Design, synthesis and evaluation of novel quinolyl chalcones as antibacterial agents

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Abstract

Some new substituted quinolinyl chalcones were synthesized and evaluated for their *in vitro* antimicrobial activity against Gram positive and Gram negative strains using a microdilution procedure. Synthesized compounds **10a-g** and **13h-q** prove to be effective with MIC (mg ml^{-1}), among them **10a**, **10b**, **10c**, **13I**, **13p** showed excellent activity against a panel of microorganisms. The newly synthesized compounds were characterized using IR, ^{1}H-NMR and elemental analysis.

Keywords: Quinoline, chalcone, pyrimidine, antimicrobial activity

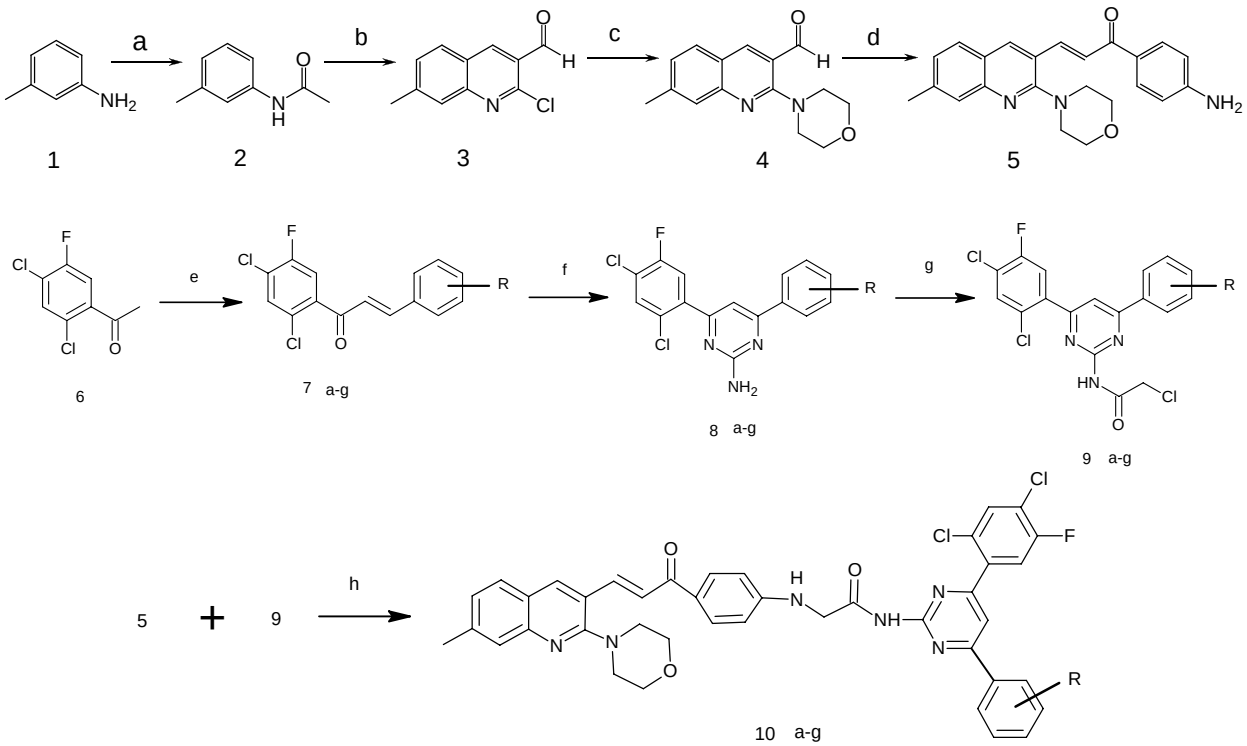
Introduction

In recent decades, problems of multi-drug resistant microorganisms have reached on alarming level in many countries around the world. A numbers of recent clinical reports describe the increasing occurrence of meticillin-resistant *S. aureus* and other antibiotic-resistant human pathogenic microorganisms in United State and European countries. Infections caused by those microorganisms pose a serious challenge to the medical community and the need for an effective therapy has led to a search for novel antimicrobial agents. In this work, we report the synthesis and biological activity of some quinolinyl chalcones and pyrimidines. Chalcones are a class of privileged structures that have a wide range of biological properties.[1] Chalcones are also reported as anticancer agents,[2] and antimalarial agents.[3-6] Quinoline-based fused heterocyclic systems are found as potential anticancer agents[7] and have antimalarial activities.[8] Pyrimidine derivatives form a component in a number of useful drugs and are associated with many biological pharmaceutical and therapeutical activities.[9] Condensed pyrimidine derivatives have been

reported as analgesics, antiviral and as anti-inflammatory agents,[10] antibacterial and antitubaculostic agents,[11] diaryl pyrimidine (DAPY'S) appears to be the more effective against wild type and various mutant strains of HIV-1.[12]

