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Antimicrobial Activity and Synthesis of Quinoline-Based Chalcones

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Abstract: A series of quinoline-based chalcones have been prepared by the condensation of quinoline-3-carbaldehydes with acetophenone and N-substituted-3-acetyl-4-hydroxy-2-quinolones with heterocyclic carbaldehydes. The prepared chalcones have been screened for antimicrobial activities against *Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus subtiles*, *Klebsiellea erogeues*, *Staphylococcus albus*, *Aspergillus flavus*, *Aspergillus niger*, *Rhodolorula rubera*, *Lipomyces lopofera* and *Candida albicans*. All the prepared chalcones have shown significant antimicrobial activities.

Key words: Acetanilides, 3-formylquinolines, acetophenone, 3-acetyl-4-hydroxy-2-quinolone, diethyl malonate, thiophene, furfural, chalcones

INTRODUCTION

Quinolines are important compounds because of their bioactive properties and medicinal uses such as antimalarial (Larsen *et al*., 1996), anti-inflammatory (Chen *et al*., 2001), antiasthmatic (Roma *et al*., 2000), antibacterial (Dube *et al*., 1998) and tyrosine kinase inhibiting agents (Billker *et al*., 1998).

Chalcones and their derivatives are also medicinally important. Many chalcone derivatives have been reported to possess antimalarial, antibacterial and antifungal properties (Katritzky, 1984). Anticancer properties of some simple chalcone derivatives have also been reported in literature (Rezig *et al*., 2000; Ducki *et al*., 1996). The synthesis of quinolinyl chalcones is scarcely reported in literature. Sayed *et al*. (1976) and Ibrahim *et al*. (1996) have synthesized a few quinolinyl chalcone derivatives by Claisen-Schmidt condensation. Dominguez *et al*. (2001) have reported the synthesis of some quinolinyl chalcones and claimed their antimalarial activity. Moussaoui *et al*. (2002) have also described the synthesis of quinolinyl chalcones and claimed their cytotoxicity in K 562 human leukaemia cell lines. The present study was aimed to prepare quinolinyl chalcones and study of their antimicrobial activities.

MATERIALS AND METHODS

All the required chemicals were purchased from Merck Company and were used as such. 2-chloro-3-formylquinolines and N-substituted-3-acetyl-4-hydroxyquinolin-2(1H)-ones were synthesized by using the methods reported in literature (Meth-Cohn and Narine, 1978) and modified by Kappe *et al*. (1994). IR spectra were recorded on Perkin Elmer spectrum-1X. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on Bruker DPX-400 instrument at 400 and 100 MHZ, respectively. Chemical shifts are reported in ppm referenced to the residual solvent signal. FAB^{+}-MS spectra were recorded on JEOL SX-102. Using Perkin-Elmer 2400-CHN Analyzer performed elemental analyses. Melting points were recorded on Gallen-kemp apparatus and were uncorrected. Aluminum coated TLC plates were purchased from Merck for monitoring of reaction and purity of compounds.

