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Biological activity of andalin (flucycloxuron), a novel chitin synthesis inhibitor, on Red Cotton Stainer *Dysdercus koenigii* (Fabricius)

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Abstract
Toxicity and morphogenetic effects at different concentrations (0.1%, 0.05%, 0.025%, 0.01%, 0.005%, 0.0025%) of Andalin (Flucycloxuron) were evaluated topically on the dorsal surface against fifth instar nymphs of *Dysdercus koenigii* (Fabr.). The data showed that Andalin was found to be toxic at all the above mentioned concentrations, the LC_{50} and LC_{90} were found to be 0.012% and 0.094% respectively. At 0.1% concentration, adult emergence was inhibited completely with delayed metamorphosis, characterized by partial moulting and abnormal wing development. Whereas, at lower concentrations the apparently normal adults showed delayed reproductive effects such as lower fecundity and zero hatchability as compared to control batches. These results highlight the need for judicious use of the compound Andalin in the management of *D. koenigii* and other similar polyphagous pests.

Keywords: Andalin; Flucycloxuron; *Dysdercus koenigii*; LC_{50}; LC_{90}; Morphogenetic effects.

Introduction

The need to protect economically important crops from the ravage of phytophagous insects by ecologically acceptable methods has led to the development of alternate strategies for insect control using an array of targets (Von Keyserlingk *et al.*, 1985; Van Beek *et al.*, 1994). The use of conventional pesticides such as organochlorines, organophosphates and carbamates, has resulted in multifarious hazard problems like toxicity to humans, pollution, bioaccumulation, poisoning and teratogenic effects of residues and the development of pesticide resistance. The non-conventional insecticides such as plant-products, growth regulators, semio-chemicals, live pathogens can possibly cut down the use of pesticides. Moreover, they are effective in small quantities, persistent, broadly toxic to insect pests, and require little labor to apply them. Many of these chemicals are more or less insect-specific and are readily decomposed in the environment, majority damage the vital systems of insects but have lower mammalian toxicity (Mitsuhashi, 1995). Because of environmental concerns related to the use of conventional insecticides, agrochemical research has focused on the discovery of more selective compounds which interfere with pest insect growth and development (Dhadialla *et al.*, 2005). Insect growth regulators (IGRs) tend to be more compatible with the biological approaches, they are metabolic disruptors, molt inhibitors and behaviors modifiers of insects. IGRs can be grouped according to their mode of action as chitin synthesis inhibitors and substances that interfere with the action of insect hormone (i.e. juvenile hormone analogs, ecdysteroids) (Tunaz and Uygun, 2004). The chitin synthesis inhibitor benzoyl-phenyl-urea (BPU) insecticides prevent the moulting process by inhibiting chitin synthesis, thereby causing abnormal endocuticular deposition and abortive moulting reported by several authors in different insect orders. Karimzadeh *et al*. (2007) studied the effects of five CSIs viz., diflubenzuron, cyromazine, lufenuron, hexaflubenzuron and triflumuron on the second instar of the Colorado potato beetle, *Leptinotarsa decemlineata* (Say) (Coleoptera: Crysomelidae). Toxicity evaluation of Radiant SC 12% and hexaflumuron EC 10% against eggs of *Pectinophora gossypiella* (Saunders) (Lepidoptera: Gelechiidae) and biological effect of these compounds on larvae, pupae and adult emergence resulted from the treated eggs were reported (El-Barkey *et al*., 2009). The morphogenic and developmental responses of lufenuron and diofenolan were reported on *Musca domestica* (Linnaeus) (Diptera: Muscidae) (Ghoneim *et al.*, 2004). The effects of lufenuron (CGA-184699) were reported against *Lobesia botrana* (Denis and Schiffermueller) (Lepidoptera: Tortricidae) (Saenz-de-Cabezon *et al.,* 2006) and desert Locusta *Schistocerca gregaria* (Forskal) (Orthoptera: Acrididae) (Bakr *et al*., 2008). From the reviewed literature, the aim of the present study is to evaluate the efficacy of a chitin synthesis inhibitor, Andalin (Flucycloxuron) on the fifth instar nymphs of *D. koenigii* (Fabricius) (Hemiptera: Pyrrhocoridae) as an alternate insecticide, which can fit in to farmer's budget as well in Integrated Pest Management (IPM) programme.

