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Full Paper

Insecticidal activity of some 3, 5-pyrazolidinedione derivatives against cotton leaf worm, *Spodoptera littoralis* (Boised.) (Lepidoptera: Noctuidae)

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Abstract

Four 3,5-pyrazolidinedione derivatives namely, 4-(4`-chlorobenzylidene)-1-phenylpyrazolidine-3,5-dione (1), 4-(4`-nitrobenzylidene)-1-phenylpyrazolidine-3,5-dione (2), 2'-(4-chlorophenyl)-1-phenyl-3,5-dioxo-1,2,3,5 tetrahydrospiropyrazole-4,3' oxirane (3) and 2'-(4-nitrophenyl)-1-phenyl-3,5-dioxo-1,2,3,5 tetrahydrospiropyrazole-4,3' oxirane (4) were prepared in pure state and bioassayed against 2nd and 4th instars larvae of cotton leaf worm, *Spodoptera littoralis* (Boised) (Lepidoptera: Noctuidae) using feeding and dipping bioassay. The results of bioassays indicated that title compounds exhibit satisfactory insecticidal activities. Among those, compound (1) exhibit the highest insecticidal activities against 2nd instar larvae, with LC_{50s} 3.23 and 0.619 mgL^{-1} for feeding, and 36.04 and 28.69 mgL^{-1} for dipping, after 48 and 72 h treatment. According to the toxicity index the compound (1) showed the highest larvicidal activity against 4th instar larvae with LC_{50s} 141.33 and 76.12 mgL^{-1} for feeding larvae, and 26.94 and 12.29 mgL^{-1} for dipping larvae after 48 and 72 h treatment. These results showed that, the 2nd larvae was more susceptible than 4th instars larvae to these compounds. In addition, the insecticidal activity of these compounds was

more effective on cotton leaf worm larvae in feeding bioassay as compared with the dipping treatment. The rest of the tested compounds possessed moderate to strong larvicidal activities against cotton leaf worm. In general, the results indicate the possible use of 3,5-pyrazolidinedione derivatives as components in integrated pest management program against *S. littoralis*.

Keywords: 3,5-pyrazolidinedione, chlorantraniliprole**;** cotton leaf worm, toxicity

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1. Introduction

The cotton leaf worm, *Spodoptera littoralis* (Boised.) (Lepidoptera: Noctuidae) is one of the most serious injuries insect pests on field crops as well as horticultural crops in greenhouse or open field in Egypt and on the most Mediterranean countries [1,2]. Consequence, the continued application of traditional pesticides for controlling this pest can often lead to the development resistance, thus bringing about enormous losses in crop production. In recent years, several insecticidal phthalic diamides (fluobendiamide, chlorantraniliprole and cyantraniliprole), [2-6] which act on the ryanodine receptor, [7-9] were discovered and commercialized, however, their insecticidal spectrum is limited. Recently, a chlorantraniliprole skeleton was found to be very significant in the discovery of novel insecticides and several modifications around its structure have been industry [10, 11]. This class of insecticides are effectively control lepidopterous insects such as cotton leave worm, especially insects that have developed resistance to older classes of insecticides [12].

Derivatives of 3,5-pyrazolidinedione posses good insecticidal activities, their substructural units are widely used in pesticide design. They are always regarded as lead compounds for the development of novel bioactive structures and widely used as insecticide [7, 13]**.** The hydrazone group is a highly efficient pharmacophore that is widely used in pesticide design. An example of such a pesticide is hydramethylnon [6, 14] the first insecticide containing a hydrazone moiety, which was commercialized in 1980. Many hydrazone derivatives with broad-spectrum activities have been reported as insecticidal agents, [15] including metaflumizone, which was discovered by BASF and commercialised in 2007 [16]. More recently, [17] described a series of substituted hydrazone derivatives possessing good activities against *Spodoptera litura* (Fabricius). **Liu**

et al. [18] also reported several hydrazone derivatives exhibiting good insecticidal activities after modification of the fluobendiamide group.

