Herbicidal, Insecticidal and Structure-Activity Relationship Studies on Pyranopyrazole and Oxinobispyrazole Derivatives

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ABSTRACT

Nine pyranopyrazole and oxinobispyrazole derivatives were synthesized and their structures were confirmed by spectral analysis. The inhibitory effects of prepared compounds were evaluated on germination and seedling growth of *Lolium temulentum*. In addition, the insecticidal activity of synthesized compounds was tested against the fourth instar larvae of *Culex pipiens*. The structure-activity relationships of compounds were disclosed. The results of herbicidal activity assay revealed that the prepared compounds caused significant reduction of *L. temulentum* seed germination. Compounds 4 and 7 showed the highest seed germination reduction at the tested concentrations (0.5, 1 and 5 mM) with complete inhibition (100%) of seed germination at 5 mM. In contrary, compounds 2 and 9 showed the weakest reduction of germination. The tested compounds also exhibited strong root growth inhibition with compound 7 being the most potent one and compound 1 being the less potent one. Similarly the tested compounds revealed pronounced inhibition of shoot growth of *L. temulentum*. Compounds 4 and 7 caused the highest shoot growth reduction at the tested concentrations. The inhibition of root growth by all compounds was greater than that of shoot growth. When tested for their insecticidal activity against the fourth instar larvae of *C. pipiens*, the tested compounds showed variable toxicity. However, compounds 4, 7 and 8 were the most potent toxicants toward the larvae, while compound 2 showed the lowest activity among the tested compounds. The results revealed that compounds bearing cyanide (CN) group at the position C-5 such as 4, 7 and 8 were the most active compounds against the tested weed and insect. In addition, the presence of phenyl moiety at N-1 significantly increased the herbicidal and insecticidal activity of compounds such as 7 and 8 compared with other compounds. Therefore, pyranopyrazole derivatives with these substitutions may be suitable for developing new pesticides.

Key words: Pyranopyrazoles, Oxinobispyrazoles, Herbicidal activity, Insecticidal activity, *Lolium temulentum*, *Culex pipiens*, Structure-activity relationship

INTRODUCTION

Pyranopyrazoles and oxinobispyrazoles are fused five-six membered rings containing nitrogen and oxygen heterocycles. They are an important category of heterocyclic compounds, which play a significant role in pharmaceutical and agricultural fields. Compounds bearing pyranopyrazole system have been found to have various biological activities, for instance antimicrobial (Mistry et al., 2012), analgesic (Kuo et al., 1984), vasodilator (Ahluwalia et al., 1997), anticancer (Zaki et al., 2004; Wang et al., 2009), anti-inflammatory (Zaki et al., 2006), molluscicidal (Abdelrazek et al., 2006 and 2007) and antifungal (Mangalagiu et al., 2001).

Lolium temulentum L., darnel, is originated in the Mediterranean and has spread widely across temperate areas wherever wheat and cereals are grown. Its spread into tropical areas of different countries is limited by prolonged high temperature and low moisture conditions (Holm et al., 1991). The seeds of *L. temulentum* have poisonous effects on man and animals when consumed in conjunction with wheat and other cereals (Ratera, 1983; Ambasta, 1994). They are remarkably similar in size and weight to the grains of wheat and other small grain crops, which make their separation difficult. When milled with wheat, it causes the flour to become grey and bitter. The poisonous compounds are considered to be two alkaloids, temulin and loline, which are present in the seed (Bor, 1960; Smith and Bernhard, 1988), and perloline in the stem (Dannhardt and Steindl, 1985). The competitive potential of *L. temulentum* has rarely been measured, but it is generally regarded as a competitive weed. Hollies (1982) revealed that grassy weeds, such as *L. temulentum*, caused yield losses of up to 17% in wheat and barley, whereas net profits were reduced by 25%. Wheat infested with *L. temulentum* can have an impaired response to N fertilization (Farnworth and Said, 1983). Moreover, *Lolium temulentum* can be a host to a variety of crop pests and diseases.

Culex is an important mosquito genus containing well-known vectors of important parasites and pathogens causing disease, such as filariasis, West Nile virus and other encephalitides. *Culex pipiens* are vectors of West Nile virus and an important pest to humans, causing allergic responses that include local skin reaction and systemic reactions such as angioedema, and urticaria (Cheng et al., 2008). In Egypt, eleven *Culex* species are widespread throughout the country

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with *C. pipiens* L., the house mosquito, being the most common (Abd El-Samie and Abd El-Baset, 2012).

