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SYNTHESIS AND IN VITRO PHARMACOLOGICAL STUDIES OF SOME NOVEL PRECURSORS OF 6, 8-DIBROMOQUINAZOLIN-4(3H) ONE

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ABSTRACT

A novel series of some precursors of 6, 8-dibromoquinazolin-4(3H)-one 61-12 have been synthesized by the based catalysed cyclisation of chromenamido 51-12 with phenylhydrazine hydrate. The overall reaction was base catalysed conventional multistep process. The title compounds have been confirmed by spectral data IR, 1H NMR, 13C NMR and elemental analysis. All the synthesized target molecules were screened for gram positive, gram negative antibacterial and fungicidal activity In Vitro by disc diffusion method. The zone of inhibition measured and calculated potency. The pharmacological strength of synthesized compounds was compared with standard drug.

KEYWORDS: Quinazolin-4(3H) one, Potency, Pyrazoline, Pharmacological, In Vitro.

INTRODUCTION

Quinazolinone, a heterocyclic compound has been extensively studied and used in certain specific biological activities. Quinazolin-4(3H) one and its derivatives constitute as an important class and found in more than 200 naturally occurring alkaloids [1]. Chalcones was well known intermediates for synthesizing various heterocyclic compounds viz. pyranones, quinolines, pyrazolines and quinazolines. The pharmaceutical importance of chalcones lies in the fact that they can be effectively utilized to enhance the bioactive moieties synthetically [2]. Quinazolin-4(3*H*) one as an important pharmacophore in medicinal chemistry and have synthetic interest because of they possess broad spectrum of pharmacological and therapeutic properties [3]. Quinazolin-4(3*H*)-one with pyrazoline moiety played vital role in medicinal chemistry. The large number of its derivatives used for anti-inflammatory and analgesics agents [4]. The halogenated derivatives of quinazolin-4(3H) ones possess potential antihyperlipidemic activity and have no significant toxic side effect at the drop sub lethal level 2 mg/kg [5]. Recently the several scientists elucidated that quinazolinone system possess variable hetrocycles at position 2 and 3 are extensively used as anti-inflammatory, anticancer [6], anti-fungal[7], HIV inhibitors[8], antioxidant[9], alziemer diseases[10] in medicinal chemistry.

Keeping these in view and encourage by the wide spectrum of therapeutic activities exhibited and literature survey of quinazoline derivatives revealed that in this study, we have synthesized some analogues of quinazolin-4(3H) ones incorporating heterocyclic moiety pyrazoline at C-3 and studied its antibacterial and antifungal activities in vitro by disc diffusion method.

METHOD AND MATERIAL

General Instrumentation

The melting points were determined in open capillary tubes and are uncorrected. All reagents were used of AR grade. The solvents were distilled prior to use. IR spectra were recorded on Perkin-Elmer 1300 FTIR spectrophotometer using KBr powder. ^{1}H NMR and ^{13}C NMR spectra of the title compounds were recorded in $CDCl_3$ on a Bruker spectrometer at 400 MHz and 75 MHz respectively, chemical shift in δ ppm. TMS used as internal standard. The purity of compounds was checked by TLC on silica gel G plates and spot visualization was done by exposing to iodine vapour. Elemental analyses of newly sysnthesized compounds were carried out on

