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Synthesis and Antimicrobial Evaluation of Pyrazoline derivatives

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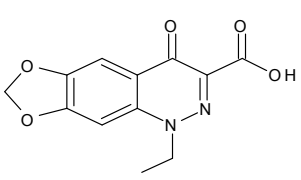
Abstract: Acetyl pyrazoline derivatives **(2a-j)** has been synthesized by the condensation of chalcones **(1a-j)** with hydrazine hydrate in glacial acetic acid, while phenyl pyrazoline derivatives **(3a-j)** has been synthesized by the cyclocondensation of phenyl hydrazine in glacial acetic acid with chalcones. All the products were screened for their antimicrobial activities.
Keywords: *N*-substituted pyrazolines, Chalcones, Antimicrobial activity.

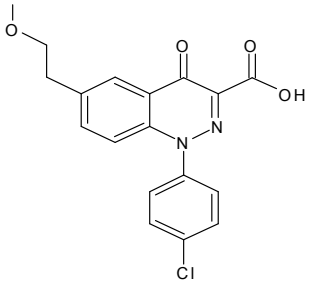
Introduction

Some cinnoline derivatives are used as a drugs such as Cinoxacin and used as antibiotics[1]. Some other derivatives of cinnolines are used as pesticide[2] such as Sinofem used as plant growth regulators. Literature survey reveals that when one biodynamic heterocyclic system was coupled with another, a molecule with enhanced biological activity was produced[3]. The chemistry of these linked bi-heterocycles has been fascinating field of investigation in medicinal chemistry, as they have been found to exhibit enhanced biological profile[4]. In view of these observations and also as a sequel to our work on the synthesis of variety of heterocycles linked with pyrazole ring[5], it was thought worthwhile to synthesize new bi-heterocycles containing pyrazole unit, in order to explore the pharmacological activity of these compounds.

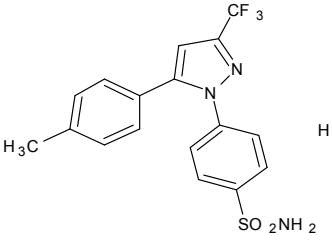
The chalcones are the convenient intermediates for the synthesis of five[6,7], six [6,8] and seven[9] member heterocycles, often have exhibited diverse biological activity. Some pyrazoline derivatives were used as antibacterial[10], antifungal[11], anti-inflammatory[12], antiamoebic[13] antidepressant[14]etc. N-substituted pyrazoline derivatives are important compounds constitute for the basic framework of drugs such as celecoxib and deracoxib are well recognized for their multifaceted pharmacological and medicinal applications[15].



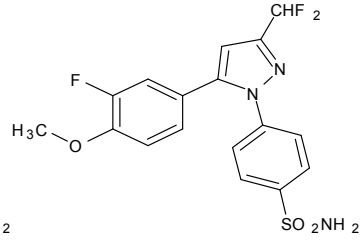
Cinoxacin



Sinofem



Celecoxib



Deracoxib

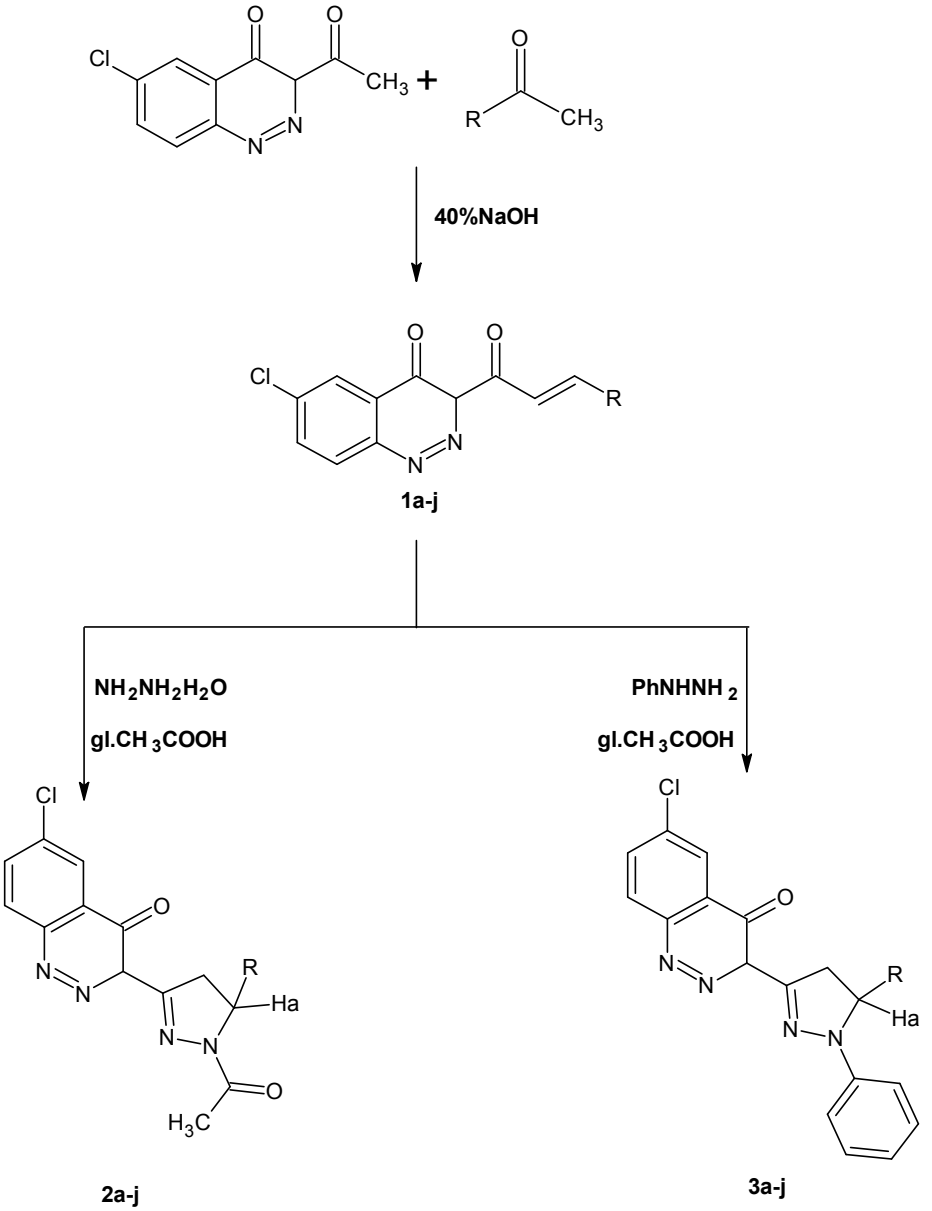
As far as the different pyrazole derivatives are concerned, 2-pyrazole derivatives became the most frequently studied[16]. Synthesis of 2-pyrazole has been reported under various conditions[17,18]. An especially popular procedure is based on the reaction of chalcones with hydrazines[19,20].

