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

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Abstract

The synthesis of six new pyrazoline derivatives was performed by reaction of the corresponding chlorones with semicarbazide hydrochloride and thiosemicarbazide. The insecticidal activity of these compounds in comparison with the bacterial insecticide (bactospine) and the pyrethroid (fenvalerate) on *S. littoralis* was studied. The findings indicated that the compound (1) \( R_1, R_2 = C_{6}H_{15}, X = O, Y = H \) 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 bactospine and 16-12 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 bactospine, 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 30 MHz and 75 MHz, respectively, in dimethyl 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-1-propenone (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\(^\circ\)C. \(^{1}\)H NMR \(\delta\) 7.35-7.80 (m, 10H), 6.55 (s, 2H), 5.40 (dd, 1H), 3.20 and 3.75 (2dd, 2H); \(^{13}\)C NMR \(\delta\) 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 needles in 90% yield, m.p. 55-57\(^\circ\)C. \(^{1}\)H NMR \(\delta\) 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\(^\circ\)C. \(^{1}\)H NMR \(\delta\) 7.30-8.35 (m, 9H), 7.85 (s, 2H), 6.65 (d, \(J = 13\) Hz, 1H) 5.80 (d, \(J = 13\)Hz, 1H).

4. 3-Cyclopropyl-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 needles in 60% yield, m.p. 284-286\(^\circ\)C. \(^{1}\)H NMR \(\delta\) 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, 3H).

5. 3-Cyclopropyl-5-(p-methylphenyl)-2-pyrazoline -
1-carboxamide: A solution of trans-1-cyclopropyl-3-(p-methoxyphenyl)-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 needles in 80% yield, m.p. 140-143°C. \[^1H\] NMR 6 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), 0.1-0.8 (m, 5H); EI/MS m/z: 243 (M+), 200 (M-CONH\_2), 199 (M-CONH\_2), 193 (199-C\_3H\_4+CH\_3), 118 (200-C = NH\), Scheme 1.

6. 1-Cyclopropyl-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 needles in 70% m.p. 189-192°C. \[^1H\] NMR 6 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 = SH), 215 (M-C = SH\_2), 200 (M-NH = NH\_2), 166 (242-C\_6H\_4), 133 (HC = CH-CH\_2), Scheme 2.

The bacterial insecticide, bactosporic FC 8500 IU/mg and the pyrethroid, fenvalerate, were used for comparison. Test insects of the susceptible strain of \textit{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 acetone 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 bactosporic 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. Calculated 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 1657-1685 cm\(^{-1}\), -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 in 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 6 and 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 \(R^1, R^2 = C_6H_5, X = O\) 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 \(R^2 = C_6H_4-p-Br\) and \(Y = Br\). Introduction of \(C_3H_5\) in \(R^1\) of both 4 and 5 as well as \(R_2 = C_6H_4-p-CH_3\) in 5 reduced their toxic effects. Also, no-cyclised compound 6 with both \(C_3H_5\) and \(C_6H_5-p-OCH_3\) 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.

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

<table>
<thead>
<tr>
<th>Compound</th>
<th>( r^1 )</th>
<th>( r^2 )</th>
<th>X</th>
<th>Y</th>
<th>LC(_{50}) (ppm) on Spodoptera larvae</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>After 2 days</td>
<td>After 7 days</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>( \text{C}_6\text{H}_5 )</td>
<td>( \text{C}_6\text{H}_5 )</td>
<td>O</td>
<td>H</td>
<td>170</td>
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<tr>
<td>2</td>
<td>( \text{C}_6\text{H}_5 )</td>
<td>( \text{C}_6\text{H}_5 )</td>
<td>S</td>
<td>H</td>
<td>460</td>
</tr>
<tr>
<td>3</td>
<td>( \text{C}_6\text{H}_5 )</td>
<td>( \text{C}_6\text{H}_4\text{p-Br} )</td>
<td>O</td>
<td>Br</td>
<td>&gt;10000</td>
</tr>
<tr>
<td>4</td>
<td>( \text{C}_6\text{H}_5 )</td>
<td>( \text{C}_6\text{H}_5 )</td>
<td>O</td>
<td>H</td>
<td>3500</td>
</tr>
<tr>
<td>5</td>
<td>( \text{C}_6\text{H}_5 )</td>
<td>( \text{C}_6\text{H}_4\text{p-CH}_3 )</td>
<td>O</td>
<td>H</td>
<td>&gt;10000</td>
</tr>
<tr>
<td>6</td>
<td>( \text{C}_6\text{H}_5 )</td>
<td>( \text{C}_6\text{H}_4\text{p-OCH}_3 )</td>
<td>S</td>
<td>S</td>
<td>&gt;1000</td>
</tr>
<tr>
<td>Bactospeine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>9400</td>
</tr>
<tr>
<td>Fenvalerate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>16</td>
</tr>
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</table>
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 potential 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 bactospine, 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 bactospine. 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$_3$H$_7$, R$^2$ = C$_6$H$_5$, X = O) followed by 1 (R$^1$, R$^2$ = C$_6$H$_5$, X = O) reduced pupation and moth emergence. While, uncylized 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, bactospene and fenvalerate on larval development of *S. littoralis*.