This study aimed to evaluate and compare the toxicity effects of 3,5-pyrazolidinedione derivatives and chlorantraniliprole against the 2nd and 4th instars larvae of cotton leaf worm, *S. littoralis* hoping to obtain compounds with more potency, low insect resistance and no environmental pollution.

2. Materials and methods

2.1. Chemistry

Four compounds were chosen in **Figure 1** to evaluate their activity as insecticides and compare with chlorantraniliprole against the 2nd and 4th instars larvae of cotton leaf worm, *S. littoralis*.

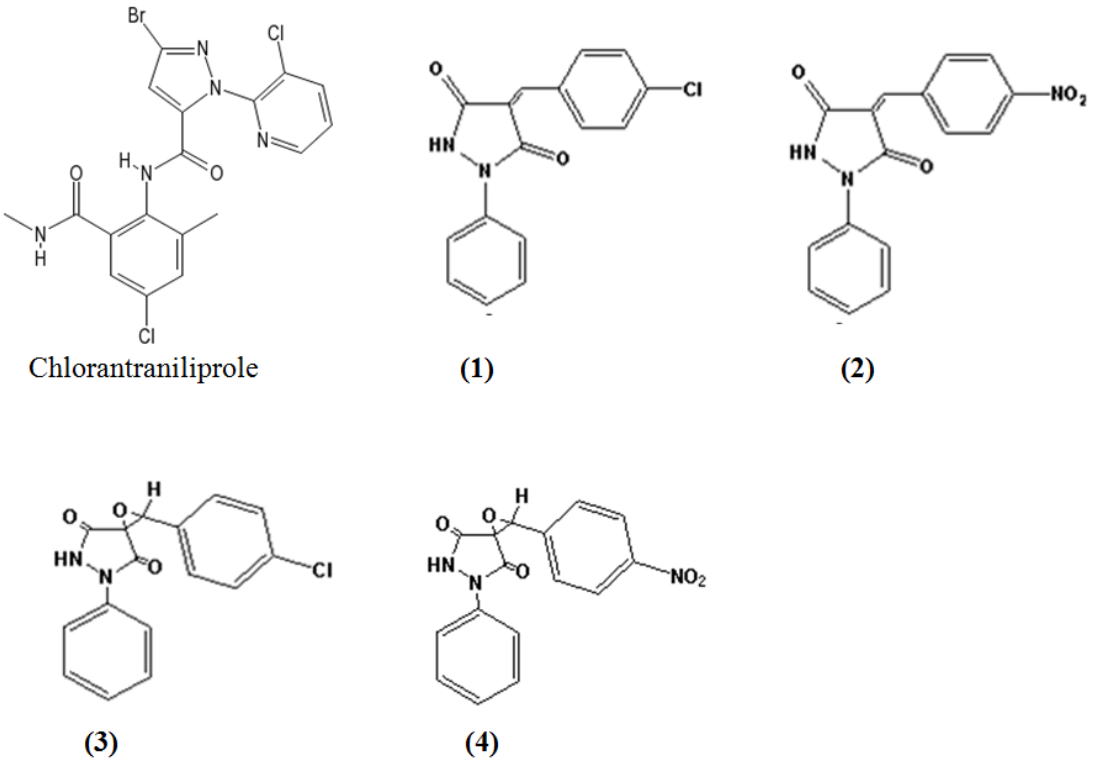


Figure 1. Chlorantraniliprole and the synthized 3,5-pyrazolidinedione derivatives, 4-(4`-chlorobenzylidene)-1-phenylpyrazolidine-3,5-dione **(1)**,4-(4`-nitrobenzylidene)-1-phenylpyrazolidine-3,5-dione **(2)**, 2'-(4-chlorophenyl)-1-phenyl-3,5-dioxo-1,2,3,5 tetrahydrospiropyrazole-4,3' oxirane **(3)** and 2'-(4-nitrorophenyl)-1-phenyl-3,5-dioxo-1,2,3,5 tetrahydrospiropyrazole-4,3' oxirane **(4)**.

