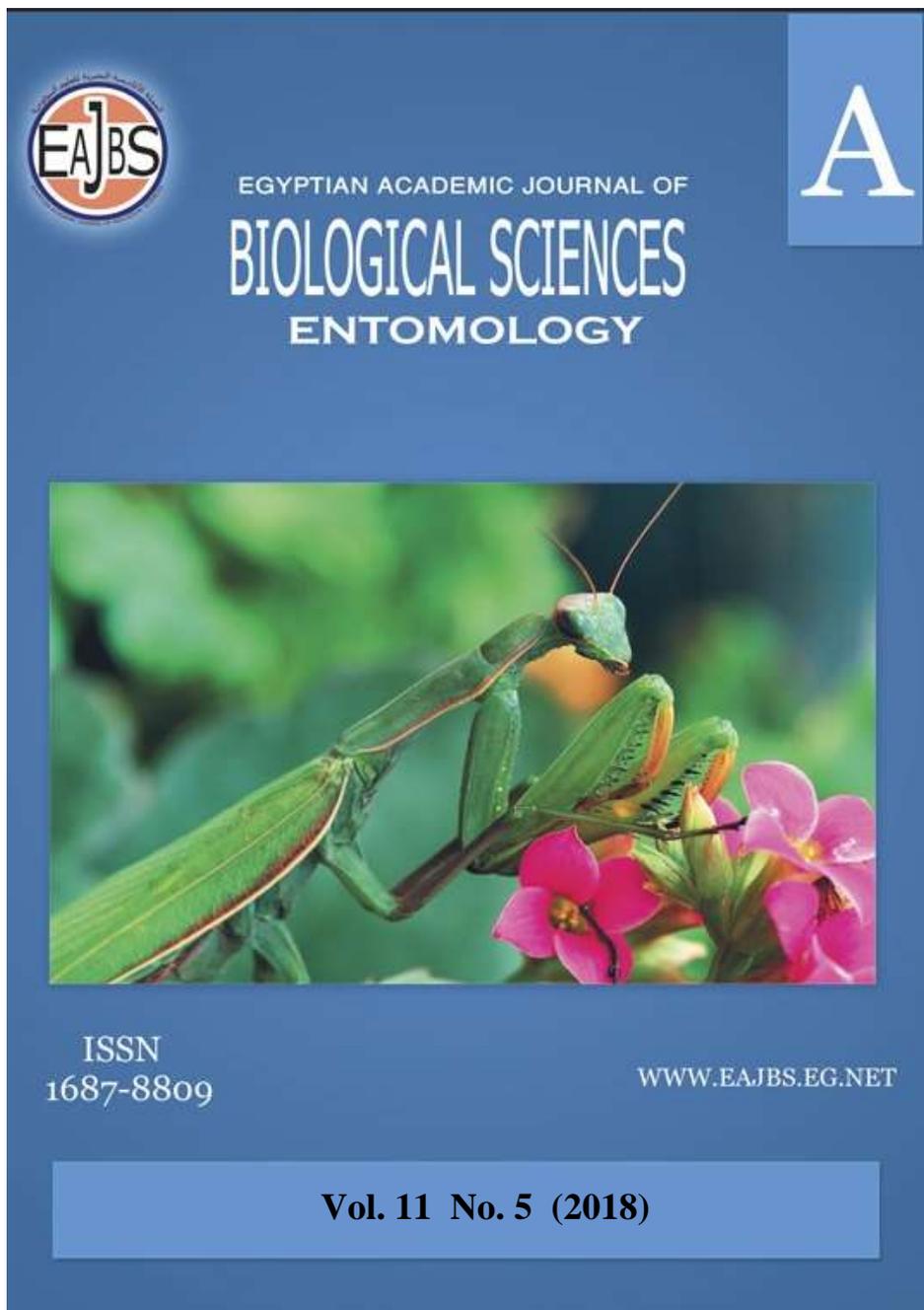


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Impairment of Development and Reproductivity of the Egyptian cotton leafworm *Spodoptera littoralis* Boisduval (Noctuidae: Lepidoptera) by Cycloheximide.

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ABSTRACT

The Egyptian cotton leafworm, *Spodoptera littoralis*, is destructive pest of cotton and various crops in Egypt and some parts of the world. The present study was carried out aiming to assess the disruptive effects of cycloheximide on survival, growth, development, metamorphosis and reproductive potential of this pest. Four doses: 180, 120, 60 and 30 µg/larva had been topically applied (once) onto the newly moulted last instar larvae. cycloheximide exhibited toxic effect on larvae, pupae and adults. Unexpectedly, no mortality was observed at the highest dose. LD₅₀ was estimated at 0.013 µg/larva. The maximal weights of the treated larvae increased and the larval growth was remarkably enhanced. The larval and pupal durations were shortened. Some larvae appeared as 'giant larvae', only at the lower two doses. They enlarged in size and appeared heavier than other treated and control larvae. They survived 2-times longer period than of the control larvae and perished without pupation. Topical treatment of larvae only with the lower two doses induced a state of suspended development, 'permanent prepupae' which failed to pupate. Cycloheximide exerted an inhibitory action on the pupation rate after treatment only with the lower three doses. Some deformed pupae were produced. The adult emergence was considerably blocked at lower three doses. The oviposition was completely prevented, at the higher two doses, but partially inhibited at the lower two doses. No fecundity could be determined at the higher two doses because no oviposition was carried out. At the lower two doses, fecundity was dramatically reduced. All eggs failed to hatch indicating complete sterility of *S. littoralis*.

INTRODUCTION

The cotton leafworm *Spodoptera littoralis* has been considered as a destructive herbivorous pest of cotton and other field crops all over the year in Egypt (Shonouda and Osman, 2000; Adham *et al.*, 2009). It is widely distributed throughout Africa, Mediterranean Europe, and several parts of Asia (Azab *et al.*, 2001). The caterpillars feed mainly on leaves, stems and also can seriously retard growth or reduce production of the cotton crop. However, during heavy infestation they can penetrate flowers and bolls (Sutanto *et al.*, 2014). To control this pest, several types of conventional insecticides have been used over the last five decades. The intensive

use of broad-spectrum insecticides against *S. littoralis* has led to the development of the insect resistance to many pesticides making their control more difficult (Aydin and Gurkan, 2006; Davies *et al.*, 2007; Mosallanejad and Smagghe, 2009). As a result of improper use, also, these insecticides usually exhibit several adverse impacts on the human health and beneficial animals as well as cause serious toxicological problems to the ecosystems (Tiryaki and Temur, 2010; Chowański *et al.*, 2014). Therefore, eco-friendly control agents have received global attention in recent years as alternative for the conventional insecticides. These alternative compounds should be characterized by lower toxicity to non-target organisms than the conventional insecticides and they should be effective at low concentrations (Attathom, 2002; Gade and Goldsworthy, 2003) as well as biodegradable into harmless compounds, which allows for avoiding the problems of environmental problems (Tiryaki and Temur, 2010; Walkowiak *et al.*, 2015; Li *et al.*, 2017).