(2E)-3-(2-chloroquinolin-3-yl)-1-phenyl-2-propen-1-one (1-a): Aqueous sodium hydroxide (2 mL, 25%) was added to a mixture of 2-chloro-3-formylquinoline (1.0 g, 5.2 mmol,), acetophenone (0.6 g, 5.2 mmol) and 25 mL ethanol (95%). The reaction mixture was stirred for 90 min at room temperature and the reaction was monitored by TLC. The pH of the reaction mixture was adjusted to 6.0 by adding 10% hydrochloric acid. The organic mass was extracted with chloroform (3×25). The chloroform layer was dried over anhydrous magnesium sulfate and evaporated. The crude product was purified by column chromatography (n-hexane/ethyl acetate 7:3). The title compound was obtained yield (1.16 g, 76%), mp 180-181°C; IR (Kbr, ν_{max} in cm^{-1}): 1665 (C = O); ^{1}H-NMR (400 MHZ, $CDCl_3$) δ: 8.5 (s, 1H, H_4), 8.23 (d, J = 15.72 Hz, 1H, H_β), 8.04 (br m, 5H, H_5, H_6, H_7, H_8, H_α), 7.65 (m, 5H, 5H of phenyl ring) ^{13}C-NMR (100 MHZ, $CDCl_3$) δ: 189.8, 147.9, 139.3, 137.5 136.2, 133.4, 131.7, 130.4, 128.9, 128.8, 128.7, 128.1, 128.0 and 126.3 mass spectrum (FAB), m/z 295 (M+2, 50%), 297 (M+2+2 17%), 258 (M-Cl, 25%), 216 (M- Ph, 10%), 176 (M-Ph-CO-CH, 15%), 105 (Ph-CO, 60%), 77 (Ph, 45%). Anal. $C_{18}H_{12}ClNO$: (293.5): Calcd; C, 73.6; H, 4.12; N, 4.77; found: C, 73.45; H, 4.04; N, 4.65%.

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(2E)-3-(2-Chloro-6-methylquinolin-3-yl)-1-phenyl-2-propen-1-one (1-b): The title compound (1-b) was prepared from 2-chloro-3-formyl-6-methylquinoline and acetophenone as described for 1-a, yield (1.26 g, 79%), mp 147°C, IR (KBr, ν_{max} in cm^{-1}): 1630 (C = O); ^{1}H-NMR (400 MHZ, $CDCl_3$) δ: 8.34 (s, 1H, H_4), 8.16 (d, 1H, J = 15.76 Hz, H_β), 8.06 (m, 2H, H_5, H_7), 7.8, (d, J = 8.5Hz, 1H, H_8) 7.59 (br m, 6H, H_α and 5H of phenyl ring), 2.53 (s, 3H CH_3). ^{13}C-NMR (100 MHZ, $CDCl_3$) δ: 189.8, 149.4, 146.4, 139.0, 137.8, 137.6, 135.5, 133.9, 133.2, 128.9, 128.8, 128.7, 128.6, 128.0, 126.9, 126.8, 125.9, 122.3 and 22.38 Mass spectrum (FAB), m/z 309, (M+2, 70%), 311, (M+2+2 30%), 273, (M+2- HCl 25%), 231, (M+2- Ph 5%). Anal. $C_{19}H_{14}ClNO$: (307.5): Calcd; C, 74.15; H, 4.58; N, 4.55; found: C, 74.05; H, 4.10; N, 4.05%.

(2E)-3-(2,7-Dichloroquinolin-3-yl)-1-phenyl-2-propen-1-one (1-c): The title compound (1-c) was prepared from 2,7-dichloro-3-formylquinoline and acetophenone as described for 1-a and purified by column chromatography with mixture of solvents (n-hexane/ethyl acetate 2:3), yield (1.24 g, 73%), mp 167-8°C; IR (Kbr, ν_{max} in cm^{-1}): 1670 (C = O); ^{1}H-NMR (400 MHZ, $CDCl_3$) δ: 8.5(s, 1H, H_4), 8.23 (d, 1H, J = 15.6Hz, H_β), 8.07 (m, 3H, H_5, H_6, H_8), 7.87 (d, J = 15.6 Hz, 1H, H_α), 7.66 (br m, 5H, 5H of phenyl ring), 7.28 (s, 1H, H_8) ^{13}C-NMR (100 MHZ, $CDCl_3$) δ: 197.8, 159.9, 146.6, 135.5, 135.3, 128.8, 128.7, 128.6, 128.5, 127.2 and 125.6 mass spectrum (FAB), m/z 329 (M+2 90%), 331 (M+2+2 30%), 292 (M- Cl 45%), 250 (M-Ph 24%), 105 (Ph-CO, 54%), 77 (Ph, 40%). Anal. $C_{18}H_{11}Cl_2NO$: (327.5): Calcd; C, 65.87; H, 3.38; N, 4.27; found: C, 65.76; H, 3.42; N, 4.25%.

