting in decreasing % of unfertilized eggs (Liu *et al*., 1987; Yoshida *et al*., 1989; Miao *et al*., 1996; Tsubouchi *et al*., 1997; Niu *et al*., 2013). In the light of the previously reviewed results, anti-JH compounds are promising candidate in the field of sericulture.

19. Summary Points:

- After discovery and isolated PI and PII from the genus *Ageratum*, (*A. houstonianum*, *A. vulgaris* and *A. conyzoides*) and *Chrysanthemum coronarium* of the plant family Asteraceae, the ageratochromenes with anti-JH property had been isolated from some plants of other families, such as Rutaceae, Lamiaceae, Hydrophyllaceae, Lamiaceae, Burseraceae, Malvaceae as well as extracts from the fungus *Penicillium brevicompactum*.
- Many anti-JH compounds can be categorized in various groups, such as precocenes, imidazoles, fluoromevalonates, benzoate and methy dodecenoate compounds, FGLamide allatostatins, benzodioxoles, bisthiolcarbamates, anti-JH compounds from microorganisms, as well as other compounds, such as Piperonyl butoxide, Pyridone, Quinolones, Lovastatin, Arborine, Allyl alcohols and Pitavastatin.
- Various anti-JH compounds had been assessed against several insects of different orders to evaluate their disruptive effects on survival, growth, development, metamorphosis and morphogenesis. Some of these compounds had been reported to exhibit dual effect (anti-JH activity and JH-like activity). Also, adult performance and reproductive biology of different insects had been disturbed by several anti-JH compounds.
- Anti-JH agents exhibit roles in the insect polyphenism, such as the wing dimorphism in aphids and planthoppers, phase transition in locusts, caste polyphenism in ants, bees and termites.
- Anti-JH compounds have some roles in behavioral patterns of insects: non-social insects (sexual behavior, feeding behavior, agonistic behavior, aggregation behavior, flight activity, migratory behavior, learning behaviour and memory), subsocial insects and social insects (honey bees and social wasps).
- Different anti-JH agents had been reported to interfere with the regulation of insect diapause
- Some anti-JH agents showed various histopathological and ultrastructural effects on flight muscles, digestive organs, endocrine organs and reproductive organs in different insects.
- Some anti-JH agents possess antifeedant properties against various insects belonging to different orders, such as Coleoptera, Hemiptera/Homoptera, Isoptera, Orthoptera and Hymenoptera.
- Anti-JH agents have regulatory roles in the general body metabolism (proteins, carbohydrates and lipida), respiratory metabolism and enzymatic activities in insects
- Some anti-JH compounds influenced the chemoreceptor organs in mouth parts and antennae as well as they disrupted the pheromone production in insects.

- The mechanisms of anti-JH compounds are yet to be debatable issue among a number of researchers allover the world because little is known about either the target site(s) or the modes of their action. Some suggestions were discussed.
- Fate and metabolism of anti-JH compounds, not only in the insect body but also in mammals, had been reviewed.
- In addition, effects of different anti-JH compounds had been studied on the insect haemogram, immune responses, host-parasite interaction, fat body structure and function, as well as the cantharidin biosynthesis.
- From the practical point of view, very few developed anti-JH compounds have been shown to be sufficiently active for the pest management programs as yet although low doses of precocenes are relatively safe for beneficial insects.
- Some anti-JH compounds, imidazoles in particular, are very important agents for the sericulture and silk research fields. Many imidazoles and their analogues had been studied in the recent 30 years for inducing trimolter silkworms (skipping off of the 5^{th} larval instar) with improved silk quality and characters.

Conclusions:

As shown the present review, many anti-JH compounds of different categories have been reported to effectively disrupt several physiological processes in insects, such as growth, development, metamorphosis, morphogenesis, reproduction, polymorphism, behavioural patterns, chemoreception, diapause, metabolism, enzymatic activities, pheromone production, *etc*. Therefore, anti-JH agents are potential insect growth regulators as well as an effective tool to study various JH-regulated physiological processes in insects. Although anti-JH compounds are selectively toxic to CA and as such interfering with the synthesis and release of JH leading to disturbance of various physiological processes in insect pests, majority of the research works on these compounds have been achieved in the laboratory and no compounds have been used under the field conditions. Unfortunately, very few developed compounds have been shown to be sufficiently active for the practical purposes in pest management programs as yet. However, precocenes and their synthetic analogues are useful compounds as an effective tool in devising 'fourth generation insecticides'. Compounds with anti-JH activity are considered as new representatives of IGRs lacking some disadvantages of juvenoid-type chemicals. However, these compounds need to be assessed against different insect pests under field conditions in future. On the other hand, some of the anti-JH analogues have been successfully used in the practical production of improved natural silk in the world.

REFERENCES

Abdelkader, M.S.A. and Lockwood, G.B. (2011): Volatile oils from the plant and hairy root cultures of *Ageratum conyzoides* L. Natural Product Research, 25: 909–917. doi:10.1080/14786419.2010.531724

Abdullah M.A.R. (2009): Toxicological and histopathological studies of *Boxus chinensis* oil and precocenes II on larvae of the red palm weevil *Rynchophorus ferrugineus* (Oliver) (Coleoptera: Curculionidae). Egyptian Academic Journal of Biological Sciences, 2(2): 45-54.

Adebayo, A.H.; Zeng, G.Z.; Zhang, Y.M.; Ji, C.J.; Akindahunsi, A.A. and Tan, N.H. (2010): Toxicological evaluation of precocene II isolated from *Ageratum conyzoides* L. (Asteraceae) in Sprague Dawley rats. African Journal of Biotechnology, 9(20): 2938-2944.

Adfa, M.; Yoshimura, T.; Komura, K. and Koketsu, M. (2010): Antitermite activities of Coumarin derivatives and Scopoletin from *Protium javanicum* Burm. f.. Journal of Chemical Ecology, 36: 720–726. doi: 10.1007/s10886-010-9807-1

Adfa, M.; Hattori, Y.; Yoshimura, T.; Komura, K. and Koketsu, M. (2011): Antifeedant and termiticidal activities of 6-Alkoxycoumarins and related analogs against *Coptotermes formosanus* Shiraki. Journal of Chemical Ecology, 37: 598–606. doi: 10.1007/s10886-011-9968-6

Agrawal, A.A. (1998): Induced responses to herbivory and increased plant performance. Nature, 270: 1201-1202. doi: 10.1126/science.279.5354.1201

Ahmed, K.S.; El Alfy, N.Z.; Ramadan, H.A.; El Gohary, H.Z., (2005): Histopathological effects of anti-juvenile hormone precocene I & II on ovaries of grasshopper *Eyprepocnemis plorans* (Charp.)(Orthoptera: Acrididae) using light and electron microscope. Journal of the Egyptian German Society of Zoology, 47(E): 107-134.

Akai, H. and Mauchamp, B. (1989): Suppressive effects of an imidazole derivative, KK-42 on JH levels in hemolymph of *Bombyx* larvae. Journal of Sericulture Science, Japan, 58: 73-74.

Akai, H. and Rembold, H. (1989): Juvenile hormone levels in *Bombyx* larvae and their impairment after treatment with an imidazole derivative KK-42. Zoological Science, 6: 615-618.

Akai, H.; Kimura, K.; Kiuchi, M. and Shibukawa A. (1984): Effects of anti-juvenoid treatment on cocoon and cocoon filaments in *Bombyx mori*. Journal of Sericulture Science, Japan, 53(6): 545-546.

Akai, H.; Kiuchi, M. and Kimura, K. (1986): Effects of anti-JH treatment on the size and fine structure of the cocoon filament of *Bombyx mori*. Journal of Sericulture Science, Japan, 55(5): 388-396.

Al-Dali, A.G.; Ghoneim, K.S.; Bakr, R.F.; Bream, A.S. and Tanani, M.A. (2008): Egg productivity of *Schistocerca gregaria* (Orthoptera: Acrididae) as affected by the non-steroidal ecdysone agonist Tebufenozide (RH- 5992). Journal of Egyptian Academic Society of Environment and Development, 9(10): 27-38.

Aliabadi, F.P.; Sahragard, A. and Ghadamyari, M. (2016): Lethal and sublethal effects of a chitin synthesis inhibitor, lufenuron, against *Glyphodes pyloalis* Walker (Lepidoptera: Pyralidae). Journal of Crop Protection, 5(2): 203-214.

Al-Mekhlafi, F.; Mashaly, A.M.; Abdel Mageed, A.; Wadaan, M.A. and Al-Mallah, N.M. (2011): Overlap effects of cyromazine concentration, treatment method and rearing temperature on the Southern cowpea weevil (*Callosobruchus maculatus* F.) reared on cowpea. African Journal of Microbiology Research, 5(32): 5848-5853. doi: 10.5897/AJMR11.703

Alrubeai, H.F. (1986): The effects of precocenes in grasshopper *Heteracris littoralis* (Orthoptera: Acrididae). International Journal of Tropical Insect Science, 7(4): 529-531. https://doi.org/10.1017/S1742758400009784

Amerasinghe, F.B. (1978): Effects of JH I and JH III on yellowing, sexual activity and pheromone production in allatectomized male *Schistocerca gregaria*. Journal of Insect Physiology, 23: 603-611. https://doi.org/10.1016/0022-1910(78)90123-3

Amiri A.; Bandani, A.R. and Ravan, S. (2010): Effect of an anti-juvenile hormone agent (Precocene I) on sunn pest, *Eurygaster integriceps* (Hemiptera: Scutelleridae) development and reproduction. African Journal of Biotechnology, 9(36): 5859-5868. https://doi.org/10.5897/AJB09.1751

Amppiah, A.S.; Fening, K.O.; Ofosu-Anim, J.; Obeng-Ofori, D. and Ntaanu, P.K. (2014): The Status of Sericulture in Ghana. JENRM, 1(2): 75-79. doi: 10.26796/jenrm.v1i0.17

Amsalem, E. and Hefetz, A. (2010): The appeasement effect of sterility signaling in dominance contests among *Bombus terrestris* workers. Behavioral and Ecological Sociobiology, 64: 1685-1694. doi: 10.1007/s00265-010-0982-4

Amsalem, E.; Malka, O.; Grozinger, C. and Hefetz, A. (2014a): Exploring the role of juvenile hormone and vitellogenin in reproduction and social behavior in bumble bees. BMC Evological Biology, 14: 45. doi: 10.1186/1471-2148-14-45

Amsalem, E.; Teal, P.; Grozinger, C.M. and Hefetz, A. (2014b): Precocene-I inhibits juvenile hormone biosynthesis, ovarian activation, aggression and alters sterility signal production in bumble bee (*Bombus terrestris*) workers. The Journal of Experimental Biology, 217: 3178-3185. doi: 10.1242/jeb.107250

Applebaum, S.W.; Avisar, E. and Heifetz, Y. (1997): Juvenile hormone and locust phase. Archives of Insect Biochemistry and Physiology, 35: 375-391. https://doi.org/10.1002/(SICI)1520-6327(1997)35:4<375::AID-ARCH3>3.0.CO;2-R

Argue, K.J.; Yun, A.J. and Neckameyer, W.S. (2013): Early manipulation of juvenile hormone has sexually dimorphic effects on mature adult behavior in *Drosophila melanogaster*. Hormones and Behavior, 64(4): 589–597. doi:10.1016/j.yhbeh.2013.08.018

Arimura, G.I.; Ozawa, R.; Shimoda, T.; Nishioka, T.; Baland, W. and Akabyshi, J.T. (2000): Herbivory induced volatiles elicit defence genes in lima bean leaves. Nature, 406: 512-515. doi:10.1038/35020072

Arivoli, S. and Tennyson, S. (2011): Larvicidal and adult emergence inhibition activity of *Abutilon indicum* (Linn.) (Malvaceae) leaf extracts against vector mosquitoes (Diptera: Culicidae). Journal of Biopesticides, 4(1): 27-35.

Armbruster, P. and Hutchinson, R.A. (2002): Pupal mass and wing length as indicators of fecundity in Aedes albopictusand *Aedes geniculatus* (Diptera: Culicidae). Journal of Medical Entomology, 39: 699- 704. https://doi.org/10.1603/0022-2585-39.4.699

Arrese, E.L. and Soulages, J.L. (2010): Insect fat body: energy, metabolism, and regulation. Annual Review of Entomology, 55: 207–225. doi: 10.1146/annurev-ento-112408-085356

Asano, S.; Kuwano, E. and Eto, M. (1984a): Anti-juvenile hormone activity of 1-citronellyl-5-phenylimidazole in the 3rd instar silkworm, *Bombyx mori* L. (Lepidoptera: Bombycidae). Applied Entomology and Zoology, 19(2): 212-220. https://doi.org/10.1303/aez.19.212

Asano, S.; Kuwano, E. and Eto, M. (1984b): Induction of precocious metamorphosis by dietary administration of 1-citronellyl-5-phenylimidazole in the 4th instar larvae of the silkworm *Bombyx mori* L. Journal of Pesticide Science, 9(3): 503-510. https://doi.org/10.1584/jpestics.9.503

Asano, S.; Kuwano, E. and Eto, M. (1986). Anti-juvenile hormone activity of imidazole compound (KK-22) and its diminution by the methoprene in the 4th instar silkworm, *Bombyx mori* L. (Lepidoptera: Bombycidae). Applied Entomology and Zoology, 21(1): 63-69. https://doi.org/10.1303/aez.21.63

Ayoade, O.; Morooka, S. and Tojo, S. (1996): Metamorphosis and wing formation in the brown planthopper, *Nilaparvata lugens*, after topical application of Precocene II. Archives of Insect Biochemistry and Physiology, 32: 485-491.

https://doi.org/10.1002/(SICI)1520-6327(1996)32:3/4<485::AID-ARCH20>3.0.CO;2-7

Ayoade, O.; Morooka, S. and Tojo, S. (1996): Induction of macroptery, precocious metamorphosis, and retarded ovarian growth by topical application of precocene II, with evidence for its non-systemic allaticidal effects in the brown plant hopper, *Nilaparvata lugens*. Journal of Insect Physiology, 42: 529-540. https://doi.org/10.1016/0022-1910(96)00135-7

Ayoade, O.; Morooka, S. and Tojo, S. (1999): Enhancement of short wing formation and ovarian growth in the genetically defined macropterous strain of the brown planthopper, *Nilaparvata lugens*. Journal of Insect Physiology, 45: 93-100.

Azambuja, P.D.; Bowers, W.S.; Ribeiro, J.M.C. and Garcia, E.S. (1982): Antifeedant activity of precocenes and analogs on *Rhodnius prolixus*. Experientia, 38(9): 1054-1055. doi: 10.1007/BF01955363

Azambuja, P.; Garcia, E.S. and Bowers, W.S. (1996): Biological activity of a furanyl anti-juvenile hormonal compound on triatominae larvae. Pesticide Science, 47: 159-164. https://doi.org/10.1002/(SICI)1096-9063(199606)47:2<159::AID-PS384>3.0.CO;2-L

Bagley, R.W. and Bauerfeind, J.C. (1972): Field experiences with juvenile hormone mimics. In: "Insect Juvenile hormone: chemistry and function" (Menn, J. and Beroza, M., eds.), pp. 113-151, New York: Academic press. https://doi.org/10.1016/B978-0-12-490950-2.50011-5

Baker, F.C.; Miller, C.A.; Tsai, L.W.; Jamieson, G.C.; Cerf, D.C. and Schooley, D.A. (1986): The effect of juvenoids, anti juvenile hormone agents, and several intermediates of juvenile hormone biosynthesis on the *in vivo* juvenile hormone levels in *Manduca sexta* larvae. Insect Biochemistry, 16: 741–747. https://doi.org/10.1016/0020-1790(86)90109-5

Bakr, R.F.A.; Guneidy, N.A.M. and El-Bermawy, S.M. (2005): Toxicological and biological activities of three IGRs against fourth larval instar of the cotton leafworm *Spodoptera littoralis* (Boisd.). Journal of Egyptian Academy of Environment and Development, 6(4): 103-132.

Balamani, E. and Nair, V.S.K. (1989): Effects of anti-juvenile hormone agents and a juvenile hormone analog on neck-ligated post-feeding last instar larvae of *Spodoptera mauritia* Boisd. (Lepidoptera: Noctuidae). 10(5): 583-589.

Baliga, B.S.; A.W. Pronczuk, and H.N. Munro, (1969): Mechanism of Cycloheximide inhibition of protein synthesis in a cell-free system prepared from rat liver. Journal of Biological Chemistry, 244(16):4480-4489.

Banerjee, S.; Kalena, G.P.; Banerji, A. and Singh, A.P. (2008): New synthetic precocenoids as potential insect control agents. Journal of Environmental Biology, 29(6): 951- 957.

Banerji, A.: (1994): Insect plant interactions: Natural insect control agents. In: "Recent advances in insect physiology and toxicology" (Gujar, G.T. ed.). Agricole Publ. Acad., New Delhi. pp. 41-47.

Banerji, A. and Goomer, N.C. (1984): Synthesis of naturally occurring 6-oxygentaed-2, 2-dimethylchromenes. Indian Journal of Chemistry, 23B: 885-886.

Banerji, A. and Kalena, G.P. (1989): Heterocycles from diacetyl phenols: Synthesis of benzodipyrans, acetyl chromenes of pyrano-(1,2) benzisoxazoles. Heterocycle, 28: 711-718.

Barton, A.E.; Wing, K.D.; Le, D.P.; Slaweki, R.A. and Feyercisen, R. (1989): Aryl-pyridylthiosemicarbazones: a new class of anti-juvenile hormone active against Lepidopteran. Experientia, 45: 580-83.

Basiouny, A. and Ghoneim, K. (2017): Juvenile hormone-like and anti-gonadotropic activities of Fluoromevalonate against the Egyptian cotton leafworm *Spodoptera littoralis* Boisd. (Lepidoptera: Noctuidae). International Journal of Agronomy and Agricultural Research, 11(4): 6-30.

Bayala, B.; Bassole, I.H.N.; Gnoula, C.; Nebie, R.; Yonli, A.; Morel, L.; Figueredo, G.; Nikiema, J.-B.; Lobaccaro, J.-M.A. and Simpore, J. (2014): Chemical composition, antioxidant, anti-Inflammatory and anti-proliferative activities of essential oils of plants from Burkina Faso. PLoS ONE 9(3): e92122. doi:10.1371/journal.pone.0092122

Bede, J.C.; Teal, P.E.; Goodman, W.G. and Tobe, S.S. (2001): Biosynthetic pathway of insect juvenile hormone III in cell suspension cultures of the sedge *Cyperus iria*. Plant Physiology, 127(2): 584–593. doi: 10.1104/pp.010264.

Begum, R. and Qamar, A. (2016): Fenoxycarb- a potent inhibitor of metamorphosis and reproduction in rice moth, *Corcyra cephalonica* (Stainton). Journal of Entomology and Zoology Studies, 4(4): 572-577.

Belles, X. and Baldellou, M.I. (1983): Precocious metamorphosis induced by precocenes on *Oxycarenus lavaterae*. Entomologia Experimentalis et Applicata, 34(2): 129-133. https://doi.org/10.1111/j.1570-7458.1983.tb03306.x

Belles, X.; Camps, F.; Casas, J. and Sanchez, F.-J. (1988): *In vivo* and *in vitro* effects of compactin in liposome carriers on juvenile hormone biosynthesis in adult females of *Blattella germanica*. Pesticide Biochemistry and Physiology, 32(1):1-10. https://doi.org/10.1016/0048-3575(88)90115-0

Bendena, W.G. and Tobe, S.S. (2012): Families of allatoregulator sequences: a 2011 perspective. Canadian Journal of Zoology, 90: 521–544. https://doi.org/10.1139/z2012-012

Benseba, F.; Kilani-Morakchi, S.; Aribi, N. and Solatani, N. (2015): Evaluation of pyriproxyfen, a juvenile hormone analog, on *Drosophila melanogaster* (Diptera: Drosophilidae): insecticidal activity, ecdysteroid contents and cuticle formation. Eur. J. Entomol., 112(4): 625–631. doi: 10.14411/eje.2015.084

Benz, G. and Ren, S.-X. (1986): Some effects of the anti-juvenile hormone fluoromevalonate in three lepidopterous species. Journal of the Swiss Entomological Society, 59: 23-30. http://doi.org/10.5169/seals-402199

Bergot, B.J.; Judy, K.J.; Schooley, D.A. and Tsai, L.W. (1980): Precocene II metabolism: comparative *in vivo* studies among several species of insects, and structure elucidation of two major metabolites. Pesticide Biochemistry and Physiology, 13(2): 95-104. https://doi.org/10.1016/0048-3575(80)90060-7

Bertuso, A.G.; Morooka, S. and Tojo, S. (2002): Sensitive periods for wing development and precocious metamorphosis after precocene treatment of brown planthopper, *Nilaparvata lugens*. Journal of Insect Physiology, 48(2): 221-229. https://doi.org/10.1016/S0022-1910(01)00167-6

Bhagyalakshmi A.; Venkata R.S.; Ramamuthi R. and Reddy P.S. (1995): Studies on the effect of hexachlorocyclohexane on the growth and silk qualities of silkworm, *Bombyx mori* L. Chemistry and Ecology, 11(2): 97-104. https://doi.org/10.1080/02757549508037689

Bilen, J.; Atallah, J.; Azanchi, R.; Levine, J.D. and Riddiford, L.M. (2013): Regulation of onset of female mating and sex pheromone production by juvenile hormone in *Drosophila melanogaster*. Proceedings of the National Academy of Sciences, USA, 110(45):18321-18326. https://doi.org/10.1073/pnas.1318119110

Binder, B.F. and Bowers, W.S. (1994): Precocene II-induced changes in the anatomy of midgut goblet cells of last instar larvae of *Helicoverpa zea* (Boddie)

(Lepidoptera: Noctuidae). International Journal of Insect Morphology and Embryology, New York, 23(1): 27-34. https://doi.org/10.1016/0020-7322(94)90006-X

Binder B.F.; Bowers, W.S. and Evans, P.H. (1991): Insect antijuvenile hormone and juvenile hormone activity from plants in the genus *Nama*. Experentia, 47(2): 199-201.