Juvenile hormone (JH), synthesized and released by the corpora allata of insects, is a hormone responsible for the regulation of different physiological processes during both postembryonic development and adult reproduction (Wheeler and Nijhout, 2003; Riddiford, 2008; El-Sheikh, *et al.*, 2011). JH along with moulting hormone (ecdysone) plays a key role in the moulting process. High JH titer maintains the "*status quo*" action which modulates a larval-larval moult, while, a low-to-absent JH titer allows ecdysone to direct a more developmentally advanced moult (Wilson, 2004). At present, the use of juvenile hormone analogues (JHAs) or insect growth regulators (IGRs), in general, is considered as a possible alternative of the conventional insecticides for controlling *S. littoralis* (Raslan, 2002). Moreover, IGRs are regarded as a 'third generation of insecticides' or biorational pesticides because they differ in their mode of action from the traditional pesticides and have low toxicity to non-target organisms (Zhou *et al.*, 2003). Because of their desirable characteristics, such as low toxicity, less environmental hazards, high selectivity, and low impact on natural enemies and human, IGRs are used to control various insect pests (Cedric, 2005; Wang and Wang, 2007). In addition, anti-JH agents are those compounds inhibiting JH-dependent developmental and reproductive processes in insects. Bede *et al.* (2001) demonstrated that the design of JH mimics or anti-JH agents is an effective strategy for insecticide discovery. As reported by many authors (Bowers, 1982; El-Ibrashy, 1982; Staal, 1982), anti-JH agents are considered as new alternatives of juvenoid-type chemicals to avoid some of their disadvantages. These chemicals are potentially efficacious for control of the major insect pests where most of the damage is caused by larval stage.

The RNA and protein synthesis inhibitor, cycloheximide (Acti-dione) was originally isolated from *Streptomyces griseus* (Baliga *et al.*, 1969). As an antibiotic, cycloheximide was earlier applied clinically in the treatment of candidiasis and meningitis. In the agricultural uses, it inhibits the growth, in culture, of many plant pathogenic fungi (MacBean, 2012). Also, cycloheximide was found to interfere with the hormonal regulation of developmental processes in insects, such as the migratory locust *Locusta migratoria* (Phillips and Loughton, 1979) and *S. gregaria* (Eid *et al.*, 1982). The stimulation of the steroidogenesis in insects is rapidly inhibited by cycloheximide (Keightley *et al.*, 1990). Early, Kelly and Lescott (1976) found that cycloheximide acts as an inhibitor of protein synthesis in the lepidopterous insects. More than three decades later, Morton and Truman (2008) reported that cycloheximide inhibited the protein synthesis necessary for the development of eclosion hormone sensitivity in the tobacco horn worm *Manduca sexta*. In insects, also, cycloheximide exhibited an anti-gonadotropic action in insects, such as the

tobacco caterpillar *Spodoptera litura* (Sridevi and Ray, 1988) and the mealworm beetle *Tenebrio molitor* (Soltani-Mazouni and Soltani, 1995). In addition, cycloheximide was recorded as a suppressive agent on the enzyme activities in insects, such as the detoxifying enzyme Glutathione S-transferase in the common cutworm *Spodoptera litura* (Wu and Lu, 2008); phenoloxidase in *Spodoptera exigua* (Shrestha and Kim, 2007) and transhydrogenase in the midgut mitochondria in *M. sexta* 5th instar larvae (Vandock *et al.*, 2010). The present study was carried out aiming at the assessment of disruptive effects of cycloheximide on survival, growth, development, metamorphosis and reproductive potential of *S. littoralis*.

MATERIALS AND METHODS

1. Experimental Insect:

A pupal sample of the Egyptian cotton leafworm, *Spodoptera littoralis* Boisd. (Lepidoptera: Noctuidae) was kindly obtained from the culture of susceptible strain maintained for several generations in Plant Protection Research Institute, Giza, Egypt. Using this sample, a culture was raised in the Department of Zoology and Entomology, Faculty of Science, Al-Azhar University, Cairo, under laboratory controlled conditions ($27\pm 2^{\circ}\text{C}$, $65\pm 5\%$ R.H., photoperiod 14h L and 10h D). Rearing procedure was carried out according to Ghoneim (1985) and improved by Bakr *et al.* (2010). Larvae were provided daily with fresh castor bean leaves *Ricinus communis*. The emerged adults were provided with cotton pieces soaked in 10% honey solution as a food source. Moths were allowed to lay eggs on *Oleander* branches. The egg patches were collected daily, and transferred into Petri dishes for another generation.

2. Cycloheximide Administration:

The RNA and protein synthesis inhibitor, cycloheximide (3-[(2R)-2-[(1S, 3S, 5S)-3, 5-dimethyl-2-oxocyclohexyl]-2-hydroxyethyl] glutarimide) was kindly provided by Dr. Heba Hassan, Prof. at Institute of Plant Protection, Giza, Egypt. Cycloheximide was diluted in acetone to prepare four doses: 180, 120, 60 and 30 $\mu\text{g}/\text{larva}$. Each dose was topically applied (once) onto the thoracic sternum of newly moulted 6th (last) instar larvae by Hamilton microapplicator (NHN 737). Groups of 20 healthy larvae were used as replicates for each dose. Control larvae had been topically applied only with 1 μl acetone. All treated and control larvae were kept individually under the previously mentioned laboratory controlled conditions. All larvae were provided with fresh castor bean leaves every day, during the feeding period. Starting from the day after treatment, all treated and control insects were observed daily to record all criteria of the study.

3. Criteria of Study:

3.1. Toxicity, Growth, Development and Metamorphosis:

Mortality in larvae, pupae and adults were determined in %. LD_{50} value was calculated using the total mortality by Microsoft office Excel, 2007, according to Finny (1971).

Coefficient of growth: Coefficient of growth was calculated according to El-Ibrashy and Aref (1985) as follows: maximal body weight (mg)/ duration (in days) for each larva.

Developmental duration: Dempster's equation (1957) was used for calculating the developmental duration (mean days \pm SD) and Richard's equation (1957) was used for calculating the developmental rate.

Pupation rate: Pupation rate was expressed in % of the developed pupae.

Adult emergence was determined in %.

Impaired morphogenesis was determined in % of deformed larvae, pupae and adults.

3.2. Reproductive parameters

The emerged adult females of *S. littoralis* were daily collected and released in plastic jars (3L) provided with sterilized cotton pieces, soaked in 10% honey solution, for feeding, as well as suitable *Oleander* branches as an oviposition site. The treated adult females were coupled with normal adult males (1:2) of the same age, at least 3 replicates, obtained from the main culture. The eggs were collected daily, and carefully transferred to Petri dishes to count eggs.