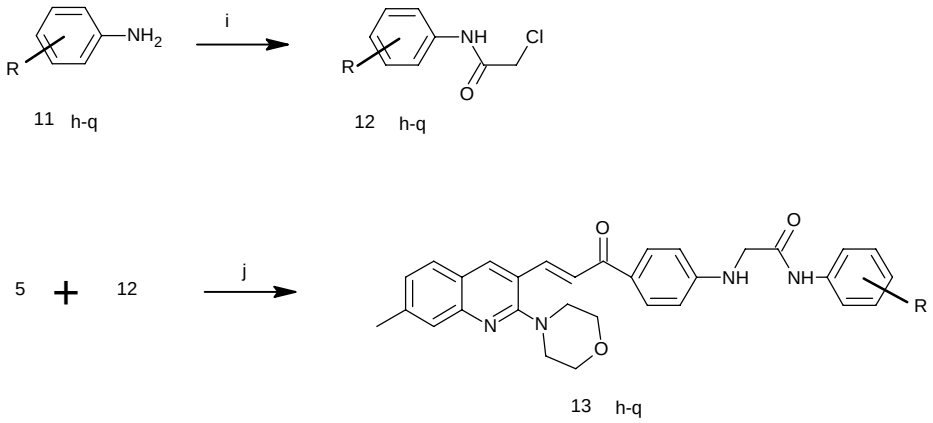
Chemistry

In this work, the main moiety, 2-chloro-3-formyl-7-methylquinoline **3** was synthesized using the Vilsmeier-Haack reagent according to the literature.[13] In the ^{1}H-NMR spectra of the chalcones, the protons of αβ unsaturated system absorbed as two doublets around δ 7.5 ppm for H-α and 8.1 ppm for H-β with coupling constant J = 15-16 Hz for the *trans* isomer. Compound **4** was obtained in high yield and purity by condensation of **3** and morpholine in DMF. The product **4** was then treated with commercially available 4-aminoacetophenone to produce **5** which, on treatment with various *N*-chloroacetyl-4-(substitutedaryl)-6-(2,4-dichloro-5-fluoroaryl)pyrimidinyl amines, which were synthesized according to literature,[14] gave **10a-g** (Series 1) and compound **5** on treatment with various *N*-chloroacetyl arylamines in the presence of potassium carbonate in DMF gave **13h-q** (Series 2). All the synthesized compounds were fully characterized by IR, ^{1}H-NMR spectroscopy and elemental analysis.



R = 10a 3,4,5-$(OCH_3)_3$**; 10b** 4-Cl**; 10c** 2-OCH_3 **; 10d** 4-CH_3**; 10e**4-OCH_3 **; 10f** 4-F**; 10g** 2-OH.

Series 1. Reagents: a) Ac_2O, AcOH, reflux, 2 h. b) DMF, $POCl_3$ (3: 12), reflux, 6 h, 80-90 ^oC. c) morpholine, DMF, K_2CO_3, reflux 3h. d) *p*-aminoacetophenone, NaOMe, MeOH, 20% NaOH, stir, 24 h. e) Ar-CHO, NaOMe, MeOH, 20% NaOH, stir, 24 h. f) guanidine nitrate, 25% NaOMe, MeOH, reflux temp, 7hr. g) chloroacetyl chloride, benzene, TEA reflux at 90 ^oC, 3h. h) K_2CO_3 , reflux, DMF, 5-10 h.



R = 13h H; **13i** 2-CH_3; **13j** 3-CH_3; **13k** 4-CH_3; **13l** 2-Cl; **13m** 3-Cl; **13n** 4-Cl; **13o** 3-NO_2; **13p** 4-NO_2; **13q** 2,4-$(NO_2)_2$.

Series 2. Reagents: i) chloroacetyl chloride, benzene, TEA, reflux, 90 °C, 3h. j) K_2CO_3 , reflux, DMF, 4 h.

