



***In Vitro* Antimicrobial Studies of Some Nitrogen Containing Heterocycles with 6, 8-Dibromo Quinazolin-4(3H) Ones**

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**ABSTRACT**

*Some nitrogen containing 6, 8-dibromoquinazolin-4(3H) ones 6a-l were synthesized by the base catalyzed cyclisation of acrylamide 5a-l with hydrazine hydrate. The overall reaction was carried out by multistep process. The base catalyzed cyclisation of acid chloride 1 with 3:5-dibromo anthranilic acid yielded benzoxazinone 2, which on reaction with hydrazine hydrate to afforded amino quinazolin-4(3H) one 3. The structural confirmation of the synthesized compounds was carried out on the basis of elemental analysis as well as IR and NMR spectra results. The title compounds were evaluated for in vitro antibacterial and antifungal activity.*

**Keywords:** Antibacterial, Antifungal, Pyrazoline, Quinazolin-4(3H) one.

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**INTRODUCTION**

Heterocyclic derivatives are pharmaceutically important compounds which were developed for better result in the medicinal chemistry. Nitrogen containing heterocycles are considered to be an important class of compounds because of their interesting diversified biological properties. One of the most frequently encountered heterocycles in medicinal chemistry is quinazolin-4(3H) one with pyrazoline and its analogs have widespread applications as antibacterial[1-2], antimalarial[3-4], antimicrobial, antifungal[5], HIV-1 integrase inhibitor[6], analgesics[7], enzyme inhibitory agent[8], anti-inflammatory, anti-breast cancer agent[9], anticancer, cardiovascular agent[10], Cox-II inhibitor[11] in medicinal chemistry. Quinazolinones system possess pyrazoline moiety at C-3 positions to yield the potential anti-tumor and antidiabetic activities [12]. Its halogenated derivatives possess potential antihyperlipidemic activity [13]. Encourage by the wide spectrum of activities exhibited these heterocycles and in continuations of our study on biologically active nitrogen heterocycle[14-20], we planned to synthesizes of new chemical entities of quinazolin-4(3H) one and prove to be enhanced biological activity.

## MATERIALS AND METHODS

**Synthesis of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-6, 8-dibromo-3, 1-benzoxazin-4(3H) one 2:** To a solution of 3-(6-chloro-2-phenylquinolin)acetyl chloride (3.16 g, 0.01 mol) in pyridine (25mL) kept on an ice bath at 0-5 °C. Add small portion of 3:5-dibromo anthranilic acid (2.95 g, 0.01 mol) and stirred for 1 h. to keep the temperature between 0-5 °C. Further reaction mixture was stirred 1 h. at room temperature. A pasty mass thus obtained was washed thoroughly with sodium bicarbonate (5 %) to remove unreacted acid. Thus solid separated was filtered, dried and recrystallised from methanol. M.P. 162 °C. Yield : 79 % IR(KBr):3073,2861(C-H),1725(C=O),1616(C=N),1327(C-N),1238(C-O-C), 782(C-Cl), 578 (C-Br) Anal. (%) for C<sub>24</sub>H<sub>13</sub>N<sub>2</sub>O<sub>2</sub>Br<sub>2</sub>Cl Calcd; C, 51.75; H, 2.33; N, 5.03; Found; C, 51.77; H, 2.34; N, 5.05.

**Synthesis of 3-Amino-2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl-6,8-dibromoquinazolin-4(3H) one 3:** To a mixture of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-6,8-dibromo-3,1-benzoxazin-4(3H) one (5.565 g, 0.01 mol) and hydrazine(99 %) (0.50 g, 0.01 mol) in 25.0 mL pyridine was heated at 180-200 °C in an oil bath for 5-6 h. The oily mass was obtained, cooled and slowly poured onto crushed acidic (HCl, 25mL) ice cold water with occasional stirring. The product obtained was filtered and washed several times with water. The crushed product was dried and recrystallised from ethanol. M.P.:145 °C. Yield: 74 % IR (KBr) : 3407(NH), 3069, 2863(C-H), 1718(C=O), 1614(C=N), 1325(C-N), 779(C-Cl), 580(C-Br). <sup>1</sup>H-NMR(CDCl<sub>3</sub>): 2.11(s, 2H, -N-NH<sub>2</sub>), 6.37-7.94(m, 11H, Ar-H), 2.62(s, 2H, -CH<sub>2</sub>). Anal. (%) for C<sub>24</sub>H<sub>15</sub>N<sub>4</sub>OBr<sub>2</sub>Cl Calcd; C, 50.48; H, 2.62; N,9.81; Found; C, 50.49; H, 2.64; N, 9.83.

**Synthesis of 2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl-3-acetamido-6,8-dibromoquinazolin-4(3H)-one 4:** To a solution of 3-Amino-2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl-6,8-dibromo quinazolin-4(3H) one (5.705 g, 0.01 mol) in dry benzene(50 ml), acetyl chloride(0.785g, 0.01mol) was added drop by drop at 0-5 °C, for 1 h with constant stirring after complete of addition, reaction mixture was kept overnight. The excess of solvent was distilled off under reduced pressure and then poured onto ice, the solid thus obtained was filtered off and recrystallized from methanol. M.P. :173 °C. Yield : 69 % IR(KBr): 3407(NH), 3063,2864(C-H),1721(C=O), 1640(C=O of -COCH<sub>3</sub>), 1323(C-N), 774(C-Cl), 576(C-I). <sup>1</sup>H-NMR(CDCl<sub>3</sub>) : 2.12(s, 1H, -N-NH-), 6.33- 7.96(m, 11H, Ar-H), 2.73(s, 3H, -COCH<sub>3</sub>), 2.63(s, 2H, -CH<sub>2</sub>). Anal. (%) for C<sub>26</sub>H<sub>17</sub>N<sub>4</sub>O<sub>2</sub>Br<sub>2</sub>Cl Calcd; C, 50.93; H, 2.77; N, 9.14; Found; C, 50.94; H, 2.79; N, 9.16.