(2E)-3-(2-Chloro-6-methoxyquinolin-3-yl)-1-phenyl-2-propen-1-one (1-d): The title compound (1-d) was prepared from 2-chloro-3-formyl-6-methoxyquinoline and acetophenone as described for 1-a, yield (1.13 g, 77%), m p 228°C; IR (KBr, ν_{max} in cm^{-1}): 1620 (C = O); ^{1}H-NMR (400 MHZ, $CDCl_3$) δ: 8.36 (s, 1H, H_4), 8.16 (d, 1H, J = 16.00Hz, H_β), 8.05 (m, 2H,H_5, H_7), 7.85(d, 9.2 Hz 1H, H_8), 7.57 (m, 4H, H_2, H_4, H_6 and H_α), 7.41(m, 2H, H_3, H_5), 3.94 (s, 3H, OCH_3) ^{13}C-NMR (100 MHZ, $CDCl_3$) δ: 189.8, 158.5, 147.8, 139.6, 138.6, 137.6, 134.9, 133.2, 129.9, 128.9, 128.8, 128.7, 126.1, 124.4, 105.3 and 55.7 mass Spectrum (FAB), m/z 325 (M+2, 100%), 327 (M+2+2, 33%), 290 (M+2-Cl 30%), 289 (M+2-HCl 90%), 245 (M-1-Ph 20%), 105 (Ph-CO 80%), 77 (Ph 43%). Anal. $C_{19}H_{14}ClNO_2$: (323.5): Calcd; C, 70.48; H, 4.36; N, 4.33; found: C, 70.46; H, 4.32; N, 4.30%.

(2E)-3-(6-Bromo-2-chloroquinolin-3-yl)-1-phenyl-2-propen-1-one (1-e): The title compound (1-e) was prepared from 6-bromo-2-chloro-3-formylquinoline and acetophenone as described for 1-a and purified by silica gel column chromatography (n-hexane/ethyl acetate (6:1)), yield (1.39 g, 72%), mp 186-7°C; IR (KBr, ν_{max} in cm^{-1}): 1675 (C = O); ^{1}H-NMR (400 MHZ, $CDCl_3$) δ: 8.4 (s, 1H, H_4), 8.2 (d, J = 15.7 Hz, 1H, H_β), 8.06 (m, 2H, H_5,H_7) 7.85 (br m, 2H, H_8, H_α), 7.65 (br m, 5H, 5H of phenyl ring). ^{13}C-NMR (100 MHZ, $CDCl_3$) δ: 189.6, 150.8, 145.7, 138.8, 137.4, 135.0, 134.9, 133.4, 130.1, 129.9, 129.1, 128.1, 127.9 and 121.1, mass spectrum (FAB), m/z 372 (M+1 10%), 374 (M+1+2, 10%), 336, (M-Cl 8%), 338 (M+2-Cl, 8%), 176 (M-Ph-CO-CH, 20%), 105 (Ph-CO, 45%), 77 (Ph, 34%). Anal. $C_{18}H_{11}BrClNO$: (372.5): Calcd; C, 58.02; H, 2.98; N, 3.76; found: C, 57.98; H, 2.91; N, 3.69%.

