SYNTHESIS AND BIOLOGICAL EFFECTS OF PYRAZOLINE DERIVATIVES AGAINST THE COTTON LEAFWORM, *SPODOPTERA LITTORALIS* BOISD.

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(Manuscript received 2 September, 1997)

Abstract

The synthesis of six new pyrazoline derivatives was performed by reaction of the corresponding chalcones with semicarbazide hydrochloride and thiosemicarbazide. The insecticidal activity of these compounds in comparison with the bacterial insecticide (bactospeine) and the pyrethroid (fenvalerate) on *S.littoralis* was studied. The findings indicated that the compound (1) (R^1, R^2 = C_6H_5, X = O,Y = H) showed the highest toxic effect followed by the thio analogue compound (2) in which X = S. Two days after treatment, their LC_{50} values were 170 and 480 ppm, which dropped to 130 and 140 ppm, respectively after 7 days. The corresponding figures ranged from 9400 to 600 ppm with bactospeine and 16-1.2 ppm with fenvalerate after 2 and 7 days, respectively. Furthermore, the synthetic pyrazolines affect the larval development with the highest potency of the derivative (2), showing ED_{50} of 40 and 12 ppm on pupation and moth emergence, respectively. In case of bactospeine, these values were 280 and 140 ppm, while reached to 0.6 and 0.27 ppm with fenvalerate, respectively.

INTRODUCTION

The cotton leafworm, *S.littoralis*, is a serious insect pest of many crops and developed resistance to different groups of insecticides. Then, it is important to synthesis new compounds and evaluate their potency on this pest. Consequently, pyrazolines were evaluated for insecticidal effects (Mulder et al., 1975; Welling et al., 1977; Grosscurt et al., 1979; Hasan et al., 1994 and 1996).

The work was carried out to synthesize some new pyrazolines and study their toxic and biological effects against *S.littoralis* in comparison with the bacterial insecticide as well as the pyrethroid, fenvalerate.

MATERIALS AND METHODS

The pyrazoline compounds were prepared according to the method of Hamada (1993). The [^{1}H] and [^{13}C] NMR data were recorded at 90 MH_Z, and 75 MH_Z, respectively in dimethy sulfoxide (DMSO) solution. The Mass spectra were carried out on Shimadzu HP 5988 (70 ev), at Microanalytical Center, Cairo University. The melting points are uncorrected. Pyrazoline derivatives studied are as follows and their structure are given in Tables 1 and 2.

1. 3,5 diphenyl-2-pyrazoline-1-carboxamide : A solution of trans-1,3 diphenyl-1propenone (0.01 mole) in dioxan was refluxed with semicarbazide hydrochloride (0.02 mole) in aqueous acetic acid for 10 hrs. The separated solid was recrystallized from methanol as colourless needles in 70% yield, m.p. 190-193^{o}C. [^{1}H] NMR δ 7.35-7.80 (m, 10H), 6.55 (s,2H), 5.40 (dd, 1H), 3.20 and 3.75 (2dd, 2H); [^{13}C] NMR δ 42.33, 59.74, 125.39, 126.39-150, 202.

2. 3,5 diphenyl-2-pyrazoline-1-thiocarboxamide : A solution of erythro-2,3-dibromo-1,3-diphenyl-1-propanone (0.01 mole) in ethanol was refluxed with thiosemicarbazide (0.04 mole) in presence of glacial acetic acid. The separated solid was recrystallized from methanol as orange needless in 90% yield, m.p. 55-57^{o}C. [^{1}H] NMR δ 10.00 (s, 2H), 6.65-7.90 (m, 10H), 4.90 (dd, 1H), 3.20 and 1.00 (2dd, 2H).

3. 4-bromo-5-(p-bromophenyl)-3- phenyl-2-pyrazoline-1-carboxamide : A solution of erythro-2,3- dibromo-3- (P-bromophenyl)-1-phenyl-1-propanone (0.01 mole) in dioxan was refluxed with semicarbazide hydrochloride (0.02 mole) in aqueous acetic acid for 14 hrs. The separated solid was recrystallized from benzene as colourless needles in 70% yield, m.p. 143-145^{o}C. [^{1}H] NMR δ 7.30-8.35 (m, 9H), 7.85 (S, 2H), 6.65 (d, J = 13 Hz, 1H) 5.80 (d, J = 13Hz, 1H).

