SYNTHESIS AND ANTI-APHID *APHIS GOSSYPII* GLOVER ACTIVITY OF SOME NEW QUINOLINE DERIVATIVES

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Abstract: A series of quinoline derivatives have been elaborated from reaction of 2-(*m*- and *p*-acetylanilino)-quinolines 6a–b with aldehydes under Claisen-Schmidt conditions followed by cyclization with phenyl hydrazine and hydroxylamine. Reaction of 6a and 6b with hydrazine, semicarbazide and thiosemicarbazide, cyanoacetylhydrazide and some subsequent condensation reactions led to diverse quinoline derivatives. Anti-Aphid *Aphis gossypii* that harm cotton crop in Egypt was screened. Compound 12 showed an LC_{50} value of 19429E-10 ppm which is much more active than Marshal (Carbosulfan), one of the broad spectrum insecticides widely used in this field.

Key words: insecticides, aphid *Aphis gossypii*, quinoline, pyrazole, thiosemicarbazide

INTRODUCTION

Cotton aphid, *Aphis gossypii* Glover (Homoptera: Aphididae), is a piercing-sucking insect that harms cotton *Gossypium barbadense* L., crop worldwide (Stoetzel *et al.* 1996; Daughtery *et al*. 1997). Damage occurs as a result of direct feeding and excretion of its honeydew. This honeydew is rich in monosaccharides and many free amino acids, resulting in associated pathogenic fungal growth and virus transmission causing more than 50 cotton plant diseases (Forlow and Henneberry 2001). Biological control (Kaplan and Eubanks 2002) through natural enemies including predators (bugs and spiders) (Weathersbee III and Hardee 1994) parasitoids (*Aphidus gifuensis*) (Ma *et al.* 2006), and pathogens such as the entomopathogenic fungus *Neozygites fresenii* are well known (Steinkraus and Zawislak 2004; Smith and Hardee 1996). Relay intercropping (Ma *et al.* 2006) of agricultural co-systems as mutualistic plant protection, and use of transgenic cotton species were valuable in protection of the crop (Runzhi *et al*. 2000). Ecological effects represented in O_3 (Menéndez *et al.* 2010) on aphid infestation as well as use of remote sensing for detection of plant damage were investigated (Reising *et al.* 2004). Chemical control, on the other hand, has gained great interest due to the widespread cultivation of cotton worldwide to satisfy the global requirements.

Despite the diversity of these insecticides (Takahashi *et al*. 2001; Conway *et al.* 2003; Zhae *et al.* 2009), *A. gossypii* could continuously evolve insecticidal resistance. Insecticides on their own have singularly failed to control this pest (Moores *et al.* 1996). Application of wide-spectrum insecticides have devastated natural enemies, thus contributing to aphid outbreaks (Liu 2000). A study was

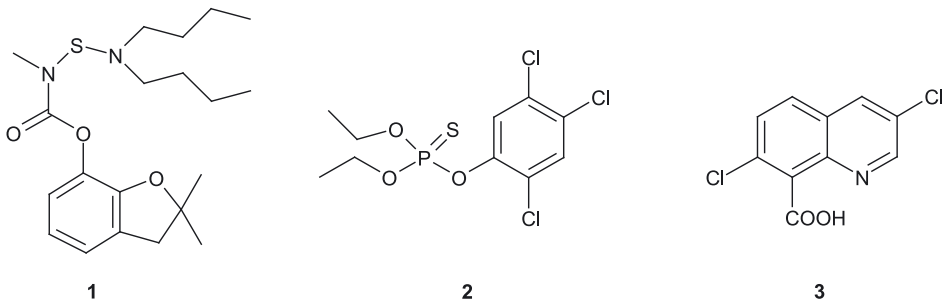

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Fig. 1. Anti-Aphid pesticides

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done in Egypt on ten insecticides of the carbamates and organophosphates families tested against adult stages of the pest collected from eight Egyptian governorates. The study showed that Marshal 1 and Dursban 2 were the most toxic insecticides (Khalid *et al.* 2005). Although, quinoline derivatives are of diverse biological activities (Lubenets *et al*. 2000), only a few, to the best of our knowledge, are of agro-applications. For instance, Quinclorac 6 is used as a herpicide (Worthing and Waiker 1987) (Fig. 1). This prompted us to synthesize a set of quinolines modified with various functionalities encountered in several pesticides, to assess their contribution as anti-aphid candidates for future protection of cotton cultivation.

MATERIALS AND METHODS

Chemistry

General

Melting points were determined on Gallenkamp apparatus and are uncorrected. Elemental analyses were performed on Flash EA1112 in ThermoFischer Center, Milan, Italy. NMR spectra were recorded on the AC200 Brucker instruments from the Technical university in Vienna, and on the varian Mercury VX-300 instrument at Cairo University. IR-spectra were recorded using JASCO FT IR-460 plus spectrometer. The mass spectra were recorded on GCMS-QP 1000Ex Shimadzu spectrometers in the microanalysis unit at Cairo University. Insecticidal activity was done in the plant protection research Institute, Agricultural Research Center, Mansoura branch, Egypt.

1-[3-(quinolin-2-ylamino)phenyl]ethanone (6a)

A mixture of 2-cholorquinoline 4 (16.3 g, 99.0 mmol) and 3-aminoacetophenone 5a (14.8 g, 109.0 mmol) and 5 drops of HCl in EtOH (30 ml) was heated under reflux for 8 hours then left to reach ambient temperature. The precipitate formed was filtered and recrystallized from benzene to afford 6a (11.0 g, 70%) as reddish crystals, m.p. 127°C. $C_{17}H_{14}N_2O$ (262).