**Synthesis of 2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl-3-substituted phenyl acryl amido-6,8-dibromoquinazolin-4(3H)-one 5a:** To a solution of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl]methyl-3-acetamido-6,8-dibromoquinazolin-4(3H)-one (6.125g, 0.01 mol) in absolute ethanol (50 ml) and add benzaldehyde (1.06g, 0.01 mol) in 2 % NaOH was refluxed for 10-12 h., cooled and poured into ice cold water. The solid thus obtained was filtered, washed with water and recrystallised from methanol. M.P.: 151 °C. Yield: 74 % IR(KBr) : 3409(NH), 3062, 2859(C-H), 1719(C=O), 1641(C=O of -COCH<sub>3</sub>), 1578 (CH=CH), 1318(C-N), 778(C-Cl), 579(C-Br). <sup>1</sup>H-NMR(CDCl<sub>3</sub>) : 2.11(s, 1H, -N-NH), 6.38- 7.91(m, 16H, Ar-H), 2.63(s, 2H, -CH<sub>2</sub>), 6.81(d, 1H, COCH=), 8.61(d, 1H, =CH-Ar). Anal; (%) C<sub>33</sub>H<sub>21</sub>N<sub>4</sub>O<sub>2</sub>Br<sub>2</sub>Cl Calcd; C, 56.53; H, 2.99; N, 7.99; Found; C, 56.54; H, 3.01; N, 8.02. The remaining 5b-l compounds were prepared by the above mention similar method.

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-(2-chloro) phenyl acryl amido-6, 8-dibromoquinazolin-4(3H)-one (5b) :** M.P.: 139-140 °C. Yield: 72 % IR(KBr) : 3366(NH), 3061, 2857(C-H), 1728(C=O), 1613(C=O of -COCH<sub>3</sub>), 1578 (CH=CH), 1316(C-N), 783(C-Cl), 574(C-Br). <sup>1</sup>H NMR(CDCl<sub>3</sub>) : 2.14(s, 1H, -N-NH), 6.38- 7.91(m, 15H, Ar-H), 3.63 (s, 2H, -CH<sub>2</sub>), 6.80(d, 1H, COCH=), 8.60(d, 1H, =CH-Ar). <sup>13</sup>C NMR: 31.5(-CH<sub>2</sub>), 36.3, 41.5(CH=CH), 160.9 (imine>C=O), 162.1 (>C=O), 173.3(imine aromatic-C), 109.20-143.16(aromatic-27C). Anal; (%) C<sub>33</sub>H<sub>20</sub>N<sub>4</sub>O<sub>2</sub>Br<sub>2</sub>Cl<sub>2</sub> Calcd; C, 53.88; H, 2.72; N,7.62; Found; C, 53.89; H, 2.74; N, 7.63.

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-(3-chloro) phenyl acryl amido-6,8-dibromoquinazolin-4(3H)-one (5c) :** M.P.: 124-125 °C. Yeild: 68 % IR(KBr) : 3369(NH), 3063, 2858(C-H), 1729(C=O), 1614(C=O of -COCH<sub>3</sub>), 1579 (CH=CH), 1316(C-N), 780(C-Cl), 576(C-Br). <sup>1</sup>H NMR(CDCl<sub>3</sub>) : 2.12(s, 1H, -N-NH), 6.38- 7.91(m, 15H, Ar-H), 3.61 (s, 2H, -CH<sub>2</sub>), 6.81(d, 1H, COCH=), 8.60(d, 1H, =CH-Ar). <sup>13</sup>C NMR: 31.3(-CH<sub>2</sub>), 36.5, 41.3(CH=CH), 161.3(immine>C=O), 162.3(>C=O), 173.1(immine aromatic-C), 109.17-143.21(aromatic-27C). Anal; (%) C<sub>33</sub>H<sub>20</sub>N<sub>4</sub>O<sub>2</sub>Br<sub>2</sub>Cl<sub>2</sub> Calcd; C, 53.88; H, 2.72; N,7.62; Found; C, 53.90; H, 2.73; N, 7.63.

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-(4-chloro) phenyl acryl amido-6,8-dibromoquinazolin-4(3H)-one (5d) :** M.P.: 144-145 °C. Yeild: 70 % IR(KBr) : 3368(NH), 3062, 2857(C-H), 1727(C=O), 1616(C=O of -COCH<sub>3</sub>), 1578(CH=CH), 1317(C-N), 781(C-Cl), 578(C-Br). <sup>1</sup>H NMR(CDCl<sub>3</sub>) :2.13(s, 1H, -N-NH), 6.38- 7.91(m, 15H, Ar-H), 3.63(s, 2H, -CH<sub>2</sub>), 6.80(d, 1H, COCH=), 8.61(d, 1H, =CH-Ar). <sup>13</sup>C NMR: 31.6(-CH<sub>2</sub>), 36.2, 41.4(CH=CH), 161.4 (immine >C=O), 162.1(>C=O), 173.2(immine aromatic-C), 109.17-143.21(aromatic-27C). Anal; (%) C<sub>33</sub>H<sub>20</sub>N<sub>4</sub>O<sub>2</sub>Br<sub>2</sub>Cl<sub>2</sub> Calcd; C, 53.88; H, 2.72; N,7.62; Found; C, 53.89; H, 2.74; N, 7.63.

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-(2-hydroxy) phenyl acryl amido-6,8-dibromoquinazolin-4(3H)-one (5e) :** M.P.: 163-164 °C. Yeild: 75 % IR (KBr) : 3553(-OH),3416(NH), 3061, 2856(C-H), 1721(C=O), 1617(C=O of -COCH<sub>3</sub>), 1579 (CH=CH), 1318(C-N), 779(C-Cl), 573(C-Br). <sup>1</sup>H NMR(CDCl<sub>3</sub>) :2.12(s, 1H, -N-NH),6.38- 7.91(m,15H, Ar-H),3.62 (s, 2H, -CH<sub>2</sub>), 6.80(d, 1H, COCH=), 8.60(d, 1H, =CH-Ar), 10.37(s, 1H,-OH). <sup>13</sup>C NMR: 31.2(-CH<sub>2</sub>), 36.3, 41.6(CH=CH), 160.9 (immine>C=O), 162.1 (>C=O), 173.2(immine aromatic-C), 109.17-143.21(aromatic-27C). Anal; (%) C<sub>33</sub>H<sub>21</sub>N<sub>4</sub>O<sub>3</sub>Br<sub>2</sub>Cl Calcd; C, 55.27; H, 2.93; N,7.81; Found; C, 55.28; H, 2.95; N, 7.83.