Materials and Methods

Breeding and maintenance of stock culture of D. koenigii (Fabricius): The adults and nymphs of *D. koenigii* were collected from the Okra field located at/near the Aligarh Muslim University campus and brought to the laboratory for present research work. These insects were kept in glass rearing jars containing 3 cm thick layer of damp sterilized sand at the bottom. The jars were placed in REMI's Environmental Chamber maintained at 28±1°C temperature and 70-80% relative humidity. The jars were covered with a piece of muslin cloth tightly fixed by means of rubber band to stop the exit of an insect. The cultures were fed on overnight soaked cotton seeds, which were changed on alternate days. When the eggs were laid, the adults were transferred to fresh rearing jars to ward-off any hindrance during egg hatching. Over-crowding was avoided for proper growth of an insect.

Sampling of experimental insects: In the present work, 4^{th} instar nymphs of *D. koenigii* were sorted out and maintained in separate jars. They moulted to 5^{th} instar after 2-3 days and the moulting was ascertained by observing the cast off exuviae and the head capsule. The newly moulted 5^{th} instar nymph were then treated with different concentrations of the selected insecticide.

Preparation of different concentrations of the chemical used: The chemical name of Andalin is 1-{α-[(*EZ*)-4-chloro-α-cyclopropylbenzylideneaminooxy]-*p*-tolyl}-3-(2,6-difluorobenzoyl) urea (ratio 50–80% (*E*)- and 50–20% (*Z*)- isomers). Technical Andalin (1%) was obtained from Duphar B.V. (Weesp, Holland). The empirical formula is $C_{25}H_{20}C_lF_2N_3O_3$. Six concentrations of Andalin viz., 0.1%, 0.05%, 0.025%, 0.01%, 0.005%, 0.0025% were prepared from 1% stock solution of Andalin by serial dilution in acetone.

Methods for estimating moulting, metamorphosis, fecundity and hatchability: After applying each dose of the Andalin topically, nymphal mortality after 24 hrs and abnormality regarding moulting and metamorphosis were recorded. Parallel control in acetone of the corresponding instars and age was also maintained for comparison. The female bugs that emerged after different dose treatment were paired with untreated males of the corresponding age. Each pair maintained in controlled condition in separate rearing jars and was also provided with soaked cotton seeds. The number of eggs laid by each female was recorded and then the eggs were transferred in separate rearing jars having damp sterilized sand at the bottom. Parallel control was also kept consisting males and females emerged from the control nymphs. The hatched and unhatched eggs were counted and percent hatchability was recorded.

Statistical analysis: The data is expressed as Mean±SE based on four replicates. The data so obtained was subjected to probit analysis as described by Finney (1971). Test of significance was performed at 1% level.