General procedure for synthesis of 7a–d

A mixture of 6a (2.98 g, 0.01 mol), the appropriate aromatic aldehyde (0.01 mol) and NaOH (1.0 g, 25.0 mmol) in EtOH 10 ml was refluxed in a water-bath for 4 h then left to reach ambient temperature. The precipitate formed was filtered and recrystallized from EtOH to afford 7a–d.

3-Phenyl-1-[3-(quinolin-2-ylamino)phenyl]prop-2-en-1-one (7a)

Obtained as yellow crystals in 65% yield; m.p. 176°C; ^{1}H NMR (200 MHz, $CDCl_3$): *d* 8.34 (s, 1H, NH), 8.04–7.26 (m, 16H, Ar, -CH = CH-), 6.99 (d, 1H, *J* 9.0 Hz, -CH = CH-). $C_{24}H_{18}N_2O$ (350).

3-(4-Methoxyphenyl)-1-[3-(quinolin-2-ylamino)phenyl]prop-2-en-1-one (7b)

Obtained as yellow crystals in 70% yield; m.p. 166°C; ^{1}H NMR (200 MHz, $CDCl_3$): *d* 8.33 (s, 1H, NH), 8.01–6.98 (m, 16H, Ar, -CH = CH-), 6.95 (d, 1H, *J* 8.8 Hz, -CH = CH-), 3.86 (s, 3H, OMe). $C_{25}H_{20}N_2O_2$ (380).

3-(4-Chlorophenyl)-1-[3-(quinolin-2-ylamino)phenyl]prop-2-en-1-one (7c)

Obtained as yellow crystals in 60% yield; m.p. 171°C; ^{1}H NMR (200 MHz, $CDCl_3$): *d* 8.43 (s, 1H, NH), 7.97–7.26 (m, 15H, Ar, -CH = CH-), 6.94 (d, 1H, *J* 8.8 Hz, -CH = CH-); EI-MS: *m/z* (%), 385 (M^+, 100), 261 (91), 219 (35). $C_{24}H_{17}ClN_2O$ (384).

3-(3-Hydroxyphenyl)-1-[3-(quinolin-2-ylamino)phenyl]prop-2-en-1-one (7d)

Obtained as colorless crystals in 75% yield; m.p. 184°C; ^{1}H NMR (200 MHz, $CDCl_3$): *d* 8.31(s, 1H, NH), 8.00–7.26 (m,15 H, Ar, -CH = CH-), 6.95 (d, 1H, *J* 8.4 Hz, -CH = CH-), 2.65 (s, 1H, OH). $C_{24}H_{18}N_2O_2$ (366).

3-[3-(Quinolin-2-ylamino)phenyl]-4,5-dihydro-1,5-diphenylpyrazole (8)

A mixture of 7a (1.75 g, 5.0 mmol) and phenylhydrazine (0.5 ml, 5.0 mmol) in EtOH (10 ml) was heated under reflux for 6 h then left to reach ambient temperature. The precipitate formed was filtered and recrystallized from MeOH to afford 8 (1.09 g, 60%) as colorless crystals; m.p.163°C. ^{1}H NMR (200 MHz, $CDCl_3$): *d* 8.06–6.80 (m, 21H, 2 Ph, 2 Ar, NH), 5.31 (dd, $J_{4,5}$ 6.4, $J_{4;5}$ 7.8 Hz, H-5_{pyr}), 3.87 (t, 1H, J_{gem} 15.8 Hz, $J_{4,5}$ 6.4 Hz, H-4_{pyr}), 3.17 (dd, 1H, J_{gem} 15.8, $J_{4;5}$ 7.8 Hz, 1 H, H-$4`_{pyr}$). $C_{30}H_{24}N_4$ (440.2).

3-[3-(Quinolin-2-ylamino)phenyl]-4,5-dihydro-5-(4-methoxyphenyl)isoxazole (9)

A mixture of 7b (1.9 g, 5.0 mmol), hydroxylamine hydrocholoride (0.34 g, 5.0 mmol) and NaOH (0.01 mol) in EtOH (15 ml) was heated under reflux for 7 h then left to reach ambient temperature. The precipitate formed was filtered and recrystillized from MeOH to afford 9 (1.3 g, 70%) as colorless crystals; m.p. 146°C. IR (KBr): 3,378 (NH_{str}), 1 607 (C = N_{str}); ^{1}H NMR (200 MHz, $CDCl_3$): *d* 8.02 (s, 1H, NH), 7.83–6.89 (m, 14H, Ar), 5.71 (dd, 1H, $J_{4,5}$ 11.0, $J_{4;5}$ 9.0 Hz, H-5_{isoxaz}), 3.88–3.69 (m, 4H, H-4_{isoxaz}, OMe), 3.36 (dd, 1H, $J_{4;5}$ 9.0, J_{gem} 16.8 Hz, H-$4`_{isoxaz}$); EI-MS: *m/z* (%): 395 (M^+, 52.6), 260 (73.2), 219 (47.4), 128 (71.1), 77(100). $C_{25}H_{21}N_3O_2$ (395.1).

1-[3-(quinolin-2-ylamino)phenyl]ethan-1-one hydrazone (10)

A mixture of 6a (2.98 g, 0.0l mol), hydrazine hydrate (3.4 g, 0.05 mol) and H_2SO_4 (0.01 ml) in EtOH (15 ml) was stirred at rt for 2 h. The precipitate formed was filtered and recrystallized from EtOh to afford 10 (2.38 g, 80%) as colorless crystals; m.p. 178°C. ^{1}H NMR (500 MHz, DMSO-*d6*): *δ* 9.54 (s, ^{1}H, NH), 8.53–6.93 (m, 12 H, Ar), 3.21 (br.s, 2H, NH_2), 2.37 (s, 3H, CH_3). $C_{17}H_{16}N_4$ (276.1).