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-(3-hydroxy) phenyl acryl amido-6,8-dibromoquinazolin-4(3H)-one (5f) :** M.P.:174-175 °C. Yeild: 71 % IR(KBr) : 3552(-OH),3415(NH), 3063, 2857(C-H), 1723(C=O), 1617(C=O of -COCH<sub>3</sub>), 1578 (CH=CH), 1317(C-N), 780(C-Cl), 575(C-Br). <sup>1</sup>H NMR(CDCl<sub>3</sub>) :2.11(s, 1H, -N-NH), 6.38- 7.91(m, 15H, Ar-H), 3.63 (s, 2H, -CH<sub>2</sub>), 6.81(d, 1H, COCH=), 8.60(d, 1H, =CH-Ar),10.36(s,1H,-OH).<sup>13</sup>C NMR: 31.4(-CH<sub>2</sub>), 36.5, 41.7 (CH=CH), 161.1 (immine>C=O),162.2 (>C=O), 173.1(immine aromatic-C), 109.17-143.21(aromatic-27C). Anal; (%) C<sub>33</sub>H<sub>21</sub>N<sub>4</sub>O<sub>3</sub>Br<sub>2</sub>Cl Calcd; C, 55.27; H, 2.93; N,7.81; Found; C, 55.29; H, 2.94; N, 7.83.

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl]methyl-3-(4-hydroxy)phenyl acryl amido-6,8-dibromoquinazolin-4(3H)-one (5g) :** M.P.: 184-185 °C. Yeild:73 % IR(KBr): 3554(-OH),3413(NH), 3064, 2856(C-H), 1721(C=O), 1616(C=O of -COCH<sub>3</sub>), 1576(CH=CH), 1318(C-N), 782(C-Cl), 577(C-Br). <sup>1</sup>H NMR(CDCl<sub>3</sub>): 2.12(s, 1H, -N-NH),6.38- 7.91(m,15H, Ar-H),3.62 (s, 2H, -CH<sub>2</sub>), 6.80(d, 1H, COCH=), 8.61(d, 1H, =CH-Ar), 10.37(s,1H,-OH).<sup>13</sup>C NMR: 31.4(-CH<sub>2</sub>), 36.5,41.3 (CH=CH), 161.1 (immine>C=O),162.1(>C=O),173.2 (immine aromatic-C), 109.17-143.21(aromatic-27C). Anal; (%) C<sub>33</sub>H<sub>21</sub>N<sub>4</sub>O<sub>3</sub>Br<sub>2</sub>Cl Calcd; C, 55.27; H, 2.93; N,7.81; Found; C, 55.28; H, 2.95; N, 7.82.

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-(2-nitro) phenyl acryl amido-6,8-dibromoquinazolin-4(3H)-one (5h) :** M.P.: 195-196 °C. Yeild: 65 % IR(KBr) : 3411(NH), 3061, 2856 (C-H), 1723(C=O), 1616(C=O of -COCH<sub>3</sub>), 1578(CH=CH), 1319(C-N),1567,1365(-NO<sub>2</sub>) 781(C-Cl), 577(C-Br). <sup>1</sup>H NMR(CDCl<sub>3</sub>): 2.13(s, 1H, -N-NH), 6.39- 7.91(m, 15H, Ar-H), 3.63 (s, 2H, -CH<sub>2</sub>), 6.80(d, 1H, COCH=), 8.61(d, 1H, =CH-Ar). <sup>13</sup>C NMR: 31.5(-CH<sub>2</sub>), 36.4, 41.3(CH=CH),161.2(immine >C=O), 162.1(>C=O), 173.1 (immine aromatic-C), 109.17-143.21(aromatic-27C). Anal; (%) C<sub>33</sub>H<sub>20</sub>N<sub>5</sub>O<sub>4</sub>Br<sub>2</sub>Cl Calcd; C, 53.12; H, 2.68; N,9.38; Found; C, 53.13; H, 2.70; N, 9.39.

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-(3-nitro) phenyl acryl amido-6,8-dibromoquinazolin-4(3H)-one (5i) :** M.P.: 187-188 °C. Yeild: 69 % IR(KBr) : 3413(NH), 3063, 2857(C-H), 1721(C=O), 1617(C=O of -COCH<sub>3</sub>), 1579(CH=CH), 1317(C-N),1566,1365(-NO<sub>2</sub>), 783(C-Cl),

578(C-Br).  $^1\text{H}$  NMR( $\text{CDCl}_3$ ): 2.12(s, 1H, -N-NH), 6.39- 7.91(m, 15H, Ar-H), 3.63(s, 2H,  $-\text{CH}_2$ ), 6.80(d, 1H,  $\text{COCH}=\text{}$ ), 8.60(d, 1H,  $=\text{CH-Ar}$ ).  $^{13}\text{C}$ NMR:31.6( $-\text{CH}_2$ ), 36.4,41.2 ( $\text{CH}=\text{CH}$ ), 161.1 (imine $>\text{C}=\text{O}$ ), 162.0( $>\text{C}=\text{O}$ ),173.2(immine aromatic-C), 109.17-143.21(aromatic-27C). Anal; (%)  $\text{C}_{33}\text{H}_{20}\text{N}_5\text{O}_4\text{Br}_2\text{Cl}$  Calcd; C, 53.12; H, 2.68; N,9.38; Found; C, 53.14; H, 2.69; N, 9.39.