There is an urgent need for developing new chemicals to protect agricultural crops and to combat human and animal disease vectors. In addition, few studies were reported in the literature on the biological activity of pyranopyrazoles and oxinobispyrazoles against agricultural and public health pests (Abdelrazek et al., 2006 and 2007; Badawy et al., 2016). Therefore, this study aims to synthesize nine pyranopyrazole and oxinobispyrazole derivatives (1-9) and evaluate their herbicidal activity against *Lolium temulentum*. The insecticidal activity of pyranopyrazoles was also tested against the fourth larval instar of *Culex pipiens*. In addition, the relationship between chemical structure and biological activity was discussed.

MATERIALS AND METHODS

1. Test weed

Seeds of a field biotype *Lolium temulentum* L. (Poaceae) were obtained from Faculty of Agriculture Farm, Alexandria, Egypt. Uniform seeds were selected for the test while undersized and damaged seeds were discarded. Germination of the seeds was tested before use and was 70% 12 days after sowing.

2. Test insect

Culex pipiens L. (Diptera: Culicidae) used in the bioassays was maintained in an insectary at the Department of Applied Entomology (Alexandria University, Egypt) for more than decade. Adults were kept in cages (50×50×50 cm) at 27±1 °C, 70±5% RH, and a photoperiod regime of 14:10 h (light/dark). The 10% sucrose solution, soaked in cotton swab, was provided as food for adult mosquitoes. A pigeon was introduced twice per week for adult blood feeding. Larvae were reared in dechlorinated water under the same temperature and light conditions and were fed daily with baby fish food. Newly emerged fourth instar larvae were used for bioassays.

3. Synthesis of pyranopyrazoles (1-9)

A general protocol for synthesis of pyranopyrazoles and oxinobispyrazoles was used for preparation of compounds 1-9 (Satyajit et al., 2013). To a mixture of 4-oxo-4*H*-benzopyran-3-carbaldehyde (0.01 mol), 3-methyl-pyrazolone, 3-methyl-1-phenylpyrazolone (0.01 mol), ammonium acetate (0.03 mol) or a few drops of piperidine were added. The mixture was heated at 190°C for 30 min. in methanol. After cooling, the obtained solid was washed with water, dried and crystallized from ethanol to obtain 3-(3,5-Dimethyl-1,7-diphenyl-4,7-dihydro-1*H*-pyrano[2,3-c;6,5-c']dipyrazol-4-yl)-chromen-4-one (1), 3-(3, 5-Dimethyl-4, 7-dihydro-1*H*-pyrano [2. 3-c; 6, 5-c'] dipyrazol-4-yl) chromen-4-one (2) and 3-(3,5-Dimethyl-1-phenyl-4,7-dihydro-1*H*-pyrano[2,3-c;6,5-c']dipyrazol-4-yl)-chromen-4-one (3). On other experiment, to a mixture of 4-oxo-4*H*-benzopyran-3-carbaldehyde (0.01 mol), pyrazolone (0.01 mol), malononitrile (0.01 mol.) or cyanoacetic acid, ethylacetoacetate, diethyl-malonate, cyanoacetamide (0.01 mol), ammonium acetate (0.03mol) or a few drops of piperidine were added. The mixture was heated at 120˚C for 30 min. in methanol. After cooling, the obtained solid was washed with water, derided and crystallized from ethanol to give 3-Methyl-6-oxo-4-(4-oxo-4*H*-chromen-3-yl)-1,6-dihydro-pyrano[2,3-*c*]pyrazole-5-carbonitrile (4), 5-Acetyl-3-methyl-4-(4-oxo-4*H*-chromen-3-yl)pyrano[2,3-*c*]pyrazol-6(1*H*)-one (5), Ethyl-3-methyl-6-oxo-4-(4-oxo-*4H*-chromen-3-yl)-1,6-dihydropyrano[2,3-*c*]pyrazole-5-carboxylate (6), 6-Amino-3-methyl-4-(4-oxo-4*H*-chromen-3-yl)-1-phenyl-1, 4-dihydropyrano [2, 3-*c*] pyrazole-5-carbonitrile (7): 3-Methyl-6-oxo-4-(4-oxo-4*H*-chromen-3-yl)-1-phenyl-1,6-dihydro-pyrano[2,3-*c*]pyrazole-5-carbonitrile (8) and 6-Amino-3-methyl-4-(4-oxo-4*H*-chromen-3-yl)-1-phenyl-1,4-dihydro-pyrano[2,3-*c*]pyrazole-5-carboxamide (9). The chemical structures (Figure 1) of prepared compounds were identified based on their spectral data of IR, ^{1}H-NMR and MS (Khurana and Chaudhary, 2012; Badawy et al., 2016).

