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Biopesticidal Potential of Nerolidol, a Sesquiterpene Compound, and its Drastic Impact on Growth and Metamorphosis of the Cotton Leafworm *Spodoptera littoralis* (Lepidoptera: Noctuidae)

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Abstract		Original Research Article

Egyptian cotton leafworm, *Spodoptera littoralis*, is one of the key pests that cause great damage to cotton plant as well as other field and vegetable crops. Plant products, as a promising alternative to the synthetic insecticides, have now been established worldwide. In this work we studied for the first time the insecticidal activity of the sesquiterpene compound, nerolidol, and its effect on growth, development and metamorphosis of *S. littoralis*. The newly moulted larvae of 5th (penultimate) or 6th (last) instar larvae were fed on castor bean leaves previously treated with seven concentrations of Nerolidol (400, 200, 100, 50, 25, 12.5 & 6.25 ppm) for 24 hr. The most important results could be summarized as follows. Nerolidol exhibited various degrees of insecticidal activity against larvae, pupae and adults, regardless the instar under treatment. Nerolidol was found more toxic after treatment of last instar larvae (LC_{50}=42.24 ppm) than after treatment of penultimate instar larvae (LC_{50}=50.01 ppm). A remarkable reduction of larval weight gain was recorded, in a dose-dependent course. Similarly, the larval growth was drastically suppressed. The larval and pupal durations were significantly prolonged. Some percentages of the treated 5th instar larvae failed to completely moult into the 6th instar, only at the higher three concentrations. Also, some larvae developed into larval-pupal intermediates. Nerolidol exerted a strong inhibitory action on the pupation rate in a dose-dependent course while the adult emergence was partially blocked, only at the higher concentrations. Nerolidol failed to exert anti-morphogenic action on *S. littoralis* after treatment of 5th instar larvae, but treatment of 6th instar larvae only with the higher two concentrations resulted in an impaired morphogenesis of some pupae.

Keywords: ecdysis, intermediates, malformation, metamorphosis, mortality, moult, pupation, toxicity.

INTRODUCTION

Cotton from the genus *Gossypium* is one of the economic crops. It is one of the major sources of fiber. Also, cotton plants produce a large amount of seeds [1]. These seeds are rich in protein and have been considered as a valuable source of oil and fodder [2]. In addition, cotton plants typically contain high content of gossypol, a terpenoid, within the glands of seed kernels [3]. The Egyptian cotton leaf worm *Spodoptera littoralis* (Boisd.) (Lepidoptera: Noctuidae) is the most destructive pest of the cotton plant and several field crops, as well as vegetables and several ornamental crops [4-7]. It is distributed in many European countries [8-10], Asia Minor and the Middle East countries [11-13]. Moreover, this insect pest has a very wide host range of at least 90 plant species of economic importance belonging to 44 families [14-16]. Over the years, the number of attacked plants by *S. littoralis* increased to more than 112 species [16, 17-20].

Although different cultural, mechanical and physical control measures have been applied for the management of *S. littoralis* in Egypt, no satisfactory results can be obtained, most farmers, however, prefer using synthetic pesticides for obtaining fast results [21-24]. Over the past 50 years, the widespread and extensive uses of many environmentally-hazardous insecticides had led to the development of quick resistance of *S. littoralis* to the many of these chemicals [25-28], beside to their hazardous residues in the

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36

environment [29, 30]. In some detail, the development of *S. littoralis* resistance to the synthetic pyrethroids, carbamates, organophosphorus and other chemical insecticides has been correlated with the development of cross-resistance in many cases [31]. Also, application of synthetic insecticides is expensive [32]. Beside to these problems, many pesticides are insoluble in water, so large quantities of organic solvents are needed and most of these solvents contaminate the ecosystem [33]. Therefore, searching for new alternative, effective and safer for human health, economic animals, non-target organisms and ecosystem, is prerequisite [34-36]. One of the chief components of Integrated Pest Management is the application of plant extracts, oils and secondary metabolites which are included in the class of 'biopesticides', in addition to certain bacteria, viruses, animals, and certain minerals [37, 38]. In this context, botanicals have been used as effective toxicants, growth regulators, antifeedants and repellents against a wide spectrum of agricultural and public health insects [39-42]. These biopesticides are effective alternative to synthetic insecticides because of their low toxicity to humans and animals, low environmental pollution and other applications. They are generally more eco-friendly alternatives for the insect control [43-45].

The monoterpenes, phenylpropenes and sesquiterpenes have reported to exhibit different biological activities against some economic insect pests as they can act as insecticides [46-48], insect growth regulators [49], antifeedants [50] and repellents [51, 52]. On the other hand, few studies were reported in the current literature on the antifeedant and growth inhibitory effects of these plant products against *S. littoralis* [45, 53-55]. In Egypt, few studies [56-58] revealed the insecticidal activities of different monoterpenes, phenylpropenes and sesquiterpenes against larvae of *S. littoralis*.

Nerolidol (3,7,11-trimethyl-1,6,10-dodecatrien-3-ol, Molecular Formula: $C_{15}H_{26}O$) is known as one of the most important acyclic sesquiterpenes. Chemically, nerolidol exists in two isomers, a *trans* form and a *cis* form [59]. It is synthesized as an intermediate in the production of (3E)-4,8-dimethy-1,3,7-nonatriene, a herbivore-induced volatile that protects plants against herbivore attacks and attracts some predatory insects [59]. The (E)-nerolidol was identified as a potent signal that elicits the plant defenses, such as the tea plant [60]. For more information, see Boncan *et al.* [61], Wroblewska-Kurdyk *et al.* [62] and Favaris *et al.* [63]. Different commercial uses of nerolidol are reported for cosmetics [64] and non-cosmetic products [65]. Also, nerolidol is widely used in the food industry as a flavor enhancer in many food products [59]. In medicine, it is currently under testing as a skin penetration enhancer for the transdermal delivery of therapeutic drugs [65, 66].

For more information, see Klopell *et al.* [67], Nogueira Neto *et al.* [68] and Javed *et al.* [69].

With regard to the pest control, Nerolidol isomers act as insect attractants [70], antifeedants [71], larvicidal [72] and ovicidal agent [73, 74]. Wróblewska-Kurdyk *et al.* [75] evaluated the effect of Nerolidol isomers on the host-plant selection behaviour of the peach potato aphid *Myzus persicae*. In a recent study, Benelli *et al.* [76] recorded a high toxicity of (E)-nerolidol against the aphid *Metopolophium dirhodum*. Depending on the results of da Silva *et al.* [77], Azamax® was more toxic than the oils of *Melaleuca leucadendra* and (E)-nerolidol against *Tetranychus urticae*. However, the oils and (E)-nerolidol were more toxic to *Plutella xylostella* than Azamax®. Recently, also, Hamadah *et al.* [78] recorded some adverse effects of nerolidol on the adult performance and reproductive potential of *S. littoralis*. The objective of the present study was to assess the insecticidal activity of Nerolidol and its effect on growth, development and metamorphosis of *S. littoralis*.