Oviposition Efficiency: Oviposition efficiency could be detected by the oviposition rate as follows:

$$\text{Number of laid eggs per } \text{♀} / \text{reproductive lifetime (in days)} \times 100$$

Reproductive Capacity: Fecundity: The laid eggs were counted for calculating the number of eggs per female. Fertility: The hatchability was usually expressed in hatching percentage of laid eggs. Sterility index: It was calculated according to Topozada *et al.* (1966) as follows:

$$\text{Sterility Index} = 100 - [(a b / A B) \times 100]$$

Where: a: mean number of eggs laid per female in the treatment. b: percentage of hatching in the treatment. A: mean number of eggs laid per female in the controls. B: percentage of hatching in the controls.

Incubation period: The laid eggs were kept in Petri dishes under the same laboratory controlled conditions, as previously mentioned. Just after the oviposition, eggs were observed until hatching for recording the incubation period (in mean days \pm SD).

4. 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

1. Toxic Effect of Cycloheximide on *S. littoralis*

After topical application of cycloheximide (once) onto the newly moulted last instar larvae, toxicity of the tested compound was expressed in mortality among larvae, pupae and adults. Mortality data were arranged in Table (1). Depending on these data, no mortality was observed at the highest dose, but different percentages of larval, prepupal, pupal and adult mortality were recorded. Larval mortality was found in a reverse relation to the dose level (15, 30 and 45% larval mortality, at 120, 60 and 30 $\mu\text{g}/\text{larva}$, respectively, vs. 00% mortality of control larvae). In a similar trend, the pupal mortality was recorded (11.8, 14.3 and 18.2% pupal mortality, at 120, 60 and 30 $\mu\text{g}/\text{larva}$, respectively, vs. 0% mortality of control pupae). An extended toxic effect of cycloheximide was exhibited on adult females, reversely correlated with the dose level (13.3, 16.7 and 33.3% adult mortality, at 120, 60 and 30 $\mu\text{g}/\text{larva}$, respectively, vs. 0% mortality of control adults). Only at the lower two doses, prepupae were subjected to the toxic effect of cycloheximide (42.9 and 27.3% prepupal mortality, at 60 and 30 $\mu\text{g}/\text{larva}$, respectively, vs. 0% mortality of control prepupae). LD₅₀ was calculated as 0.013 $\mu\text{g}/\text{larva}$.

2. Effect of Cycloheximide on Growth and Developmental of *S. littoralis*:

2.1. Affected Growth:

After topical application of cycloheximide doses onto the newly moulted last instar larvae, data of the maximal weight (max.wt), duration and coefficient of growth of treated and control larvae were assorted in Table (2). In the light of these data, the max. wt increased in no certain trend. This increasing max.wt was statistically significant at the doses 120 and 60 $\mu\text{g}/\text{larva}$ (745.9 ± 128.2 and 349.8 ± 78.2 mg, respectively, vs. 295.6 ± 31.8 mg of control larvae). On the other hand, cycloheximide remarkably enhanced the treated larvae to grow in higher CG (118.9 ± 18.9 , 189.3 ± 35.2 , 088.2 ± 23.7 and 081.6 ± 12.6 , at 180, 120, 60 and 30 $\mu\text{g}/\text{larva}$, respectively, vs. 074.1 ± 9.5 of control larvae).

2.2. Affected Duration and Developmental Rate:

Depending on the data of Table (2), topical application of cycloheximide resulted in shortened larval duration, especially at the higher two doses (2.8 ± 0.8 and 4.1 ± 0.3 days, at 180 and 120 $\mu\text{g}/\text{larva}$, respectively, vs. 4.2 ± 0.4 of control larvae). According to data assorted in Table (3), the pupal duration was remarkably shortened, as a response to cycloheximide treatment, regardless the dose level (7.50 ± 3.5 , 7.39 ± 1.4 , 8.00 ± 0.8 and 7.35 ± 1.1 days, at 180, 120, 60 and 30 $\mu\text{g}/\text{larva}$, respectively, vs. 8.44 ± 0.7 of control pupae). As obviously shown in the same table, the developmental rate of pupae was considerably enhanced after larval treatment with cycloheximide.

2.3. Disturbed Developmental Program:

After topical application of 60 and 30 $\mu\text{g}/\text{larva}$ of cycloheximide onto last instar larvae, some larvae appeared as a strange phenotype larvae, 'giant larvae' (huge permanent larval phenotype), which were heavier than other treated and control larvae, only at the lower two doses (652.8 ± 81.2 and 545.9 ± 62.1 mg, at 60 and 30 $\mu\text{g}/\text{larva}$, respectively, compared to 295.6 ± 31.8 mg of control larvae). These giant larvae had a darker colour than that of other larvae and survived 2-times longer period than control larvae (8.9 ± 0.9 and 10.1 ± 1.1 days, at 60 and 30 $\mu\text{g}/\text{larva}$, respectively, vs. 4.2 ± 0.4 days of control larvae) and perished without transformation into pupa or even prepupae.

As clearly seen in the aforementioned table, also, topical treatment of larvae only with the lower two doses induced a state of suspended development, as expressed in 'permanent prepupae' (42.9 and 27.3% permanent prepupae, at 60 and 30 $\mu\text{g}/\text{larva}$, respectively). These developmentally suspended prepupae survived 10 days and perished with no symptom of pupation.

3. Effect of Cycloheximide on Metamorphosis and Morphogenesis of *S. littoralis*:

3.1. Affected Metamorphosis:

On the basis of data arranged in Table (3), cycloheximide exerted an inhibitory action on the pupation rate after treatment of last instar larvae only with the lower three doses (85, 40 and 40% pupation of treated larvae, at 120, 60 and 30 $\mu\text{g}/\text{larva}$, respectively, vs. 100% pupation of control larvae).

Data presented in Table (3) revealed the failure of cycloheximide to affect the adult emergence at the highest dose level. In contrast, it exhibited a blocking effect on this crucial metamorphosis process, with other doses (86.7, 83.3 and 66.7% adult emergence from pupae of treated larvae, at 120, 60 and 30 $\mu\text{g}/\text{larva}$, respectively, vs.

100% adult emergence of control congeners).

3.2. Disrupted Morphogenesis:

Depending on the data of Table (3), cycloheximide failed to exhibit morphogenic efficiency on the present insect after treatment of larvae with the majority of doses levels. Only at 120 µg/larva, the tested compound exhibited morphogenic efficiency on pupae, since deformed pupae were produced (11.8% deformed pupae, at 120µg/larva, compared to 0% deformations of control pupae).

