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Synthesis and *In Vitro* Antimicrobial Evaluation of Pyrazole Clubbed Quinoline

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ABSTRACT

In present study, a novel series of *6-bromo-2,7,8-trichloro-3-(3'-phenyl-4',5'-dihydro-1H-pyrazol-5'-yl)quinoline*$_{(a\text{-}i)}$. These novel synthesized entities were elicited by IR, ^{1}H NMR, ^{13}C NMR, C,H,N Analyzer and mass spectra. The entities produced in laboratory were screened with strains of bacteria and fungi like *Staphylococcus aureus, Bacillus Megaterium, Proteus vulgaris, Escherichia coli, and Aspergillus niger* respectively. Out of nine different entities synthesized five derivatives showed excellent antibacterial activity and rest of them showed moderate antimicrobial activity.

Keywords: antifungal agents, pyrazolines, antibacterial agents, chalcones

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INTRODUCTION

There is a huge demand for the development of antimicrobial drugs in the market due to the increasing number of the infections caused by the rapid development of the microbes having the resistance property towards the presently available antibiotics[1].Heterocyclic rings since years have played an important role in serving as a key template in the development of important therapeutic agents[2]. Pyrazoles are the kind of motifs which possesses multi pharmacological activities[3,4]. Pyrazoles on combining with different heterocyclic compounds results in the formation of biologically active entities[5,6].

Scientists have also reported several quinolines to be excellent antimicrobial agent[7,8], antimalerial agent[9] and antimycobactrial agent[10]. Quinolines with different subsistent act as antagonist for endothelin[11] as well as lukotriene D4 receptor[12]. Recent research work also reports that pyrazole on getting attached to a quinoline ring can exhibit very good antimicrobial activity[13].

Keeping this excellent antimicrobial property[14] of pyrazole substituted quinoline into consideration; a series of novel entities showing similar or high antimicrobial activity have been synthesized by versatile[15] method. The structures of these biologically active compounds were confirmed with the help of IR, ^{1}H NMR, ^{13}C NMR, C,H,N Analysis and mass spectral data.

MATERIALS AND METHODS

Materials and physical measurements

All chemicals required for synthesis were obtained from Merck ltd and SD Fine chemicals ltd. Melting points of synthesized compounds were determined by open tube capillary method. The purity of the entities synthesized was monitored by using TLC plates (silica gel G) in the solvent system Toluene: Acetone (2:8). The spots were observed by exposing it to UV light and iodine chamber. The IR spectra were obtained by using Perkin-Elmer Infrared Spectrometer (KBr pellet). The ^{1}H NMR and ^{13}C NMR were recorded by Bruker Spectrometer-400 MHz with DMSO as solvent and TMS as internal standard. Elemental analysis (% C, H, N) was carried out by Perkin-Elmer 2400 CHN Analyzer. Mass spectra were obtained by using Schimadzu mass spectrometer.

Methods of preparation and physical data of synthesized compounds

Synthesis of *2,7,8-trichloro-6-bromoquinoline-3-carbaldehyde* (I)

Compound **I** was prepared from 3-bromo-4,5-dichloroacetanilide according to literature method[16]. Compound **(I):** Yield: 92%; m.p. 178°C; Anal. Calcd. for $C_{10}H_3BrCl_3NO$**:** C, 35.39; H,

0.89; N, 4.13; Cl, 31.34. Found: C, 35.36; H, 0.86; N, 4.11; Cl, 31.32. IR (KBr, cm^{-1}): 1596 (C=N str. of quinoline ring), 754 (C-Cl str.); ^{1}H NMR (400 MHz, DMSO, δ, ppm): 7.89 (1H, s, Ar-H), 8.75 (1H, s, Ar-H), 9.58 (1H, s, CHO); ^{13}C NMR (400 MHz, DMSO, δ, ppm**):** 121.4 (c_6), 126.7 (c_{10}), 130.5 (c_3), 131.0 (c_5), 131.6 (c_8), 142.0 (c_7), 142.2 (c_4), 143.6 (c_9), 150.4 (c_2); MS (m/z): 340 (M^+).

General procedure for the Synthesis of different substituents of *(Z)-3-(6-bromo-2, 7, 8-trichloro-quinoline-3'-yl)-1-phenylpre-2-en-1-one* (II)$_{a-i}$

To a well stirred solution of **(I)** (0.01 mol) in 25 ml ethanol; differently substituted Acetophenone (0.01 mol) were added. 40% NaOH added till the solution became basic. The reaction mixture was stirred for 24 Hrs. The contents were poured into ice cold water acidified, filtered and crystallized from ethanol.

(Z)-3-(6-bromo-2,7,8-trichloroquinolin-3-yl)-1-(4-hydroxyphenyl)prop-2-en-1-one (II)$_a$: Yield: 86%; m.p. 128°C; Anal. Calcd. for $C_{18}H_9BrCl_3NO_2$: C, 47.25; H, 1.98; N, 3.06; Cl, 23.25. Found: C, 47.23; H, 1.96; N, 3.04; Cl, 23.23; IR (KBr, cm^{-1}): 3076 (C-H str. Of phenyl ring)**,** 2960 (C-H of alkane), 1666 (C=O str.) 1590 (C=N str. of quinoline ring), 668 (C-Br str.), 777 (C-Cl str.); ^{1}H NMR (400 MHz, DMSO, δ, ppm): 8.35 (1H, s, quinoline ring), 8.80 (1H,s, quinoline ring), 6.89 (1H, d, phenyl ring), 6.93 (1H,d,phenyl ring), 8.09 (1H, d, phenyl ring), .06 (1H, d, phenyl ring), 5.39 (1H, s, -OH), 7.15 (1H, d, C=C, J=8.8Hz) 7.61 (1H, d, C=C, J=8.7Hz); ^{13}C NMR (400 MHz, DMSO, δ, ppm): 116.7 (c_{13}), 116.7 (c_{15}), 121.9 (c_6), 123.5 (c_{10}), 127.3 ($c_{4'}$), 129.9 (c_5), 130.5 (c_{11}), 131.6 (c_{12}), 131.6 (c_{16}), 131.9 (c_8), 134.5 (c_4), 134.8 (c_3), 139.5 (c_7), 141.8(c_9), 145.6 ($c_{5'}$), 151.4 (c_2),164.6 (c_{14}), 189.0 ($c_{3'}$); MS (m/z) 457.5 (M^+)