MATERIALS AND METHODS
The insect culture
A sample of Egyptian cotton leaf worm *Spodoptera littoralis* (Boisd.) (Lepidoptera: Noctuidae) pupae was kindly obtained from the culture of susceptible strain maintained for several generations in Plant Protection Research Institute, Agricultural Research Center, Doqqi, Giza, Egypt. In the laboratory of Insect Physiology, Faculty of Science, Al-Azhar University, Cairo, a culture was established under laboratory controlled conditions (27 ± 2^oC, $65\pm5\%$ R.H., photoperiod 14 h L and 10 h D). Rearing procedure was carried out according to Ghoneim [79] and improved by Bakr *et al.* [80]. Egg patches were kept in Petri dishes until hatching. The hatched larvae were transferred into glass containers containing a layer of dry saw dust and tightly covered with muslin cloth secured with rubber bands. For feeding, larvae were provided daily with fresh castor bean leaves *Ricinus communis*. The developed pupae were collected and placed in clean jars provided with a layer of moistened saw dust. All jars had been kept in suitable cages provided with branches of fresh Tafla plant, *Nerium oleander*, as oviposition sites. The emerged adults were provided with 10% honey solution on a cotton wick as a food source. Moths were allowed to mate and lay eggs on branches. The egg patches were collected daily, and transferred into Petri dishes for the next generation.

The tested compound and concentration preparation
The tested nerolidol 98% (an acyclic Sesquiterpene) in the present study was purchased from ABCR GmbH, Karlsruhe, Germany. It has the chemical name: (*cis* + *trans*) [3, 7, 11-Trimethyl-1, 6, 10-dodecatrien-3-ol] and Formula: $C_{15}H_{26}O$. Five ml of Tween 60 were added (as emulsifier) to 5 ml of ethyl

alcohol (95%). Then, these solvents were mixed thoroughly with 5 ml of nerolidol. For obtaining a stock solution, 90 ml of distilled water was added to the mixture for preparing a concentration of 4.8 % nerolidol, emulsion. The stock solution was diluted with distilled water in volumetric flasks for preparation of a series of concentrations: 400.00, 200.00, 100.00, 50.00, 25.00, 12.50 & 6.25 ppm.

Bioassay of nerolidol

Bioassay of nerolidol was carried out against the newly moulted 5th (penultimate) larvae and newly moulted 6th (last) larvae. Discs of fresh castor bean leaves were dipped in each concentration for 5 minutes and air dried before introduction to larvae as food for 24 hr under the aforementioned laboratory conditions. Control larvae received leaf discs after dipping in Tween 60 and alcohol (95 %) solution for 5 minutes. Ten replicates of treated and control larvae (one larva/replicate) were kept separately in glass vials. Then, mortality and biological parameters were recorded daily.

Insecticidal activity

All mortalities of treated and control (larvae, pupae and adults) were recorded every day and corrected according to Abbott's formula [81] as follows:

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

The LC$_{50}$ was calculated for total mortality by Microsoft® office Excel (2007), according to Finny [82].

Growth, development and metamorphosis

Larval body weight gain: Each individual larva (treated or control) was carefully weighed every day using a digital balance for recording the weight gain as follows:

Initial body weight (before the beginning of experiment) - final body weight (at the end of experiment).

Growth rate: It was calculated according to Waldauer [83] as follows:
Fresh weight gain during the feeding period/Feeding period x mean fresh body weight of larva

Developmental duration and rate: Dempster's equation [84] was applied for calculating the developmental duration, and Richard's equation [85] was used for calculating the developmental rate.

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

Adult emergence: number of successfully emerged adults was expressed in % according to Jimenez-Peydro *et al*. [86] as follows:
[No. of completely emerged adults / No. of pupae] × 100

Morphogenesis: The deranged metamorphosis and morphogenesis programs were detected and calculated in larval-pupal or pupal-adult intermediates (%). Also, pupal deformation was calculated in %. Features of impaired programs were recorded in photos.

STATISTICAL ANALYSIS OF DATA
Data obtained were analyzed by the Student's *t*-distribution, and refined by Bessel correction [87] for the test significance of difference between means using GraphPad InStat© v. 3.01 [88].

RESULTS
Insecticidal activity of nerolidol against *S. littoralis*
After treatment of newly moulted penultimate (5th) instar larvae of *S. littoralis* with seven concentration levels of nerolidol, data of the insecticidal activity were summarized in Table (1). According to these data, nerolidol exhibited acute toxicity on the 5th instar larvae only at the higher two concentration levels (50 & 20% larval mortality, at 400 & 200 ppm, respectively, vs. 0% mortality of control congeners). Stronger toxicity was observed on the successfully moulted last instar larvae, since mortality % increased parallel to the concentration level, with an exception of the lowest concentration level (50, 50, 40, 40, 30 & 20% larval mortality, at 400, 200, 100, 50, 25 & 12.5 ppm, respectively, *vs*. 0% mortality of control larvae). A weak toxic effect was exhibited by nerolidol on the developed pupae and emerged adult moths (see Table 1). LC$_{50}$ value was calculated in 50.01 ppm.

After treatment of newly moulted last (6th) instar larvae of *S. littoralis* with seven concentration levels of nerolidol, data of the insecticidal activity against all developmental stages were arranged in Table (2). In the light of these data, nerolidol exhibited a considerably toxic effect on larvae, in a dose-dependent course, with an exception of the lowest concentration level (80, 70, 60, 50, 30 & 20% larval mortality, at 400, 200, 100, 50, 25 & 12.5 ppm, respectively, in comparison with 0% mortality of control larvae). Nerolidol displayed a pupicidal effect only after larval treatment with the higher two concentration levels. In

respect of the successfully emerged adult moths, only the higher three concentration levels caused various degrees of toxicity against adults (50, 50 & 20% adult mortality, at 200, 100 & 50 ppm, respectively, *vs*. 0% mortality of control adults). LC_{50} value was determined in 42.24 ppm.

In the light of data of both tables 1 & 2, nerolidol was found more toxic after treatment of 6th instar larvae than its toxicity after treatment of 5th instar larvae. In other words, the last instar was more sensitive to Nerolidol toxicity than penultimate instar.

Effect of nerolidol on growth, development, metamorphosis and morphogenesis of *S. littoralis*

After treatment of 5th instar larvae with seven concentration levels of nerolidol, data of weight gain, growth, development, metamorphosis and morphogenesis were assorted in Table (3). Data of similar criteria were arranged in Table (4), after treatment of 6th instar larvae with nerolidol.

Effect on the weight gain and growth

Data of Table (3) revealed a remarkable reduction of larval weight gain (wtg), after treatment of 5th instar larvae with nerolidol, in a dose-dependent course (48.19±2.11, 56.33±1.74, 62.14±1.09, 65.64±0.98, 73.25±1.76, 81.72±1.09 & 84.15±2.05 mg, at 400, 200, 100, 50, 25, 12.5, 6.25 ppm, respectively, *vs*. 86.19±2.71mg of control larvae). Similarly, nerolidol suppressed the larval growth rate (GR), in a dose-dependent course (3.00±0.01, 4.34±0.56, 5.43±0.56, 6.19±0.78, 8.95±0.16, 9.65±0.26 & 10.36±0.42, at 400, 200, 100, 50, 25, 12.5, 6.25 ppm, respectively, *vs*. 12.49±0.53 of control larvae). In addition, wtg of the successfully moulted 6th instar larvae had been subjected to a strong reducing action of nerolidol. Also, these larvae appeared with pronouncedly regressed GR (for detail, see 3).

After treatment of 6th instar larvae with nerolidol, data of Table (4) revealed a drastic reduction of the larval wtg (142.13±2.77, 162.68±3.19, 188.24±4.08, 193.51±1.19, 211.18±3.67, 226.20±4.15 & 233.14±0.28 mg, at 400, 200, 100, 50, 25, 12.5, 6.25 ppm, respectively, *vs*. 234.28±2.01 mg of control larvae) and considerably regressed GR.