1-[3-(quinolin-2-ylamino)phenyl]ethan-1-one semicarbazone (11a)

A mixture of 6a (2.98 g, 0.0l mol), semicarbazide (1.11 g, 0.01 mol) and sodium acetate (0.01 mol) in EtOH (15 ml) was heated under reflux 2 h while stirring, then left to reach ambient temperature. The precipitate formed was filtered and recrystallized from MeOH to afford 11a (0.72 g, 65%) as colorless crystals; m.p. 218°C). IR (KBr): 3,427–3,314 (NH_{str}), 3185 (NH_{2str}), 1678 (C = O_{str}),

1571 (C = N_{str}); ^{1}H NMR (200 MHz, DMSO-d_6): *d* 9.49 (s, 1H, NHCO-), 8.44–7.32 (m, 11H, NH, Ar), 3.78 (br.s, 2H, NH_2), 2.25 (s, 3H, CH_3); EI-MS: *m/z* (%): 319 (M^+, 66.7), 234 (66.7). $C_{18}H_{17}N_5O$ (319).

1-[4-(quinolin-2-ylamino)phenyl]ethan-1-one thiosemicarbazone (11b)

A mixture of 6b (2.98 g, 0.0l mol) and thiosemcarbazide (0.91 g, 0.01 mol) in EtOH (20 ml) containing H_2SO_4 (0.01 ml) was stirred at ambient temperature for 3 h. The precipitate formed was filtered and recrystallized from EtOH to afford 11b (2.0 g, 70%) as yellow crystals; m.p. 219°C. IR (KBr): 3,261–3,423 (NH_{str}), 3,062 (NH_{2str}), 1,605 (C = N_{str}), EI-MS: *m/z* (%): 335 (M^+, 1.0). $C_{18}H_{17}N_5S$ (335).

1-[4-(quinolin-2-ylamino)phenyl]ethan-1-one N-phenylmethylene]semicarbazone (12)

A mixture of 11b (3.35 g, 0.0l mol) and benzaldehyde (1.06 g, 0.01 mol) in EtOH (10 ml) was heated under reflux for 3 h then left at ambient temperature overnight. The precipitate formed was filtered and recrystallized from aqueous EtOH to afford 12 (2.17 g, 65%) as colorless crystals; m.p. 181°C. ^{1}H NMR (200 MHz, DMSO-*d6*): δ 10.20 (s, 1H, -N = CH-), 8.23–8.02 (2s, 2 H, 2 NH), 7.87–7.43 (m, 15H, Ar), 2.46 (s, 3H, CH_3); EI-MS: *m/z* (%): 423 (M+, 0.1), 261 (100), 219 (23), 128 (77.24). $C_{25}H_{21}N_5S$ (423).

2-cyano-N′-{1-[3-(quinolin-2-ylamino)phenyl]ethylidene}acetohydrazide (13)

A mixture of 6a (2.987 g, 0.0l mole) and cynoacetohydrazide (0.99 g, 0.01 mole) in dry EtOH (30 ml) containing H_2SO_4 (0.01 ml) was stirred for 2 h at ambient temperature. The precipitate formed was filtered off and recrystallized from MeOH to afford 13 (2.24 g, 75%) as reddish crystals; m.p. 224°C**.** ^{1}H NMR (200 MHz, DMSO-d_6): *d* 11.17 (s, 1 H, NHCO-), 11.0 (s, 1H, NH), 8.44–7.34 (m, 10H, Ar), 4.29 (s, 2H,- CH_2), 2.39 (s, 3H, CH_3); EI-MS: *m/z* (%): 342.5 M^+, 2), 303 (3.31), 261 (100), 219 (10.05), 128 (1.98); $C_{20}H_{17}N_5O$ (343).

2-Cyanomethyl-5-[3-(quinolin-2-ylamino)phenyl]-5-methyl-1,3,5-oxadiazol-3,4(2H) (14)

A mixture of 13 (3.43 g, 0.0l mole) and Et_3N (5 ml) in dioxin (20 ml) was heated under reflux for 4 h then allowed to reach ambient temperature. The precipitate formed was filtered and recrystallized from MeOH to afford 14 (2.09 g, 60%) as colorless crystals; m.p. 230°C. IR (KBr): 3,343–3,450 (NH*str*), 2,264 (CN_{str}), 1,683 (C = O_{str}), 1,543 (C = N_{str}); ^{1}H NMR (200 MHz, DMSO-d_6): *d* 11.11 (s, 1 H, N-H), 9.55 (s, 1H, N-H), 8.56–7.08 (m, 10H, Ar), 4.33 (s, 1H, -CH_2-), 2.35 (s, 3H, CH_3). EI-MS: *m/z* (%): 343 (M^+, 25.8). $C_{20}H_{17}N_5O$ (343).

2-Cyano-2-(hydroxyimino)-N′-{1-[3-(quinolin-2-ylamino)phenyl]ethylidene}acetohydrazide (15)

A solution of 13 (3.43 g, 0.01 mole) in dioxin (10 ml) containing HCl (5 ml) was treated with a solution of $NaNO_2$ (0.7 g) in H_2O (5ml) at 0°C while stirring. The precipitate formed was recrystallized from EtOH to afford 15 (2.4 g, 70%) as colorless crystals; m.p. 174°C. IR (KBr): 3,363 (NH_{str}), 1,672 (C = O_{str}), 1,538 (C = N_{str}); ^{1}H NMR (200 MHz, DMSO-d_6): *d* 9.70 (s, 1H, N-NH-), 8.69 (s, 1H, NH), 8.10–7.08 (m, 10H, Ar), 3.36 (s, 1H, OH), 2.51 (s, 3H, CH_3). $C_{20}H_{16}N_6O_2$ (372).

