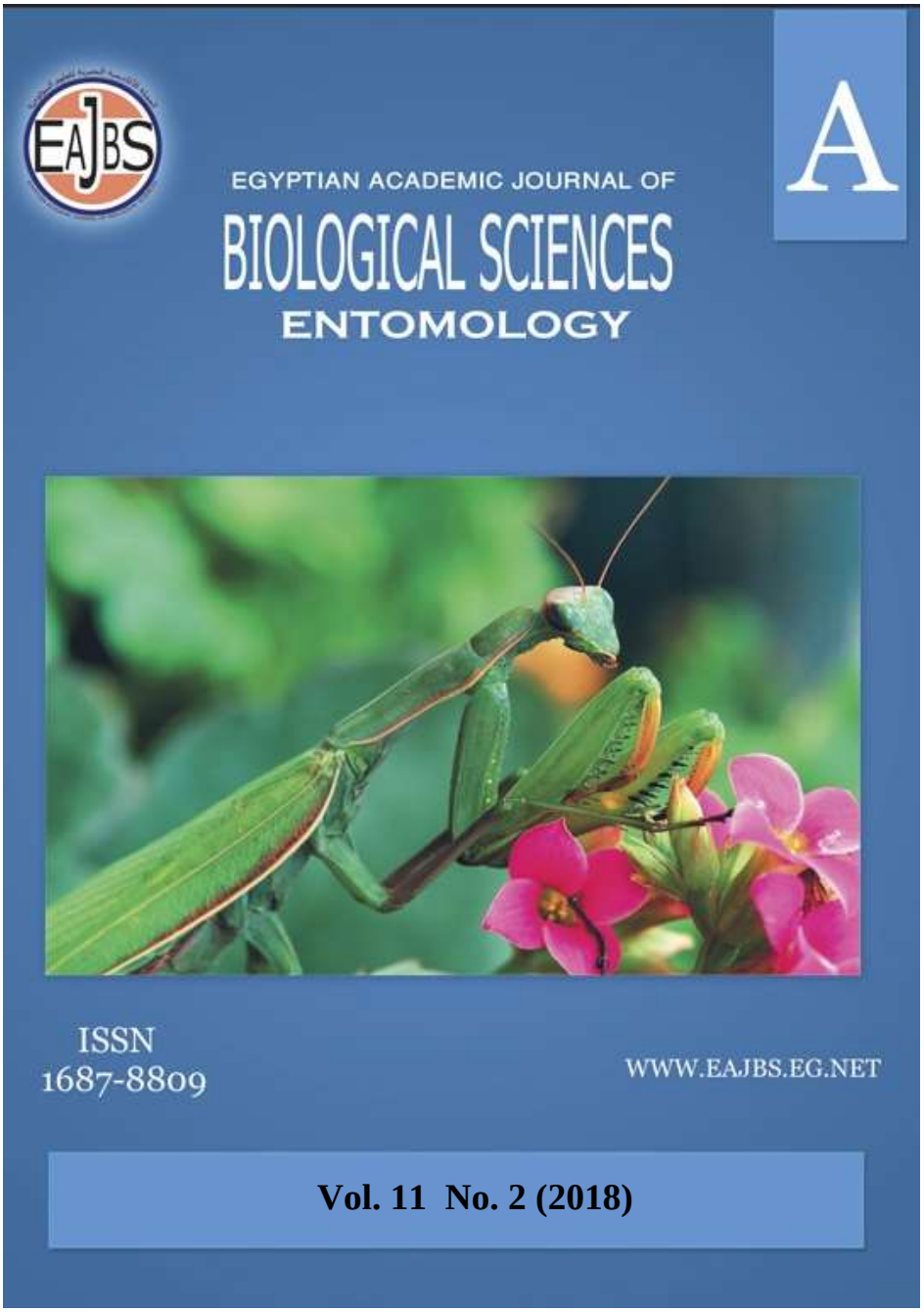

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Toxicity And Physiological Activity of Methoprene, A Juvenile Hormone Analog, Against Development and Metamorphosis of The Grey Flesh Fly, *Parasarcophaga argyrostoma* (Robineau- Desvoidy)(Diptera: Sarcophagidae).

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ABSTRACT

The grey flesh fly *Parasarcophaga argyrostoma* plays a role in human cutaneous wounds and eye myiasis and it is also known as parasitoid of various animals. The present study aimed to investigate the efficacy of Methoprene on survival, development and metamorphosis of this fly species. Five dose levels (10.0, 5.0, 1.0, 0.1 and 0.01µg/larva) of Methoprene was topically applied onto the early last instar larvae and prepupae. Methoprene exhibited larvicidal, pupicidal and adulticidal activities against *P. argyrostoma*. LD_{50} values were found 0.155 and 0.258 µg/insect after topical treatment of early last instar larvae and prepupae, respectively. The maximal body weight of treated larvae was considerably decreased. The duration of treated larvae was prolonged. The coefficient of growth of treated larvae was depressed. The pupal duration was remarkably prolonged. Some larval-pupal intermediates had been produced, only at the higher two doses. Topical treatment of prepupae only with the lower two doses induced a state of 'permanent prepupae'. The treated last instar larvae pupated in regressed rate. The pupation rate was slightly regressed after topical treatment of prepupae only with the lower two doses. The adult emergence of flies was completely blocked after topical treatment of either the early last instar larvae or prepupae with the highest dose of Methoprene. At other dose levels, the adult eclosion of flies was partially blocked. Different percentages of deformed pupae and adults were recorded.

INTRODUCTION

Flesh flies (Diptera: Sarcophagidae) differ from most flies in that they are ovoviviparous, opportunistically depositing hatched maggots instead of eggs. From the sanitary point of view, flesh flies are of relevant importance. Their impact on human and animal health is well known for their potential ability as myiasis

producers (Guimarães et al., 1983) and for their role as vector of pathogens (Greenberg, 1971). On the other hand, they are among the most useful insects for forensic investigations (Wells et al., 2001). The grey flesh fly *Parasarcophaga argyrostoma* (Robineau-Desvoidy) is worldwide in distribution including Europe, North America, Chile, Africa, India, Argentina, the Hawaiian Islands, and the Marshall Islands (Lopes, 1961). The adult flies visit decaying substances, faeces and also feed on flowers. Larvae normally develop in decaying meat but are also known as parasitoids of various animals (Povolny and Verves, 1997). *P. argyrostoma* has received much attention due to its role in human cutaneous wounds and eye myiasis (Razmjou et al., 2007; Gómez-Hoyos et al., 2012). Interest in the study of *P. argyrostoma* maggots has increased with the step forward in forensic entomology, where they are considered potential indicators of the time of death (Wells et al., 2001; Buenaventura et al., 2009).

Insecticides, such as organophosphates and carbamates, are in use extensively in agriculture and medicine since World War II. The intensive and indiscriminate uses of many broad-spectrum conventional insecticides led to several drastic problems, such as the environmental hazards, destruction of the natural enemies, like parasites, predators, birds, fishes and mammals, serious toxicological problems to humans, as well as the development of insect resistance toward different insecticides (Davies et al., 2007; Costa et al., 2008; Mosallanejad and Smagghe, 2009). Therefore, alternative materials have been initiated recently to minimize the insecticide hazards and introduce of new effective and safer ways with negligible effects on the ecosystem (Derbalah et al., 2014).