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-(4-nitro) phenyl acryl amido-6,8-dibromoquinazolin-4(3H)-one (5j)** : M.P.: 203-205  $^\circ\text{C}$ . Yeild: 67 % IR(KBr) : 3413(NH), 3062, 2859(C-H), 1723(C =O), 1616(C=O of  $-\text{COCH}_3$ ), 1579 ( $\text{CH}=\text{CH}$ ),1567,1368( $-\text{NO}_2$ ),1318(C-N), 782(C-Cl), 577(C-Br).  $^1\text{H}$  NMR( $\text{CDCl}_3$ ): 2.13(s, 1H, -N-NH), 6.39- 7.91(m, 15H, Ar-H), 3.62 (s, 2H,  $-\text{CH}_2$ ), 6.81(d, 1H,  $\text{COCH}=\text{}$ ), 8.61(d, 1H,  $=\text{CH-Ar}$ ).  $^{13}\text{C}$ NMR:31.4( $-\text{CH}_2$ ),36.3,41.3 ( $\text{CH}=\text{CH}$ ),161.2 (imine $>\text{C}=\text{O}$ ), 162.1 ( $>\text{C}=\text{O}$ ),173.3(immine aromatic-C),109.17-143.21(aromatic-27C). Anal; (%) $\text{C}_{33}\text{H}_{20}\text{N}_5\text{O}_4\text{Br}_2\text{Cl}$  Calcd; , 53.12; H, 2.68; N,9.38; Found; C, 53.13; H, 2.70; N, 9.40.

**Spectral data of 2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl-3-(2-methoxy)phenyl acryl amido-6,8-dibromoquinazolin-4(3H)-one (5k)** : M.P.:156-157  $^\circ\text{C}$ . Yeild: 78 % IR(KBr) : 3412(NH), 3061, 2858(C-H), 1721(C =O), 1614(C=O of  $-\text{COCH}_3$ ),1579( $\text{CH}=\text{CH}$ ),1319(C-N),1244,1109(C-O-C),781(C-Cl),579(C-Br).  $^1\text{H}$ -NMR( $\text{CDCl}_3$ ): 2.12(s, 1H, -N-NH),6.39- 7.91(m,15H, Ar-H), 3.63 (s, 2H,  $-\text{CH}_2$ ),6.80(d,1H,  $\text{COCH}=\text{}$ ), .61(d,1H,  $=\text{CH-Ar}$ ), 3.78(s,3H,- $\text{OCH}_3$ ).  $^{13}\text{C}$ NMR:31.5( $-\text{CH}_2$ ),36.5,41.6( $\text{CH}=\text{CH}$ ), 59.6( $-\text{OCH}_3$ ) 161.2 (imine  $>\text{C}=\text{O}$ ), 162.1 ( $>\text{C}=\text{O}$ ),173.1(immine aromatic-C),109.17-143.21(aromatic-27C).Anal;(%)  $\text{C}_{34}\text{H}_{23}\text{N}_4\text{O}_3\text{Br}_2\text{Cl}$  Calcd; C, 55.85; H, 3.14; N,7.66; Found; C, 55.86; H, 3.15; N, 7.67.

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-(4-methoxy) phenyl acryl amido-6,8-dibromoquinazolin-4(3H)-one (5l)** : M.P.: 167-168  $^\circ\text{C}$ . Yeild: 76 % IR(KBr) : 3411(NH), 3063, 2858(C-H), 1721(C =O), 1616(C=O of  $-\text{COCH}_3$ ), 1579( $\text{CH}=\text{CH}$ ), 1317(C-N),1245,1108(C-O-C),778(C-Cl), 577(C-Br).  $^1\text{H}$  NMR( $\text{CDCl}_3$ ): 2.13(s, 1H, -N-NH), 6.39- 7.91(m, 15H, Ar-H), 3.62 (s, 2H,  $-\text{CH}_2$ ), 6.80(d, 1H,  $\text{COCH}=\text{}$ ), 8.61(d, 1H,  $=\text{CH-Ar}$ ), 3.79(s,3H,- $\text{OCH}_3$ ).  $^{13}\text{C}$  NMR: 31.6( $-\text{CH}_2$ ), 36.6, 41.4 ( $\text{CH}=\text{CH}$ ),59.7( $-\text{OCH}_3$ ),161.1(immine  $>\text{C}=\text{O}$ ),162.3 ( $>\text{C}=\text{O}$ ), 173.2(immine aromatic-C), 109.17-143.21 (aromatic-27C). Anal; (%) $\text{C}_{34}\text{H}_{23}\text{N}_4\text{O}_3\text{Br}_2\text{Cl}$  Calcd; C, 55.85; H, 3.14; N,7.66; Found; C, 55.87; H, 3.15; N, 7.68.

**Synthesis of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-(5-phenyl-4, 5-dihydro-1H-pyrazol-3-yl amino)-6,8-dibromoquinazolin-4(3H)-one 6a** : To a solution of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-substituted phenyl acryl amido-6,8-dibromoquinazolin-4(3H)-one (7.005 g, 0.01 mol) in methanol, add hydrazine hydrate(99 %) (1.0 g,0.02 mol) and few drops of glacial acetic acid. The reaction mixture was refluxed for 8-10 h., distilled and cooled. The separated solid was filtered, washed with water and recrystallised from methanol. M.P.: 166  $^\circ\text{C}$ . Yeild: 72 % IR(KBr): 3368(N-H),3061,2856(C-H),1723 (C=O),1617(C=N), 1317(C-N), 780(C-Cl),577(C-Br).  $^1\text{H}$  NMR( $\text{CDCl}_3$ ): 2.13(d,1H, $=\text{N-NH}$ ), 8.31(s,1H,-N-NH), 2.63(s,2H, $-\text{CH}_2$ ), 3.06 (d,1Ha), 3.48(d,1Hb), 6.54(t,1Hx), 6.43-7.95(m,16H,Ar-H).  $^{13}\text{C}$  NMR: 31.4 ( $-\text{CH}_2$ ), 36.4, 41.3, 161.2 (pyrazol-C), 162.1 ( $>\text{C}=\text{O}$ ), 173.1(immine aromatic-C) 109.17-143.21(aromatic-27C). Anal; (%)  $\text{C}_{33}\text{H}_{23}\text{N}_6\text{OBr}_2\text{Cl}$  Calcd; C, 55.42; H, 3.22; N,11.75; Found; C, 55.44; H, 3.24; N, 11.76.

The remaining 6b-l compounds were prepared by the above mention similar method.