Effect on the developmental durations and rate

Data of Table (3) revealed a remarkably prolonged larval duration after treatment of 5th instar larvae with only higher three concentration levels of Nerolidol (48.19±2.11, 56.33±1.74, 62.14±1.09, 65.64±0.98, 73.25±1.76, 81.72±1.09 & 84.15±2.05 days of treated larvae, at 400, 200, 100, 50, 25, 12.5 & 6.25 ppm, respectively, *vs*. 2.31±0.48 days of control larvae). Also, the successfully moulted 6th instar larvae passed a general prolonged period, but significantly prolonged period only after treatment with the higher two

concentration levels of nerolidol (9.00±0.33 & 8.67±0.48 days of treated larvae, at 400 & 200 ppm, respectively, *vs*. 7.81±0.67 days of control larvae). In addition, the successfully developed pupae after treatment of 5th instar larvae with all nerolidol concentration levels, except the lowest one, survived significantly prolonged period (8.19±0.36, 7.87±0.16, 7.74±0.25, 7.49±0.53 & 7.28±0.67 days of treated pupae, at 200, 100, 50, 25 & 12.5 ppm, respectively, *vs*. 6.87±0.33 days of control pupae).

A similar prolongation of pupal duration was determined after treatment of 6th instar larvae with nerolidol. This prolonged duration was found in a dose-dependent course (8.52±0.47, 8.28±0.24, 7.96±0.10, 7.78±0.25, 7.53±0.42 & 7.23±0.34 days of treated pupae, at 200, 100, 50, 25, 12.5 & 6.25 ppm, respectively, *vs*. 6.87±0.33 days of control pupae, see Table 4).

With regard to the developmental rate (DR), data of Table (3) displayed a strong suppressing action of nerolidol on DR of treated 5th instar larvae, proportional to the increasing concentration level. A similar regression of DR was recorded for 6th instar larvae after treatment with nerolidol (for detail, see Table 4).

Effect on the developmental program

Data of Table (3) included a criterion of the disrupted developmental program, failure of ecdysis. For some detail, some percentages of the treated 5th instar larvae failed to completely moult into the 6th instar, only after treatment with the higher three concentration levels of nerolidol (20, 20 & 10% failed larvae to moult, at 400, 200 & 100 ppm, respectively, compared to 0% failure of control larvae). As shown in Fig. (1), these 6th instar larvae appeared with rudimentary 5th instar exuvia and abdominal constrictions.

Another feature of disrupted developmental program is the production of larval-pupal intermediates. Depending on data of Table (3), treatment of 5th instar larvae with Nerolidol were induced to produce different intermediate creatures. With exception of the lower two concentration levels, these intermediates were produced in increasing percentage with the increasing concentration level (30, 30, 20, 10 & 10% of larval-pupal intermediates, at 400, 200, 100, 50 & 25 ppm, respectively).

In addition, a similar feature of disrupted developmental program was recorded after treatment of 6th instar larvae. The larval-pupal intermediates were increasingly produced as the concentration level was increased, with exception of the lowest concentration level of nerolidol (70, 50, 40, 40, 20 & 10% of intermediates, at 400, 200, 100, 50, 25 & 12.5ppm, respectively, see Table 4). Irrespective of the larval instar under treatment, the important features of these

intermediates had been observed with pupal abdomen and larval head and thorax (see Fig. 2).

Effect on the metamorphosis

Pupation

Depending on data assorted in Table (3), nerolidol exerted a strong inhibitory action on pupation, since pupation rate was regressed in a dose-dependent course, after treatment of 5th instar larvae, with exception of the lowest concentration level (30, 40, 60, 70 & 80% pupation, at 200, 100, 50, 25 & 12.5 ppm, respectively, *vs.* 100% pupation of control congeners). A similar inhibitory effect was exhibited by nerolidol on the pupation after treatment of 6th instar larvae. As obviously seen in Table (4), the pupation blocking increased proportional to the increasing nerolidol concentration level (20, 30, 40, 50, 70 & 80% pupation, at 400, 200, 100, 50, 25 & 12.5 ppm, respectively, *vs.* 100% pupation of control congeners).

Adult emergence

It may be important to mention that the adult emergence is a prerequisite process of the insect metamorphosis. On the basis of data assorted in both tables (3 & 4), nerolidol had a weak blocking potency on adult emergence after treatment of 5th instar larvae or 6th instar larvae. For some detail, the adult emergence was partially blocked after treatment of 5th instar larvae only with the higher two concentration levels of nerolidol (66.67 & 83.33% adult emergence, at 200 & 100 ppm, respectively, *vs.* 100% emergence of control congeners, Table 3). Also, treatment of 6th instar larvae only with 200 ppm nerolidol resulted in 66.67% emerged adults while 100% emerged adults were recorded at other concentrations (Table 4).

Effect on the morphogenesis program

As seen in Table (3), nerolidol failed to exert anti-morphogenic action on *S. littoralis* after treatment of 5th instar larvae. On the other hand, treatment of 6th instar larvae only with the higher two concentration levels of Nerolidol impaired the morphogenesis of some pupae (100.00 & 33.33% deformed pupae, at 400 & 200 ppm, respectively, *vs.* 0% deformation of control pupae, see Table 4). As observed in Fig. (3), the malformed pupae developed with bent abdomens, hump-backs or with last larval exuvia attached to head and mouth parts.

Table-1: Insecticidal activity (%) of Nerolidol against *S. littoralis* after treatment of newly moulted penultimate (5th) instar larvae

Conc. (ppm)	Larval mortalities		Pupal mortality	Adult mortality	Total mortality	Corrected mortality	LC$_{50}$ (ppm)
	5th instar	6th instar					
400.00	50.00	100.00	---	---	100.00	100.00	
200.00	20.00	62.50	33.33	0.00	80.00	80.00	
100.00	0.00	40.00	0.00	16.67	70.00	70.00	
50.00	0.00	40.00	16.67	0.00	50.00	50.00	50.01
25.00	0.00	30.00	0.00	0.00	30.00	30.00	
12.50	0.00	20.00	0.00	0.00	20.00	20.00	
6.25	0.00	0.00	0.00	0.00	0.00	0.00	
Control	0.00	0.00	0.00	0.00	0.00	--	

Conc.: concentration. ---: no developed pupae or adults.

Table-2: Insecticidal activity (%) of Nerolidol against *S. littoralis* after treatment of newly moulted last instar larvae

Conc. (ppm)	Larval mortality	Pupal mortality	Adult mortality	Total mortality	Corrected mortality	LC$_{50}$ (ppm)
400.00	80.00	100.00	---	100.00	100.00	
200.00	70.00	33.33	50.00	90.00	90.00	
100.00	60.00	0.00	50.00	80.00	80.00	
50.00	50.00	0.00	20.00	60.00	60.00	42.24
25.00	30.00	0.00	0.00	30.00	30.00	
12.50	20.00	0.00	0.00	20.00	20.00	
6.25	0.00	0.00	0.00	0.00	0.00	
Control	0.00	0.00	0.00	0.00	--	

Conc. ---: see footnote of Table (1).