It is well known that the moulting, growth, development and metamorphosis of insects are controlled 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). It is the balance in levels of MH and JH that define the outcome of each developmental transition. During 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 triggers the larval-pupal and pupal-adult molts (Riddiford et al., 2003; Dubrovsky, 2005). In addition, JHs regulate many aspects of insect physiology and behaviour, including various forms of polymorphism, sex pheromone biosynthesis, diapause, migration, reproduction, metabolism and innate immunity (Mitsuoka et al., 2001; Goodman and Granger, 2005; Raikhel et al., 2005; Truman and Riddiford, 2007; Riddiford, 2008; Flatt et al., 2008; Zhan et al., 2011; Denlinger et al., 2012; Amsalem et al., 2014).

Screening new targets involved in JH-biosynthesis within the CA has been a subject of study during the last four decades (Bede et al., 2001). So, compounds that interact with JH, stimulate JH-biosynthesis, inhibit JH-biosynthesis or interfere with its catabolism can be utilized as new insecticides against insect pests (Nandi and Chakravarty, 2011). All these compounds can be collectively called as 'insect growth regulators' (IGRs) (Dhadialla et al., 1998; Khan and Qamar, 2012). 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 (Nicholas et al., 1999; Martins and Silva, 2004; Wang and Liu, 2016).

On the basis of the mode of action, IGRs had been grouped in three categories: (i) Juvenile hormone analogues (JHAs) (also called as Juvenoids), (ii) Ecdysteroids

or ecdysone agonists and (iii) Chitin synthesis inhibitors (CSIs) or moult inhibitors (Wing and Aller, 1990; Dhadialla et al., 1998; Oberlander and Silhacek, 2000). Later, Tunaz and Uygun (2004) classified IGRs into CSIs and substances that interfere with the action of insect hormones (i.e. JHAs, and ecdysteroids).

Because of their desirable characteristics, such as low toxicity, almost no apparent side effect on non-target organisms especially vertebrates, less environmental pollution, high selectivity, and low impact on natural enemies and human health, IGRs are used to control various insect pests (Wang and Wang, 2007; Ghasemi et al., 2010; Taleh et al., 2015; Resmitha and Meethal, 2016). Many IGRs have shown potentiality against different lepidopterous insects (Talikoti et al., 2012; Ghoneim et al., 2017a; Hassan et al., 2017; Tanani et al., 2017).

Methoprene belongs to the synthetic terpenoid class of compounds. Methoprene is a molecule that closely resembles insect juvenile hormone (Budavari, 1989; Crosby and Minyard, 1991). The insect growth regulating properties of methoprene were first described in 1973 and registered as a biological pesticide by the EPA in 1975 (Crosby and Minyard, 1991). It was later re-classified by the EPA as a biochemical pesticide (Glare and O'Callaghan, 1999). Methoprene is a highly effective compound mimicking the juvenile hormone, i.e., a JHA, for regulation of growth and development as well as many of the physiological and behavioural effects of JH in insects (Wyatt and Davey, 1996; Zera and Zhao, 2004). When used as a pesticide, methoprene acts by disrupting the molting cycle of some insects and other arthropods, including parasites (Struger et al., 2007). Methoprene has been successfully used to control some species of mosquitoes (Ross et al., 1994a,b; Ali et al., 1995; Ritchie, 1997; Pinkney et al., 2000; Nishiura et al., 2003), but is effective against a range of insects, including the orders Diptera, Lepidoptera and Coleoptera (Glare and O'Callaghan, 1999).

Chemical control of *P. argyrostoma* by conventional insecticides is difficult because of the larvae being protected inside wounds or bodies, and the high mobility of the adults. Searching for alternative pest management agents is necessary. Therefore, the present study was designed as a contribution in searching for control measure alternative to the conventional insecticides against *P. argyrostoma*. Objective of the present study was to investigate the efficacy of methoprene on survival, development and metamorphosis of this fly species.

MATERIALS AND METHODS

Experimental Insect:

A culture of the grey flesh fly *Parasarcophaga argyrostoma* (Robineau-Desvoidy) (Diptera: Sarcophagidae) was established under controlled laboratory conditions (28±0.1^{o}C, 65±5% R.H.). It was originated by a sample of susceptible strain pupae obtained from the continuously maintained culture for several years at the Department of Entomology, Faculty of Science, Cairo University. The rearing routine work and daily manipulation were carried out according to Zohdy and Morsy (1982a, b). Larvae (maggots) and pupae (puparia) were confined in plastic vials covered with muslin and supplied with a small piece of red meat mixed with a suitable amount of bran dust. The food was renewed daily. Adult flies were confined in wooden cages (30x30x30 cm) with wire gauze sides.

Methoprene Administration:

Methoprene has the chemical name: 1, isopropyl 2E, 4E-11 methoxy-3,7, 11-trimethyl-2, 4-dodecadienoates, with the molecular formula: $C_{19}H_{34}O_3$. Common

trade names include Altosid®, Apex®, Diacon®, Dianex®, Precor®, and Z-515®. Methoprene of 98.5% purity was purchased from Sigma-Aldrich Co., Egypt.
Methoprene was diluted with acetone to prepare five dose levels: 10.0, 5.0, 1.0, 0.1 and 0.01µg/larva. Thirty replicates (one larva/ replicate) of healthy larvae of the early last (3^{rd}) instar and similar number of prepupae were topically treated, individually, with each dose using Hamilton microapplicator (NHN 737). Similar number of replicates of early last instar larvae and prepupae had been topically treated with 1µ acetone only as controls. Treated and control insects were kept under the previously mentioned laboratory conditions. All treated and control insects were checked daily for feeding of larvae and recording all criteria of study.

Criteria of Study:

1. Toxicity of Methoprene:

Toxicity was determined by observed mortality. All mortalities of treated and control (larvae, pupae and adults) were recorded every day and total mortality was corrected according to Abbott's formula (Abbott, 1925) as follows:

$$\% \text{ of corrected mortality} = \frac{\% \text{ of test mortality} - \% \text{ of control mortality}}{100 - \% \text{ of control mortality}} X100$$

The LC_{50} value was calculated for general mortality by Microsoft office Excel, 2007, according to Finny (1971).

2. Larval Growth:

Coefficient of growth (mean±SD) was calculated according to El-Ibrashy and Aref (1985) as follows: maximal body weight (mg) of full grown larvae/ duration (in days).

3. Developmental and Metamorphic Parameters:

Developmental durations had been calculated (mean days±SD) using Dempster's equation (1957).

Pupation rate was expressed in % of the developed pupae. Adult emergence was determined in %.

All of the possible aberrations of metamorphosis and morphogenesis, such as larval-pupal or pupal-adult intermediates, permanent insects, and malformed pupae, were calculated in %.