4. 3-Cyclopropryl-5-phenyl-2-Pyrazoline -1 Carboxamide : A solution of trans-1-cyclopropyl-3- Phenyle -2-propenone (0.01 mole) in dioxan was refluxed with semicarbazide hydrochloride (0.02 mole) in aqueous acetic acid for about 12 hrs. The separated solid was recrystallized from methanol as colourless needless in 60% yield, m.p. 284-286^{o}C. [^{1}H] NMR δ 7.00-7.65 (m,5H), 6.66 (s,2H), 5.50 (dd, 1H), 3.20 and 3.75 (2dd, 2H), 0.55-2.15 (m, 5H).

5. 3 - Cyclopropryl - 5 - (p-methylphenyl)-2 -pyrazoline -

1-carboxamide: A solution of *trans*-1-cyclopropy-3-(p-methylphenyl)-2-propenone (0.01 mole) in dioxan was refluxed with semicarbazide hydrochloride (0.02 mole) in aqueous acetic acid for about 6 hrs. The separated solid was recrystallized from methanol as colourless needless in 80% yield, m.p. 140-143°C.[^{1}H] NMR δ 6.70-7.59 (M,4H), 6.00 (s, 2H), 5.15 (dd, 1H) 3.15 and 2.45 (2dd, 2H), 2.25 (s, 3H), 0.1-0.9 (m, 5H); EL/MS m/z: 243 (M+), 200 (M-CONH2),199 (M-$CONH_2$), 143 (199-(C_3H_5+CH_3), 118 (200∇C = NN), Scheme 1.

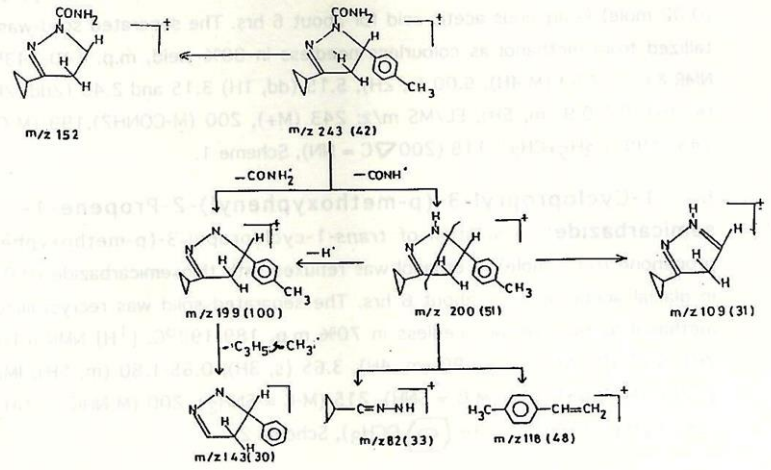
6. 1-Cyclopropryl-3-(p-methoxyphenyl)-2-Propene-1- thiosemicarbazide: A solution of *trans*-1-cyclopropyl-3-(p-methoxyphenyl)-2-propenone (0.01 mole) in ethanol was refluxed with thiosemicarbazide (0.02 mole) in glacial acetic acid for about 6 hrs. The separated solid was recrystallized from methanol as pale yellow needless in 70% m.p. 189-192°C. [^{1}H] NMR δ 10.55 (s, 2H), 6.75 (D, 2H), 7.25-7.90 (m, 4H), 3.65 (s, 3H), 0.65-1.80 (m, 5H); IM/MS m/z: 242 (M-OCH_3), 216 (M-C = SNH), 215 (M-C = SNH_2), 200 (M-NHC = SNH_3), 166 (242-C_6H_4), 133 (HC = CH-  OCH_3), Scheme 2.