Results and Discussion

Chemistry:

The synthesis of acetyl pyrazoline and phenyl pyrazoline from chalcone was performed following the steps shown in reaction scheme-I. In the initial step, chalcones **(1a-j)** were synthesized by condensing 3-acetyl-6-chlorocinnolin-4(3*H*)-one with aromatic aldehydes in the presence of catalytic amount of alcoholic KOH solution at RT[21-23]. On the basis of synthesis and biological data of our work[24,25], and in continuation of our ongoing work on 2-pyrazole & cinnoline derivatives, we inspire to synthesize some new compounds bearing 6-chlorocinnolin-4(3*H*)-one as a basic core. The compounds **(2a-j)** were synthesized by reacting chalcones with hydrazine hydrate in presence of glacial acetic acid[26] while **(3a-j)** were synthesized by reacting chalcone with phenyl hydrazine in glacial acetic acid [27].

The purity of all the synthesized compounds was checked by TLC. The structures of the synthesized compounds were assigned on the basis of spectral data like IR, ^{1}H NMR, mass and elemental analysis and all the newly synthesized compounds were in full agreement with the proposed structures.



Reaction Scheme-I

Table I –Antimicrobial screening results of compounds (2a-j) and (3a-j)

Compd.	Zones of inhibition in mm				
	Antibacterial activity				Antifungal activity
	B. mega	*B. substilis*	*P. vulgaris*	*E. coli*	*A. niger*
2a	17	16	16	18	19
2b	19	20	21	16	17
2c	14	12	16	16	15
2d	12	15	17	14	24
2e	15	14	17	12	17
2f	10	11	13	14	18
2g	18	14	16	20	19
2h	12	11	13	17	17
2i	16	18	15	17	14
2j	16	14	14	15	12
3a	16	13	11	12	24
3b	15	18	22	14	18
3c	16	14	18	12	20
3d	18	17	23	16	20
3e	18	17	23	16	20
3f	14	16	24	16	17
3g	18	16	23	15	15
3h	17	14	22	14	19
3i	15	18	24	14	16
3j	14	15	22	14	16
Ampicillin	20	24	21	22	00
Norfloxacin	18	17	25	24	00
Benzyl	20	18	15	18	00
Amoxicillin	21	24	25	25	00
Griseofulvin	00	00	00	00	24

Biological Screening

Antimicrobial activity:

The antimicrobial activity was assayed by using the cup-plate agar diffusion method[29] by measuring the zone of inhibition in mm. All the compounds were screened in vitro for their antimicrobial activity against varieties of bacterial strains such *Bacillus megaterium* ATCC 14518, *Bacillus substilis* ATCC 23857, *Escherichia coli* ATCC 25922, *Proteus vulgaris* ATCC 29213 and fungi *Aspergillus niger* ATCC 9029 at 40 µg/mL concentration. Standard drugs like Ampicillin, Amoxicillin, Norfloxacin, Benzyl penicillin and Greseofulvin were used for the comparison purpose **(Table I)**.

Compounds **2b**, **2g**, **3d**, **3e** and **3g** were found to be active. Among the compounds **2b** is found to be more potent while **2a** and **3h** were moderately active against *Bacillus megaterium*, in the series **2b** is potent and **2g**, **3d** and **3e** moderately active against *Bacillus subs*tilis. Compounds **3i** and **3f** active, while compounds **3d**, **3e** and **3g** were moderately active against *Proteus vulgaris*. Compounds **2d** and **3a** were active while compounds **3c**, **3d** and **3e** were moderately active against *Aspergillus niger*.

Experimental

Melting points were determined in open capillary on an electro thermal apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker AC-300 MHz FT NMR spectrometer. Chemical shifts are expressed in δ ppm downfield from internal TMS as reference. ^{1}H NMR data are reported in order: multiplicity (bs, broad singlet; s, singlet; d, doublet; t, triplet; m, multiplet; exchangeable by D_2O). IR spectra were recorded on a Shimadzu FTIR-8400 instrument in KBr disc and only noteworthy absorption levels (cm^{-1}) are listed. Mass spectra were recorded on a GCMS-QP2010 spectrophotometer. Elemental analysis was performed on a Carlo Erba EA 1108 elemental analyzer. The results of elemental analyses (C, H, N) were within ± 0.4 % of the theoretical values. TLC was performed on silica gel PF_{254} plates (Merck).

Preparation of (*E*)-3-Aryl-1-(6-chloro-4(3*H*)-one-cinnolin-3-yl)-prop-2-en-1-ones (1a-j): It is prepared as per reported method[28] .