(Z)-3-(6-bromo-2,7,8-trichloroquinolin-3-yl)-1-(4-nitrophenyl)prop-2-en-1-one (II)$_b$: Yield: 84%; m.p. 172°C; Anal. Calcd. for $C_{18}H_8BrCl_3N_2O_3$: C, 44.44; H, 1.66; N, 5.76; Cl, 16.42. Found: C, 44.42; H, 1.64; N, 5.74; Cl, 16.40; IR (KBr, cm^{-1}): 3040 (C-H str. Of phenyl ring)**,** 2929 (C-H of alkane), 1658 (C=O str.), 1595 (C=N str. of quinoline ring), 679 (C-Br str.), 770 (C-Cl str.); ^{1}H NMR (400 MHz, DMSO, δ, ppm): 8.35 (1H, s, quinoline), 8.80 (1H,s, quinoline ring), 8.43 (1H, d, phenyl ring), 8.47 (1H,d,phenyl ring), 8.10 (1H, d, phenyl ring), 8.12 (1H, d, phenyl ring), 7.15 (1H, d, C=C, J=8.8Hz) 7.61 (1H, d, C=C, J=8.7Hz); ^{13}C NMR (400 MHz, DMSO, δ, ppm): 121.9 (c_6), 123.5 (c_{10}), 124.7 (c_{13}), 124.7 (c_{15}),127.3 ($c_{4'}$), 129.9 (c_5), 130.6 (c_{12}), 130.6 (c_{16}), 131.9 (c_8), 134.5 (c_4), 134.8 (c_3), 139.5 (c_7), 141.8(c_9), 144.7 (c_{11}),145.6 ($c_{5'}$), 151.4 (c_2),153.6 (c_{14}), 189.2 ($c_{3'}$); MS (m/z) 486.5 (M^+)

(Z)-3-(6-bromo-2,7,8-trichloroquinolin-3-yl)-1-(2-chlorophenyl)prop-2-en-1-one (II)$_c$: Yield: 85%; m.p. 132°C; Anal. Calcd. for $C_{18}H_8BrCl_4NO$: C, 45.42; H, 1.69; N, 2.94; Cl, 29.79. Found:

C, 45.40; H, 1.67; N, 2.92; Cl, 29.77; IR (KBr, cm^{-1}): 3030 (C-H str. Of phenyl ring), 2935 (C-H of alkane), 1690 (C=O str.), 1570 (C=N str. of quinoline ring), 683 (C-Br str.), 740 (C-Cl str.); ^{1}H NMR (400 MHz, DMSO, δ, ppm): 8.35 (1H, s, quinoline ring), 8.80 (1H,s, quinoline ring), 7.69 (1H, d, phenyl ring), 7.83 (1H,d,phenyl ring),7.52 (1H, t, phenyl ring), 7.67 (1H, t, phenyl ring), 7.15 (1H, d, C=C, J=8.8Hz) 7.61 (1H, d, C=C, J=8.7Hz); ^{13}C NMR (400 MHz, DMSO, δ, ppm): 121.9 (c_6), 123.5 (c_{10}), 127.3 ($c_{4'}$), 127.7 (c_{13}), 129.9 (c_5), 131.5 (c_8),131.6 (c_{12}), 131.7 (c_{15}), 131.9 (c_{16}), 134.5 (c_4), 134.8 (c_3), 135.6 (c_{14}), 137.6 (c_{11}), 139.5 (c_7), 141.8(c_9), 145.6 ($c_{5'}$), 151.4 (c_2), 189.2 ($c_{3'}$); MS (m/z) 477 (M^+)

(Z)-3-(6-bromo-2,7,8-trichloroquinolin-3-yl)-1-(4-methoxyphenyl)prop-2-en-1-one $(II)_d$: Yield: 79%; m.p. 149°C; Anal. Calcd. for $C_{19}H_{11}BrCl_3NO_2$: C, 45.42; H, 2.35; N, 2.97; Cl, 22.55. Found: C, 45.40; H, 2.33; N, 2.95; Cl, 22.53; IR (KBr, cm^{-1}): 3250(C-H str. Of phenyl ring), 2935 (C-H of alkane), 1641 (C=O str.), 1562 (C=N str. of quinoline ring), 671 (C-Br str.), 758 (C-Cl str.); ^{1}H NMR (400 MHz, DMSO, δ, ppm): 8.35 (1H, s, quinoline ring), 8.80 (1H,s, quinoline ring), 8.15 (1H, d, phenyl ring), 8.12 (1H,d,phenyl ring), 7.20 (1H, d, phenyl ring), 7.25 (1H, d, phenyl ring) 7.15 (1H, d, C=C, J=8.8Hz) 7.61 (1H, d, C=C, J=8.7Hz), 3.83 (3H, m, -OCH_3); ^{13}C NMR (400 MHz, DMSO, δ, ppm): 55.8 (-OCH3), 114.7 (c_{13}), 114.9 (c_{15}),121.9 (c_6), 123.5 (c_{10}), 127.3 ($c_{4'}$), 129.9 (c_5), 130.6 (c_{11}), 131.0 (c_{12}), 131.0 (c_{16}), 131.5 (c_8),134.5 (c_4), 134.8 (c_3), 139.5 (c_7), 141.8(c_9), 145.6 ($c_{5'}$), 151.4 (c_2), 166.6 (c_{14}), 189.2 ($c_{3'}$); MS (m/z) 471.5 (M^+)