Statistical Analysis of Data:

Data obtained were analyzed by the Student's *t*-distribution, and refined by Bessel correction (Moroney, 1956) for the test significance of difference between means.

RESULTS

Lethal effect of methoprene on *P. argyrostoma*:

After topical application of methoprene (once) onto the early last (3^{rd}) instar larvae, data of the lethal effect was expressed as mortalities of larvae (maggots), pupae (puparia) and adult flies and assorted in Table (1). After topical application of methoprene (once) onto prepupae, data of mortalities were arranged in Table (2).

1. Larvicidal Effect of Methoprene:

Depending on data of Table (1), treatment of last instar larvae with methoprene caused different percentages of larval mortality in a dose-dependent course (10, 15, 35, 40 and 45% mortality, at 0.01, 0.1, 1.0, 5.0 and 10.0 µg/larva, respectively, *vs*.

05% mortality of control larvae). Methoprene had high initial killing power, since the majority of larval mortality was observed during the first 24 h post-treatment.

2. Pupicidal Effect of Methoprene:

According to data listed in Table (1), an extended toxic effect of methoprene was exhibited on pupae, since different pupal mortalities were recorded, in no certain trend, after treatment of last instar larvae. The strongest toxic effect was exhibited at the highest dose (100% pupal mortality, *vs*. 5.3% mortality of control pupae). After topical application of prepupae with methoprene, the pupal mortalities were recorded in a dose-dependent manner. The extreme mortal potency of methoprene was exhibited at the highest dose level (10, 15, 30, 60 and 100% pupal mortality, at 0.01, 0.1, 1.0, 5.0 and 10.0 µg/prepupa, respectively, *vs*. 5.0% mortality of control pupae).

3. Adulticidal Effect of Methoprene:

As obviously shown in Tables (1 and 2), no adult mortality could be recorded at the highest dose level of methoprene because no adults emerged, may be due to the complete death of pupae, regardless the time of treatment. The tested compound exhibited increasing adulticidal effect by the increasing dose level applied onto the early last instar larvae (25.0, 31.3, 41.7 and 50.0% adult mortality, at 0.01, 0.1, 1.0 and 5.0 µg/larva, respectively, *vs*. 0% mortality of control adult flies, Table 1). According to data distributed in Table (2), the extended toxic effect of methoprene on adult flies appeared in no certain trend (16.7, 29.4. 42.9 and 37.5% adult mortality, at 0.01, 0.1, 1.0 and 5.0 µg/larva, respectively, *vs*. 0% mortality of control adult flies).

Depending on the corrected mortality, after treatment of last instar larvae, methoprene exerted lethal potency against *P. argyrostoma* parallel to the dose level (33.3, 38.9, 61.1, 72.2 and 100% corrected mortality, at 0.01, 0.1, 1.0, 5.0 and 10.0 µg/larva, respectively, Table 1). In a similar trend, the lethal potency of methoprene increased by increasing dose level, after treatment of prepupae (21.1, 36.8, 57.9, 73.7 and 100% corrected mortality, at 0.01, 0.1, 1.0, 5.0 and 10.0 µg/prepupa, respectively).

The calculated LD_{50} values of methoprene were found 0.155 and 0.258 µg/insect after topical treatment of last instar larvae and prepupae, respectively. Therefore, the early last instar larvae were more sensitive to the toxicity of methoprene than prepupae.

Table (1): Toxic effect (%) of methoprene on *P. argyrostoma* after topical treatment of the early last instar larvae.

Dose (µg/larva)	Larval mortality	Pupal mortality	Adult mortality	Total mortality	Corrected mortality	LD_{50} (µg/larva)
10.0	45	100.0	---	100	100	0.155
5.0	40	16.7	50.0	75	72.2	
1.0	35	07.7	41.7	65	61.1	
0.1	15	05.9	31.3	45	38.9	
0.01	10	11.1	25.0	40	33.3	
Control	05	05.3	00.0	10	---	

---: No adult mortality could be calculated because no adult flies emerged.

Table (2): Toxic effect (%) of methoprene on *P. argyrostoma* after topical treatment of the prepupae.

Dose (µg/larva)	Pupal mortality	Adult mortality	Total mortality	Corrected mortality	LD_{50} (µg/larva)
10.0	100	---	100	100	0.258
5.0	60	37.5	75	73.7	
1.0	30	42.9	60	57.9	
0.1	15	29.4	40	36.8	
0.01	10	16.7	25	21.1	
Control	05	00.0	05	---	

---: See footnote of Table (1).

Effect of Methoprene on The Larval Growth in *P. argyrostoma*:

After topical application of methoprene doses (once) onto the early last instar larvae, data of the maximal body weight (max. wt), duration and coefficient of growth (CG) of the treated and control larvae were assorted in Table (3). In the light of these data, max. wt considerably decreased, almost in a dose-dependent course (116.5±3.51, 103.7±12.26, 102.9±14.80, 094.2±16.09 and 068.7±4.42 mg of treated larvae, at 0.01, 0.1, 1.0, 5.0 and 10.0 µg/larva, respectively, in comparison with 116.5±6.13 mg of control larvae). With regard to the larval duration, data of the same table clearly show a slightly or remarkably prolongation, depending on the dose of methoprene (4.00±0.43, 3.60±0.50, 3.62±0.63 and 3.73±0.62 days of treated larvae, at 0.01, 0.1, 1.0 and 5.0 µg/larva, respectively, *vs*. 3.55±0.50 days of control larvae). An exceptional case of significantly shortened larval duration was recorded at the highest dose of methoprene (2.85±0.66 days of treated larvae, *vs*. 3.55±0.50 days of control larvae).

As exiguously shown in the same table, CG of the treated larvae was slightly or pronouncedly depressed, depending on the dose level of methoprene. The potent inhibitory action was exerted on the larval growth at the doses 0.01, 1.0 and 5.0 µg/larva (29.91±5.32, 29.16±4.46 and 26.18±4.67, respectively, *vs*. 37.3±13.04 CG of control larvae).

Table (3): Larval growth of *P. argyrostoma* after topical application of methoprene onto the early last instar larvae.

Dose (µg/larva)	Weight (mean mg±SD)*	Duration (mean days±SD)	Coefficient of growth (mean±SD)
10.0	068.7±4.42 d	2.85±0.66 c	33.02±19.06 a
5.0	094.2±16.09 d	3.73±0.62 a	26.18±04.67 b
1.0	102.9±14.80 c	3.62±0.63 a	29.16±04.46 b
0.1	103.7±12.26 b	3.60±0.50 a	32.64±12.03 a
0.01	116.5±3.51 a	4.00±0.43 b	29.91±05.32 b
Control	116.5±6.13	3.55±0.50	

Mean±SD followed with the same letter a: insignificantly different (P >0.05), b: significantly different (P<0.05), c: highly significantly different (P<0.01), d: very highly significantly different (P<0.001)

Effect of Methoprene on The Development of *P. argyrostoma*:

After topical application on methoprene onto the early last instar larvae, data of

the affected development was summarized in Table (4). After topical application on methoprene onto the prepupae, data of the affected development was assorted in Table (5).