Table-3: Growth and development of *S. littoralis* after treatment of the newly moulted 5th instar larvae with Nerolidol

Conc. (ppm)	Larval instar									Pupal stage			Adult emergence (%)
	5th				6th								
	(mean mg ± SD)	Duration (mean days ± SD)	Growth rate (mean± SD)	Failure of ecdysis (%)	(mean mg ± SD)	Duration (mean days ± SD)	Growth rate (mean± SD)	Develop. Rate	Larval-pupal Inter. (%)	Pupation (%)	Pupal deformities (%)	Pupal duration (mean days ± SD)	
400.00	48.19±2.11 d	3.18±0.21 c	3.00±0.01 d	20.00	169.15±3.74 d	9.00±0.33 c	12.36±0.27 d	11.11	30.00	---	---	---	---
200.00	56.33±1.74 d	3.00±0.56 b	4.34±0.56 d	20.00	174.23±2.14 d	8.67±0.48 b	13.56±0.31 d	11.53	30.00	30.00	0.00	8.19±0.36 d	66.67
100.00	62.14±1.09 d	2.94±0.67 b	5.43±0.56 d	10.00	197.88±5.06 d	8.33±0.07 a	15.12±0.46 d	12.00	20.00	40.00	0.00	7.87±0.16 d	83.33
50.00	65.64±0.98 d	2.56±0.07 a	6.19±0.78 d	0.00	213.40±3.02 d	8.12±0.15 a	18.23±0.76 d	12.32	10.00	60.00	0.00	7.74±0.25 d	100.00
25.00	73.25±1.76 d	2.36±0.16 a	8.95±0.16 d	0.00	225.08±2.44 d	8.00±0.33 a	20.37±0.63 d	12.50	10.00	70.00	0.00	7.49±0.53 d	100.00
12.50	81.72±1.09 d	2.41±0.33 a	9.65±0.26 d	0.00	230.60±3.18 a	7.92±0.46 a	22.15±0.86 b	13.10	0.00	80.00	0.00	7.28±0.67 d	100.00
6.25	84.15±2.05 a	2.33±0.11 a	10.36±0.42 d	0.00	230.67±4.33 a	7.85±0.56 a	24.39±1.27 a	13.20	0.00	100.00	0.00	7.00±0.13 a	100.00
Control	86.19±2.71	2.31±0.48	12.49±0.53	0.00	230.68±2.55	7.81±0.67	25.27±0.56	12.82	0.00	100.00	0.00	6.87±0.33	100.00

Conc., ---: See footnote of Table (1). Develop. Developmental. Inter.: Intermediate. Mean ± SD followed with letter: a: insignificant (P >0.05), b: significant (P<0.05), c: highly significant (P<0.01), d: extremely significant (P<0.001)

Table-4: Growth and development of *S. littoralis* after treatment of the newly moulted 6th instar larvae with Nerolidol

Conc. (ppm)	Larval instar					Pupal stage			Adult emergence (%)
	Weight gain (mean mg ± SD)	Duration (mean days ± SD)	Growth rate (mean± SD)	Develop. Rate	Larval-pupal Inter. (%)	Pupation (%)	Pupal deformities (%)	Pupal duration (mean days ± SD)	
400.00	142.13±2.77 d	9.17±0.08 d	9.26±0.75 d	10.91	70.00	20.00	100.00	---	---
200.00	162.68±3.19 d	9.05±0.33 d	11.58±0.36 d	11.05	50.00	30.00	33.33	8.52±0.47 d	66.67
100.00	188.24±4.08 d	8.56±0.41 d	14.44±0.57 d	11.68	40.00	40.00	0.00	8.28±0.24 d	100.00
50.00	193.51±1.19 d	8.33±0.11 c	16.67±0.33 d	12.00	40.00	50.00	0.00	7.96±0.10 d	100.00
25.00	211.18±3.67 d	7.74±0.21 b	19.56±0.39 d	12.92	20.00	70.00	0.00	7.78±0.25 d	100.00
12.50	226.20±4.15 d	7.67±0.52 a	22.18±0.81 b	13.04	10.00	80.00	0.00	7.53±0.42 d	100.00
6.25	233.14±0.28 a	7.56±0.33 a	23.46±0.37 b	13.23	0.00	100.00	0.00	7.23±0.34 c	100.00
Control	234.28±2.01	7.20±0.63	25.27±0.56	13.89	0.00	100.00	0.00	6.87±0.33	100.00

Conc.: see footnote of Table (1). Develop.. Inter., a, b, c, d: see footnote of Table (3).

Fig-1: Failure of ecdysis of *S. littoralis* 5th instar larvae after treatment with higher concentrations of Nerolidol. (A): Normal 5th instar larva. (B) Normal 6th instar larva. (C, D, E, F & G): Various symptoms of incompletely moulted 6th instar larvae with old 5th instar cuticles and abdominal constrictions.
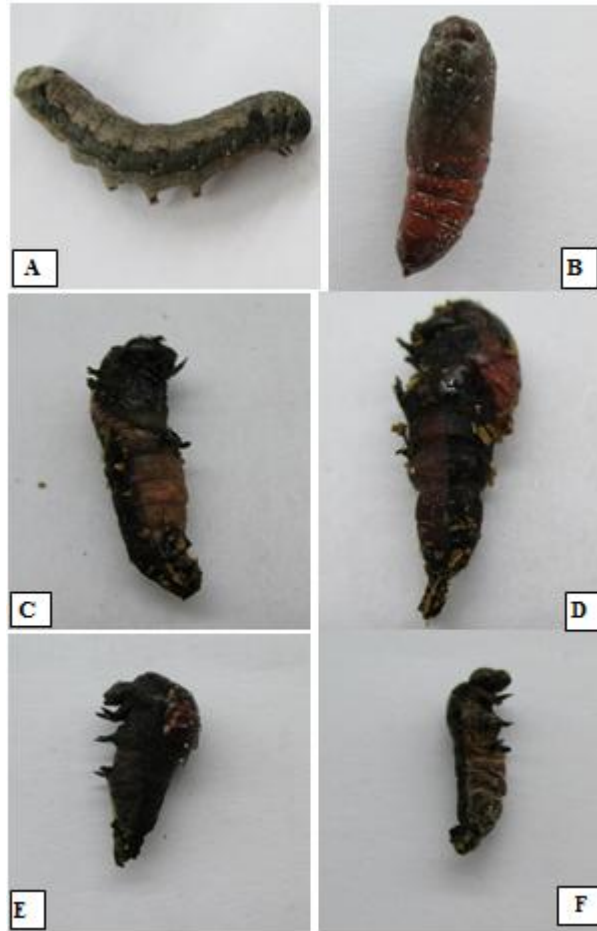
Fig-2: Larval-pupal intermediates of *S. littoralis* as features of disturbed metamorphosis program by Nerolidol, regardless the concentration or larval instar under treatment. (A) Normal last instar larva. (B) Normal pupa. (C, D, E & F): Various larval-pupal intermediates (pupal abdomen with larval thorax and head).
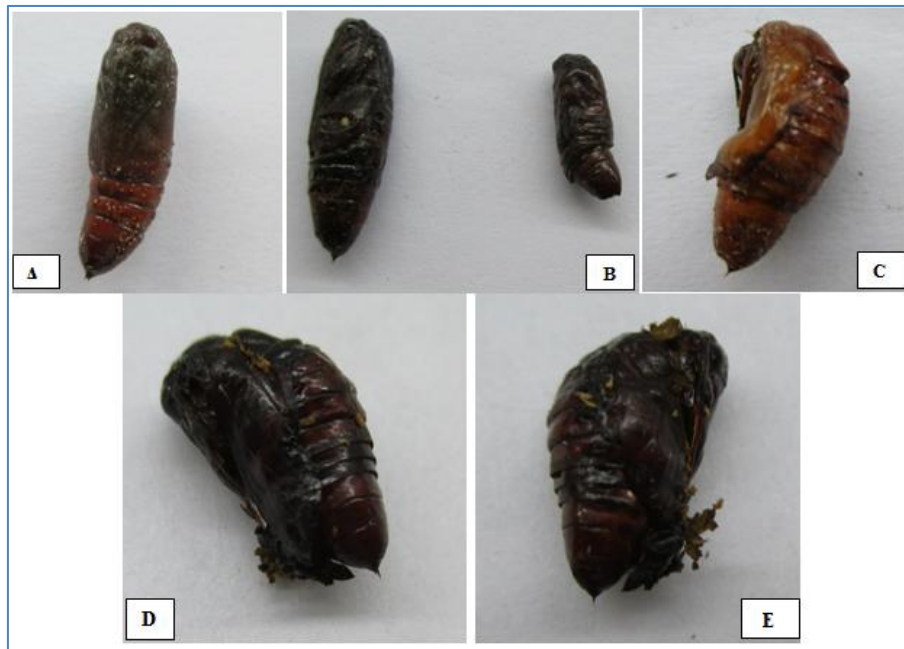
Fig-3: Pupal deformations of *S. littoralis* produced by Nerolidol after treatment of last instar larvae with higher concentrations. (A) Normal pupa. (B) Normal pupa (at left) and dwarf pupa with bent abdomen (at right). (C) Hump- back pupa. (D & E) Hump-back pupa with last larval cuticle attached to head and mouth parts