4. Phytotoxic Bioassay

A bioassay based on germination and subsequent seedling growth was carried out to study the phytotoxic effects of the nine pyranopyrazoles and oxinobispyrazoles on seeds of *Lolium temulentum* (Abdelgaleil et al., 2009) The solutions of tested pyranopyrazoles were initially prepared in dimethyl sulfoxide (DMSO) and then diluted with distilled water containing 0.02% of an emulsifying agent (Triton-X 100) to give the concentrations of 0.5, 1 and 5 mM. The treatments with distilled water containing DMSO (0.5% v/v) and Triton-X 100 (0.02%) were taken as the controls. The use of DMSO and Triton-X 100 at these concentrations did not reduce germination or plant growth compared to a water only control. Three replicates, each of 20 seeds, were prepared for each treatment using glass Petri dishes (9 cm) lined with Whatman No. 2 filter paper. Six milliliters of each concentration was added to individual Petri dishes. Afterward, Petri dishes were placed in the bottom of 0.1 mm thick polyethylene bags (15 by 30 cm) that were expanded to contain air and then closed at the top with rubber bands to prevent the loss of moisture. The Petri dishes were placed in a growth chamber at 22±2 °C with a 12-h photoperiod. Twelve days after sowing, the germination was determined by counting the number of germinated seeds and the lengths of root and shoot were

measured. The growth reduction percentages of root and shoot lengths were calculated from the following equation: R (%) = [1 − T/C]×100; where T is the root or shoot length of treatment (cm) and C is the root or shoot length of control (cm).

5. Insecticidal bioassay

The larval mortality bioassay was carried out using the recommended method of the World Health Organization (WHO, 1996). Stock solutions of the tested pyranopyrazoles and oxinobispyrazoles were prepared in dimethyl sulfoxide (DMSO). Groups of 20 *C. pipiens* fourth instar larvae were separately put into 200-ml plastic cups containing 100 ml of distilled water. The tested compounds solutions in 0.1 ml DMSO were added to each cup and suspended with Tween-20 (0.1 ml), with gentle shaking to ensure a homogeneous test solution. The compounds were tested at concentrations 125, 250 and 500 mg/L. The control was prepared with distilled water containing the same amount of DMSO and Tween-20. There were three replicates for each concentration. Treated and control larvae were held in the same conditions used for colony rearing. Larval mortalities were recorded 24 and 48 h post-treatment. Larvae were considered dead when they did not respond to stimulus or did not rise to the surface of the solution.

6. Statistical analysis

Germination percentages, root and shoot lengths, and mortality percentages were subjected to one-way analysis of variance followed by Student–Newman–Keuls test (Cohort Software Inc. 1985) to determine significant differences among mean values at the probability level of 0.05.

RESULTS AND DISCUSSION

1. Effect of pyranopyrazoles and oxinobispyrazoles on seed germination

The effect of the nine pyranopyrazoles and oxinobispyrazoles (1-9) on the seed germination of *L. temulentum* 12 days after sowing is given in Table 1. The results reveal that the tested pyranopyrazoles and oxinobispyrazoles caused significant reduction of seed germination at the tested concentrations except compound 9 at concentrations 0.5 and 1mM. At 0.5 mM, compound 7 gave the highest reduction in seed germination, followed by 1 and 3, while 9, 5 and 2 were the less effective compounds at this concentration. Compound 7 caused the highest seed germination reduction at concentration of 1 mM with 28.3% seed germination. In contrary, 8 had the weakest effect on seed germination at 1 mM. In the case of 5 mM, compounds 4 and 7 caused complete inhibition (100%) of seed germination. Compounds 1, 8 and 6 caused strong reduction of seed germination at this concentration with 13.3, 18.3 and 20.0% seed germination, respectively, whereas 3, 9 and 2 were the less effective compounds at this concentration.