1. Pupal Development:

The pupal (puparial) duration can be used as a good indicator of the pupal development, i.e., shorter duration may denote faster rate and *vice versa*. At the highest dose level of methoprene, no pupal duration could be measured because no adult flies emerged, regardless the time of treatment.

Depending on the data assorted in Table (4), the pupal duration was remarkably prolonged after topic application of methoprene onto the early last instar larvae (12.60±0.80, 15.66±0.47, 15.13±0.45 and 14.33±0.81 days of treated pupae (puparia) , at 0.01, 0.1, 1.0 and 5.0 µg/larva, respectively, *vs*. 11.36±0.48 days of control pupae).

According to the data of Table (5), the pupal duration was considerably prolonged after treatment of the prepupae with methoprene (13.00±1.04, 15.08±0.27, 14.47±0.93 and 14.50±0.50 days of treated pupae, at 0.01, 0.1, 1.0 and 5.0 µg/larva, respectively, *vs*. 12.08±0.73 days of control pupae). Depending on these data, methoprene exerted an inhibitory effect on the successfully formed pupae, since they developed in slower rate than that of the control pupae, regardless the time of treatment.

2. Disrupted Developmental Program:

2.1. Larval-pupal Intermediates:

As clearly seen in Table (4), topical treatment of the last instar larvae with the higher two doses of methoprene impaired the process of larval-pupal transformation since some larval-pupal intermediates were produced (20 and 10% intermediates, at 10.0 and 5.0 µg/larva, respectively). These intermediate creatures perished just after production.

2.2. Permanent Prepupae:

As obviously shown in Table (5), topical treatment of prepupae only with the lower two doses of methoprene induced a state of suspended development, as expressed in 'permanent prepupae' (10.5 and 10.0% permanent prepupae, at 0.1 and 0.01 µg/prepupa, respectively). These permanent prepupae suffered the adverse action of methoprene along 12 days and eventually perished without external feature of puparium formation.

Effect of Methoprene on Metamorphosis And Morphogenesis of *P. argyrostoma*:

1. Pupation Process:

On the basis of data arranged in Table (4), the methoprene-treated last instar larvae pupated in a slightly or drastically regressed rate, depending on the dose level (78.57, 64.29, 92.86, 78.57 and 92.31% pupation (pupariation), at 0.01, 0.1, 1.0, 5.0 and 10.0 µg/larva, respectively, *vs*. 100% pupation of control larvae). The pupation inhibition could be calculated as 21.43, 35.71, 7.14, 21.43 and 7.69%, at 0.01, 0.1, 1.0, 5.0 and 10.0 µg/larva, respectively). On the other hand, the pupation rate was slightly regressed after topical treatment of prepupae only with the lower two doses of methoprene (92.86 and 92.86% pupation of treated larvae, at 0.01 and 0.1 µg/prepupa, *vs*. 100% pupation of control prepupae).

2. Adult Emergence:

Depending on data of Tables (4 & 5), the adult emergence of flies was completely blocked after topical treatment of either the early last instar larvae or prepupae with the highest dose of methoprene. Also, the adult eclosion of flies was drastically blocked, in no certain trend, after treatment of last instar larvae with other methoprene doses (26.66, 17.69, 33.33 and 45.47%, at 5.0, 1.0, 0.1 and 0.01 µg/larva, respectively, *vs*. 94.95% emergence of control adult flies) (Table 4). After topical treatment of prepupae with other doses of methoprene, the adult eclosion was

correlated directly to the dose level, i.e., the inhibitory action of methoprene increased as the dose level was elevated (100, 55.39, 48.62 and 44.29% emergence, at 0.01, 0.1, 1.0 and 5.0 µg/prepupa, respectively, *vs*. 100% emergence of control adult flies, Table 5).

3. Disrupted Morphogenesis:

As highlighted by data of Table (4), methoprene displayed anti-morphogenic efficiency on the developed pupae, since different %s of deformed pupae were produced after treatment of last instar larvae, but in no certain trend (3.33, 10.0, 10.0, 13.33 and 3.33% deformed pupae, at 0.01, 0.1, 1.0, 5.0 and 10.0 µg/larva, respectively, *vs*. 0% malformation of control pupae). In contrast, methoprene failed to exhibit similar efficiency on the pupal morphogenesis, after treatment of prepupae, since no deformed pupae were observed, Table 5).

With regard to the disruptive effect of methoprene on the adult morphogenesis, data of Table (4) unambiguously revealed that topical treatment of last instar larvae only with the doses 5.0 and 1.0 µg/larva of methoprene deranged the morphogenesis of the emerged adult flies as recorded in 6.7 and 6.7% deformed adults, respectively (*vs*. 0% deformation of control adult flies). Also, topical treatment of the prepupae with the same two doses led to 20.5% malformed adult flies (compared to 0% deformity of control adult flies, Table 5).

Table (4): Development and metamorphosis of *P. argyrostoma* after topical application of methoprene onto the early last instar larvae.

Dose (µg/larva)	Larval-pupal inter. (%)	Pupation rate (%)	Pupal Duration (mean days±SD)	Deformed pupae (%)	Adult emergence (%)	Deformed adults (%)
10.0	20	92.31	--- *	3.33	00.00	---
5.0	10	78.57	14.33±0.81 c	13.33	26.66	6.7
1.0	00	92.86	15.13±0.45 c	10.0	17.69	6.7
0.1	00	64.29	15.66±0.47 c	10.0	33.33	0.0
0.01	00	78.57	12.60±0.80 b	3.33	45.47	0.0
Control	00	100	11.36±0.48	00.00	94.95	0.0

a, c: See footnote of Table (3). Larval-pupal inter.: Larval-pupal intermediates, they perished without pupation. *: The pupal duration could not be measured because no adults emerged.

Table (5): Development and metamorphosis of *P. argyrostoma* after topical application of methoprene onto the prepupae

Dose (µg/larva)	Permanent prepupae (%)*	Pupation rate (%)	Pupal Duration (mean days±SD)	Deformed pupae (%)	Adult emergence (%)	Deformed adults (%)
10.0	00.0	100	--- **	0	00.00	---
5.0	00.0	100	14.50±0.50 c	0	44.29	20.5
1.0	00.0	100	14.47±0.93 c	0	48.62	20.5
0.1	10.5	92.86	15.08±0.27 c	0	55.39	00.0
0.01	10.0	92.86	13.00±1. 04 b	0	100	00.0
Control	00.0	100	12.08±0.73	0	100	00.0

b, c: See footnote of Table (3). *: Permanent prepupae perished without pupation. **: The pupal duration could not be measured because no adults emerged.