Experimental Section

General Procedures. All chemicals were of analytical grade and used directly. All melting points were determined in PMP-DM scientific melting point apparatus and are uncorrected. The completion of reaction was monitored by thin-layer chromatography (TLC) using silica gel-G coated Al-plates (0.5 mm thickness, Merck) and spots were visualized under UV radiation. Infrared spectra were recorded on a Perkin Elmer RX-1 model spectrophotometer using KBr pellets. ^{1}H NMR spectra were acquired on a Bruker Avance-2 model spectrophotometer using $CDCl_3$ as a solvent and TMS as internal reference (chemical shifts in δ, ppm).

Preparation of 3-formyl-7-methyl-2-morpholinoquinoline (4). To a well-stirred solution of morpholine (0.1 mol, 8.71 ml) and 2-chloro-3-formyl-7-methylquinoline **3** (0.1 mol, 20.5 g.) in DMF (25mL) were stirred at 35 ^{o}C for 4 h. The pH was adjusted using sodium bicarbonate. After cooling, the resulting solid was filtered, dried and recrystallized from ethanol to obtain compound **4**, yield 68%, as yellowish white solid. Mp 178 ^{o}C.

1-(4-aminophenyl)-3-(2-morpholino-7-methylquinolin-3-yl)-2-propen-1-one (**5).** To a solution of 4-aminoacetophenone (0.1 mol 13.5 g), **4** (0.1 mol, 25.6 g), methanol (98 ml) and 20% NaOH solution (20 ml) was stirred for 0.5 h at room temperature and left overnight. After the completion of reaction, it was poured into ice water, acidified, filtered and recrystallized from ethanol to give a pale yellow powder. Yield 70%, Mp 209 ^{o}C.

Compound (10a). General method

To a mixture of **5** (0.01 mol, 3.73 g.) in DMF and the respectively **9a** was heated at 90 ^{o}C in the presence of sodium bicarbonate for 5-10 h and the resulting mixture was poured into ice cold

water and stirred for 30 minute then dry and washed with methanol and recrytallised from acrylonitrile. Yield 78%, as a brown solid. Mp 189 ^{o}C. Anal. Calcd for $C_{44}H_{39}N_6O_6FCl_2$: C, 63.08%; H, 4.69%; N, 10.03%. found: C, 63.05%; H, 4.64%; N, 10.01%; **NMR CDCl$_3$**: 2.38 (s, 3H, Me), 3.69 (t, 4H, -CH_2), 3.60 (t, 4H, -CH_2), 4.00 (s, 9H, OMe), 4.05 (s, 2H, -CH_2), 5.96 (s, 1H, -NH), 7.06 (s, 1H, H_5), 7.14 (s, 1H, H_6), 7.33 (s, 1H, H_8), 7.8 (s, 1H, -CH), 7.88-8.52 (m, 7H, Ar-H), 9.62 (s, 1H, -NH), 8.1 (s, 1H, -CH). **IR (KBr)/cm $^{-1}$**: 3328 cm^{-1}(-NH-), 1575 cm^{-1} (-C=C-), 1635 cm^{-1} (-C=N-), 725 cm^{-1}(-C-Cl), 1098 cm^{-1} (-C-F-), 1684 cm^{-1}(>C=O-), 1130 cm^{-1} (-CH_2-O-CH_2-).

Compound (10b). Yield 70%**,** brown; mp 202; Anal. Calcd for $C_{41}H_{33}N_6O_3FCl_2$: C, 62.96%; H, 4.12%; N, 10.75%. found: C, 62.93%; H, 4.10%; N, 10.73%; **NMR CDCl$_3$**: 2.33 (s, 3H, Me), 3.70 (t, 4H, -CH_2), 3.62 (t, 4H, -CH_2), 4.15 (s, 2H, -CH_2), 5.98 (s, 1H, -NH), 7.10 (s, 1H, H_5), 7.15 (s, 1H, H_6), 7.33 (s, 1H, H_8), 7.82 (s, 1H, -CH), 7.88-8.52 (m, 7H, Ar-H), 9.59 (s, 1H, -NH), 8.12 (s, 1H, -CH). **IR (KBr)/cm $^{-1}$**: 3330 cm^{-1} (-NH-), 1560 cm^{-1} (-C=C-), 1648 cm^{-1} (-C=N-) , 723 cm^{-1}(-C-Cl-), 1080 cm^{-1} (-C-F-), 1689 cm^{-1}(>C=O-), 1125 cm^{-1}(-CH_2-O-CH_2-).