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-[5-(2-chloro) phenyl-4, 5-dihydro-1H-pyrazol-3-yl amino]-6,8-dibromoquinazolin-4(3H)-one(6b)**: M.P.: 149-150  $^\circ\text{C}$ . Yeild: 70 % IR(KBr):3369(N-H),3063,2861(C-H),1725(C=O),1616(C=N), 1316(C-N), 782(C-Cl), 580(C-Br).  $^1\text{H}$  NMR( $\text{CDCl}_3$ ): 2.11(d,1H, $=\text{N-NH}$ ),8.29(s,1H,-N-NH),3.63(s,2H, $-\text{CH}_2$ ), 3.05 (d,1Ha), 3.46(d,1Hb), 6.51 (t,1Hx), 6.43-7.95(m,15H,Ar-H).  $^{13}\text{C}$  NMR: 31.5( $-\text{CH}_2$ ), 36.3, 41.5, 161.1 (imine pyrazol-C), 162.2 ( $>\text{C}=\text{O}$ ),173.3(immine aromatic-C), 109.17-143.21(aromatic-27C). Anal; (%)  $\text{C}_{33}\text{H}_{22}\text{N}_6\text{OBr}_2\text{Cl}_2$  Calcd; C, 52.87; H, 2.93; N,11.21; Found; C, 52.88; H, 2.95; N, 11.23.



**Spectral data of 6c: 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-[5-(3-chloro) phenyl-4,5-dihydro-1H-pyrazol-3-yl amino]-6,8-dibromoquinazolin-4(3H)-one(6c) :** M.P.: 139-140 °C. Yield: 67 % IR(KBr): 3371(N-H),3062, 2857(C-H),1721 (C=O),1616(C=N), 1316(C-N), 782(C-Cl),577(C-Br). <sup>1</sup>H NMR(CDCl<sub>3</sub>):2.13(d,1H,=N-NH),8.30(s,1H,-N-NH),3.63(s,2H,-CH<sub>2</sub>), 3.06 (d,1Ha), 3.47(d,1Hb),6.53 (t,1Hx), 6.43-7.95(m,15H,Ar-H). <sup>13</sup>C NMR: 31.3(-CH<sub>2</sub>), 36.4, 41.3, 161.3 (imine pyrazol-C),162.2 (>C=O),173.1(imine aromatic-C), 109.17-143.21(aromatic-27C). Anal; (%)C<sub>33</sub>H<sub>22</sub>N<sub>6</sub>OBr<sub>2</sub>Cl<sub>2</sub> Calcd; C, 52.87; H, 2.93; N,11.21; Found; C, 52.89; H, 2.95; N, 11.22.

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-[5-(4-chloro) phenyl-4,5-dihydro-1H-pyrazol-3-yl amino]-6,8-dibromoquinazolin-4(3H)-one(6d):** M.P.:158-160 °C. Yield: 69 % IR(KBr):3369(N-H),3063,2861(C-H),1723(C=O),1615(C=N),1317(C-N), 780(C-Cl),579(C-Br). <sup>1</sup>H NMR (CDCl<sub>3</sub>): 2.12(d,1H,=N-NH),8.31(s,1H,-N-NH),3.62(s,2H,-CH<sub>2</sub>), 3.05 (d,1Ha), 3.45(d,1Hb), 6.51(t,1Hx), 6.43-7.95(m,15H,Ar-H).<sup>13</sup>C NMR: 31.4(-CH<sub>2</sub>), 36.2, 41.5, 161.2 (imine pyrazol-C),162.1 (>C=O), 173.1(imine aromatic-C), 109.17-143.21(aromatic-27C). Anal; (%)C<sub>33</sub>H<sub>22</sub>N<sub>6</sub>OBr<sub>2</sub>Cl<sub>2</sub> Calcd; C, 52.87; H, 2.93; N,11.21; Found; C, 52.88; H, 2.94; N, 11.23.

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-[5-(2-hydroxy) phenyl-4, 5-dihydro-1H-pyrazol-3-yl amino]-6,8-dibromoquinazolin-4(3H)-one(6e) :** M.P.:183-184 °C.Yield: 73 % IR(KBr):3551(O-H),3413(N-H),3063,2858 (C-H),1723(C=O),1616 (C=N), (C-N), 780(C-Cl),579(C-Br).<sup>1</sup>H NMR(CDCl<sub>3</sub>): 2.13(d,1H,=N-NH), 8.31(s,1H,-N-NH), 3.63(s,2H,-CH<sub>2</sub>), 3.06(d,1Ha), 3.47 (d,1Hb),6.53(t,1Hx), 6.43-7.95(m,15H,Ar-H),10.38(s,1H,-OH). <sup>13</sup>C NMR: 31.4(-CH<sub>2</sub>), 36.5, 41.3, 161.2 (pyrazol-C), 162.1(>C=O),173.3(imine aromatic-C) 109.17-143.21(aromatic-27C). Anal; (%) C<sub>33</sub>H<sub>23</sub>N<sub>6</sub>O<sub>2</sub>Br<sub>2</sub>Cl Calcd; C, 54.21; H, 3.14; N,11.49; Found; C, 54.23; H, 3.15; N, 11.51.

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-[5-(3-hydroxy) phenyl-4, 5-dihydro-1H-pyrazol-3-yl amino]-6, 8-dibromoquinazolin-4(3H)-one (6f) :** M.P.: 191-193 °C.Yield: 71 %IR (KBr): 3547(O-H), 3411(N-H), 3062, 2857 (C-H), 1721(C=O), 1617 (C=N), 1316(C-N), 782(C-Cl), 578(C-Br). <sup>1</sup>H NMR(CDCl<sub>3</sub>): 2.11(d,1H,=N-NH), 8.31(s,1H,-N-NH), 3.63 (s,2H,-CH<sub>2</sub>), 3.05(d,1Ha), 3.47(d,1Hb),6.52(t,1Hx), 6.43-7.95(m,15H,Ar-H),10.37(s,1H,-OH). <sup>13</sup>C NMR: 31.4(-CH<sub>2</sub>), 36.5, 41.5, 161.2 (imine pyrazol-C), 162.1(>C=O), 173.2 (imine aromatic-C) 109.17-143.21 (aromatic-27C). Anal; (%)C<sub>33</sub>H<sub>23</sub>N<sub>6</sub>O<sub>2</sub>Br<sub>2</sub>Cl Calcd; C, 54.21; H, 3.14; N,11.49; Found; C, 54.22; H, 3.16; N, 11.50.