DISCUSSION

Disrupted Survival of *P. argyrostoma* by Methoprene:

Toxicity of several insect growth regulators (IGRs) against various insect species had been reported, such as the toxic effects of Fenoxycarb against the hymenopterous parasitoid *Phanerotoma ocularis* (Moreno et al., 1993a), the rice meal moth *Corcyra cephalonica* (Begum and Qamar, 2016) and the desert locust *Schistocerca gregaria* (Ghoneim and Ismail, 1995a). Toxic effects of Flufenoxuron (El-Naggar, 2013), Lufenuron (Bakr et al., 2013), Buprofezin (Nasr et al., 2010) and Cyromazine (Tanani et al., 2015) were reported against the Egyptian cotton leafworm *Spodoptera littoralis*. Toxic effects of Pyriproxyfen were reported against the Sunn pest *Eurygaster integriceps* (Mojaver and Bandani, 2010) and the lawn armyworm *Spodoptera mauritia* (Resmitha and Meethal, 2016). Also, toxicities of various IGRs were reported against different insects, such as Kinoprene against the common house mosquito *Culex pipiens* (Hamaidia and Soltani, 2014); Flufenoxuron and Methoprene against the black cutworm *Agrotis ipsilon* (Khatter, 2014); Lufenuron against the red flour beetle *Tribolium castaneum* (Gado et al., 2015); the lesser mulberry snout moth *Glyphodes pyloalis* (Aliabadi et al., 2016) and the corn earworm *Helicoverpa armigera* (Vivan et al., 2016); Tebufenozide (RH-5992) against the Mediterranean flour moth *Ephestia kuehniella* (Tazir et al., 2016); Cyromazine against the flies *Musca domestica*, *Stomoxys calcitrans* and *Fannia canicularis* (Donahue et al., 2017); Novaluron against the pink bollworm *Pectinophora gossypiella* (Ghoneim et al., 2017a) and olive leaf moth *Palpita unionalis* (Ghoneim et al., 2017b).

Results of the present study were, to some extent, in agreement with those previously reported results, since methoprene exhibited larvicidal, pupicidal and adulticidal activities against *P. argyrostoma*. Topical treatment of the early last instar larvae with methoprene resulted in larval mortality, in a dose-dependent course. Moreover, methoprene had high initial killing power, since the majority of larval mortality was observed during the first 24 h post-treatment. Also, different pupal mortalities were recorded. In addition, methoprene exhibited a chronic toxicity against the adult flies. Such effect was intensified by increasing dose applied onto the early last instar larvae but appeared in no certain trend after treatment of prepupae.

In larvicidal activity of methoprene against *P. argyrostoma*, in the current study, was in corroboration with some reported results of methoprene larvicidal activity against some insects, such as the mosquito *Culex molestus* (Farghal and Temerak, 1981), the common house mosquito *Culex pipiens* (Gelbic et al., 2002), the Asian tiger mosquito *Aedes albopictus* (Khan et al., 2016), the black cutworm *Agrotis ipsilon* (Khatter, 2014) and *C. cephalonica* (Tripathi and Tiwari, 2006). Also, the present result of methoprene pupicidal activity against *P. argyrostoma* agreed with those reported pupicidal activity of methoprene against some insects, such as the yellow fever mosquito *Aedes aegypti* (Braga et al., 2005) and *C. cephalonica* (Tripathi and Tiwari, 2006). In addition, exposure of 3rd instar larvae of the flesh fly *Sarcophaga ruficornis* to different concentrations of Barium carbonate resulted in larval and pupal mortalities (Singh et al., 2017).

The larval deaths of *P. argyrostoma*, in the current investigation, may be attributed to the prevention of moulting larvae to swallow volumes of air for splitting the old cuticle and expand the new one during ecdysis (Linton et al., 1997). Also, the larval deaths may be due to the prevented feeding and continuous starvation (Ghoneim et al., 2000). The pupal deaths of *P. argyrostoma* can be directly related to

the hormonal activity of the tested compound or may be due to some secondary factors, such as suffocation, bleeding and desiccation due to imperfect exuvation, and for failure of vital homeostatic mechanisms (Sehnal, 1983; Smagghe and Degheele, 1994). The adult mortalities of *P. argyrostoma* can be explained by the retention and distribution of methoprene in the insect body as a result of direct and rapid transport *via* the haemolymph to other tissues, and/or by lower detoxification capacity of adults against the tested compound (Osman et al., 1984).

LC_{50} (or LD_{50}) values of IGRs are variable against different insect species. For examples, LC_{50} values of Novaluron and Lufenuron (chitin synthesis inhibitors, CSIs) against the tobacco cutworm *Spodoptera litura* were determined as 350.45 and 453.78 ppm, respectively (Sharma and Pathania, 2014); LC_{50} of Hexaflumuron (CSI) against *H. armigera* was 8.47 mg /L (Taleh et al., 2015); LC_{50} of Methoxyfenozide (ecdysteroid) against *C. pipiens* was calculated in 24.54 µg/L (Hamaidia and Soltani, 2016); LD_{50} values of RH-5849 and Tebufenozide (ecdysteroids) against *E. kuehniella* were 0.05 and 0.005 µg/insect, respectively (Tazir et al., 2016); LC_{50} values of Noviflumuron and Novaluron (CSIs) were 0.153 and 0.342 ppm after treatment of 1-day old eggs of *P. gossypiella* (Hamadah and Ghoneim, 2017); etc. In the current investigation, LD_{50} values of methoprene (a juvenoid) against *P. argyrostoma* were found 0.155 and 0.258 µg/insect, after topical treatment of the early last instar larvae and prepupae, respectively.

In insects, 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.

In addition, the early last instar larvae of *P. argyrostoma* were more sensitive to methoprene than prepupae, in the present study. This finding coincided with many results reporting that the early larval instars of different flies were more susceptible than the later ones to some IGRs, such as the house fly *Musca domestica* (Fouda et al., 1991), the green bottle fly *Lucilia cuprina* (Friedel and McDonell, 1985), the little house fly *Fannia* spp. (Meyer et al., 1987) and the Mediterranean fruit fly *Ceratitis capitata* (Vinuela et al., 1993).

Growth Inhibition in *P. argyrostoma* by Methoprene:

In the current investigation, the maximal body weight of methoprene-treated larvae of *P. argyrostoma* considerably decreased, almost in a dose-dependent course. Also, the coefficient of growth of the treated larvae was slightly or drastically depressed, depending on the dose level of methoprene. The decreased body weight of methoprene-treated larvae of *P. argyrostoma*, in the present study, disagreed with the reported increasing weight gain of the mulberry silk worm *Bombyx mori* last instar larvae after treatment of 4th instar larvae with methoprene (Miranda et al., 2002). On the other hand, the present result was, to some extent, in conformity with those reported results of reduced larval body weight in *C. capitata* after treatment of larvae with Cyromazine (Vinuela et al., 1993), *P. argyrostoma* after treatment of 3rd instar larvae with Pyriproxyfen (Ismail, 1995) or chlorfluazuron (Ghoneim and Ismail, 1995b).