Results

Effects on survival rate and mortality: The mean of the total nymphal mortality and adult mortality by the application of different concentrations of Andalin (flucycloxuron) on 5^{th} instar nymphs of *D. koenigii* along with control (acetone) and untreated insects is given in Table 1. The highest concentration i.e. 0.1% Andalin gave 21% nymphal mortality after 24 hours of treatment and 96% total mortality up to adult emergence. The survived 4% adults died with malformed wings. The lowest concentration (0.0025%) showed only 3% mortality after 24hrs of the treatment and the total mortality before adult emergence with 0.0025% Andalin was 23%. Fig 1 shows the regression between concentration strength and nymphal death of 5^{th} instars which yield a positive linear correlation ($y = 167.66x + 5.4542$, $R^2 = 0.9013$). The mortality during 5^{th} instar nymph-adult moult was quite high i.e. 94.94%, 76.47% and 56.82% at concentrations of 0.1%, 0.05% and 0.025% Andalin respectively and the concentration v/s mortality during fifth to adult moult showed (Fig 2) a linear positive correlation ($y = 729.12x + 29.413$, $R^2 = 0.9053$). The LC_{50} and LC_{90} values of Andalin during 5^{th}-adult moulting were found to be 0.012% and 0.094% respectively (Table 1). The nymphal mortality of *D. koenigii* with the application of Andalin was found to be dose-dependent. The mean total mortality of the control insects up to adult emergence was only 6% and is more than the mortality of untreated batch (2%) which may be due to acetone irritability (Table 1). Fig 3 shows the regression between concentration v/s total mortality up to adult emergence which yields positive linear correlation (y = 702.43x + 33.797, R^2 = 0.8739). The lowest dose of Andalin (0.0025%) produced maximum number of adults i.e. 77% whereas the highest dose produced only 4%. Out of the 77% adults formed at lowest concentration, 18.18% were malformed and rest 81.82% showed no morphogenic abnormalities. The regression between concentration v/s malformed adults showed positive linear correlation (y = 793.11x + 25.161, R^2 = 0.9563) (Fig 4).

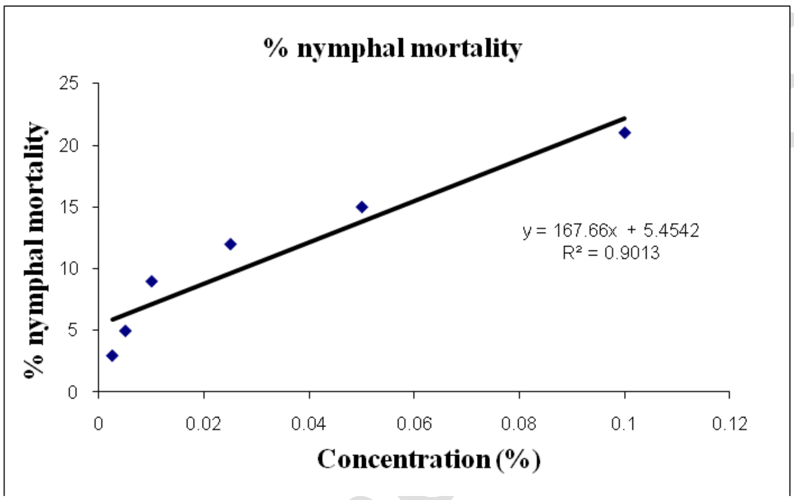


Fig 1. Showing % nymphal mortality at different concentrations of Andalin on the 5th instar nymphs of *D. koenigii.*

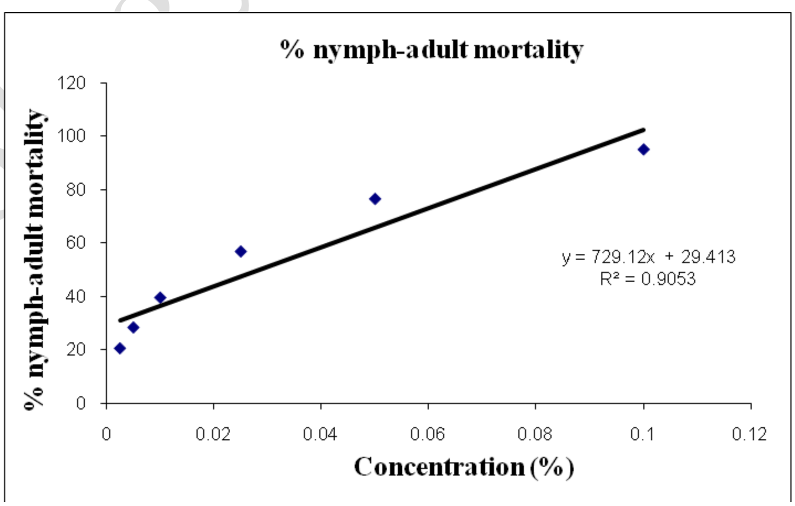


Fig 2. Showing % nymph-adult mortality at different concentrations of Andalin on the 5th instar nymphs of *D. koenigii.*