3-{(E)-3-(Furan-2-yl)acryloyl}-4-hydroxy-1-methylquinolin-2(1*H*)-one (2-a): A mixture of 3-acetyl-4-hydroxy-1-metylquinolin-2(1H)-one (2.17 g, 0.01 mol), furfral (0.96 g, 0.01 mol), piperidine (1-2 drops) and 1-butanol (25 mL) was refluxed for 6 h. The reaction mixture was cooled and allowed to settle the precipitates. Precipitates were filtered under suction and washed with cold 1-butanol. The crude product was purified by column (chloroform/n-hexane 2:1), yield (2.00 g, 68%), mp 160-162°C (Lit. mp 106°C, Ibrahim *et al.* (1996)), IR (KBr, ν_{max}): 1610 cm^{-1} (C = O); ^{1}H-NMR(300 MHZ, $CDCl_3$) δ: 8.5 (d, J = 15.6 Hz, 1H, H_β), 8.2 (d, J = 8.1 Hz, 1H, H_5), 7.45 (d, 1H, J = 15.6 Hz, H_α) 7.68 (m, 1H, H_6), 7.56 (m, 1H, H_7), 7.28 (d, J = 7.5Hz, 1H, H_8), 7.25 (m, 1H, H_3) 6.78 (d, J = 3.6 Hz, 1H, H_5), 6.53 (d, J = 8.7Hz, 1H, H_4), 3.41, (s, 3H, N-CH_3). ^{13}C-NMR (75MHz, $CDCl_3$) δ: 194, 176.12, 161.61, 152.19, 145.56, 141.66, 134.81, 130.9, 126.15, 122.78, 122.00, 116.59, 116.12, 114.20, 112.8, 105.56 and 29.16. Anal. $C_{17}H_{13}NO_4$: (295): Calcd; C, 69.15; H, 4.44; N, 4.74; found: C, 68.87; H, 4.38; N, 4.69%.

1-Ethyl-4-hydroxy-{(E)-3-(thiophen-2-yl) acryloyl} quinolin-2(1*H*)-one (2-b): The title compound (2-b) was prepared from 3-acetyl-1-ethyl-4-hydroxyquinolin-2(1H)-one and 2-formylthiophene as described for 2-a and purified by column chromatography (ethyl acetate/n-hexane 3:2), yield (2.21, 67%), mp 162-4°C, IR (KBr, ν_{max}): 1607.9 cm^{-1} (C = O); ^{1}H-NMR(300 MHZ, $CDCl_3$) δ: 8.52 (d, 1H, J = 15.6 Hz, 1H, H_β), 8.24 (dd, J = 1.8, 8.1 Hz, 1H, H_5), 8.11 (d, J = 15.6 Hz, 1H, H_α) 7.68 (m, 1H, H_6), 7.47 (d, 4.8Hz 1H, H_6), 7.41 (d, J = 3.3 Hz, 1H, H_8), 7.29 (d, J = 8.4 Hz, 1H H_3) 7.21 (m, 1H, H_5), 7.1 (dd, J = 1.5, 3.6Hz, 1H, H_4), 4.33 (q, J = 7.2Hz, 2H, N-$C\underline{H}_2CH_3$), 1.41 (t, J = 7.2Hz, 3H, $NCH_2C\underline{H}_3$), ^{13}C-NMR (75 MHZ, $CDCl_3$) δ: 193.6, 176.02, 161.22, 141.04, 140.72, 137.56, 130.83, 132.2, 129.87, 128.32, 126.4, 124.32, 121.84, 116.29, 114.09, 37.14 and 12.84. Anal. Calcd; $C_{18}H_{15}NO_3S$: (325): C, 66.44; H, 4.65; N, 4.30; found: C, 66.23; H, 4.54; N, 4.26%