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-[5-(4-hydroxy) phenyl-4, 5-dihydro-1H-pyrazol-3-yl amino]-6,8-dibromoquinazolin-4(3H)-one(6g):** M.P.: 197-198 °C.Yield: 74 % IR(KBr): 3552(O-H), 3411(N-H), 3061,2859 (C-H),1725(C=O), 1616 (C=N),1317(C-N), 780(C-Cl), 579(C-Br). <sup>1</sup>H NMR(CDCl<sub>3</sub>): 2.13(d,1H,=N-NH), 8.31(s,1H,-N-NH), 3.63 (s,2H,-CH<sub>2</sub>), 3.06(d,1Ha), 3.45(d,1Hb),6.51(t,1Hx), 6.43-7.95(m,15H,Ar-H), 10.38(s,1H,-OH). <sup>13</sup>C NMR: 31.6(-CH<sub>2</sub>), 36.3,41.6, 161.1(imine pyrazol-C),162.2(>C=O),173.1(imine aromatic-C), 109.17-143.21(aromatic-27C). Anal; (%)C<sub>33</sub>H<sub>23</sub>N<sub>6</sub>O<sub>2</sub>Br<sub>2</sub>Cl Calcd; C, 54.21; H, 3.14; N,11.49; Found; C, 54.22; H, 3.16; N, 11.50.

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-[5-(2-nitro) phenyl-4, 5-dihydro-1H-pyrazol-3-yl amino]-6,8-dibromoquinazolin-4(3H)-one(6h):** M.P.: 179-180 °C.Yield: 66 % IR(KBr): 3413(N-H),3063,2859(C-H),1721(C=O),1616(C=N), 1567, 1363(-NO<sub>2</sub>), 1317(C-N),781(C-Cl),577(C-Br).<sup>1</sup>H NMR(CDCl<sub>3</sub>): 2.13(d,1H,=N-NH), 8.31(s,1H,-N-NH), 3.63(s,2H,-CH<sub>2</sub>), 3.05(d,1Ha), 3.46(d,1Hb),6.51(t,1Hx), 6.43-7.96(m,15H,Ar-H).<sup>13</sup>C NMR : 31.5(-CH<sub>2</sub>), 36.3,41.2,161.2(imine pyrazol-C),162.1(>C=O),173.2(imine aromatic-C), 109.17-143.21(aromatic-27C). Anal; (%) C<sub>33</sub>H<sub>22</sub>N<sub>7</sub>O<sub>3</sub>Br<sub>2</sub>Cl Calcd; C, 52.13; H, 2.89; N,12.90; Found; C, 52.15; H, 2.90; N, 12.92.

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-[5-(3-nitro) phenyl-4, 5-dihydro -1H-pyrazol-3-yl amino]-6,8-dibromoquinazolin-4(3H)-one(6i) :** M.P.: 194-195 °C.Yield: 70 % IR (KBr):3411(NH), 3062, 2857(C-H), 1723(C=O), 1617(C=N), 1565, 1362(-NO<sub>2</sub>), 1316(C-N), 780(C-Cl),

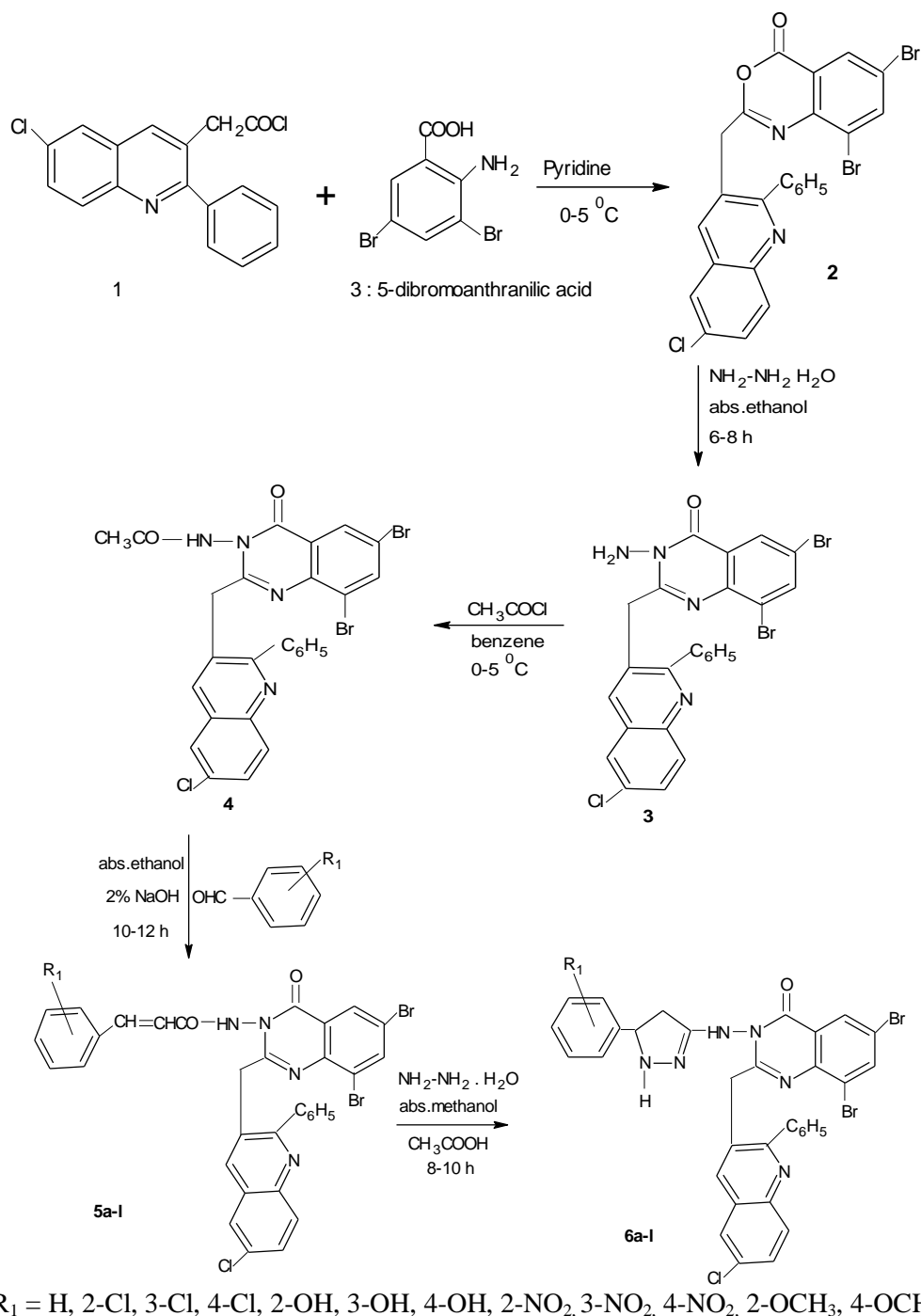
574(C-Br).  $^1\text{H}$  NMR( $\text{CDCl}_3$ ): 2.12(d,1H,=N-NH), 8.33(s,1H,-N-NH), 3.63 (s,2H,-CH<sub>2</sub>), 3.06(d,1Ha), 3.46(d,1Hb),6.52(t,1Hx), 6.43-7.96(m,15H,Ar-H).  $^{13}\text{C}$  NMR: 31.4(-CH<sub>2</sub>), 36.1, 41.4, 161.1(immine pyrazol-C), 162.3(>C=O), 173.2(immine aromatic-C), 109.17-143.21 (aromatic-27C). Anal; (%) C<sub>33</sub>H<sub>22</sub>N<sub>7</sub>O<sub>3</sub>Br<sub>2</sub>Cl Calcd; C, 52.13; H, 2.89; N,12.90; Found; C, 54.15; H, 2.91; N, 12.92.