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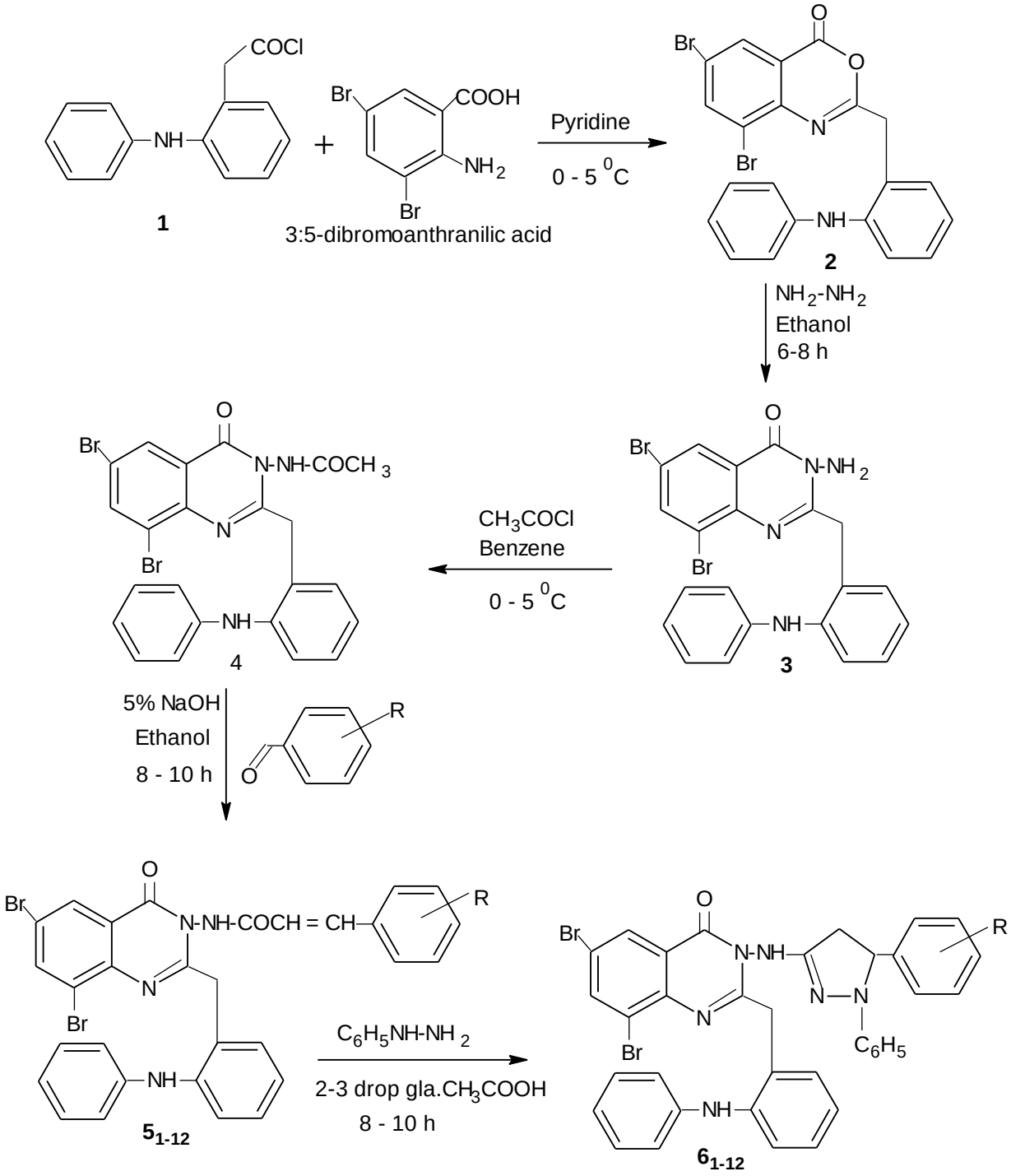
Carlo Ebra 1108 analyzer and the result were varying within ± 0.04 % of the calculated values. The starting compound **1** was prepared according to the reported method (Furniss et al., 1989)[11].

Scheme I Synthetic Pathway for Target Molecule



R= -H, 2-OH, 3-OH, 4-OH, 2-Cl, 3-Cl, 4-Cl, 2-NO_2, 3-NO_2, 4-NO_2, 2-OCH_3, 4-OCH_3

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Experimental section

2-(2-phenylamino)phenyl methyl–6,8-dibromo-3,1-benzoxazin-4(*H*) one 2

To solution of 2–(2-phenylamino) phenyl acetyl chloride (2.45 g, 0.01 mol) in pyridine(25ml) kept on an ice bath at 0-5 ^{0}C. Add each small portion of 3:5-dibromo anthranilic acid (2.94 g, 0.01 mol) was added portion wise and stirred for 1 h. to maintain temprature 0-5 ^{0}C. Further reaction mixture was stirred 1h at room temperature. A pasty mass thus obtained which was washed thoroughly with sodium bicarbonate (5%) to remove unreacted acid. A solid separated was filtered, dried and recrystalised from methanol.

M.P.:161 ^{0}C Yeild: 69 % IR(KBr): 3407(NH),3073,2861(C-H),1725(C=O),1614 (C=N), 1323(C-N),1236(C-O-C), 750(NH wag), 614(C-Br). Anal. (%) for $C_{21}H_{14}N_2O_2Br_2$ Calcd; C, 51.85; H, 2.88; N, 5.76; Found; C, 51.87; H, 2.89; N, 5.77.

3-Amino 2-(2-phenylamino)phenyl methyl-6,8–dibromo quinazolin–4(3*H*) one 3

To a mixture of 2-(2-phenyl amino) phenyl methyl–6,8-dibromo-3,1-benzoxazine-4(*H*)-one (4.86 g, 0.01 mol) and hydrazine hydrate (99 %) (0.50 g, 0.01mol) in 25.0 ml pyridine was heated at 180-200 ^{0}C in an oil bath for 5 - 6 h. The oily mass was 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 recrystallized from ethanol.