DISCUSION
Biopesticidal potential of nerolidol against *S. littoralis*

Different monoterpenes, phenylpropenes and sesquiterpenes had been reported to exhibit insecticidal activities against *Spodoptera littoralis* [20, 45, 56, 58, 89, 90]. For examples, 5,6-dihydroxy-3,4-7 trimethoxy flavones (isolated from *Artemisia maritima*) was found to be toxic against 2nd and 4th instar larvae of *S. littoralis* [91]. The *trans*-ethyl cinnamate, thymol, carvacrol, trans-anethole and piperitone revealed contact toxicities against the 3rd larval instar of *S. littoralis* [56, 89]. Also, γ-terpinene and terpinen-4-ol caused contact toxicities against the 4th larval instar of *S. littoralis* [56, 57] and (−)-carvone and 1,8-cineole showed strong contact toxicities against the 3rd larval instar of *S. littoralis* [58]. Toxicity of linoleic acid against the larvae of *S. littoralis* was reported by Yousef *et al*. [92]. Different isolated compounds from the essential oil of *Schinus terebinthifolius*, such as α-pinene, α-terpinene, β-ocimene, limonene, terpinen-4-olα-terpineol, citronellol, thymol and carvacrol had high insecticidal activities against *S. littoralis* [93, 94]. Pavela [89] evaluated the acute toxicity of 32 volatile compounds against 3rd instar larvae of *S. littoralis* and reported that α-pinene, *p*-cymene, γ-terpinene, thymol and carvacrol (applied at 300μg/larva) caused 100% mortality within 24 hr. As recorded by Pavela *et al*. [90], thymol, carvacrol, geranyl acetate, (E)-Nerolidol or phenolic monoterpenes showed significant toxic effects on larvae of *S. littoralis*. Recently, Abdelgaleil *et al*. [45] found Cuminaldehyde, (−)-carvone and 1,8-cineole as highly active toxicants against the 2nd larval instar of *S. littoralis*. Recently, also, Hamadah, *et al*. [78] treated the newly moulted larvae of 5th and 6th instar larvae of *S. littoralis* with seven concentrations of nerolidol. This sesquiterpene compound exhibited an adulticidal activity, only at the higher concentrations.

In addition to *S. littoralis*, various plant products had been reported to exhibit toxicities against different insects, such as Pogostone against *Spodoptera litura* and *Spodoptera exigua* [95]; Biostop Moustiques® against 4th instar larvae of susceptible and resistant strains of the mosquito *Anopheles gambiae* [96]; some sesquiterpene lactones and monoterpenoids against 4th instar larvae of the fly *Bradysia odoriphaga* [97]; carvacrol, (−)-α-bisabolol and chamazulene against *Diaphorina citri* [98]; some Sesquiterpene lactone compounds against *Spodoptera frugiperda* [99], as well as Azamax® was more toxic than the oils of *Melaleuca leucadendra* and (E)-nerolidol against *Tetranychus urticae*. However, the oils and (E)-nerolidol were more toxic to *Plutella xylostella* than Azamax® [77]. Also, Tang *et al*. [100] recorded a high toxicity of Concanavalin, a legume lectin, against the potato psyllid *Bactericera cockerelli*. Cinnamon oil and its components had the highest contact toxicity against *Drosophila suzukii*, whereas lemongrass oil, its main components,

and farnesol were less toxic, and geraniol was the least toxic [101].

Results of the present study were, to a great extent, in agreement with the previously reported results, because treatment of newly moulted penultimate (5th) instar larvae with nerolidol resulted in different mortalities of the treated larvae, only at the higher two concentrations. Moreover, the tested compound exhibited stronger toxicity against the successfully moulted last instar larvae while a weak toxic effect was exhibited on the developed pupae and emerged adult moths. In addition, treatment of newly moulted last (6th) instar larvae with nerolidol resulted in a considerable larval mortality, in a dose-dependent course. Also, this compound displayed a pupicidal effect only at the higher two concentrations. Nerolidol caused various degrees of toxicity against adults, only at the higher concentrations.

Also, the present results were in corroboration with some reported results of the insecticidal activity of another sesquiterpene compound, Farnesol, against various insects and mites [102, 103]. For examples, the (E,E)-α-Farnesene and a mixture of Farnesol isomers caused considerable toxicities against nymphs of the black bean aphid *Aphis fabae* and the peach potato aphid *Myzus persicae* [104]; Farnesol (isolated from *Stellera chamaejasma*) was recorded with remarkably insecticidal activity against the aphids *Aphis craccivora* and *Leucania separata* [105]; Awad [106] reported that Farnesol showed a significant dose-dependent increase in mortality of the black cutworm *Agrotis ipsilon* 4th instar larvae; the high dose of Farnesol reduced the survival of the nymphs of the red cotton stainer bug *Dysdercus koenigii* to 70% after 24h of exposure and increasing mortality during subsequent days [107]. Recently, Ghoneim *et al*. [108] recorded serious insecticidal activity of Farnesol against different development stages of *S. littoralis*. For the pure compounds (isolated from *Warburgia ugandensis* extracts), the larger grain borer *Prostephanus truncates* was most susceptible to polygodial and warbuganal which caused 64.3 and 61.7% deaths, respectively [109].

To interpret the insecticidal activity of nerolidol against *S. littoralis*, in the present investigation, some suggestions could be provided. The larval mortality may be attributed to the failure of larvae to moult owing to the inhibition of chitin synthesis [110, 111]. The larval mortality may be attributed to the inability of moulting larvae to swallow volumes of air for splitting the old cuticle and expand the new one during ecdysis [112]. Also, the larval deaths might be due to the prevented feeding and continuous starvation [113]. The pupal mortality in *S. littoralis*, in the current study, could be directly or indirectly relate to activities of nerolidol against some vital processes, such as suffocation, bleeding and desiccation owing to imperfect exuvation,

failure of vital homeostatic mechanisms, *etc.* [114]. The adult mortality of *S. littoralis* could be explained by the retention and distribution of nerolidol 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 [115].