2.2. Insects

Strain of cotton leaf worm, *S. littoralis* used in this study was maintained in Plant Protection Laboratory, Faculty of Agriculture, Assiut University, Egypt for more than fifteen years without exposure to insecticides. It is reared on castor leaves as described by [19].

2.3. Laboratory bioassay

The insecticidal activities of the title compounds against the 2nd and 4th of cotton leaf worm were tested by feeding and dipping larvae bioassay methods [20]. Reported here are the results of laboratory tests to determine the concentrations of these chemical compounds which are required to kill 50% (LC_{50}) of 2nd and 4th of cotton leaf worm with a modification in the toxicity tests. Six concentrations of aqueous solution of each compound plus 0.05% Triton X-100 as a surfactant were used.

Feeding bioassay: In the feeding bioassay, 2nd and 4th instar larvae of cotton leaf worm were used. Serial concentrations of chlorantraniliprole (Coragen© 20% SC was produced by DuPont™ de Nemours Co.) and compound 1-4 were prepared using TritonX-100 (0.05 %) as detergent and tap water as solvent. Parts of castor bean leaves were dipped for 10 s in each concentration to be tested and then transferred to Petri-dishes containing filter paper for half an hour where the treated leaves were allowed to dry. Selected larvae were allowed to feed for 24 h on the treated leaves and then allowed to feed for another 24 and 48 h on untreated fresh leaves.

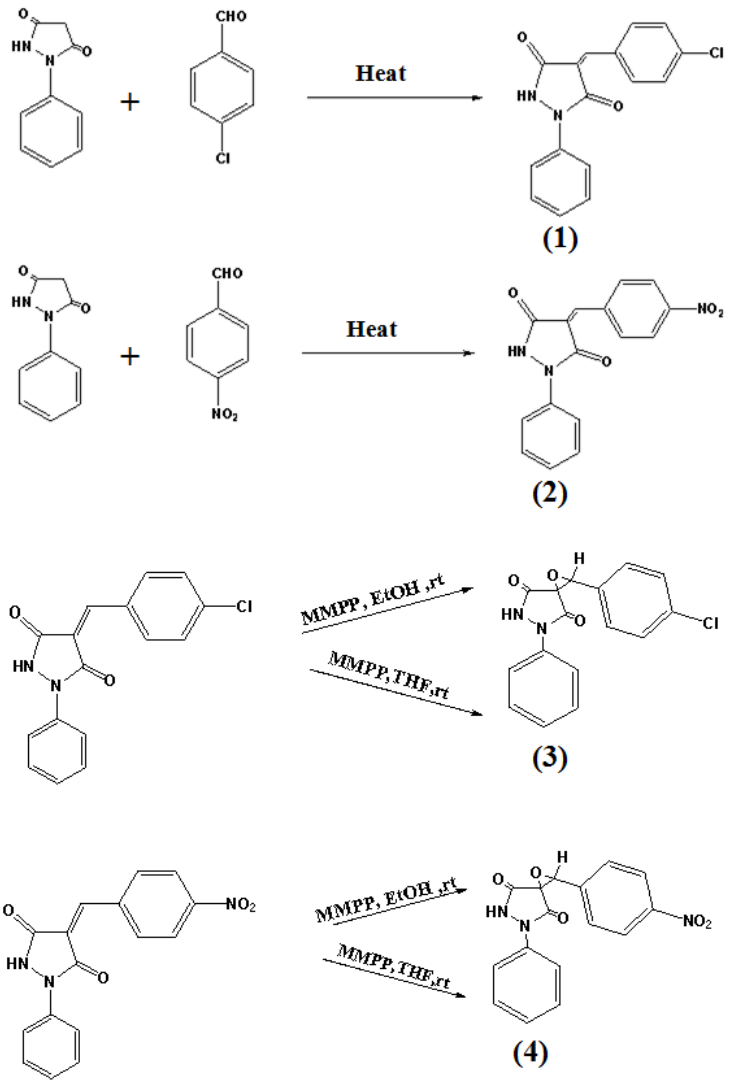
Dipping larvae bioassay: Serial concentrations of chlorantraniliprole and compound 1-4 were prepared. A total of 20 2nd and 4th instar larvae of cotton leaf worm, nearly of the same size, were dipped for 10 s in each concentration three times. The treated larvae were allowed to dry at room temperature for about 0.5 h. Control batches of larvae were similarly dipped in a solution of distilled water plus 0.05% Triton X-100. After the treated batches of larvae had dried, they were individually transferred to Petri dishes (9 cm diameter) and held for 24 h at 22 ± 2 °C, 60 ± 5% relative humidity and photoperiod of 12:12 (light/ dark). Larvae mortality was recorded 48 and 72 h after treatment. The larva was considered dead if no movement was detected when it was touched with a small brush. The toxicity experiment of each compound was repeated twice and the results were corrected by **Abbott's** formula [21]. Median lethal concentrations (LC_{50}) and slope values of chemical compounds were determined by the Probit regression analysis using the software SPSS (Version 16.0 for windows, SPSS Inc., Chicago, the USA) and expressed as parts per million mgL^{-1} (ppm) [22]. Toxicity ratio is defined as the ratio of chlorantraniliprole's LC_{50} value for baseline toxicity and the compounds' LC_{50} value.