M.P. :118-119 ^{0}C Yeild : 64 % IR(KBr) : 3403(NH), 3068, 2869(C-H), 1721(C=O), 1612(C=N), 1321(C-N), 611(C-Br).^{1}HNMR($CDCl_3$)**:** 9.79(s,1H, -NH), 2.1(s, 2H, -N-NH_2), 6.42-7.96(m, 11H, Ar-H), 2.71(s, 2H, -CH_2). Anal. (%) for $C_{21}H_{16}N_4OBr_2$ Calcd; C, 50.40; H, 3.20; N, 11.20; Found; C, 50.42; H, 3.21; N, 11.21.

2-(2-phenylamino)phenyl methyl-3-acetamido-6,8-dibromo quinazolin-4(3*H*)-one 4

To solution of 3-amino-2-(2-phenylamino)phenyl methyl-6,8–dibromo quinazolin–4(3*H*) one **(**5.00 g, 0.01 mol) in dry benzene(50 ml), acetyl chloride(0.785g, 0.01mol) was added dropwish at 0-5 ^{0}C, for 1 h with constant stirring after completion of addition the 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 recrystalized from methanol.

M.P**. :**173-174 ^{0}C Yeild **:** 69 % IR(KBr): 3407(NH), 3062,2859(C-H),1727(C=O), 1645 (C=O of –$COCH_3$),1320(C-N), 613(C-Br). ^{1}H-NMR($CDCl_3$) **:** 9.78(s, 1H, -NH), 2.12(s, 1H, -N-NH), 6.42- 7.96(m, 11H, Ar-H), 2.70(s, 3H, -CH_3), 2.71(s, 2H, -CH_2). Anal. (%) for $C_{23}H_{18}N_4O_2Br_2$ Calcd;C,50.92; H, 3.32; N, 10.33; Found; C, 50.93; H, 3.34; N, 10.34.

2-(2-phenyl)amino)phenyl methyl-3-(phenyl acryl amido)-6,8-dibromo quinazolin-4(3*H*)-one 5_1

A solution of 2-(2-phenylamino)phenyl methyl-3-acetamido-6,8-dibromo quinazolin-4(3*H*)-one **(**5.42g, 0.01 mol) in absolute ethanol (50 ml) and add benzaldehyde (0.01 mol) in 2 % NaOH was refluxed for 10-12 h, cooled and poured into ice cold water. The solid obtained was filtered, washed with water and recrystalized from methanol.

M.P**. :**162-163 ^{0}C Yeild **:** 71 % IR(KBr) : 3411(NH), 3061, 2852(C-H), 1719(C =O), 1653(C=O of –$COCH_3$), 1576 (CH=CH), 1316(C-N), 611(C-Br).^{1}H-NMR($CDCl_3$)**:** 9.78(s, 1H, -NH), 2.11(s, 1H, -N-NH), 6.42- 7.96(m, 16H, Ar-H), 2.61 (s, 2H, -CH_2), 6.80(d, 1H, COCH=), 8.62(d, 1H, =CH-Ar). Anal. (%) for $C_{30}H_{22}N_4O_2Br_2$ Calcd; C, 57.14; H, 3.49; N, 8.89; Found; C, 57.15; H, 3.51; N, 8.90.

The remaining $5_{2\text{-}12}$ compounds were prepared by the above mention similar method.

2-(2-phenylamino)phenylmethyl-3–[(1,5-diphenyl)-4,5-dihydro-1*H*-pyrazol-3-yl amino] -6,8-dibromoquinazolin-4(3*H*)-one 6_1

To a solution of 2-(2-phenyl amino) phenyl methyl-3-(5-phenyl chromen amido)-6,8-dibromoquinazolin-4(3*H*) one (6.30g, 0.01 mole) in methanol, add phenylhydrazine hydrate (99 %) (2.16 g, 0.02 mole) and few drop of glacial acetic acid. The reaction mixture was refluxed for 8-10 h. After reaction mixture were distilled and cooled. The separated solid was filtered, washed with water and recrystallized from methanol.