Also, it may be important to explicate the toxicity of nerolidol, in the present work, leading to mortality of larvae, pupae and/or adults of *S. littoralis*, by its inhibition of Acetylcholinesterase (AchE), one of the most recognized insecticidal mechanisms, since many terpenoid compounds have been reported to inhibit AchE activity in insects resulting in death [116-119]. Moreover, toxicity of the tested Sesquiterpene compound, nerolidol, can be mediated through: i) inhibition of AchE activity which leads ultimately to impaired neurotransmission, ii) depletion of the activity of antioxidant enzymes leading to accumulation of Reactive oxygen species and peroxidation of membrane lipids and iii) Binding to octopamine receptors or GABA-gated chloride channels and iv) inhibition of cytochrome P450-mediated detoxification [120-122]. In addition, nerolidol might induce the apoptosis in *S. littoralis* midgut cells leading to death [100].

With regard to LC_{50} values of nerolidol against *S. littoralis*, in the current study, the tested compound was remarkably more toxic after treatment of last (6th) instar larvae than treatment of penultimate (5th) instar larvae. In other words, the last instar larvae were more susceptible to the insecticidal potency of nerolidol than the penultimate instar larvae. This result based on the LC_{50} values which were determined in 42.24 ppm and 50.01 ppm, respectively. A similar result was reported for the same insect by Ghoneim *et al.* [108] since Farnesol exhibited stronger insecticidal activity after treatment of 6th instar larvae (LC_{50} = 33.67 ppm) than treatment of 5th instar larvae (LC_{50} = 36.56 ppm). On the other hand, results of the current study on *S. littoralis* revealed that the 6th instar larvae were more sensitive to nerolidol than 5th instar larvae. The present result disagreed with many reported results on insects, in particular Lepidoptera, since the earlier larval instars had been recorded more sensitive to the toxicity of different plant compounds than the later larval instars. Unfortunately, there is no conceivable interpretation of this finding right now!! However, different LC_{50} values had been determined for various plant products against several insects. For examples, some naphtooquinone derivatives exhibited different toxicities on *S. littoralis* larvae and isovalerylshikonin was significantly more toxic (LD_{50} = 0.8μg/cm^2) than isobutyrylshikonin (LD_{50} = 7.3μg/cm^2) [19]. Farnesol exhibited toxicity against *A. craccivora* and *L. separata*, with LC_{50} values of 20.2 and 15.2 mg L^{-1}, respectively [105]. The plant compounds, 1-desacetylwilforgine, wilforgine, 1-desacetylwilforine and wilforine showed insecticidal activities to the 3rd

instar larvae of mosquito *Culex pipiens*, with LC_{50}= 25.70, 25.40, 22.58 and 14.57 μg/ml, respectively and to adults of *Musca domestica*, with LC_{50}= 87.29, 70.19, 47.80 and 21.00 μg g/ml, respectively [123]. Among eleven terpene ketones, thymoquinone exhibited the highest toxicity against adults of *Sitophilus zeamais*, with LC_{50}=16.5μg/cm^2 and LC_{50} 13.8 μL/L air (24hr after treatment) of contact and fumigant methods, respectively [124]. As reported by AlShebly *et al.* [125], epi-β-bisabolol showed high toxicity against the early 3rd instar larvae of the mosquito *Anopheles stephensi* (LC_{50}=14.68 μg/ml), the mosquito *Aedes aegypti* (LC_{50}=15.83 μg/ml) and the mosquito *Culex quinquefasciatus* (LC_{50}= 17.27 μg/ml). Baranitharan *et al.* [126] isolated Methyl 4-piperidineacetate among identified seven compounds in the ethanolic extract of *Punica granatum*. After treatment of 3rd instar larvae of the mosquito *C. quinquefasciatus*, LC_{50} was found to be 110.36 ppm. In a recent study of Benelli *et al.* [76], Phytol was the most effective against the aphid *Metopolophium dirhodum* (LC_{50}= 1.4 mL L^{-1}), followed by (E)-nerolidol (LC_{50}= 3.5 mL L^{-1}) and spathulenol (LC_{50} = 4.3 mL L^{-1}). It may be important to mention that the LC_{50} values depend on several factors, such as susceptibility of the insect and its treated stage or instar, lethal potency of the tested compounds or products and their concentrations, method and time of treatment or exposure, as well as the experimental conditions [108, 127].

Reduced weight gain and inhibited growth of *S. littoralis* by nerolidol

Some plant products were reported to reduce the weight of larval, pupal and adult stages of various insects [128]. In the present study on *S. littoralis*, a remarkable reduction of larval weight gain was recorded after treatment of 5th instar or 6th instar larvae with the sesquiterpene compound, nerolidol, in a dose-dependent course. This result was in agreement with many reported results of reduced larval body weight of *S. littoralis* after treatment with Farnesol [108] and Linoleic acid (= omega-6 fatty acid) [92] or allyl cinnamate 0.05% [129]. Feeding of *S. littoralis* larvae and the migratory locust *Locusta migratoria* nymphs on diet treated with Gibberellic acid (GA$_3$) resulted in remarkably reduced larval body weight in both insects [130]. In addition, feeding of *A. ipsilon* larvae on a food plant treated with Farnesol, the larval body weight was reduced [131]. The body weight gain of the lesser mealworm *Alphitobius diaperinus* larvae was reduced after feeding on diet treated with β-damascone (isolated from Bulgarian rose oil) or its synthetic derivatives γ- and δ-halolactones [132].

To explicate the reduction of weight gain of *S. littoralis* larvae after treatment with nerolidol, in the current study, the treated larvae might suffer gut alterations, suggesting that such larvae stopped feeding and consequently lost weight [4]. Another suggestion is

a post-ingestion toxic effect of nerolidol, causing poor utilization of food by these larvae or inhibiting important vital processes, causing the weight loss [133].

With regard to the growth, different plant products were reported to exhibit inhibitory effects on the growth of insect larvae [128]. In the present study, nerolidol was found a strong growth inhibitor against *S. littoralis*, after treatment of 5th instar or 6th instar larvae. This result was consistent with the reported results of inhibited growth of the same insect after treatment with different plant products. For example, some triterpenes caused growth inhibition of *S. littoralis* larvae, such as limonoids from *Khaya senegalensis*, *Chukrasia tabularis* and *Swietenia mahogany* [5, 134]. Various monoterpenes, phenylpropenes, sesquiterpenes and some terpenoid compounds showed inhibitory effects on the growth of *S. littoralis* [20, 54, 135, 136, 137]. Isobutyrylshikonin and isovalerylshikonin inhibited the growth of *S. littoralis* larvae [19]. After treatment of 5th or 6th instar larvae of *S. littoralis* with Farnesol, serious reduction of the larval growth rate [108]. Abdelgaleil *et al*. [45] evaluated the growth inhibitory activities of seven monoterpenes, two phenylpropenes and two sesquiterpenes on 2nd instar larvae of *S. littoralis*. All compounds drastically inhibited the growth of larvae. The cuminaldehyde, 1,8-cineole and eugenol were the most potent growth inhibitors.