Also, the present result of inhibited growth of *P. argyrostoma*, after treatment of last instar larvae with methoprene, was in accordance with those reported results of inhibited larval growth of some insects by the inhibitory action of various IGRs, such as *S. littoralis* by Flufenoxuron (Bakr et al., 2010), Lufenuron (Adel, 2012), and Novaluron (Ghoneim et al., 2015); *P. demoleus* by Diofenolan (Singh and Kumar, 2011); *S. litura* by Chlorfluazuron (Perveen, 2012); *Ae. aegypti* and *C. pipiens*

(Farnesi et al., 2012; Djeghader et al., 2014) and *A. ipsilon* by methoprene (Khatter, 2014). The inhibited growth of *P. argyrostoma* by methoprene, in the current study, may be a result of the blocked release of morphogenic peptides, causing alteration in the ecdysteroid and juvenoid titres (Barnby and Klocke, 1990). Also, methoprene may affect the tissues and cells undergoing mitosis (Nasiruddin and Mordue, 1994).

Disturbed Development of *P. argyrostoma* by Methoprene:

1. Affected Developmental Durations:

The larval and/or pupal durations of several insects had been prolonged as a response to larval treatment with methoprene. For examples, methoprene treatment of *C. molestus* larvae resulted in prolonged larval and pupal periods (Farghal and Temerak, 1981). After topical application of methoprene onto *C. cephalonica* larvae, the larval duration was prolonged (Tripathi and Tiwari, 2006). After topical application of methoprene onto larvae of *B. mori* 48h after 4th larval ecdysis, duration of the 5th (last) larval instar was prolonged (Miranda et al., 2002). Methoprene (0.1-5.0 µg/insect) topically applied on the newly moulted 5th instar larvae of *S. litura* caused a slight effect on the 5th instar duration, while the application to the newly moulted 6th (last) larvae resulted, in dose-dependent prolongation in the last instar duration (Yoshiga and Tojo, 2001). Treatment of *Ae. aegypti* larvae with methoprene resulted in prolongation of the pupal duration in dose-dependent course (Braga et al., 2005). Results of the present study on *P. argyrostoma* were, to a great extent, concomitant to the previously reported results, since the duration of methoprene-treated larvae was slightly or remarkably prolonged, depending on the dose level. Also, the pupal duration was considerably prolonged after topical application of methoprene onto either the early last instar larvae or prepupae. In other words, methoprene exerted a retarding action on the development of pupae, since they developed in slower rate than that of control pupae.

Also, our results of prolonged larval duration of *P. argyrostoma* corroborated with the reported results of prolonged larval duration in some insect species by various IGRs, such as *S. littoralis* after treatment of penultimate or last instar larvae with Novaluron (Ghoneim et al., 2015) and Cyromazine (Tanani et al., 2015); the fall armyworm *Spodoptera frugiperda* by Methoxyfenozide (Zarate et al., 2011); *P. gossypiella* by Pyriproxyfen (Sabry and Abdou, 2016) and Noviflumuron or Novaluron (Hamadah and Ghoneim, 2017). In addition, our results of prolonged pupal duration and retarded development of *P. argyrostoma* were in agreement with many reported results of retarded development of several insect species by various IGRs, such as *S. littoralis* by Diflubenzuron (Aref et al., 2010), Lufenuron (Gaaboub et al., 2012), Novaluron (Ghoneim et al., 2015) and Cyromazine (Tanani et al., 2015); *C. pipiens* by Kinoprene (Hamaidia and Soltani, 2014); *A. ipsilon* by methoprene and Flufenoxuron (Khatter, 2014); *P. gossypiella* by Buprofezin (Al-Kazafy, 2013); Teflubenzuron (El-Khayat et al., 2015) and Chromafenozide (Salem, 2015). Recently, the developmental duration was prolonged indicating a retarded development in some of other insects by IGRs, such as *G. pyloalis* by Lufenuron (Aliabadi *et al*., 2016); *C. pipiens* by Methoxyfenozide (Hamaidia and Soltani, 2016); *C. cephalonica* by Fenoxycarb (Begum and Qamar, 2016); *P. gossypiella* by Lufenuron and Pyriproxyfen (Sabry and Abdou, 2016) and Novaluron (Ghoneim *et al*., 2017a); and *P. unionalis* by Novaluron (Ghoneim *et al*., 2017b); *etc*.

On the contrary, the present results disagreed with the reported results of shortened larval duration of some insects after treatment with different IGRs, such as the red palm weevil *Rhynchophorus ferrugineus* by Lufenuron and Diofenolan (Tanani, 2001), *A. ipsilon* by Flufenoxuron (El-Sheikh, 2002), *S. gregaria* by

Lufenuron (Bakr et al., 2008), *P. gossypiella* by Methoxyfenozide (Sabry and Abdou, 2016) and *P. unionalis* by Novaluron (Ghoneim et al., 2017b).

In the current study, retarded development of *P. argyrostoma* by methoprene, as expressed in prolonged pupal duration, may be attributed to the indirect interference of this IGR with neuroendocrine organs responsible for the synthesis and release of tropic hormones, like prothoracicotropic hormone (Subrahmanyam et al., **1989**). In general, the prolongation of larval or pupal duration may be due to the persistence of juvenile hormone (JH) and its elevated level in the haemolymph where it is only in the absence of JH that ecdysone could be activated and lead to the formation of the next stage (Kuwano et al., 2008). Also, methoprene might exhibit a delaying effect on the pupariation of prepupae of *P. argyrostoma*. On the other hand, the final step of chitin biosynthesis pathway was inhibited by this IGR and the precursor was not converted into chitin leading to a prolongation of developmental duration (Djeghader et al., 2014).

2. Derangement of the Developmental Program:

2.1. Production of larval-pupal Intermediates:

In the present study on *P. argyrostoma*, topical treatment of the last instar larvae with methoprene impaired the process of larval-pupal transformation, since some larval-pupal intermediates were produced, only at the higher two doses (10.0 and 5.0 µg/larva). These mosaic intermediates perished soon after formation. Our result was, to a great extent, in agreement with some of the reported larval-pupal intermediates in a number of insect pests after treatment with various IGRs, such as *H. armigera* after treatment with Hexaflumuron (Taleh et al., 2015); *S. littoralis* after treatment with Novaluron (Ghoneim et al., 2015) and Cyromazine (Tanani et al., 2015); *C. cephalonica* after treatment with Fenoxycarb (Begum and Qamar, 2016); as well as *P. gossypiella* (Ghoneim et al., 2017a) and *P. unionalis* (Ghoneim et al., 2017b) after treatment with Novaluron. In Diptera, some larval-pupal intermediates were formed after treatment of 3rd instar larvae of *P. argyrostoma* with 150 µg/larva of chlorfluazuron (Ghoneim and Ismail, 1995b). Also, treatment with some juvenoids induced the production of larval-pupal intermediates or larviform pupae in the stable fly *Stomoxys calcitrans* and the flesh fly *Sarcophaga bullata* (Wright, 1970; Weaver and Begley, 1982).