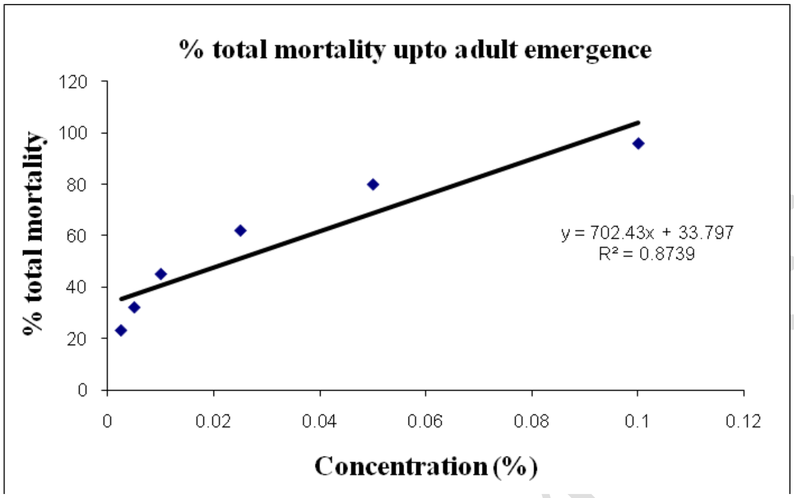


Fig 3. Showing % total mortality before adult emergence at different concentrations of Andalin on the 5th instar nymphs of *D. koenigii.*

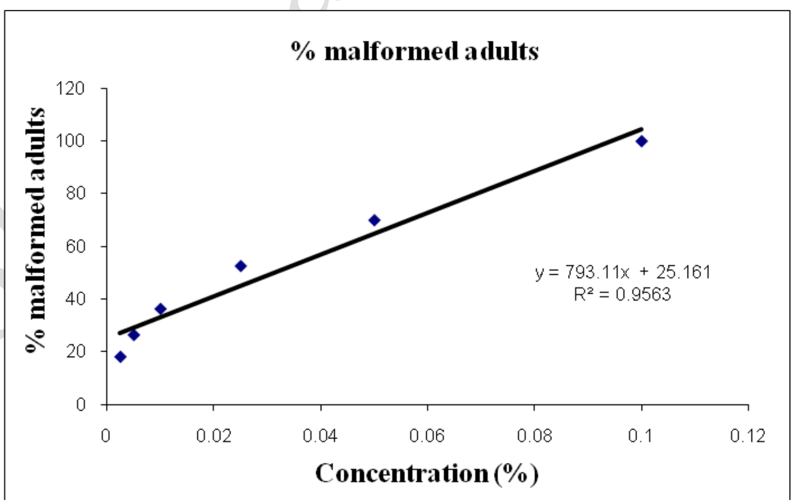


Fig 4. Showing % total malformed adults with Andalin treatment on the 5th instar nymphs of *D. koenigii.*

Table 1. Showing nymphal mortality and adult malformation following the topical application of different concentrations of Andalin on freshly moulted (12-16 hours) 5th instar nymphs of *D. koenigii.*