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-[5-(4-nitro) phenyl-4, 5-dihydro-1H-pyrazol-3-yl amino]-6,8-dibromoquinazolin-4(3H)-one(6j):** M.P.: 211-212 °C.Yeild: 68 % IR (KBr):3413(NH), 3061, 2859(C-H), 1722(C=O), 1616(C=N), 1563, 1361(-NO<sub>2</sub>), 1316(C-N), 782(C-Cl), 576(C-Br).  $^1\text{H}$  NMR( $\text{CDCl}_3$ ): 2.12(d,1H,=N-NH), 8.31(s,1H,-N-NH), 3.63(s,2H,-CH<sub>2</sub>), 3.05(d,1Ha), 3.47(d,1Hb),6.52(t,1Hx), 6.43-7.96(m,15H,Ar-H).  $^{13}\text{C}$  NMR: 31.6(-CH<sub>2</sub>), 36.2, 42.3, 161.2(immine pyrazol-C), 162.2(>C=O), 173.1(immine aromatic-C), 109.17-143.21 (aromatic-27C). Anal; (%) C<sub>33</sub>H<sub>22</sub>N<sub>7</sub>O<sub>3</sub>Br<sub>2</sub>Cl Calcd; C, 52.13; H, 2.89; N,12.90; Found; C, 52.15; H, 2.90; N, 12.91.

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-[5-(2-methoxy) phenyl-4, 5-dihydro-1H-pyrazol-3-yl amino]-6,8-dibromoquinazolin-4(3H)-one(6k):** M.P.: 168-169 °C. Yeild: 73 % IR(KBr): 3411 (N-H),3063,2857 (C-H), 1723 (C=O), 1616 (C=N),1317 (C-N), 1243, 1109(C-O-C), 780(C-Cl), 576(C-Br).  $^1\text{H}$  NMR( $\text{CDCl}_3$ ):2.13(d,1H,=N-NH), 8.31(s,1H,-N-NH) 3.63(s,2H,-CH<sub>2</sub>), 3.06(d,1Ha), 3.46(d,1Hb), 6.52(t,1Hx), 6.43-7.96 (m,15H,Ar-H), 3.80(s,3H,-OCH<sub>3</sub>).  $^{13}\text{C}$ NMR: 31.3(-CH<sub>2</sub>), 36.6, 42.4, 161.1(immine pyrazol-C), 162.2(>C=O), 173.3 (immine aromatic-C), 58.4(-OCH<sub>3</sub>), 109.17-143.21(aromatic-27C). Anal; (%) C<sub>34</sub>H<sub>25</sub>N<sub>6</sub>O<sub>2</sub>Br<sub>2</sub>Cl Calcd; C, 54.80; H, 3.35; N,11.28; Found; C, 54.81; H, 3.37; N, 11.30.

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-[5-(4-methoxy) phenyl-4,5-dihydro-1H-pyrazol-3-yl amino]-6,8-dibromoquinazolin-4(3H)-one(6l) :** M.P.:176-177 °C. Yeild: 75 % IR (KBr): 3413(N-H), 3063, 2857 (C-H), 1723(C=O), 1614(C=N), 1317 (C-N), 1243,1108 (C-O-C), 782(C-Cl), 577(C-Br). $^1\text{H}$  NMR( $\text{CDCl}_3$ ):2.13(d,1H,=N-NH) ,8.31 (s,1H,-N-NH), 3.63(s,2H,-CH<sub>2</sub>), 3.06(d,1Ha), 3.467d,1Hb),6.53(t,1Hx), 6.43-7.96(m,15H,Ar-H), 3.80(s,3H,-OCH<sub>3</sub>).  $^{13}\text{C}$  NMR: 31.2(-CH<sub>2</sub>), 36.5, 42.5, 161.3(immine pyrazol-C), 162.1(>C=O), 173.1 (immine aromatic-C), 58.2(-OCH<sub>3</sub>), 109.17-143.21(aromatic-27C). Anal; (%)C<sub>34</sub>H<sub>25</sub>N<sub>6</sub>O<sub>2</sub>Br<sub>2</sub>Cl Calcd; C, 54.80; H, 3.35; N,11.28; Found; C, 54.82; H, 3.36; N, 11.29.