Bitsch, C. and Bitsch, J. (1984): Antigonadotropic and antiallatal effects of precocene II in the firebrat, *Thermobia domestica* (Thysanura, Lepismatidae). Journal of Insect Physiology, 30(6):463-470. DOI: 10.1016/0022-1910(84)90026-X

Bloch, G.; Borst, D.W.; Huang, Z.; Robinson, G.E.; Cnaani, J. and Hefetz, A. (2000): Juvenile hormone titers, juvenile hormone biosynthesis, ovarian development and social environment in *Bombus terrestris*. Journal of Insect Physiology, 46: 47-57. https://doi.org/10.1016/S0022-1910(99)00101-8

Bloch, G.; Shpigler, H.; Wheeler, D.E. and Robinson, G.E. (2009): Endocrine influences on the organization of insect societies. In: "Hormones, Brain and Behavior"(Arnold, A.P.; Etgen, A.M.; Fahrbach, S.E. and Rubin, R.T. eds.). second ed., Academic Press, San Diego, pp. 1027–1068.

Bowers, W.S. (1976): Discovery of insect anti-allatotropins. In: "The Juvenile Hormones" (Gilbert, L.I., ed.). New York, NY: Plenum Press, pp. 394-408.

Bowers, W.S. (1982): Toxicology of the precocenes. In: "Insecticide Mode of Action" (Coats, J.R. ed.), New York, Academic Press, pp. 403-427.

Bowers W.S. (1983): The precocenes. In: "Endocrinology of Insects"(Downer, R.G.H. and Laufer, H. eds.). Alan R. Liss, Inc., New York, pp. 517-523.

Bowers, W.S. (1985): Anti-hormones. In: "Comprehensive Insect Physiology, Biochemistry and Pharmachology" (Kerkut, G.A. and Gilbert, L.I., eds.), Pergamon Press, Oxford, pp. 551-564.

Bowers, W.S. (1992): Insecticidal compounds from plants. In: "Phytochemical resources for medicine and agriculture" (Nigg, H.K. and Segler, D., eds.). Plenum Press, New York, pp. 227-235.

Bowers, W.S. and Aregullin, M. (1987): Discovery and identification of an antijuvenile hormone from *Chrysanthemum conorarium*. Memórias do Instituto Oswaldo Cruz., 82(III): 51-54.

Bowers, W.S.; Ohta, T.; Cleere, J.S. and Marsella, P.A. (1976): Discovery of insect anti-juvenile hormones in plants. Science, 193: 542–547. http://www.jstor.org/stable/1742746

Bowers, W.S.; Unnithan, G.C.; Fukushima, J.; Toda, J. and Sugiyama, T (1995): Synthesis and biological activity of furanyl anti-juvenile hormonal compounds. Pesticide Science, 43: 1-11. https://doi.org/10.1002/ps.2780430102

Bownes M (2004): The regulation of yolk protein gene expression in *Drosophila* and other flies in higher Diptera. In: "Reproductive Biology of Invertebrates"(Raikhel, A.S.; Sappington, T.W. and Enfield, N.H., eds.), Science Publishers, USA. p.95.

Boyd, D.R.; Sharma, N.D.; Boyle, R.; Evans, T.A.; Malone, J.F.; McCombe, K.M.; Dalton, H. and Chima, J. (1996): Chemical and enzyme-catalysed syntheses of enantiopure epoxide and diol derivatives of chromene, 2,2-dimethylchromene, and 7-methoxy-2,2-dimethylchromene (precocene-1). Journal of the Chem. Society-Perkin Transactions, 1(14): 1757-1765. doi: 10.1039/p19960001757

Bradley, J.T. and Haynes, H.W. (1991): Precocene-induced effects on ovarian development in crickets. Comparative Biochemistry and Physiology, 98A: 213-219.

Braendle, C.; Davis, G.K.; Brisson, J.A. and Stern, D.L. (2006): Wing dimorphism in aphids. Heredity, 97: 192–199. doi:10.1038/sj.hdy.6800863

Breed, M.D.; Smith, T.A. and Torres, A. (1992): Guard honey bees: role in nestmate recognition and replacement. Annals of Entomological Society of America, 85: 633-637.

Brooks, G.T. (1987): Progress on insect control chemicals from juvenile hormone research. Journal of Pesticide Science, 12:113-123.

Brooks, G.T. and McCaffery, A.R. (1990): The precocene antijuvenile hormones (Allatotoxins): a case history in insect toxicology. In: "Chromatography and isolation of insect hormones and pheromones" (McCaffery, A.R. and Wilson, I.D., eds). Plenum Press: New York, pp: 33-43.

Brooks, G.T.; Pratt, G.E.; Ottridge, A.P. and Mace, D.W. (1984a): The inhibition of JH III biosynthesis in corpora allata of the cockroach *Periplaneta americana in vitro*. Proceedings of 1984 Brighton Crop Protection Conference, 3: 881-886.

Brooks, G.T.; Pratt, G.E.; Ottridge, A.P. and Cocks, J.A. (1984b): Effects of inhibitors on JH III biosynthesis in corpora allata of the cockroach *Periplaneta americana* L. *in vitro*. Journal of Pesticide Seience (Tokyo), 9: 211-214.

Broughton, S.J.; Piper, M.D.; Ikeya, T.; Bass, T.M.; Jacobson, J.; Driege, Y.; Martinez, P.; Hafen, E.; Withers, D.J.; Leevers, S.J. and Partridge, L. (2005): Longer lifespan, altered metabolism, and stress resistance in *Drosophila* from ablation of cells making insulin-like ligands. Proceedings of the National Academy of Sciences, USA, 102(8): 3105-3110. https://doi.org/10.1073/pnas.0405775102

Burks, C.S.; Evans, L.D.; Kim, Y. and Krafsur, E.S. (1992): Effects of Precocene and methoprene application in young-adult *Musca autumnalis*. Physiological Entomology, 17: 115-120. https://doi.org/10.1111/j.1365-3032.1992.tb01187.x

Burt, M.E.; Kuhr, R.J. and Bowers, W.S. (1978): Metabolism of precocene II in the cabbage looper and European corn-borer. Pesticide Biochemistry Physiology, 9: 300–303. https://doi.org/10.1016/0048-3575(78)90010-X

Burt, M.E.; Kuhr, R.J. and Bowers, W.S. (1979): Distribution and Metabolism of Precocene II in the brown cockroach (*Periplaneta brunnea* Burmeister). Bulletin of Environmental contamination and Toxicology, 22: 586-589.

Cachero, S.; Ostrovsky, A.D.; Yu, J.Y.; Dickson, B.J. and Jefferis, G.S. (2010): Sexual dimorphism in the fly brain. Current Biology, 20(18):1589–1601. https://doi.org/10.1016/j.cub.2010.07.045

Caldwell, R.L. and Rankin, M.A. (1972): Effects of a juvenile hormone mimic on flight in the milk-weed bug, *Oncopeltus fasciatus*. General and Comparative Endocrinology, 19: 601-605. https://doi.org/10.1016/0016-6480(72)90264-X

Camps, F.; Conchillo, A. and Messeguer, A. (1985): Preparation of Precocene 2 and 3,4-Epoxyprecocene 2 Deuterated Analogues at C-3, C-4 and C-3, C-4. Zeitschrift für Naturforschung, 40b: 556-558.

Cantín, Á.; Moya, P.; Castillo, M.A.; Primo, J.; Miranda, M.A. and Primo-Yúfera, E. (1999): Isolation and synthesis of N-(2-methyl-3-oxodec-8-enoyl)-2-pyrroline and 2-(hept-5-enyl)-3-methyl-4-oxo-6,7,8,8a-tetrahydro-4 H-pyrrolo[2,1- b]1,3-oxazine – two new fungal metabolites with *in vivo* anti-juvenile-hormone and insecticidal activity. European Journal of Organic Chemistry, 1: 221-226. https://doi.org/10.1002/(SICI)1099-0690(199901)1999:1<221::AID-EJOC221>3.0.CO;2-Y

Capinera, J.L. (2008): Sericulture. Encyclopedia of Entomology, pp: 3345-3348. ©Springer Science+Business, Media B.V. doi: 10.1007/978-1-4020-6359-6_4136

Carbone M.A.; Jordan K.W.; Lyman R.F.; Harbison S.T.; Leips J.; Morgan T.J.; DeLuca M.; Awadalla P. and Mackay T.F. (2006): Phenotypic variation and natural selection at catsup, a pleiotropic quantitative trait gene in *Drosophila*. Current Biology, 16: 912-919. https://doi.org/10.1016/j.cub.2006.03.051

Carney, R.L. and Brown, T.L. (1989): US Patent 4,877,899

Carrel, J.E.; Doom, J.P. and McCormick, J.P. (1986): Cantharidin biosynthesis in a blister beetle: inhibition by 6-fluoromevalonate causes chemical disarmament. Experientia, 42(7): 853-854. doi: 10.1007/BF01941552

Castillo, M.; Moya, P.; Couillaud, F.; Garcerá, M.D. and Martínez-Pardo, R. (1998): A heterocyclic oxime from a fungus with anti-Juvenile hormone activity. Archives of Insect Biochemistry and Physiology, 37:287–294. https://doi.org/10.1002/(SICI)1520-6327(1998)37:4<287::AID-ARCH4>3.0.CO;2-O

Castillo, M.-A.; Moya, P.; Cantín, A.; Miranda, M.A.; Primo, J.; Hernández, E. and Primo-Yúfera, E. (1999): Insecticidal, anti-juvenile hormone, and fungicidal activities of organic extracts from different *Penicillium* species and their isolated active components. Journal of Agriculture and Food Chemistry, 47(5): 2120-2124. doi: 10.1021/jf981010a

Cavalcante, V.M.S. and Regis, L.N. (1992): The reproductive capacity of *Panstrongylus megistus* (Hemiptera: Reduviidae) males treated with precocenes. Memórias do Instituto Oswaldo Cruz, 87(4): 467-472. http://dx.doi.org/10.1590/S0074-02761992000400002

Ceccato, P.; Cressman, K.; Giannini, A. and Trzaska, S. (2007): The desert locust upsurge in West Africa (2003-2005): Information on the desert locust early warning system and the prospects for seasonal climate forecasting. International Journal of Pest Management, 53(1): 7-13. https://doi.org/10.1080/09670870600968826

Chamseddin, K.H.; Khan, S.; Nguyen, M.L.H. and Bauer, J. (2012): Takeout-dependent longevity is associated with altered juvenile hormone signaling. Mechanisms of ageing and development, 133: 11-12. https://doi.org/10.1016/j.mad.2012.08.004

Chang, F.; Hsu C.L.; Jurd, L. and Williamson, D.L. (1984): Effects of precocene and benzyl-1,3-benzodioxole derivatives on sex attractancy in the Mediterranean fruit fly (Diptera: Tephritidae). Annals of Entomological Society of America, 77: 147-151. https://doi.org/10.1093/aesa/77.2.147

Chang, F.; Jang, E.B.; Hsu, C.L.; Ma, M. and Jurd, L. (1994): Benzodioxole-1,3-benzodioxole derivatives and their effects on the reproductive physiology of insects. Archives of Insect Biochemistry and Physiology, 27: 39–51. https://doi.org/10.1002/arch.940270106

Chen, Y.R.; Chen, S.C.; Chang, H.W.; Sun, G. and Kou, R. (2005a): Effect of exogenous juvenile hormone III and precocene II on agonistic behavior and the corpora allata *in vitro* activity in the male lobster cockroach *Nauphoeta cinerea* (Dictyoptera: Blaberidae, Oxyhaloinae). Zoological Studies, 44: 409-416.

Chen, Z.; Madden, R.D. and Dillwith, J.W. (2005b): Effect of precocene II on fatty acid metabolism in the pea aphid, *Acyrthosiphon pisum*, under cold stress. Journal of Insect Physiology, 51(4): 411-416. https://doi.org/10.1016/j.jinsphys.2005.02.006

Chenevert, R.; Perron, J.M.; Paquin, R1; Robitaille, M. and Wang, Y.K. (1980): Activity of precocene analogues on *Locusta migratoria* (Forsk.). Expeientia, 36: 379-380.

Chowański, S.; Kudlewska, M.; Marciniak, P. and Rosiński, G. (2014): Synthetic insecticides- is there an alternative? Polish Journal of Environmental Studies, 23(2): 291-302.

Chowański, S.; Lubawy, J.; Urbański, A. and Rosiski, G. (2016): Cardioregulatory functions of neuropeptides and peptide hormones in insects. Protein and Peptide Letters, 23(10): 913-931. doi: 10.2174/0929866523666160728102842

Clark, D. (2000): Synthesis of (−)-Brevioxime. Tetrahedron, 56(34): 6181–6184. https://doi.org/10.1016/S0040-4020(00)00586-X

Clive, D.L.J. and Hisaindee, S. (2000): Synthesis of racemic brevioxime and related model compounds. Journal of Organic Chemistry, 65: 4923-4929. doi: 10.1021/jo0003551

Cnaani, J.; Robinson, G.E.; Bloch, G.; Borst, D. and Hefetz, A. (2000): The effect of queen-worker conflict on caste determination in the bumblebee *Bombus terrestris*. Behavioral and Ecological Sociobiology, 47: 346-352. http://www.jstor.org/stable/4601753

Coats, S.A.; Mutchmor, J.A. and Tollefson, J.H. (1987): Regulation of migratory flight by juvenile hormone mimic and inhibitor in the Western corn rootworm (Coleoptera: Chrysomelidae). Annals of Entomological Society of America, 80: 697-708. https://doi.org/10.1093/aesa/80.5.697

Connat, J.L. (1988): Effects of different anti-juvenile hormone agents on the fecundity of the female cattle tick *Boophilus microplus*. Pesticide Biochemistry and Physiology, 30: 28-34. https://doi.org/10.1016/0048-3575(88)90056-9

Connat, J.-L. and Nepa, M.-C. (1990): Effects of different anti-juvenile hormone agents on the fecundity of the female tick *Ornithodoros moubata*. Pesticide Biochemistry and Physiology, 37: 266-274. https://doi.org/10.1016/0048-3575(90)90133-M

Cornette, R.; Gotoh, H.; Koshikawa, S. and Miura, T. (2008): Juvenile hormone titers and caste differentiation in the damp-wood termite *Hodotermopsis sjostedti* (Isoptera, Termopsidae). Journal of Insect Physiology, 54: 922-930.

Couillaud, F. (1991): Evidence for regulation of juvenile hormone biosynthesis operating before mevalonate in locust corpora allata. Molecular and Cellular Endocrinology, 77(1-3):159–166. doi: 10.1016/0303-7207(91)90070-9.

Couillaud, F.; Mauchamp, B. and Girardie, A. (1987): Biological, radiochemical and physicochemical evidence for the low activity of disconnected corpora allata in locust. Journal of Insect Physiology, 33: 223-228. https://doi.org/10.1016/0022-1910(87)90041-2

Cusson, M.; Sen, S.E. and Shinoda, T. (2013): Juvenile hormone biosynthetic enzymes as targets for insecticide discovery. In: "Advanced technologies for managing insect pests"(Ishayya, I.; Palli, S.R. and Horowitz, A.R., eds), Springer, pp. 31-55.

Czoppelt, C. and Rembold, H. (1985): Effect of precocene 2 on sensibilized honey bee larvae. Mitteilungen der Deutschen Gesellschaft für Allgemeine und Angewandte Entomologie,

Dai, H.; Wu, X. and Wu, S. (2001): The change of juvenile hormone titer and its relation with wing dimorphism of brown planthopper, *Nilaparvata lugens*. Acta Ecologica Sinica, 44: 27-32.

Dale, J.F. and Tobe, S.S. (1986): Biosynthesis and titre of juvenile hormone during the first gonotrophic cycle in isolated and crowded *L. migratoria* females. Journal of Insect Physiology, 32: 763-769. https://doi.org/10.1016/0022-1910(86)90079-X

Damalas, C.A. and Eleftherohorinos, I.G. (2011): Pesticide exposure, safety issues, and risk assessment indicators. International Journal of Environmental Research and Public Health, 8(5): 1402-1419. doi: 10.3390/ijerph8051402

Darvas, B.; Kuwano, E.; Eto, M.; Tag al-din, M.H. and Timar, T. (1990): Effects of some anti-juvenile hormone agents (Precocenes-2, J-2710, KK-110) on post embryonic development of *Neobellieria bullata*. Agricultural and Biological Chemistry; 54(11): 3045-3047. https://doi.org/10.1080/00021369.1990.10870450

DeBaun, J.R.; Bova, D.L.; Tseng, C.K. and Menn, J.J. (1978): Metabolism of [ring_14C] Ordram (molinate) in the rat. 2. Urinary metabolite identification. Journal of Agricultural and Food Chemistry, 26(5): 1098-1104. doi: 10.1021/jf60219a007

De Kort, C.A.D. (1990): Thirty-five years of diapause research with the Colorado potato beetle. Entomologia Experimentalis et Applicata, 56:1-13. https://doi.org/10.1111/j.1570-7458.1990.tb01376.x

De Loof, A.; Van Loon, J. and Vanderroost, C. (1979): Influence of ecdysterone, precocene and compounds with juvenile hormone activity on induction, termination and maintenance of diapause in the parasitoid wasp, *Nasonia vitripennis*. Physiological Entomology, 4(4): 319-328. https://doi.org/10.1111/j.1365-3032.1979.tb00623.x

Deb, D.C. and Chakravorty, S. (1982): Effect of precocene II, applied independently or subsequent to hydroprene treatment, on the morphogenesis of female reproductive organs of *Corcyra cephalonica*. Journal of Insect Physiology, 28(8): 703-712. https://doi.org/10.1016/0022-1910(82)90149-4

Debernard, S.; Rossignol, F. and Couillaud, F. (1994): The HMG-CoAreductase inhibitor fluvastatin inhibits insect juvenile hormone biosynthesis. General and Comparative Endocrinology, 95(1): 92-98. doi: 10.1006/gcen.1994.1105

Denlinger, D.L. (2000): Molecular regulation of insect diapause. In: "Environmental Stressors and Gene Responses"(Storey, K.B. and Storey, J.M., eds.), Elsevier, Amsterdam, pp. 259–275.

Denlinger, D.L.; Yocum, G.D. and Rinehart, J.P. (2012): Hormonal control of diapause. In: "Insect Endocrinology" (Lawrence, I.G., ed.). Academic Press, San Diego, CA, USA, pp: 430-463.

Denno, F. and Perfect, T.J. (1994): Planthoppers: their Ecology and Management. Chapman and Hall, New York, 799 pp.

Dietz, A.; Hermann, H.R. and Blum, M.S. (1979): The role of exogenous JH I, JH III and anti-JH (Precocene II) on queen induction in 4.5-day-old worker honey bee larvae. Journal of Insect Physiology, 25: 503-512. https://doi.org/10.1016/S0022-1910(79)80009-8

Dixon, A.F.G. (1987): Seasonal development in aphids. In: "Aphids, their biology, natural enemies and control"(Minks, A.K. and Harrewijn, P., eds.). Elsevier, Amsterdam, vol. 2A, pp: 315-320.

Donahue, W.A.Jr.; Showler, A.T.; Donahue, M.W.; Vinson, B.E. and Osbrink, W.L.A. (2017): Lethal effects of the insect growth regulator Cyromazine against three species of filth flies, *Musca domestica*, *Stomoxys calcitrans*, and *Fannia*

canicularis (Diptera: Muscidae) in cattle, swine, and chicken manure. J. Econ. Entomol., tow294. doi: https://doi.org/10.1093/jee/tow294

Dorn, A. (1982): Precocene-induced effects and possible role of juvenile hormone during embryogenesis of the milkweed bug *Oncopeltus fasciatus*. General and Comparative Endocrinology, 46(1): 42-52. https://doi.org/10.1016/0016-6480(82)90161-7

Dubrovsky, E.B. (2005): Hormonal cross talk in insect development. Trends in Endocrinology and Metabolism, 16: 6-11. https://doi.org/10.1016/j.tem.2004.11.003

Dubrovsky, E.B.; Dubrovskaya, V.A. and Berger, E.M. (2004): Hormonal regulation and functional role of *Drosophila* E75A orphan nuclear receptor in the juvenile hormone signaling pathway. Developmental Biology, 268: 258-270. https://doi.org/10.1016/j.ydbio.2004.01.009

Duportets, L.; Dufour, M.-C.; Bécard, J.-M.; Gadenne, C. and Couillaud, F. (1996): Inhibition of male corpora allata activity and sexual pheromone responsiveness in the black cutworm, *Agrotis ipsilon*, by the hypocholesterolemic agent, fluvastatin. Insect Biochemistry and Physiology, 32(3-4): 601-611. https://doi.org/10.1002/(SICI)1520-6327(1996)32:3/4<601::AID-ARCH31>3.0.CO;2-E

Duportets, L.; Dufour, M.C.; Couillaud, F. and Gadenne, C. (1998): Biosynthetic activity of corpora allata, growth of sex accessory glands and mating in the male moth *Agrotis ipsilon* (Hufnagel). Journal of Experimental Biology, 201: 2425–2432.