Table 1. Effect of pyranopyrazoles and oxinobispyrazoles on *Lolium temulentum* seed germination 12 days after sowing[a]

Conc	Seed germination % ± SE[b]		
mM	1	2	3
0	70.0±0.0a	70.0±0.0a	70.0±0.0a
0.5	41.7±1.66b	60.0±2.89b	41.7±4.44b
1	48.3±6.05b	41.7±1.66c	51.7±7.31b
5	13.3±1.66c	30.0±2.89d	36.7±6.01b
Conc	Seed germination % ± SE		
mM	4	5	6
0	70.0±0.0a	70.0±0.0a	70.0±0.0a
0.5	58.3±6.01b	61.7±4.41b	53.3±1.67b
1	45.0±2.89c	51.7±3.34bc	38.3±4.41c
5	0.0±0.0d	25.0±5.01c	20.0±2.89d
Conc	Seed germination % ± SE		
mM	7	8	9
0	70.0±0.0a	70.0±0.0a	70.0±0.0a
0.5	31.7±4.41b	56.7±4.41b	65.0±5.78a
1	28.3±1.66b	55.0±2.89b	53.3±4.41a
5	0.0±0.0c	18.3±1.67c	31.7±4.41b

[a] Data are expressed as means ± SE from experiments with three replicates of 20 seeds each.
[b] Mean values within a column sharing the same letter are not significantly different at the 0.05 probability level.

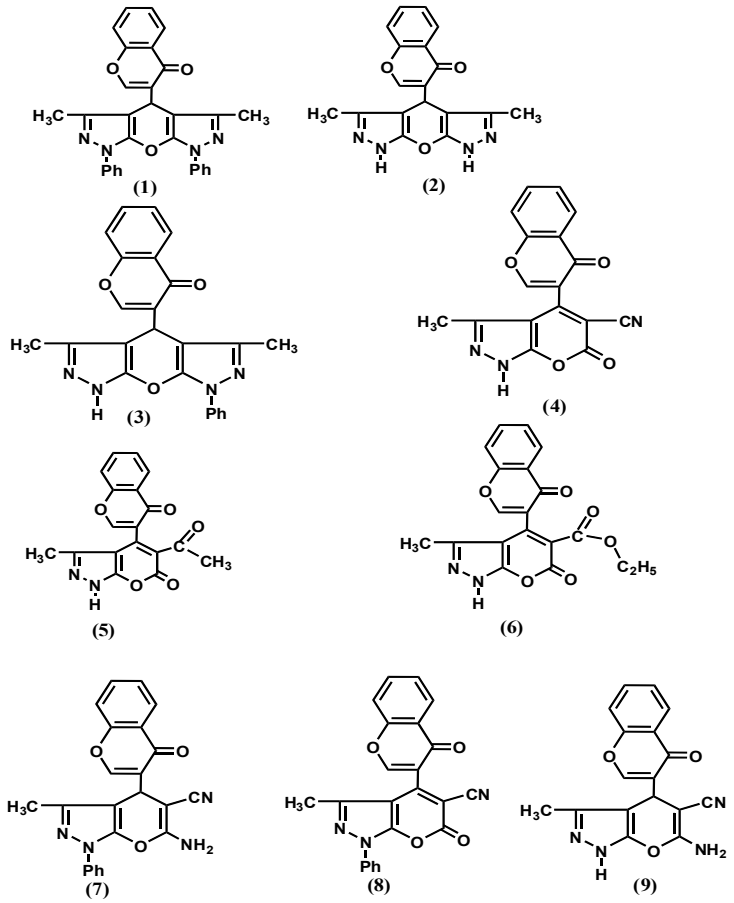

Figure 1. The chemical structures of pyranopyrazoles and oxinobispyrazoles(1-9)

2. Effect of pyranopyrazoles and oxinobispyrazoles on root growth

The results showed that the tested compounds exhibited significant reduction of root growth of *L. temulentum* at all tested concentrations compared to control, except for compound 4 at the lowest concentration (0.5 mM) and compound 1 at concentrations 0.5 and 1 mM (Table 2).