General procedure for synthesis of 1-Acetyl-3-(6-chlorocinnolin-4(3*H*)-one-3-yl)-5-aryl-4,5-dihydro-1*H*-pyrazoles (2a-j): To the mixture of (2*E*)-1-(6-Chlorocinnolin-4(3*H*)-one)-3-aryl-prop-2-en-1-ones **(1a-j)** (0.01 mol) in glacial acetic acid (25 mL) and hydrazine hydrate (0.01 mol) was refluxed in oil bath for 8 hrs. The resulting solution was poured onto crushed ice, thus the solid separated was filtered under vacuum and crystallized from ethanol to give analytically pure product.

1-Acetyl-3-(6-chlorocinnolin-4(3*H*)-one-3-yl)-5-phenyl-4,5-dihydro-1*H*-pyrazoles (2a): Yield 75 %; m.p. 164-167 °C; Anal. Calcd. for $C_{19}H_{15}ClN_4O_2$: C, 62.21; H, 4.12; N, 15.27. Found: C, 62.19, H, 4.11, N, 15.25; IR (KBr, cm^{-1}): 3033 (C=C-H stretching of aromatic ring), 2923 (-C-H stretching of $-COCH_3$ group), 1668 (-C=O stretching of $-COCH_3$ group), 1658 (-C=O stretching of cinnolin ring), 1570 (C=C- stretching of aromatic ring), 771 (C-Cl); ^{1}H-NMR (300 MHz, $CDCl_3$, δ ppm): 2.1 (3H, s, $-COCH_3$), 3.05-3.10 (1H, dd, $-CH_2-$, J = 17.6, 4.8 Hz), 3.71-3.77 (1H, dd, $-CH_2-$, J = 17.7, 11.53 Hz), 5.26-5.30 (1H, dd, -Cha, J = 11.57, 5.07 Hz), 6.87-6.72 (5H, m, Ar-H), 7.13-7.19 (4H, m, Ar-H); MS (*m*/*z*, (relative abundance, %)): 366 (M+, 42.5) 305, 213, 180, 163, 155 (Base Peak, 100).

1-Acetyl-3-(6-chlorocinnolin-4(3*H*)-one-3-yl)-5-(3-bromophenyl)-4,5-dihydro-1*H*- pyrazoles (2b): Yield 92 %; m.p. 158-160°C; Anal. Calcd. for $C_{19}H_{14}BrClN_4O_2$: C, 51.20; H, 3.17; N, 12.57. Found: C, 51.17, H, 3.15, N, 12.55; IR (KBr, cm^{-1}): 3025 (C=C-H stretching of aromatic ring), 2936 (-C-H stretching of $-COCH_3$ group), 1658 (-C=O stretching of $-COCH_3$ group), 1655 (-C=O stretching of cinnolin ring),1574 (C=C- stretching of aromatic ring), 765 (-C-Cl); ^{1}H-NMR (300 MHz, $CDCl_3$, δ ppm): 2.2 (3H, s, $-COCH_3$), 3.01-3.06 (1H, dd, $-CH_2-$, J = 17.1, 5.2 Hz), 3.67-3.72 (1H, dd, $-CH_2-$, J = 17.4, 11.43 Hz), 5.77-5.80 (1H, dd, -Cha, J = 11.61, 5.01 Hz) 6.83-6.88 (4H, m, Ar-H), 7.35-7.41 (4H, m, Ar-H); MS (*m*/*z*, (relative abundance, %)): 445 (M+, 38.5) 302, 219, 179, 163, 155 (Base Peak, 100).

1-Acetyl-3-(6-chlorocinnolin-4(3*H*)-one-3-yl)-5-(2-chlorophenyl)-4,5-dihydro-1*H*- pyrazoles (2c): Yield 89 %; m.p. 170-172°C; Anal. Calcd. for $C_{19}H_{14}Cl_2N_4O_2$: C, 56.87; H, 3.52; N, 13.96. Found: C, 56.85, H, 3.49, N, 13.94; IR (KBr, cm^{-1}): 3035 (C=C-H stretching of aromatic ring), 2929 (-C-H stretching of $-COCH_3$ group), 1649 (-C=O stretching of $-COCH_3$ group), 1651 (-C=O stretching of cinnolin ring), 1568 (C=C- stretching of aromatic ring), 769 (-C-Cl); ^{1}H-NMR (300 MHz, $CDCl_3$, δ ppm): 2.37 (3H, s, $-COCH_3$), 3.07-3.12 (1H, dd, $-CH_2-$, J = 17.5, 5.1 Hz), 3.74-3.79 (1H, dd, $-CH_2-$, J = 17.1, 11.47 Hz), 6.03-6.06 (1H, dd, -CHa, J = 11.53, 4.98 Hz), 7.23-7.27 (4H, m, Ar-H), 7.49-7.53 (4H, m, Ar-H); MS (*m*/*z*, (relative abundance, %)): 401 (M+, 39.5) 309, 221, 179, 162, 155 (Base Peak, 100).

1-Acetyl-3-(6-chlorocinnolin-4(3*H*)-one-3-yl)-5-(3-chlorophenyl)-4,5-dihydro-1*H*- pyrazoles (2d): Yield 74 %; m.p. 184-186°C; Anal. Calcd. for $C_{19}H_{14}Cl_2N_4O_2$: C, 56.87; H, 3.52; N, 13.96. Found: C, 56.86, H, 3.48, N, 13.95; IR (KBr, cm^{-1}): 3025 (C=C-H stretching of aromatic ring), 2938 (-C-H stretching of $-COCH_3$ group) , 1638 (-C=O stretching of $-COCH_3$ group), 1659 (-C=O stretching of cinnolin ring),1556 (C=C- stretching of aromatic ring), 774 (-C-Cl); ^{1}H-NMR (300 MHz, $CDCl_3$, δ ppm): 2.34 (3H, s, $-COCH_3$), 3.02-3.07 (1H, dd, $-CH_2-$, J = 17.4, 5.2 Hz), 3.68-3.73 (1H, dd, $-CH_2-$, J = 17.6, 11.39 Hz), 5.86-5.89 (1H, dd, -CHa, J = 11.58, 4.93 Hz), 7.08-7.11 (4H, m, Ar-H), 7.28-7.30 (4H, m, Ar-H); MS (*m*/*z*, (relative abundance, %)): 401 (M+, 37.5) 308, 221, 179, 161, 155 (Base Peak, 100).