Edwards, J.P. and Price, N.R. (1983): Inhibition of juvenile hormone III biosynthesis in *Peripalneta americana* with the fungal metabolite compactin (ML-236B). Insect Biochemistry, 13(1): 185-189.

Edwards, J.P.; Bergot, B.J. and Staal, G.B. (1983): Effects of three compounds with anti-juvenile hormone activity and a juvenile hormone analogue on endogenous juvenile hormone levels in the tobacco horn worm, *Manduca sexta* Journal of Insect. Physiology, 29(1): 83-89. https://doi.org/10.1016/0022-1910(83)90109-9

Edwards, J.P.; Cerf, D.C. and Staal, G.B. (1985): Inhibition of oötheca production in *Periplaneta americana* (L.) with the anti juvenile hormone fluoromevalonate. Journal of Insect Physiology, 31(9): 723-728. https://doi.org/10.1016/0022-1910(85)90053-8

Eid, M.A.; Salem, M.S.; El-Ibrashy, M.T. and Abdel-Hamid, M. (1982): Effects of precocene II, Cycloheximide and C16-JH on the growth rate and adult morphometrics of *Schistocerca gregaria* Forsk. Bulletin of Entomological Society of Egypt (Economic Series), 13: 95-105.

Eizaguirre, M.; López, C.; Schafellner, Ch. and Sehnal, F. (2007): Effects of ecdysteroid agonist RH-2485 reveal interactions between ecdysteroids and juvenile hormones in the development of *Sesamia nonagrioides*. Archives of Insect Biochemistry and Physiology, 65: 74-84. https://doi.org/10.1002/arch.20181

El-Gammal A.M. (1983): Studies on recent control measures against the desert locust, *Schistocerca gregaria* Forskal. Ph.D. Thesis (Agric.), Cairo University.

El-Gammal, A.M.; Abdel-Fattah, T.A.; Mohamed, M.T. and El-Gawhary, H.M. (2004): The Anti-juvenile hormone action of Cycloheximide (RNA and protein synthesiss inhibitor) in some nymphal instars of *Schistocerca gregaria* Forskal). Egyptian Journal of Agricultural Research, 82(4):1561-1572.

El-Ibrashy (1982): Juvenile hormone mimics in retrospect and antagonists in prospect. Journal of Applied Entomology, 94: 217-236. https://doi.org/10.1111/j.1439-0418.1982.tb02569.x

Elliot, H.J. (1975): Corpus allatum and ovarian growth in a polymorphic paedogenetic insect. Nature, 257: 390-391. doi:10.1038/257390b0

Erezyilmaz, D.F.; Riddiford, L.M. and Truman, J.W. (2006): The pupal specifier broad directs progressive morphogenesis in a direct-developing insect. Proceedings of the National Academy of Sciences of USA, 103(18): 6925-6930. https://doi.org/10.1073/pnas.0509983103

Ergen G. (2001): The effects of precocene II on the fine structure of corpus allatum in adult female *Anacridium aegyptium* L. (Orthoptera: Acridiae). Turkish Journal of Zoology, 25: 95-103.

Farag, A.I. and Varjas, L. (1983): Precocious metamorphosis and moulting deficiencies induced by an anti-JH compound FMev in the fall webworm, *Hyphantria cunea*. Entomologia Experimentalis et Applicata, 34: 65-70. https://doi.org/10.1111/j.1570-7458.1983.tb03291.x

Faraq, A.I.; Darwish, E.T.E. and Hegab, A.M. (1985): On the action of precocene 2 and fenarimol on the cabbage aphid, *Brevicoryne brassicae* (L.) and its parasitoid *Diaeretiella rapae* (M'Intosh). Anz. Schidlingskde, Pflanzenschutz, Umweltschutz, 58: 152-155.

Farazmand, H. (2009): Effect of insect growth regulators on digestive system of Colorado potato beetle larvae, *Leptinotarsa decemlineata* (Say) (Col., Chrysomelidae). Journal of Entomological Research, 1(2): 109-118.

Farazmand, H. and Chaika, S. Yu. (2008): Effects of Precocene-I and II on the development of Colorado potato beetle, *Leptinotarsa decemlineata* (Col.: Chrysomelidae). Applied Entomology and Phytopathology, 76(1): 14pp.

Farazmand, H. and Chaika, S. Yu. (2011): Effects of precocene I and II on the sensory system of antennae and mouthparts of Colorado potato beetle larvae, *Leptinotarsa decemlineata* (Col.: Chrysomelidae). Journal of Entomological Society of Iran, 31(1): 41-56.

Feldlaufer, M.F. and Eberle, M.W. (1980): Insecticidal effect of Precocene II on the human body louse, *Pediculus humanus*. Transactions of the Royal Society of Tropical Medicine and Hygiene, 74(3): 398-399. https://doi.org/10.1016/0035-9203(80)90110-8

Ferkovich, S.M.; Oberlander H., and Roller R.R. (1977): Release of a juvenile hormone binding protein by fat body of the Indian meal moth *Podia interpunctella in vitro*. Journal of Insect Physio1ogy, 123:297-302. https://doi.org/10.1016/0022-1910(77)90045-2

Feyereisen, R. and Farnsworth, D.E. (1987): Precursor supply for insect juvenile hormone III biosynthesis in a cockroach. Journal of Biological Chemistry, 262: 2676-2681.

Feyereisen, R.; Johnson, G.; Koener, J.; Stay, B. and Tobe, S.S. (1981): Precocenes as pro-allatocidins in adult female *Diploptera punctata*: a functional and ultrastructural study. Journal of Insect Physiology, 27(12): 855-868. https://doi.org/10.1016/0022-1910(81)90087-1

Figueroa, C.C.; Prunier-Leterme, N.; Rispe, C.; Sepulveda, F.; Fuentes-Contreras, E.; Sabater-Munoz, B.; Simon, J.-C. and Tagu, D. (2007): Annotated expressed sequence tags and xenobiotic detoxification in the aphid *Myzus persicae* (Sulzer). Insect Science, 14: 29-45. https://doi.org/10.1111/j.1744-7917.2007.00123.x

Flatt, T. and Heyland, A. (2011): Mechanisms of life history evolution: the genetics and physiology of life history traits and trade-offs. Oxford University Press, 506 pp.

Flatt, T.; Tu, M.P. and Tatar, M. (2005): Hormonal pleiotropy and the juvenile hormone regulation of *Drosophila* development and life history. Bioessays, 27: 999-1010. https://doi.org/10.1002/bies.20290

Flatt, T.; Heyland, A.; Rus, F.; Porpiglia, E.; Sherlock, C.; Yamamoto, R.; Garbuzov, A.; Palli, S.R.; Tatar, M. and Silverman, N. (2008): Hormonal regulation of the humoral innate immune response in *Drosophila melanogaster*. Journal of Experimental Biology, 211: 2712-2724. doi: 10.1242/jeb.014878

Fluri, P. (1983): Precocene II has no anti-juvenile hormone effects in adult honey bees. Experientia, 39: 919-920.

Fujita, N.; Furuta, K.; Shiraishi, H.; Hong, S.; Shiotsuki, T. and Kuwano, E. (2005): Synthesis and anti-juvenile hormone activity of ethyl 4-[2-(6-methyl-3-pyridyloxy)alkyloxy]benzoates. Journal of Pesticide Science USA, 30: (3): 192-198. https://doi.org/10.1584/jpestics.30.192

Fujita, N.; Ashibe, K.; Yamada, N.; Shiotsuki, T.; Kiuchi, M. and Kuwano, E. (2007): Juvenile hormone activity of ethyl 4-(2-aryloxyhexyloxy)benzoate with precocious metamorphosis-inducing activity. Bioscience, Biotechnology and Biochemistry, 71: 2333-2334. https://doi.org/10.1271/bbb.70265

Fujita, N.; Furuta, K.; Ashibe, K.; Yoshida, S.; Yamada, N.; Shiotsuki, T.; Kiuchi, M. and Kuwano, E. (2008): Juvenile hormone activity of optically active ethyl 4-(2-benzylalkyloxy)-benzoates inducing precocious metamorphosis. Journal of Pesticide Science, 33(4): 383-386. https://doi.org/10.1584/jpestics.G08-22

Furuta, K.; Shirahashi, H.; Ashibe, K.; Yamashita, H.; Nishikawa, M.; Fujita, N.; Yamada, N. and Kuwano, E. (2006): Synthesis and Anti–Juvenile Hormone Activity of Alkyl 4–(2–Phenoxyalkyloxy)benzoates and Related Compounds. Journal of Faculty of Agriculture, Kyushu University, 51(2): 303-308.

Furuta, K.; Ashibe, K.; Shirahashi, H.; Fujita, N.; Yamashita, H.; Yamada, N. and Kuwano, E. (2007): Synthesis and anti-juvenile hormone activity of ethyl 4-(2-benzylalkyloxy)benzoates and their enantiomers. Journal of Pesticide Science, 32: 99-105. https://doi.org/10.1584/jpestics.G06-46

Furuta, K.; Fujita, N.; Ibushi, T.; Shiotsuki, T.; Yamada, N. and Kuwano, E. (2010): Synthesis and anti-juvenile hormone activity of ethyl 4-[(6-substituted 2,2-dimethyl-2H-chromen-7-yl)methoxy]benzoate. Journal of Pesticide Science, 35: 405-411. https://doi.org/10.1584/jpestics.G09-71

Gäde, G. and Goldsworthy G.J. (2003): Insect peptide hormones: a selective review of their physiology and potential application for pest control. Pest Management Science, 59(10):1063-1075. doi: 10.1002/ps.755

Gao, N. and Hardie, J. (1996): Pre- and post-natal effects of precocenes on aphid morphogenesis and differential rescue. Archives of Insect Biochemistry and Physiology, 32: 503-510. https://doi.org/10.1002/(SICI)1520-6327(1996)32:3/4<503::AID-ARCH22>3.0.CO;2-F

Garcera, M.D.; Ibanez, P.; Martinez, R. and Cunat, P. (1989): Effects of juvenile hormone and precocene II on the metabolic rate of the digestive system, fat body and ovaries of the insect *Oncopeltus fasciatus*. Revista Espanola de Fisiologia, 45: 357-362.

Garcera, M.D.; Ibanez, P.; Martinez, R. and Cunat, P. (1991): Changes induced on the metabolic rate of three insect species by juvenile hormone and precocene II treatments. Revista Espanola de Fisiologia, 47: 31-36.

Garcia, M.L.M.; Melloh, Fl.P. and Mellom, B.C.M. (1988): Effect of precocene II, ecdysone and juvenile hormone on the glycogen concentration in pupae of *Stomoxys calcitrans* (Diptera: Muscidae). Memorias do Instituto Oswaldo Cruz, 83: 451-454. http://dx.doi.org/10.1590/S0074-02761988000400010.

Garside, C.S.; Nachman, R.J. and Tobe, S.S. (2000): Injection of Dip-allatostatin or Dip-allatostatin pseudopeptides into mated female *Diploptera punctata* inhibits endogenous rates of JH biosynthesis and basal oocyte growth. Insect Biochemistry and Molecular Biology, 30: 703-710. https://doi.org/10.1016/S0965-1748(00)00041-2

Gaur, R. and Kumar, K. (2009): Effect of precocene on morphogenesis in housefly, *Musca domestica* Linn. Entomon, 34: 107-110.

Gayathri-Elayidam, U. and Muraleedharen, D. (2001): Influence of juvenile hormone on the early embryonic development of *Dysdercus cingulatus* Fabr. (Heteroptera: Pyrrhocoridae). Entomon, 26:173-182.

Gellissen, G. and Wyatt, G.R. (1981): Production of lipophorin in the fat body of adult *Locusta migratoria*: comparison with vitellogenin. Canadian Journal of Biochemistry, 59: 648-654. https://doi.org/10.1139/o81-090

Gelman, D.B.; Bell, R.A.; Demillo, A.B. and Kochansky, J.P. (1995): Effect of KK-42 on growth, development, molting and metamorphosis of the European corn borer, *Ostrinia nubilalis* (Hubner). Archives of Insect Biochemistry and Physiology, 28: 1-15. https://doi.org/10.1002/arch.940280102

Ghoneim, K.S. (1988): Anti-JH effects of Cycloheximide in *Schistocerca gregaria* Forskal (Orthoptera: Acrididae). Journal of Faculty of Education, Ain Shams University, Egypt 13: 93-102.

Ghoneim, K. (2014): Cantharidin as promising chemotherapeutic agent in the modern medicine: a comprehensive review. Journal of Science, 4(5): 272-292.

Ghoneim, K. (2015): Disturbed Acetylcholinesterase activity in haemolymph and fat bodies of *Schistocerca gregaria* (Forskal)(Orthoptera: Acrididae) by extracts of pomegranate *Punica granatum* Linn. and toothpick weed *Ammi visnaga* L. Review of Knowledge Economy, 2(1): 39-53.

Ghoneim, K. and Basiouny, A. (2017): Insecticidal and antijuvenile hormone activities of Precocene II against the grasshopper *Euprepocnemis plorans plorans* (Charp.) (Orthoptera: Acrididae). International Journal of Trend in Scientific Research and Development, 1(6): 510-524.

Ghoneim, K. and Bosly, H.A.M. (2017): Disruptive impact of Precocene I (juvenile hormone-antagonist) on the adult performance and reproductive potential of the Egyptian cotton leafworm *Spodoptera littoralis* Boisduval (Lepidoptera: Noctuidae). Egyptian Academic Journal of Biological Sciences (A. Entomology), 10(6): 1-25.

Ghoneim, K.; Amer, M.; Al-Daly, A.; Mohammad, A.; Khadrawy, F. and Mahmoud, M. (2014a): Disrupted survival, growth and development of desert locust *Schistocerca gregaria* (Forskal) (Orthoptera: Acrididae) by extracts from toothpick weed *Ammi visnaga* Lamarck (Apiaceae). International Journal of Biosciences, 5(1): 397-414. doi: 10.12692/ijb/5.1.397-414

Ghoneim, K.; Tanani, M.; Hamadah, Kh.; Basiouny, A. and Waheeb, H. (2014b): Inhibited reproductive capacity of Egyptian cotton leaf worm *Spodoptera littoralis* (Boisd.) (Lepidoptera: Noctuidae) by the chitin synthesis inhibitor Novaluron. Egyptian Academic Journal of Biological Sciences (A. Entomology), 7(2): 105-118.

Ghoneim, K.; Hamadah, Kh.; El-Hela, A.; Mohammad, A. and Amer, M. (2015): Efficacy of *Nigella sativa* (Ranunculaceae) extracts on adult performance and phase transition of the desert locust *Schistocerca gregaria* (Orthoptera: Acrididae). International Journal of Research Studies in Zoology, 1(2): 29-44.

Ghoneim, K.; Hassan, H.A.; Tanani, M.A. and Bakr, N.A. (2017a): Toxic and disruptive effects of Novaluron, a chitin synthesis inhibitor, on development of the pink bollworm *Pectinophora gossypiella* (Saunders)(Lepidoptera: Gelechiidae). International Journal of Entomology Research, 2(2): 36-47.

Ghoneim, K.; Hamadah, Kh.; Mansour, A.N. and Abo Elsoud, A.A. (2017b): Toxicity and disruptive impacts of Novaluron, a chitin synthesis inhibitor, on development and metamorphosis of the olive leaf moth *Palpita unionalis* (Hübner) (Lepidoptera: Pyralidae). International Journal of Trend in Research and Development, 4(3): 184-193.

Ghosh, A.; Chowdhury, N. and Chandra, G. (2012): Plant extracts as potential mosquito larvicides. Indian Journal of Medical Research, 135: 581-598.

Gilbert, L.I.; Granger, N.A. and Roe, R.M. (2000): The juvenile hormones: historical facts and speculations on future research directions. Insect Biochemistry and Molecular Biology, 30: 617-644. doi: 10.1016/S0965-1748(00)00034-5

Gillett, S.D. and Phillips, M.L. (1977): Faeces as a source of a locust gregarization stimulus. Effects on social aggregation and on cuticular colour of nymphs of the desert locust, *Schistocerca gregaria* (Forsk.) Acrida, 6: 279-286.

Giridhar, K.; Mahanya, J.C.; Kantharaju, B.M. and Nagesh, S. (2010): Raw silk production. Indian Silk, 8(1): 27-29.

Goewie, E.A.; Beetsma, J. and de Wilde, J. (1978): Wirkung von precocene II auf die Kastendifferenzierung der Honigiene (*Apis mellifera*). Mitteilungen der deutschen Gesellschaft fur allgemeine und angewande Entomologie, 1: 304-305.

Goodman, W.G. and Granger N.A. (2005): The juvenile hormones. In: "Comprehensive molecular insect science" (Gilbert, L.I.; Iatrou, K. and Gill, S.S., eds). Elsevier, Boston, Vol 3, pp: 320-408.

Gordon, S.D.; Rogers, S. and Windmill, J. (2012): Hearing differences of gregarious and solitary locusts (*Schistocerca gregaria*), an example of epigenetic effects. Frontiers in Behavioral Neuroscience, Conference Abstract: Tenth International Congress of Neuroethology. doi: 10.3389/conf.fnbeh.2012.27.00122

Gotoh, H.; Cornette, R.; Koshikawa, S. and Miura, T. (2008): Effects of precocenes on the corpora allata and the JH titer in the damp-wood termite *Hodotermopsis sjostedti* (Isoptera: Termopsidae). Sociobiology, 52(2): 345-356. http://agriknowledge.affrc.go.jp/RN/3020068181

Granger, N.A.; Janzen, W.P. and Ebersohl, R. (1995): Biosynthetic products of the corpus allatum of the tobacco hornworm, *Manduca sexta*. Insect Biochemistry and Molecular Biology, 25(4): 427-439. https://doi.org/10.1016/0965-1748(94)00076-B

Greenspan, R.J. (1995): Understanding the genetic construction of behavior. Scientific American, 272(4): 72-78.

Grossniklaus-Bürgin, C. and Lanzrein, B. (1990): Endocrine interrelationship between the parasitoid *Chelonus* sp. and its host *Trichoplusia ni*. Archives of Insect Biochemistry and Physiology, 14: 201-216.

Gu, S.H.; Chow, Y.S. and Lin, F.J. (1995): Fluctuations in the biosyn-thetic activity of the prothoracic gland in recessive trimolters of the silkworm, *Bombyx mori*.

Journal of Experimental Zoology, 271: 211-219. https://doi.org/10.1002/jez.1402710308

Hales, D.F. and Mittler, T.E (1981): Precocious metamorphosis of the aphid *Myzus persicae* induced by the precocene analogue 6-methocy-7-ethoxy-2,2-dimethylchromene. Journal of Insect Physiology, 27: 333-337. https://doi.org/10.1016/0022-1910(81)90079-2

Halpin, R.A.; El-Naggar, S.F.; McCombe, K.M.; Vyas, K.P.; Boyd, D.R. and Jerina, D.M. (1982). Resolution and assignment of absolute configuration to the (+)- and (-)-*cis* and *trans* 3,4-diol metabolites of the antijuvenile hormone precocene I. Tetrahedron Letters, 23: 1655-1658. https://doi.org/10.1016/S0040-4039(00)87182-8

Halpin, R.A.; Vyas, K.P.; El-Nagger, S.F. and Jerina, D.M. (1984): Metabolism and hepatotoxicity of the naturally occurring benzo[b]pyran precocene I. Chemico-Biological Interactions, 48(3): 297-315.

Hamadah, Kh.; Tanani, M.; Ghoneim, K.; Basiouny, A. and Waheeb, H. (2015): Effectiveness of Novaluron, chitin synthesis inhibitor, on the adult performance of Egyptian cotton leafworm, *Spodoptera littoralis* (Boisd.)(Lepidoptera: Noctuidae). International Journal of Research Studies in Zoology, 1(2): 45-55.

Hamadah, Kh.; Ghoneim, K.; Mansour, A.N. and Abo Elsoud, A.A. (2017): Deranged adult performance and reproductive potential of the olive leaf moth *Palpita unionalis* (Hübner)(Lepidoptera: Pyralidae) by the non-steroidal ecdysone agonist, Methoxyfenozide. International Journal of Information Research and Review, 4(6): 4228-4240.

Hamaidia, K. and Soltani, N. (2014): Laboratory evaluation of a biorational insecticide, Kinoprene, against *Culex pipiens* Larvae: effects on growth and development. Annual Research & Review in Biology, 4(14): 2263-2273. doi: 10.9734/ARRB/2014/9729

Hamaidia, K. and Soltani, N. (2016): Ovicidal activity of an insect growth disruptor (methoxyfenozide) against *Culex pipiens* L. and delayed effect on development. Journal of Entomology and Zoology Studies, 4(4): 1202-1207.