Table 1. Toxic effect (%) of cycloheximide after topical treatment of the newly moulted last instar larvae of *S. littoralis*.

| Dose (µg/larva) | Larval mortality | Prepupal mortality | Pupal mortality ♀♀ | Adult mortality ♀♀ | Total mortality | LD ₅₀ (µg/larva) |
|-----------------|------------------|--------------------|--------------------|--------------------|-----------------|-----------------------------|
| 180 | 00.0 | 00.0 | 00.0 | 00.0 | 00.0 | 0.013 |
| 120 | 15 | 00.0 | 11.8 | 13.3 | 35 | |
| 60 | 30 | 42.9 | 14.3 | 16.7 | 75 | |
| 30 | 45 | 27.3 | 18.2 | 33.3 | 80 | |
| Control | 00.0 | 00.0 | 00.0 | 00.0 | 0.00 | |

Table 2. Growth of *S. littoralis* after topical application of cycloheximide onto the newly moulted last instar larvae.

| Dose (µg/larva) | Maximal body weight (mean mg±SD)* | Duration (mean days±SD) | Coefficient of growth (mean±SD) |
|-----------------|-----------------------------------|-------------------------|---------------------------------|
| 180 | 338.7±98.0 a | 2.8±0.8 c | 118.9±18.9 c |
| 120 | 745.9±128.2 c | 4.1±0.3 a | 189.3±35.2 c |
| 60 | 349.8±78.2 b | 4.3±0.6 a | 088.2±23.7 b |
| 30 | 334.7±33.1 a | 4.2±0.4 a | 081.6±12.6 a |
| Control | 295.6±31.8 | 4.2±0.4 | 074.1±9.5 |

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). *: Giant larvae were excluded from calculation.

Table 3. Development and metamorphosis of *S. littoralis* after topical application of cycloheximide onto the newly moulted last instar larvae.

| Dose (µg/larva) | Giant larvae (%)* | Permanent prepupae (%)** | Pupation rate ♀♀ (%) | Pupal Duration (mean days±SD) | Pupal Develop. | Deformed pupae (%)*** | Adult emergence (%) |
|-----------------|-------------------|--------------------------|----------------------|-------------------------------|----------------|-----------------------|---------------------|
| 180 | 00.0 | 00.0 | 100 | 7.50±3.5 c | 13.33 | 00.0 | 100 |
| 120 | 00.0 | 00.0 | 85 | 7.39±1.4 c | 13.53 | 11.8 | 86.7 |
| 60 | 20.0 | 42.9 | 40 | 8.00±0.8 b | 11.95 | 00.0 | 83.3 |
| 30 | 10.0 | 27.3 | 40 | 7.35±1.1 c | 13.61 | 00.0 | 66.7 |
| Control | 00.0 | 00.0 | 100 | 8.44±0.7 | 11.85 | 00.0 | 100 |

b, c: See footnote of Table (2). Pupal develop.: pupal developmental rate. *: Giant larvae were remarkably heavier than treated larvae. They lived 2-fold period of treated larvae and perished

without pupation. **: Permanent prepupae lived 10 days and perished without pupation. ***: Sexually unknown pupae.

4. Effect of Cycloheximide on Reproductive Potential of *S. littoralis*:

After topical application of cycloheximide onto the newly moulted last instar larvae, data of the most important parameters of reproductive potential of the emerged adult females were summarized in Table (4).

Oviposition rate: Depending on these data, the oviposition efficiency of females was completely prohibited at the higher two doses of cycloheximide. At the lower two doses, oviposition rate of females was remarkably regressed (58.2 and 70.0% oviposition, at 60 and 30 $\mu\text{g}/\text{larva}$, respectively, vs. 100% oviposition of control adult females).

Reproductive capacity: The functional compartments of reproductive capacity taken into consideration herein were fecundity (mean eggs/ ♀) and fertility (hatching %). According to the data of Table (4), no fecundity of females could be determined because no oviposition was carried out, at the higher two doses of cycloheximide. On the other hand, dramatically reduced fecundity of adult females was recorded at the lower two doses (102.8 ± 49.4 and 104.6 ± 18.9 eggs/ ♀ , at 60 and 30 $\mu\text{g}/\text{larva}$, respectively, vs. 1259.2 ± 120.3 eggs/control ♀). With no exception, all eggs failed to hatch indicating complete sterility of *S. littoralis* as a response to strong anti-gonadotropic action of cycloheximide. Thus, no incubation period could be measured for treated insects.

Table 4. Reproductive potential of *S. littoralis* as influenced by cycloheximide doses topically applied onto the newly moulted last instar larvae.

| Dose ($\mu\text{g}/\text{larva}$) | Oviposition Rate (%) | Fecundity (mean eggs \pm SD) | Hatchability (%) | Sterility index (%) | Incubation period (mean days \pm SD) |
|-------------------------------------|----------------------|--------------------------------|------------------|---------------------|--|
| 180 | 00.0 | 000.0 | --- | 100 | --- |
| 120 | 00.0 | 000.0 | --- | 100 | --- |
| 60 | 58.2 | 102.8 ± 49.4 d | 00.0 | 100 | --- |
| 30 | 70.0 | 104.6 ± 18.9 d | 00.0 | 100 | --- |
| Control | 100 | 1259.2 ± 120.3 | 98.3 | --- | 3.5 ± 0.4 |

d: very highly significantly different ($P < 0.001$)

DISCUSSION

1. Disrupted Survival of *S. littoralis* by Cycloheximide:

Toxicities of several insect growth regulators (IGRs) had been reported against various insect species. For examples, 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 *S. littoralis*. Pyriproxyfen was reported to be toxic against the Sunn pest *Eurygaster integriceps* (Mojaver and Bandani, 2010) and the lawn armyworm *Spodoptera mauritia* (Resmitha and Meethal, 2016). Also, other IGRs exhibited different toxicities 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); tebufenozide (RH-5992) against the

Mediterranean flour moth *Ephestia kuehniella* (Tazir *et al.*, 2016); lufenuron against the lesser mulberry snout moth *Glyphodes pyloalis* (Aliabadi *et al.*, 2016) and the corn earworm *Helicoverpa armigera* (Vivan *et al.*, 2016); fenoxycarb against the rice meal moth *Corcyra cephalonica* (Begum and Qamar, 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).

In addition, toxicities of various anti-juvenile hormone (anti-JH) compounds had been reported against several insects, such as precocenes against several mosquito species (Yasyukevich and Zvantsov, 1999) and the Colorado potato beetle *Leptinotarsa decemlineata* (Farazmand and Chaika, 2008); precocene II (PII) against the lepidopterous pest *Pericallia ricini* (Khan and Kumar, 2000), the red palm weevil *Rhynchophorus ferrugineus* (Abdullah, 2009), the grey flesh fly *Parasarcophaga dux* (Nassar *et al.*, 1999), and the Asian tiger mosquito *Aedes albopictus* (Liu and Liu, 2014) as well as some synthesized analogues of Fluoromevalonate (Shuto *et al.*, 1988) against the mulberry silkworm *Bombyx mori*. After exposure of the newly moulted 2nd or 4th (penultimate) instar nymphs of the grasshopper *Euprepocnemis plorans* to some doses of PII, various mortalities were recorded among the treated nymphs and the emerged adults (Ghoneim and Basiouny, 2017). Results of the present study on *S. littoralis* were, to some extent, in agreement with those previously reported results, but all larval, pupal and adult mortalities were reversely correlated with the dose level of cycloheximide. Moreover, no mortality was observed at the highest dose. However, the larval deaths of *S. littoralis*, 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, these larval deaths may be due to the prevented feeding and continuous starvation of the insect (Ghoneim *et al.*, 2000). The pupal deaths can be directly related to the hormonal activity of the tested cycloheximide or may be due to other causes, such as suffocation, bleeding and desiccation due to imperfect exuvation, and for failure of vital homeostatic mechanisms (Smagghe and Degheele, 1994). The adult mortalities can be explained by the retention and distribution of cycloheximide 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).