Compound (10c). Yield 62%**,** brown**;** mp 165; Anal. Calcd for $C_{42}H_{35}N_6O_4FCl_2$: C, 64.87%; H, 4.54%; N, 10.81%. found: C, 64.84%; H, 4.51%; N, 10.79%; **NMR CDCl$_3$:** 2.37 (s, 3H, Me), 3.66 (t, 4H, -CH_2), 3.59 (t, 4H, -CH_2), 4.01 (s, 3H, OMe), 4.06 (s, 2H, -CH_2), 5.96 (s, 1H, -NH), 7.06 (s, 1H, H_5), 7.14 (s, 1H, H_6), 7.33 (s, 1H, H_8), 7.8 (s, 1H, -CH), 7.33 (s, 1H, H_8), 7.88-8.52 (m, 7H, Ar-H), 9.62 (s, 1H, -NH), 8.1 (s, 1H, -CH). **IR (KBr)/cm $^{-1}$:**3340 cm^{-1}(-NH-), 1580 cm^{-1} (-C=C-), 1645 cm^{-1} (-C=N-), 730 cm^{-1}(-C-Cl-), 1090 cm^{-1} (-C-F-), 1684 cm^{-1}(>C=O-), 1140 cm^{-1}(-CH_2-O-CH_2-).

Compound (10d). Yield 70%**,** brown**;** mp 168; Anal. Calcd for $C_{42}H_{35}N_6O_3FCl_2$: C, 66.23%; H, 4.63%; N, 11.03%. found: C, 66.21%; H, 4.62%; N, 10.01%; **NMR CDCl$_3$:** 2.32 (s, 3H, Me), 2.38 (s, 3H, Me), 3.69 (t, 4H, -CH_2), 3.60 (s, 4H, -CH_2), 4.08 (s, 2H, -CH_2), 5.92 (s, 1H, -NH), 7.08 (s, 1H, H_5), 7.15 (s, 1H, H_6), 7.30 (s, 1H, H_8), 7.86 (s, 1H, -CH), 7.34 (s, 1H, H_8), 7.88-8.52 (m, 7H, Ar-H), 9.58 (s, 1H, -NH), 8.12 (s, 1H, -CH). **IR (KBr)/cm $^{-1}$:** 3330 cm^{-1}(-NH-), 1575 cm^{-1} (-C=C-), 1635 cm^{-1} (-C=N-), 720 cm^{-1}(-C-Cl-), 1098 cm^{-1} (-C-F-), 1678 cm^{-1}(>C=O-), 1150 cm^{-1}(-CH_2-O-CH_2-).

Compound (10e). Yield 65%**,** brown**;** mp 194; Anal. Calcd for $C_{42}H_{35}N_6O_4FCl_2$ C, 64.87%; H, 4.54%; N, 10.81%. found: C, 64.85%; H, 4.50%; N, 10.78%; **NMR CDCl$_3$:** 2.36 (s, 3H, Me), 3.66 (t, 4H, -CH_2), 3.59 (t, 4H, -CH_2), 4.01 (s, 3H, OMe), 4.09 (s, 2H, -CH_2), 5.92 (s, 1H, -NH), 7.09 (s, 1H, H_5), 7.15 (s, 1H, H_6), 7.33 (s, 1H, H_8), 7.8 (s, 1H, -CH), 7.33 (s, 1H, H_8), 7.88-8.52 (m, 7H, Ar-H), 9.62 (s, 1H, -NH), 8.1 (s, 1H, -CH). **IR (KBr)/cm $^{-1}$:** 3320 cm^{-1}(-NH-), 1566 cm^{-1} (-C=C-), 1630 cm^{-1} (-C=N-), 732 cm^{-1}(-C-Cl-), 1088 cm^{-1} (-C-F-), 1673 cm^{-1}(>C=O-), 1150 cm^{-1}(-CH_2-O-CH_2-).

Compound (10f). Yield 70%**,** brown**;** mp 210; Anal. Calcd for $C_{41}H_{33}N_6O_3F_2Cl_2$: C, 62.96%; H, 4.12%; N, 10.75%. found: C, 62.94%; H, 4.09%; N, 10.73%; **NMR CDCl$_3$:** 2.36 (s, 3H, Me), 3.66 (t, 4H, -CH_2), 3.59 (t, 4H, -CH_2), 4.12 (s, 2H, -CH_2), 6.01 (s, 1H, -NH), 7.12 (s, 1H, H_5), 7.19 (s, 1H, H_6), 7.38 (s, 1H, H_8), 7.8 (s, 1H, -CH), 7.33 (s, 1H, H_8), 7.88-8.52 (m, 7H, Ar-H), 9.67 (s, 1H, -NH), 8.12 (s, 1H, -CH). **IR (KBr)/cm $^{-1}$:** 3327 cm^{-1}(-NH-), 1576 cm^{-1} (-C=C-),

1655 cm^{-1} (-C=N-), 721 cm^{-1}(-C-Cl-), 1065 cm^{-1} (-C-F-), 1679 cm^{-1}(>C=O-), 1146 cm^{-1}(-CH_2-O-CH_2-).