The formation of larval-pupal intermediates, in the present study, indicated a disturbing activity of methoprene against the development program of *P. argyrostoma*. The production of these intermediates can be interpreted, generally, by the interference of this juvenoid with the hormonal regulation of pupation program (Al-Sharook et al., 1991). However, some conceivable scenarios can be described herein. (1) Methoprene might inhibit the development program *via* an ecdysteroid reduction and/or interference with the release of the neurosecretion (Josephrajkumar et al., 1999). (2) The production of these intermediates indicated a juvenile property of methoprene disrupting the perfect larval-pupal transformation. (3) The production of these mosaic creatures in *P. argyrostoma* may be explicated by an inhibitory effect of methoprene on the DNA synthesis (Mitlin et al., 1977) or the chitin biosynthesis and chitin synthase (Mayer et al., 1980). (4) The moult induction had lethal consequences because the induction of a rapid moult did not provide enough time for the completion of larval-pupal transformation. Thus, the insects moulted to nonviable forms between the stages (Tateishi et al., 1993). Moults 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).

2.2. Induction of Permanent Prepupae:

In insects, a symptom of suspended development attracts a great attention of some entomologists. This feature is usually expressed as 'permanent larvae'. The induction of permanent nymphs or larvae was recorded in some insect species as a response to some IGRs or botanicals. Some authors (Salem et al., 1985; El-Gammal and Taha, 1984; Abou El-Ela, 1993) observed permanent nymphs of *S. gregaria* (Orthoptera) after treatment with certain IGRs. Permanent larvae of the European corn borer *Ostrinia nubilalis* (Lepidoptera) were induced depending upon the dose of Fenoxycarb (JHA) and the timing of application onto the 5^{th} instar larvae (Gadenne et al., 1990). Permanent larvae of *P. argyrostoma* (Diptera) were induced after topical treatment with 100 µg/larva of chlorfluazuron (CSI)(Ghoneim and Ismail, 1995b).

Among botanicals, some plant extracts, or isolated plant products, had been reported to induce permanent nymphs or larvae in various insects, such as the large milkweed bug *Oncopeltus fasciatus* (Hemiptera) after injection of azadirachtin into the newly moulted last instar nymphs (Dorn et al., 1986); *O. fasciatus* and the cotton stainer bug *Dysdercus peruvianus* (Hemiptera) after topical application of *Manilkara subsericea* extracts onto 4^{th} instar nymphs (Fernandes et al., 2013); *S. litura* (Lepidoptera) after treatment of larvae with acetone leaf extract of *Withania somnifera* (Gaur and Kumar, 2010); and the confused flour beetle *Tribolium confusum* (Coleoptera) after treatment of 5^{th} instar and 6^{th} instar larvae with 1µg/µl of Andrographolide (a terpenoid isolated from the leaves of *Andrographis paniculata*)(Lingampally et al., 2013). Feeding of larvae of the greater wax moth *Galleria mellonella* (Lepidoptera), for a long time, on a diet treated with the JH analogue [methyl 2,7dimethyl-9-(2-oxolanyl) 2,4 nonadienoate; 0.1 mg/g of diet] induced permanent larvae (Slama and Lukas, 2013).

In the present study on *P. argyrostoma*, topical treatment of prepupae only with the lower two doses of methoprene (0.1 and 0.01 µg/prepupa) induced a state of suspended development in some prepupae, known as 'permanent prepupae'. These suspended prepupae suffered the adverse action of methoprene along 12 days and eventually perished without any external feature of puparium formation.

To understand the production of the 'permanent prepupae' in *P. argyrostoma*, it is noteworthy to mention herein that the pupariation (puparium formation) in cyclorrhaphous Diptera differs greatly from tanning which occurs after pupal ecdysis in other Diptera and different holometabolous insects. Pupariation occurs in between the prepupa and pupal apolysis (Zdarek, 1985; Raabe, 1989). In the present study, production of the 'permanent prepupae' may be explained by the inhibitory action of methoprene on the prothoracic gland (ecdysone-producing gland) and hence the ecdysone could not be synthesized and/or released. It is well known that the absence of ecdysone leads to failure of ecdysis. In general, the tested compound might disrupt the ecdysteroid metabolism or might alternatively act directly to inhibit the release of ecdysis-triggering hormone (Gaur and Kumar, 2010; Gibbens et al., 2011).

Perturbation of Metamorphosis and Morphogenesis in *P. argyrostoma* by Methoprene:

1. Interrupted Pupation:

In the present study on *P. argyrostoma*, the methoprene-treated last instar larvae pupated in a slightly or drastically regressed rate (decreasing pupation %), depending on the dose level. On the other hand, the pupation rate was slightly regressed after topical treatment of prepupae only with the lower two doses of methoprene (0.1 and 0.01 µg/prepupa).

This result was, to a great extent, consistent with those reported results of regressed pupation rate in some insects by the action of various IGRs, such as *E. kuehniella* by Fenoxycarb (Moreno et al., 1992); *P. argyrostoma* by Pyriproxyfen (Ismail, 1995) and Chlorfluazuron (Ghoneim and Ismail, 1995b); the diamondback moth *Plutella xylostella* by Hexaflumuron (Mahmoudvand et al., 2012); *S. littoralis* by Novaluron (Ghoneim et al., 2015); *G. pyloalis* by Lufenuron (Aliabadi et al., 2016) and Fenoxycarb (Singh and Tiwari, 2016); the whitefly parasitic wasp *Encarsia formosa* by Pyriproxyfen and Fenoxycarb (Wang and Liu, 2016); *P. gossypiella* (Ghoneim et al., 2017a) and *P. unionalis* (Ghoneim et al., 2017b) by Novaluron. The regressed pupation rate in *P. argyrostoma* after larval treatment with methoprene, in the present study, might be due to an inhibitory effect of this compound on the synthesis of specific storage proteins by fat body during the last larval instar and their deposition at the time of pupariation (Gupta, 1985)

2. Impaired Adult Emergence:

The adult emergence of *P. argyrostoma* was reported to be completely or partially blocked after larval treatment with certain doses of different IGRs, such as Pyriproxyfen (Ismail, 1995), Chlorfluazuron (Ghoneim and Ismail, 1995b), Hydroprene, Kinoprene and Methoprene (El-Sherif, 1986). On the other hand, Methoprene was reported to inhibit the adult emergence after larval treatment of other insect species, such as *C. molestus* (Farghal and Temerak, 1981), the lesser mealworm *Alphitobius diaperinus* (Edwards and Abraham, 1985), *Ae. aegypti* (Braga et al., 2005), *C. cephalonica* (Tripathi and Tiwari, 2006), the southern house mosquito *Culex quinquefasciatus* and *Ae. albopictus* (Khan et al., 2016; Bibbs et al., 2017). In addition, the adult emergence was slightly or drastically blocked after larval treatment of different insects with various IGRs, such as *E. kuehniella* by Fenoxycarb (Moreno et al., 1992); *P. xylostella* after treatment with Hexaflumuron (Mahmoudvand et al., 2012); *D. melanogaster* after treatment with Pyriproxyfen (Benseba et al., 2015); *S. littoralis* after larval treatment with Novaluron (Ghoneim et al., 2015); *G. pyloalis* after treatment with Lufenuron (Aliabadi et al., 2016); *C. quinquefasciatus* and *Ae. albopictus* after treatment with Pyriproxyfen (Khan et al., 2016); *P. gossypiella* after treatment with Novaluron (Hassan et al., 2017) and *P. unionalis* after treatment with Methoxyfenozide (Hamadah et al., 2017). After exposure of 3rd instar larvae of *S. ruficornis* to different concentrations of Barium carbonate, the adult emergence was considerably blocked (Singh et al., 2017). The adult emergence in the F1 generation of the same fly species was blocked after topical application of Pyriproxyfen onto the parental generation (Singh and Kumar, 2015).

