Journal of Plant Protection and Pathology

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Biological Activity of some Synthetic Cyanoacetamide Derivatives against some Cotton Pests

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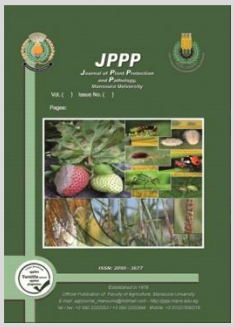

ABSTRACT

The continuous searching for new compounds that more effective is very important in the pest control field. That is because of the resistance in many pests to several pesticides. In the search for new biologically active compounds, extensive research is based on the synthesis of heterocyclic molecules. In this work, three new cyanoacetamide derivatives were synthesized and confirmed by IR spectra, mass spectra and elemental analysis. These compounds were; **(1)**: 2-cyano-N-(2-hydroxyphenyl) acetamide, **(2):** (E)-2-cyano-N-(2-hydroxyphenyl)-3-(methylthio)-3-(phenylamino) acrylamide and **(3):** 1-(2-hydroxyphenyl)-4,6-dimethyl-2-oxo-1,2-dihydropyridine-3-carbonitrile. They were tested as active ingredients against the 3rd instar larvae of cotton leafworm *Spodoptera littoralis* (Boisd) and the adult stage of cotton mealybug *Phenacoccus solenopsis* under laboratory conditions. Based on the mortality percentages and LC_{50} values, all compounds had high toxicity against *Phenacoccus solenopsis* after 48 hours of treatment. While the second compound was more toxic against *Spodoptera littoralis* compared with other both compounds that had a very low toxicity.

***Keywords**:* Pesticidal efficacy; Cyanoacetamide; *Phenacoccus solenopsis*; *Spodoptera littoralis*.

INTRODUCTION

Many researchers in the pest control field interest to search for new compounds that are more toxic against pests. That is because of the excessive use of pesticides, this led to the emergence of resistant individuals from pests to these pesticides. Cyanoacetamide and their related heterocyclic derivatives have generated a great deal of attention due to their interesting biological activity (Nazish *et al*., 2015), their pharmaceutical activities include: antimicrobial (Khalil *et al.,* 2010), antifungal, antibacterial (Darwish *et al.,* 2014), anti-inflammatory (Roifman *et al.,* 2000), antitumor properties (Cocco *et al.,* 2000), carbonic anhydrase inhibitory (Alafeefy *et al.,* 2013), anticancer (Mohamed *et al.,* 2017). Analgesic properties (Ismail *et al.,* 2007), Also they have agriculture activities such as; herbicidals (Geissler *et al.,*1980) and molluscicidal activity (Fadda *et al*., 2018a), rodenticidal activity (Fadda *et al*., 2018b). In addition it was reported by (Fadda *et al*., 2017) that cyanoacetamide derivatives have an insecticidal activity on the second instar larvae of cotton leafworm, *Spodoptera littoralis*. In this work, the Egyptian cotton leafworm and the cotton mealybug (Fig. 1) will be used to test the insecticidal activity of the synthetic cyanoacetamide derivatives. The Egyptian cotton leafworm, *Spodoptera littoralis*, Boisd. (Lepidoptera: Noctuidae) is considered as one of the most injurious and widespread pests of different crops in Egypt. Also, it is important insect pest of cotton in Southern Europe, Africa and the Middle East. This pest attacks cotton and many of field crops and vegetables and ornamental plants. The larvae feed on leaves also can retard growth or reduce the production of the cotton crop. (Meisner and Nemny, 1992 & Hosny *et al.*, 1986). On the other hand, the cotton mealybug, *Phenacoccus solenopsis* Tinsley (Hemiptera: Pseudococcidae) is considered a polyphagous insect pest. one hundred fifty-four plant species were attacked by the cotton mealybug including field crops, vegetables, ornamentals, weeds, bushes, and trees (Saini *et al*., 2009 & Arif *et al*., 2009). As well as economic damage caused by it mainly to cotton, brinjal, okra, tomato, sesame, sunflower and, China rose (Arif *et al*., 2009). The present study aimed to synthesize and characterize newer some cyanoacetamide derivatives and tested their insecticidal activity against *Spodoptera littoralis* and *Phenacoccus solenopsis* under laboratory condition.