Compound (10g). Yield 60%**,** brown**;** mp 155; Anal. Calcd for $C_{41}H_{33}N_6O_4FCl_2$: C, 62.49%; H, 4.36%; N, 11.01%. found: C, 62.47%; H, 4.33%; N, 10.98%; **NMR $CDCl_3$:** 2.33 (s, 3H, Me), 3.68 (t, 4H, -CH_2), 3.58 (t, 4H, -CH_2), 4.08 (s, 2H, -CH_2), 6.01 (s, 1H, -NH), 7.14 (s, 1H, H_5), 7.11 (s, 1H, H_6), 7.35 (s, 1H, H_8), 7.82 (s, 1H, -CH), 7.32 (s, 1H, H_8), 7.88-8.52 (m, 7H, Ar-H), 9.65 (s, 1H, -NH), 8.18 (s, 1H, -CH). **IR (KBr)/cm $^{-1}$:** 3332 cm^{-1}(-NH-), 1576 cm^{-1} (-C=C-), 1638 cm^{-1} (-C=N-), 712 cm^{-1}(-C-Cl-), 1092 cm^{-1} (-C-F-), 1663 cm^{-1}(>C=O-), 1159 cm^{-1}(-CH_2-O-CH_2-).

General procedure for *N*-chloroacetyl arylamines (12h-q)

In benzene (30 ml), chloroacetyl chloride (0.03 mol, 3.38 g, 2.4 ml) and 2-3 drops of TEA were added and the mixture was stirred on a water bath for 10 mins. A solution of arylamine (0.02 mol) in benzene (30 ml) was added dropwise and the mixture heated at reflux for 2 h then cooled. The resulting white precipitate was filtered and washed with benzene, purified by recrystallization from alcohol.

Compound (13h). Compound **5** (0.01 mol, 3.73 g.) and the *N*-chloroacetyl aryl amine **12h** were heated at reflux in DMF (25 ml) at 90 °C in the presence of sodium bicarbonate for 5-10 h and the resulting mixrture was poured into ice cold water and stirred for 30 min then dry and washed with methanol and recrytallisation form acrylonitrile or ethanol, yield 65%, brown solid. Mp 220-225 ^{o}C. Anal. Calcd for $C_{31}H_{30}N_4O_3$: C, 73.44%; H, 5.92%; N, 11.05%. found: C, 73.41%; H, 5.89%; N, 11.02%; **NMR $CDCl_3$**: 2.40 (s, 3H, Me), 9.64 (s, 1H, -NH), 5.97 (s, 1H, -NH), 4.08 (s, 2H, -CH_2), 7.61 (m, 4H, Ar-H), 7.24 (m, 4H, Ar-H), 3.71 (t, 4H, -CH_2), 3.62 (t, 4H, -CH_2), 8.12 (d, 1H, -CH), 7.5 (d, 1H, -CH), 7.12-8.28 (m, 4H, Ar-H). **IR (KBr)/cm $^{-1}$**: 3336 cm^{-1}(-NH-), 1580 cm^{-1} (>C=O), 1638 cm^{-1} (-C=N-), 1335 cm^{-1}(-C-CH_3), 1111 cm^{-1}(-CH_2-O-CH_2-).

Compound (13i). Yield 71%**,** brown; mp 230; Anal. Calcd for $C_{32}H_{32}N_4O_3$: C, 73.84%; H, 6.14%; N, 10.75%. found: C, 73.81%; H, 6.12%; N, 10.73%; **NMR $CDCl_3$**: 2.38 (s, 3H, Me), 2.42 (s, 3H, Me), 9.64 (s, 1H, -NH), 6.07 (s, 1H, -NH), 4.05 (s, 2H, -CH_2), 7.58 (m, 4H, Ar-H), 7.21 (m, 4H, Ar-H), 3.79 (t, 4H, -CH_2), 3.68 (t, 4H, -CH_2), 8.10 (d, 1H, -CH), 7.49 (d, 1H, -CH), 7.12-8.28 (m, 4H, Ar-H). **IR (KBr)/cm $^{-1}$:** 3342 cm^{-1}(-NH-), 1588 cm^{-1} (>C=O), 1635 cm^{-1} (-C=N-), 1343 cm^{-1}(-C-CH_3), 1123 cm^{-1}(-CH_2-O-CH_2-).