Compound 3 caused the highest root growth reduction at 0.5 mM with 57% growth inhibition. Similarly, compounds 6, 5, 8 and 7 displayed strong root growth reduction at this concentration with 50.4, 49.8, 46.5 and 46.3 % growth reduction, respectively. In contrast, compound 4 revealed the lowest reduction of root growth at this concentration. At 1 mM, compound 7 was the most potent root growth inhibitor, followed by compounds 8 and 4 with 76.2, 71.7 and 67.7% growth reduction, respectively. Compound 1 had the weakest effect on root growth. Compounds 4 and 7 caused complete root growth inhibition at 5 mM. Likewise, compounds 8, 9, 6 and 5 displayed strong effect on root growth (reduction > 90%). In contrary, compound 1 revealed the weakest effect of root growth at this concentration.

3. Effect of pyranopyrazoles and oxinobispyrazoles on shoot growth

The results demonstrate that the pyranopyrazoles and oxinobispyrazoles had pronounced effect on shoot growth of *L. temulentum*. The tested compounds (1-9) caused significant reduction of shoot growth at the tested concentrations, except compound 1 at 0.5 and 1 mM, and compound 2 at 0.5 mM (Table 3). Compound 7 (growth inhibition = 44.5%) was the most active at 0.5 mM, followed by compound 8 (growth inhibition = 31.8%), while compound 1 (growth inhibition = 5.2%) was the less effective one among the tested compounds. In addition, compounds 7, 6 and 4 caused the highest shoot growth reduction at 1 mM. In contrary, compounds 1 and 3 had the lowest growth reduction at this concentration. At 5 mM, compounds 4 and 7 caused complete inhibition of shoot growth. Compounds 8, 6 and 2 showed strong reduction of shoot growth, while compound 3 was the less effective one at 5 mM.

The results of the present study indicated that compounds (1-9) had herbicidal activity against *L.*

temulentum. These results are supported by the study of Badawy et al. (2016) who mentioned that the tested compounds caused reduction on seed germination and seedling growth of *Portulaca oleracea*.

Despite the lack of reported studies on herbicidal activity of the tested pyranopyrazoles and oxinobispyrazoles, some pyrazoles were described to possess herbicidal activity. For example, Ma et al. (2010) synthesized a series of novel *N*-(2,2,2)-trifluoroethylpyrazole derivatives and evaluated their herbicidal activity against dicotyledonous and monocotyledonous weeds.

Table 2. Effect of pyranopyrazoles and oxinobispyrazoles on *Lolium temulentum* root growth 12 days after sowing[a]

Conc	1		2		3	
mM	Root length (cm)	R (%)[b]	Root length (cm)	R (%)	Root length (cm)	R (%)
0	5.12±0.26a	0.0	5.12±0.26a	0.0	5.12±0.26a	0.0
0.5	3.91±0.31a	23.6	3.0±0.19b	41.4	2.18±0.29b	57.4
1	3.87±0.43a	24.4	2.83±0.17b	44.7	2.75±0.25b	46.3
5	2.43±0.28b	52.5	0.71±0.39c	86.1	1.24±0.26c	75.8
Conc	**4**		**5**		**6**	
mM	**Root length (cm)**	**R (%)**	**Root length (cm)**	**R (%)**	**Root length (cm)**	**R (%)**
0	5.12±0.26a	0.0	5.12±0.26a	0.0	5.12±0.26a	0.0
0.5	4.63±0.35a	9.6	2.57±0.22b	49.8	2.54±0.23b	50.4
1	1.65±0.34b	67.7	1.77±0.26c	65.4	1.75±0.39b	65.8
5	0.0±0.0c	100.0	0.5±0.0d	90.2	0.3±0.12c	94.1
Conc	**7**		**8**		**9**	
mM	**Root length (cm)**	**R (%)**	**Root length (cm)**	**R (%)**	**Root length (cm)**	**R (%)**
0	5.12±0.26a	0.0	5.12±0.26a	0.0	5.12±0.26a	0.0
0.5	2.37±0.12b	46.3	2.74±0.26b	46.5	3.20±0.14b	37.5
1	1.22±0.22c	76.2	1.45±0.19c	71.7	1.98±0.16c	61.3
5	0.0±0.0d	100.0	0.13±0.09d	97.5	1.03±0.07d	79.9

[a] Data are expressed as means ± SE from experiments with three replicates of 20 seeds each.
[b] I = reduction.
[c] Mean values within a column sharing the same letter are not significantly different at the 0.05 probability level.