1-Acetyl-3-(6-chlorocinnolin-4(3*H*)-one-3-yl)-5-(4-chlorophenyl)-4,5-dihydro-1*H*- pyrazoles (2e): Yield 71 %; m.p. 164-166°C; Anal. Calcd. for $C_{19}H_{14}Cl_2N_4O_2$: C, 56.87; H, 3.52; N, 13.96. Found: C, 56.87, H, 3.49, N, 13.95; IR (KBr, cm^{-1}): 3011 (C=C-H stretching of aromatic ring), 2936 (-C-H stretching of $-COCH_3$ group), 1625 (-C=O stretching of $-COCH_3$ group), 1658 (-C=O stretching of cinnolin ring), 1563 (C=C- stretching of aromatic ring), 772 (-C-Cl); ^{1}H-NMR (300 MHz, $CDCl_3$, δ ppm): 2.43 (3H, s, $-COCH_3$), 3.09-3.14 (1H, dd, $-CH_2-$ J = 17.2, 4.93 Hz), 3.69-3.74 (1H, dd, $-CH_2-$, J = 17.7, 11.46 Hz), 5.67-5.70 (1H, dd, -CHa, J = 11.47, 5.13 Hz), 6.86-6.88 (4H, m, Ar-H), 7.22-7.29 (4H, m, Ar-H); MS (*m*/*z*, (relative abundance, %)): 401 (M+, 38.5) 307, 229, 177, 163, 155 (Base Peak, 100).

1-Acetyl-3-(6-chlorocinnolin-4(3*H*)-one-3-yl)-5-(3,4-dimethoxyphenyl)-4,5-dihydro-1*H*-pyrazoles (2f): Yield 74 %; m.p. 202-204°C; Anal. Calcd. for $C_{21}H_{19}ClN_4O_2$: C, 59.09; H, 4.49; N, 13.13. Found: C, 59.06, H, 4.48, N, 13.11; IR (KBr, cm^{-1}): 3013 (C=C-H stretching of aromatic ring), 2935 (-C-H stretching of $-COCH_3$ group), 1629 (-C=O stretching of $-COCH_3$ group), 1648 (-C=O stretching of cinnolin ring), 1567 (C=C- stretching of aromatic ring), 770 (-C-Cl); ^{1}H-NMR (300 MHz, $CDCl_3$, δ ppm): 2.43 (3H, s, $-COCH_3$), 2.97-3.02 (1H, dd, $-CH_2-$, J = 17.5, 5.4 Hz), 3.67 (6H, s, Ar-OCH_3), 3.76-3.82 (1H, dd, $-CH_2-$, J = 18.1, 11.41 Hz), 5.68-5.71 (1H, dd, -CHa, J = 11.50,

5.09 Hz), 6.73-6.80 (3H, m, Ar-H), 7.58-7.66 (4H, m, Ar-H); MS (*m*/*z*, (relative abundance, %)): 427 (M+, 32.5) 295, 239, 181, 163, 155 (Base Peak, 100).

1-Acetyl-3-(6-chlorocinnolin-4(3*H*)-one-3-yl)-5-(4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazoles (2g): Yield 83 %; m.p. 186-188°C; Anal. Calcd. For $C_{20}H_{17}ClN_4O_3$: C, 60.53; H, 4.32; N, 14.12. Found: C, 60.51, H, 4.31, N, 14.11; IR (KBr, cm^{-1}): 3027 (C=C-H stretching of aromatic ring), 2917 (-C-H stretching of $-COCH_3$ group), 1618 (-C=O stretching of $-COCH_3$ group), 1652 (-C=O stretching of cinnolin ring), 1559 (C=C- stretching of aromatic ring), 773 (-C-Cl); ^{1}H-NMR (300 MHz, $CDCl_3$, δ ppm): 2.4 (3H, s, $-COCH_3$), 3.01-3.06 (1H, dd, $-CH_2-$, J = 17.8, 5 Hz), 3.72-3.77 (1H, dd, $-CH_2-$, J = 17.8, 11.55 Hz), 3.84 (3H, s, Ar-OCH_3), 5.54-5.57 (1H, dd, -CHa, J = 11.56, 5.04 Hz), 6.91-6.99 (4H, m, Ar-H), 7.28-7.32 (4H, m, Ar-H); MS (*m*/*z*, (relative abundance, %)): 397 (M+, 46.5) 289, 249, 171, 163, 155 (Base Peak, 100).