Compound (13j). Yield 77%**,** brwon**;** mp 228; Anal. Calcd for $C_{32}H_{32}N_4O_3$: C, 73.84%; H, 6.14%; N, 10.75%. found: C, 73.82%; H, 6.11%; N, 10.72%; **NMR $CDCl_3$**: 2.38 (s, 3H, Me), 2.33 (s, 3H, Me), 9.66 (s, 1H, -NH), 5.88 (s, 1H, -NH), 4.01 (s, 2H, -CH_2), 7.51 (m, 4H, Ar-H), 7.26 (m, 4H, Ar-H), 3.83 (t, 4H, -CH_2), 3.62 (t, 4H, -CH_2), 8.10 (d, 1H, -CH), 7.49 (d, 1H, -CH), 7.12-8.28 (m, 4H, Ar-H). **IR (KBr)/cm $^{-1}$**: 3348 cm^{-1}(-NH-), 1581 cm^{-1} (>C=O), 1631 cm^{-1} (-C=N-), 1347 cm^{-1}(-C-CH_3), 1121 cm^{-1}(-CH_2-O-CH_2-).

Compound (13k). Yield 55%**,** brwon**;** mp 222; Anal. Calcd for $C_{32}H_{32}N_4O_3$: C, 73.84%; H, 6.14%; N, 10.75%. found: C, 73.83%; H, 6.10%; N, 10.73%; **NMR $CDCl_3$**: 2.35 (s, 3H, Me), 2.47 (s, 3H, Me), 9.63 (s, 1H, -NH), 6.12 (s, 1H, -NH), 4.09 (s, 2H, -CH_2), 7.5 (m, 4H, Ar-H),

7.24 (m, 4H, Ar-H), 3.80 (t, 4H, -CH_2), 3.68 (t, 4H, -CH_2), 8.10 (d, 1H, -CH), 7.54 (d, 1H, -CH), 7.12-8.28 (m, 4H, Ar-H). **IR (KBr)/cm $^{-1}$**: 3328 cm^{-1}(-NH-), 1557 cm^{-1} (>C=O), 1649 cm^{-1} (-C=N-), 1325 cm^{-1}(-C-CH_3), 1108 cm^{-1}(-CH_2-O-CH_2-).

Compound (13l). Yield 65%**,** brwon**;** mp 165; Anal. Calcd for $C_{32}H_{29}N_4O_3Cl$: C, 67.76%; H, 5.36%; N, 10.35%. found: C, 67.74%; H, 5.34%; N, 10.33%; **NMR CDCl$_3$**: 2.38 (s, 3H, Me), 9.60 (s, 1H, -NH), 5.96 (s, 1H, -NH), 4.13 (s, 2H, -CH_2), 7.58 (m, 4H, Ar-H), 7.21 (m, 4H, Ar-H), 3.79 (t, 4H, -CH_2), 3.64 (t, 4H, -CH_2), 8.10 (d, 1H, -CH), 7.49 (d, 1H, -CH), 7.12-8.28 (m, 4H, Ar-H). **IR (KBr)/cm $^{-1}$**: 3342 cm^{-1}(-NH-), 1588 cm^{-1} (>C=O), 1635 cm^{-1} (-C=N-), 1343 cm^{-1}(-C-CH_3), 1123 cm^{-1}(-CH_2-O-CH_2-), 711 cm^{-1}(-C-Cl-).

Compound (13m). Yield 73%**,** brwon**;** mp 218; Anal. Calcd for $C_{31}H_{29}N_4O_3Cl$: C, 67.76%; H, 5.36%; N, 10.35%. found: C, 67.73%; H, 5.32%; N, 10.32%; **NMR CDCl$_3$**: 2.38 (s, 3H, Me), 9.56 (s, 1H, -NH), 6.07 (s, 1H, -NH), 3.92 (s, 2H, -CH_2), 7.58 (m, 4H, Ar-H), 7.18 (m, 4H, Ar-H), 3.85 (t, 4H, -CH_2), 3.68 (t, 4H, -CH_2), 8.10 (d, 1H, -CH), 7.49 (d, 1H, -CH), 7.12-8.28 (m, 4H, Ar-H). **IR (KBr)/cm $^{-1}$**: 3322 cm^{-1}(-NH-), 1578 cm^{-1} (>C=O), 1631 cm^{-1} (-C=N-), 1323 cm^{-1}(-C-CH_3), 1117 cm^{-1}(-CH_2-O-CH_2-), 718 cm^{-1}(-C-Cl-).