Scheme I



## APPLICATIONS

**Antimicrobial Activity:** The *in vitro* antimicrobial activity of synthesized compounds 6a-l was carried out by cup-plate method (Barry 1976). Antibacterial activity was screened against two gram positive bacteria *S.aureus* ATCC 9144 and *Bacillus Subtilis* ATCC 6633) and two gram negative bacteria (*E. coli* ATCC 25922 and *P.aeruginosa* ATCC 9027), by measuring the zone of inhibition on agar plates at two different

concentrations 100 and 50  $\mu\text{g/ml}$ . Antifungal activity also screened for two fungal species, *Candida albicans* ATCC 10231 and *Aspergillus niger* ATCC 6275, by measuring the zone of inhibition on agar plates at two different concentrations 20 and 10  $\mu\text{g mL}^{-1}$ . Penicillin-G and fluconazole were used as standard for antibacterial and antifungal activity respectively.

**Table: 3** Anti-bacterial activity of compound 6a-l

Compd	R <sub>1</sub>	Zone of inhibition in (mm)											
		<i>S. aureus</i> ATCC9144			<i>B. subtilis</i> ATCC6633			<i>E.coli</i> ATCC25922			<i>P.aeruginosa</i> ATCC9027		
		C <sub>H</sub>	C <sub>L</sub>	Pot %	C <sub>H</sub>	C <sub>L</sub>	Pot %	C <sub>H</sub>	C <sub>L</sub>	Pot %	C <sub>H</sub>	C <sub>L</sub>	Pot %
6a	H	12	10	46.40	13	11	49.15	13	11	49.15	13	11	49.15
<b>6b</b>	<b>2-Cl</b>	<b>18</b>	<b>15</b>	<b>66.43</b>	<b>19</b>	<b>17</b>	<b>68.41</b>	14	11	54.16	15	12	52.44
<b>6c</b>	<b>3-Cl</b>	<b>17</b>	<b>14</b>	<b>62.99</b>	<b>18</b>	<b>16</b>	<b>64.52</b>	14	12	51.09	15	12	52.44
<b>6d</b>	<b>4-Cl</b>	<b>19</b>	<b>17</b>	<b>68.41</b>	<b>20</b>	<b>18</b>	<b>72.52</b>	15	12	52.44	15	13	54.16
6e	2-OH	13	11	49.15	15	12	52.44	12	10	46.40	13	11	49.15
6f	3-OH	12	10	46.40	13	11	49.15	12	10	46.40	13	11	49.15
6g	4-OH	13	11	49.15	15	12	52.44	13	11	49.15	15	12	52.44
6h	2-NO <sub>2</sub>	15	13	54.16	15	13	54.16	<b>18</b>	<b>16</b>	<b>64.52</b>	<b>18</b>	<b>16</b>	<b>64.52</b>
6i	3-NO <sub>2</sub>	15	12	52.44	15	13	54.16	<b>17</b>	<b>15</b>	<b>60.87</b>	<b>18</b>	<b>17</b>	<b>62.05</b>
6j	4-NO <sub>2</sub>	15	13	54.16	16	14	57.41	<b>18</b>	<b>15</b>	<b>66.43</b>	<b>19</b>	<b>16</b>	<b>69.92</b>
6k	2-OCH <sub>3</sub>	16	14	57.41	16	14	57.41	14	12	51.09	15	13	54.16
6l	4-OCH <sub>3</sub>	16	13	59.98	16	13	59.98	15	12	52.44	16	14	57.41
<b>Penicillin-G</b>		27	22	100	27	22	100	27	22	100	27	22	100

C<sub>H</sub> Zone of inhibition at concentration 100  $\mu\text{g mL}^{-1}$ , C<sub>L</sub> Zone of inhibition at concentration 50  $\mu\text{g mL}^{-1}$ , potency of compound(%) as compared to penicillin-G.

**Table: 4** Antifungal activity of compound 6a-l

Compd	R <sub>1</sub>	Zone of inhibition in (mm)					
		<i>C.albicans</i> ATCC 10231			<i>A.niger</i> ATCC 6275		
		C <sub>H</sub>	C <sub>L</sub>	Pot %	C <sub>H</sub>	C <sub>L</sub>	Pot %
6a	H	<b>18</b>	<b>16</b>	<b>70.63</b>	<b>19</b>	<b>17</b>	<b>74.85</b>
6b	2-Cl	13	11	52.86	14	12	56.03
6c	3-Cl	12	10	49.89	12	10	49.89
6d	4-Cl	14	12	56.03	14	12	56.03
6e	2-OH	12	10	49.89	13	11	52.86
6f	3-OH	13	11	52.86	14	12	56.03
6g	4-OH	15	13	59.36	15	13	59.36
6h	2-NO <sub>2</sub>	12	10	49.89	13	11	52.86
6i	3-NO <sub>2</sub>	11	09	47.09	13	11	52.86
6j	4-NO <sub>2</sub>	13	11	52.86	14	12	56.03
6k	2-OCH <sub>3</sub>	<b>16</b>	<b>14</b>	<b>62.91</b>	<b>16</b>	<b>13</b>	<b>65.57</b>
6l	4-OCH <sub>3</sub>	<b>16</b>	<b>12</b>	<b>63.96</b>	<b>17</b>	<b>15</b>	<b>66.67</b>
<b>Fluconazole</b>		25	21	100	25	21	100

C<sub>H</sub> Zone of inhibition at concentration 20  $\mu\text{g/ml}$ , C<sub>L</sub> Zone of inhibition at Concentration 10  $\mu\text{g/ml}$ , potency of compound (%) as compared to fluconazole.



## CONCLUSIONS

We have used simple and convenient methods with simple work up and producing clean products for the synthesis of novel heterocycles 6, 8-dibromoquinazolin-4(3H) ones derivatives **6a-l**. The active pharmacophore pyrazoline and quinoline present in a newly synthesized compounds possessed good antibacterial and antifungal activity *in vitro*. The chloro group on phenyl nucleus at *ortho*, *meta* and *para* position showed very good activity against gram positive bacteria, on the other hand side nitro group on phenyl nucleus at *ortho*, *meta* and *para* position displayed higher activity against gram negative bacteria compared to standard. *Phenyl* nucleus, *ortho* and *para* methoxy substituted compounds showed very good antifungal activity. Overall results lead to focus on identified for active inhibitor and better future for improvement of further research on these molecules.

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