Concentration (%)	Mortality after 24 hrs of 5th instar nymphs Mean±SE	Mortality during 5th-adult moult Mean±SE	Total mortality upto adult emergence Mean±SE (% mortality)	Total number of adult emerged Mean±SE (% total adult emerged)	Number of adult with malformed wings Mean±SE (% malformed adults)	Total number of normal adults formed Mean±SE (% normal adults formed)
0.1	5.25±0.25	18.75±0.25	24.00±0.00 (96)	1.00±0.00 (4)	1.00±0.00 (100)	Nil (0)
0.05	3.75±0.25	16.25±0.61	20.00±0.41 (80)	5.00±0.41 (20)	3.50±0.50 (70)	1.50±0.64 (30)
0.025	3.00±0.41	12.50±0.50	15.50±0.28 (62)	9.50±0.28 (38)	5.00±0.41 (52.63)	4.50±0.29 (47.37)
0.01	2.25±0.25	9.00±0.41	11.25±0.25 (45)	13.75±0.25 (55)	5.00±0.41 (36.36)	8.75±0.48 (63.64)
0.005	1.25±0.25	6.75±0.25	8.00±0.41 (32)	17.00±0.41 (68)	4.50±0.28 (26.47)	12.50±0.64 (73.53)
0.0025	0.75±0.25	5.00±0.41	5.75±0.47 (23)	19.25±0.47 (77)	3.50±0.28 (18.18)	15.75±0.63 (81.82)
Control (Acetone)	1.25±0.25	0.25±0.25	1.50±0.28 (6)	23.50±0.28 (94)	0.50±0.28 (2.13)	23.00±0.58 (97.87)
Untreated	0.25±0.25	0.25±0.25	0.50±0.28 (2)	24.50±0.28 (98)	0.00±0.00 (0)	24.50±0.29 (100)

Note: 100 insects treated in 4 replicates of 25 each.

Effect on moulting and metamorphosis: The bar diagram (Fig 5) represents the mortality during 5th–adult moult of Andalin treated 5th instar nymphs which is in the order of 0.1%>0.05%>0.025>0.01>0.005>0.0025%. The mortality during 5th instar nymph to adult moult is due to incomplete or partial moulting and finally death of the intermediate within 24-48 hours of moulting (Fig 7-12). The 5th instar nymphs which died also showed some dose-dependent morphogenic abnormality such as shrunk abdomen (Fig 6-A) or swollen abdomen (Fig 6-B). The malformation during 5th–adult moulting with 0.1% Andalin treated 5th instar nymph is shown in Fig 7 (A and B). The deformity includes incomplete moulting which is characterized by old cuticle (exuviae) attached to the last few segments of the abdomen, legs, proboscis, antennae etc., also the body was deformed (Fig 7-B). In the lower concentrations of Andalin i.e., 0.05%, 0.025% and 0.01%, partial moulting occurred where the exuviae failed to detach from the lower region of the body. The body did not curve too much as in case of higher concentrations, only slightly deformed body was seen (Fig 8-A, 9-A, 10-A). Abnormality of wings which includes crumpled wings also occurred (Fig, 8-B, 9-B & 10-B). At a concentration of 0.005 % Andalin, the exuviae remained attached only to the legs (Fig 11-B), Fig 11-A shows crippled, totally damaged hind wings which are extremely reduced in size with the treatment of 0.005% Andalin. In case, where complete ecdysis occurred, different types of wings and legs abnormality were observed. With the application of 0.0025% Andalin, the adults showed wings and legs deformation (Fig 12-B). The forewings and hind wings were crumpled and reduced in size as compared to the normal adult. Also, the deformity of the legs was seen and sometimes the legs became either straight or curved whereas in normal adults the legs are bent at a certain angle.