(Z)-3-(6-bromo-2,7,8-trichloroquinolin-3-yl)-1-(4-bromrophenyl)prop-2-en-1-one $(II)_e$: Yield: 76%; m.p. 147°C; Anal. Calcd. for $C_{18}H_8Br_2Cl_3NO$: C, 41.54; H, 1.55; N, 2.69; Cl, 20.44. Found: C, 41.52; H, 1.55; N, 2.67; Cl, 20.42; IR (KBr, cm^{-1}): 3262 (C-H str. Of phenyl ring), 2952 (C-H of alkane), 1642 (C=O str.), 1558 (C=N str. of quinoline ring), 689 (C-Br str.), 766 (C-Cl str.); ^{1}H NMR (400 MHz, DMSO, δ, ppm): 8.35 (1H, s, quinoline ring), 8.80 (1H,s, quinoline ring), 8.05 (1H, d, phenyl ring), 8.03 (1H,d,phenyl ring), 7.83 (1H, d, phenyl ring), 7.79 (1H, d, phenyl ring) 7.15 (1H, d, C=C, J=8.8Hz) 7.61 (1H, d, C=C, J=8.7Hz); ^{13}C NMR (400 MHz, DMSO, δ, ppm): 121.9 (c_6), 123.5 (c_{10}), 127.3 ($c_{4'}$), 128.6 (c_{14}), 129.9 (c_5), 130.2 (c_{16}), 130.2 (c_{12}), 131.5 (c_8), 132.2 (c_{15}), 132.2 (c_{13}), 134.5 (c_4), 134.8 (c_3), 136.6 (c_{11}), 139.5 (c_7), 141.8(c_9), 145.6 ($c_{5'}$), 151.4 (c_2), 189.2 ($c_{3'}$); MS (m/z) 520.5 (M^+)

(Z)-3-(6-bromo-2,7,8-trichloroquinolin-3-yl)-1-(4-fluorophenyl)prop-2-en-1-one $(II)_f$: Yield: 86%; m.p. 126°C; Anal. Calcd. for $C_{18}H_8BrCl_3FNO$: C, 47.50; H, 1.75; N, 3.05; Cl, 23.15. Found: C, 47.48; H, 1.73; N, 3.03; Cl, 23.13; IR (KBr, cm^{-1}): 3255 (C-H str. Of phenyl ring), 2946 (C-H of alkane), 1668 (C=O str.), 1566 (C=N str. of quinoline ring), 675 (C-Br str.), 777

(C-Cl str.); ^{1}H NMR (400 MHz, DMSO, δ, ppm): 8.35 (1H, s, quinoline ring), 8.80 (1H,s, quinoline ring), 7.43 (1H, d, phenyl ring), 7.52 (1H,d,phenyl ring), 7.87 (1H, d, phenyl ring), 7.92 (1H, d, phenyl ring) 7.15 (1H, d, C=C, J=8.8Hz) 7.61 (1H, d, C=C, J=8.7Hz); ^{13}C NMR (400 MHz, DMSO, δ, ppm): 121.9 (c_6), 123.5 (c_{10}), 127.3 ($c_{4'}$), 129.9 (c_5), 131.8 (c_{16}), 131.8 (c_{12}), 131.5 (c_8), 116.2 (c_{15}), 116.2 (c_{13}), 134.5 (c_4), 134.8 (c_3), 133.6 (c_{11}), 139.5 (c_7), 141.8(c_9), 145.6 ($c_{5'}$), 151.4 (c_2), 168.6 (c_{14}), 189.2 ($c_{3'}$); MS (m/z) 459.5 (M^+)

(Z)-3-(6-bromo-2,7,8-trichloroquinolin-3-yl)-1-(4-chlorophenyl)prop-2-en-1-one $(II)_g$: Yield: 88%; m.p. 139°C; Anal. Calcd. for $C_{18}H_8BrCl_3NO$: C, 45.42; H, 1.69; N, 2.94; Cl, 29.79. Found: C, 45.40; H, 1.67; N, 2.92; Cl, 29.77; IR (KBr, cm^{-1}): 3298 (C-H str. Of phenyl ring), 2962 (C-H of alkane), 1678 (C=O str.), 1569 (C=N str. of quinoline ring), 677 (C-Br str.), 776 (C-Cl str.); ^{1}H NMR (400 MHz, DMSO, δ, ppm): 8.35 (1H, s, quinoline ring), 8.80 (1H,s, quinoline ring), 7.43 (1H, d, phenyl ring), 7.52 (1H,d,phenyl ring), 7.87 (1H, d, phenyl ring), 7.92 (1H, d, phenyl ring) 7.15 (1H, d, C=C) 7.61 (1H, d, C=C, J=8.7Hz); ^{13}C NMR (400 MHz, DMSO, δ, ppm): 121.9 (c_6), 123.5 (c_{10}), 127.3 ($c_{4'}$), 129.2 (c_{15}), 129.2 (c_{13}), 129.9 (c_5), 130.8 (c_{16}), 130.8 (c_{12}), 131.5 (c_8), 134.5 (c_4), 134.8 (c_3), 136.2 (c_{11}), 139.5 (c_7), 140.1 (c_{14}) 141.8(c_9), 145.6 ($c_{5'}$), 151.4 (c_2), 189.2 ($c_{3'}$); MS (m/z) 476 (M^+)

(Z)-3-(6-bromo-2,7,8-trichloroquinolin-3-yl)-1-(4-methylphenyl)prop-2-en-1-one $(II)_h$: Yield: 81%; m.p. 159°C; Anal. Calcd. for $C_{19}H_{11}BrCl_3NO$: C, 50.09; H, 2.43; N, 3.07; Cl, 17.54. Found: C, 50.07; H, 2.41; N, 3.05; Cl, 17.54; IR (KBr, cm^{-1}): 3366 (C-H str. Of phenyl ring), 2947 (C-H of alkane), 1600 (C=O str.), 1552 (C=N str. of quinoline ring), 668 (C-Br str.), 758 (C-Cl str.); ^{1}H NMR (400 MHz, DMSO, δ, ppm): 8.35 (1H, s, quinoline ring), 8.80 (1H,s, quinoline ring), 7.83 (1H, d, phenyl ring, 7.91 (1H, d, phenyl ring), 7.62 (1H,d,phenyl ring), 7.67 (1H, d, phenyl ring), 7.81 (1H, d, phenyl ring) 7.15 (1H, d, C=C, J=8.8Hz) 7.61 (1H, d, C=C, J=8.7Hz) 7.72 (1H, m, phenyl ring); ^{13}C NMR (400 MHz, DMSO, δ, ppm): 21.5 (-CH_3), 121.9 (c_6), 123.5 (c_{10}), 127.3 ($c_{4'}$), 129.2 (c_{15}), 129.2 (c_{13}), 129.2 (c_{11}),129.8 (c_{16}), 129.8 (c_{12}), 129.9 (c_5), 131.5 (c_8), 134.5 (c_4), 134.8 (c_3), 139.5 (c_7), 144.1 (c_{14}) 141.8(c_9), 145.6 ($c_{5'}$), 151.4 (c_2), 189.2 ($c_{3'}$); MS (m/z) 455.5 (M^+)