The bacterial insecticide, bactospeine FC 8500 I.U/mg and the pyrethroid, fenvalerate, were used for comparison. Test insects of the susceptible strain of *S.littoralis* were reared in the laboratory on artificial diet (Hegazi, 1976) and the 4th instar larvae were used in the tests.

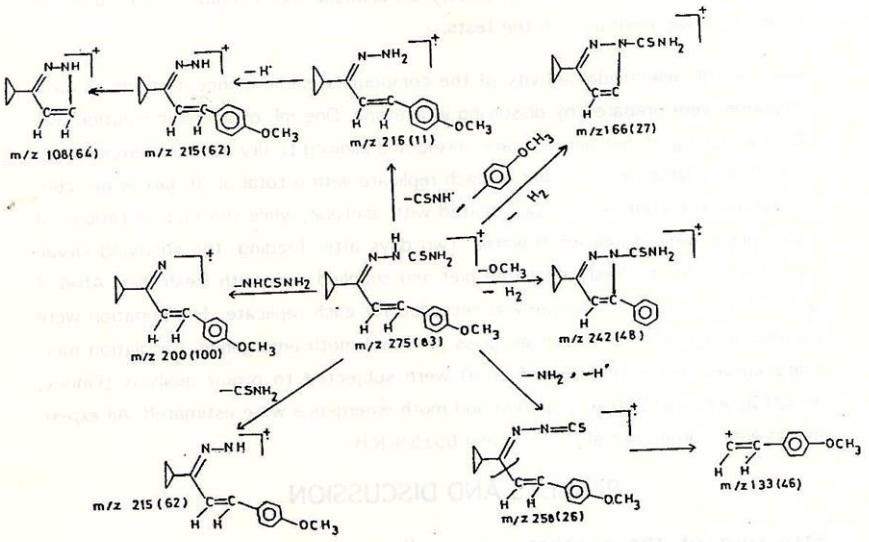
For the insecticidal activity of the compounds, series concentrations of each compound were prepared by dissolving in acetone. One ml. of acetonic solution was added into 10 g of diet per replicate, mixed and allowed to dry at room temperature. After that, 5 larvae were added to each replicate with a total of 30 larvae per concentration. The control diet was treated with acetone, while the concentrations of bactospeine were dissolved in water. Two days after feeding, the surviving larvae were transferred to fresh untreated diet and supplied daily with fresh diet. After 2 and 7 days, mortality of larvae was recorded for each replicate. The pupation were counted and transferred to clean glass jars until moth emergence. Caculation mortality curves and estimation of LC50 were subjected to probit analysis (Finney, 1952) as well as ED50 on pupation and moth emergence were estimated. All experiments were carried out at 27±1°C and 65±5% R.H.

RESULTS AND DISCUSSION

Structure of the synthetic pyrazolines



Scheme 1. Mass spectrum of compound (5)



Scheme 2. Mass spectrum of compound (6)

These compounds were derivatives of chalcones which containing olefinic double bond. The latter acts as center for nucleophilic attack from hydrazide moiety of semicarbazide and thiosemicarbazide to form pyrazolines. The structure was confirmed using infrared spectra, showing the-C = N at 1569-1661 cm^{-1}, -C=O-at 1657-1685cm^{-1}, -C= S-at 1243, 1244 cm^{-1} and NH at 3401-3491 cm^{-1} and -C=C at 1585 cm^{-1}. Also, structure was confirmed using ^{1}H-NMR and MS spectra. For example, the mass spectra of compounds 5 and 6 were shown is Scheme 1 and 2, respectively.

Insecticidal effects of compounds

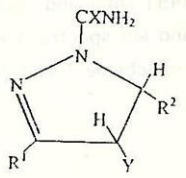
Data in Table 1 show LC50 values of the compounds studied on *Spodoptera* larvae after 2 and 7 days of treatment. Concerning the synthetic pyrazolines, the highest toxic effects were noticed with derivatives 1 and 2 with LC50 of 170-130 and 480-140 ppm after 2 and 7 days, respectively. The corresponding figures were 3500-2700 ppm with derivative 4. The weakest effects were obtained with compounds 3, 5 and 6and their LC50 were above 10000 ppm after 2 days. The derivatives 3 and 6 still gave >10000 ppm after 7 days, while it was 6000 ppm with 5. Similar results were obtained with Tsuboi et al., (1993a &b), who stated that some synthetic pyrazolines showed high toxic effects on *Spodoptera* larvae.