Against insects, LC₅₀ (or LD₅₀) values of IGRs are variable. For examples, LC₅₀ values of novaluron and lufenuron against the tobacco cutworm *Spodoptera litura* were determined as 350.45 and 453.78 ppm, respectively (Sharma and Pathania, 2014); LC₅₀ of hexaflumuron against *H. armigera* was 8.47 mg /L (Taleh *et al.*, 2015); LC₅₀ of methoxyfenozide against *C. pipiens* was calculated in 24.54 µg/L (Hamaidia and Soltani, 2016); LD₅₀ values of RH-5849 and tebufenozide against *E. kuehniella* were 0.05 and 0.005 µg/insect, respectively (Tazir *et al.*, 2016); LC₅₀ values of noviflumuron and novaluron were 0.153 and 0.342 ppm after treatment of 1-day old eggs of *P. gossypiella* (Hamadah and Ghoneim, 2017); etc. In addition, variable LC₅₀ (or LD₅₀) values were recorded for different anti-JH compounds against various insects. For examples, LC₅₀ values of PI and PII against *A. albopictus* were estimated in 41.63 and 43.55 µg/ml, respectively (Liu and Liu, 2014); LC₅₀ values of PII and PI against the book louse *Liposcelis bostrychophila* were calculated in 30.4 and 64.0 µg/cm², respectively (Lu *et al.*, 2014); LC₅₀ of PI against the cat flea *Ctenocephalides felis* was estimated in 10.97 ppm (Rust and Hemsarh, 2017); LC₅₀ values of the anti-JH agent Pitavastatin against *M. sexta* and

the viviparous cockroach *Diploptera punctata* were estimated at 5.23, and 395.2 μM , respectively (Li *et al.*, 2017); etc. LD₅₀ values of PII against *E. plorans* were 0.388 and 17.022 $\mu\text{g}/\text{cm}^2$ after topical treatment of newly moulted 2nd and 4th instar nymphs, respectively (Ghoneim and Basiouny, 2017). In the current investigation, LD₅₀ of cycloheximide against *S. littoralis* was calculated in 0.013 $\mu\text{g}/\text{larva}$. However, LD₅₀ (or LC₅₀) 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.

2. Influenced Growth and Development of *S. littoralis* by Cycloheximide:

2.1. Disturbed Growth:

After topical application of cycloheximide doses onto the newly moulted last instar larvae of *S. littoralis*, in the present investigation, the maximal body weights of the treated larvae increased, in no certain trend. Also, cycloheximide remarkably enhanced the treated larvae to grow higher rate than control larvae. These results were found contradictory to many reported results of the inhibited larval growth in different insect species by various IGRs, such as *S. littoralis* by flufenoxuron (Bakr *et al.*, 2010), lufenuron (Adel, 2012) and novaluron (Ghoneim *et al.*, 2015); the common lime butterfly *Papilio demoleus* by diufenolan (Singh and Kumar, 2011), *S. litura* by chlorfluazuron (Perveen, 2012), the yellow fever mosquito *Aedes aegypti* (Farnesi *et al.*, 2012), *C. pipiens* by novaluron (Djehader *et al.*, 2014) and kinoprene (Hamaidia and Soltani, 2014). Also, our results of increasing body weights and enhanced growth of *S. littoralis* larvae disagreed with those reported results of growth inhibition in some insects by some anti-JH compounds, such as the mealworm beetle *Tenebrio molitor* by several chromene derivatives (Roberto *et al.*, 1998); *A. aegypti*, *Anopheles sacharovi* and *An. stephensi* by PI and PII (Yasyukevich and Zvantsov, 1999) and *M. sexta* by the anti-allatostatins, fluvastatin, lovastatin and pitavastatin (Li *et al.*, 2017). After exposure of the newly moulted 2nd or 4th instar nymphs of *E. plorans* to different doses of PII, the nymphal growth had been inhibited (Ghoneim and Basiouny, 2017). Likewise, some IGRs failed to affect the growth of different insects, such as *M. domestica* (Ghoneim *et al.*, 1991), the American cockroach *Periplaneta americana* and the milkweed bug *Oncopeltus fasciatus* (Darvas *et al.*, 1992), the African armyworm *Spodoptera exempta*, the beet armyworm *Spodoptera exigua* and *L. decemlineata* (Smagghe and Degheele, 1994).

The increasing body weights of cycloheximide-treated last instar larvae of *S. littoralis*, in the present study, might be due to a stimulatory action of the tested compound on the larvae to consume more amount of food. This suggestion may be substantiated by the finding of Ghoneim and Tanani (2017) who recorded considerably increased body weight of the last instar nymphs of the desert locust *Schistocerca gregaria* after treatment with chromafenozide (ecdysteroid agonist). Also, cycloheximide might exert a retarding action on the functions of the malpighian tubules in *S. littoralis* leading to storage of the water and some ions in the insect body, thus the body weight increased (Chapman and de Borer, 1995). Interpretation of the reduced larval growth of insects after treatment with some IGRs and anti-JH compounds is available (Lange *et al.*, 1983; Barnby and Klocke, 1990; Nasiruddin and Mordue, 1994). However, a reliable explication of the promoting action of cycloheximide on larval growth of *S. littoralis*, in the present investigation, is not available right now!!!