(Z)-3-(6-bromo-2,7,8-trichloroquinolin-3-yl)-1-(phenyl)prop-2-en-1-one $(II)_i$: Yield: 78%; m.p. 171°C; Anal. Calcd. for $C_{18}H_{19}BrCl_3NO$: C, 48.96; H, 2.05; N, 3.17; Cl, 24.09. Found: C, 48.94; H, 2.03; N, 3.15; Cl, 24.07; IR (KBr, cm^{-1}): 3382 (C-H str. Of phenyl ring), 2958 (C-H of alkane), 1684 (C=O str.), 1586 (C=N str. of quinoline ring), 675 (C-Br str.), 768 (C-Cl str.); ^{1}H NMR (400 MHz, DMSO, δ, ppm): 8.35 (1H, s, quinoline ring), 8.80 (1H,s, quinoline ring), 7.43 (1H, d, phenyl ring), 7.52 (1H,d,phenyl ring), 7.97 (1H, d, phenyl ring), 7.91 (1H, d, phenyl

ring), 7.99 (1H, m, phenyl ring) 7.15 (1H, d, C=C, J=8.8Hz) 7.61 (1H, d, C=C, J=8.7Hz) 2.45 (3H, m, $-CH_3$); ^{13}C NMR (400 MHz, DMSO, δ, ppm): 121.9 (c_6), 123.5 (c_{10}), 127.3 ($c_{4'}$), 129.2 (c_{15}), 129.2 (c_{13}), 128.8 (c_{16}), 128.8 (c_{12}), 129.9 (c_5), 131.5 (c_8), 134.5 (c_4), 134.8 (c_3), 134.1 (c_{14}) 139.5 (c_7), 141.8(c_9), 145.6 ($c_{5'}$), 151.4 (c_2), 189.2 ($c_{3'}$); MS (m/z) 441.5 (M^+)

General procedure for the Synthesis of *6-bromo-2,7,8-trichloro-3-(3'-phenyl-4', 5'dihydro-1H-pyrazole-5'-yl)quinoline* (III)$_{a-i}$

Mixture of differently substituted 3-(6-bromo-2,7,8-trichloro-quinoline-3'-yl)-1-phenylpre-2-en-1-one **(II)**$_{a-i}$ (0.01mol) and hydrazine hydrate (0.04 mol) in *ethanol* (30 ml) were refluxed for 12 Hrs. The product were filtered, washed with hot methanol and recrystallized from 1, 4-dioxane.

6-bromo-2,7,8-trichloro-3-{3'-(p-hydroxyphenyl)-4',5'dihydro-1H-pyrazol-5'-yl}quinoline.

(III)$_a$: Yield: 79%; m.p. 189°C; Anal. Calcd. for $C_{18}H_{11}BrCl_3N_3O$: C, 45.48; H, 2.35; N, 8.91; Cl, 22.55. Found: C, 45.45; H, 2.32; N, 8.88; Cl, 22.52; IR (KBr, cm^{-1}): 3246 (NH str. of pyrazole ring), 1596 (C=N str. of quinoline ring), 1649 (C=N str. of pyrazole ring), 686 (C-Br str.), 754 (C-Cl str.); ^1H NMR (400 MHz, DMSO, δ, ppm): 1.72 (1H, d, pyra. Ring, J=15.5Hz), 1.88 (1H, d, pyra. ring, J=15.6Hz), 3.80 (1H,t, pyra. Ring, J=12.6Hz), 7.86 (1H, d, phenyl ring), 6.56 (1H, t, phenyl ring), 6.59 (1H, t, phenyl ring), 7.90 (1H, d, phenyl ring), 6.94 (1H, d, pyra NH ring), 7.82 (1H, m, quinoline ring), 8.56 (1H, m, quinoline ring), 9.70 (1H, s, -OH); ^{13}C NMR (400 MHz, DMSO, δ, ppm): 42.6 ($c_{4'}$), 44.9 ($c_{5'}$), 116.0 (c_{13}), 116.0 (c_{15}), 120.7 (c_6), 123.6 (c_{10}), 126.6 (c_{11}), 129.0 (c_5), 130.6 (c_{12}), 130.6 (c_{16}), 131.6 (c_8), 135.0 (c_3), 135.1 (c_4), 138.2 (c_7), 142.7 (c_9), 151.4 ($c_{3'}$), 154.0 (c_2), 160.9 (c_{14}); MS (m/z) 472 (M^+).

6-bromo-2,7,8-trichloro-3-{3'-(p-nitrophenyl)-4',5'dihydro-1H-pyrazol-5'-yl}quinoline (III)$_b$: Yield: 76%; m.p. 177°C; Anal. Calcd. for $C_{18}H_{10}BrCl_3N_4O_2$: C, 43.19; H, 2.01; N, 11.19; Cl, 21.25. Found: C, 43.17; H, 1.99; N, 11.17; Cl, 21.23; IR (KBr, cm^{-1}): 3250 (NH str. of pyrazole ring), 1590 (C=N str. of quinoline ring), 1645 (C=N str. of pyrazole ring), 683 (C-Br str.), 750 (C-Cl str.); ^1H NMR (400 MHz, DMSO, δ, ppm**):** 1.70 (1H, d, pyra. ring, J=15.5Hz), 1.86 (1H, d, pyra. ring, J=15.6Hz), 3.82 (1H, t, pyra. Ring, J=12.8Hz), 8.06 (1H, d, phenyl ring), 8.26 (1H, d, phenyl ring), 8.12 (1H, t, phenyl ring), 8.29 (1H, t, phenyl ring) 6.89 (1H, m, pyra NH ring), 7.78 (1H, m, quinoline ring), 8.60 (1H, m, quinoline ring); ^{13}C NMR (400 MHz, DMSO, δ, ppm): 42.6 ($c_{4'}$), 44.9 ($c_{5'}$), 120.7 (c_6), 123.6 (c_{10}), 124.5 (c_{15}), 124.5 (c_{13}), 129.0 (c_5), 130.2 (c_{12}), 130.2 (c_{16}), 131.6 (c_8), 135.0 (c_3), 135.1 (c_4), 138.2 (c_7), 140.3 (c_{11}), 142.7 (c_9), 150.6 (c_{14}), 151.4 ($c_{3'}$), 154.0 (c_2); MS (m/z) 501 (M^+).