Hamnett, A.F. and Pratt, G.E. (1983): The absolute configuration of precocene I dihydrodiols produced by metabolism of precocece I by corpora allata of *Locusta migratoria in vitro*. Life Sciences, 32: 2147-2153. https://doi.org/10.1016/0024-3205(83)90395-8

Hanelova, J. (2005): Parental care of true bugs from the family Acanthosomatidae (Heteroptera). Unpublished M.Sc. thesis, Charles University in Prague, Department of Zoology, 103 pp. (in Czech).

Harano, K.-I.; Tanaka, S.; Watari, Y. and Saito, O. (2012): Phase-dependent locomotor activity in first-stadium nymphs of the desert locust, *Schistocerca gregaria*: Effects of parental and progeny rearing density. Journal of Insect Physiology, 58: 718-725. doi:10.1016/j.jinsphys.2012.02.007

Hardie, J. (1986): Morphogenetic effects of precocenes on three aphid species. Journal of Insect Physiology, 32: 813-818. https://doi.org/10.1016/0022-1910(86)90085-5

Hardie, J.; Baker, F.C.; Jamieson, G.C.; Lees, A.D. and Schooley, D.A. (1985): The identification of an aphid juvenile hormone, and its titre in relation to photoperiod. Physiological Entomology, 10: 297-302. https://doi.org/10.1111/j.1365-3032.1985.tb00050.x

Hardie, J.; Honda, K.; Timar, T. and Varjas, L. (1995): Effects of 2,2-dimethylchromene derivatives on wing determination and metamorphosis in the

pea aphid, *Acyrthosiphon pisum*. Archives of Insect Biochemistry and Physiology, 30: 25-40. https://doi.org/10.1002/arch.940300103

Hardie, J.; Gao, N.; Timar, T.; Sebok, P. and Honda, K. (1996): Precocene derivatives and aphid morphogenesis. Archives of Insect Biochemistry and Physiology, 32: 493–501. https://doi.org/10.1002/(SICI)1520-6327(1996)32:3/4<493::AID-ARCH21>3.0.CO;2-6

Hartfelder, K. (1990): Regulatory steps in caste development of eusocial bees. In: "Social Insects - an Evolutionary Approach to Castes and Reproduction"(Engels, W. ed.), Heidelberg: Springer, pp. 245–264.

Hartfelder, K. (2000): Insect juvenile hormone: from '*status quo*' to high society. Brazilian Journal of Medical and Biological Research, 33: 157-177. http://dx.doi.org/10.1590/S0100-879X2000000200003

Hartfelder, K. and Emlen, D.J. (2012): Endocrine control of insect polyphenism. ©2012 Elsevier B.V., Chapter 11, pp: 464-522. doi: 10.1016/B978-0-12-384749-2.10011-1

Hartman, H.B. and Suda, M. (1973): Pheromone production and mating behavior by allatectomized males of the cockroach, *Nauphoeta cinerea*. Journal of Insect Physiology, 19: 1417-1422. https://doi.org/10.1016/0022-1910(73)90172-8

Hassan, H.A.; Ghoneim, K.; Tanani, M.A. and Bakr, N.A. (2017): Impairing effectiveness of the chitin synthesis inhibitor, Novaluron, on adult performance and reproductive potential of the pink bollworm *Pectinophora gossypiella* (Saunders) (Lepidoptera: Gelechiidae). Journal of Entomology and Zoology Studies, 5(2): 581-592.

Haunerland, N.H. and Bowers, W.S. (1985): Comparative studies on pharmacokinetics and metabolism of the anti-juvenile hormone precocene II. Archives of Insect Biochemistry and Physiology, 2: 55-63. https://doi.org/10.1002/arch.940020106

Hebbalkar, D.S. and Sharma, R.N. (1991): Effects of age sex oogenetic cycles body weight juvenoids and precocene II on the oxygen consumption of red cotton bug *Dysdercus koenigii* F. Indian Journal of Experimental Biology, 29: 962-966.

Hegazi, E.M.; El-Singaby, N.R. and Khafagi, W.E. (1998): Effects of precocenes (I and II) and juvenile hormone I on *Spodoptera littoralis* (Boisd.) (Lep.; Noctuidae) larvae parasitized by *Microplitis rufiventris* Kok. (Hym.; Braconidae). Journal of Applied Entomology, 122: 453-456. doi: 10.1111/j.1439-0418.1998.tb01525.x

Hegazi, E.M. and Khafagi, W.E. (1998): Precocene II and possible function of *Microplitis rufiventris* Kok. (Hym., Brac.) teratocytes. Archives of Phytopathology and Plant Protection, 32: 49-58. http://www.tandfonline.com/loi/gapp20

Hegazi E.M.; El-Shazli, A.Y.; Hafez, M.B. and Abd El-Aziz, G.M. (2000): Influence of precocene II on the estimated changes within haemocytes population of parasitized *Spodoptera littoralis* larvae by *Microplitis rufiventris*. Archives of Phytopathology and Plant Protection, 33(4): 351-360. doi: 10.1080/03235400009383355

Henderson, G.R. (1998): Primer pheromones and possible soldier caste influences on the evolution of sociality in lower termites. In: "Pheromone Communication in Social Insects" (Vander Meer, R.K.; Breed, M.D.; Espelie, K.E. and Winston, M.L., eds.). Westview Press, Boulder, pp.: 314-330.

Hirai, M.; Kamineura, M.; Kikuchi, K.; Yasukochi, Y.; Kiruchi, M.; Shinoda, T. and Shiotsuki, T. (2002): cDNA cloning and characterization of *Bombyx mori* juvenile hormone esterase; an inducible gene by the imidazole insect growth regulator KK-42. Insect Biochemistry and Molecular Biology, 32(6): 627-35. https://doi.org/10.1016/S0965-1748(01)00141-2

Hiramatsu, Y.; Adfa, M.; Ninomiya, M.; Yoshimura, T. and Koketsu, M. (2013): Effects of 2,2-dimethylchromenes against the feeding behavior of *Coptotermes formosanus* Shiraki. Journal of Pesticide Science, 38(4): 228–231. https://doi.org/10.1584/jpestics.D13-050

Hiruma, K.; Yagi, S. and Endo, A. (1983): ML-236B (Compactin) as an inhibitor of juvenile hormone biosynthesis. Applied Entomology and Zoology, 18(1): 111-115. https://doi.org/10.1303/aez.18.111

Hodek, I. (2002): Controversial aspects of diapause development. European Journal of Entomology, 99: 163-173. doi: 10.14411/eje.2002.024

Hoffmann K.H. and Lorenz, M.W. (1998): Recent advances in hormones in insect pest control. Phytoparasitica, 26(4): 323–330.

Hsia, M.T.S.; Grossman, S. and Schrankel, K.R. (1981): Hepatotoxicity of the antijuvenile hormone precocene II and the generation of dihydrodiol metabolites. Chemo-Biological Interactactions, 37: 265-277. https://doi.org/10.1016/0009-2797(81)90113-7

Hsu, C.L. and Chang, F. (1982): Interference with JH production as a possible cause for the effect of Precocene II on sex attractancy in the Mediterranean fruit fly (Diptera: Tephritidae). Annals of Entomological Society of America, 75: 363-365. https://doi.org/10.1093/aesa/75.4.363

Hsu, C.-L.; Chang, F.; Mower, H.F.; Groves, L.J. and Jurd, L. (1989): Effect of orally administered 5-Ethoxy-6-[4-Methoxyphenyl] Methyl-1,3-Benzodioxole on reproduction of the Mediterranean fruit fly (Diptera: Tephritidae). Journal of Economic Entomology, 82(4): 1046-1053. https://doi.org/10.1093/jee/82.4.1046

Hsu, C.-L.; Chang, F.; Hunter, W. and Hou, R.F. (1990): Cytological effects of J2581 (5-ethoxy-6-ethoxy-6-[4-methoxyphenyl] methyl-1,3-benzodioxole) on spermatogenesis in the oriental fruit fly, *Dacus dorsalis* Hendel. Comparative Biochemistry and Physiology Part C: Comparative Pharmacology, 96(1): 27-31. https://doi.org/10.1016/0742-8413(90)90039-C

Hu, B.-Z.; Xu, Y.; Zheng, X.-R. and Shi, W.-P. (2012): Molt disruption and mortality of *Locusta migratoria* var. *manilensis* (Meyen) (Orthoptera: Acrididae) caused by insect growth regulators. African Journal of Biotechnology, 11(16): 3882-3887. http://dx.doi.org/10.5897/AJB11.2854

Huang, Z.Y. and Robinson, G.E. (1992): Honeybee colony integration: worker-worker interactions mediate hormonally regulated plasticityin division of labor. Proceedings of the National Academy of Sciences of USA (PNAS), 89: 11726-11729. https://doi.org/10.1073/pnas.89.24.11726

Huang Z.Y.; Robinson, G.E. and Borst, D.W. (1994): Physiological correlates of division of labor among similarly aged honey bees. Journal of Comparative Physiology A, 174:731-739.

Huang, Q.; Qian, X.; Song, G. and Cao, S. (2003): The toxic and antifeedant activity of 2h-pyradazin-3-one-substituted 1,3,4,-oxidazoles against armyworm *Pseudaletia separate* (Walker) and other insects and mites. Pest Management Science, 59(8):933-939.

Hult, E.F.; Weadick, C.J.; Chang, B.S.W. and Tobe, S.S. (2008): Reconstruction of ancestral FGLamide-type insect allatostatins: A novel approach to the study of allatostatin function and evolution. Journal of Insect Physiology, 54: 959-968. doi: 10.1016/j.jinsphys.2008.04.007

Hwangbo, D.S.; Gersham, B.; Tu, M.P.; Palmer, M. and Tatar, M. (2004): *Drosophila* dFOXO controls lifespan and regulates insulin signaling in the brain and fat body. Nature, 429: 562-566. doi:10.1038/nature02549

Ignell, R.; Couillaud, F. and Anton, S. (2001): Juvenile hormone mediated plasticity of aggregation behaviour and olfactory processing in adult desert locusts. Journal of Experimental Biology, 204(2): 249-259.

Iqbal, M.C.M.; Jayasasinghe, U.L.B.; Herath, H.M.T.B.; Wiljesekara, K.B. and Fujimoto, Y. (2004): A fungistatic chromene from *Ageratum conyzoides*. Phytoparasitica, 32: 119-126. doi: 10.1007/BF02979776

Ishiguro, H.; Fujita, N.; Kim, I-H.; Shiotsuki, T. and Kuwano, E. (2003): Ethyl 4-[2-(6-Methyl-3-pyridyloxy)butyloxy]benzoate, a novel anti-juvenile hormone agent. Biosciences, Biotechnology and Biochemistry, 67: 2045-2047. doi: 10.1271/bbb.67.2045

Islam, M.S. (1995): Endocrine manipulation in crowd-reared desert locust *Schistocerca gregaria* (Forskal). II. Effects of Precocene on mortality and reproductive parameters. Bangladesh Journal of Zoology, 23: 199-208.

Ismail, S.H.; Hassanali, A.; Osir, E. and Tawfik, A. (1997): Effects of anti-juvenile hormone (Precocene II) treatment on phase changes and pheromone production in the desert locust, *Schistocerca gregaria* (Forskal) (Orthoptera: Acrididae). Journal of insect Physiology, 43(12): 1177-1182. doi: 10.1016/S0022-1910(97)00079-6

Isman, M.B.; Yan, J.Y. and Proksch, P. (1986): Toxicity of natural chromene derivatives to a grasshopper. Naturwissenschaften, 73: 500-501. doi: 10.1007/BF00367198

Jaffe, K. (1980): Effects of Cycloheximide on protein synthesis and memory consolidation in praying mantids. Physiology and Behavior, 25: 367-371. doi: 10.1016/0031-9384(80)90275-9

Jalba, H.C. (2016): Scenario of sericulture industry in Maharashtra State, India. Journal of Entomology and Zoology Studies, 4(1): 601-605.

Jaya; Prakash B. and Dubey N.K. (2011): Evaluation of chemically characterized essential oils of *Coleus aromaticus*, *Hyptis suaveolens* and *Ageratum conyzoides* against storage fungi and aflatoxin contamination of food commodities. International Journal of Food Science and Technology, 46: 754-760. https://doi.org/10.1111/j.1365-2621.2011.02557.x

Jennings, R.C. and Ottridge, A.P. (1984): The synthesis of the epoxide and some other possible metabolites of precocene I. Journal of Chemical Society, Perkin Transactions, I: 1733. doi: 10.1039/P19840001733

Jian, H.; Gong-yin, Y.; Yong-li, L.; Yue-xian, F. and Cui, H. (1999): Effect of Jinlu, an imidazole derivate on ultrastructure of larval silk gland cells of *Antheraea yamamai* (Lep.: Saturniidae). Journal of Chinese Electron Microscopy Society, 18: 583-594.

Joiner, R.L.; Vinson, S.B. and Benskin, J.B. (1973): Teratocytes as a source of juvenile hormone activity in a parasitoid-host relationship. Nature, 246: 120-121. doi:10.1038/newbio246120a0

Jokubaitis, L.A. (1996): Development and pharmacology of fluvastatin. British Journal of Clinical Practice. Supplement, 77A: 11-15.

Jurberg, J.; Galvão, C.; Bowers, W.S.; Garcia, E.S. and Azambuja, P. (1997): Biomorphological alterations induced by an anti-juvenile hormonal compound, 2-(2-ethoxyethoxy)ethyl furfuryl ether, on three species of Triatominae larvae (Hemiptera, Reduviidae). Memórias do Instituto Oswaldo Cruz, Rio de Janeiro, 92(2): 263-268. http://dx.doi.org/10.1590/S0074-02761997000200022

Jurd, L.; Fye, R.L. and Morgan, J.Jr. (1979): New types of insect chemosterilants. Benzylphenols and benzyl-1,3-benzodioxole derivatives as additives to housefly diet. Journal of Agticulture and Food Chemistry, 27:1007-1016. doi: 10.1021/jf60225a053

Kadono-Okuda, K.; Kuwano, E.; Eto, M. and Yamashita, O. (1987): Inhibitory action of an imidazole compound on ecdysone synthesis in prothoracic glands of the silkworm, *Bombyx mori*. Development, Growth and Differentiation, 29: 527-533. https://doi.org/10.1111/j.1440-169X.1987.00527.x

Kadano-Okuda, K.; Amornsak, W. and Yamashita, O. (1994): Controlled ecdysteroid accumulation in eggs of silkworm, *Bombyx mori*, by an imidazole compound (KK-42), and embryogenesis in these eggs. Archives of Insect Biochemistry and Physiology, 25: 121-135. https://doi.org/10.1002/arch.940250205

Kai, Z.P.; Huang, J.; Tobe, S.S. and Yang, X.L. (2009): A potential insect growth regulator: synthesis and bioactivity of an allatostatin mimic. Peptides, 30(7):1249-1253. doi: 10.1016/j.peptides.2009.03.010.

Kai, Z.P.; Huang, J.; Xie, Y.; Tobe, S.S.; Ling, Y.; Zhang, L.; Zhao, Y.C. and Yang, X.L. (2010): Synthesis, biological activity, and hologram quantitative structure–activity relationships of novel allatostatin analogues. Journal of Agriculture and Food Chemistry, 58(5):2652–2658. doi: 10.1021/jf902156k

Kai, Z.P.; Xie, Y.; Huang, J.; Tobe, S.S.; Zhang, J.R. and Ling Y. (2011): Peptidomimetics in the discovery of new insect growth regulators: studies on the structure–activity relationships of the core pentapeptide region of allatostatins. Journal of Agriculture and Food Chemistry, 59: 2478-2485. doi: 10.1021/jf200085d

Kamaruzzaman, A.; Reza, A.; Mondal, K. and Parween, S. (2006): Morphological abnormalities in *Tribolium castaneum* (Herbst) and *Tribolium confusum* Jacquelin du Val Duval due to cyromazine and pirimiphos-methyl treatments alone or in combination. Invertebrate Survival Journal, 3: 97-102.

Kambhampati, S.; Mackauer, M. and Nair, K.K. (1984): Precocious metamorphosis and wing formation in the pea aphid, *Acyrthosiphon pisum*, induced by precocene analogue 7-ethoxy-6methoxy-2,2-dimethylchromene. Archives of Insect Biochemistry and Physiology, 1: 115-147. https://doi.org/10.1002/arch.940010204

Kanda, T.; Kiguchi, K.; Murayama, J.; Aoki, A.; Takahashi, T.; Kanda, C.; Wu, Y.C.; Kuwano, E. and Eto, M. (1985): Induction of precocious trimolting silkworms by anti-juvenile hormone and the physical properties of the cocoon filament and fabrics. Sanshi Shikenjo Hokoku, 30(1):123-149.

Kandil, M.A.; Ahmed, A.F. and Moustafa, H.Z. (2012): Toxicological and biochemical studies of lufenuron, chlorfluazuron and chromafenozide against *Pectinophora gossypiella* (Saunders). Egyptian Academic Journal of Biological Sciences, 4(1): 37- 47.

Kaneko, Y.; Furuta, K.; Kuwano, E. and Hiruma, K. (2011): An anti-juvenile hormone agent, ethyl 4-(2-benzylhexyloxy)benzoate, inhibits juvenile hormone synthesis through the suppression of the transcription of juvenile hormone

biosynthetic enzymes in the corpora allata in *Bombyx mori*. Insect Biochemistry and Molecular Biology, 41(10):788-794. doi: 10.1016/j.ibmb.2011.05.009

Kappler, C.; Kabbouh, M.; Hetru, C.; Durst, F. and Hofftriann, J.A. (1988): Characterization of three hydroxylases involved in the final steps of biosynthesis of the steroid hormone ecdysone in *Locusta migratoria* (Insecta, Orthoptera). Journal of Steroid Biochemistry, 31: 891-898. https://doi.org/10.1016/0022-4731(88)90330-5

Karadogan, B. and Parsons, P.J. (2001): Synthesis of racemic brevioxime and related analogues. Tetrahedron, 57(41): 8699-8703. doi: 10.1016/S0040-4020(01)00835-3

Kartal M.; Altun M.L. and Kurucu S., (2003): HPLC method for the analysis of harmol, harmalol, harmine and harmaline in the seeds of *Peganum harmala* L. Journal of Pharmaceutical and Biomedical Analysis, 31: 263-269. https://doi.org/10.1016/S0731-7085(02)00568-X

Kawaguchi, Y.; Banno, Y.; Doira, H. and Fuji, H. (1993): Manifestation of characteristics in the giant egg mutant of *Bombyx mori* (Lepidoptera: Bombycidae). 4: Surface structure of eggshell in Ge egg. Japan Journal of Applied Entomology and Zoology, 37: 91-95.

Keightley, D.A.; Lou, K.J. and Smith, W.A. (1990): Involvement of translation and transcription in insect steroidogenesis. Molecular and Cellular Endocrinology, 74: 229-237. https://doi.org/10.1016/0303-7207(90)90228-Z

Kelly, T.J. and Fuchs, M.S. (1978): Precocene is not a specific anti-gonadotropic agent in adult female *Aedes aegypti*. Physiological Entomology, 3: 297-301. https://doi.org/10.1111/j.1365-3032.1978.tb00162.x

Kelly, D.C. and Lescott, T. (1976): The Effects of inhibitors of nucleic acid and protein synthesis on the replication of *Spodoptera frugiperda* nuclear polyhedrosis virus in cultured *Spodoptera frugiperda* cells. Intervirology, 7: 360-365. doi:10.1159/000149978

Kennedy, J.S. and Stroyan, H.L.G. (1959): Biology of aphids. Annual Review of Entomology, 4: 139-160. https://doi.org/10.1146/annurev.en.04.010159.001035

Khafagi, W. (2000): Reproductive potential of the parasitic wasp *Microplitis rufiventris* Kok. reared in hosts treated with the growth regulator precocene II. Anzeiger für Schädlingskunde, 73(2): 55-57. https://doi.org/10.1046/j.1439-0280.2000.00055.x

Khafagi, W.E. (2004): Effects of juvenile hormone I, precocene I and precocene II on the progeny of *Microplitis rufiventris* Kok. female when administered *via* its host, *Spodoptera littoralis* (Boisd.). Journal of Applied Entomology, 128: 6-10. https://doi.org/10.1046/j.1439-0418.2003.00795.x

Khafagi, W.E. and Hegazi, E.M. (1999): Latent effects of precocenes (I and II) and juvenile hormone I on *Spodoptera littoralis* (Boisd.) larvae. Archives of Phytopathology and Plant Protection 32(4):337-350. doi: 10.1080/03235409909383302

Khafagi, W.E. and Hegazi, E.M. (2001): Effects of juvenile hormones I & II and precocenes I & II on the immune response of *Spodoptera littoralis* larvae to supernumerary larvae of the solitary parasitoid, *Microplitis rufiventris* Kok. Journal of Insect Physiology, 47: 1249–1259. doi: 10.1016/S0022-1910(01)00110-X

Khafagi, W.E. and Hegazi, E.M. (2004): Effects of juvenile hormone I and precocene I & II on *Microplitis rufiventris* when administered *via* its host, *Spodoptera*

littoralis. BioControl, 49: 517–536. doi: 10.1023/B:BICO.0000036435.76314.ad

Khan, M.A. (1988): Brain-controlled synthesis of juvenile hormone in adult insects. Entomologia Experimentalis et Applicata, 46: 3–17. https://doi.org/10.1111/j.1570-7458.1988.tb02262.x

Khan, I.A. and Kumar, K. (2000): Precocene II acts as insect growth regulator in polyphagous pest, *Pericallia ricini* F. (Lepidoptera: Arctiidae). The Proceedings of the National Academy of Sciences, India, 70(B): 279-285.