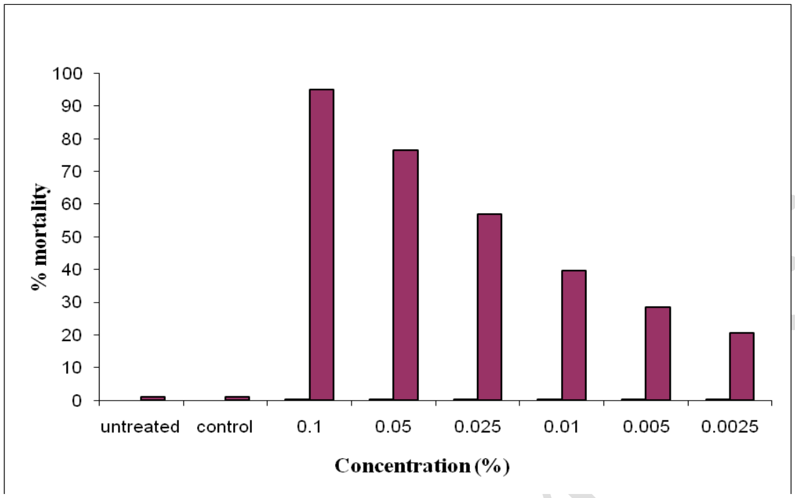
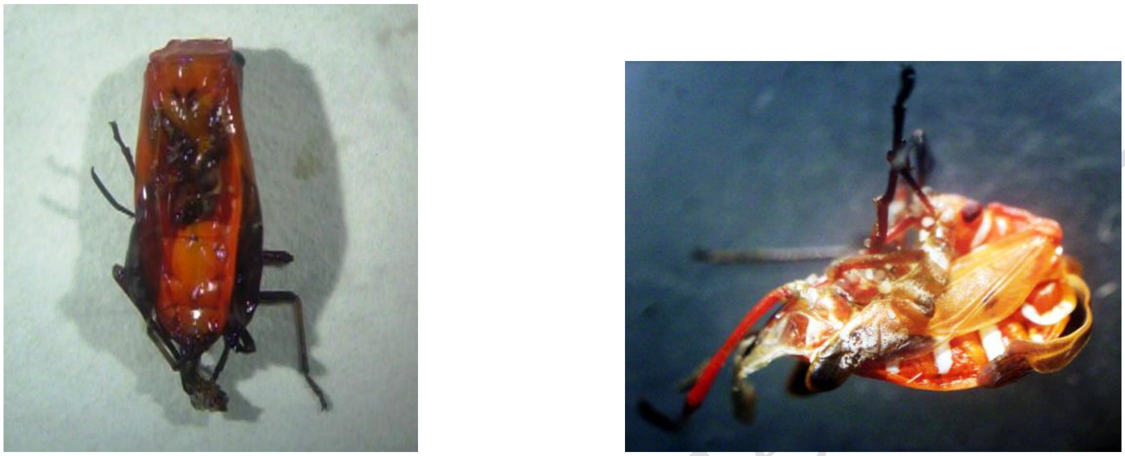


Fig 5. Showing % mortality during nymphal-adult moult with Andalin treatment at different concentrations on 5th instar nymphs of *D. koenigii.*

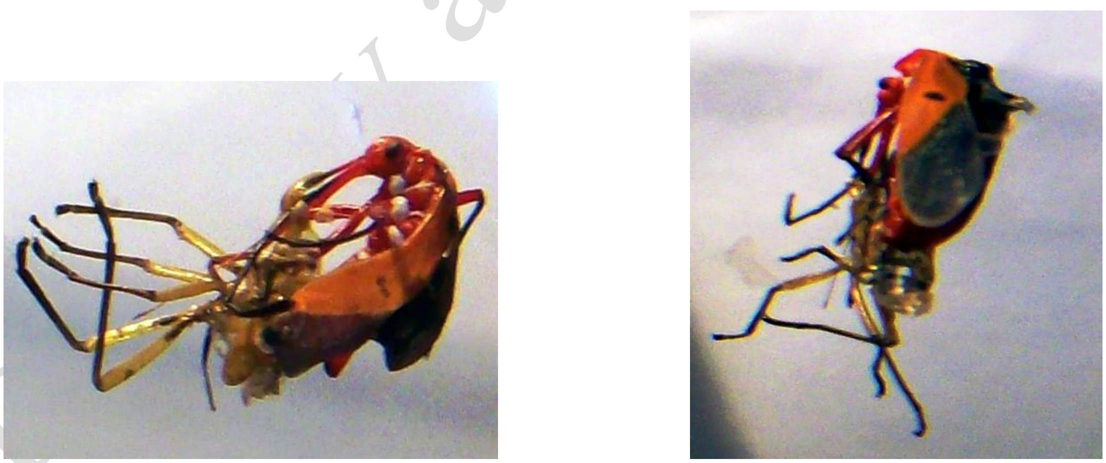
A B

Fig 6A-6B. Showing nymphal abnormality after 24 hrs of Andalin treatment at varying concentrations on 5th instar nymphs of *D. koenigii*.