1-Acetyl-3-(6-chlorocinnolin-4(3*H*)-one-3-yl)-5-[4-(methylsulfanyl)phenyl]-4,5-dihydro-1*H*-pyrazoles (2h): Yield 77 %; m.p. 186-188°C; Anal. Calcd. for $C_{20}H_{17}ClN_4O_2S$: C, 58.18; H, 4.15; N, 13.57. Found: C, 58.17, H, 4.13, N, 13.55; IR (KBr, cm^{-1}): 3029 (C=C-H stretching of aromatic ring), 2911 (-C-H stretching of $-COCH_3$ group), 1617 (-C=O stretching of $-COCH_3$ group), 1656 (-C=O stretching of cinnolin ring), 1552 (C=C- stretching of aromatic ring), 775 (-C-Cl); ^{1}H-NMR (300 MHz, $CDCl_3$, δ ppm): 2.47 (3H, s, $-COCH_3$), 2.73 (s, 3H, Ar-SCH_3), 2.98-3.03 (1H, dd, $-CH_2-$, J = 17.2, 5.07 Hz), 3.65-3.70 (1H, dd, $-CH_2-$, J = 17.9, 11.42 Hz), 5.77-5.80 (1H, dd, -CHa, J = 11.52, 5.14 Hz), 7.29-7.37 (4H, m, Ar-H), 7.58-7.66 (4H, m, Ar-H); MS (*m*/*z*, (relative abundance, %)): 412 (M+, 39.5) 289, 259, 187, 164, 155 (Base Peak, 100).

1-Acetyl-3-(6-chlorocinnolin-4(3*H*)-one-3-yl)-5-(3-nitrophenyl)-4,5-dihydro-1*H*-pyrazoles (2i): Yield 72 %; m.p. 168-170°C; Anal. Calcd. for $C_{19}H_{14}ClN_5O_4$: C, 55.42; H, 3.43; N, 17.01. Found: C, 55.40, H, 3.41, N, 17.00; IR (KBr, cm^{-1}): 3014 (C=C-H stretching of aromatic ring), 2926 (-C-H stretching of $-COCH_3$ group), 1628 (-C=O stretching of $-COCH_3$ group), 1650 (-C=O stretching of cinnolin ring), 1549 (C=C- stretching of aromatic ring), 768 (-C-Cl); ^{1}H-NMR (300 MHz, $CDCl_3$, δ ppm): 2.35 (3H, s, $-COCH_3$), 3.08-3.13 (1H, dd, $-CH_2-$, J = 17.6, 5.3 Hz), 3.79-3.84 (1H, dd, $-CH_2-$, J = 17.4, 11.39 Hz), 5.83-5.86 (1H, dd, -CHa, J = 11.49, 4.98 Hz), 7.76-7.79 (4H, m, Ar-H), 8.04-8.13 (4H, m, Ar-H); MS (*m*/*z*, (relative abundance, %)): 412 (M+, 39.5) 289, 259, 187, 164, 155 (Base Peak, 100).

1-Acetyl-3-(6-chlorocinnolin-4(3*H*)-one-3-yl)-5-(2-hydroxyphenyl)-4,5-dihydro-1*H*-pyrazoles (2j): Yield 80 %; m.p. 244-245°C; Anal. Calcd. for $C_{19}H_{15}ClN_4O_3$: C, 59.61; H, 3.95; N, 14.64. Found: C, 59.59, H, 3.93, N, 14.62; IR (KBr, cm^{-1}): 3014 (C=C-H stretching of aromatic ring), 2924 (-C-H stretching of $-COCH_3$ group), 1629 (-C=O stretching of $-COCH_3$ group), 1658 (-C=O stretching of cinnolin ring), 1547 (C=C- stretching of aromatic ring), 769 (-C-Cl); ^{1}H-NMR (300 MHz, $CDCl_3$, δ ppm): 2.26 (3H, s, $-COCH_3$), 3.06-3.11 (1H, dd, $-CH_2-$, J = 17.4, 5.2 Hz), 3.73-3.78 (1H, dd, $-CH_2-$, J = 17.1, 11.41 Hz), 4.19 (1H, s, OH), 5.69-5.72 (1H, dd, -CHa, J = 11.59, 5.10 Hz), 7.02-7.07 (4H, m, Ar-H), 7.83-7.86 (4H, m, Ar-H); MS (*m*/*z*, (relative abundance, %)): 383 (M+, 29.5) 296, 268, 196, 174, 155 (Base Peak, 100).

General procedure for synthesis of 1-Phenyl-3-(6-chlorocinnolin-4(3*H*)-one-3-yl)-5-aryl-4,5-dihydro-1*H*-pyrazoles (3a-j): To the mixture of 6-chloro-3-[(2*E*)-3-(4-methoxyphenyl)prop-2-enoyl]cinnolin-4(3*H*)-one (3.4 gm, 0.01 mol) in glacial acetic acid (25 mL) and phenyl hydrazine (0.92 gm, 0.01 mol) was refluxed for 8 hrs. The resulting solution was poured on to crushed ice, thus the solid separated was filtered and crystallized from ethanol to give analytically pure product.

1-Phenyl-3-(6-chlorocinnolin-4(3*H*)-one-3-yl)-5-phenyl-4,5-dihydro-1*H*-pyrazoles (3a): Yield 75 %; m.p. 158-160°C; Anal. Calcd. for $C_{23}H_{17}ClN_4O$: C, 68.91; H, 4.27; N, 13.98. Found: C, 68.89, H, 4.25, N, 13.94; IR (KBr, cm^{-1}): 3033 (C=C-H stretching of aromatic ring), 2923 (pyrazoine $-CH_2$), 1668 (-C=O stretching of cinnolin ring), 1570 (C=C- stretching of aromatic ring), 771 (-C-Cl); ^{1}H-NMR (300 MHz, $CDCl_3$, δ ppm): 2.83-2.88 (1H, dd, $-CH_2-$, J = 16.27, 7.69 Hz), 3.63-3.68 (1H, dd, $-CH_2-$, J = 16.31, 12.14 Hz), 5.27-5.31 (1H, dd, J = 12.09, 7.79 Hz, -CH), 6.92-6.97 (5H, m, Ar-H), 7.01-7.04 (5H, m, Ar-H), 7.18-7.29 (4H, m, Ar-H) MS (*m*/*z*, (relative abundance, %)): 401 (M+, 29.5) 386, 369, 307 (Base Peak, 100), 298, 163.