Apart from *S. littoralis*, many studies recorded different inhibitory effects of various plant compounds on the larval growth of some insects. For examples, treatment of the early larvae of *S. frugiperda* with gedunin, photogedunin or Toosendanin resulted in the larval growth inhibition, in a dose-dependent course [138]. The growth inhibition in *Bactrocera cucurbitae* larvae was documented in dose-dependent course by Kaur and Rup [139] after treatment with Gibberellic acid (GA₃) or Coumarin, kinetin, GA₃ and 3-indoleacetic acid. Feeding of *S. litura* larvae on an artificial diet fortified with Miraculan resulted in suppression of larval growth [140]. Corzo *et al*. [141] recorded regressed growth rate of *S. frugiperda* larvae by feeding on some sesquiterpenoids. Szołyga *et al*. [142] showed that α- and β-thujone inhibited the growth of *A. diaperinus*. Treatment of *S. frugiperda* larvae with Jasmonic acid reduced the larval growth [143]. Treatment of 3rd instar larvae of *S. litura* with Alantolactone and isoalantolactone, and two eudesmane-type sesquiterpene lactones resulted in the inhibition of larval growth [144]. It was also reported that the eudesmane sesquiterpenes inhibited the growth of *S. frugiperda* [145]. Our result was in corroboration with the previously reported results but disagreed with few studies which recorded some inducing effects of certain plant compounds on the larval growth of some insects, such as cucurbitacin-C (an oxygenated triterpene) which had been appeared to promote the growth of *S. exigua* larvae [146].

The explication of growth inhibition of *S. littoralis* larvae by nerolidol, in the current study, could be provided as follows. The growth inhibition might be a result of the retardation and/or delay in release of certain peptides from neurohaemal organs, causing alteration in the hemolymph ecdysteroid and juvenoid titers [147].

Prolonged developmental durations and retarded developmental rate of *S. littoralis* by nerolidol

In the present study, a remarkably prolonged larval duration was recorded after treatment of 5th instar or 6th instar larvae with only higher three concentrations of the sesquiterpenoid compound, nerolidol. Also, the developed pupae lived significantly prolonged duration after treatment of 5th instar larvae with nerolidol. The compound exerted a strong suppressing action on the developmental rate, regardless the larval instar under treatment. These results were, to some extent, in agreement with many reported results of prolonged larval and/or pupal duration in different insects after treatment with some plant compounds, such as *S. littoralis* after treatment with 5,6-dihydroxy-3,4-7 trimethoxy flavone [91]; *A. ipsilon* after feeding on leaves sprayed with Farnesol [131]; *S. litura* larvae after feeding on an artificial diet fortified with Miraculan [140] and after treatment with higher concentrations of Alantolactone and isoalantolactone [144] or Erucin (4-Methylthiobutyl isothiocyanate) [148]; *Schistocerca gregaria* after feeding on clover leaves treated with Farnesol [102]; *Galleria mellonella* larvae after injection of Abscisic acid into the haemocoel [149]; *A. diaperinus* after feeding on diet treated with β-damascone or its synthetic derivatives γ- and δ-halolactones [41]. Recently, Ghoneim *et al*. [108] treated the 5th or 6th instar larvae of *S. littoralis* with Farnesol and recorded remarkably prolonged larval and pupal durations, in a dose-dependent course. In contrast, the present results disagreed with some reported results of significantly shortened larval and pupal durations after treatment with some plant compounds, such as *S. litura* and *S. exigua* after treatment with Pogostone [95] and the domestic mosquito *C. pipiens* after treatment with Saponin [150].

In the present study, prolongation of the larval and pupal durations and retarded development of *S. littoralis*, after larval treatment with nerolidol, could be interpreted by some scenarios. Nerolidol might indirectly interfere with the neuroendocrine organs responsible for the synthesis and release of tropic hormones, like prothoracicotropic hormone [151]. The final step of chitin biosynthesis pathway could be inhibited by nerolidol and the precursor was not converted into chitin for moulting leading to a prolongation of the developmental duration [152]. Also, the prolongation of larval duration might be due to reduced food intake, caused by phagodeterrence of nerolidol [153], or by a deviation of part of the taken food to the detoxification metabolism [154]. With decreased food ingestion and low biomass conversion,

the insect takes longer to reach the critical weight for ecdysis, leading to the prolongation of larval duration [133]. In addition, nerolidol might exhibit a delaying effect on the pupal transformation into adults [112]. In other words, the prolongation of pupal duration might be due to an elevated titer of juvenile hormone in the haemolymph. Only in the absence of JH in haemolymph, ecdysone could be activated and led to the production of the next stage [155].

Disrupted developmental program of *S. littoralis* by nerolidol
Ecdysis failure of larvae
The failure of larval ecdysis is a criterion of the disrupted developmental program in insects. Depending on the currently available literature, no information was found on this development criterion, as an effect of sesquiterpene compounds or other plant compounds, except a study of Ghoneim *et al*. [108] who reported that some 5th instar larvae of *S. littoralis* (20%) failed to completely moult into the next instar, after treatment only with the highest concentration level (400 ppm) of Farnesol. A similar result was recorded in the present study, since some percentages of the treated 5th instar larvae failed to completely moult into the 6th instar, only after treatment with the higher three concentrations of nerolidol. These 6th instar larvae were observed with rudimentary 5th instar exuvia and abdominal constrictions.

For the interpretation of this ecdysis failure of treated *S. littoralis* larvae, it may be important to mention that the moulting hormone "ecdysone" plays a key role in the shedding of old cuticle in a phenomenon called "ecdysis" or "moulting". Nerolidol might exhibit serious disturbances during larval moulting, indicating disruption of the function of larval endocrine system, thereby preventing completion of moulting [151]. For some detail, nerolidol might suppress the activity of ecdysone in larvae leading to the failure of moult and ultimately died [156, 157, 158, 159, 160]. On the other hand, failure of ecdysis of *S. littoralis* larvae, in the current study, may be attributed to an inhibitory effect of nerolidol on the chitin formation [6, 111] or to the inability of larvae to shed their exocuticle during ecdysis [112].

Production of intermediate creatures
Another feature of disrupted developmental program in insects is the production of larval-pupal or/and pupal-adult intermediates. The formation of some intermediates had been reported for different insect species as response to the disruptive effects of some botanicals [161, 162], such as *Tribolium confusum* after treatment of 5th instar larvae (production of larval-pupal intermediates) or 6th instar larvae or 0-hr-old pupae (production of pupal-adult intermediates) with 1μg/μl of Andrographolide (a terpenoid) [163]. Also, larval treatment of *S. litura* with the same plant compound led

to the production of larval-pupal intermediates, at all concentrations [164]. Recently, Ghoneim *et al*. [108] observed some larval-pupal intermediates after treatment of 5th instar or 6th instar larvae with Farnesol, in a dose-dependent course. Results of the present study on *S. littoralis* were, to a great extent, agreed with these reported results, since the treatment of 5th instar or 6th instar larvae of *S. littoralis* with nerolidol led to the production of some larval-pupal intermediates increasingly with the increasing concentration. Irrespective of the larval instar under treatment, the important features of these intermediates had been observed with pupal abdomen and larval head and thorax.

To explicate the production of larval-pupal intermediates in *S. littoralis* by nerolidol, in the present study, this sesquiterpene compound might interfere with the pupal moulting and development *via* the disturbance of hormonal regulation, such as the moulting hormone, leading to an ecdysteroid reduction [163]. However, it may be important to provide some suggestions for explicating this criterion of disrupted development program. (1) Nerolidol might inhibit the development program *via* the interference with the release of the neurosecretion [165]. (2) The production of these intermediates might indicate a juvenile hormone-like activity of nerolidol retarding the perfect larval-pupal transformation. (3) Nerolidol might interfere with the chitin biosynthesis and chitin synthase leading to moulting into non-viable forms between stages [166]. (4) The production of these mosaic creatures in *S. littoralis* may be explicated by an inhibitory effect of nerolidol on the DNA synthesis. (5) 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 non-viable forms between the stages [166]. Molts had been induced during the early phase of the last instar to produce larval-like individuals, while those formed in the late phase generate pupal-like individuals [167]. (6) Nerolidol might cause a misexpression of *br*-C which then leads to improper expression of one or more downstream effector genes controlled by *br*-C gene products. Symptoms of the impaired development, like larval-pupal intermediates, are the end results [168, 169].