Khan, I.A. and Kumar, K. (2005): Effect of precocene II on imaginal differentiation in flesh fly, *Sarcophaga ruficornis* F. (Diptera: Sarcophagidae). Entomon, 30: 187-191.

Khan, G.Z.; Khan, I.; Khan, I.A.; Alamzeb; Salman, M. and Kalim Ullah, (2016): Evaluation of different formulations of IGRs against *Aedes albopictus* and *Culex quinquefasciatus* (Diptera: Culicidae). Asian Pacific Journal of Tropical Biomedicine, 6(6): 485-491. https://doi.org/10.1016/j.apjtb.2016.04.008

Khatter, N.A. (2014): Effect of two insect growth regulators on the development of *Agrotis ipsilon* Hufn. (Lepidoptera: Noctuidae). Journal of Harmonized Research in Applied Sciences, 2(1): 20-28.

Kiehlmann, E.; Conn, J.E. and Borden, J.H. (1982): 7-Ethoxy-6-methoxy-2,2-dimethyl-2H- benzopyran. Organic Preparations and Procedures International, 14: 337-342. https://doi.org/10.1080/00304948209354926

Kight, S.L. (1998): Precocene II modifies maternal responsiveness in the burrower bug, *Sehirus cinctus* (Heteroptera). Physiological Entomology, 23: 38-42. https://doi.org/10.1046/j.1365-3032.1998.2310038.x

Kiguchi, K.; Mori, T. and Akai, H. (1984): Effects of anti-juvenile hormone "ETB" on the development and metamorphosis of the silkworm, *Bombyx mori*. Journal of Insect Physiology, 30: 499-506. https://doi.org/10.1016/0022-1910(84)90031-3

Kimura, K.; Ote, M.; Tazawa, T. and Yamamoto, D. (2005): Fruitless specifies sexually dimorphic neural circuitry in the *Drosophila* brain. Nature, 438(7065): 229-233. doi: 10.1038/nature04229

Kiss, I.; Fodor, A.; Timar, T.; Hosztafi, S.; Sebok, P.; Torok, T.; Viragh, E. and Berenyi, M. (1988): Biological activity of precocene analogues on *Locusta migratoria*. Experientia, 44: 790-792. doi: 10.1007/BF01959168

Kiuchi, M.; Kimura, K. and Akai, H. (1985): Induction of trimolters from a tetramolter strain of *Bombyx mori* by anti-juvenoid treatment. Journal of Sericultural Science of Japan, 54(1):77-81. https://doi.org/10.11416/kontyushigen1930.54.77

Kiuchi, M.; Abe, S. and Akai, H. (1986): Growth and food efficiency in precocious trimolter silkworms induced by the administration of an anti-JH compound. Journal of Sericultural Science of Japan, 55(3): 246-251. https://doi.org/10.11416/kontyushigen1930.55.246

Koopmanshap, A.B.; Oouchi, H.; de Kort, C.A.D. (1989): Effects of a juvenile hormone analogue on the eggs, post-embryonic development, metamorphosis and diapause induction of the Colorado potato beetle, *Leptinotarsa decemlineata*. Entomologia Experimentalis et Applicata, 50: 255-263. https://doi.org/10.1111/j.1570-7458.1989.tb01200.x

Korb, J.; Roux, E.A. and Lenz, M. (2003): Proximate factors influencing soldier development in the basal termite *Cryptotermes secundus* (Hill). Insectes Sociaux, 50: 299-303. doi: 10.1007/s00040-003-0674-4

Kostal, V. (2006): Eco-physiological phases of insect diapause. Journal of Insect Physiology, 52: 113–127. https://doi.org/10.1016/j.jinsphys.2005.09.008

Koul, O. and Smirle, M.J. (1994): Allomones in insect plant interactions. In: "Recent advance in insect physiology and toxicology" (Gujar, G.T., ed.). Agricole. Publ. Acad. New Delhi, pp.: 14-33.

Kramer, S.J. and Staal, G.B. (1981): *In vitro* studies on the mechanism of action of anti-juvenile hormone agents in larvae of *Manduca sexta*. In: "Juvenile Hormone Biochemistry" (Pratt G.E.; Brooks, G.T., eds.) Amsterdam: Elsevier North-Holland, pp. 425–437.

Kramer, S.J.; Baker, F.C.; Miller, C.A.; Cerf, D.C.; Schooley, C.A. and Menn, J.J. (1983): Juvenile hormone antagonists. In: "Pesticide Chemistry: Human Welfare and Environment: Synthesis and Structure-Activity Relationships"(Doyle, P. and Fujita, T. eds.). Pergamon Press, Oxford, NewYork, pp: 177–182. https://doi.org/10.1016/B978-0-08-029222-9.50028-7

Krecek, J.; Hrdy, I.; Jarolim, V. and Wimmer, Z. (1981): Antagonistic interaction between a juvenile hormone analogue and precocene I in *Prorhinotermes simplex* (Isoptera). Acta Entomologica Bohemoslovaca, 78: 266-269.

Kulkarni, S.A. and Paradkar, M.V. (1992): Efficient synthesis of precocenes. Synthetic Communications, 22(11): 1555-1562. https://doi.org/10.1080/00397919208021628

Kumar, N. (2014): Biological potential of a weed *Ageratum houstonianum* Mill: a review. Indo American Journal of Pharmaceutical Research, 4(6): 2683-2689.

Kumar, K. and Khan, I.A. (2004): Effect of precocene on development of ovarian follicles in flesh fly, *Sarcophaga ruficornis* F. Indian Journal of Experimental Biology, 42(1): 74-80.

Kuwano, E. and Eto, M. (1983): Terpenoid imidazoles: New anti-juvenile hormones and insecticidal compounds. Proceedings of 10th International Congress for Plant Protection, Brighton, 1: 278.

Kuwano E.; Takeya, T. and Eto, M. (1983): Terpenoid imidazoles: new antijuvenile hormones. Agricultural and Biological Chemistry, 47: 921-923. https://doi.org/10.1080/00021369.1983.10865749

Kuwano, E.; Takeya, R. and Eto, M. (1984): Synthesis and anti-juvenile hormone activity of 1-citronellyl-5-substituted imidazoles. Agricultural and Biological Chemistry, 48(12): 3115-3119. https://doi.org/10.1271/bbb1961.48.3115

Kuwano, E.; Takeya, R. and Eto, M. (1985): Synthesis and anti-juvenile hormone activity of 1-substituted-5-[(*E*)-2,6-dimethyl-1,5-heptadienyl] imidazoles. Agricultural and Biological Chemistry, 49: 483-486. https://doi.org/10.1271/bbb1961.49.483

Kuwano, E.; Tanaka, Y.; Kikuchi, M. and Eto, M. (1988): Effects of anti- juvenile hormones and related compounds on development in the larvae of *Bombyx mori*. Journal of Faculty of Agriculture, Kyushu University, 33(1,2): 17-28.

Kuwano, E.; Kiguchi, M. and Eto, M. (1990): Synthesis and anti-juvenile hormone activity of 1-neopentyl-5-substituted imidazoles. Journal of Faculty of Agriculture, Kyushu University, 35(1-2): 35-41.

Kuwano, E.; Hisano T.; Eto M.; Suzki K.; Unnithan G.C. and Bowers, W.S. (1992): Insect growth regulating activity of 1,5-disubstituted imidazole against *Bombyx mori* and *Oncopeltus fasciatus*. Pesticide Science, 34: 263-268. https://doi.org/10.1002/ps.2780340312

Lainé, L.V. and Wright, D.J. (2003): The life cycle of *Reticulitermes* spp. (Isoptera: Rhinotermitidae): what do we know? Bulletin of Entomological Research 93(4):267-378. doi: 10.1079/BER2003238

Lange, A.B.; Phillips, D.R. and Loughton, B.G. (1983): The effects of precocene II on early adult development in male *Locusta*. Journal of Insect Physiology, 29(1): 73-81. https://doi.org/10.1016/0022-1910(83)90108-7

Langewald, J. and Schmutterer, H. (1995): Colour change in the desert locust, *S. gregaria* (Forsk.), induced by topical treatment with azadirachtin-enriched neem oil in semi-field trails in Benin at different population densities. Journal of Applied Entomology, 119: 221-226. https://doi.org/10.1111/j.1439-0418.1995.tb01274.x

Langley, P.A. and Pimley, R.W. (1986): A role for juvenile hormone and the effects of so-called anti-juvenile hormones in *Glossina morsitans*. Journal of Insect Physiology, 32: 727-734. https://doi.org/10.1016/0022-1910(86)90115-0

Le Conte, Y. and Hefetz, A. (2008): Primer pheromones in social Hymenoptera. Annual Review of Entomology, 53: 523-542.

Lee, S.S. and Tan, M.L. (1981): Precocene II induced effects on the ovary and fat body of female *Oxya japonica* (Orthoptera Acrididae). Acrida, 10: 25-32.

Lee, S.-H.; Oh, H.-W.; Fang, Y.; An, S.-B.; Park, D.-S.; Song, H.-H.; Oh, S.-R.; Kim, S.-Y.; Kim, S.; Kim, N.; Raikhel, A.S.; Je, Y.H. and Shin, S.W. (2015): Identification of plant compounds that disrupt the insect juvenile hormone receptor complex. www.pnas.org/cgi/doi/10.1073/pnas.1424386112

Lee, S.-H.; Lim, H.N.; Choi, J.Y.; Park, D.H.; Ahn, B.H.; Fang, Y.; Kim, J.H.; Park, M.G.; Woo, R.M.; Lee, B.R.; Kim, W.J.; Ko, Y.K.; Lee, Ill Y. and Je, Y.H. (2018): Mosquitocidal activity of penfluridol as juvenile hormone antagonist. Journal of Asia-Pacific Entomology, 21: 130-133.

Lehmann, Ph.; Lyytinen, A.; Piiroinen, S. and Lindström, L. (2015): Is a change in juvenile hormone sensitivity involved in range expansion in an invasive beetle? Frontiers in Zoology, 12: 20. doi: 10.1186/s12983-015-0113-1

Leighton T.E.; Marks, D. and Leighton, F. (1981): Pesticides: Insecticides and fungicides are chitin synthesis inhibitors. Science, 213: 905-907. doi: 10.1126/science.213.4510.905

Li, Q.-J.; Guan, Z.-H. and Guan, H. (1993): Effect of precocene II on vitellogenesis of housefly *Musca domestica vicina*. Acta Entomologica Sinica, 36: 129-137. http://www.insect.org.cn/EN/Y1993/V36/I2/129

Li, Y.; Zhang, Z.; Robinson, G.E. and Palli, S.R. (2007): Identification and characterization of a juvenile hormone response element and its binding proteins. Journal of Biological Chemistry, 282: 37605-37617. doi: 10.1074/jbc.M704595200

Li, B.; Wang, Y.; Liu, H.; Xu, Y.; Wei, Z.; Chen, Y. and Shen, W. (2010): Resistance comparison of domesticated silkworm (*Bombyx mori* L.) and wild silkworm (*Bombyx mandariana* M.) to phoxim insecticide. African Journal of Biotechnology, 9(12): 1771-1775. doi: 10.5897/AJB10.1955

Li, M.; Mead, E.A. and Zhu, J. (2011): Heterodimer of two bHLH-PAS proteins mediates juvenile hormone-induced gene expression. Proceedings of the National Academy of Sciences, USA (PNAS), 108(2): 638-643. https://doi.org/10.1073/pnas.1013914108

Li, Y.-M.; Kai, Z.-P.; Huang, J. and Tobe, S.S. (2017): Lepidopteran HMG-CoA reductase is a potential selective target for pest control. PeerJ., 5: e2881; doi: 10.7717/peerj.2881

Lin, H.; Chen, D.Z.; Zhu, X.X.; Hou, N.J.; Chen, G.H. and Zhuang, D.H. (1991): Induction of DNA-dependent RNA polymerase and RNA synthesis by "Kang-20" treatment in the silkworm, *Bombyx mori*. Acta Entomologica Sinica, 34(4):385-390.

Lindsey, R., 2002. Locusts. Available from http://earth.Observatory.NASA.Gov/Observatory/.

Liu, T.-X. and Chen, T.-Y. (2001): Effects of the insect growth regulator fenoxycarb on immature *Chrysoperla rufilabris* (Neuroptera: Chyrsopidae). Florida Entomologist, 84(4): 628–633. doi: 10.2307/3496394

Liu, X.C. and Liu, Z.L. (2014): Evaluation of larvicidal activity of the essential oil of *Ageratum conyzoides* L. aerial parts and its major constituents against *Aedes albopictus*. Journal of Entomology and Zoology Studies; 2 (4): 345-350.

Liu, G.F.; Chen, W.X.; Lu, X.F. and Li, R.Q. (1987): Studies on the reelability of trimolting cocoons induced by SM-1 and the physical properties of its filament in *Bombyx mori*. Acta Sericologica Sinica, 13 (3):144-149.

Loher, W. (1961): The chemical acceleration of the maturation process and its hormonal control in the male of the desert locust. Proceedings of the Royal Society B: Biological Sciences, 153: 380-397. doi: 10.1098/rspb.1961.0008

Lorenz, M.W.; Kellner, R. and Hoffmann, K.H. (1995): Identification of two allatostatins from the cricket, *Gryllus bimaculatus* de Geer (Ensifera, Gryllidae): additional members of a family of neuropeptides inhibiting juvenile hormone biosynthesis. Regulatory Peptides, 57: 227-236. https://doi.org/10.1016/0167-0115(95)00036-B

Lu, X.F. and Li, R.Q. (1987): Study on the fine filament size silk of trimolter silkworms induced by SM-1 inducer. Acta Sericologica Sinica, 13(2): 71-75.

Lu, X.F. and Xiao, Q. (1997): Comparison of cocoon quality of genetic trimolter and induced trimolter silkworms. Silk Technology, 5(4): 5-7.

Lu, X.N.; Liu, X.C.; Liu, Q.Z. and Liu, Z.L. (2014): Isolation of insecticidal constituents from the essential oil of *Ageratum houstonianum* Mill. against *Liposcelis bostrychophila*. J.Chem., Article ID 645687,6 pp. http://dx.doi.org/10.1155/2014/645687

Luna, J.-C.; Robinson, V.-A.; Martinez, A.-M.; Schneider, M.-I.; Figueroa, J.-I.; Smagghe, G.; Vinuela, E.; Budia, F. and Pineda, S. (2011): Long-term effects of methoxyfenozide on the adult reproductive processes and longevity of *Spodoptera exigua* (Lepidoptera: Noctuidae). Journal of Economic Entomology, 104(4): 1229-1235. doi: 10.1603/EC10450.

MacBean, C. (2012): The Pesticide Manual. 16th ed., British Crop Production Council, 557 pp.

Mao, L.; Henderson, G. and Dong, S.-L. (2010): Studies of precocene I, precocene II and biogenic amines on formosan subterranean termite (Isoptera: Rhinotermitidae) presoldier/soldier formation. Journal of Entomological Science, 45: 27-34. https://doi.org/10.18474/0749-8004-45.1.27

Martínez, T. and Garcerá, M.D. (1987): Effects of precocene II on female-specific hemolymph polypeptides in *Oncopeltus fasciatus*. Insect Biochemistry and Physiology, 6(1): 49-58. https://doi.org/10.1002/arch.940060106

Masner, P.; Bowers, W.S.; Kalin, M. and Muhle, T. (1979): Effect of precocene II on the endocrine regulation of development and reproduction in the bug, *Oncopeltus fasciatus*. General and Comparative Endocrinology, 37: 156-166. https://doi.org/10.1016/0016-6480(79)90103-5

Massuod, W.A.M. (2014): Larvicidal potentiality of the bandotan (*Ageratum conyzoides*) leaves for controlling the three species of mosquitoes (*Aedes aegypti*, *Culex quinoefasciatus* and *Anopheles maculates*). MSc. Thesis, Bioscience, Sebeles Maret University, Surakata, 49pp.

Mathai, S. and Nair, V.S.K. (1984): Morphogenetic effects of precocene II on the larval stages of *Spodoptera mauritia* Boisd. (Lepidoptera: Noctuidae). In: Proceedings of Fifth All India Symposium on Developmental Biology (Agarwal, S.K. and Goel, S.C., eds.). pp. 59-66.

Mathai, S. and Nair, V.S.K. (2005): Treatment of larvae with repeated doses of precocene II induces precocious metamorphic changes in *Spodoptera mauritia* (Lepidoptera: Noctuidae). Archives of Insect Biochemistry and Physiology, 1: 199-203. https://doi.org/10.1002/arch.940010210

Mathai, S.; Santha, P.C. and Nair, V.S.K. (1989): Antigonadotropic effects of precocene II in *Spodoptera mauritia* Boisd. (Lepidoptera: Noctuidae). Proceedings of the Indian National Science Academy, B55: 91-95.

Mattson, M.P. and Furukawa, K. (**1997**): Anti-apoptotic actions of cycloheximide: blockade of programmed cell death or induction of programmed cell life? Apoptosis, 2: 257-264.

Menn, J.J. (1980): Contemporary frontiers in chemical pesticide research. Journal of Agriculture and Food Chemistry, 28: 2-8. doi: 10.1021/jf60227a012

Menn, J.J. (1985): Prospects of exploitation of insect antijuvenile hormones for selective insect control. In: "Approaches to New Leads for Insecticides" (von Keyserlingk et al., eds.). ©Springer-Verlag Berlin Heidelberg. doi: 10.1007/978-3-642-70821-3_4

Meola, R.W. and Petralia, R.S. (1980): Juvenile hormone induction of biting behavior in *Culex* mosquitoes. Science, 209: 1548-1550. http://dx.doi.org/10.1126/science.209.4464.1548

Meuser, S. and Pflüger, H.J. (1998): Programmed cell death specifically eliminates one part of a locust pleuroaxilliary muscle after the imaginal moult. Journal of Experimental Biology, 201: 2367-2382.

Miao, Y.G.; Yu, S.W.; Ren, X.N. and Pan, W.X. (1996): Studies on the mechanism of anti-juvenile hormone and molting hormone to silkworm (*Bombyx mori* L.). Journal of Zhejiang Agriculture University, 22(4): 345-348.

Miao, Y.; Jiang, L. and Bharathi, D. (2001): Effects of Jinlu, an anti-juvenile hormone on the growth, ultra structure of the corpora allata and prothoracic gland of silkworm, *Bombyx mori* L. Journal of Zhejiang University (Science), 2(3): 294-297.

Minakuchi, C. and Riddiford, L.M. (2006): Insect juvenile hormone action as a potential target of pest management. Journal of Pesticide Science, 31(2):77-84. https://doi.org/10.1584/jpestics.31.77

Minakuchi, C.; Zhou, X. and Riddiford, L.M. (2008): Krüppel homolog 1 (Kr-h1) mediates juvenile hormone action during metamorphosis of *Drosophila melanogaster*. Mechanisms of Development, 125: 91-105. doi: 10.1016/j.mod.2007.10.002

Mitsuoka, T.; Takita, M.; Kanke, E. and Kawasaki, H. (2001): Ecdysteroid titer, responsiveness of prothoracic gland to prothoracicotropic hormone (PTTH), and PTTH release of the recessive trimolter strain of *Bombyx mori* in extra-ecdysed larvae by JHA and 20E application. Zoological Science, Japan, 18(2): 235-240. https://doi.org/10.2108/zsj.18.235

Miura, T. (2004): Proximate mechanisms and evolution of caste polyphenism in social insects: From sociality to genes. Ecological Research, 19:141-148. https://doi.org/10.1111/j.1440-1703.2003.00618.x

Miyajima, T.; Yamamoto, T.; Mase, K.; Iizuka, T.; Nozaki, M. and Kiuchi, M. (2001): Induction of trimolting larvae by the imidazole compound, triflumizole, in the silkworm races with a thin cocoon filament, Hakugin and Honobono, and the resulted cocoon characters. The Journal of Sericultural Science of Japan, 70(1): 37-42.

Miyake, T. and Mitsui, T. (1995): Multiple physiological activity of an anti-juvenile hormone, precocene 2 on the white-backed rice planthopper. Journal of Pesticide Science, 20: 17-24.

Mojaver, M. and Bandani, A.R. (2010): Effects of the insect growth regulator pyriproxyfen on immature stages of sunn pest, *Eurygaster integriceps* Puton (Heteroptera: Scutelleridae). Munis Entomology and Zoology, 5(1): 187-197. http://www.munisentzool.org

Mondal, K. and Parween, S. (2000): Insect growth regulators and their potential in the management of stored-product insect pests. Integrated Pest Management Review, 5: 255-295.