In case of bactospeine, LC50 were 9400 and 600 ppm after 2 and 7 days, respectively, while these values were 16 and 1.2 ppm with fenvalerate.

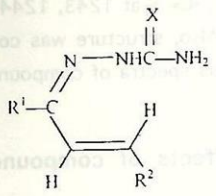
The above results indicate that the highest effects of synthetic pyrazolines were noticed with the derivative 1, in which R^1, R^2 = C_6 H_5, X = O and followed by the thio analogue 2 where X = S.Then, the pyrazoline ring with two phenyl groups gave the highest insecticidal effects. The results agree with those obtained by Grosscurt et al., (1979), who mentioned that pyrazolines having a phenyl group as a ring substituent have higher insecticidal activity. The results in Table 1 also demonstrate that presence of the lowest electronegative atom (O) in compound 1 gave the highest initial effect after 2 days. Furthermore, the lowest effect of derivative 3 attributed to R^2 = C_6 H_4-p-Br and Y = Br. Introduction of C_3H_5 in R^1 of both 4 and 5 as well as R_2 = C_6 H_4-p-CH_3 in 5 reduced their toxic effects. Also, no-cyclised componud 6 with both C_3 H_5 and C_6 H_5-p-OCH_3 groups gave the lowest activity.

Previous studies showed the substituent effects on the insecticidal activity. Grosscurt et al., (1979) mentioned that the 3,4-diphenyl derivatives give rise to products with much better insecticidal properties than those with phenyl substitu-

Table 1. The toxic effects of synthetic pyrazolines, bactospeine and fenvalerate on *Spodoptera* larvae.



(A)



(B)

General structure of pyrazolines studied (A = no. 1-5, B = no.6)

Compound	R^1	R^2	X	Y	LC_{50} (ppm) on *Spodoptera* larvae	
					After 2 days	After 7 days
1	C_6H_5	C_6H_5	O	H	170	130
2	C_6H_5	C_6H_5	S	H	480	140
3	C_6H_5	C_6H_4-p-Br	O	Br	>10000	>10000
4	C_3H_5	C_6H_5	O	H	3500	2700
5	C_3H_5	C_6H_4-p-CH_3	O	H	>10000	6000
6	C_3H_5	C_6H_4-p-OCH_3	S	S	>1000	>10000
Bactospeine					9400	600
Fenvalerate					16	1.2

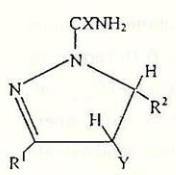
tion at only the 3 position or even those with 3,4-diphenyl substitution. Hasan et al., (1996) indicated that substituents of the N-1 atom in the pyrazoline ring has a specific role for the potentional insecticidal effects.

Concerning the effects of compounds tested on larval development, various effects on pupation and moth emergence were illustrated in Table 2. With regard to pyrazolines studied, the highest effects were detected with 2 and 4 giving ED_{50} values on pupation with 40 and 42 ppm, while they were 12 and 30 ppm on moth emergence, respectively. On the contrary, compounds 5 and 6 showed the weakest effects with ED_{50} of 1300 and 1000 ppm on pupation which dropped to 800 and 520 ppm to moth emergence, respectively. The compounds 1 and 2 gave the moderate effects. In case of bactospeine, ED_{50} ranged from 280 to 140 ppm to pupation and moth emergence, respectively. These values were 0.6 and 0.27 ppm with fenvalerate, respectively.