Impaired metamorphosis of *S. littoralis* by nerolidol
Inhibited pupation
As reported by some studies, pupation rate of different insects was suppressed after treatment with plant extracts or plant-derived compounds [144, 148, 170]. In the present study, nerolidol exerted a strong inhibitory action on pupation, since pupation rate was regressed in a dose-dependent course, after treatment of 5th instar or 6th instar larvae. The pupation impediment increased proportional to the increasing nerolidol concentration. This result was in accordance with some reported results of inhibited pupation of some insects

after treatment with various plant products. For examples, treatment of the *S. frugiperda* larvae with doses 0.2-5.0µg/mL of eucalyptin, chrysin, eucalyptin, quercetin, luteolin, and betulinic and oleanolic acids considerably reduced the pupation [171]. Addition of alantolactone and isoalantolactone to the diet of 3rd instar larvae of *S. litura* significantly reduced the pupation% [144]. A reduction of pupation was recorded in *S. litura* after larval feeding on Miraculan-treated diet [140]. Also, reduction of pupation was observed in *G. mellonella* after injection of ABA into the larval haemocoel [149]. After treatment of 5th or 6th instar larvae of *S. littoralis* with Farnesol, the pupation rate was drastically suppressed [108].

To understand the regressed pupation rate of *S. littoralis*, in the current investigation, nerolidol might exert a suppressive action on the chitin synthesis and prevented the normal deposition of new cuticle during apolysis [172]. For some detail, nerolidol might exert an inhibitory action on the prothoracic gland (ecdysone-producing gland) and hence the ecdysone could not be synthesized and/or released. In other words, nerolidol might block the release of morphogenic peptides, causing disturbance in titers of both ecdysteroids and juvenoids [173]. Also, nerolidol might disrupt the ecdysteroid metabolism or might alternatively act directly to inhibit the release of ecdysis-triggering hormone [174]. In addition, reduction of the pupation rate of *S. littoralis* might be due to inhibitory effect of nerolidol on the synthesis of specific storage proteins in fat body during the last larval instar and their deposition at the time of pupation [175].

Blocked adult emergence
It is known from the literature sources that the adult emergence of different insects was completely or partially blocked by various plant extracts [170, 156, 176-180, 144, 181-183]. In the present study, nerolidol appeared to have a weak blocking potency on the adult emergence because partially blocked adult emergence was recorded only at the higher concentrations of Nerolidol, irrespective of the larval instar under treatment. The present result was in agreement with many reported results of significantly blocked adult emergence after larval treatment with some plant products or compounds, such as *S. littoralis* after treatment of 2nd instar larvae of *S. littoralis* with 5,6-dihydroxy-3,4-7 trimethoxy flavones [91] and after treatment of 5th or 6th instar larvae with Farnesol (Sesquiterpene compound) [108].

Apart from *S. littoralis*, significantly blocked adult emergence of *S. frugiperda* was recorded by Céspedes *et al.* [138] after treatment of the neonate larvae with gedunin, photogedunin epimeric mixture, photogedunin acetates mixture or Toosendanin, and Salazar *et al.* [171] after treatment with eucalyptin, chrysin, eucalyptin, and quercetin, luteolin, and

oleanolic acids. Also, partially blocked adult emergence of *T. confusum* was observed after treatment of 5th or 6th instar larvae with Andrographolide (a terpenoid) [163]. The adult emergence of *S. litura* and *S. exigua* had been blocked after larval treatment with Pogostone [95]. Blocked adult emergence of *H. armigera* and *S. litura* had been reported after treatment larvae with Flindersine (an alkaloid) [184]. Also, blocked adult emergence of *S. litura* was recorded after feeding of 2nd instar larvae on fresh food treated with Allyl isothiocyanate (an isothiocyanate) [180] or after treatment of 3rd instar larvae with alantolactone and isoalantolactone (sesquiterpenes) [144]. Djeghader *et al.* [150] reported a blocked adult emergence of *C. pipiens* after treatment of 4th instar larvae with Saponin. In addition, a similar result on *B. cucurbitae* was recorded by Kaur and Rup [139] after treatment the larvae with the plant growth regulators, Cn, kinetin, GA$_3$ and IAA. Among the pure compounds (isolated from *Warburgia ugandensis* extracts), polygodial and ugandensolide exhibited significantly higher blocking effects on adult emergence of the larger grain borer *Prostephanus truncates* [109].

Prior to the interpretation of blocked adult emergence of *S. littoralis*, in the present study, it may be important to mention that the adult emergence is a prerequisite process of the insect metamorphosis. This crucial physiological process has been regulated by the eclosion hormone. Disturbance of this hormone partially or completely arrest the adults to emerge [165]. For interpretation of the blocking of adult emergence after treatment of 5th or 6th instar larvae of *S. littoralis*, in the present study, nerolidol might exhibit a disturbing effect on the normal metabolism of insect hormones during the development of the immatures leading to failure of adult emergence. In particular, nerolidol might disturb the adult eclosion hormone release and/or inhibition of the neurosecretion [165, 185]. On the molecular basis, nerolidol might cause misexpression of certain genes, particularly the broodcomplex (*br-C*) transcription factor gene, leading to symptoms of impaired metamorphosis, like blocking of adult emergence [168, 169].

Perturbed morphogenesis program of *S. littoralis* by nerolidol
As reported in the current literature, plant extracts of different families or isolated plant compounds drastically affect the morphogenesis of pupae in several insects, as appeared in pupal deformities [158, 163, 186, 151, 171, 180, 160]. In the present study, nerolidol failed to exert anti-morphogenic action on *S. littoralis* after treatment of 5th instar larvae. On the other hand, treatment of 6th instar larvae with the higher two concentrations of nerolidol impaired the morphogenesis of some pupae. The malformed pupae developed with bent abdomens, hump-backs or with last larval exuvia attached to head and mouth parts. The present result was in corroboration with some reported results of

malformed pupae of different insects after treatment with various plant compounds, such as *S. littoralis* after treatment of 5th or 6th instar larvae of with Farnesol [108]; *S. frugiperda* after treatment of larvae with eucalyptin, chrysin, eucalyptin, quercetin, luteolin, and oleanolic acids [171] and *S. litura* after treatment of larvae with Andrographolide [164].

To explicate the disruption of pupation program in *S. littoralis*, in the present study, nerolidol might inhibit the chitin synthesis or/and might prevent the normal deposition of new cuticle during apolysis leading to the pupal deformities [172]. The anti-morphogenic effect of nerolidol might be due to the disturbance of release of ecdysteroids responsible for the form of developing pupae [138]. In this regard, nerolidol might block the release of morphogenic peptides, causing alteration in titers of juvenoids required for the perfect pupal transformation [173].

CONCLUSION

Depending on results of the present study, nerolidol exhibited considerably toxic effect on *S. littoralis*, caused serious reduction of larval weight gain and detrimentally inhibited growth and development; disturbed development program, remarkably suppressed pupation, partially blocked adult emergence, and deformed pupae. Therefore, nerolidol could be recommended as an eco-friendly alternative to synthetic insecticides for the management of this dangerous pest.

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