6-bromo-2,7,8-trichloro-3-{3'-(o-chlorophenyl)-4',5'dihydro-1H-pyrazol-5'-yl}quinoline (III)$_c$: Yield: 78%; m.p. 183°C; Anal. Calcd. for $C_{18}H_{11}BrCl_4N_3$: C, 44.20; H, 2.02; N, 8.56; Cl, 28.92.

Found: C, 44.17; H, 2.00; N, 8.54; Cl, 28.90; IR (KBr, cm^{-1}): 3255 (NH str. of pyrazole ring), 1588 (C=N str. of quinoline ring), 1640 (C=N str. of pyrazole ring), 690 (C-Br str.), 772 (C-Cl str.)**;** ^{1}H NMR (400 MHz, DMSO, δ, ppm**):** 1.70 (d, 1H, pyra. ring, J=15.5Hz), 1.92 (d, 1H, pyra. ring, J=15.6Hz), 3.80 (t, 1H, pyra. ring, J=12.8Hz), 7.79 (1H, d, phenyl ring), 7.42 (1H, t, phenyl ring), 7.49 (1H, t, phenyl ring), 7.53 (1H, d, phenyl ring) 6.92 (m, 1H, pyra NH ring), 7.82 (1H, m, quinoline ring), 8.48 (1H, m, quinoline ring); ^{13}C NMR (400 MHz, DMSO, δ, ppm): 42.6 ($c_{4'}$), 44.9 ($c_{5'}$), 120.7 (c_6), 123.6 (c_{10}), 127.5 (c_{15}), 128.6 (c_{13}), 129.0 (c_5), 130.2 (c_{16}) 131.6 (c_8), 132.6 (c_{14}), 133.2 (c_{12}), 135.0 (c_3), 135.1 (c_4), 137.5 (c_{11}), 138.2 (c_7), 142.7 (c_9), 151.4 ($c_{3'}$), 154.0 (c_2), ; MS (m/z) 491 (M^+).

6-bromo-2,7,8-trichloro-3-{3'-(p-methoxyphenyl)-4',5'dihydro-1H-pyrazol-5'-yl}quinoline $(III)_d$: Yield: 69%; m.p. 168°C; Anal. Calcd. for $C_{19}H_{13}BrCl_3N_3O$: C, 47.00; H, 2.70; N, 8.59; Cl, 21.90. Found: C, 44.17; H, 2.00; N, 8.54; Cl, 28.90; IR (KBr, cm^{-1}): 3298 (NH str. of pyrazole ring), 1569 (C=N str. of quinoline ring), 1589 (C=N str. of pyrazole ring), 695 (C-Br str.), 766 (C-Cl str.); ^{1}H NMR (400 MHz, DMSO, δ, ppm**):** 1.73 (d, 1H, pyra. ring, J=15.5Hz), 1.86 (d, 1H, pyra. ring, J=15.6Hz), 3.70 (t, 1H, pyra. ring, J=12.6Hz), 7.95 (1H, d, phenyl ring), 7.90 (1H, d, phenyl ring), 7.03 (1H, d, phenyl ring), 7.09 (1H, d, phenyl ring) 6.94 (m, 1H, pyra NH ring), 7.80 (1H, m, quinoline ring), 8.56 (1H, m, quinoline ring); 3.72 (s, 3H, methoxy); ^{13}C NMR (400 MHz, DMSO, δ, ppm): 42.6 ($c_{4'}$), 44.9 ($c_{5'}$), 114.5 (c_{15}), 114.5 (c_{13}), 120.7 (c_6), 123.6 (c_{10}), 126.4 (c_{11}), 129.0 (c_5), 130.3 (c_{12}), 130.3 (c_{16}), 135.0 (c_3), 135.1 (c_4), 131.6 (c_8), 138.2 (c_7), 142.7 (c_9), 151.4 ($c_{3'}$), 154.0 (c_2), 163.2 (c_{14}); MS (m/z) 486.5 (M^+).

6-bromo-2,7,8-trichloro-3-{3'-(p-bromophenyl)-4',5'dihydro-1H-pyrazol-5'-yl}quinoline $(III)_e$: Yield: 65%; m.p. 196°C; Anal. Calcd. for $C_{18}H_{10}Br_2Cl_3N_3$: C, 40.45; H, 1.89; N, 7.86; Cl, 19.9. Found: C, 40.43; H, 1.87; N, 7.84; Cl, 19.9; IR (KBr, cm^{-1}): 3359 (NH str. of pyrazole ring), 1578 (C=N str. of quinoline ring), 1636 (C=N str. of pyrazole ring), 689 (C-Br str.), 773 (C-Cl str.); ^{1}H NMR (400 MHz, DMSO, δ, ppm): 1.79 (d, 1H, pyra. ring, J=15.5Hz), 1.97 (d, 1H, pyra. ring, J=15.6Hz), 3.80 (t, 1H, pyra. ring, J=12.6Hz), 7.72 (1H, d, phenyl ring), 7.58 (1H, d, phenyl ring), 7.76 (1H, d, phenyl ring), 7.62 (1H, d, phenyl ring) , 6.92 (m, 1H, pyra NH ring), 7.80 (1H, m, quinoline ring), 8.54 (1H, m, quinoline ring); ^{13}C NMR (400 MHz, DMSO, δ, ppm): 42.6 ($c_{4'}$), 44.9 ($c_{5'}$), 120.7 (c_6), 123.6 (c_{10}), 125.4 (c_{14}), 129.0 (c_5), 131.3 (c_{16}), 131.3 (c_{12}), 131.5 (c_{13}), 131.5 (c_{15}), 131.6 (c_8), 133.4 (c_{11}), 135.0 (c_3), 135.1 (c_4), 138.2 (c_7), 142.7 (c_9), 151.4 ($c_{3'}$), 154.0 (c_2); MS (m/z) 535.5 (M^+).