2-cyano-2-(4-chlorophenyldiazeneyl)-N›-{1-[3-(quinolin-2-ylamino)phenyl]ethylidene}acetohydrzide (16)

A mixture of 13 (3.43 g, 0.01 mol), NaOAc (3 g, 0.3 mol) in dioxane (20 ml) was stirred at 0°C then treated with *p*-chlorobenzene diazzonium chloride (0.01 mol). The precipitate formed was recrystallized from EtOH to afford 16 (2.22 g, 65%) as colorless crystals; m.p.170°C. IR (KBr): 3,366–3,230 (NH_{str}), 2,215 (CN_{str}), 1,690 (C = O_{str}), 1,599 (C = N_{str}); ^{1}H NMR (500 MHz, DMSO-*d6*): δ 12.72, 12.06, 10.48, 9.64 (4s, 3H, 3 N-H *D_2O exchangeable*), 8.53–7.01 (m, 15 H, Ar), 2.34(s, 3H, CH_3). $C_{26}H_{20}ClN_7O$ (481).

Toxicological studies

Samples of cotton leaves infested with cotton aphid, *A. gossypii* were collected from the cotton fields of the Dakahlia Governorate, Egypt, in June, 2008 and transferred to the laboratory. The slide dip technique adopted by Thistlewood *et al.* (1992) was applied to evaluate the efficiency of the tested modified heterocyclic compounds, in addition to the recommended insecticide Marshal (carbosulfan) 25% WP, against aphids. A piece of double-faced scotch tape was pressed tightly to the surface of a glass slide, using a moist brush. At least six concentrations for each compound were used. Three replicates with 10 apterous adults (1–2-days-old) each, were made for each concentration. The aphids were stuck to the tape on their backs so that their legs and antennae were free. Slides with aphids were dipped into a beaker containing compound solutions which were mixed with Triton X at a concentration of 0.3%. The aphids were immersed for 10 seconds to ensure complete wetting. Control aphids were similarly dipped in water with Triton X at a concentration of 0.3%. When withdrawn, slides were placed down, on their edges, on absorbent paper towelling and then allowed to dry at room temperature. The treated slides were then placed into a glass slide holding chamber to conserve the moisture. Mortality counts were tallied after 24 hours of treatment. Aphids responding to touch from a brush were considered alive. Mortality data were corrected according to the Abbott formula (Abbot 1952) and the corrected mortality percentage of each compound was statistically computed according to Finney (1971). From which the corresponding concentration probit lines (LC-p lines) were estimated in addition to determination of 25, 50 and 90% mortalities. Slope values of tested compounds were also estimated. In addition, the efficiency of different compounds was measured by comparing the tested compound with the most effective compound by using the following equation: Toxicity index = LC_{50} of the most effective compound/LC_{50} of the tested compound x 100, Sun *et al.* (1950).

RESULTS AND DISCUSSION

Chemistry

For our endeavor, substrates 6a and 6b (Kamel *et al.* 1986) were obtained by nucleophilic substitution of 2-chloroquinoline 4 with the appropriate acetylaniline derivative 5a–b, in refluxing EtOH containing drops of HCl. The acetyl moieties in these derivatives are active enough to carry diverse functionalizations that might lead to new insecticide candidates. The first group that we thought about was the chalcone derivatives 7a–d, and some of their derived heterocycles 8–9 (Fig. 2), were then prepared. Compounds 7a–d were obtained in 60–75% yields *via* condensation of 6a with the appropriate aldehyde under Claisen-Schmidt condensation conditions, with modified NaOH proportion into 2.5 equivalents as the substrate is a hydrochloride form. ^{1}H NMR spectra of 7a–d showed a doublet for one of the two olefinic protons at δ 6.94–6.99 ppm (J 8.4–9.0 Hz). The second one was overlapping, as the imine proton, with the aromatic protons in the range δ 7.26–8.43 ppm. The methoxy protons of 7b were observed as singlet at 3.86 ppm, and the molecular ion peak of 7c was observed as the base peak at m/z 385. Pyrazole **8** was obtained in 60% yield *via* Michael-addition of phenyl hydrazine to 6a in refluxing EtOH (Fig. 2). The methylene protons of the pyrazole moeity, H-4$_{Pyrazole}$, were diastereotopic. They appeared as a pair of doublet-of-doublets at δ 3.17 and 3.87 ppm with common germinal coupling constant, J_{gem}, of 15.8 Hz. The pyrazole proton H-5 was observed consequently, as doublet-of-doublet at higher shift, δ 5.31 ppm, with two different J values of 6.4 and 7.8 Hz. Isoxazole 9 (Fig. 2), was obtained in 70% yield by treatment of 7b with hydroxylamine hydrochloride. The H-4 methylene protons of the isoxazole moiety were diastereotopic as in the pyrazole ring in the ^{1}H NMR spectrum with the exception of the overlapping of one of these protons with the methoxy protons giving a multiplet at δ 3.69–3.88 ppm. H-5 was observed, as expected, at higher shift, δ 5.71 ppm, compared with 8, δ 5.31 ppm, due to the electronegativity difference between oxygen and nitrogen. The molecular ion peak for 9, m/z 395, was observed at an intensity of 52%.