Monger, D.J.; Lim, W.A.; Kezdi, F.A and Law, J.H. (1982): Compactin inhibits insect HMGCoA reductase and juvenile hormone biosynthesis. Biochemical and Biophysical Research Communications, 105: 1374-1380. https://doi.org/10.1016/0006-291X(82)90939-1

Moore, P.J.; Reagan-Wallin, N.L.; Haynes, K.F. and Moore, A.J. (1997): Odour conveys status on the cockroaches. Nature, 389: 25. doi:10.1038/37888

Morton, D.B. and Truman, J.W. (2008): Effect of cycloheximide on eclosion hormone sensitivity and the developmental appearance of the eclosion hormone and cGMP regulated phosphoproteins in the CNS of the tobacco hornworm, *Manduca sexta*. Journal of Receptor and Signal Transduction Research, 15: 773-86. doi: 10.3109/10799899509079906

Mosallanejad, H. and Smagghe, G. (2009): Biochemical mechanisms of methoxyfenozide resistance in the cotton leafworm *Spodoptera littoralis*. Pest Management Science, 65: 732-736. doi: 10.1002/ps.1753

Moya P.; Castillo, M.; Primo-Yufera, E.; Couillaud, F.; Martinez-Manez, R.; Garcera, M.D.; Miranda, H.A.; Primo, J. and Martinez-Pardo, R. (1997): Brevioxime: a new juvenile hormone biosynthesis inhibitor isolated from *Penicillium brevicompactum*. Journal of Organic Chemistry, 62: 8544-8545. doi: 10.1021/jo970397y

Mukhopadhyay B.; Roychoudhary, N. and Chakravorty, S. (1988): Effects of juvenoids and precocene-II in the growth and differentiation of female reproductive system of green stink bug *Nezara viridula* (Linn.). Zoologische Jahrbücher. Abteilung für allgemeine Zoologie und Physiologie der Tiere, 93: 337-345.

Murakoshi, S.; Kamikado, T. and Tamure, S. (1977): Change in moltinism and integument colour of silkworm larvae, *Bombyx mori* L. by some quinolone alkaloids. Japan Journal of applied Entomology and Zoology, 21: 230-232. https://doi.org/10.1303/jjaez.21.230

Muraleedharan, D.; Varghese, A.; Abraham, G. and Mathews, R.A. (1986): Effect of precocene-II on endocrines, feeding and digestion in the semilooper caterpillar, *Achoea janata*. In: "Insect Neurochemistry and Neurophysiology". Springer, pp 307-314. doi: 10.1007/978-1-4612-4832-3_39

Muthukrishnan, J.; Seifert, K.; Hoffmann, K.H. and Lorenz, M.W. (1999): Inhibition of juvenile hormone biosynthesis in *Gryllus maculates* by *Glycosmis pentaphylla* leaf compounds. Phytochemistry, 50: 249-254.

Nachman, R.J.; Garside, C.S. and Tobe, S.S. (1999): Hemolymph and tissue-bound peptidase-resistant analogs of the insect allatostatins. Peptides, 20: 23–29. https://doi.org/10.1016/S0196-9781(98)00149-1

Nachman, R.J.; Strey, A.; Isaac, E.; Pryor, N.; Lopez, J.D.; Deng, J.G.; Coast, G.M. (2002): Enhanced *in vivo* activity of peptidase-resistant analogs of the insect kinin neuropeptide family. Peptides, 23: 735–745. https://doi.org/10.1016/S0196-9781(01)00654-4

Nagendraradhya, B.S. and Jagadeesh Kumar, T.S. (2013): Effect of topical administration of JH mimic and performance of qualitative and quantitative traits CSR_2 and MG_{408} Bivoltine breeds of the silkworm, *Bombyx mori* L. International Journal of Science, Environment and Technology, 2(2): 185-195.

Nair, V.S.K. and Rajalekshmi, E. (1988): Effects of fluoromevalonate on penultimate and last instar larvae of *Spodoptera litura* Boisd. Indian Journal of Experimental Biology, 27: 170-173.

Nair, K.S.; Vijayan, V.A.; Nair, J.S.; Trivedy, K. and Chinya, P.K. (2000): Influence of a plant based juvenile hormone mimic, ω-formyl longifolene oxime citronellyl ether on silkworm, *Bombyx mori* L. Sericologia, 40(4): 551-557.

Nandi, P.S. and Chakravarty, K. (2011): Juvenoids and anti-Juvenoids as third generation pesticide to control lepidopteran field crop pests. Indian Streams Research Journal, 1(6): 15pp. doi: 10.9780/22307850

Nassar M.M.; Hafez S.T.; Farrag A.M. and Abahussain M.O. (1999): Efficacy of BaySir-8514 and precocene II against the grey flesh fly *Parasarcophaga dux* (Thomson) (Diptera: Sarcophagidae). Journal of the Egyptian Society of Parasitology, 29(3): 697-707.

Nave, J.F.; d'Orchymont, H.; Ducep, J.B. and Jung, M.J. (1985): Mechanism of inhibition of cholesterol bisynthesis by 6-fluoromevalonate. Biochemistry Journal, 227: 247-254.

Nijhout, H.F. (1994): Insect hormones. Princeton: Princeton Univ. Press, New Jersey, 280 pp.

Nijhout, H.F. and Wheeler, D.E. (1982): Juvenile hormone and the physiological basis of insect polymorphisms. The Quarterly Review of Biology, 57: 109-133. http://www.jstor.org/stable/2829551

Niu, R.H.; Wu, Z.P.; Yin, P.F.; Wang, G.H. and Tan, J.Z. (2013): Analysis of cocoon and silk quality of trimolter silkworms induced by anti-juvenile hormone. Advanced Materials Research, 796: 57-61. https://doi.org/10.4028/www.scientific.net/AMR.796.57

Nogueira, J.H.C.; Goncalez, E.; Galleti, S.R.; Facanali, R.; Marques, M.O.M. and Felícioa, J.D. (2010): *Ageratum conyzoides* essential oil as aflatoxin suppressor of *Aspergillus flavus*. International Journal of Food Microbiology, 137: 55-60. https://doi.org/10.1016/j.ijfoodmicro.2009.10.017

Nolte, D.J. (1963): A pheromone for melanization of locusts. Nature, 16: 660-661. doi:10.1038/200660a0

Norris, M.S. and Pener, M.P. (1965): An inhibitory effect of allatectomized males and females on the sexual maturation of young male adults of *S. gregaria* (Forskal). Nature, 208: 1122-1130. doi: 10.1038/2081122a0

Nouzova, M.; Rivera-Perez, C. and Noriega, F.G. (2015): Allatostatin-C reversibly blocks the transport of citrate out of the mitochondria and inhibits juvenile

hormone synthesis in mosquitoes. Insect Biochemistry and Molecular Biology, 57: 20-26. doi: 10.1016/j.ibmb.2014.12.003

Oberlander, H. and Silhacek, D. (2000): Insect growth regulators. In: "Alternatives to pesticides in stored-product IPM" (Subramanyam, B. and Hagstrum, D.W. eds.). Kluwer Academic Publishers, Boston. pp. 147-163.

O'Brien, R.D. (1967) Insecticides: action and metabolism. New York, Academic Press. 346pp.

Ohta, T.; Kuhr, R.J.; Bowers, W.S. (1977): Radiosynthesis and metabolism of the insect anti-juvenile hormone, precocene II. Journal of Agriculture and Food Chemistry, 25: 478-481. doi: 10.1021/jf60211a059

Okunade, A.L. (2002): *Ageratum conyzoides* L. (Asteraceae). Fitoterapia, 73: 1-16. https://doi.org/10.1016/S0367-326X(01)00364-1

Oliveira, R.C.; Vollet-Neto, A.; Oi, C.A.; van Zweden, J.S.; Nascimento, F.; Brent, C.S. and Wenseleers, T. (2017): Hormonal pleiotropy helps maintain queen signal honesty in a highly eusocial wasp. Scientific Reports, 7: 1654, 12pp. doi:10.1038/s41598-017-01794-1

Onayade, O.A.; Looman, A.; Schefer, J.J.C. and Svendsen, A. (1989): Precocene I and other constituents of the essential oil of *Platostoma africanum*. Planta Medica, 55: 553-555. doi: 10.1055/s-2006-962093

Oostra, V.; Mateus, A.R.; van der Burg, K.R.L.; Piessens, T.; van Eijk, M.; Brakefield, P.M.; Beldade, P. and Zwaan, B.J. (2014): Ecdysteroid hormones link the juvenile environment to alternative adult life histories in a seasonal insect. American Naturalist, 184: 79-92.

Osman, K.S.A. (1988): Effect of precocene-3 on the hormonal regulation of oogenesis and larval mortality in *Aiolopus thalassinus* (Fabr.) (Saltatoria: Acrididae). Mitteilungen der Deutschen Gesellschaft für Allgemeine und Angewandte Entomologie, 6: 464-487.

Osman, E.E.; Rarwash, I. and El- Samadisi, M.M. (1984): Effect of the anti-moulting agent "Dimilin" on the blood picture and cuticle formation in *Spodopterea littoralis* (Boisd.) larvae. Bulletin of Entomological Society of Egypt (Economic Series), 14: 3-46.

Pallabi, K. and Sharma, S. (2017): Eri silkworm (*Philosamia ricini*) rearing and comparative analysis of its economic parameters based on different food plants in Deosal village, Mayong Block, Morigaon District, Assam, India. International Journal of Science and Research, 6(5): 1737-1740.

Pallos, F.M.; Letchworth, P.E. and Menn, J.J. (1976): Novel non-terpenoid insect growth regulators. Journal of Agricultural and Food Chemistry, 24: 218-221. doi: 10.1021/jf60204a020

Parthasarathy, R. and Palli, S.R. (2007): Stage- and cell-specific expression of ecdysone receptors and ecdysone-induced transcription factors during midgut remodeling in the yellow fever mosquito, *Aedes aegypti*. Journal of Insect Physiology, 53: 216-229. https://doi.org/10.1016/j.jinsphys.2006.09.009

Parween, S.; Faruki, S.I. and Begum, M. (2001): Impairment of reproduction in the red flour beetle, *Tribolium castaneum* (Herbst.) (Coleoptera: Tenebrionidae) due to larval feeding on triflumuron-treated diet. Journal of Applied Entomology, 125: 1-4.

Passera, L. (1982): Endocrine regulation of caste determination in ants. In: "Social insects in the tropics". Proceedings of the First International Symposium (Jaisson, P., ed.). Presses de l'Universite Paris XIII, Paris, Vol 1, pp: 41-62.

Passera, L. and Suzzoni, J.P. (1979): Le rôle de la reine de *Pheidole pallidula* (Nyl.) (Hymenoptera, Formicidae) dans la sexualisation du couvain après traitement per l'hormone juvénile. Insectes Sociaux, 26: 343–353. doi: 10.1007/BF02223553

Pathak, S.C. and Bhandari, R. (2002): Effect of frontal ganglionectomy and administration of precocene II and exogenous juvenile hormone on reproductive behaviour in male *Blattella germanica* Linn. (Blattoidea: Blattellidae). Entomon, 27: 11-19.

Pearce, A.N.; Huang, Z.Y. and Breed, M.D. (2001): Juvenile hormone and aggression in honey bees. Journal of Insect Physiology, 47: 1243-1247. https://doi.org/10.1016/S0022-1910(01)00109-3

Pener, M.P. (1991): Locust phase polymorphism and its endocrine relations. Advances in Insect Physiology, 23:1-79. https://doi.org/10.1016/S0065-2806(08)60091-0

Pener, M.P. and Lazarovici, P. (1979): Effect of exogenous juvenile hormones on mating behavior and yellow color in allatectomized adult male desert locusts. Physiological Entomology, 4: 251-261. https://doi.org/10.1111/j.1365-3032.1979.tb00202.x

Pener, M.P. and Simpson, S.J. (2009): Locust phase polyphenism: an update. Advances in Insect Physiology, 36: 1-286. https://doi.org/10.1016/S0065-2806(08)36001-9

Pener, M.P.; Desberg, D.; Lazarovici, P.; Reuter, C.C.; Tsai, L.W.; Baker, F.C. (1986): The effect of a synthetic precocene on juvenile hormone III titre in late *Locusta* eggs. Journal of Insect Physiology, 32: 853-857. https://doi.org/10.1016/0022-1910(86)90100-9

Pener, M.P.; Ayali, A. and Ben-Ami, E. (1992): Juvenile hormone is not a major factor in locust phase changes. In "Insect Juvenile Hormone Research"(Mauchamp, B.; Couillaud, B. and Baehr, J.C., eds.). Paris: Inst. Natl. Recherche Agron, pp.: 125-134.

Phillips, D.R. and Loughton, B.G. (1979): The effect of inhibition of RNA and protein synthesis on the development of larvae of *Locusta migratoria*. Insect Biochemistry, 9(2): 241-245. https://doi.org/10.1016/0020-1790(79)90056-8

Pineda, S.; Martinez, A.M.; Figueroa, J.I.; Schneider, M.I.; Estal, P. Del; Vinuela, E.; Gomez, B.; Smagghe, G. and Budia, F. (2009): Influence of azadirachtin and methoxyfenozide on life parameters of *Spodoptera littoralis*. Journal of Economic Entomology, 102(4): 1490-1496. https://doi.org/10.1603/029.102.0413

Piulachs, M.D.; Vilaplana, L.; Bartolome, J.M.; Carreno, C.; Martin, D.; Rosario, G.M.; Herranz, R.; Garcia-Lopez, M.T.; Andreu, D. and Belles, X. (1997): Ketomethylene and methyleneamino pseudopeptide analogs of insect allatostatins inhibit juvenile hormone and vitellogenin production in the cockroach *Blattella germanica*. Insect Biochemistry and Molecular Biology, 27: 851–858. doi: 10.1016/S0965-1748(97)00067-2

Polgar, L.; Mackaur, M. and Volkl, W. (1991): Diapause induction in 2 species of aphid parasitoids-the influence of aphid morph. Journal of Insect Physiology, 37(9): 699-702. https://doi.org/10.1016/0022-1910(91)90047-4

Polivanova, Å.N. (1982): The influence of precocene on embryonic development in *Eurygaster integriceps*. Doklady Akademii Nauk SSSR, 263(2): 501-503.

Polivanova, Å.N. (1991): Possibilities of using specific biological effects of precocene-containing plants on the greenhouse whitefly (*Trialeurodes*

vaporariorum Westw.) to control its aboundance. Doklady Akademii Nauk SSSR , 316(6): 1501-1505.

Polivanova, Å.N. (1997): Specific features of *Myzus persicae* (Homoptera, Aphididae) development on plants synthesizing Precocenes, inhibitors of insect juvenile hormone. Zoologicheskij Zhurna, l76(7): 777-784.

Polivanova, Å.N. and Triseleva, T.A. (1985): Suppression of the migratory flight behavior of overwintered adults of *Eurygaster integnceps* Puton (Insecta, Heteroptera) by precocene. Doklady Akademii Nauk SSSR, 279: 247-250.

Polivanova, Å.N. and Triseleva, T.A. (1992): Morph-physiological and behavioral effects juvenile hormone deficiency in insect ontogenesis. Successes of Modern Biology, 112(5 & 6): 774-784.

Palivanova, E.N.; Bocharova, E.V. and Triseleva, T.A. (1983): Influence of precocenes II on the corpora allata and oocyte development in overwintering bugs *Eurygaster integriceps*. Doklady Biological Sciences, 269(1): 197-199.

Pradeep, A.R. and Nair, V.S.K. (1989): Morphogenetic effects of precocenes II in the brown planthopper, *Nilaparvata lugens* Stal. (Homoptera: Delphacidae). The Proceedings of the National Academy of Sciences, India, Section B: B55 (5-6): 381-386.

Pradeep, A.R. and Nair, V.S.K. (2000a): Antigonadotropic effects of precocene 2: allaticidal action in females of *Nilaparvata lugens* (Stal). Philippine Entomologist, 14(2): 175-183.

Pradeep, A.R.1 and Nair, V.S.K. (2000b): Antifeedant effects of precocene II in the brachypterous females of the rice brown planthopper, *Nilaparvata lugens* (Stål) (Homoptera: Delphacidae). Journal of Entomological Research, 24(2): 195-198.

Pratt, G.E.; Jennings, R.C.; Hamnett, A.F. and Brooks, G.T. (1980): Lethal metabolism of precocene I to a reactive epoxide by locust corpora allata. Nature, 284: 320-323. doi:10.1038/284320a0

Pratt, G.E.; Jennings, R.C. and Hamnett, A.F. (1981): The mode of action of precocenes. In: "Regulation of insect development and behaviour" (Sehnal, F.; Zabza, A.; Menn, J.J. and Cymborowski, B., eds.). Wroclaw: Tech. Univ. Press). pp: 347-356.

Pratt, G.E.; Farnsworth, D.E.; Fok, K.F.; Siegel, N.R.; McCormack, A.L.; Shabanowitz, J.; Hunt, D.F. and Feyereisen, R. (1991): Identity of a second type of allatostatin from cockroach brains: an octadecapeptide amide with a tyrosine-rich address sequence. Proceedings of the National Academy of Sciences of the USA (PNAS), 88: 2412-2416.

Proksch, P.; Proksch, M.; Towers, G.H.N. and Rodriguez, E. (1983): Phototoxic and insecticidal activities of chromenes and benzofurans from *Encelia*. Journal of Natural Products, 46: 331–334. doi: 10.1021/np50027a006

Punzo, F. (1980): Neurochemical changes associated with learning in *Schistocerca americana* (Orthoptera: Acrididae). Journal of the Kansas Entomological Society, 53(4): 787-796. http://www.jstor.org/stable/25084110

Punzo, F. and Jellies, J. (1980): Effects of cycloheximide-induced protein synthesis inhibition on the phototactic behavior of *Tenebrio molitor* (Coleoptera: Tenebrionidae) and *Popilius disjunctus* (Coleoptera: Passalidae). Journal of the Kansas Entomological Society, 53(3): 597-606. http://www.jstor.org/stable/25084077

Qin, L.; Liu, Y.Q.; Zhang, T.; Li, H.; Ren, Y.L. and Gao, Y.Z. (1999): Study on application of imidazole derivative on Chinese tusser (*Antheraea pernyi*). Journal of Shenyang Agricultural University, 30: 31-34.

Quistad, G.B.; Cerf, D.C.; Schooley, D.A. and Staal, G.B. (1981): Fluoromevalonate acts as an inhibitor of insect juvenile hormone biosynthesis. Nature, 289: 176-177. doi: 10.1038/289176a0

Quistad, G.B.; Staiger, L.E. and Cerf, D.C. (1982): Preparation and biological activity of potential inhibitors of insect juvenile hormone biosynthesis. Journal of Agriculture and Food Chemistry, 30: 1151-1154. doi: 10.1021/jf00114a037

Quistad, G.B.; Cerf, D.C.; Kramer, S.J. and Schooley, D.A. (1985): Design of novel insect anti juvenile hormones: Allylic alcohol derivatives. Journal of Agricultural and Food Chemistry, 33(1): 47-50. doi: 10.1021/jf00061a014

Rachinsky, A. (1994): Octopamine and serotonin influence on corpora allata activity in honey bee (*Apis mellifera*) larvae. Journal of Insect Physiology, 40: 549-554. https://doi.org/10.1016/0022-1910(94)90141-4

Rachinsky, A. (1996): Brain and suboesophageal ganglion extracts affect juvenile hormone biosynthesis in honey bee larvae (*Apis mellifera carnica*). Zoology-Analysis of Complex Systems, 99: 277-284.

Raikhel, A.S.; Brown, M.R. and Belles, X. (2005): Hormonal control of reproductive processes. In: "Comprehensive Molecular Insect Science" (Gilbert, L.I.; Iatrou, S.S. and Gill, S.S., eds.). Oxford, UK: Elsevier. Vol. 3, pp: 433-492.

Rankin, M.A. (1980). Effects of precocene-I and precocene-II on flight behavior in *Oncopeltus fasciatus*, the migratory milkweed bug. Journal of Insect Physiology, 26: 67-73. https://doi.org/10.1016/0022-1910(80)90111-0

Rankin, M.A. and Rankin, S.M. (1980): Some factors affecting presumed migratory flight activity of the convergent lady beetle, *Hippodamia convergens* (Coccinellidae, Coleoptera). Biology Bulletin, 158: 336-369. https://doi.org/10.2307/1540862

Rankin, S.M.; Chambers, J. and Edwards, J.P. (1997): Juvenile hormone in earwigs: roles in oogenesis, mating, and maternal behaviors. Archives of Insect Biochemistry and Physiology, 35(4): 427-442. https://doi.org/10.1002/(SICI)1520-6327(1997)35:4<427::AID-ARCH6>3.0.CO;2-O

Readio, J.; Meola, R.W. and Jurd, L. (1987): Assessment of six benzyl-1,3-benzodioxole compounds for anti-juvenile hormone activity in *Culex pipiens*. Journal of the American Mosquito Control Association, 3(1):15-19.

Rembold, H.; Czoppelt, C. and Sharma, G.K. (1979): Precocene II is no anti-juvenile hormone in the honey bee, *Apis mellifera*. Zeitschrift für Naturforschung C, 34(12): 1261-1263. https://doi.org/10.1515/znc-1979-1231.