6-bromo-2,7,8-trichloro-3-{3'-(p-fluorophenyl)-4',5'dihydro-1H-pyrazol-5'-yl}quinoline $(III)_f$: Yield: 72%; m.p. 176°C; Anal. Calcd. for $C_{18}H_{10}BrCl_3N_3F$: C, 45.67; H, 2.13; N, 8.87; Cl, 22.46.

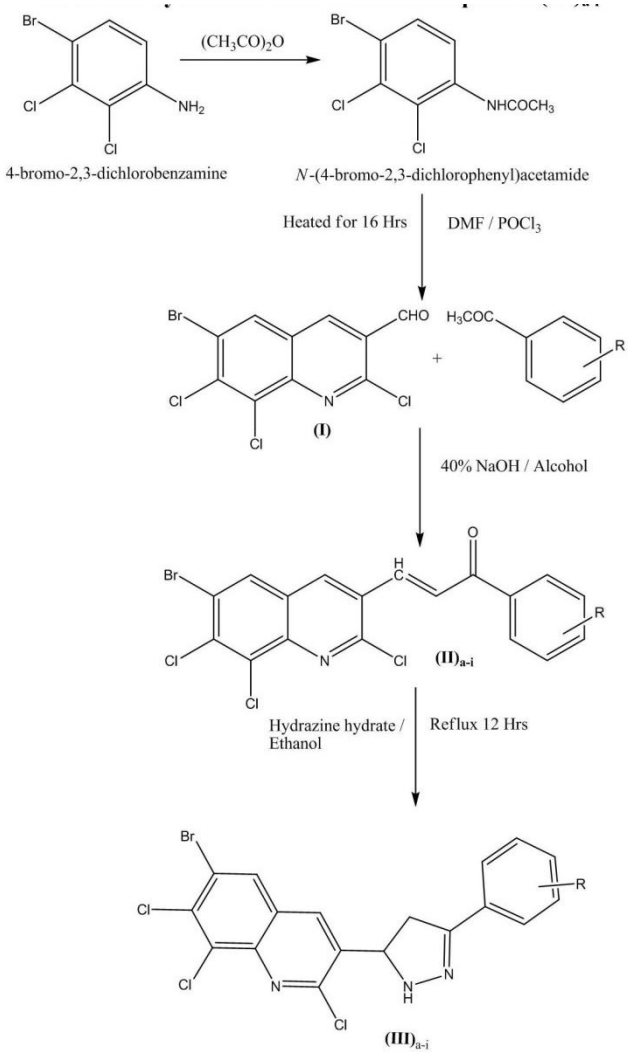
Found: C, 45.65; H, 2.11; N, 8.85; Cl, 22.44; IR (KBr, cm^{-1}): 3394 (NH str. of pyrazole ring), 1567 (C=N str. of quinoline ring), 1656 (C=N str. of pyrazole ring), 695 (C-Br str.), 779 (C-Cl str.); ^{1}H NMR (400 MHz, DMSO, δ, ppm): 1.76 (d, 1H, pyra. ring, J=15.5Hz), 1.94 (d, 1H, pyra. ring, J=15.6Hz), 3.88 (t, 1H, pyra. ring, J=12.6Hz), 7.81 (1H, d, phenyl ring), 7.86 (1H, d, phenyl ring), 7.39 (1H, d, phenyl ring), 7.42 (1H, d, phenyl ring) 6.93 (m, 1H, pyra NH ring), 7.82 (1H, m, quinoline ring), 8.56 (1H, m, quinoline ring); ^{13}C NMR (400 MHz, DMSO, δ, ppm): 42.6 ($c_{4'}$), 44.9 ($c_{5'}$), 115.9 (c_{13}), 115.9 (c_{15}), 120.7 (c_6), 123.6 (c_{10}), 129.0 (c_5), 129.4(c_{11}), 130.8 (c_{16}), 130.8 (c_{12}), 131.6 (c_8), 135.0 (c_3), 135.1 (c_4), 138.2 (c_7), 142.7 (c_9), 151.4 ($c_{3'}$), 154.0 (c_2), 165.4 (c_{14}); MS (m/z) 474.5 (M^+).

6-bromo-2,7,8-trichloro-3-{3'-(p-chlorophenyl)-4',5'dihydro-1H-pyrazol-5'-yl}quinoline $(III)_g$: Yield: 75%; m.p. 193°C; Anal. Calcd. for $C_{18}H_{10}BrCl_4N_3$: C, 44.12; H, 2.06; N, 8.58; Cl, 28.94. Found: C, 44.10; H, 2.06; N, 8.56; Cl, 28.92; IR (KBr, cm^{-1}): 3359 (NH str. of pyrazole ring), 1581 (C=N str. of quinoline ring), 1642 (C=N str. of pyrazole ring), 684 (C-Br str.), 776 (C-Cl str.); ^{1}H NMR (400 MHz, DMSO, δ, ppm): 1.70 (d, 1H, pyra. ring, J=15.5Hz), 1.90 (d, 1H, pyra. ring, J=15.6Hz), 3.82 (t, 1H, pyra. ring, J=12.6Hz), 7.99 (1H, d, phenyl ring), 7.92 (1H, d, phenyl ring), 7.56 (1H, d, phenyl ring), 7.52 (1H, d, phenyl ring) 6.90 (m, 1H, pyra NH ring), 7.80 (1H, m, quinoline ring), 7.84 (1H, m, quinoline ring); ^{13}C NMR (400 MHz, DMSO, δ, ppm): 42.6 ($c_{4'}$), 44.9 ($c_{5'}$), 120.7 (c_6), 123.6 (c_{10}), 128.9 (c_{13}), 128.9 (c_{15}), 129.0 (c_5), 130.6 (c_{16}), 130.6 (c_{12}), 131.6 (c_8), 132.2(c_{11}), 135.0 (c_3), 135.1 (c_4), 136.6 (c_{14}), 138.2 (c_7), 142.7 (c_9), 151.4 ($c_{3'}$), 154.0 (c_2); MS (m/z) 491 (M^+).