The second class of derivatives whose synthesis we thought about is the carbazides. Their derivatives and analogues, as some semicarbazides and thiosemicarbazides, are commercially available insecticides. Therefore, the acetyl moieties of 6a–b are quite suitable to graft quinoline with these active motif and related groups. Thus, condensation of 6a with excess of hydrazine hydrate in refluxing EtOH contained a drop of conc?. H_2SO_4 afforded hydra-

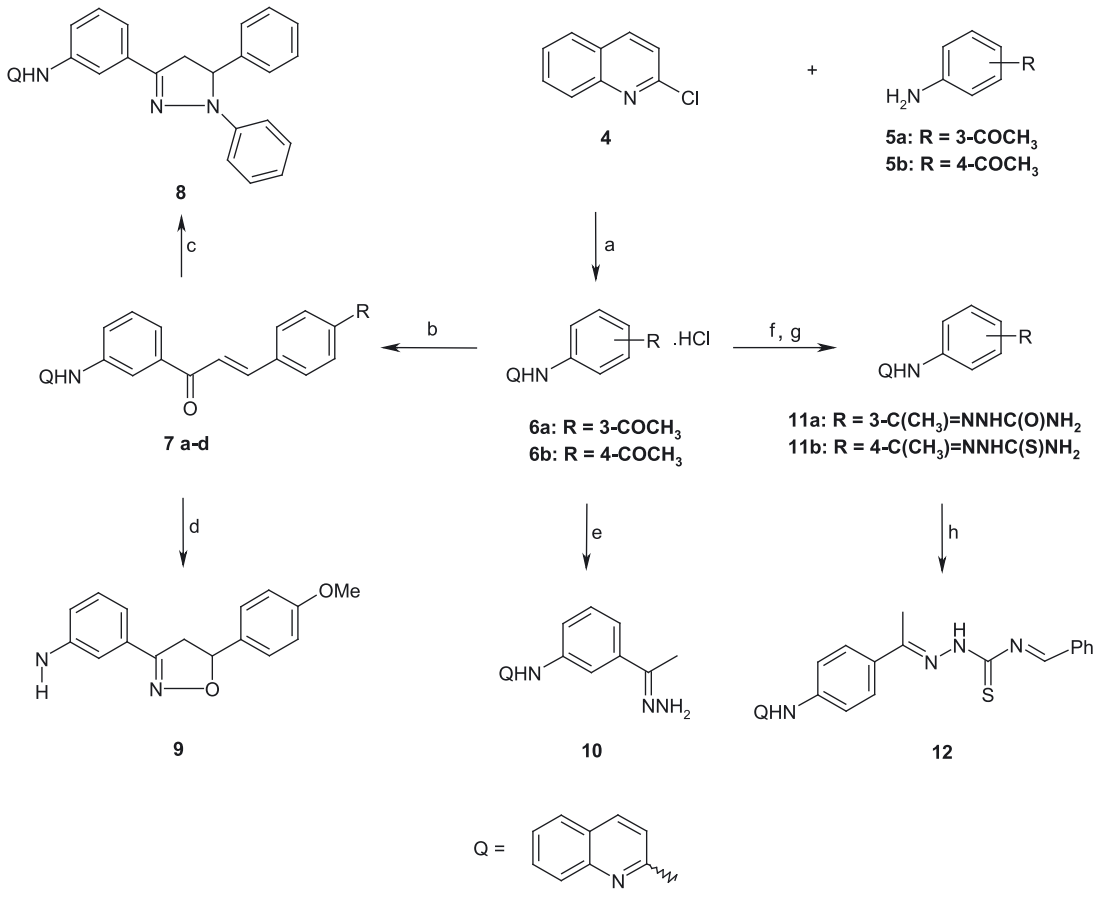

Fig. 2. Reagents and conditions: (a) EtOH, HCl, rfx., 70% for 6a; (b) PhCHO, NaOH, EtOH, 7a (65%), *p*-MeOC$_6$H$_4$CHO, NaOH, EtOH 7b (70%), *p*-ClC$_6$H$_4$CHO, NaOH, EtOH 7c (60%), *m*-HOC$_6$H$_4$CHO, NaOH, EtOH 7d (75%); (c) 7a, PhNHNH$_2$, EtOH, rfx., 60%; (d) 7b, NH$_2$OH.HCl, NaOH, EtOH, rfx., 70%; (e) N_2H_4. H_2O, H_2SO_4, 80%; (f) 6a, Semicarbazide, EtOH, rfx., 65%; (g) 6b, Thiosemicarbazide, EtOH, rfx., 60%; (h) 11b, BzH, EtOH, rfx., 65%

zone 10 (Fig. 2), in 80% yield. ^{1}H NMR revealed a singlet at δ 2.37 ppm for the methyl group protons, a multiplet for the aromatic protons at δ 6.93–8.53 ppm and a D_2O exchangeable proton singlet at δ 9.54 corresponding to the hydrazone moiety NH_2-group. Semicarbazone 11a (Fig. 2), was obtained in 65% yield by refluxing 6a with semicarbazide in EtOH. IR-spectrum showed stretching bands for the groups NH at 3,314–3,427, NH_2 at 3,185, C = O at 1678 and C = N at 1571 cm. MS revealed a molecular ion peak at *m/z* 319 with intensity of 66% while ^{1}H NMR showed D_2O exchangeable broad singlets at δ 6.60 ppm for the NH_2 group, 9.59 and 11.20 ppm for the two NH groups. Thiosemicarbazone 11b (Fig. 2), was obtained analogously from 6b and thiosemicarbazide in 70% yield. IR-spectrum revealed stretching bands at 3,261–3,423 for the NH group, 3,062 for the NH_2 group and 1,660 cm for the C = N group. Molecular ion peak of *m/z* 335 was observed at an intensity of 1%. Condensation of 11b with benzaldehyde in refluxing EtOH afforded Schiff-like-base 12 (Fig. 2), in 65% yield. MS showed the molecular ion peak *m/z* 423 at an intensity of 0.1%, whereas, the characteristic aldimine proton signal was observed satisfactorily in the ^{1}H NMR spectrum as singlet at δ 10.20 ppm.