2.2. Affected Developmental Durations:

In insects, the developmental rate is usually reversely related to the developmental duration, i.e. shorter duration indicates faster rate and *vice versa*. As reported by many studies, larval duration in several insect species (holometabolous or hemimetabolous) had been prolonged as a response to the action of different IGRs, such as the fall armyworm *Spodoptera frugiperda* as a response to methoxyfenozide (Zarate *et al.*, 2011); *S. littoralis* as a response to novaluron (Ghoneim *et al.*, 2015) and cyromazine (Tanani *et al.*, 2015); *G. pyloalis* as a response to lufenuron (Aliabadi *et al.*, 2016); *C. pipiens* as a response to methoxyfenozide (Hamaidia and Soltani, 2016); *C. cephalonica* as a response to fenoxycarb (Begum and Qamar, 2016); *P. gossypiella* as a response to pyriproxyfen (Sabry and Abdou, 2016) and novaluron (Hamadah and Ghoneim, 2017). Also, treatment of some insects with anti-JH compounds resulted in prolongation of the larval duration, such as 5th nymphal instar in *O. fasciatus* after treatment with PI (Bowers and Aldrich, 1980); 4th instar nymphs of *S. gregaria* after treatment with PII (Eid *et al.*, 1982); three latter instars of the fall webworm *Hyphantria cunea* after treatment with fluoromevalonate (Farag and Varjas, 1983); 6th instar larvae of *S. mauritia* after treatment with PII (Mathai and Nair, 1984); 5th instar nymphs of the grasshopper *Aiolopus thalassinus* after treatment with PIII (Osman, 1988); larval period of *S. litura* after treatment with PI, PII and ethoxyprococene (a synthetic analog of P II) (Srivastava and Kumar, 1999); etc. Results of the present study were inconsistent with these reported results, since the topical application of cycloheximide onto the newly moulted last instar larvae of *S. littoralis* resulted in shortened larval duration, especially at the higher two doses (180 and 120 µg/larva). Also, the pupal duration was remarkably shortened, regardless the dose level as well as developmental rate of pupae was considerably promoted. On the other hand, our results were concomitant to results of shortened larval duration of some insects after treatment with different IGRs, such as *Rh. ferrugineus* after treatment with lufenuron and diufenolan (Tanani, 2001), *A. ipsilon* after treatment with flufenoxuron (El-Sheikh, 2002), *S. gregaria* after treatment with lufenuron (Bakr *et al.*, 2008), *P. gossypiella* after treatment with methoxyfenozide (Sabry and Abdou, 2016) and *P. unionalis* after treatment with novaluron (Ghoneim *et al.*, 2017b). Also, the present results were, to a great extent, in agreement with those reported results of shortened larval duration after treatment with some anti-JH compounds, such as *P. dux* after treatment of the 3rd instar larvae with PII (Nassar *et al.*, 1999) and the flesh fly *Sarcophaga ruficornis* after treatment of the last instar larvae with PI, PII and PIII (Srivastava and Kumar, 1996). The shortened larval and pupal duration of *S. littoralis*, in the current investigation, might be due to a response of these stages for avoiding the adverse action of cycloheximide, as a xenobiotic agent. Also, cycloheximide (RNA and protein synthesis inhibitor) might prevent the formation of nuclear receptors in the cells, leading to disturbance in *S. littoralis* developmental durations (Riddiford and Truman, 1993).

2.3. Derangement of the Development Program:

Giant larval phenotype:

Some juvenile hormone analogues (JHAs), chitin synthesis inhibitors (CSIs), ecdysteroid agonists and botanicals had been reported to induce a giant larval phenotype in some insects. For examples, methoprene promoted the production of giant larvae in the cabbage looper *Trichoplusia ni* (Newitt *et al.*, 1986). In *M. sexta*,

the inhibition of juvenile hormone esterase (JHE) by a trifluoroketone inhibitor resulted in the appearance of giant larvae (Abdel-Aal and Hammock, 1986), which were also observed following JHA application (Hatakoshi *et al.*, 1988). Feeding of *S. littoralis* larvae on food supplemented with the *Cynodon dactylon* extracts resulted in the appearance of giant larvae (Aref, 2009). Methoprene, pyriproxyfen, RH-5849 and tebufenozide were assessed against *T. castaneum*, the lesser grain borer *Rhyzopertha dominica* and the rice weevil *Sitophilus oryzae*. All compounds induced the production of giant larvae which failed to pupate (Kostyukovskya *et al.*, 2000). Some larvae of the greater wax moth *Galleria mellonella*, which consumed large amounts of a diet treated with JHA [methyl 2,7-dimethyl-9-(2-oxolanyl) 2,4 nonadienoate], appeared as giant larvae (Slama and Lukas, 2013). Potent inhibitors of JHE, including phosphoramidothiolate-type and trifluoromethylketone were synthesized. Treatment with several compounds of these inhibitors resulted in the appearance of giant larvae (Sparks *et al.*, 1983; Abdel-Aal and Hammock, 1986; Linderman *et al.*, 1987; Roe *et al.*, 1997; Kamita *et al.*, 2003). Treatment of 2nd instar larvae of *S. littoralis* with sub-lethal doses of triflumuron and methoxyfenozide resulted in the appearance of some giant pupae (Khattar, 2015).

Results of the current investigation on *S. littoralis* were, to a great extent, in resemblance to the previously reported results, since topical application of cycloheximide onto last instar larvae induced some larvae to appear in a strange phenotype, 'giant larvae', only at the lower two doses (60 and 30 µg/larva). These giant larvae enlarged in size and appeared heavier than other treated and control larvae. They had darker colour than that of other larvae, survived 2-times longer period and perished without transformation into pupa or even prepupae. For understanding the induction of these giant larvae of *S. littoralis*, it is important to know that JHs are metabolized in lepidopterous larvae and immature stages of other insects (Hammock, 1985; Abdel-Aal and Hammock, 1986). As the stimulation or inhibition of JH degradation by JHE would also modify JH titer in haemolymph and influence the development of an insect, any factor that interferes with the presence of JHE is harmful for insect development. Mechanistically, JHAs have been hypothesized to function as inhibitors of JHE (Kamita *et al.*, 2011). These enzymes are required to reduce JH titer below the *status quo* level that is important for normal moulting to occur (El-Sheikh *et al.*, 2016).

Moreover, cycloheximide exhibited JH-like activity inducing impairment in the hormonal regulation of moulting process, thus giant larvae had appeared. In some detail, this juvenilizing effect can be explained by a depressing action of cycloheximide on the activity of one or more JHEs (Phillips and Loughton, 1979). This suggestion can be substantiated by the finding of Sandburge *et al.* (1975) who reported that the esterase activity was inhibited when cycloheximide was injected into the 4th instar nymphs of the migratory locust *Locusta migratoria* causing a high titer of JH in the haemolymph. Thus, induction of giant larvae in the present study indicated that cycloheximide can be considered as JH mimic against *S. littoralis*. In addition, cycloheximide might inhibit the ecdysteroidogenesis, since some authors (Caceres *et al.*, 2011; Gibbens *et al.*, 2011) reported that this giant larval phenotype was commonly observed in ecdysteroidogenesis-deficient 3rd instar larvae of the vinegar fly *Drosophila melanogaster* and could be rescued by ecdysone feeding.

Permanent prepupae:

In insects, a symptom of suspended development attracts a great attention of some entomologists. This feature is usually expressed in 'permanent larvae'. The induction

of permanent larvae or nymphs was recorded in some insect species as a response to some IGRs or botanicals. Some authors (Salem *et al.*, 1985a; El-Gammal and Taha, 1984; Abou El-Ela, 1993) observed permanent nymphs of *S. gregaria* after treatment with certain IGRs. Permanent larvae of the European corn borer *Ostrinia nubilalis* were induced depending upon the dose of fenoxycarb and the timing of application onto the 5th instar larvae (Gadenne *et al.*, 1990). Permanent larvae of the grey flesh fly *Parasarcophaga argyrostoma* were induced after topical treatment with 100 µg/larva of chlorfluazuron (Ghoneim and Ismail, 1995). Among botanicals, some plant extracts or isolated plant products had been reported to induce permanent nymphs in various insects, such as *O. fasciatus* (Hemiptera) after injection of the newly moulted last instar nymphs with azadirachtin (Dorn *et al.*, 1986); *O. fasciatus* and the cotton stainer bug *Dysdercus peruvianus* after topical application of *Manilkara subsericea* (Sapotaceae) extracts onto 4th instar nymphs (Fernandes *et al.*, 2013); *S. litura* (Lepidoptera) after treatment of larvae with acetone leaf extract of *Withania somnifera* (Solanaceae) (Gaur and Kumar, 2010); and the confused flour beetle *Tribolium confusum* (Coleoptera) after treatment of 5th instar and 6th instar larvae with 1 µg/µl of Andrographolide (a terpenoid isolated from the leaves of *Andrographis paniculata*, Acanthaceae) (Lingampally *et al.*, 2013). Feeding of *G. mellonella* larvae, for a long time, on a diet treated with the JH analogue [methyl 2,7-dimethyl-9-(2-oxolanyl) 2,4 nonadienoate; 0.1 mg/g of diet] induced permanent larvae (Slama and Lukas, 2013). Apart from IGRs and botanicals, El-Gammal *et al.* (1986) observed permanent nymphs in *S. gregaria* after exposure of gamma irradiation against the 3rd instar nymphs.