Compound (13n). Yield 78%**,** brwon**;** mp 249; Anal. Calcd for $C_{31}H_{29}N_4O_3Cl$: C, 67.76%; H, 5.36%; N, 10.35%. found: C, 67.73%; H, 5.34%; N, 10.31%; **NMR CDCl$_3$**: 2.34(s, 3H, Me), 9.52(s, 1H, -NH), 6.02(s, 1H, -NH), 3.97 (s, 2H, -CH_2), 7.55 (m, 4H, Ar-H), 7.13 (m, 4H, Ar-H), 3.83 (t, 4H, -CH_2), 3.64 (t, 4H, -CH_2), 8.10 (d, 1H, -CH), 7.44 (d, 1H, -CH), 7.12-8.28 (m, 4H, Ar-H). **IR (KBr)/cm $^{-1}$**: 3352 cm^{-1}(-NH-), 1598 cm^{-1} (>C=O), 1643 cm^{-1} (-C=N-), 1343 cm^{-1}(-C-CH_3), 1133 cm^{-1}(-CH_2-O-CH_2-), 704 cm^{-1}(-C-Cl-).

Compound (13o). Yield 80%**,** brwon**;** mp 257; Anal. Calcd for $C_{31}H_{29}N_5O_5$: C, 67.45%; H, 5.25%; N, 12.69%. found: C, 67.41%; H, 5.22%; N, 12.67%; **NMR CDCl$_3$**: 2.42 (s, 3H, Me), 9.64 (s, 1H, -NH), 6.03 (s, 1H, -NH), 4.01 (s, 2H, -CH_2), 7.58 (m, 4H, Ar-H), 7.21 (m, 4H, Ar-H), 3.79 (t, 4H, -CH_2), 3.64 (t, 4H, -CH_2), 8.10 (d, 1H, -CH), 7.47 (d, 1H, -CH), 7.12-8.28 (m, 4H, Ar-H). **IR (KBr)/cm $^{-1}$**: 3352 cm^{-1}(-NH-), 1572 cm^{-1} (>C=O), 1645 cm^{-1} (-C=N-), 1339 cm^{-1}(-C-CH_3), 1126 cm^{-1}(-CH_2-O-CH_2-).

Compound (13p). Yield 76%**,** brwon**;** mp 232; Anal. Calcd for $C_{31}H_{29}N_5O_5$: C, 67.45%; H, 5.25%; N, 12.69%. found: C, 67.42%; H, 5.21%; N, 12.67%; **NMR CDCl$_3$**: 2.33 (s, 3H, Me), 9.67 (s, 1H, -NH), 6.07 (s, 1H, -NH), 4.05 (s, 2H, -CH_2), 7.58 (m, 4H, Ar-H), 7.21 (m, 4H, Ar-H), 3.72 (t, 4H, -CH_2), 3.68 (t, 4H, -CH_2), 8.10 (d, 1H, -CH), 7.49 (d, 1H, -CH), 7.12-8.28 (m, 4H, Ar-H). **IR (KBr)/cm $^{-1}$**: 3332 cm^{-1}(-NH-), 1578 cm^{-1} (>C=O), 1652 cm^{-1} (-C=N-), 1345 cm^{-1}(-C-CH_3), 1123 cm^{-1}(-CH_2-O-CH_2-).

Compound (13q). Yield 69%**,** brwon**;** mp 242; Anal. Calcd for $C_{31}H_{28}N_6O_7$: C, 72.75%; H, 4.69%; N, 14.08%. found: C, 72.71%; H, 4.67%; N, 14.06%; **NMR CDCl$_3$**: 2.42 (s, 3H, Me), 9.69 (s, 1H, -NH), 6.07 (s, 1H, -NH), 4.02 (s, 2H, -CH_2), 7.54 (m, 4H, Ar-H), 7.21 (m, 4H, Ar-H), 3.74 (t, 4H, -CH_2), 3.68 (t, 4H, -CH_2), 8.10 (d, 1H, -CH), 7.42 (d, 1H, -CH), 7.12-8.28 (m, 5H, Ar-H). **IR (KBr)/cm $^{-1}$**: 3344 cm^{-1}(-NH-), 1578 cm^{-1} (>C=O), 1635 cm^{-1} (-C=N-), 1341 cm^{-1}(-C-CH_3), 1112 cm^{-1}(-CH_2-O-CH_2-).