1-Phenyl-3-(6-chlorocinnolin-4(3*H*)-one-3-yl)-5-(3-bromophenyl)-4,5-dihydro-1*H*-pyrazoles (3b): Yield 72%; m.p. 150-152°C; Anal. Calcd. for $C_{23}H_{16}BrClN_4O$: C, 57.58; H, 3.36; N, 11.68. Found: C, 57.56, H, 3.35, N, 11.64 IR (KBr, cm^{-1}): 3025 (C=C-H stretching of aromatic ring), 2936 (pyrazoine $-CH_2$), 1658 (-C=O stretching of cinnolin ring), 1574 (C=C- stretching of aromatic ring), 765 (-C-Cl); ^{1}H-NMR (300 MHz, $CDCl_3$, δ ppm): 2.76-2.81 (1H, dd, $-CH_2-$, J = 16.17, 7.63 Hz), 3.69-3.74 (1H, dd, $-CH_2-$, J = 16.21, 12.18 Hz), 5.73-5.77 (1H, dd, -CH, J = 12.14, 7.73 Hz), 7.19-7.23 (4H, m, Ar-H), 7.32-7.36 (4H, m,

Ar-H), 7.66-7.73 (5H, m, Ar-H); MS (*m*/*z*, (relative abundance, %)): 480 (M+, 41.5) 376, 363, 307 (Base Peak, 100), 283, 169.

1-Phenyl-3-(6-chlorocinnolin-4(3*H*)-one-3-yl)-5-(2-chlorophenyl)-4,5-dihydro-1*H*-pyrazole (3c): Yield 74%; m.p. 144-146°C; Anal. Calcd. for $C_{23}H_{16}Cl_2N_4O$: C, 63.46; H, 3.70; N, 12.87. Found: C, 63.44, H, 3.68, N, 12.85; IR (KBr, cm^{-1}): 3035 (C=C-H stretching of aromatic ring), 2929 (pyrazoine -CH_2), 1649 (-C=O stretching of cinnolin ring), 1568 (C=C- stretching of aromatic ring), 769 (-C-Cl); ^{1}H-NMR (300 MHz, $CDCl_3$, δ ppm): 2.65-2.70 (1H, dd, -CH_2-, J = 16.24, 7.73 Hz), 3.36-3.41 (1H, dd, -CH_2-, J = 16.27, 12.09 Hz), 5.54-5.58 (1H, dd, -CH, J = 12.21, 7.74 Hz), 6.98-7.05 (4H, m, Ar-H), 7.17-7.21 (4H, m, Ar-H), 7.34-7.39 (5H, m, Ar-H); MS (*m*/*z*, (relative abundance, %)): 435 (M+, 43.5) 383, 363, 307 (Base Peak, 100), 263, 149.

1-Phenyl-3-(6-chlorocinnolin-4(3*H*)-one-3-yl)-5-(3-chlorophenyl)-4,5-dihydro-1*H*-pyrazoles (3d): Yield 73%; m.p. 122-124°C; Anal. Calcd. for $C_{23}H_{16}Cl_2N_4O$: C, 63.46; H, 3.70; N, 12.87. Found: C, 63.45, H, 3.64, N, 12.84; IR (KBr, cm^{-1}): 3025 (C=C-H stretching of aromatic ring), 2938 (pyrazoine -CH_2), 1638 (-C=O stretching of cinnolin ring), 1556 (C=C- stretching of aromatic ring), 774 (-C-Cl); ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 2.73-2.78 (1H, dd, -CH_2-, J = 16.33, 7.75 Hz), 3.42-3.47 (1H, dd, -CH_2-, J = 16.23, 12.17 Hz), 5.89-5.93 (1H, dd, -CH, J = 12.18, 7.75 Hz), 7.13-7.418 (4H, m, Ar-H), 7.28-7.73 (4H, m, Ar-H), 7.67-7.73 (5H, m, Ar-H); MS (*m*/*z*, (relative abundance, %)): 435 (M+, 43.5) 383, 363, 307 (Base Peak, 100), 263, 149.

1-Phenyl-3-(6-chlorocinnolin-4(3*H*)-one-3-yl)-5-(4-chlorophenyl)-4,5-dihydro-1*H*-pyrazoles (3e): Yield 78%; m.p. 124-126°C; Anal. Calcd. for $C_{23}H_{16}Cl_2N_4O$: C, 63.46; H, 3.70; N, 12.87. Found: C, 63.43, H, 3.67, N, 12.85; IR (KBr, cm^{-1}): 3011 (C=C-H stretching of aromatic ring), 2936(pyrazoine -CH_2), 1625 (-C=O stretching of cinnolin ring), 1563 (C=C- stretching of aromatic ring), 772 (-C-Cl); ^{1}H-NMR (300 MHz, $CDCl_3$, δ ppm): 2.81-2.86 (1H, dd, -CH_2-, J = 16.21, 7.71 Hz), 3.53-3.58 (1H, dd, -CH_2-, J = 16.17, 12.15 Hz), 5.57-5.61 (1H, dd, -CH, J = 12.23, 7.63 Hz), 7.08-7.11 (5H, m, Ar-H), 7.57-7.59 (4H, m, Ar-H), 7.93-7.97 (4H, m, Ar-H); MS (*m*/*z*, (relative abundance, %)): 435 (M+, 43.5) 383, 363, 307 (Base Peak, 100), 263, 149.