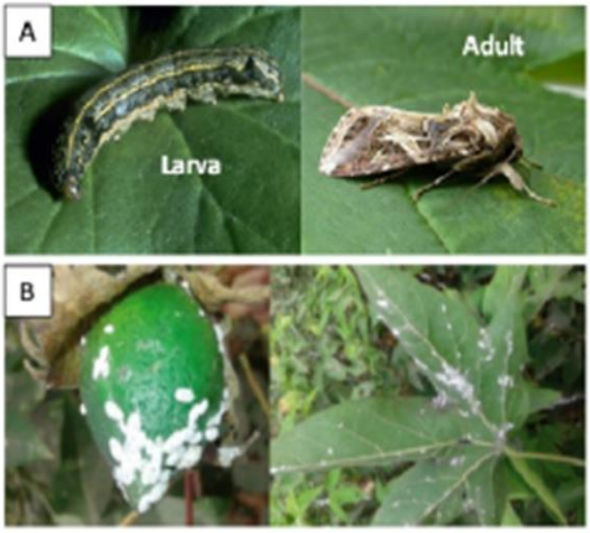

Figure 1. The Egyptian cotton leafworm *Spodoptera littoralis* (A) and the cotton mealybug *Phenacoccus solenopsis* (B)

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DOI: 10.21608/jppp.2020.95610

MATERIALS and METHODS

1. Chemistry

All melting points were uncorrected and measured on a Gallenkamp melting point apparatus. IR spectra (KBr) were recorded with a Perkin–Elmer model 157 infrared spectrophotometer. Mass spectra were acquired with GCMS-QP1000 EX and Jeol JMS600 spectrometers at 70 eV. Elemental analysis was performed by the micro-analytical center of the Faculty of Science, Mansoura University.

Synthesis of 2-Cyano - N- (2-hydroxyphenyl) acetamide (Compound : 1).

A mixture of o-aminophenol (0.01 mole, 1.09 g), and 3-(3,5-dimethyl-1H-pyrazol-1-yl)-3-oxopropanenitrile (0.01 mole, 0.16 g) was heated in benzene under reflux for 4 hours. The formed solid product was crystalline material filtered off and washed with benzene to afford the corresponding acetamide derivative (Compound : 1). Yield 95 %; mp 280 °C; IR (KBr): v/cm-1 = 2271 (CN), 3276 (NH), 1H NMR (400 MHz, DMSO-d6): δ/ppm = 4.00 (s, 2H, CH2), 9.57 (s, H, NH), 9.93 (s, H, OH), 6.77–7.84 (m, 4H, Ar–H), MS m/z (%): 176 (31.01), 136 (18.33), 109 (100.00), 107 (11.56), 77 (1.41).

Synthesis of (E)-2-cyano-N-(2-hydroxyphenyl)-3-(methylthio)-3-(phenylamino) acrylamide (Compound : 2).

This compound was prepared from stirring of compound (1) (0.01mol, 1.76g) with potassium hydroxide (0.01mol, 0.56 g) in 30ml dimethyl foramide for 30 min. then phenyl isothiocynate (0.01mol, 1.34 g) was added to the later mixture and complete stirring for 6 hours, after that dimethyl sulphate (0.01mol, 1.26g) was added with continuing in stirring for additional 3 hours. The reaction mixture was poured onto ice water and filtered off the formed solid product, dried and recrystallized from ethanol to afford compound (2). Orange crystals; yield 75 %; mp 170 °C; IR (KBr): ν/cm^{-1} = 3423 (OH), 3302, 3106 (2NH), 2219 (CN), 1649 (C=O). MS m/z (%): 325 (30.36), 297 (100.00), 251 (74.10), 161 (41.69), 151 (81.04), 137 (31.12).

Synthesis of 1-(2-hydroxyphenyl)-4,6-dimethyl-2-oxo-1,2-dihydropyridine-3-carbonitrile (Compound: 3).

Refluxing of equimolar amounts of compound (1) (0.01mol, 1.76g) and acetyl acetone (0.01mol, 1g) in 30ml ethanol in the presence of few drops from pipredine for 3 hours. Crystalline product was formed on hot filtered off and dried to give compound (3). Brown crystals; yield 50 %; mp 175 °C; IR (KBr): ν/cm^{-1} = 3480 (OH), 2226(CN), 1746 (C=O), ^{1}H NMR (400 MHz, DMSO-*d6*): δ/ppm = 2.0 (s, H, CH_3), 2.4 (s, H, CH_3), 6.5 (s, H, CH), 10.0 (s, H, OH), 6.93–7.34 (m, 8H, Ar–H).