1-ethyl-4-hydroxy-3-{3-(thiophen-3-yl)acryloyl}quinolin-2(1H)-one (2-c): The title compound (2-c) was prepared from 3-acetyl-1-ethyl-4-hydroxyquinolin-2(1H)-one and 3-formylthiophene as described for 2-a and purified by column chromatography (ethyl acetate/n-hexane 3:1), yield (2.01 g, 62%), mp 140°C, IR (KBr, ν_{max}): 1612.9 cm^{-1} (C = O); ^{1}H-NMR (300 MHZ, $CDCl_3$) δ: 8.54 (d, 1H, J = 15.6 Hz, H_β), 8.28 (dd, 1H, J = 1.8, 8.1 Hz, H_5), 8.01 (d, J = 15.6 Hz, 1H, H_α) 7.68 (m, 1H, H_6), 7.74 (br m, 2H, H_6, H_7), 7.55 (dd, J = 0.9, 5.1Hz,1H, H_8), 7.37 (br-m, 3H, H_2, H_4, H_5), 4.35 (q, J = 7.2Hz, 2H, N-CH_2-CH_3), 1.39 (t, J = 7.2Hz, 3H, N-CH_2-CH_3), ^{13}C-NMR (75 MHZ, $CDCl_3$) δ: 194.54, 176.05, 161.35, 140.75, 138.81, 138.51, 133.77, 129.94, 128.00, 126.94, 123.69, 124.32, 121.89, 116.37, 114.43, 105.54, 37.18 and 12.83. Anal. $C_{18}H_{15}NO_3S$: (325): Calcd; C, 66.44; H, 4.65; N, 4.30; O, 14.75; S, 9.85; found: C, 66.05; H, 4.54; N, 4.21%.

RESULTS AND DISCUSSION

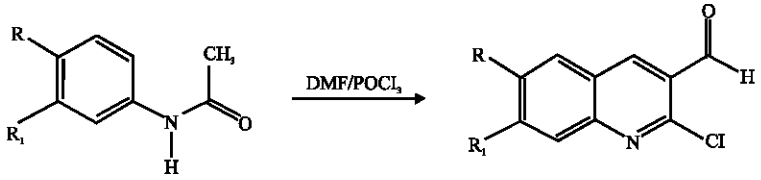
During the present study a series of chalcones were prepared by condensing 3-formylquinolines with acetophenone and 3-acetyl-4-hydroxyquinolin-2(1H)-one with different heterocyclic aldehydes. For this purpose a series of substituted 2-chloro-3-formylquinolines were prepared from acetanilide derivatives using Meth-Cohn and Narine (1978) procedures (Scheme 1). The required acetanilides were prepared by direct condensation of anilines with acetic acid in the presence of orthophosphoric acid (Munawar *et al*., 2005).

The prepared quinolines were condensed with acetophenone in the presence of ethanolic sodium hydroxide to give a series of chalcone derivatives in good yield (Scheme 2).

N-Substituted-3-acetyl-4-hydroxyquinolin-2(1H)-one derivatives were prepared by a modified Kappe *et al*. (1994) method and condensed with thiophen-2-carbaldehyde, thiophen-3-carbaldehyde and furfural in the presence of piperidine in 1-butanol to obtain α,β-unsaturated carbonyl compounds (Scheme 3).

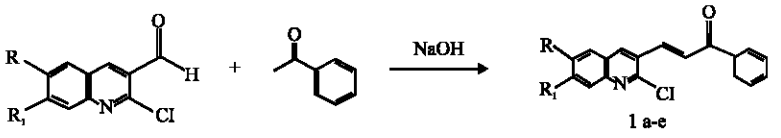
In ^{1}HNMR spectra of these compounds, the protons of α, β unsaturated carbonyl compounds have given two doublets in the range 7.5 ppm for H_α and 8.5 ppm for H_β with coupling constant in the range (15-16 Hz). It is inferred that they are trans isomers. The rest of signals for protons have appeared in the expected regions. Additional structure elucidation is supported by ^{13}CNMR spectra. A signal in the range δ (194-189) ppm in ^{13}CNMR of all the compounds that indicates carbonyl group is present. Interestingly the mass spectra of the prepared chalcones have shown the most intense signal $(M+2)^+$ in 1(a-d) compounds and not in 1-e. Probably this is due to the hydrogenation of α,β unsaturated chalcones in glycerol matrix in the ionization chamber followed by ionization of the saturated chalcones. Meili and Seibi (1984) have reported similar hydrogenation by glycerol in FAB-spectra of several compounds.