1-Phenyl-3-(6-chlorocinnolin-4(3*H*)-one-3-yl)-5-(3,4-dimethoxyphenyl)-4,5-dihydro-1*H*-pyrazoles (3f): Yield 75%; m.p. 124-126°C; Anal. Calcd. for $C_{25}H_{21}ClN_4O_3$: C, 65.15; H, 4.59; N, 12.16. Found: C, 65.13, H, 4.57, N, 12.14; IR (KBr, cm^{-1}): 3013 (C=C-H stretching of aromatic ring), 2935 (pyrazoine -CH_2), 1629 (-C=O stretching of cinnolin ring), 1567 (C=C-stretching of aromatic ring), 770 (-C-Cl); ^{1}H-NMR (300 MHz, $CDCl_3$, δ ppm):3.03-3.08 (1H, dd, -CH_2-, J = 16.13, 7.67 Hz), 3.21-3.26 (1H, dd, -CH_2-, J = 16.25, 12.07 Hz), 3.78 (6H, s, -OCH_3), 5.21-5.25 (1H, dd, -CH, J = 12.09, 7.73 Hz), 6.87-6.92 (3H, m, Ar-H), 7.13-7.17 (5H, m, Ar-H), 7.74-7.81 (4H, m, Ar-H); MS (*m*/*z*, (relative abundance, %)): 461 (M+, 43.5) 423, 353, 307 (Base Peak, 100), 283, 129.

1-Phenyl-3-(6-chlorocinnolin-4(3*H*)-one-3-yl)-5-(4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazoles (3g): Yield 70%; m.p. 124-126°C; Anal. Calcd. for $C_{24}H_{19}ClN_4O_2$: C, 66.90; H, 4.44; N, 13.00. Found: C, 66.89, H, 4.42, N, 12.98; IR (KBr, cm^{-1}): 3027 (C=C-H stretching of aromatic ring), 2917 (pyrazoine -CH_2), 1618 (-C=O stretching of cinnolin ring), 1559 (C=C-stretching of aromatic ring), 773 (-C-Cl); ^{1}H-NMR (300 MHz, $CDCl_3$, δ ppm): 2.97-3.02 (1H, dd, -CH_2-, J = 16.20, 7.70 Hz), 3.72-3.77 (1H, dd, -CH_2-, J = 16.23, 12.10 Hz), 3.81 (3H, s, -O-CH_3), 5.16-5.20 (1H, dd, -CH, J = 12.14, 7.72 Hz), 6.93-6.98 (4H, m, Ar-H), 7.26-7.30 (5H, m, Ar-H), 7.74-779 (4H, m, Ar-H); MS (*m*/*z*, (relative abundance, %)): 431 (M+, 33.5) 378, 353, 307 (Base Peak, 100), 293, 139.

1-Phenyl-3-(6-chlorocinnolin-4(3*H*)-one-3-yl)-5-[4-(methylsulfanyl)phenyl]-4,5-dihydro-1*H*-pyrazoles (3h): Yield 75%; m.p. 110-112°C; Anal. Calcd. for $C_{24}H_{19}ClN_4OS$: C, 64.49; H, 4.28; N, 12.54. Found: C, 64.47, H, 4.26, N, 12.52; IR (KBr, cm^{-1}): 3029 (C=C-H stretching of aromatic ring), 2911 (pyrazoine -CH_2), 1617 (-C=O stretching of cinnolin ring), 1552 (C=C-stretching of aromatic ring), 775 (-C-Cl); ^{1}H-NMR (300 MHz, $CDCl_3$, δ ppm): 2.45 (3H, s, -SCH_3), 2.91-2.96 (1H, dd, -CH_2-, J = 16.31, 7.79 Hz), 3.75-3.80 (1H, dd, -CH_2-, J = 16.26 12.18 Hz), 5.27-5.31 (1H, dd, -CH, J = 12.17, 7.69 Hz,), 7.03-7.11 (5H, m, Ar-H), 7.42-7.48 (4H, m, Ar-H), 7.83-7.88 (4H, m, Ar-H); MS (*m*/*z*, (relative abundance, %)): 447 (M+, 39.5) 388, 353, 307 (Base Peak, 100), 293, 139.

1-Phenyl-3-(6-chlorocinnolin-4(3*H*)-one-3-yl)-5-(3-phenoxyphenyl)-4,5-dihydro-1*H*-pyrazoles (3i): Yield 71%; m.p. 118-120°C; Anal. Calcd. for $C_{29}H_{21}ClN_4O_2$: C, 65.43; H, 4.17; N, 12.21. Found: C, 65.41, H, 4.19, N, 12.18; IR (KBr, cm^{-1}): 3014 (C=C-H stretching of aromatic ring), 2926 (pyrazoine -CH_2), 1628 (-C=O stretching of cinnolin ring), 1549 (C=C-stretching of aromatic ring), 768 (-C-Cl); ^{1}H-NMR (300 MHz, $CDCl_3$, δ ppm): 2.97-3.02 (1H, dd, -CH_2-, J = 16.29, 7.74 Hz), 3.18-3.23 (1H, dd, -CH_2-, J = 16.15, 12.19 Hz), 5.23-5.27 (1H, dd, -CH, J = 12.25, 7.82 Hz), 6.74-6.77 (5H, m, Ar-H), 7.19-7.26 (5H, m, Ar-

H), 7.34-7.39 (4H, m, Ar-H), 7.71-7.78 (4H, m, Ar-H); MS (*m*/*z*, (relative abundance, %)): 493 (M+, 41.5) 478, 453, 307 (Base Peak, 100), 283, 149.