2.Biological activity:

The tested insect pests:

The present work was established to test the toxicity of the synthesized compounds under laboratory conditions against some cotton insect pests. A laboratory strain of cotton leafworm *S. littoralis* (Boisd.) and the cotton mealybug *P. solenopsis* (Tinsley) were managed under regular ailments connected with 25 ± 1 °C and 60% to 70% ± 5 % RH and kept down any contaminants by chemical compounds until eventually any time connected with review in order to obtain a susceptible and homogenous stress (EL-Defrawi *et al.,* 1964).

Preparing the concentration of the compounds:

Each compound was prepared as a stock solution by dissolving it in ethyl alcohol 70% with heating. A series of different concentrations of three synthesized compounds were prepared by diluting them in water. They were 4000, 2000, 1000, and 500 ppm in case of *S. littoralis* treatment but they were 2000, 1000, 500 and, 200 ppm in case of the *P. solenopsis* treatment.

Toxicity bioassay:

The toxicity bioassay test was conducted by leaf dipping method as mentioned by Abdullah (2019). Clean caster leaves were dipped in each concentration of the synthesized compounds for 30 second, other group leaves were dipped in solution of water-ethanol without compounds as the control treatment. Then all leaves allow to air-drying. The air-dry leaves were put in plastic cups. Then twenty individuals of the 3rd instar larvae of *S. littoralis* and the same count of the adult stage of *P. solenopsis* were put on the leaves separately. All cups were covered by muslin. Each treatment were replicated four times. The survival individuals of both insect pests were recorded for seven days in case of *S. littoralis* and two days in case of *P. solenopsis*. The mortality percentages were daily recorded and corrected by Abbott's formula (Abbott, 1925). Median lethal concentration (LC_{50}), slope values and 95% fiducially limits were estimated by Finney's probit analysis method (Finney, 1971). Also, the toxicity index was calculated according to Sun's equation (1950).

$$\text{Mortality \%} = \frac{\text{Control survival - Treatment survival}}{\text{Control survival}} \text{ X } 100$$

$$\text{Toxicity index} = \frac{\text{LC}_{50} \text{ of the most effective compound}}{\text{LC}_{50} \text{ of the tested compound}} \text{ X } 100$$

RESULTS AND DISCUSSION

1.Chemistry:

The compound (1): 2-cyanomethyl hydroxyphenyl, was obtained by cyanoactylation of 2-hydroxy phenol (as primary aromatic amine) with 3-(3,5-dimethyl-1H-pyrazol-1-yl)-3-oxopropanenitrile in refluxing toluene, and which then successfully used for the preparation of N-cyanoacetamide derivatives (Fadda *et al.,* 2012).

The reaction between 2-cyanoacetamide derivatives and aryl isothiocyanates under basic conditions afforded intermediate salt which is alkylated using methyl iodide or dimethyl sulfate to yield 3-aryl, 2-cyano, 3-methylthio acrylamide derivative (2) (Elgemeie *et al.,* 2008). In addition, when the cyanoacetamide 1 was reacted with acetylacetone in ETOH in the presence of a catalytic amount of triethylamine, the cyclocondensation reaction occurred and the 2-pyridinone derivatives 3 were smoothly afforded. It can be postulated that the reaction initially proceeds via a nucleophilic attack to form the Michael adduct which in turn cyclized and eliminated two water molecules, affording the final product (3) (Ried and Meyer, 1957). The structures of compounds (1, 2 & 3) were established and confirmed by their elemental analysis and spectral data (Fig. 2)

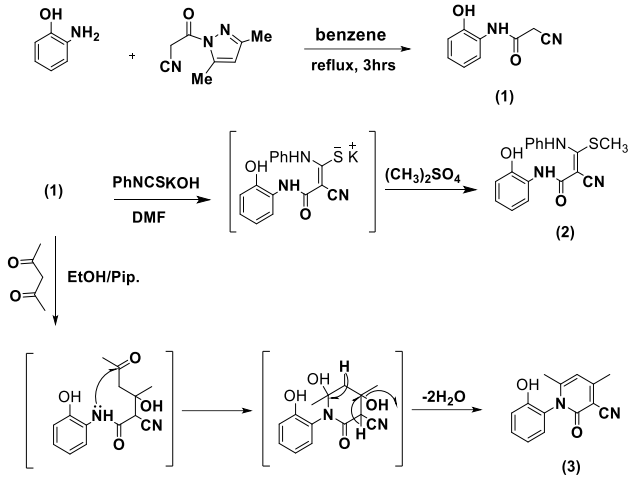

Figure 2. Scheme: Synthesis of cyanoacetamide derivatives.