Results of the present study on *P. argyrostoma* was, to a great extent, in agreement with the previously reported results, since the emergence of adult flies was completely blocked after topical treatment of either the early last instar larvae or prepupae with the highest dose (10.0 µg/larva) of Methoprene. After treatment of last instar larvae with other doses, adult eclosion of the flies was detrimentally blocked, in no certain trend. After topical treatment of prepupae with other doses, the adult eclosion was inversely correlated to the dose level.

In this regard, it is important to emphasize that the adult emergence in insects is a crucial physiological process and regulated by the eclosion hormone. The disturbance of this hormone partially or completely arrests the adults to emerge. The present result of blocked adult emergence of *P. argyrostoma* can be interpreted by the disturbing effect of methoprene on the adult eclosion hormone release and/or inhibition of the neurosecretion (Al-Sharook et al., 1991; Josephrajkumar et al.,

1999). On the molecular basis, JH mimics and anti-JH compounds may cause misexpression of certain genes, particularly the *brood* complex (*br*-C) transcription factor gene, leading to symptoms of impaired metamorphosis, like blocking of adult emergence (Wilson, 2004; Nandi and Chakravarty, 2011).

3. Disturbance of Morphogenesis:

3.1. Morphogenic Disorders of Pupae:

In the present study on *P. argyrostoma*, Methoprene displayed an anti-morphogenic activity against the developed pupae, since different percentages of deformed pupae were produced after treatment of last instar larvae. In contrast, Methoprene failed to exhibit similar activity, after treatment of prepupae. This result was in a partial resemblance with the reported results of impaired pupal morphogenesis in the parasitoid *Ph. ocularis* after treatment with Fenoxycarb (Moreno et al., 1993b); *T. castaneum* and *T. confusum* after treatment with Cyromazine (Kamaruzzaman et al., 2006), *S. frugiperda* after feeding of 5th instar larvae on a diet treated with Methoxyfenozide (Zarate et al., 2011), *C. cephalonica* after topical application of last instar larvae with Fenoxycarb (Begum and Qamar, 2016), *P. gossypiella* after treatment of the full grown larvae with Novaluron (Ghoneim et al., 2017a) and *P. unionalis* after treatment of newly moulted last instar larvae with Novaluron (Ghoneim et al., 2017b).

For interpretation of the anti-morphogenic activity of Methoprene against the pupae of *P. argyrostoma*, as appeared in pupal deformities, after topical treatment of early last instar larvae, in the present study, the tested compound might exert suppressive action on the chitin synthesis and prevented the normal deposition of new cuticle during apolysis leading to the production of pupal deformities (Retnakaran et al., 1985). In addition, Methoprene might block the release of morphogenic peptides, causing alteration in titres of ecdysteroids and juvenoids (Barnby and Klocke, 1990). However, the failure of Methoprene to impair the pupal morphogenesis after treatment of prepupae, in the present study, but after treatment of the early last instar larvae, indicated that the pupal morphogenesis program of *P. argyrostoma* usually takes place during the first half of last larval instar.

3.2. Morphogenic Disorders of Adults:

The corrupted adult morphogenesis, as expressed in the production of deformed adults, was widely reported, after treatment of various insects with different IGRs, such as *S. littoralis* after treatment with Methoxyfenozide (Pineda et al., 2004), Flufenoxuron (Bakr et al., 2010) and Novaluron (Hamadah et al., 2015); *Rh. ferrugineus* after treatment with Diofenolan (Tanani, 2001); the eastern spruce budworm *Choristoneura fumiferana* after treatment with Tebufenozide and Methoxyfenozide (Sundaram et al., 2002); *T. castaneum* and *T. confusum* after treatment with Cyromazine (Kamaruzzaman *et al*., 2006); *E. integriceps* after treatment with Pyriproxyfen (Mojaver and Bandani, 2010); *S. frugiperda* after treatment with Methoxyfenozide (Zarate et al., 2011); *A. kuehniella* after treatment with Hexaflumuron (Ashouri et al., 2014); *H. armigera* after treatment with Hexaflumuron (Taleh *et al*., 2015); *C. cephalonica* after treatment with Fenoxycarb (Begum and Qamar, 2016); *etc*. Singh and Kumar (2015) reported the development of deformed adults in the F1 generation of *S. ruficornis* after topically applying Pyriproxyfen to the parental generation. In addition, the developed adults of the mosquito *C. quinquefasciatus*, after larval treatment with Fenoxycarb, were incapable to fly (Schaefer et al., 1987).

Results of the present investigation on *P. argyrostoma* were compatible with

the previously reported results of arrested adults, since methoprene exhibited anti-morphogenic activity against adults. After topical treatment of either last instar larvae or prepupae only with the doses 5.0 and 1.0 µg/larva, some of the emerged adult flies appeared anomalous morphologically. The deformed adult flies were observed with a poor ability to fly. The present result agreed, also, with the reported anti-morphogenic activity of Methoprene against some of other insects, such as *Sitotroga cerealella* (Stockel and Edwards, 1981), *T. confusum* (Smet et al., 1989) and the rice moth *Corcyra cephalonica* (Tripathi and Tiwari, 2006).

For interpretation of the anti-morphogenic action of Methoprene on the adult flies of *P. argyrostoma*, as appeared in adult deformities in the present study, this juvenoid might exert an adverse action on the hormonal balance during the adult differentiation, in particular the disturbance of ecdysteroid titre which led to changes in lysosomal enzyme activity causing overt morphological abnormalities (Josephrajkumar et al., 1999). In addition, other suggestions can be appreciated, such as the exogenously increasing of JH titre causing imbalance with ecdysteroids. Also, the chitin synthase might be inhibited by metabolites of the tested compound (Cohen and Casida, 1980), inhibition of DNA synthesis (Mitlin et al., 1977) and/or inhibition of facilitated diffusion and active transport across cell membranes of nucleosides and amino acids (Mayer et al., 1988). On the other hand, Sehnal (1983) suggested that juvenoids (like methoprene, in the present study) do not interfere with the function and growth of insect cells but prevent their imaginal differentiation. Thus, the hormonal unbalance in adult *P. argyrostoma*, by larval or prepupal treatment with methoprene, in the current investigation, might explain the formation of the anomalous adult flies (Staal, 1975).

Conclusion:

Depending on the obtained results in the present study, methoprene exhibited acute and chronic lethal potency against different developmental stages of *P. argyrostoma*. Also, the tested juvenoid exerted disruptive effects on growth, development and metamorphosis of pupae and adult flies. Therefore, methoprene may be an effective compound for remedial control of this medically serious fly.

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