Some anti-JH compounds had been reported to induce permanent larvae or nymphs in some insect species, such as the grasshopper *E. plorans* in which exposure of the newly moulted 2nd instar nymphs to 20 µg/cm² of PII induced some 'permanent nymphs' in both 2nd and 4th instars (Ghoneim and Basiouny, 2017). In the present study, topical treatment of *S. littoralis* larvae only with the lower two doses of cycloheximide (60 and 30 µg/larva) induced some 'permanent prepupae'. These developmentally suspended prepupae survived 10 days and perished with no symptom of pupation. To understand the appearance of permanent prepupae in the current investigation, cycloheximide exerted an inhibitory action on the prothoracic gland (ecdysone-producing gland) and hence the ecdysone could not be synthesized and/or released. Also, 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).

3. Impaired Metamorphosis and Morphogenesis of *S. littoralis* by Cycloheximide:

Pupation and pupal deformation:

In the present study on *S. littoralis*, cycloheximide exerted a suppressive action on pupation, since the pupation rate was drastically regressed after topical treatment of the newly moulted last instar larvae with the lower three doses (120, 60 and 30 µg/larva). This result was, to a great extent, consistent with those reported results of regressed pupation rate of some insects by various IGRs, such as 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. In the current study, also, cycloheximide exhibited weak anti-morphogenic efficiency on *S. littoralis* because some deformed pupae were produced only at 120µg/larva. This result was in a partial resemblance with the reported results of impaired pupal morphogenesis in *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 fenoxycarb onto last instar larvae (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). Also, the present result was, to some extent, in agreement with those reported results on the impaired morphogenesis in some insects by a number of anti-JH compounds, such as *T. ni* (Sparks *et al.*, 1987) and *S. mauritia* (Nair and Rajalekshmi, 1988) after treatment of last instar larvae with FMev; *A. thalassinus* after topical application of PIII onto eggs or 5th instar nymphs (Osman, 1988); *S. ruficornis* after administration of PI, PII or PIII to the last instar larvae (Srivastava and Kumar, 1996); *S. litura* after treatment of larvae with PI or PII (Srivastava and Kumar, 1999); *P. dux* after topical application of PII onto the 3rd instar larvae (Nassar *et al.*, 1999); and *E. integriceps* after treatment of nymphs with PI (Amiri *et al.*, 2010). For interpretation of the regression of pupation rate and production of the deformed pupae in *S. littoralis*, as caused by cycloheximide 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, cycloheximide might block the release of morphogenic peptides, causing alteration in titers of ecdysteroids and juvenoids (Barnby and Klocke, 1990).

Adult emergence:

The adult emergence of many insect species was partially or completely blocked after larval treatment with various IGRs, such as *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) and cyromazine (Tanani *et al.*, 2015); *G. pyloalis* after treatment of the 4th instar larvae of with lufenuron (Aliabadi *et al.*, 2016); *Culex quinquefasciatus* and *A. albopictus* after treatment with pyriproxyfen and methoprene (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). Results of the present study on *S. littoralis* were, to a great extent, in agreement with the previously reported results, since the adult emergence was detrimentally blocked after treatment of last instar larvae with the majority of cycloheximide doses. Also, our results agreed with those reported results of blocking action of some anti-JH compounds on the adult emergence of various insects, such as *S. ruficornis* by PII (Khan and Kumar, 2005) and *B. mori* by KK-42 (a terpenoid imidazoles)(Kadono-Okuda *et al.*, 1987).

In this context, 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 appeared in partial or complete arresting of adults to emerge. The present result of blocked adult emergence of *S. littoralis* can be interpreted by the disturbing effect of cycloheximide on the normal metabolism of insect hormones during the development of the immatures leading to failure of adult emergence (Trigo *et al.*, 1988). In particular, cycloheximide might disturb the adult

eclosion hormone release and/or inhibition of the neurosecretion (Al-Sharook *et al.*, 1991; Josephraj Kumar *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).

4. Deteriorated Reproductive Potential of *S. littoralis* by Cycloheximide:

Reproduction in insects is mainly controlled by JH, which is responsible for vitellogenesis and other reproductive processes (Ghoneim *et al.*, 2014). It is interesting to categorize the effects of IGRs on the insect reproduction into: i) reproductive behaviour, ii) oviposition, iii) egg hatchability (ovicidal and embryocidal), and iv) adult sterilization (Mondal and Parween, 2000). On the other hand, ecdysteroids have essential functions in the insect reproductive processes, *viz.*, vitellogenesis, ovulation of matured eggs and spermatocyte growth (Wigglesworth, 1984; Hagedorn, 1985).

4.1. Reduction of Oviposition Efficiency:

In insects, the oviposition rate can be used as an informative indicator of the oviposition efficiency of adult females (Ghoneim *et al.*, 2014). In the current study, the oviposition efficiency of *S. littoralis* females was completely prohibited, after larval treatment with the higher two doses (160 and 120 µg/larva) of cycloheximide. At the lower two doses, the oviposition rate was remarkably regressed. This result was, to a great extent, in conformity with the reported results of inhibited oviposition efficiency of some insects by various IGRs, such as *S. littoralis* by flufenoxuron (Bakr *et al.*, 2010) and novaluron (Ghoneim *et al.*, 2014); *S. gregaria* by flufenoxuron and lufenuron (Soltani-Mazouni and Soltani, 1994) or tebufenozide (Al-Dali *et al.*, 2008); the Indian meal moth *Plodia interpunctella* by RH-5849 (Smagghe and Degheele, 1994); the bean beetle *Callosobruchas maculatus* by cyromazine (Al-Mekhlafi *et al.*, 2011); *P. gossypiella* by novaluron (Hassan *et al.*, 2017) and *P. unionalis* by methoxyfenozide (Hamadah *et al.*, 2017). 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). In contrast, the present result disagreed with the results of stimulated oviposition of the two-spotted field cricket *Gryllus bimaculatus* by some ecdysteroid agonists (Behrens and Hoffmann, 1983). The prohibited oviposition efficiency of *S. littoralis*, in the present study, can be understood as a result of the inhibition of ovarian DNA synthesis or to the interference of cycloheximide with vitellogenesis *via* certain biochemical processes, since this compound was known as RNA and protein synthesis inhibitor (Phillips and Loughton, 1979; Soltani-Mazouni and Soltani, 1995; Morton and Truman, 2008; MacBean, 2012). Also, cycloheximide might exert a reverse action to that exerted by the ecdysteroid agonists which stimulate the neurosecretory cells to release a myotropic ovulation hormone (Parween *et al.*, 2001).