Condensation of 6a with cyanoacetohydrazide was studied (Fig. 2), the reaction was conducted in refluxing EtOH affording the active methylene containing derivative 13 in 75% yield. The molecular ion peak, *m/z* 342 was observed at an intensity of 2%. ^{1}H NMR spectrum showed that amide proton was observed as two singlets at δ 11.17 and 11.01 ppm due to tautomerism, while, the protons of the active methylene moiety were observed as a singlet at δ 4.29 ppm. Treatment of 13 with Et_3N in refluxing dioxane afforded oxadiazole 14 in favour of a pyrazolone. This was deduced based on the persistence of the active methylene protons signal in ^{1}H NMR spectrum and change in melting point of 13.

Finally, condensation of 13, with nitrous acid prepared *in situ* at 0°C, afforded oxime 15 in 70% yield (Fig. 3). The two NH proton signals, ^{1}H NMR spectrum, were observed at δ 9.70 and δ 8.69 ppm while oxime-OH was observed at δ 3.36 ppm. Azo-dye derivative 16 was obtained by coupling of 13 with benzene diazonium chloride at 0°C in 65% yield. Disappearance of the active methylene protons signal, ^{1}H NMR spectrum, was decisive for this coupling (Nawwar *et al.* 1993; Shafik *et al.* 2006; Abd El Salam *et al.* 2009).

Toxicological studies

Toxocological assay of compounds 6–16, table 1 revealed that the thiosemicarbazide Shiff base derivative 12 is the most toxic one in this quinoline series with LC_{50} value of 19,429x10^{-10} ppm which is much more toxic than Marshal. Coming next to this derivative and with a nearby range of toxicity is the hydrazone 10, semicarbazide 11a and then the pyrazole 8. These derivatives are more toxic than Marshal but very less toxic than 12. The cyanoacetylhydrazone series (Fig. 3), was found to be a whole series that was more toxic than Marshal. Oxadiazole 14 was the most toxic one and followed 8 directly, and separated from the rest of the series with the hydroxylated chalcone like derivative 7d. This chalcone derivative was the only active derivative among the other chalcones

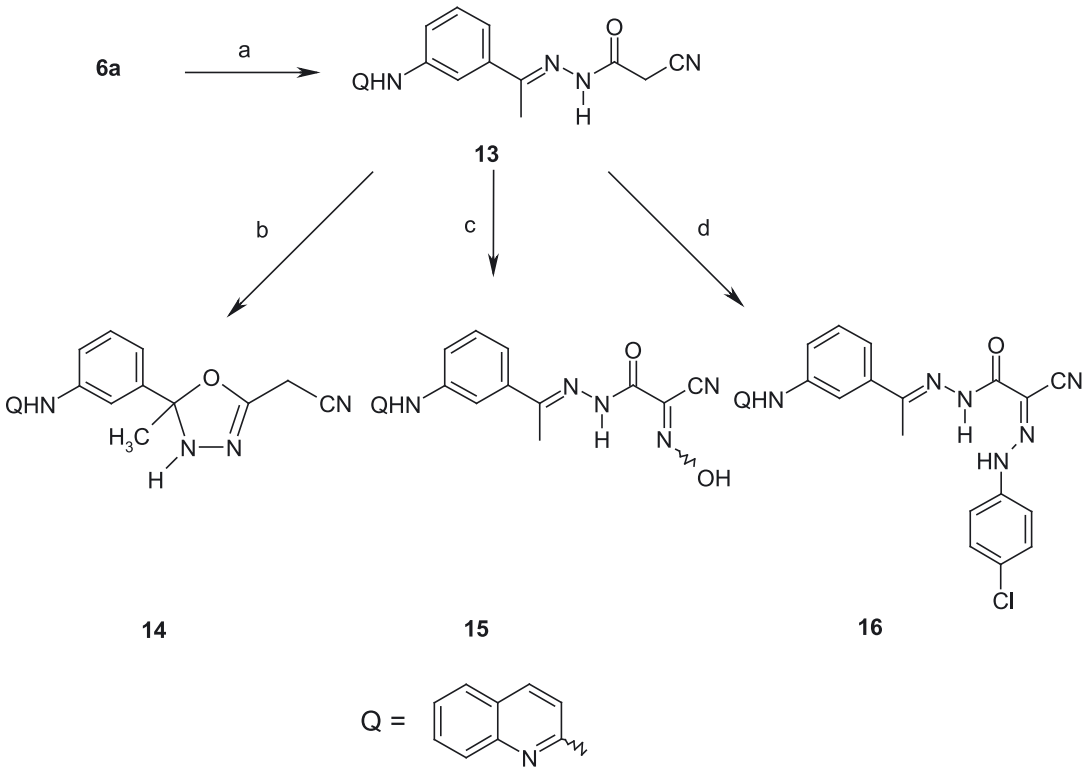

Fig. 3. Reagents and conditions: (a) EtOH, rfx., 75% for 13; (b) Et_3N, Dioxane, rfx., 60% for 14; (c) $NaNO_2$, HCl, 0°C, 70% for 15; (6) *p*-ClC_6H_4N=NCl, NaOAc, 0°C, 65% for 16