6-bromo-2,7,8-trichloro-3-{3'-(p-methylphenyl)-4',5'dihydro-1H-pyrazol-5'-yl}quinoline $(III)_h$: Yield: 70%; m.p. 178°C; Anal. Calcd. for $C_{19}H_{13}BrCl_3N_3$: C, 48.60; H, 2.79; N, 8.95; Cl, 22.65. Found: C, 48.58; H, 2.77; N, 8.93; Cl, 22.63; IR (KBr, cm^{-1}): 3386(NH str. of pyrazole ring), 1574 (C=N str. of quinoline ring), 1637 (C=N str. of pyrazole ring), 688 (C-Br str.), 776 (C-Cl str.). ^{1}H NMR (400 MHz, DMSO, δ, ppm): 1.74 (d, 1H, pyra. ring, J=15.5Hz), 1.90 (d, 1H, pyra. ring, J=15.6Hz), 3.80 (t, 1H, pyra. ring, J=12.5Hz), 7.71 (1H, d, phenyl ring), 7.76 (1H, d, phenyl ring), 7.28 (1H, d, phenyl ring), 7.32 (1H, d, phenyl ring), 6.88 (m, 1H, pyra NH ring), 7.54 (1H, m, quinoline ring), 8.38 (1H, m, quinoline ring); 4.28 (s, 3H, methyl); ^{13}C NMR (400 MHz, DMSO, δ, ppm): 42.6 ($c_{4'}$), 44.9 ($c_{5'}$), 120.7 (c_6), 123.6 (c_{10}), 129.0 (c_5), 129.2 (c_{15}), 129.2 (c_{16}) 129.2 (c_{12}), 129.2 (c_{13}), 131.2(c_{11}), 131.6 (c_8), 135.0 (c_3), 135.1 (c_4), 138.2 (c_7), 140.6 (c_{14}), 142.7 (c_9), 151.4 ($c_{3'}$), 154.0 (c_2); MS (m/z) 470.5 (M^+).

6-bromo-2,7,8-trichloro-3-{3'-phenyl-4',5'dihydro-1H-pyrazol-5'-yl}quinoline

$(III)_i$: Yield: 69%; m.p. 191°C; Anal. Calcd. for $C_{18}H_{11}BrCl_3N_3$: C, 47.46; H, 2.43; N, 9.22; Cl, 23.35. Found: C, 47.44; H, 2.41; N, 9.20; Cl, 23.33; IR (KBr, cm^{-1}): 3379(NH str. of pyrazole ring), 1578 (C=N str. of quinoline ring), 1616 (C=N str. of pyrazole ring), 695 (C-Br str.), 752 (C-Cl str.). ^{1}H NMR (400 MHz, DMSO, δ, ppm): 1.74 (d, 1H, pyra. ring, J=15.5Hz), 1.94 (d, 1H, pyra. ring, J=15.6Hz), 3.80 (t, 1H, pyra. ring, J=12.6Hz), 7.58 (1H, d, phenyl ring), 7.68 (1H, d, phenyl ring), 7.28 (1H, d, phenyl ring), 7.32 (1H, d, phenyl ring), 7.36 (1H, m, phenyl ring), 6.88 (m, 1H, pyra NH ring), 7.54 (1H, m, quinoline ring), 8.38 (1H, m, quinoline ring); 4.28 (s, 3H, methyl); ^{13}C NMR (400 MHz, DMSO, δ, ppm): 42.6 ($c_{4'}$), 44.9 ($c_{5'}$), 120.7 (c_6), 123.6 (c_{10}), 128.8 (c_{13}), 128.8 (c_{15}), 129.0 (c_5), 129.2 (c_{16}), 129.2 (c_{12}), 131.5(c_{11}), 131.6 (c_8), 131.6 (c_{14}), 135.0 (c_3), 135.1 (c_4), 138.2 (c_7), 142.7 (c_9), 151.4 ($c_{3'}$), 154.0 (c_2); MS (m/z) 456.5 (M^+).



Scheme-1: Synthetic route of the final compounds $(III)_{a-i}$.

Compound	R	Compound	R	Compound	R
$(III)_a$	p-OH	$(III)_d$	p-OCH_3	$(III)_g$	p-Cl
$(III)_b$	p-NO_2	$(III)_e$	p-Br	$(III)_h$	p-CH_3
$(III)_c$	o-Cl	$(III)_f$	p-F	$(III)_i$	H

RESULTS AND DISCUSSION

Synthesis

The titled entities $(III)_{a-i}$ was synthesized in four steps. The first steps involves the conversion of 4-bromo-2,3-dichloroaniline to 4-bromo-2,3-dichloroacetanilide using acetic anhydride. The 4-bromo-2,3-dichloroacetanilide thus obtained on reaction in presence of DMF and $POCl_3$ resulted in 2,7,8-trichloro-6-bromoquinoline-3-carbaldehyde(**I**). Compound **(I)** on further reaction with differently substituted acetophenone resulted in formation of different substituent of **(**Z)-3-(6-bromo-2, 7, 8-trichloro-quinoline-3'-yl)-1-phenylpre-2-en-1-one $\mathbf{(II)}_{a-i}$. Finally compound **(II)** on further reaction with hydrazine hydrate in presence of ethanol resulted in final product 6-bromo-2, 7, 8-trichloro-3-(3'-phenyl-4', 5'dihydro-1*H*-pyrazole-5'-yl) quinoline $\mathbf{(III)}_{a-i}$. The procedure is given in Scheme-1.

Characterization

The Intermediates $(II)_{a-I}$ showed Z-geometry which resulted in the formation of pyrazole derivative on further reaction. The formation of Z-geometry of the chalcones can be easily justified on comparing with the literature[17] that the coupling constant value J=8.8Hz and J=8.7Hz for each of the hydrogen attached to the carbon atoms of chalcones in vicinity to each other.