Table 3. Effect of pyranopyrazoles and oxinobispyrazoles on *Lolium temulentum* shoot growth 12 days after sowing[a]

Conc	1		2		3	
mM	Shoot length (cm)	R (%)[b]	Shoot length (cm)	R (%)	Shoot length (cm)	R (%)
0	7.82±0.24a	0.0	7.82±0.24a	0.0	7.82±0.24a	0.0
0.5	7.41±0.26a	5.2	6.88±0.26ab	12.0	6.09±0.24b	22.1
1	7.22±0.54a	7.7	6.18±0.59b	21.0	6.74±0.32b	13.8
5	3.70±0.32b	52.7	2.83±0.09c	63.8	4.48±0.52c	42.7
Conc	**4**		**5**		**6**	
mM	**Shoot length (cm)**	**R (%)**	**Shoot length (cm)**	**R (%)**	**Shoot length (cm)**	**R (%)**
0	7.82±0.24a	0.0	7.82±0.24a	0.0	7.82±0.24a	0.0
0.5	6.0±0.50b	23.3	6.29±0.27b	19.6	6.11±0.20b	21.9
1	4.38±0.25c	44.0	6.21±0.41b	20.6	4.26±0.50c	45.5
5	0.0±0.0d	100.0	3.56±0.18c	54.5	2.31±0.36d	70.5
Conc	**7**		**8**		**9**	
mM	**Shoot length (cm)**	**R (%)**	**Shoot length (cm)**	**R (%)**	**Shoot length (cm)**	**R (%)**
0	7.82±0.24a	0.0	7.82±0.24a	0.0	7.82±0.24a	0.0
0.5	4.34±0.33b	44.5	5.33±0.33b	31.8	6.32±0.24b	19.2
1	3.48±0.25c	55.5	4.81±0.23b	38.5	5.03±0.29c	35.7
5	0.0±0.0d	100.0	0.91±0.50c	88.4	3.35±0.16d	57.2

[a] Data are expressed as means ± SE from experiments with three replicates of 20 seeds each.
[b] R = reduction.
[c] Mean values within a column sharing the same letter are not significantly different at the 0.05 probability level

Some of the tested compounds exhibited better herbicidal activity by soil application than the commercial herbicide, metolachlor. Kang et al. (2015) stated that pyrazoles exhibited excellent herbicidal activities at the concentration of 100 mg/L, and compound 5-chloro-2-((3-methyl-1-(2,2,2-trifluoroethyl)-1H-pyrazol-5-yl)oxy)pyrimidine showed bleaching activity to green weeds. In addition, pyrazole derivatives were described to have herbicidal activities against *Brassica napus*, *Echinochloa crusgalli*, *E. oryzicola*, *Lindernia procumbens*, *Eleocharis acicularis*, *Sagittaria pygmaea*, *Cyperus serotinus*, *C. difformis, Eleocharis acicularis*, *E. kuroguwai*, *Monochoria vaginalis*, *Rotala indica*, *Elatine triandra*, *Ammannia multiflora* and *Scirpus juncoides* (Kudo et al., 1999; Ohno et al., 2004; Xu et al., 2012).

The results indicated that the tested pyranopyrazoles and oxinobispyrazoles exhibited greater inhibitory effects on seedling growth than on seed germination. A similar finding was described by Leather and Einhellig (1985) who demonstrated that bioassays determining seedling growth of many allelochemicals are usually more sensitive than those measuring germination. In addition, all of the tested compounds had greater inhibitory effects on root growth than on shoot growth. These results are supported by our earlier studies of inhibitory effects of essential oils, sesquiterpenes and monoterpenes on seedling growth (Abdelgaleil et al., 2009 and 2014; Saad et al., 2012; Gouda et al., 2016). This finding might be predictable, because it is likely that roots are the first to absorb the allelochemicals compounds from the media (Turk and Tawaha 2002).