Table 1. Toxicity index of compounds 6–16 against *A. gossypii*

Componds[1]	LC_{25}	LC_{50}	LC_{90}	Slope	Toxicity index [%][2]
12	35,694E-17	19,429E-10	12,220E+3	0.1±0.058	100
10	81,034E-11	0.0008	326.702	0.227±0.063	0.243
11a	73,380E-16	0.0019	17,259E+9	0.08±0.055	0.102
8	53,930E-14	0.0022	78,512E+5	0.102±0.056	0.088
14	52,740E-19	0.013	44,387E+17	0.054±0.054	0.015
7d	0.013	0.831	2,373.394	0.371±0.062	0.0002
15	0.0004	0.993	33,390E+2	0.196±0.056	0.0002
16	0.0034	1.663	21,055E+1	0.251±0.058	0.0001
13	0.017	7.655	87,934E+1	0.253±0.058	0.000025
Marshal	6.807	184.734	97,840.292	0.470±0.091	0.000001
11b	13.041	268.236	83,887.89	0.514±0.091	72,432E-11
7a	791.667	1,445.496	4,537.717	2.580±1.015	13,441E-11
7b	321.521	1,540.632	30,246.865	0.991±0.246	12,611E-11
6b	0.057	4,652.192	99,768E+8	0.137±0.058	41,763E-12
6a	8.104	5,086.203	10,524E+5	0.214±0.068	38,199E-12
9	13.0	43,300E+1	16,969E+10 x	44,871E-14	44,871E-14
7c	445.962	63,730E+1	62,976E+7	0.214±0.076	30,486E-14

[1] compounds are arranged according to the decrease in their toxicities relative to the active compound 12 using Marshal as a reference
[2] toxicity index – (LC_{50} of the tested compound/LC_{50} of the most active compound) x 100

compared with the reference insecticide. This result adds an impact to the intriguing biological activity (Jang *et al.* 2007) of chalcones which is attributed, in most cases, to the affinity of its enone-system to free sulfohydryl groups in proteins (Aly *et al.* 2006) which might target some insect proteins elaborating this insecticidal activity. Following 7d in toxicity were oxime 15 then the azo-dye derivative 16, and finally cyanoacetylhydrazone 13 which was still more toxic than Marshal. Although, 12 showed the highest anti-aphid activity, its thiosemicarbazide precursor 11b was less toxic than the reference insecticide and so were the rest of the chalcones 7a–c and oxazoline 9.

In general, treatment of the cotton aphids, *Aphis gossypii* (Glover) with these quinoline derivatives, in comparison with the recommended insecticide, Marshal (Carbosulfan) 25% WP resulted in two groups (Table 1). The first group is more toxic than the insecticide Marshal, The compounds of the first group are 12, 10, 11a, 8, 14, 7a, 15, 16 and 13. The second group is less toxic than Marshal. The compounds of the second group are 11b, 7a, 7b, 6b, 6a, 9 and 7c.

These results reflect the impact of these derivatives as new insecticide candidates for cotton cultivation which are in accordance with our hypothesis.

CONCLUSIONS

Condensation reactions of 2-acetylanilinoquinolines were good leads for new quinoline derivatives grafted with several functionalities frequently encountered in commercial pesticides. Some of these derivatives were more toxic than Marshal which is one of the best anti-aphid pesticides on the market. These results put quinoline derivatives of these series, as leads for developing new potential pesticides.

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REFERENCES

Abbott W.S. 1925. A method of computing the effectiveness of an insecticide. J. Econ. Entomol. 18 (2): 265–267.

Abd El Salam H.A., Shaker N.O., El-Telbani E.M., Nawwar G.A.M. 2009. Facile synthesis of heterocycles having bacteriocidal activity incorporating oleic acid residues. J. Chem. Res. 6: 400–404.

Aly M.R.E., Rochaix P., Amessou M., Johannes L., Florent J.-C. 2006. Synthesis of globo- and isoglobotriosides bearing a cinnamoylphenyl tag as novel electrophilic thiol-specific carbohydrate reagents. Carbohydr. Res. 341 (12): 2026–2036.

Conway H.E., Kring T.J., McNew R. 2003. Effect of Imidacloprid on wing formation in the cotton aphid (Homoptera: Aphidiae). Florida Entomol. 68 (4): 474–476.

Daughtery M.L., Jones R.K., Moyer J.W., Daub M.E., Barker J.R. 1997. Tospoviruses strike the greenhouse industry: INSV has become a major pathogen on flower crops. Plant Dis. 81 (11): 1220–1230.

Finney D.J. 1971. Probit Analysis. A Statistical Treatment of the Sigmoid Response Curve. 7th ed., Cambridge Univ. Press, England: 145–146.

Forlow J.L., Henneberry T.J. 2001. Cotton Aphid Biology and Honeydew Production. Arizona Cotton Report: 282–289.

Jang S., Jung J.C., Oh S. 2007. Synthesis of 1,3-diphenyl-2-propen-1-one derivatives and evaluation of their biological activities. Bioorg. Med. Chem. 15 (12): 4098–4105.

Kamel M., Nabih I., Gadalla K.Z., Ashour M.M. 1986. New pyrazolinylanilinoquinolines and other related products of possible antibacterial activity. Pharmazie 41 (1): 55–56.

Kaplan I., Eubanks M.D. 2002. Disruption of cotton aphid (Homoptera: Aphididae) – natural enemy dynamics by red imported fire ants (Hymenoptera: Formicidae). Environ. Entomol. 31 (6): 1175–1183.