Antimicrobial activity: The newly synthesized compounds were screened for their antibacterial and antifungal activities against the organisms: *Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus subtiles*,



R = H, CH_3, OCH_3, Br
R_1 = H, Cl

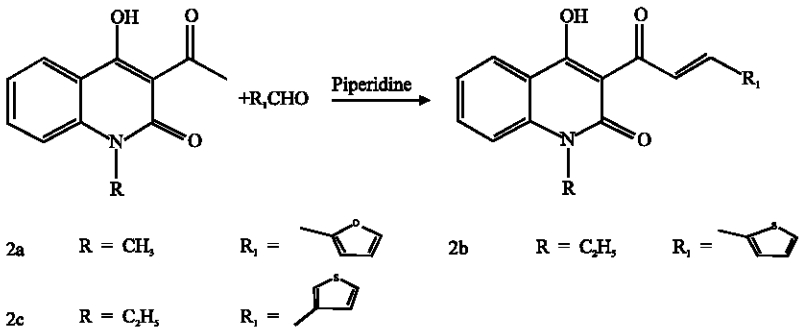
Scheme 1: Synthesis of quinoline carbaldehydes



1a. R = R^1 = H 1b. R = CH_3, R^1 = H 1c. R = H, R^1 = Cl

1d. R = OCH_3, R^1 = H 1e. R = Br, R^1 = H

Scheme 2: Synthesis of chalcones



Scheme 3: Chalcones with five membered heterocyclic compounds

Table 1: *In vitro* antimicrobial activity (bacteria) of newly prepared chalcones (1a-e and 2a-c) (μg disc^{-1}) by disc-diffusion assay and diameter of zone of inhibition (mm)

Compound	*E. coli*	*P. aeruginosa*	*B. subtiles*	*K. erogeues*	*S. albus*
1-a	8	7	3	-	6
1-b	7	7	3	-	6
1-c	12	10	3	2	10
1-d	7	6	5	-	7
1-e	10	9	4	-	8
2-a	11	12	8	6	12
2-b	13	14	13	7	14
2-c	13	14	13	8	15
Ofloxacin	24	23	26	23	21

-: No inhibition

Table 2: ANOVA for the effect of different compounds for their antibacterial activity against five bacterial species

Sources of variation	df	SS	MS	F-values
Treatments	44	5476	124.7	187.00***
Chemicals (C)	8	4360	545.0	818.00***
Bacterial species (B)	4	814	203.7	305.00***
C×B	32	301	9.420	14.12***
Error	90	60	0.667	
Total	135	18326		

***: Significant at $p \leq 0.001$, df: degree of freedom, SS: Sum of Squares, MS: Mean Squares

Klebsiellea erogeues, *Staphylococcus albus*, *Aspergillus flavus*, *Aspergillus niger*, *Rhodolorula rubera*, *Lipomyces lopofera* and *Candida albicans*. Using the disc-diffusion method (Karaman *et al*., 2003) carried out the antimicrobial tests. Suspension of (100 μL) containing 10^8 cfu mL^{-1} of bacteria, 10^6 cfu mL^{-1} of fungi was spread on Mueller-Hinton agar (MHA) medium and Sabouraud's Dextrose Agar (SDA) medium, respectively. The discs (6 mm in diameter), impregnated with 10 μL of the test compounds (1000 μg disc^{-1}) at the concentration of 100 mg mL^{-1} were placed on the inoculated agar. Negative controls were prepared using the same solvent (DMF), which was employed to dissolve the test compounds. Ofloxacin (5 μg disc^{-1}) and Clotrimazole (10 μg disc^{-1}) were used as positive reference standards to determine the sensitivity of each microbial species tested. The inoculated plates were incubated at 37°C for 24 h and 27°C for 72 h for bacterial and fungal strains, respectively. Antimicrobial activities were evaluated by measuring the diameter of zone of inhibition against test organisms and results were given in Table 1, 3 and 4.