Renuga, B.F. and Sahayaraj, K. (2009): Influence of botanicals in total head protein of *Spodoptera litura* (Fab.). Journal of Biopesticides, 2(1): 52-55.

Resmitha, C. and Meethal, K.V. (2016): Toxicity of insect growth regulator, Pyriproxyfen, on larvae of *Spodoptera mauritia* Boisd. (Lepidoptera: Noctuidae). International Journal of Agriculture Innovations and Research, 5(1): 173-176.

Richard, D.S.; Jones, J.M.; Barbarito, M.R.; Cerula, S.; Detweiler, J.P.; Fisher, S.J.; Brannigan, D.M. and Scheswohl, D.M. (2001): Vitellogenesis in diapausing and mutant *Drosophila melanogaster*: further evidence for the relative roles of ecdysteroids and juvenile hormones. J. Insect Physiol., 47: 905-913. doi:10.1016/S0022-1910(01)00063-4

Riddiford, L.M. (1994): Cellular and molecular actions of juvenile hormone. I. General considerations and premetamorphic actions. In: "Advances in Insect Physiology"(Evans, P.O., ed.). Academic Press, London. vol. 24, pp. 213-274.

Riddiford, L.M. (2008): Juvenile hormone action: A 2007 perspective. Journal of Insect Physiology, 54: 895-901. https://doi.org/10.1016/j.jinsphys.2008.01.014

Riddiford, L.M.; Roseland, C.R.; Thalberg, S. and Curtis, A.T. (1983): Actions of two juvenile hormone antagonists on lepidopteran epidermis. Journal of Insect Physiology, 29: 281-286. https://doi.org/10.1016/0022-1910(83)90096-3

Riddiford, L.M.; Hiruma, K. and Zhou, X. and Nelson, C.A. (2003): Insights into the molecular basis of the hormonal control of molting and metamorphosis from *Manduca sexta* and *Drosophila melanogaster*. Insect Biochemistry and Molecular Biology, 33:1327-1338. https://doi.org/10.1016/j.ibmb.2003.06.001

Ringo, J.; Werczberger, R.; Altaratz, M. and Segal, D. (1991): Female sexual receptivity is defective in juvenile hormone-deficient mutants of the apterous gene of *Drosophila melanogaster*. Behavior Genetics, 21(5):453-469. DOI: 10.1007/BF01066724

Ringo, J.; Talyn, B. and Brannan, M. (2005): Effects of precocene and low protein diet on reproductive behavior in *Drosophila melanogaster* (Diptera: Drosophilidae). Annals of Entomological Society of America, 98: 601-607. https://doi.org/10.1603/0013-8746(2005)098[0601:EOPALP]2.0.CO;2

Roberto, C.F.; Sosa, M.E.; Favier, L.S.; Penna, F.; Guerreiro, E.; Giordano, O.S. and Tonn, C.E. (1998): Growth inhibitory activities of benzofuron and chromene derivatives towards *Tenebrio molitor*. Journal of Natural Products, 61: 1209-1211. DOI: 10.1021/np9800248

Rose, U. (2004): Morphological and functional maturation of a skeletal muscle regulated by juvenile hormone. The Journal of Experimental Biology, 207: 483-495. doi: 10.1242/jeb.00754

Roseler, P.F. (1991): Reproductive competition during colony establishment. In: "The social biology of wasps"(Rose, K.G. and Matthews, R.W. eds.). Ithaca, NY and London: Comstock Publishing Associates, pp: 309-335.

Rup, P.J. and Bangla, V. (1995): An investigation on the influence of methoprene and precocene-II on protein, glycogen and trehalose content of developing banana fruit fly, *Zaprionus paravittiger* (Godbole and Vaidya). Journal of Insect Science, 8: 140-143.

Rust, M.K. and Hemsarth, W.L.H. (2017): Intrinsic activity of IGRs against larval cat fleas. Journal of Medical Entomology, 54(2): 418-421. DOI: https://doi.org/10.1093/jme/tjw201

Sabry, K.H. and Abdou, G.Y. (2016): Biochemical and toxic characterization of some insect growth regulators to the pink bollworm, *Pectinophora gossypiella* (Saunders). American-Eurasian Journal of Sustainable Agriculture, 10(1): 8-14.

Sahota, T.S. and Farris, S.H. (1980): Inhibition of flight muscle degeneration by precocene II in the spruce bark beetle, *Dendroctonus rufipennis* (Kirby) (Coleoptera: Scolytidae). Canadian Journal of Zoology, 58(3): 378-381. https://doi.org/10.1139/z80-048

Salem, M.S.; El-Ibrashy, M.T. and Abdel-Hamid, M. (1982a): Disruption and abnormalities induced by precocene II, Cycloheximide and/or C 16-JH in the desert locust, *Schistocerca gregaria* Forsk. Bulletin of Entomological Society of Egypt (Economic Series), 13: 127-136.

Salem, M.S.; Eid, M.A.; El-Ibrashy, M.T. and Abdel-Hamid, M. (1982b): Effect of precocene II, Cycloheximide on flight and coxal muscles respiratory metabolism in the adult desert locust, *Schistocerca gregaria* Forsk. Bulletin of Entomological Society of Egypt (Economic Series), (13):117-125.

Samaranayaka-Ramasamy, M. and Chaudhury, M.F.B. (1982): Precocene induced sterility in F1 generation of *Glossina morsitans morsitans*. Journal of Insect Physiology, 28(6): 559-565. https://doi.org/10.1016/0022-1910(82)90037-3

Sánchez, C.M.; J.M.P. Martín,; Jin, J.-S.; Dávalos, A.; Zhang, W.; de la Peña, G.; Martínez-Botas, J.; Rodríguez-Acebes, S.; Suárez, Y.; Hazen, M.J.; Gómez-Coronado, D.; Busto, R.; Cheng, Y.-C. and Lasunción, M.A. (2015): Disruption of the mevalonate pathway induces dNTP depletion and DNA damage. Biochimica et Biophysica Acta, 1851: 1240-1253.

Santha, P.C. and Nair, V.S.K. (1991): Precocene-induced changes in the cerebral neurosecretory cells of *Spodoptera mauritia* Boisd. (Lepidoptera: Noctuidae). Zoologischer Anzeiger, 226: 163-173.

Sariaslani, F.S.; McGee, L.R. and Ovenall, D.W. (1987): Microbial transformation of precocene II: Oxidative reactions by *Streptomyces griseus*. Applied and Environmental Microbiology, 53(8): 1780-1784.

Saxena, R.C.; Sharma, M.; Kumar, M.L.; Bansal, S.K. and Shrivastava, D. (1994): Developmental effects of 6, 7-dimethoxy-2,2-dimethyl chromene on the preimaginal stages of *Anopheles stephensi*. Proceedings of Academy of Environmental Biology, 3:181-184.

Schal, C.; Burns, E.L. and Blomquist, G.J. (1990): Endocrine regulation of female contact sex pheromone production in the German cockroach, *Blattella germanica*. Physiological Entomology, 15: 81-91. https://doi.org/10.1111/j.1365-3032.1990.tb00495.x

Schal, C.; Burns, E.L.; Gadot, M.; Chase, J. and Blomquist, G.J. (1991): Biochemistry and regulation of pheromone production in *Blattella germanica* (L.) (Dictyoptera: Blattellidae). Insect Biochemistry, 21(1): 73-79. https://doi.org/10.1016/0020-1790(91)90066-N

Schmidt, M.H.H. and Dikic, I. (2010): Assays to monitor degradation of the EGF receptor. In: "Methods in Molecular Biology" (Patel, T.B. and Bertics, P.J., eds.), Epidermal growth factor receptor: methods and protocols, Humana Press, Totowa, N.J., vol. 327, pp: 131-138.

Schooneveld H. (1979): Precocene-induced collapse and resorption of corpora allata in nymphs of *Locusta migratoria*. Experientia, 35: 363-364.

Schrankel, K.R.; Grossman, S.J. and Hsia, M.T. (1982): Precocene II nephrotoxicity in the rats. Toxicological Letters, 12: 95-100. https://doi.org/10.1016/0378-4274(82)90170-9

Schwedes, C.C. and Carney, G.E. (2012): Ecdysone signaling in adult *Drosophila melanogaster*. Journal of Insect Physiology, 58: 293–302. https://doi.org/10.1016/j.jinsphys.2012.01.013

Seinsche, A.; Dyker, H.; Losel, P.; Backhaus, D.; Scherkenbeck, J. (2000): Effect of helicokinins and ACE inhibitors on water balance and development of *Heliothis virescens* larvae. Journal of Insect Physiology, 46: 1423-1431. https://doi.org/10.1016/S0022-1910(00)00065-2

Sevala, N.L. and Davey, K.G. (1990): The action of juvenile hormone on the follicle cells of *Rhodnius prolixus* involves protein kinase C and calcium. In: "Insect Neurochemistry and Neurophysiology" (Borkovel, A.B. and Master, E.P., eds.), NJ: Humana. pp: 323-328.

Sevela, N.L.; Davey, K.G. and Prestwich, G.D. (1995): Photoaffinity level and characterisation of a juvenile hormone binding protein in the membranes of follicle cells of *Locusta migratoria*. Insect Biochemistry and Molecular Biology, 25: 267-273. DOI: 10.1016/0965-1748(94)00065-P

Shen, Z.Y.; Li, R.Q.; Lu, X.F. and Dai, Z.Y. (1990): Effect of trimolting silkworm inducer SM-1 on the regulation mechanisms of the silk fibroin synthesis of silkworm Ⅱ. Acta Sericologica Sinica, 16(2): 85-89.

Shiotsukia, T.; Yukuhirob, F.; Kiuchib, M. and Kuwanoc, E. (1999): Effect of 1-(4-phenoxyphenoxypropyl)imidazole (KS-175) on larval growth in the silkworm *Bombyx mori*. Journal of Insect Physiology, 45(12): 1049-1055. https://doi.org/10.1016/S0022-1910(99)00088-8

Shuto, A.; Kuwano, E. and Eto, M. (1988): Synthesis of two optical isomers of the insect anti-juvenile hormone agent fluoromevalonolactone (FMev) and their biological activities. Agricultural and Biological Chemistry, 52(4): 915-919. DOI: 10.1080/00021369.1988.10868759

Sieber, R. and Benz, G. (1980): The hormonal regulation of the larval diapause in the codling moth, *Laspeyresia pomonella* (Lep. Tortricidae). Journal of Insect Physiology, 26(3): 213-218. https://doi.org/10.1016/0022-1910(80)90083-9

Siegel, M.R. and Sisler, H.D. (1963): Inhibition of protein synthesis *in vitro* by cycloheximide. Nature, 200: 675-676. doi:10.1038/200675a0

Singh, D. and Bhathal, S.S. (1994): Role of insect growth regulators in integrated pest management. Journal of Insect Science, 7(1): 1-9.

Singh, S. and Kumar, K. (2011): Anti-JH compounds and insect pest management. In: "Emerging Trends in Zoology" (Srivastava, U.C. and Kumar, S., eds.). Narendra Publishing House, pp: 335-350.

Singh, S. and Rao, P.J. (1999): Effect of *Artemisia vulgaris* on development and reproduction of *Spodoptera litura* and *Schistocerca gregaria*. Indian Journal of Entomology, 61(4): 305-311.

Singh, S. and Rao, P.J. (2000): Effect of *Ageratum conyzoides* on development and reproduction of *Spodoptera litura*. Indian Journal of Entomology, 62(3): 231-238.

Singh, A. and Tiwari, S.K. (2016): Role of Fenoxycarb, a juvenile hormone analogue, on the developmental stages of rice-moth, *Corcyra cephalonica* Staint. (Lepidoptera: Pyralidae). International Journal of Zoological Investigations, 2(2): 267-280.

Sirugue D.; Bonnard, O.; le Quere, J.L.; Farine, J.P. and Brossut, R. (1992): 2-Methylthiazolidine and 4-ethylguaiacol, male sex pheromone components of the cockroach *Nauphoeta cinerea* (Dictyoptera, Blaberidae): a reinvestigation. Journal of Chemical Ecology, 18: 2261-2276. DOI: 10.1007/BF00984949

Sláma, K. (1971): Insect juvenile hormone analogues. Annual Review of Biochemistry, 40: 1079-1102. DOI: 10.1146/annurev.bi.40.070171.005243

Sláma, K. (1978): The principles of antihormone action in insects. Acta entomologica Bohemoslovaca, 75: 65-82.

Smith, R.L. (1997): Evolution of paternal care in the giant water bugs (Heteroptera: Belostomatidae). In: "The evolution of social behavior in insects and arachnids"(Choe, J.C. and Crespib J., eds.). Cambridge, Cambridge University Press, pp: 116-149.

Soderlund, D.M.; Messeguer, A. and Bowers, W.S. (1980): Precocene II metabolism in insects (*Trichoplusia ni*): synthesis of potential metabolites and identification of initial *in vitro* biotransformation products. Journal of Agricultural and Food Chemistry, 28(4): 724-731. DOI: 10.1021/jf60230a053

Sohn, H.D.; Ahn, K.H. and Lee, K.R. (1991): Effects of methoprene and Precocene 2 on juvenile hormone esterase activity in the hemolymph of silkworm *Bombyx mori*. Korean Journal of Entomology, 21: 1-10.

Soltani, N. (1984): Effects of ingested diflubenzuron on the longevity and peritrophic membrane of adult mealworms (*Tenebrio molitor* L.). Pest Management Science, 15: 221-225. https://doi.org/10.1002/ps.2780150302

Soltani-Mazouni, N. and Soltani, N. (1995): Protein synthesis in the fat body of *Tenebrio molitor* (L.) during oocyte maturation: Effect of diflubenzuron, cycloheximide and starvation. Journal of Stored Products Research, 31(2): 117-122. https://doi.org/10.1016/0022-474X(94)00046-V

Soltani-Mazouni, N.; Amrani, L.; Boudra, I. and Zeguine, K. (2000): Inhibitory activity of an imidazoles compound on ecdysiosynthetic organs in meal worms under *in vivo* and *in vitro* conditions. Sciences & Technologie, Université Mentouri, Constantine, Algérie, 14: 125-128.

Sparks, T.C.; Roe, R.M.; Buehler, A. and Hammock, B.D. (1987): The evaluation of anti-juvenile hormones using last stadium larvae of the cabbage looper *Trichplusia ni* (Hubner). Insect Biochemistry, 17(7): 1011-1016. https://doi.org/10.1016/0020-1790(87)90112-0

Sreejith, P.S.; Praseeja, R.J. and Asha V.V. (2012): A review on the pharmacology and phytochemistry of traditional medicinal plant, *Glycosmis pentaphylla* (Retz.) Correa. Journal of Pharmacy Research, 5(5): 2723-2728.

Sridevi, R. and Ray, A. (1988): Protein synthesis in the male accessory reproductive glands of *Spodoptera litura* (Noctuidae: Lepidoptera). International Journal of Tropical Insect Science, 9(5): 635-637.

Srivastava, S. and Kumar, K. (1996): Effect of precocenes on metamorphosis of flesh fly, *Sarcophaga ruficornis* F. Indian Journal of Experimental Biology, 34: 547-553.

Srivastava, S. and Kumar, K. (1997): Precocene I and II induced metamorphosis in a noctuid moth, *Spodoptera litura* Fabr. Proceedings of Natural Academy of Science, India, 67(B): 213-226.

Srivastava, S. and Kumar, K. (1999): Juvenilizing effects of ethoxyprecocene in a lepidopteran insect. Indian Journal of Experimental Biology, 37(4): 379-383.

Srivastava, K. and Upadhyay, V.B. (2013a): Effect of phytoecdysteroid on silk producing potential of multivoltine mulberry silkworm *Bombyx mori*. The Bioscan, 8(1): 43-47.

Srivastava, K. and Upadhyay, V.B. (2013b): Phytoecdysteroid changes protein content in the larvae of *Bombyx mori*. Journal of Applied Biosciences, 39(1): 51-54.

Staal, G.B. (1982): Insect control with growth regulation interfering with the endocrine system. Entomologia Expermentalis et Applicata, 31: 15-23. https://doi.org/10.1111/j.1570-7458.1982.tb03115.x

Staal, G.B. (1986): Anti-juvenile hormone agents. Annual Review of Entomology, 31: 391-429.

Staal, G.B.; Henrick, C.A.; Bergot, B.J.; Cerf, D.C.; Edwards, J.P. and Kramer, S.J. (1981): Relationship and interactions between JH and anti-JH analogues in Lepidoptera. Int. "Conference on Regulation of Insect Development and Behaviour (Karpaz, P.; Sehnal, F.; Zabza, A.; Menn, J.J. and Cymborowski, B., eds). Worclaw: Technical University Press, pp: 323-340.

Stay, B. and Tobe, S.S. (2007): The role of allatostatins in juvenile hormone synthesis in insects and crustaceans. Annu. Rev. Entomol. 52: 277–99. doi:10.1146/annurev.ento.51.110104.151050.

Stay, B.; Tobe, S.S.; Bendena, W.G. (1994): Allatostatins: identification, primary structures, functions and distribution. Advances in Insect Physiology, 25: 267-337. https://doi.org/10.1016/S0065-2806(08)60066-1

Suzuki, K.; Fujisawa, T.; Kurihara, M.; Abe, S. and Kuwano, E. (1989): Artificial hatching in silkworm, *Antheraea yamamai*: application of KK-42 and its analogs. In: "Wild Silk moths"(Aki, H. and Wu, Z.S., eds.). The 88. International Society for Wild Silkmoths, Tokyo, Japan, pp: 79-84.

Sword, G.A.; Lecoq, M. and Simpson, S.J. (2010): Phase polyphenism and preventative locust management. Journal of Insect Physiology, 56: 949-957. https://doi.org/10.1016/j.jinsphys.2010.05.005

Szczepanik, M.; Obara, R.; Szumny, A.; Gabryś, B.; Halarewicz-Pacan, A.; Nawrot, J. and Wawrzeńczyk, C. (2005): Synthesis and insect antifeedant activity of precocene derivatives with lactone moiety. Journal of Agricultural and Food Chemistry, 53: 5905-5910. DOI: 10.1021/jf058034j

Tallamy, D.W. (2001): Evolution of exclusive paternal care in Arthropods. Annual Review of Entomology, 46: 139-165. DOI: 10.1146/annurev.ento.46.1.139

Tallamy, D.W.; Monaco, E.L. and Pesek, J.D. (2002): Hormonal control of egg dumping and guarding in the lace bug, *Gargaphia solani* (Hemiptera: Tingidae). Journal of Insect Behavior, 15: 467-475.

Tan, Z.D.; Kong, L.W.; Fan, H.L.; Gong, X.X.; Han, Y.D. and Yan, R.A. (1992): Induction of 3-molt silkworm by using of SD-Ⅲ and its effect on silk quality. Acta Sericologia Sinica, 18(4): 237-242.

Tanaka, S. (2001): Endocrine mechanisms controlling body-color polymorphism in locusts. Archives of Insect Biochemistry and Physiology, 47: 139-149. https://doi.org/10.1002/arch.1045

Tanaka, S. (2006): Corazonin and locust phase polyphenism. Applied Entomology and Zoology, 41:179-193. DOI: 10.1303/aez.2006.179

Tanani, M. and Ghoneim, K. (2017): Impaired adult performance and reproduction of the pink bollworm ***Pectinophora gossypiella*** (Saunders) (Lepidoptera: Gelechiidae) after treatment of eggs with the chitin synthesis inhibitors, Noviflumuron and Novaluron. International Journal of Modern Research and Reviews, 5(3): 1513-1526.

Tarrant, C.; Cupp, E.W. and Bowers, W.S. (1982): The effects of precocene II on reproduction and development of triatomine bugs (Reduviidae: Triatominae). American Journal of Tropical Medicine and Hygiene, 31(2): 416-420. DOI: 10.4269/ajtmh.1982.31.416

Tarver, M.R.; Schmelz, E.A.; Rocca, J.R. and Scharf, M.E. (2009): Effects of soldier-derived terpenes on soldier caste differentiation in the termite (*Reticulitermes flavipes*). Department of Entomology, Faculty Publications, Paper 1. http://dx.doi.org/10.1007/s10886-009-9594-8

Tatar, M.; Kopelman, A.; Epstein, D.; Tu, M.-P.; Yin, C.-M. and Garofalo, R.S. (2001a): A mutant *Drosophila* insulin receptor homolog that extends life-span and impairs neuroendocrine function. Science, 292: 107-110. https://doi.org/10.1126/science.1057987

Tatar, M.; Priest, N. and Chien, S. (2001b): Negligible senescence during reproductive dormancy in *D. melanogaster*. American Naturalist, 158: 248-258. DOI: 10.2307/3079203

Tateishi, K.; Kiuchi, M. and Takeda, S. (1993): New cuticle formation and moult inhibition by RH-5849 in the common cutworm, *Spodoptera litura* (Lepidoptera: Noctuidae). Applied Entomology and Zoology, 28: 177-184. https://doi.org/10.1303/aez.28.177

Tawfik AI. (2012): Hormonal control of the phase polyphenism of the desert locust: a review of current understanding. Open Entomology Journal, 6: 22-41. DOI: 10.2174/1874407901206010022

Tawfik, A.I. and Sehnal, F. (2003): A role for ecdysteroids in the phase polymorphism of the desert locust. Physiological Entomology, 28: 19-24. https://doi.org/10.1046/j.1365-3032.2003.00316.x

Tawfik, A.I.; Tanaka, S.; de Loof, A.; Schoofs, L.; Baggerman, G.; Waelkens, E.; Derua, R.; Milner, Y.; Yerushalmii, Y. and Pener, M.P. (1999): Identification of the gregarization-associated dark pigmentotropin in locusts through an albino mutant. Proceedings of the National Academy of Sciences of USA (PNAS), 96: 7083-7087. https://doi.org/10.1073/pnas.96.12.7083

Tawfik, A.I.; Osir, E.O. and Hassanali, A. (2014): Effects of anti-juvenile hormone (Precocene II) treatment on phase changes and pheromone production in the desert locust, *Schistocerca gregaria* (Forskal) (Orthoptera: Acrididae). The Open Entomology Journal, 8: 10-16. DOI: 10.1016/S0022-1910(97)00079-6

Tazir, A.; Kirane-Amrani, L. and Soltani, N. (2016): Impact of two bisacylhydrazines on development of *Ephestia kuehniella* Zeller, 1879 (Lepidoptera: Pyralidae) with respect to cuticular thickness and protein. Journal of Entomology and Zoology Studies, 4(6): 626-631.