Khalid M.S., Hassanein A.A., Abou-Yousef H.M. 2005. Anti-Aphid *Aphis gossypii* activity of Marshal and Dursban insecticides against some adults collected from Egypt. J. Agric. Sci. Mansoura Uni. 30 (11): 7083–7088.

Liu T.X. 2000. Population dynamics of *Bemisia argentifolii* (Homoptera: Aleyrodidae) on spring collard and relationship to yield in the lower Rio Grande valley of Texas. J. Econ. Entomol 93 (3): 750–756.

Lubenets V.I., Stadnitskaya N.E., Novikov V.P. 2000. Synthesis of thiosulfonates belonging to quinoline derivatives Russ. J. Org. Chem. 36 (6): 851–853.

Ma X. M., Liu X.X., Zhang Q.W., Zhao J.Z., Cai Q.N., Ma Y.A., Chen D.M. 2006. Assessment of cotton aphids, *Aphis gossypii*, and their natural enemies on aphid-resistant and aphid-susceptible wheat varieties in a wheat–cotton relay intercropping system. Entomol. Exp. Appl. 121 (3): 235–241.

Menéndez A.I., Romero A.M., Folcia A.M., Martinez-Ghersa M.A. 2010. Aphid and episodic O_3 injury in arugula plants (*Eruca sativa* Mill) grown in open-top field chambers. Agric. Ecosyst. Enviro. 135 (1–2): 10–14.

Moores G.D., Gao X., Debenholm I., Devonshire A.L. 1996. Characterisation of insensitive acetylcholinesterase in insecticide-resistant cotton aphids, *Aphis gossypii* Glover (Homoptera: Aphididae). Pest Biochem. Physol. 56 (2): 102–110.

Nawwar G.A.M., Haggag B.M., Swellem R.H. 1993. Synthesis and molluscicidal activity of new derivatives of 1-(Hydroxy/substituted Phenyl)-3-arylpropenones. Arch. Pharm. 326 (10): 831–836.

Reising D., Godfrey L., Keillor K. 2004. Beltwide Cotton Conferences, San Antonio, TX: 1524-1527.

Runzhi Z., Hongbin L., Changyan T., Guangxue Z. 2000. Biological mechanism of controlling cotton aphid (Homoptera: aphididae) by the marginal alfalfa zone surrounding cotton field. Chinese Sci. Bull. 45 (4): 355–358.

Shafik N.A., Chabaka L.M., Nawwar G.A.M. 2006. Salicylanilides and their heterocyclic analogues with molluscicidal activity. Afindad 63 (523): 523–529.

Smith M.T., Hardee D.D. 1996. Influence of fungicides on development of an entomopathogenic fungus (Zygomycetes: Neozygitaceae) in the cotton aphid (Homoptera: Aphididae). Environ. Entomol. 25 (3): 677–687.

Steinkraus D.C., Zawislak J. 2004. Summaries of arkansas cotton res.: AAES Res. Ser. 533: 220–223.

Stoetzel M.B., Miller G.L., OBrien P.J, Graves J.B. 1996. Aphids (Homoptera: Aphididae) colonizing cotton in the United States. Florida Entomol. 79 (2): 193–206.

Sun Y.P. 1950. Toxicity index – an improved method of comparing the relative toxicities of insecticides. J. Econ. Entomol. 43 (1): 45–53.

Takahashi H., Murahashi K., Take T., Asai M., Yamada T. 2001. Efficiency of acetamiprid tablet against cotton aphid on cucumber by various application methods. J. Pestic. Sci. 26 (4): 371–375.

Thistlewood H.A., Pree D.J., Crawford L.A. 1992. Comparison of slide dip and Petri dish *assays* for measuring resistance to permethrin in *Amblyseius fallacies* (Acari: Phytoseiidae) J. Econ. Entomol. 85 (6): 2051–2057.

Weathersbee III A.A., Hardee D.D. 1994. Abundance of Cotton Aphids (Homoptera: Aphididae) and associated biological control agents on six cotton cultivars. J. Econ. Entomol. 87 (1): 258–265.

Worthing C.R., Waiker S.B. 1987. The Pesticide Manual: A World Compendium. 8th ed. The British Crop Protection Council, 220 pp.

Zhae Y., Li Y., Wang S., Li Z. 2009. Design, synthesis, and insecticidal activity of novel neonicotinoid derivatives containing N-oxalyl groups. Arkivoc xi: 152–164.

POLISH SUMMARY

SYNTEZA NOWYCH POCHODNYCH ZWIĄZKÓW GUINOLINY I ICH AKTYWNOŚĆ PRZECIWKO *AHPIS GOSSYPII* (GLOVER)

Opracowano serię pochodnych związków quinoliny w wyniku reakcji 2-(m i p-acetylanilino)-quinolin 6a-b z aldehydami według Clainsen-Schmidt'a, a następnie poprzez cyklizację z fenylohydrazyną i hydroksyloaminą. Reakcja 6a i 6b z hydrazyną, semikarbazydem i tiosemikarbazydem, cyjanoacetylohydrazydem oraz kolejne reakcje kondensacji doprowadziły do powstania pochodnych związków quinoliny. Przedmiotem badań była ocena ich skuteczności przeciwko mszycy *Apis gossypii*, szkodnikowi upraw bawełny w Egipcie. Komponent 12 o wartości LC_{50} dla 19429E-10 ppm okazał się bardziej skuteczny niż preparat Marchal (karbosulfan), jeden z powszechnie stosowanych insektycydów w zwalczaniu *A. gossypii*.