A B

Fig 7A-7B. Showing malformation during 5th-adult moult with 0.1% Andalin treatment on 5th instar nymphs of *D. koenigii.*



A B

Fig 8A-8B. Showing malformation during 5th-adult moult with 0.05% Andalin treatment on 5th instar nymphs of *D. koenigii*.

A

B

Fig 9A-9B. Showing malformation during 5th-adult moult with 0.025% Andalin treatment on 5th instar nymphs of *D. koenigii*.

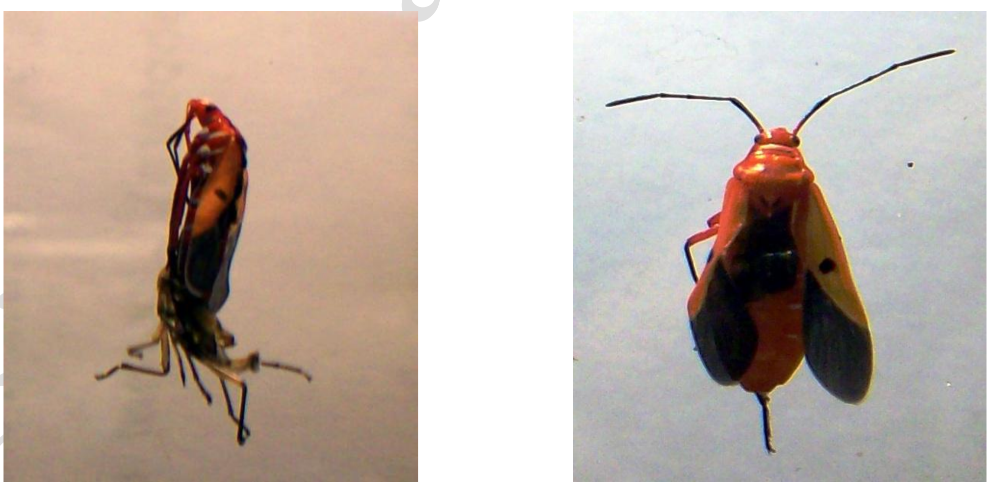
A

B

Fig 10A-10B. Showing malformation during 5th-adult moult with 0.01% Andalin treatment on 5th instar nymphs of *D. koenigii*.

A B

Fig 11A-11B. Showing malformation during 5th-adult moult with 0.005% Andalin treatment on 5th instar nymphs of *D. koenigii*.



A B

Fig 12A-12B. Showing malformation during 5th-adult moult with 0.0025% Andalin treatment on 5th instar nymphs of *D. koenigii*.

Effects on fecundity and hatchability: At 0.1% Andalin concentration, only 4% adult emerged which possessed malformed wings and legs and died within 24 hours of emergence that is why no mating occurred and hence no fecundity. In case with 0.05 % and 0.025 % Andalin treatment, normal adult emergence was only 30% and 47.37% respectively. In the former dose (0.05%), the apparently normal adults thus formed could not survive more than 24-48 hours and during this period no mating occurred and ultimately no oviposition. Whereas, in the latter concentration (0.025%) though normal adults mated but they failed to lay eggs and died within 4-5 days. Therefore, no fecundity was recorded in the females emerged from 5th instar nymphs treated with 0.1%, 0.05% and 0.025% Andalin. At lower concentrations of Andalin i.e. 0.01%, 0.005% and 0.0025%, an average of 27.75±1.25, 38.74±0.85 and 47.75±1.70 number of eggs were laid as compared to control and untreated females which laid an average of 132.25±0.85 and 144.25±1.49 eggs respectively (Table 2). The reduction in the fecundity was highly significant at 0.01% ($t=8.2929$, $P<0.01$), 0.005% ($t=10.4641$, $P<0.01$) & 0.0025% Andalin ($t=8.1319$, $P<0.01$). The average number of eggs laid by the females emerged from 0.01% Andalin treated 5th instar nymphs dropped to a quarter (approximately) of the control and about one-fifth of the untreated. The females emerged from the lowest concentration (0.0025%) of Andalin treated 5th instar nymphs also showed more than half and one-third decrement in the average number of eggs laid as compared to controlled and untreated fecundity respectively.