2. Toxicity of the synthesized cyanoacetamide derivatives:

Tables 1, 2, 3 and 4 illustrated the insecticidal efficacy of synthesized cyanoacetamide derivatives against *S. littoralis* and *P. solenopsis*. The data presented in Table 1 showed that high mortality percentage (82%) of *S. littoralis* caused by compound (2) at 4000 ppm after 7 days of treatment but the mortality percentages were less with the other both compounds at the same concentration and time (21% and 43%). These data agree with the LC_{50} values in Table 2 and Fig. 3 which indicates that compound (2) was approved to be the most toxic compound to the 3rd instar larvae of *S. littoralis* with LC_{50} value at 1106 ppm. Also, the toxicity index revealed the same result which was 3%, 100%, 21% to compound 1, 2, and 3, respectively.

In case of cotton mealybug, data posted in Tables 3 and 4 illustrate that compounds (1) and (2) gave the nearest value of mortality percentage followed by compound (3) which were 98%, 99% and 95.7% respectively at 2000 ppm after 48 hours. Whereas, the LC_{50} values showed that compound (1) was approved to be the most toxic compound with LC_{50} value of 213 ppm followed by compound (2) and (3) with LC_{50} values of 249 and 428 ppm respectively as shown in Table 4 and Fig 4. In addition, the toxicity index showed the same result which was 100%, 85.5%, 49.76% to compound 1, 2, and 3, respectively. The toxic of cyanoacetamide derivatives may be referred to the presence of $S(CH_3)$ and CN groups in their structure as mentioned by Fadda *et al.,* (2017). They added that both groups S(CH3) and CN are among electron-withdrawing groups. Where, the results of the insecticidal activity demonstrated that the presence of electron-withdrawing groups or atoms is essential for improving insecticidal activity, such as in the heterocyclic compounds. Also, they reported that cyanoacetamide derivatives have an insecticidal activity on the second instar larvae of cotton leafworm, *Spodoptera littoralis.*

Table 1. Efficacy of synthesized cyanoacetamide derivatives against the 3rd instar larvae of *S. littoralis* under laboratory condition.

Concentration (ppm)	Cyanoacetamide derivatives								
	Compound (1)			Compound (2)			Compound (3)		
	Mortality % of *S. littoralis* after days								
	3 days	5 days	7 days	3 days	5 days	7 days	3 days	5 days	7 days
500	0	5	5	0	10	27	0	0	4
1000	0	8	9	31	39	47	0	8	12
2000	9	12	14	42	59	66	10	22	26
4000	13	18	21	57	68	82	19	31	43

Table 2. Toxicity of the synthesized cyanoacetamide derivatives against of the 3rd instar larvae of *S. littoralis* under laboratory condition after 7 days.

Cyanoacetamide derivatives	LC_{50} (ppm)	Confidence limits		Slope ±	Toxicity Index (%)
		Lower	Upper		
Compound (1)	36015	11181	2569929	0.851 ± 0.25	3.00
Compound (2)	1106	905	1322	1.694 ± 0.21	100.00
Compound (3)	5216	3859	8572	1.616 ± 0.24	21.00

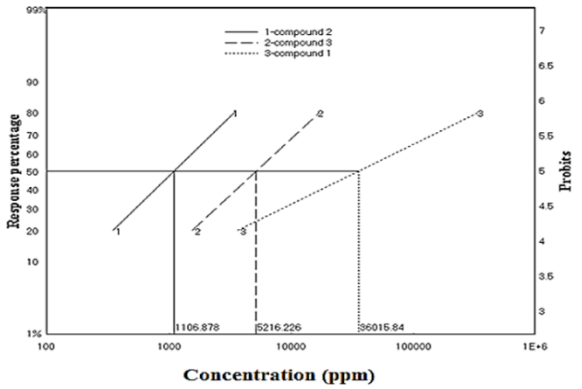

Fig. 3. Toxicity lines of the synthesized compounds with the 3rd instar larvae of *S. littoralis* under laboratory condition after 7 days.