Biological assays

1. Compounds

Test compounds were dissolved in DMSO (12.5%) at an initial concentration of 20 mg ml $^{-1}$ and then were serially diluted in culture medium.

2. Cells

Bacterial strains *Staphylococcus aureus, Bacillus subtillis, Escherichia coli, Salmonella typhosa*.

3. Antibacterial assays

The MICs of the chemical compounds assays were carried out as described by Clause[15] with minor modifications. Ampicillin trihydrate was used as reference antibacterial agent. Solutions of the test compounds and reference drug were dissolved in DMSO at a concentration of 20 mg ml^{-1}. The twofold dilution of the compounds and reference drug were prepared (20, 10, 5.0, 2.5, 1.25, 0.625, 0.31, 0.15, 0.07, 0.03, 0.019, 0.01, 0.005 >) mg ml^{-1}. Antibacterial activities of the bacterial strains were carried out in Muller– Hinton broth (Difco) medium, at pH 6.9, with an inoculum of (1– 2) × 10^3 cells ml $^{-1}$ by the spectrophotometric method and an aliquot of 100 µl was added to each tube of the serial dilution. The chemical compounds-broth medium serial tube dilutions inoculated with each bacterium were incubated on a rotary shaker at 37 °C for 24 h at 150 rpm. The minimum inhibitory concentrations of the chemical compounds were recorded as the lowest concentration of each chemical compounds in the tubes with no growth (i.e. no turbidity) of inoculated bacteria.

Table 1. Antimicrobial Activity

Sr.No.	Minimum Inhibitory Concentration in mgml^{-1}			
	S. aureus	***B. subtillis***	***E. coli***	***S. typhosa***
10a	0.03	0.015	0.15	1.25
10b	0.31	0.07	1.25	0.625
10c	0.625	0.015	5.0	2.5
10d	2.5	2.5	0.03	5.0
10e	0.15	5.0	2.5	5.0
10f	0.15	0.625	1.25	1.25
10g	2.5	2.5	5.0	0.625
13h	-	10	1.25	-
13i	2.5	-	0.625	5.0
13j	1.25	-	2.5	10
13k	1.25	5.0	2.5	1.25
13l	2.5	1.25	0.015	2.5
13m	0.015	0.625	2.5	0.625
13n	0.625	0.07	5.0	2.5
13o	2.5	2.5	10	1.25

Table 1. Continued

Sr.No.	Minimum Inhibitory Concentration in $mgml^{-1}$			
	S. aureus	***B. subtillis***	***E. coli***	***S. typhosa***
13p	2.5	5.0	5.0	0.015
13q	1.25	1.25	2.25	5.0
Ampicillin trihydrate	0.019	0.005	0.005	0.01

Conclusions

A series of quinolinyl chalcones were prepared and tested for their *in vitro* antibacterial activity against the four strains of bacteria (gram +ve, gram –ve). Five compounds of the obtained series showed high *in vitro* antimicrobial activity. Compound (**10a**) showed excellent activity against *Staphylococcus aureus* and *Bacillus subtillis*, compound (**10b**) showed good activity against *Bacillus subtillis*, compound (**10c**) showed excellent activity against *Bacillus subtillis*, compound (**13l**) showed excellent activity against *Escherichia coli* and compound (**13p**) showed excellent activity against *Salmonella typhosa*. The presence of more than one electron-withdrawing group on the aromatic ring in Series 1 in general increased the antimicrobial activity compared to compounds with electron-donating groups. The presence of electron-donating group on the aromatic ring in Series 2 in general decreased the antimicrobial activity compared to compounds with electron-withdrawing groups. Based upon the results, it will also be necessary to optimize the by substituting a series of electron-withdrawing groups on the aromatic ring and selectively modifying the quinoline nucleus. The substitution in the C-2, C-3, and C-4 positions in Series 1 and C-2 and C-4 positions in Series 2 in of the phenyl ring seems to be very important for antibacterial effect, as well as the presence and the position of –NHCO- group in the connecting linker between the aromatic ring seems to be very important for antibacterial effect.

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