4. Insecticidal activity of pyranopyrazoles and oxinobispyrazoles on *Culex pipiens* fourth instar larvae

Pyranopyrazoles and oxinobispyrazoles (1-9) were tested for their toxicity against the fourth instar larvae of *C. pipiens*. In general, all of the tested compounds showed insecticidal activity. However the toxicity was compound, concentration and time dependent. After 24 h of treatment at 125 mg/L, compound 7 exhibited the highest larval mortality, followed by compounds 4 and 8 (Table 4). Similarly, compounds 7 and 8 showed the highest toxicity at this concertation after 48 h of treatment, while compound 2 had the least toxicity. The tested compounds caused higher larval toxicity at 250 mg/L with compound 7 being the most potent after 24 h, followed by compounds 4 and 8. After 48 h of treatment, compound 7 caused complete larval mortality and compounds 1, 4 and 8 showed strong insecticidal activity. All of the tested compounds revealed potent toxicity against *C. pipiens* larvae at 500 mg/L after 24 h except compounds 2 and 9. After 48 h, compounds 1 and 7 caused complete larval mortality. In addition, compounds 4, 5 and 8 displayed strong insecticidal activity, while compound 2 was the less effective one at this concentration.

To the best of our knowledge there were no reported studies on the insecticidal activity of synthetized pyranopyrazoles and oxinobispyrazoles (1-9) against *C. pipiens* or other insects. Nevertheless, many pyrazoles have been stated to have insecticidal activity against different insect species. Song et al. (2012) evaluated the insecticidal or acaricidal activity some pyrazoles containing 4,5-dihydrooxazole moieties against *Helicoverpa armigera*, *Plutella xylostella*, *Aphis craccivora*, *Culex pipiens pallens* and *Tetranychus cinnabarinus*. Some of the prepared compounds showed high insecticidal activity against the tested insects and spider mite. In addition, pyrazole derivatives exhibited notable control of *P. xylostella*, *H. armigera*, *C. pipiens pallens*, *Laphygma exigua*, *Spodoptera litura*, *Nilaparvata lugens* and *Rhopalosiphum maidis* (Wu et al. 2012).

Table 4. Mortality percentages of *Culex pipiens* fourth instar larvae after 24 and 48 h of treatment with pyranopyrazoles and oxinobispyrazoles at different concentrations

Compound	Mortality (%) ± SE[a]					
	125 mg/L		250 mg/L		500 mg/L	
	24 h	48 h	24 h	48 h	24 h	48 h
1	20.0±0.0c	53.3±6.67b	26.7±6.67c	80.0±5.78b	80.0±5.78b	100.0±0.0a
2	0.0±0.0d	6.7±6.67cd	0.0±0.0d	53.3±6.67c	13.3±6.67d	53.3±6.7c
4	36.7±3.34b	40.0±0.0b	43.3±3.34b	73.3±3.34b	66.7±3.34b	86.7±3.34a
5	10.0 ±0.0d	50.0±0.0b	10.0±0.0d	50.0±0.0c	70.0±5.78b	96.7±3.34a
7	63.3±3.34a	80.0±5.78a	76.7±3.34a	100.0±0.0a	100.0±0.0a	100.0±0.0a
8	30.0±5.78b	73.3±6.67a	36.7±3.34b	80.0±5.78b	66.7±8.83b	90.0±5.78a
9	0.0±0.0d	20.0±0.0c	20.0±0.0c	46.7±6.67c	33.3±3.34c	66.7±6.67b
Control	0.0±0.0d	0.0±0.0d	0.0±0.0d	0.0±0.0d	0.0±0.0d	0.0±0.0d

[a] Means within each column followed by the same letter are not significantly different (P=0.05).

Moreover, the insecticidal or acaricidal activities of pyrazole derivatives against *Nephotettix cincticeps*, *Tetranychus urtica* and *Periplaneta americana* have been described (Verma and Nayal, 2003; Ohno et al., 2010).

The structure-herbicidal activity relationship examination of the tested compounds revealed that the compounds containing two pyrazole rings or oxinobispyrazoles such as 1, 2 and 3 were less active than compounds containing one pyrazole ring or pyranopyrazoles (4-9) against *L. temulentum*. Among the bi-pyrazole (1-3), compound 1 which bearing no phenyl moiety was more active than compound 2 which bearing one phenyl moiety at N-1 and both compounds were more active than 3 which bearing two phenyl moieties at N-1 and N-1`. The presence of cyanide (CN) group at C-5 increased the herbicidal activity of compound 4 comparing with 5 and 6. Compounds 4 and 8 revealed similar herbicidal activity against *L. temulentum*, indicating that the substitution of H by phenyl at N-1 had no significant effect on the herbicidal activity. However, the presence of phenyl at N-1 strongly enhanced the activity of compound 7 comparing with compound 9.