Table 2. Showing fecundity and hatchability of female emerged from the treated 5th instar nymphs of *D. koenigii* with Andalin.

Concentration (%)	Number of eggs laid (Mean±SE)	Number of eggs hatched (Mean±SE)	% hatching
0.1	Nil	Nil	Nil
0.05	Nil	Nil	Nil
0.025	Nil	Nil	Nil
0.01	27.75±1.25	Nil	Nil
0.005	38.75±0.85	Nil	Nil
0.0025	47.75±1.70	Nil	Nil
Control (Acetone)	132.25±0.85	127.50±2.50	96.41
Untreated	144.25±1.49	141.50±1.26	98.09

Discussion

Insect growth regulators are bio-rational compounds that are species-specific and highly selective in action (Staal, 1975) and act by disrupting the normal development of several species of insects (Henrick *et al.*, 1973). The effects of these Insect growth regulators, more precisely, the chitin synthesis inhibitors which interfere with chitin biosynthesis in insects (Post and Vincent 1973; Post *et. al.*, 1974; Deul *et al*., 1978; Hajjar and Casida, 1978; Gijswijt *et al.,* 1979) have been worked out on a number of species of insect pests. The results of these studies revealed that there is a wide range of responses and susceptibility with respect to different insect species against a chitin synthesis inhibitor. Thus, it becomes inevitable to find out the most effective chemicals against particular species of insect pests which do not adversely affect the environment and are also bio-degradable. In the present investigation, six concentrations (0.1%, 0.05%, 0.025%, 0.01%, 0.005% and 0.0025%) of Andalin (Flucycloxuron) which is a chitin synthesis inhibitor were tested topically on the 5th instar nymphs of *D. koenigii* (F.). Different concentrations resulted in different mortality rate after 24 hours of the treatment. The Andalin treated nymphs of *D. koenigii* showed varying degree of inhibitory and delayed effects. The morphogenetic effects of flucycloxuron (Andalin) to *D. koenigii* include incomplete moulting, deformed nymphs and adults with exuviae attached to the body and varying degree of wing growth inhibition. In another study, the efficacy of Flucycloxuron, Diflubenzuron and Halofenozide was tested and it was reported that flucycloxuron was the most toxic chitin synthesis inhibitor against *Tenebrio molitor* (Linnaeus), also the adult showed highest absorption through the cuticle for flucycloxuron among the three chitin synthesis inhibitors (Soltani *et al*., 1993; Chebira *et al.,* 2006). The growth inhibitory effects of flucycloxuron have also been demonstrated in non-insect species, a ciliated protist, *Paramecium* sp. (Rouabhi *et al.,* 2005). In the present study, the Andalin treated nymphs of *D. koenigii* showed moulting inhibition and in the attempt to moult from nymph-adult mortality occurred. They failed to ecdyse due to inhibition of the synthesis of new cuticle. Diflubenzuron, for instance, when directly applied to *Mandusa* epidermal cells in vitro, inhibited endocuticular deposition. Three sites have been proposed for describing the mode of action of diflubenzuron and other chitin synthesis inhibitors namely: inhibition of chitin synthetase (or its biosynthesis), inhibition of proteases (or its biosynthesis) and inhibition of UDP-N-acetylglucosamine transport through the membrane (Miyamoto *et al.,* 1993). Earlier, reports showed that the release of UDP-N-acetylamine from the epithelial cells was inhibited by diflubenzuron (Mitsui *et al.,* 1984). Further, it was suggested that the compound interferes with the transport system of UDP-N-acetyl amine across the membrane (Eto, 1990).

It is concluded that Andalin treated 5^{th} instar nymphs of *D. koenigii* with different concentrations showed mortality, moulting abnormality and nymphal and adult malformation. Thus, Andalin can be recommended for use as an effective insect growth regulator in IPM modules for this pest.

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