Table 3: Antimicrobial activities of prepared compounds

Compounds	*E. coli*	*P. aeruginosa*	*B. subtiles*	*K. erogeues*	*S. albus*
1-a	8e	7f	3f	e	6f
1-b	7e	7f	3ef	e	6ef
1-c	12bc	10d	3ef	2d	10d
1-d	7e	6g	5d	e	7ef
1-e	10cd	9e	4de	e	8e
2-a	11d	12c	8c	6c	12c
2-b	13b	14b	13b	7c	14b
2-c	13b	14b	13b	8b	15b
Ofloxacin	24a	23a	26a	23a	21a

In a column values with different values show a significant difference ($p \leq 0.05$) as determined by Duncan's Multiple Range Test

Table 4: *In vitro* antimicrobial activities (fungi) of newly prepared chalcones (1a-e and 2a-c) (μg disc^{-1}) by disc-diffusion assay and diameter of zone of inhibition (mm)

Compounds	*A. niger*	*A. flavus*	*R. rubra*	*L. lopofera*	*C. albicans*
1-a	5	3	7	6	4
1-b	6	4	8	4	3
1-c	11	6	8	5	5
1-d	6	4	9	4	3
1-e	9	5	8	4	4
2-a	10	9	11	7	8
2-b	12	10	14	10	9
2-c	12	9	13	9	9
Clotrimazole	16	16	17	18	18

On the basis of the observed zone of inhibition values, it can be concluded that there is a significant differences in the antibacterial and antifungal potentials of prepared quinolinyl chalcones. The difference among the responses of different prepared compounds is also significant (Table 2 and 5).

Among the prepared compounds 2a, 2b and 2c have shown more antibacterial and antifungal activities against the tested microbes than rest of the compounds. This is might be because of structural features. Probably quinolones rapidly inhibit DNA synthesis by promoting the DNA gyrase cleavage resulting in bacterial deaths. The responses of the prepared compounds are less than standard; a fourth generation agent with improved gram-positive coverage. The relative responses of different compounds against each microbial species are shown (Table 3 and 6).

Table 5: ANOVA for the effect of 9 different compounds for their antifungal activity against five fungal species

Sources of variation	df	SS	MS	F-values
Treatments	44	2346	53.00	109.00***
Chemicals (C)	8	1910	239.00	488.00***
Bacterial species (B)	4	296	74.00	151.00***
C×B	32	140	4.36	8.93***
Error	90	44	0.49	
Total	135	12067		

***: Significant at $p \leq 0.001$, df: degree of freedom, SS: Sum of Squares, MS: Mean Squares

Table 6: Antifungal activity of prepared compounds

Compound	*A. niger*	*A. flavus*	*R. rubra*	*L. lopofera*	*C. albicans*
1-a	5e	3e	7e	6d	4de
1-b	6d	4e	8de	4ef	3ef
1-c	11d	6e	8de	5ef	5ef
1-d	6bc	4d	9e	4e	3d
1-e	9de	5e	8d	4f	4f
2-a	10c	9c	11c	7d	8c
2-b	12b	10b	14b	10b	9bc
2-c	12b	9bc	13b	9c	9b
Clotrimazole	16a	16a	17a	18a	18a

In a column values with different values show a significant difference ($p \leq 0.05$) as determined by Duncan's Multiple Range Test

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REFERENCES

Billker, O., V. Lindo, M. Panico, A.E. Etiene, T. Paxton, A. Dell, M. Rogers, R.E. Sinden and H.R. Morris, 1998. Identification of xanthurenic acids the putative inducer of malaria development in the mosquito. Nature, 392: 289-292.

Chen, Y.L., K.C. Fang, J.Y. Sheu, S.L. Hsu and C.C. Tzeng, 2001. Synthesis and antibacterial evaluation of certain quinolone derivatives. J. Med. Chem., 44: 2374-2377.

Dominguez, J.N., J.E. Charris, G. Lobo, N.G. Dominguez, M.M. Moreno, F. Riggione, E. Sanchez, J. Olson and P.J. Rosenthal, 2001. Synthesis of quinolinyl chalcones and their evaluation of their antimalarial activity. Eur. J. Med. Chem., 36: 555-560.