3. Results and discussion

3.1. Synthesis

The synthetic procedures for the title compounds are outlined in **Scheme1** [23].The

structure of the synthesized compounds wass spectral and elemental analyses [23]. elucidated and confirmed on the basis of their



Scheme 1. Synthesis of the 3,5-pyrazolidinedione derivatives, 4-(4`-chlorobenzylidene)-1-phenylpyrazolidine-3,5-dione **(1)**, 4-(4`-nitrobenzylidene)-1-phenylpyrazolidine-3,5-dione **(2)**, 2'-(4-chlorophenyl)-1-phenyl-3,5-dioxo-1,2,3,5 tetrahydrospiropyrazole-4,3' oxirane **(3)** and 2'-(4-nitrorophenyl)-1-phenyl-3,5-dioxo-1,2,3,5 tetrahydrospiropyrazole-4,3'oxirane **(4)**.MMPP: Magnesium monoperoxy phthalate hexahhydrate, EtOH: Ethanol, THF: Tetrahydrofuran, rt: room temperature.

3.2. Insecticidal activity

3.2.1. Toxicity test for the 2nd larvae of cotton leaf worm, S. litoralis

Insecticidal activities of chlorantraniliprole and the tested compounds against the the 2nd larvae of cotton leaf worm are given in **Tables (1** and **2)**. The four compounds showed strong to weak insecticidal activities against the 2nd larvae of cotton leaf worm since some of them were as active as chlorantraniliprole after 48 and 72 h of treatment with LC_{50} values ranged from 3.23 to 3152.19 and from 0.619 to 1124.11 mgL^{-1} for feeding bioassay, whereas, for dipping larvae bioassay LC_{50} values ranged from 36.04 to 3384.27 and from 28.69 to 1309.75 mgL^{-1}. The LC_{50} value of chlorantraniliprole was 2.25 and 0.225 mgL^{-1} for feeding bioassay, and 4.98 and 1.25 for dipping bioassay after 48 and 72 h of treatment. The above results revealed that the insecticidal activity of compound **1** against the 2nd larvae of cotton leaf worm was similar to that of chlorantraniliprole for feeding bioassay after 48 and 72 h of treatment. In addition chlorantraniliprole and the synthsized of the 3,5-pyrazolidinedione derivatives were active on chewing pest insects primarily by ingestion and secondarily by contact. These results agree with [17] which described a series of substituted hydrazone derivatives possessing good activities against *Spodoptera litura* (Fabricius). [2] stated that chlorantraniliprole showed more toxic effect in feeding test of 2nd and 4th larval instars of cotton leaf worm under laboratory conditions.

Table 1. Insecticidal activity of chlorantraniliprole and compounds **1-4** against the 2nd larvae of cotton leaf worm, *S. litoralis* after 48 h of feeding and dipping larvae bioassay treatment.