Table 3, Efficacy of synthesized cyanoacetamide derivatives against adult stage of *P. solenopsis* under laboratory condition.

Cyanoacetamide derivatives	Concentrations of compounds (ppm)			
	200	500	1000	2000
	Mortality percentage of *P. solenopsis* after 48 hours			
Compound (1)	47.00	79.00	93.00	98.00
Compound (2)	38.00	81.00	96.00	99.00
Compound (3)	19.80	56.50	82.60	95.70

Table 4. Toxicity of the synthesized cyanoacetamide derivatives against adult stage of *P. solenopsis* under laboratory condition after 48 hours.

Cyanoacetamide derivatives	LC_{50} (ppm)	Confidence limits		Slope ±	Toxicity Index (%)
		Lower	Upper		
Compound (1)	213	164	259	2.24 ± 0.23	100.00
Compound (2)	249	208	287	± 0.312.95	85.50
Compound (3)	428	369	490	± 0.232.56	49.76

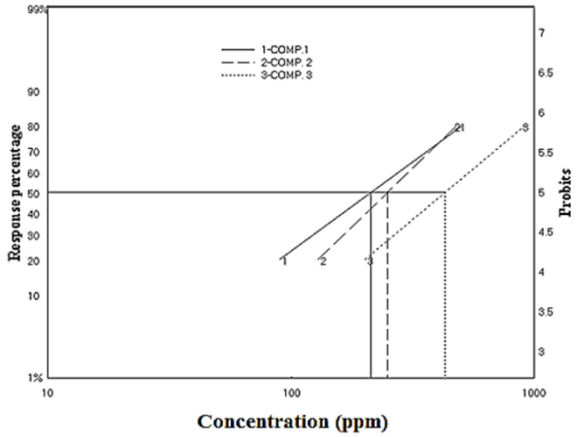

Fig. 4. Toxicity lines of the synthesized compounds with adult stage of *P. solenopsis* under laboratory condition after 2 days.

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الكفاءة البيولوجية لبعض مشتقات السيانوأسيتاأميد المخلقة على بعض أفات القطن

رضا عبدالعظيم الشرقاوي ورضا راضي حسن عبدالله

معهد بحوث وقاية النباتات – مركز البحوث الزراعية – الدوقي – الجيزة – مصر

البحث المستمر عن مركبات جديدة أكثر فاعلية يعتبر من الأمور المهمة في مجال مكافحة الآفات. وذلك بسبب ظاهرة المقاومة التي توجد في العديد من الآفات تجاه بعض المبيدات الحشرية. ويعتمد البحث عن مركب نشط بيولوجيا على تخليق جزيئات حلقية غير متجانسة فانها تكون فعالة كمبيدات للافات الحشرية. في هذه الدراسة تم تخليق ثلاثة مركبات جديدة من مشتقات السيانواسيتاأميد طبقا لطريقة التحضير القياسية وهم : (1): 2-cyano-N-(2-hydroxyphenyl) acetamide (2): (E)-2-cyano-N-(2-hydroxyphenyl)-3-(methylthio)-3-(phenylamino) acrylamide (3): 1-(2-hydroxyphenyl)-4,6-dimethyl-2-oxo-1,2-dihydropyridine-3-carbonitrile. وتم إثبات التركيب الكيميائي لها باستخدام التقنيات الطيفية (الأشعة تحت الحمراء، ومطياف الكتلة، والرنين النووي المغناطيسي). تم اختبار السمية لهذة المركبات على العمر اليرقي الثالث لدودة ورق القطن والطور البالغ من حشرة بق القطن الدقيقي تحت الظروف المعملية. أظهرت النتائج أن المركب الثاني كان أكثر سمية على العمر اليرقي الثالث لدودة ورق القطن حيث كانت قيمة التركيز النصفي المميت له هي 1106 جزء فى المليون وكانت نسبة الموت 82% فى حين أن المركبان الأول والثالث أحدثا نسبة موت ضئيلة جدا بعد سبعة أيام من المعاملة. بينما أظهرت المركبات الثلاثة فعالية عالية وصلت الى أكثر من 95% نسبة موت لحشرة بق القطن الدقيقي بعد 48 ساعة.