Tércio, J.; Ferreira, B.; Catani, V. and Comasseto, J.V. (1987): Synthesis of 2,2-Dimethyl-2H-thiochromenes, the sulfur analogs of precocenes. Synthesis, 2: 149-153. doi: 10.1055/s-1987-27866

Tillman, J.A.; F. Lu,; L.M. Goddard,; et al. (2004): Juvenile hormone regulates *de novo* isoprenoid aggregation pheromone biosynthesis in pine bark beetles, *Ips* spp., through transcriptional control of HMG-CoA reductase. Journal of Chemical Ecology, 30: 2459-2494. DOI: 10.1007/s10886-004-7945-z

Timar, T. and Jaszberenyi, J.C. (1988): A novel synthesis of precocenes. Efficient synthesis and regioselective O-alkylation of dihydroxy-2,2-dimethyl-4-chromanones. Journal of Heterocyclic Chemistry, 25(3): 871-877. https://doi.org/10.1002/jhet.5570250333

Tiryaki, D. and Temur, C. (2010): The fate of pesticide in the environment. Journal of Biological and Environmental Sciences, 4(10): 29-32.

Trabalon, M. and Campan, M. (1984): Etude de la receptivite sexuelle de la femelle *Calliphora vomitoria* (Diptera, Calliphoridae) au tours du premier cycle gonadotrope. I: Approaches comportementale et physiologique. Behavior, 90: 241-258.

Triseleva, T.A. (2003): Effect of plants synthesizing biologically active substances - precocenes - on insects. Biological Bulletin, 30(3): 275-280.

Triseleva, T.A. (2007): Influence of Precocene II on the sensory system of antennae and mouthparts in larvae of the fruit tree tortricid *Archips podana* Scop. (Lepidoptera: Tortricidae). Izvestiia Akademii nauk. Seriia biologicheskaia/Rossiiskaia akademiia nauk, 34(5): 557-562. DOI: 10.1134/S106235900705007X

Triseleva, T.A. (2012): Antijuvenile influence of the precocene on the development of adult antennae in the apple surface eating tortricid *Archips podana* Scop. (Lepidoptera: Tortricidae). Izvestiia Akademii nauk. Seriia biologicheskaia/Rossiiskaia akademiia nauk, 5: 501-508.

Trivedy, K.; Remadevi, O.K.; Magadam, S.B. and Datta, R.K. (1993): Effect of juvenile hormone analogue, Labomin on the growth and economic characters of silkworm, *Bombyx mori* L. Indian Journal of Sericulture, 32(2): 162-168.

Trivedy, K.; Nair, K.S.; Ahsan, M.M. and Datta, R.K. (1997): A juvenile hormone mimic modulated enhancement in silk productivity in silkworm, *Bombyx mori* L. Indian Journal of Sericulture, 36(1): 35-38.

Truman, J.W. and Riddiford, L.M. (1974): Hormonal mechanisms underlying insect behaviour. Advances in Insect Physiology, 10: 297-352. https://doi.org/10.1016/S0065-2806(08)60132-0

Truman, J.W. and Riddiford, L.M. (2007): The morphostatic actions of juvenile hormone. Insect Biochemistry and Molecular Biology, 37: 761-770. https://doi.org/10.1016/j.ibmb.2007.05.011

Tsubouchi, K.; Akahane, T. and Imai, T. (1997): High strength silk fiber obtained from super fine filament of silkworm cocoon treated with bioactive substances. Japan Agricultural Research Quarterly, 31(2):133-136.

Tunaz, H. and Uygun, N. (2004): Insect growth regulators for insect pest control. Turkish Journal of Agriculture and Forestry, 28: 377-387.

Unnithan, G.C.; Bern, H.A. and Nair, K.K. (1977): Ultrastructural analysis of the neuroendocrine apparatus of *Oncopeltus fasciatus* (Heteroptera). Acta Zoologica, 52: 117-143. https://doi.org/10.1111/j.1463-6395.1971.tb00553.x

Unnithan, G.C.; Nair, K.K. and Syed, A. (1980): Precocene-induced metamorphosis in the desert locust, *Schistocerca gregaria*. Experientia, 36: 135-156.

Unnithan, G.C.; Andersen, J.F.; Hisane, T.; Kuwano, E. and Feyereisen, R. (1995): Inhibition of juvenile hormone biesynthesis and methyl farnesoate epoxidase activity by 1,5-disubstituted imidazoles in the cockroach *Diploptera punctata*. Pesticide Science, 43: 13-19.

Uvarov, B.P. (1921). A revision of the genus *Locusta* L. (=*Pachytylus* Fieb.), with a new theory as to periodicity and migrations of locusts. Bulletin of Entomological Research, 12: 135-163. https://doi.org/10.1017/S0007485300044989

Uvarov, B.P. (1966): Grasshoppers and locusts. A Handbook of General Acridology. I. The Univ. Press, Cambridge, 481 pp.

Vainker, S. (2004): Chinese silk: a cultural history. 1st ed., Rutgers University Press, New Brunswick, N.J., 224pp.

Vajrala, N.; Bottomley, P.J.; Stahl, D.A.; Arp, D.J. and Sayavedra-Soto, L.A. (2014): Cycloheximide prevents the *de novo* polypeptide synthesis required to recover from acetylene inhibition in *Nitrosopumilus maritimus*. FEMS Microbiology and Ecology, 88: 495-502. https://doi.org/10.1111/1574-6941.12316

Van Der Gaag, N. (2000): Pick your poison. New Internationalist, 323: 9-11.

Van Mellaert, H.; De Loof, A. and Jurd, L. (1982): Sterilising effects of new compounds with antijuvenile hormone activity. Mededelingen van de Faculteit Landbouwwetenschappen, Rijksuniversiteit, Gent, 47: 459-465.

Van Mellaert, H.; De Loof, A. and Jurd, L. (1983): Anti-juvenile hormone effects of newly described chemosterilants: Benzyl-1,3-benzodioxoles and benzylphenols. Entomologia Experimentalis et Applicata, 33: 83-88. https://doi.org/10.1111/j.1570-7458.1983.tb03237.x

Villella, A. and Hall, J.C. (2008): Neurogenetics of courtship and mating in *Drosophila*. Advances in Genetics, 62: 67-184. https://doi.org/10.1016/S0065-2660(08)00603-2

Vinson, S.B. (1970): Development and possible functions of teratocytes in the host-parasite association. Journal of Invertebrate Pathology, 16: 93-101. https://doi.org/10.1016/0022-2011(70)90212-0

Waibel, M.; Floreano, D.; Magnenat, S. and Keller, L. (2006): Division of labour and colony efficiency in social insects: effects of interactions between genetic architecture, colony kin structure and rate of perturbations. Proceedings of the Royal Society B: Biological Sciences 273(1595):1815-1823. DOI: 10.1068/rspb.2006.3513

Walker, W.F. (1978): Mating behavior in *Oncopeltus fasciatus* (Dallas) effects of diet, photoperiod, juvenoids and precocene II. Physiological Entomology, 3: 147-155. https://doi.org/10.1111/j.1365-3032.1978.tb00144.x

Walkowiak, K.; Spochacz, M. and Rosinski, G. (2015): Peptidomimetics- A new class of bioinsecticides. Postepy Biologii Komorki, 42(2): 235-254.

Wang, F.-H. and Gong, H. (2001): Termination of pupal diapause in the bollworm *Helicoverpa armigera* by precocene. Entomologia Sinica, 8(4): 309-314.

Wang, X. and Kang, L. (2014): Molecular mechanisms of phase change in locusts. Annual Review of Entomology, 59: 225-243. DOI: 10.1146/annurev-ento-011613-162019

Wang, Q. L. and Liu, T.-X. (2016): Effects of three insect growth regulators on *Encarsia formosa* (Hymenoptera: Aphelinidae), an endoparasitoid of *Bemisia tabaci* (Hemiptera: Aleyrodidae). Journal of Economic Entomology, 109(6): 2290-2297. DOI: 10.1093/jee/tow216

Wang, F. and Schnal, F. (2001): Effects of the imidazole derivative KK-42 on the female and embryos of *Schistocerca gregaria*. Entomological Science, 4: 387-392.

Wang, Y. and Wang, M. (2007): The research of IGRs. World Pesticide, 29: 8-11.

Wang, Z.; Chen, X. and Haunerland, N.H. (1993): Flight muscle development in juvenile and adult forms of the desert locust, *Schistocerca gregaria*. Journal of Insect Physiology, 39: 325-333. https://doi.org/10.1016/0022-1910(93)90063-W

Weaver, R.J. and Audsley, N. (2009): Neuropeptide regulators of juvenile hormone synthesis: Structures, functions, distribution, and unanswered questions. In: "Trends in Comparative Endocrinology and Neurobiology". Annals of of the New York Academy of Sciences, 1163: 316-329. doi: 10.1111/j.1749-6632.2009.04459.x

Weers, P.M.M.; Beal, J. van and der Horst, D.J. van (1994): Effects of precocene and ecdysterone on locust apolipophorin-III synthesis. Proceedings of Experimental and Appllied Entomology, 5: 57-72.

Wheeler, D.E. (1986) Developmental and physiological determinants of caste in social Hymenoptera: evolutionary implications. American Naturalist, 128:13-34.

Wheeler, D.E. (1990): The developmental basis of worker polymorphism in fire ants. Journal of Insect Physiology, 36: 315–322. https://doi.org/10.1016/0022-1910(90)90012-5

Wiepz, G.J.: Guadaramma, A.G.; Fulgham, D.L. and Bertics, P.J. (2010): Purification and assay of kinase-active EGF receptor from mammalian cells by immunoaffinity chromatography. In: "Methods in Molecular Biology" (Patel, T.B. and Bertics, P.J., eds.). vol. 327, pp: 25-38, Humana Press, Totowa, NJ

Williams C.M. (1967): Third generation pesticides. Scientific American, 217: 13-17. http://www.jstor.org/stable/24926053

Wilson, T.G. (2004): The molecular site of action of juvenile hormone and juvenile hormone insecticides during metamorphosis: how these compounds kill insects. Journal of Insect Physiology, 50(2/3):111-121. DOI: 10.1016/j.jinsphys.2003.12.004

Wilson, T.G.; Landers, N.H. and Happy G.M. (1983): Precocenes I and II: inhibition of vitellogenic oocyte development in *Drosophila melanograster*. Journal of Insect Physiology, 29: 249-254. https://doi.org/10.1016/0022-1910(83)90091-4

Wittstock, S.; Kaatz, H.H. and Menzel, R. (1993): Inhibition of brain protein synthesis by cycloheximide does not affect formation of long-term memory in honeybees after olfactory conditioning. Journal of Neuroscience, 13: 1379-1386. https://doi.org/10.1523/JNEUROSCI.13-04-01379.1993

Woodard, H.D. and Rankin, M.A. (1980): Effect of precocene II on circadian rhythms of feeding and mating behavior in the milkweed bug, *Oncopeltus fasciatus*. Experientia, 36: 554-555. DOI: 10.1007/BF01965796

Wu, J.M.; Wu, Z.D.; Xu, J.L. and Cao, M.X. (1991): The effect of trimolter inducer KK-42 on the endocrine system in the silkworm *Bombyx mori*. Acta Entomologica Sinica, 34(3): 278-283. http://www.insect.org.cn/EN/Y1991/V34/I3/278

Wu, Z.; Liu, L.; Chen, G. and Tan, J. (2013): Induction, development and regulation of trimolters: Great progress in the domesticated silkworm (*Bombyx mori* L.). African Journal of Biotechnology, 12(11): 1171-1177. https://doi.org/10.5897/AJB2012.10090

Wu, X.Q.; Huang, J.; Wang, M.Z.; Zhang, Z.; Li, X.L. and Yang, X.L. (2016): Synthesis, bioactivity and functional evaluation of linker-modified allatostatin analogs as potential insect growth regulators. Chinese Chemical Letters, 27: 559-562. https://doi.org/10.1016/j.cclet.2016.02.010

Wu, X.; Wang, M.; Huang, J.; Zhang, L.; Zhang, Z.; Ling, Y.; Yang, X. and Tobe, S.S. (2017): A potential insect growth regulator for cockroach control: design, synthesis and bioactivity of N-terminal-modified allatostatin analogues. Pest Management Science, 73: 500-505. https://doi.org/10.1002/ps.4444

Wyatt, G.R. (1988): Vitellogenin synthesis and the analysis of juvenile hormone in locust fat body. Canadian Journal of Zoology, 66: 2600-2610. https://doi.org/10.1139/z88-384.

Wyatt, G.R. and Davey, K.G. (1996): Cellular and molecular actions of juvenile hormone. II: roles of juvenile hormone in adult insects. Advances in Insect Physiology, 26:1-155. https://doi.org/10.1016/S0065-2806(08)60030-2.

Xiang, Z.H.; Huang, J.T.; Xia, J.G. and Lu, C. (2005): Biology of Sericulture. Forestry Publishing House, Beijing, China.

Xie, Y.; Kai, Z.P.; Tobe, S.S.; Deng, X.L.; Ling, Y. and Wu, X.Q. (2011): Design, synthesis and biological activity of peptidomimetic analogs of insect allatostatins. Peptides, 32: 581-586. https://doi.org/10.1016/j.peptides.2010.10.016.

Xie, Y.; Zhang, L.; Zhang, C.; Wu, X.; Deng, X.; Yang, X. and Tobe, S.S. (2015): Synthesis, biological activity, and conformational study of N-methylated allatostatin analogues inhibiting juvenile hormone biosynthesis. Journal of Agricultural and Food Chemistry, 63: 2870-2876.

Xie, Y.; Wang, M.; Zhang, L.; Wu, X.; Yang, X. and Tobe, S.S. (2016): Synthesis and biological activity of FGLamide allatostatin analogs with Phe3 residue modifications. Journal of Peptide Science, 22: 600-606. https://doi.org/10.1002/psc.2906.

Xu, Y.S. and Xu, J.L. (2001): New progress in insect anti-juvenile hormone. China Sericulure, 22(1): 56-57.

Yagi, K.J.; Kwok, R.; Chan, K.K.; Setter, R.R.; Myles, T.G. and Tobe, S.S. (2005): Phe-Gly-Leu-amide allatostatin in the termite *Reticulitermes flavipes*: content

in brain and corpus allatum and effect on juvenile hormone synthesis. Journal of Insect Physiology, 51: 357-365. https://doi.org/10.1016/j.jinsphys.2004.12.006

Yagi, K.J.; Elliott, K.L.; Teesch, L.; Tobe, S.S. and Stay, B. (2008): Isolation of cockroach Phe-Gly-Leu-amide allatostatins from the termite *Reticulitermes flavipes* and their effect on juvenile hormone synthesis. Journal of Insect Physiology, 54: 939-948. https://doi.org/10.1016/j.jinsphys.2008.01.013

Yaguchi, A.; Yoshinari, T.; Tsuyuki, R.; Takahashi, H.; Nakajima, T.; Sugita-Konishi, Y.; Nagasawa, H. and Sakuda, S. (2009): Isolation and identification of precocenes and piperitone from essential oils as specific inhibitors of trichothecene production by *Fusarium graminearum*. Journal of Agricultural and Food Chemistry, 57(3): 846–851. DOI: 10.1021/jf802813h

Yamada, N.; Maeda, K.; Masumoto, M.; Inagaki, Y. and Furuta, K. (2016): Anti-juvenile hormone activity of ethyl 4-[(7-substituted 1,4-benzodioxan-6-yl)methyl]benzoates and their effect on the juvenile hormone titer in the hemolymph of the silkworm, *Bombyx mori*. Journal of Pesticide Science, 41(2): 38-43. DOI: 10.1584/jpestics.D15-072

Yamamoto, R.; Bai, H.; Dolezal, A.G.; Amdam, G. and Tatar, M. (2013): Juvenile hormone regulation of *Drosophila* aging. BMC Biology, 11: 85. https://doi.org/10.1186/1741-7007-11-85

Yasyukevich, V.V. and Zvantsov, A.B. (1999): Effects of antihormones on the susceptibility of *Anopheles sacharovi* mosquitoes to the malaria causative organism *Plasmodium gallinaceum*. Meditsinskaya Parazitologiya i Parazitarnye Bolezni, 68: 46-48.

Yin, C.-M.; Zou, B.-X. and Stoffolano, J.G. (1989): Precocene II treatment inhibits terminal oocyte development but not vitellogenin synthesis and release in the black blowfly, *Phormia regina* Meigen, Journal of Insect Physiology, 35: 465-469. https://doi.org/10.1016/0022-1910(89)90053-X

Yin, C.-M.; Zou, B.-X. and Stoffolano, J.G. (1990): Precocene II Suppresses the Biosynthesis of Juvenile Hormone, Ecdysteroids and Vitellogenin in the Black Blowfly, *Phormia regina* Meigen. In: "Insect Neurochemistry and Neurophysiology"(Borkovec A.B., Masler E.P., eds)· Insect Neurochemistry and Neurophysiology, pp: 373-376. https://doi.org/10.1007/978-1-4612-4512-4_47

Yoshida, M.; Nakanishi, K. and Suemitsu, K. (1989): Physicochemical properties of three molter raw silk changed by anti-JH. Kiito Kensa Kenkyu Hokoku, 42:11-19.

Yoshida, T.; Shiotsuki, T. and Kuwano, E. (2000): Synthesis and precocious metamorphosis-inducing activity of 3-(1-alkenyl)pyridines. Journal of Pesticide Science, 25: 253-258. https://doi.org/10.1584/jpestics.25.253

Zarate, N.; Diaz, O.; Martinez, A.M.; Figueroa, J.I.; Schneider, M.I.; Smagghe, G.; Vinuela, E.; Budia, F. and Pineda, S. (2011): Lethal and sublethal effects of Methoxyfenozide on the development, survival and reproduction of the fall armyworm, *Spodoptera frugiperda* (J.E. Smith) (Lepidoptera: Noctuidae). Neotropical Entomology, 40(1): 129-137. http://dx.doi.org/10.1590/S1519-566X2011000100020.

Zera, A.J. (2007): Endocrine analysis in evolutionary-developmental studies of insect polymorphism: hormone manipulation versus direct measurement of hormonal regulators. Evolutionary Development, 9: 499-513. https://doi.org/10.1111/j.1525-142X.2007.00181.x

Zera, A.J. and Denno, R.F. (1997): Physiology and ecology of dispersal polymorphism in insects. Annual Review of Entomology, 42: 207-231.

Zhang, D. (1989): Impact of teratocytes from *Microplitis croceipes* (Cresson)(Hymenoptera: Braconidae) on the larval development of *Heliothis virescens* (F.)(Lepidoptera: Noctuidae). M.Sc.Thesis, University of Kentucky, Lexington, KY.

Zhang, Q.; Nachmanc, R.J.; Kaczmarek, K.; Zabrocki, J. and Denlingera, D.L. (2011): Disruption of insect diapause using agonists and an antagonist of diapause hormone. Proceedings of the National Academy of Sciences of USA, 108(41): 16922-16926.

Zhao, L.-Q. and Zhu, D.-H. (2013): Effects of application of juvenile hormone and precocene on physiological trade-offs between flight muscle and reproductive development in the wing-dimorphic cricket *Velarifictorus ornatus* (Orthoptera: Gryllidae). Acta Entomologica Sinica, 56(6): 622-629. http://www.insect.org.cn/EN/Y2013/V56/I6/622

Zhou, F.; Zhu, G.; Zhao, H.; Wang, Z.; Xue, M.; Li, X.; Xu, H.; Ma, X. and Liu, Y. (2016): Sterilization effects of adult-targeted baits containing insect growth regulators on *Delia antiqua*. Scientific Reports, 6: 32855; 9pp. doi: 10.1038/srep32855.

Zhuang, D.H.; Xiang, M.H.; Gui, Z.Z. and Chen, G.H. (1992): The effect of trimolter by treatment with anti-juvenile hormone (AJH) analogue (YA20) and it's quality of cocoon filament in silkworm, *Bombyx mori*. Acta Sericologica Sinica, 18(2): 93-99.