On the other hand, the presence of two phenyl moieties on N-1 and N-1` in compound 1 increased the toxicity of compound 1 to *C. pipiens* larvae comparing with 2 which bearing no phenyl. Comparing the toxicity of compounds 4 and 5 indicated that the substitution at C-5 either by CN or $COCH_3$ had no notable effect on the toxicity. Moreover, the presence of phenyl ring at N-1 in compound 7 increased the toxicity of the compound compared with compound 9.

In summary, nine pyranopyrazoles and oxinobispyrazoles (1-9) were prepared and tested for their herbicidal activity against *L. temulentum* and their insecticidal activity against *C. pipiens*. Among the tested compounds, 4, 6, 7, and 8 showed promising herbicidal activity against *L. temulentum*. In addition, compounds 1, 5, 7 and 8 displayed the highest insecticidal activity against *C. pipiens* larvae. These compounds seem promising and warrant further studies in the future.

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الملخص العربي

دراسات على النشاط الإبادى ضد الحشائش والحشرات والعلاقة بين التركيب الكيميائي والنشاط لمركبات البايرانوبايرازول والأوكسينوبايرازول

سمير عبد العظيم عبد الجليل، يونس محمود بدوى

فى هـذه الدراسـة تـم تحـضير ٩ مركبـات مـن البايرانوبايرازول والأوكسينوبايرازول وتم التعـرف علـى التركيب الكيميائى بواسطة طرق التحليل الطيفى المختلفـة. تم تقييم التأثير التثبيطى لهذه المركبات على إنبـات بـذور ونمو بادرات حشيشة الصامة. بالإضافة إلى تقييم النـشاط الإبادى الحشرى للمركبات المحضرة على العمـر اليرقـى الرابع لبعوضة الكيولكس. كما تـم دراسـة العلاقـة بـين التركيب الكيميائى والنشاط الإبادى للمركبـات المحـضرة. أوضحت النتائج أن المركبات المحـضرة أحـدثت خفـضاً معنوياً فى إنبات بذور حشيشة الـصامة. المركبـان ٤ و٧ أظهرا أعلى نسبة خفض فى الإنبات على كل التركيـزات المستخدمة (٠,٥ و١ و٥ مللى مولر)، كمـا سـببا هـذان المركبان منعاً تاماً لإنبات البذور على تركيز ٥ مللى مولر. على النقيض من ذلك فـإن المركبـان ٢ و٩ كانـا أقـل المركبات تثبيطاً لإنبات البذور. كما أظهـرت المركبـات المختبرة أيضا تثبيطاً قوياً لنمو المجموع الجذرى للحشيشة وكان مركب ٧ أعلى المركبات تثبيطاً فى حين مركـب ١ أقل المركبات تثبيطاً. بالمثل فإن المركبات سـببت خفـضاً قوياً لنمو المجموع الخضرى لحشيشة الصامة. المركبان ٤ و٧ أحدثا أعلى خفض فى نمو المجموع الخضرى على كل التركيزات المختبرة. كل المركبات المختبرة سببت خفـضاً أعلى فى نمو الجذور عن نمو المجموع الخضرى. وعنـد إختبار النشاط الإبادى الحشرى للمركبات ضد العمر اليرقى الرابع لبعوضة الكيولكس فإن المركبات المحضرة أظهرت سمية متفاوتة. بالرغم من أن مركبات ٤ و٧ و٨ كانت أعلى المركبات سمية ضد اليرقات، بينما مركـب ٢ كـان أقـل المركبات سمية على يرقات الحشرة مـن بـين المركبـات المختبرة. أوضحت النتائج أن المركبات التى تحتوى علـى مجموعة سيانيد CN علـى ذرة الكربـون رقـم ٥ مثـل مركبات ٤ و٧ و٨ كانت أكثر المركبـات فعاليـة ضـد حشيشة الصامة وبعوضة الكيولكس. كما أن وجـود حلقـة الفينايل على ذرة النيروجين رقم ١ يؤدى إلى زيادة النشاط الإبادى الحشرى والنشاط الإبادى ضد الحشائش كمـا فـى مركبى ٧ و٨ مقارنة بالمركبات الأخرى. لذلك فإن مركبات البايرانوبايرازول التى تحتوى هذه الإستبدالات ربما تكـون مناسبة لتطوير بعض المبيدات الجديدة.