	Feeding larvae bioassay			**Dipping larvae bioassay**		
Compd	**Slope ± SE**	**LC_{50} (mgL^{-1})**	**Toxicity ratio**	**Slope ± SE**	**LC_{50} (mgL^{-1})**	**Toxicity Ratio**
Chlorantr-aniliprole	0.83±0.02	2.25	1	0.82±0.03	4.98	1
1	0.42±0.03	3.23	0.70	0.69±0.04	36.04	0.138
2	0.68±0.02	3152.19	0.0007	0.55±0.03	3384.27	0.002
3	0.75±0.03	1373.47	0.002	0.65±0.02	1977.94	0.001
4	0.31±0.03	1465.21	0.0002	0.75±0.02	2125.51	0.002

Notes: toxicity ratio is defined as the ratio of chlorantraniliprole's LC_{50} value for baseline toxicity and the compounds' LC_{50} value.

Table 2. Insecticidal activity of chlorantraniliprole and compounds **1-4** against the 2nd larvae of cotton leaf worm, *S. litoralis* after 72 h of feeding and dipping larvae bioassay treatment.

	Feeding larvae bioassay			Dipping larvae bioassay		
Compd	**Slope ± SE**	**LC_{50} (mgL^{-1})**	**Toxicity ratio**	**Slope ± SE**	**LC_{50} (mgL^{-1})**	**Toxicity Ratio**
Chlorantr-aniliprole	0.84±0.02	0.225	1	0.93±0.02	1.25	1
1	0.63±0.03	0.619	0.363	0.58±0.03	28.69	0.043
2	0.86±0.02	1233.03	0.0002	0.72±0.04	1309.75	0.001
3	0.86±0.02	1054.57	0.0002	0.72±0.04	1189.17	0.001
4	0.61±0.03	1124.11	0.0002	0.55±0.02	1265.15	0.0009

3.2.2. Toxicity test for the 4th larvae of cotton leaf worm, S. litoralis

The toxicity effects of chlorantraniliprole and the tested compounds of 3,5-pyrazolidinedione derivatives against the 4th larvae of cotton leaf worm are given in **Tables (3 and 4).** The four 3,5-pyrazolidinedione derivatives showed strong to weak larvaicidal activities against the 4th larvae of cotton leaf worm . Some of them were as active as or more than chlorantraniliprole after 48 and 72 h of treatment with LC_{50} values ranged from 26.94 to 3215.42 and from 12.29 to 2015.16 mgL^{-1} for feeding bioassay. For dipping larvae bioassay the LC_{50} values ranged from 141.33 to 4254.81 and from 76.12 to 2151.11 mgL^{-1}. Whereas that of chlorantraniliprole was 33.25 and 12.35 mgL^{-1} for feeding bioassay and 76.45 and 21.45 mgL^{-1} for dipping bioassay after 48 and 72 h of treatment. Based on the LC_{50s} values, compound (1) exhibited the highest toxicity index compared with chlorantraniliprole against the 4th larvae of cotton leaf worm for feeding bioassay after 48 and 72 h of treatment, while, compound 2 showed the least efficient one. The above results revealed that the insecticidal activity of compound **1** against the 4th larvae of cotton leaf worm was 1.234 and 1.004-fold than that of chlorantraniliprole for feeding larvae bioassay after 48 and 72 h of treatment respectively.

Table 3. Insecticidal activity of chlorantraniliprole and compounds **1-4** against the 4th larvae of cotton leaf worm, *S. litoralis* after 48 h of feeding and dipping larvae bioassay treatment.

	Feeding larvae bioassay			**Dipping larvae bioassay**		
Compd	**Slope ± SE**	**LC_{50} (mgL^{-1})**	**Toxicity ratio**	**Slope ± SE**	**LC_{50} (mgL^{-1})**	**Toxicity Ratio**
Chlorantr-aniliprole	0.88±0.02	33.25	1	0.84±0.12	76.45	1
1	0.56±0.03	26.94	1.234	0.58±0.04	141.33	0.541
2	0.68±0.02	3215.42	0.010	0.55±0.03	4254.81	0.018
3	0.57±0.02	1456.22	0.023	0.79±0.03	2150.96	0.035
4	0.81±0.03	1856.52	0.018	0.65±0.02	2465.31	0.031

Table 4. Insecticidal activity of chlorantraniliprole and compounds **1-4** against the 4th larvae of cotton leaf worm, *S. litoralis* after 72 h of feeding and dipping larvae bioassay treatment.