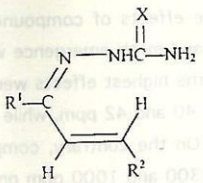
Consequently, all pyrazolines studied except 5 and 6 gave high effects to pupation and adult emergence in comparison with bactospeine. The above findings indicate that derivative 2, which containing two phenyl groups at R^1, R^2 and X = S inhibited the larval development more than the other derivatives. Furthermore, derivative 4 in which ($R^1 = C_3H_5$, $R^2 = C_6H_5$, X= O) followed by 1 (R^1, $R^2 = C_6H_5$, X = O) reduced pupation and moth emergence. While, uncyclized compound 6 gave the lowest effect. Concerning their mode of action, the pyrazoline compounds have various kinds of nerve effect, including blockage of the voltage-dependent sodium (Salgado, 1990 and 1992) and calcium channels (Zhang and Nicholson, 1993).

In general, the results indicate the possible use of pyrazoline compounds, bacterial and chemical insecticides as components in IPM programmes against *S.littoralis*.

Table 2. Effects of synthetic pyrazolines, bactospeine and fenvalerate on larval development of *S.littoralis*.



(A)



(B)

General structure of pyrazolines studied (A = no. 1-5, B = no.6)

					ED_{50} (ppm)	
Compound	R^1	R^2	X	Y	On % pupation	On % moth emergence
1	C_6H_5	C_6H_5	O	H	160	96
2	C_6H_5	C_6H_5	S	H	40	12
3	C_6H_5	C_6H_4-p-Br	O	Br	170	130
4	C_3H_5	C_6H_5	O	H	42	30
5	C_3H_5	C_6H_4-p-CH3	O	H	1300	800
6	C_3H_5	C_6H_4-p-OCH3	S	S	1000	520
Bactospeine					280	140
Fenvalerate					0.6	0.27

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تصنيع والتأثيرات البيولوجية لمشتقات البيرازولين ضد دودة ورق القطن

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يستهدف البحث تطبيق مركبات البيرازولين فى برامج مكافحة الآفات الحشرية حيث تناولت الدراسة التأثيرات السامة لبعض مركبات البيرازولين المصنعة بالإضافة إلى مقدرة تلك المركبات فى تثبيط تطور اليرقات إلى عذارى وحشرات كاملة ومقارنة ذلك مع تأثيرات المبيد البكتيرى (باكتوسبين)والمبيد البيروثرويد (فينفاليريت).

ولقد أظهرت النتائج تصنيع ٦ مشتقات للبيرازولين (خمس منها ذات تركيب حلقى، بينما السادس غير حلقى) وإختلفت المجاميع الإستبدالية على تلك المشتقات. وأظهرت نتائج التأثير السام لمركبات البيرازولين القوة النسبية العالية لمشتق (١) والذى يحتوى على المجاميع الإستبدالية التالية: مجموعتى فينايل وذرة أكسيجين ضد اليرقات المعاملة ويليه النظير الكبريتى (المشتق ٢).حيث كانت قيم LC50 بعد يومين من المعاملة كما يلى : ١٧٠ ، ٤٨٠ جزء فى المليون للمركبين المذكورين على التوالى، بينما إنخفضت إلى ١٣٠ ، ١٤٠، جزء فى المليون على التوالى بعد ٧ أيام. وتراوحت القيم المماثلة مع الباكتوسبين من ٩٤٠٠ إلى ٦٠٠ جزء فى المليون، بينما فى الفينفاليريت من ١٦ إلى ١,٢ جزء فى المليون بعد ٢، ٧ أيام على التوالى.

كذلك أظهرت مشتقات البيرازولين المصنعة فعالية ضد تطور اليرقات مع الفعالية العالية للمشتق (٢) والذى يحتوى على الكبريت معطياً قيم ED50تعادل ٤٠ ، ١٢ جزء فى المليون ضد تكوين العذارى والفراشات على التوالى. ولقد تراوحت تلك القيم مابين ٢٨٠ إلى ١٤٠ جزء فى المليون عند تطبيق الباكتوسبين بينما كانت تعادل ٠,٦ – ٠,٢٧ جزء فى المليون بإستخدام الفينفاليريت.