Let us consider one of the derivatives of the resulted product and discuss the spectral study. Taking into consideration compound $\mathbf{(III)}_i$ the IR spectra study shows a stretching vibration at 3379cm^{-1} indicating the presence of secondary amine present in pyrazole ring. The strong absorption peak observed at 1578 cm^{-1} indicates the presence of –C=N- in quinoline ring and the one observed at 1616cm^{-1} showed the presence of –C=N- in pyrazole ring. The absorption at 6985cm^{-1} and 752cm^{-1} are due to presence of C-Br and C-Cl respectively. The ^1H NMR spectrum of compound $\mathbf{(III)}_i$ showed a multiplet at δ = 7.38-7.58 indicating the presence of five protons in phenyl ring. A triplet at δ = 6.88 showed the presence of proton attached with N in pyrazole ring. Two protons present in quinoline nucleus showed its presence between δ = 7.58-8.34. The final compound $\mathbf{(III)}_i$ shows a varied chemical shifts of carbon from δ = 154.0-44.9. The carbon nucleus C-2, C-6, C-7, C-8 under the influence of electronegative environment shows downfield shift. The carbon present in vicinity to the nitrogen containing hydrogen in pyrazole nucleus showed chemical shift value δ = 44.9. The carbon directly attached to nitrogen in pyrazole nucleus (C-3') shows δ = 151.6. Carbon enumeration of the compound $\mathbf{(III)}_i$ is

described in figure-1.

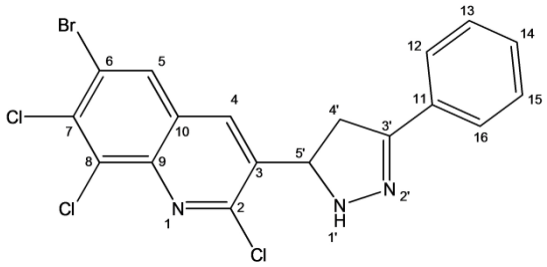


Figure-1:Carbon enumeration of final compound

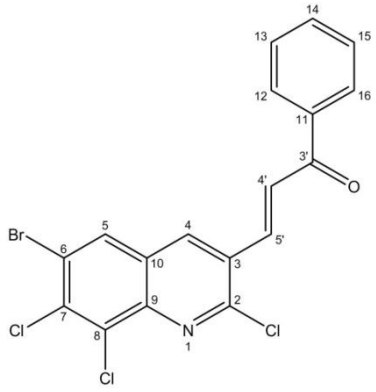


Figure-2:Carbon enumeration of compound II

Table-1:Data of Antibacterial and antifungal activity of synthesized compounds $(III)_{a-i}$ against standard drugs Ampicillin and Griseofulvin

Strains	**$(III)_a$**	**$(III)_b$**	**$(III)_c$**	**$(III)_d$**	**$(III)_e$**	**$(III)_f$**	**$(III)_g$**	**$(III)_h$**	**$(III)_i$**	**Std.1**
S.aureus	19	15	20	18	14	13	19	15	12	23
B.mega	20	15	10	23	13	9	10	12	14	22
P.valgaris	10	14	9	17	18	11	13	18	13	21
E.coli	20	17	14	13	11	16	10	15	19	25
Strain	**$(III)_a$**	**$(III)_b$**	**$(III)_c$**	**$(III)_d$**	**$(III)_e$**	**$(III)_f$**	**$(III)_g$**	**$(III)_h$**	**$(III)_i$**	**Std.2**
A.niger	13	16	9	12	21	13	10	20	18	25

Std.1= Ampicillin, Std.2= Griseofulvin, Zone of inhibition: in mm.

Antimicrobial activity

The results of the antimicrobial studies by agar cup method procured **(Table-1)** clearly indicate the significant activity of the synthesized compounds as antibacterial and antifungal agents. The antimicrobial activity was compared with standard drugs viz. Ampicillin for antibacterial activity and Griseofulvin for antifungal activity.

Antibacterial activity

The purified compounds were screened for their antibacterial activity. The nutrient agar prepared by the usual method, was inoculated aseptically with 0.5ml of 24 Hrs. old subcultures of

S.aureus, B.mega, P.valgaris and E.coli in separate conical flasks at 45°C and was mixed well by gentle shaking. The content was poured on petri dish (13cm in diameter) and allowed to set for 2 Hrs. The cups (10mm in diameter) were formed by the help of borar in agar medium and filled with 0.04ml (40 µg) solution of sample in DMF. The plates were incubated at 37°C for 24 Hrs. and the zone of inhibition of bacterial growth were measured in millimeter and presented in the table-1. Compounds $(III)_a$, $(III)_c$, $(III)_d$, $(III)_g$ corresponding to functional group substitutions p–OH, o-Cl, p-OCH_3, p-Cl respectively exhibited excellent activity when compared with the standard drug Ampicillin. The remaining compound $(III)_b$, $(III)_e$, $(III)_f$, $(III)_h$, $(III)_i$ relating to substituent p-NO_2, p-Br, p-F, p-CH_3, p-H exhibited moderate activity. Above data states o-Cl and p-Cl substituent to be the best one among all the synthesized compounds along with p-OH and p-OCH_3 functional groups. Among the biological active moieties synthesized derivatives consisting p-F and p-NO_2 substituent exhibited least activity among all the biological active motifs.

Antifungal activity

A.niger was employed for testing antifungal activity using cup-plate method. The culture was maintained on Sabouraud's agar slants, sterilized Sabouraud's agar medium was inoculated with 72 Hrs. old 0.5 ml suspension of fungal spores in separate flask. About 25 ml of inoculated medium was evenly spreaded in a petri dish and allowed to set for 2 Hrs. The plates were incubated at 30°C for 48 Hrs. After the completion of incubation time, the zone of inhibition was measured in mm. Compounds **$(III)_b$**, **$(III)_e$**, **$(III)_h$**, **$(III)_i$** exhibited excellent antifungal activity, these compounds possessed functional group viz. p-Br, p-CH_3, H, p-NO_2 whereas **$(III)_a$**, **$(III)_d$**, **$(III)_f$**, showed moderate activity while **$(III)_c$**, **$(III)_g$** exhibited low or poor activity. The compounds with functional group p-OH, P-OCH_3 and p-F exhibited moderate activity.

CONCLUSION

Among the newly synthesized moieties, it is observed that the one showing good antimicrobial activities can be further modified for more potent result than the existing one. The anti tubercular studies for these motifs can be made possible. The cytotoxicity studies of these moieties can be undertaken.

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