Dube, D., M. Bloun, C. Brideau, C. Chan, S. Desmarais, D. Eithier, J.P. Falgueyeret, R.W. Friesen, M. Girad, Y. Girad, J. Guay, P. Tagri and R.N. Yong, 1998. Quinolines as potent 5-lipoxygenase inhibitor: Synthesis andbiological profile. Bioorg. Med. Chem. Lett., 8: 1255-1260.

Ducki, S., J.A. Hadfield, N.J. Lawrence, C.Y. Liu, A.T. Mc Gown and X. Zang, 1996. Isolation of E-1-(4^{l}-hydroxyphenyl0-but-1-en-3-one from scutellaria barbata. Planta Medica, 62: 185-186.

Ibrahim, S.S., H.A. Allimony and E.S. Othman, 1996. 3-Acryolyl-1,2-dihydro-4-hydroxy-1-methyl-2-oxo quinoline derivatives and their behaviour towards some nucleophiles. Chem. Papers, 51: 33-42.

Kappe, T., R. Aiger, P. Hohengassner and W. Stadlbauer, 1994. Synthesis of 3-acyl-4-hydroxy-2(1H) quinolones. J. Parkat. Chem., 336: 596-601.

Karaman, I., F. Sahin, M. Gulluce, H. Ogutcu, M. Sengul and Adiguzel, 2003. Antimicrobial activity of aqueous and methanol extracts of *Junipreus oxycedrus* L. J. Ethnopharmacol., 85: 231-235.

Katritzky, A.R., 1984. Rees C.W. Comprehensive Heterocyclic Chemistry Pergamon Press, Oxford, pp: 25-85.

Larsen, R.D., E.G. Corley, A.O. King, J.D. Carrol, P. Davis, T.R. Verhoeven, P.J. Reider, M. Labelle, J.Y. Gauthier, Y.B. Xiang and R. Zamboni, 1996. Practical route to a new class of LTD_4 Receptor Antagonists J. Org. Chem., 61: 3398-3405.

Meili, J. and J. Seibi, 1984. A new versatile matrix for fast atom bombardment analysis. Org. Mass Spectrom, 19: 581-582.

Meth-Cohn, O. and B. Narine, 1978. A versatile new synthesis of quinolines thieno pyridines and related fused pyridines. Tetrahedron Lett., 23: 2045-2048.

Moussaoui, F., A. Belfaitah, A. Debache and S. Rhouati, 2002. Synthesis and characterization of some new aryl quinolinyl α, β unsaturated ketones. J. Soc. Alger. Chim., 12: 71-78.

Munawar, M.A., M. Azad, S. Ashraf, M.A. Khan and A.M. Zafar, 2005. Direct condensation of anilines with carboxylic acids in phosphoric acid. J. Scientific Res. (Pak.), 34: 29-32.

Rezig, R., M. Chebah, S. Rhouati, S. Ducki and N.J. Lawrence, 2000. Synthesis of some quinolinyl acyl α, β unsaturated ketones. J. Soc. Alger. Chem., 10: 111-120.

Roma, G., M.D. Braccio, G. Grossi, F. Mattioli and M. Chia, 2000. 1,8-Naphthyridines (IV). 9-substituted N, N-dialkyl-5-(alkylamino or cycloalkylamino) [1,2,4] triazolo[4,3-a][1,8]naphthridine-6-carboxamides, new compounds with anti aggressive and potent anti inflammatory activities. Eur. J. Med. Chem., 35: 1021-1035.

Sayed, A.A., S.M. Sami, A. Elfayoumi and E.A. Mohamed, 1976. The behaviour of some 3-substituted 4-hydroxy-1-alkyl (or phenyl) carbostyrils towards amines and hydrazines. Egypt. J. Chem., 19: 811-826.