![General structure of pyrazolines studied](image)

(A) (B)

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

<table>
<thead>
<tr>
<th>Compound</th>
<th>R¹</th>
<th>R²</th>
<th>X</th>
<th>Y</th>
<th>ED₅₀ (ppm)</th>
<th>On % pupation</th>
<th>On % moth emergence</th>
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<tbody>
<tr>
<td>1</td>
<td>C₆H₅</td>
<td>C₆H₅</td>
<td>O</td>
<td>H</td>
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<td>100</td>
<td>96</td>
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<tr>
<td>2</td>
<td>C₆H₅</td>
<td>C₆H₅</td>
<td>S</td>
<td>H</td>
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<td>40</td>
<td>12</td>
</tr>
<tr>
<td>3</td>
<td>C₆H₅</td>
<td>C₆H₄-p-Br</td>
<td>O</td>
<td>Br</td>
<td>170</td>
<td>170</td>
<td>130</td>
</tr>
<tr>
<td>4</td>
<td>C₆H₅</td>
<td>C₆H₅</td>
<td>O</td>
<td>H</td>
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<td>42</td>
<td>30</td>
</tr>
<tr>
<td>5</td>
<td>C₆H₅</td>
<td>C₆H₄-p-CH₃</td>
<td>O</td>
<td>H</td>
<td>1300</td>
<td>1300</td>
<td>800</td>
</tr>
<tr>
<td>6</td>
<td>C₆H₅</td>
<td>C₆H₄-p-CH₃</td>
<td>S</td>
<td>S</td>
<td>1000</td>
<td>1000</td>
<td>520</td>
</tr>
<tr>
<td>Bactospene</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>280</td>
<td>280</td>
<td>140</td>
</tr>
<tr>
<td>Fenvalerate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.6</td>
<td>0.6</td>
<td>0.27</td>
</tr>
</tbody>
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REFERENCES


تصنيع والتاثيرات البيولوجية لمشتقات الفيتيانيولين

نجرى عماد م. محبوب، و.د. محمد ف. و.د. أسامة

1 كلية التربية - جامعة الإسكندرية - الإسكندرية.

2 د. د.بيجوث وقادة النباتات - دائرة البحث الزراعية - الصناعية - الإسكندرية.

يستهدف البحث تطبيق مناطق الفيتيانيولين في برنامج مكافحة الأطعمة الضارة حيث
تنقل المواد النباتية السامة لبعض مناطق الفيتيانيولين المصنعة بالإضافة إلى مقدرة تلك
المركبات في تثبيط تطور الهياجات إلى دقيق وحشرات كامنة ومقاومة تلك تأثيرات الفيتيانيولين
(الإلكتاينز) (العديد الفيتيانيولين (نيفتالين)}}.

وقد أظهرت النتائج طبيعة 1 مشتقات الفيتيانيولين (حس إذا مسح ردود تكبير حضي، بينما
الأساس غير حضي) وإختلاف الجوانب الاستهدافية على ذلك مشاهدات. وأظهرت نتائج التأثير السام
لمركبات الفيتيانيولين القوة العالية للعمال (1) والذي يحتوي على الجامبي الإبداعية
الخليفة، مجموعتي فيتاوي وناجفة أسيس تين هاد هامالم لهاماملا وجاء في المجموع_two
نحاطت في المجموعة كما يلي: 180 جم في المليون للكميين
العديد الفيتيانيولين. بينما إمتلكت إلى 170 جم في المليون على القتالي بعد 7 أيام.
وتحاول التأثير مع الفيتيانيولين من 70 إلى 90 جم في المليون بينما في
الفيتاليولين من 17 إلى 24 جم في المليون.

كذلك أظهرت مشتقات الفيتيانيولين المصنعة فعالية ضد تطور النباتات مع الفعالالية
المادية (1) والذي يحتوي على التكبير مع العلم: 170 جم في المليون عند تكبير
العديد وفرشات على القتالي، ولقد تأرجح تلك القمي من 16 إلى 20 جم في المليون عند
تحليق البليكسيسين بينما كانت معدلات 1 - 27 جم في المليون باستخدام الفيتاليولين.