4.2. Suppression of Reproductive Capacity:

Inhibited fecundity:

There are many reported results of prohibited fecundity (mean number of eggs/female) in several insects after larval treatment with various IGRs, such as *S. littoralis* after treatment with lufenuron (Gaaboub *et al.*, 2012) or novaluron

(Ghoneim *et al.*, 2014). Also, fecundity of other insect species was reduced by various IGRs, such as *E. kuehniella* by tebufenozide (Khebbeb *et al.*, 2008); *S. litura* by methoxyfenozide (Shahout *et al.*, 2011); the gypsy moth *Lymantria dispar* by methoxyfenozide (Ouakid *et al.*, 2016); *D. koenigi* by flufenoxuron (Khan and Qamar, 2011); *A. kuehniella* by hexaflumuron (Ashouri *et al.*, 2014); *P. xylostella* by pyriproxyfen (Mahmoudvand *et al.*, 2015); *T. castaneum* (Gado *et al.*, 2015) and *D. antique* (Zhou *et al.*, 2016) by lufenuron and *C. cephalonica* by fenoxycarb (Begum and Qamar, 2016); etc. With regard to anti-JH compounds, fecundity of some insects was prohibited after larval treatment with a number of these compounds, such as *P. dux* by PII (Nassar *et al.*, 1999), the brown planthopper *Nilaparvata lugens* by PII (Pradeep and Nair, 2000), *E. integriceps* by PI (Amiri *et al.*, 2010) and *L. decemlineata* by H17 (Lehmann *et al.*, 2015). Results of the present investigation were, to some extent, in corroboration with those reported results, since topical application of the higher two doses of cycloheximide (160 and 120 µg/larva) onto last instar larvae of *S. littoralis* completely prevented the oviposition of the adult females and subsequently no fecundity was determined. In addition, fecundity was dramatically reduced, at the lower two doses. On the contrary, our result disagreed with some reported results of the failure of some IGRs and anti-JH compounds to affect the fecundity in various insects, such as fenoxycarb against the honey bee *Apis mellifera* (Thompson *et al.*, 2005), methoxyfenozide against *S. exigua* (Christian-Lius and Pineda, 2010) and novaluron against the brown marmorated stink bug *Halyomorpha halys* (Kamminga *et al.*, 2012). These diverse effects can be attributed to the potency of IGRs and their modes of action, susceptibility of the insect species, time of treatment and other factors.

To understand the dramatic inhibition of fecundity of *S. littoralis*, after larval treatment with cycloheximide in the current investigation, it is interesting to mention that JH is necessary for post-eclosion development of the vitellogenin-producing adult fat body. In many insects, including *S. littoralis*, JH modulates fecundity at least in part because JH is prerequisite hormone for inducing the yolk proteins uptake into oocytes (Soller *et al.*, 1997), while ecdysone, produced from egg follicles, induces yolk protein mRNA expressed in the fat body (Bownes, 2004; Raikhel *et al.*, 2005; Schwedes and Carny, 2012). The fecundity inhibition in *S. littoralis* might be due to the interference of cycloheximide with one or more processes from the ovarian follicle development to the egg maturation. Cycloheximide might cause some disorders in the ovaries, including cell death in the germarium, resorption of oocytes in the pre-vitellarium and vitellarium (Zhou *et al.*, 2016). Cycloheximide might inhibit the synthesis and metabolism of proteinaceous constituents during oogenesis (Salem *et al.*, 1997). Also, it might exert an inhibitory action against the function of authentic gonadotropic hormone (JH in adults) responsible for the synthesis of vitellogenins and vitellogenesis (Di Ilio *et al.*, 1999).

Reduced fertility:

Fertility (egg hatching % or egg viability) is another important parameter of the reproductive capacity in insects. Fertility of some insects had been reduced as a result of larval treatments with some IGRs, such as *P. gossypiella* by lufenuron, methoxyfenozide and chromafenozide (Kandil *et al.*, 2012) or novaluron (Hassan *et al.*, 2017); *S. littoralis* by chlorfluazuron (Sammour *et al.*, 2008), methoxyfenozide (Pineda *et al.*, 2009), lufenuron (Gaaboub *et al.*, 2012), triflumuron (El-Naggar, 2013) or novaluron (Ghoneim *et al.*, 2014); *S. litura* by chromafenozide (Shahout *et al.*, 2011); *E. kuehniella* by tebufenozide (Khebbeb *et al.*, 2008); *D. koenigi* by

flufenoxuron (Khan and Qamar, 2011), *C. maculata* by cyromazine (Al-Mekhlafi *et al.*, 2011), *A. kuehniella* by hexaflumuron (Ashouri *et al.*, 2014); *C. pipiens* (Hamaidia and Soltani, 2016) and *L. dispar* (Ouakid *et al.*, 2016) by methoxyfenozide; *P. unionalis* by methoxyfenozide (Hamadah *et al.*, 2017); etc. Also, fertility of some insects had been reduced by some anti-JH compounds, such as *E. integriceps* by PI (Amiri *et al.*, 2010); and *D. flavidus* by phenolic chromene and hydroxyethyl chromene (isolated from *A. conyzoides*) (Okunade, 2002). Bowers and Aregullin (1987) isolated an anti-JH compound, polyacetylenic sulfoxide, from *C. coronarium*, which produced sterile adults in *O. fasciatus*. In the present study, cycloheximide potency exceeded over the potencies of all previously reported IGRs and anti-JH compounds, since it caused complete sterility in *S. littoralis*, since no eggs could hatch, regardless the dose level. Thus, cycloheximide was found extremely strong anti-gonadotropic agent against this insect. This finding confirmed some of the previous findings of a number of studies, since cycloheximide exhibited an anti-gonadotropic action also against *S. litura* (Sridevi and Ray, 1988) and *T. molitor* (Soltani-Mazouni and Soltani, 1995).

Conclusion:

Depending on the obtained results, cycloheximide exhibited a moderate toxic effect on larvae, pupae and adults of *S. littoralis*. It impaired the development program and prohibited the adult emergence. Moreover, it exerted an extreme anti-gonadotropic action causing complete sterilization of this pest. On the other hand, a disadvantage was recorded for cycloheximide, since it enhanced the larval growth in this pest. Some safety reports mentioned that the use cycloheximide in agricultural applications is now decreasing due to the recent findings of health risks at low doses. Therefore, for recommendation to use of cycloheximide in the IPM program against *S. littoralis*, intensive research should be conducted in the foreseeable future to assess its hazards to human, domestic animals, beneficial arthropods and environmental systems.

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