1-Phenyl-3-(6-chlorocinnolin-4(3*H*)-one-3-yl)-5-[4-(dimethylamino)phenyl]-4,5-dihydro-1*H*-pyrazoles (3j): Yield 70%; m.p. 164-166°C; Anal. Calcd. for $C_{25}H_{22}ClN_5O$: C, 67.64; H, 5.00; N, 15.78. Found: C, 67.62, H, 4.99, N, 15.76; IR (KBr, cm^{-1}): 3014 (C=C-H stretching of aromatic ring), 2924 (pyrazoine -CH_2), 1629 (-C=O stretching of cinnolin ring), 1547 (C=C-stretching of aromatic ring), 769 (-C-Cl); ^{1}H-NMR (300 MHz, $CDCl_3$, δ ppm): 2.79 (6H, s, -CH), 2.07-2.12 (1H, dd, -CH_2-, J = 16.32, 7.77 Hz), 3.63-3.68 (1H, dd, -CH_2-, J = 16.27, 12.16 Hz), 5.36-5.40 (1H, dd, -CH, J = 12.27, 7.78 Hz), 6.83-6.88 (4H, m, Ar-H), 7.21-7.26 (5H, m, Ar-H), 7.81-7.87 (4H, m, Ar-H); MS (*m*/*z*, (relative abundance, %)): 444 (M+, 33.5) 398, 343, 307 (Base Peak, 100), 293, 139.

Conclusions

To summarize, a new class of 1-Acetyl-3-(6-chlorocinnolin-4(3*H*)-one-3-yl)-5-(3-bromophenyl)-4,5-dihydro-1*H*-pyrazoles (**2b)** were synthesized. The newly synthesized heterocycles exhibited moderate to promising antimicrobial activity against standard strains. These results make interesting lead molecules for further synthetic and biological evaluation. It can be concluded that this class of compounds certainly holds great promise towards the pursuit to discover novel classes of antimicrobial agents. Further studies to acquire more information concerning structure–activity relationships are in progress.

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References

1. F. Vargas, T. Z. Carlos Rivas, A. Ramirez, T. Cordero, Y. Diaz, C. Izzo, Y. M. Cardenas, V. Lopez, L. Gomez, J. Ortega, A. Fuentes; J. Photochem and Photobiology, 2008, 92: 90.
2. A. Robert, A. William, US 4379929 (Cl. 544-234; CO7D237/28), 1983 12 Apr, Appl. 245,564. 19,1981, 9
3. C.W. Bird, Tetrahedron; 1992, 48: 340.
4. F. Abdelrazek, P. Metz, N. Metwally, S. El-Mahrouky; Arch. Pharm., 2006, 339: 460.
5. H. Perreault, L. Ramaley, F. Benoit, P. Sim, R. Boyd: Org. Mass Spect., 2005, 27: 96.
6. A. Nehad, A. El-Latif, A. El-Galil, E. Amr, A. Ibrahiem; Monatsh. Chem., 2007, 138: 559.
7. B. J. Gaede, M. Dermott; Het. Chem., 1993, 30: 49.
8. K. Shibata, I. Katsuyama, H. Izoe, M. Matsui, H J Muramatsu; Het. Chem., 1993, 30: 277.
9. X. Jiaxi, C. Wang, Q Zhang; Het. Chem., 2001, 6: 557.
10. H. F. Havaldar, N. K. Khatri; Asian J. Chem., 2007, 19: 5093.
11. B. A. Altan, P. Erhan, U. Abbasoglu; J. Pharm. of Gazi University., 2001, 18: 115.
12. A. Mohammad, H. Kumar, S A Khan; Bioorg. Med. Chem. Lett., 2008, 18: 918.
13. H. Kakul, A. Mohammad, A. Amir; Eur. J. Med. Chem., 2008, 43: 393.
14. Y. Prasad, K. P. Rajendra, Ravi, Deepti, A. Ramana, M Venkata; Asian J. Chem., 2007, 19: 4790.
15. S. Micheal, G. S. Sattari, F Jamali; J. Pharm. Sci., 2001, 4: 1.
16. T. K. Dave, S. D. Tala, J. D. Akbari, M. F. Dhaduk, H S Joshi; International J. Syn. Charac., 2008, 1: 147.
17. L. C. Raiford, W. J. Peterson; J. Org. Chem., 1936, 1: 544.
18. R. H. Wiley, C. H. Jarboe, F. N. Hayes, E. Hansbury, J. T. Nielsen, P. X. Callahan, M. C. Sellars; J. Org. Chem., 1958, 23: 732.
19. A. E. Sammour; Tetrahedron, 1964, 20: 1067.
20. I. Bhatnagar, M. V. George; Tetrahedron., 1968, 24: 1293.
21. D. H. Vyas, M. F. Dhaduk, S. D. Tala, J. D. Akbari, H. S. Joshi; Indian J. Het. Chem., 2007, 17: 169.
22. D. H. Vyas, S. D. Tala, M. F. Dhaduk, J. D. Akbari, H. S. Joshi; J. Indian Chem. Soc., 2007, 84: 1140.
23. D. J. Paghdar, S. D. Tala, M. F. Dhaduk, J. D. Akbari, H. S. Joshi; Indian J. Het. Chem., 2007, 17: 113.
24. P. T. Chovatia, J. D. Akbari, P. K. Kachhadia, P. D. Zalavadia, H. S. Joshi, J. Serb. Chem. Soc., 2007, 71: 713.
25. M. R. Patel, J. D. Akbari, D. H. Purohit, H. S. Joshi; J. Indian Chem. Soc., 2007, 84: 1169.

26. A. Levai, J. Jeko; Arkivoc, 2007, 4: 134.
27. N. Rayyes, A. Ai-Johary; J. Chem. Eng. Data., 1985, 30: 500.
28. S. G. Franzblau, R. S. Witzig, J. C. McLaughlin, P. Torres, G. Madico, A. Hernandez, M. T. Degnan, M. B. Cook, V. K. Quenzer, R. M. Freguson, R. H. Gilman; J. Clin. Microbiol., 1998, 36: 362.
29. Barry A L, The Antimicrobial Susceptibility test: Principle and Practices, edited by Illus Lea and Febiger, Philodalphia pa, (USA), 1976 p.180