	Feeding larvae bioassay			**Dipping larvae bioassay**		
Compd.	**Slope ± SE**	**LC_{50} (mgL^{-1})**	**Toxicity ratio**	**Slope ± SE**	**LC_{50} (mgL^{-1})**	**Toxicity Ratio**
Chlorantr-aniliprole	0.72±0.03	12.35	1	0.94±0.02	21.45	1
1	0.50±0.04	12.29	1.004	0.61±0.03	76.12	0.281
2	0.94±0.03	2015.16	0.061	0.81±0.03	2251.11	0.001
3	0.84±0.02	1105.86	0.011	0.71±0.02	1678.55	0.013
4	0.61±0.03	1258.18	0.009	0.55±0.02	1369.22	0.016

3.2.3. Structure-action relationship

As an extension of this approach, the structure-activity relationships (SAR) were also discussed on the basis of the toxicity values in **Tables 1 -4** as well**.** According to the general framework structure, it is appeared that the 4-chlorobenzylidene derivative **1** is more active, against the 2nd

and 4th larvae of cotton leaf worm, *S. litoralis*, than the other 4-(4`-nitrobenzylidene)-1-phenylpyrazolidine-3,5-dione (2), 2'-(4-chlorophenyl)-1-phenyl-3,5-dioxo-1,2,3,5 tetrahydrospiropyrazole-4,3' oxirane (3) and 2'-(4-nitrorophenyl)-1-phenyl-3,5-dioxo-1,2,3,5 tetrahydrospiropyrazole-4,3' oxirane (4) synthesized derivatives. The high activity associated with compounds **1** may be due to the presence of Chlorine atom in the structure beside the other common features of all compounds. The insecticidal activity of phenylpyrazolidine-3,5-dione derivative **1** and **3** is higher than that of **2 and 4** analog, this may be due to the presence of chlorine atom which may cause the insecticidal activity.

Conclusion

In conclusion, a series of, 4-(4`-chlorobenzylidene)-1-phenylpyrazolidine-3,5-dione (1), 4-(4`-nitrobenzylidene)-1-phenylpyrazolidine-3,5-dione (2), 2'-(4-chlorophenyl)-1-phenyl-3,5-dioxo-1,2,3,5 tetrahydrospiropyrazole-4,5 oxirane (3) and 2'-(4-nitrorophenyl)-1-phenyl-3,5-dioxo-1,2,3,5 trahydrospiropyrazole-4, 5 oxirane **(4)** analogs which contain 3,5-pyrazolidinedione moiety were designed and chemically synthesized. The toxicity of these compounds were estimated against the 2nd and 4th larvae of cotton leaf worm, *S. litoralis* and indicated that some of the target compounds exhibited excellent insecticidal activities, while some compounds revealed moderate larvicidial activities. Compound **1** revealed the best insecticidal activity against cotton leaf worm, which exceeded that of the commercial pesticides (Compared with chlorantraniliprole in this study). The high activity associated with compound **1** may be due to the presence of the chlorine atom attached to the benzyl cycle in its molecular structure. Our research demonstrated that new chlorobenzylidene, nitrobenzylidene, 4-chlorophenyl and 4-nitrophenyl derivatives containing 3,5-pyrazolidinedione moiety could effectively control cotton leaf worm, and this emphasis other studies done by [6, 7, 13, 17]. In addition chlorantraniliprole and the synthesized 3,5-pyrazolidinedione derivatives were active on chewing pest insects primarily by ingestion and secondarily by contact. These results showed that, 3,5-pyrazolidinedione have insecticidal effects on the cotton leaf worm, *S. litoralis* and may be used as alternatives conventional insecticides in integrated pest management programs for controlling this pest.

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