M.P.: 128-129 ^{0}C Yield: 70%. IR(KBr):3369(N-H), 3062, 2858(C-H),1716(C=O),1614 (C=N), 1315(C-N),611(C-Br). ^{1}H NMR($CDCl_3$): 3.06(d, 1Ha), 3.42 (d,1Hb), 6.43(t, 1Hx), 3.62 (s, 2H, -CH_2), 8.18(s, 1H, -N –NH), 9.86 (s, 1H, - NH), 6.42-7.96(m,21H, Ar- H). ^{13}C NMR: 30.4(CH_2-C), 35.6, 41.4, 161.1(pyrazole-3C), 109.21-143.20(Ar-30C), 162.32 (C=O,C), 173.6(immine-C). Anal. (%) for $C_{36}H_{28}N_6OBr_2$ Calcd; C, 60.00; H, 3.88; N, 11.66; Found; C, 60.01; H, 3.90; N, 11.67.

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The remaining $6_{2\text{-}12}$ compounds were prepared by the above mention similar method.

2-(2-phenyl amino) phenyl methyl -3-[5-(2-hydroxy phenyl)-1-phenyl-4, 5-dihydro-1*H*-pyrazol-3-yl-amino]-6,8-dibromoquinazolin-4(3*H*)-one 6_2

M.P.: 136-137 ^{0}C Yeild: 73 % IR(KBr):3548(O-H), 3381(N-H), 3072, 2858 (C-H), 1721 (C=O), 1614(C=N), 1319(C-N), 609(C-Br). ^{1}HNMR($CDCl_3$): 3.07(d,1Ha),3.45 (d,1Hb), 6.43(t,1Hx), 3.61(s, 2H, -CH_2),8.18(s,1H, -N –NH), 9.84 (s, 1H, -NH), 6.42-7.94 (m,20H, Ar- H), 10.3(s,1H, -OH). ^{13}C NMR: 30.5 (CH_2-C), 35.7, 40.8, 161.1 (pyrazole–3C), 109.21-143.20 (Ar-30C), 162.3 (C = O,C), 173.0 (immine - C). $C_{36}H_{28}N_6O_2Br_2$ anal % calcd : C 58.69, H 3.80, N 11.41 found C 58.70 H 3.81 N 11.43.

2-(2-phenylamino) phenyl methyl -3-[5-(3-hydroxy phenyl)-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl-amino]-6,8-dibromoquinazoline-4(3*H*)-one 6_3

M.P.:149-150 ^{0}C Yeild: 67 % IR(KBr): 3549(O-H), 3370(N-H), 3062, 2861(C-H), 1720 (C=O),1614(C=N),1325(C-N), 613(C-Br). ^{1}H NMR($CDCl_3$): 3.09(d,1Ha), 3.45(d,1Hb), 6.43 (t,1Hx), 3.63 (s, 2H, -CH_2), 8.17(s, 1H, -N –NH), 9.86 (s, 1H, - NH), 6.42-7.96 (m, 20H, Ar- H),10.27(s,1H, -OH). ^{13}C NMR: 30.5(CH_2-C), 35.7, 41.4, 161.1(pyrazole-3C), 109.21-143.20 (Ar-30C), 162.3 (C = O,C), 173.6 (immine -C). $C_{36}H_{28}N_6O_2Br_2$ anal % calcd : C 58.69, H 3.80, N 11.41 found C 58.71 H 3.82 N 11.42.

2-(2-phenyl amino) phenyl methyl -3-[5-(4-hydroxy phenyl)-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl-amino]-6,8-dibromoquinazolin-4(3*H*)-one 6_4

M.P.: 155-156 ^{0}C Yeild: 69 % IR(KBr):3543(O-H),3389(N-H),3058,2862 (C-H), 1723 (C=O), 1613(C=N),1321(C-N), 611(C-Br). ^{1}H NMR($CDCl_3$): 3.06(d,1Ha),3.41(d,1Hb), 6.45(t,1Hx), 3.60 (s, 2H, -CH_2), 8.19(s, 1H, -N–NH), 9.87 (s, 1H, - NH), 6.42-7.94(m, 20H, Ar- H), 10.27(s,1H, -OH). ^{13}C NMR: 30.4(CH_2-C), 34.8, 41.6, 160.9(pyrazole-3C), 109.21-143.20(Ar-30C), 162.1 (C=O,C), 173.4 (immine - C). $C_{36}H_{28}N_6O_2Br_2$ anal % calcd : C 58.69, H 3.80, N 11.41 found C 58.70 H 3.82 N 11.42.

2-(2-phenyl amino) phenyl methyl -3-[5-(2-chloro phenyl)-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl-amino]-6,8-dibromoquinazolin-4(3*H*)-one 6_5

M.P.: 124-125 ^{0}C Yeild : 76 % IR(KBr):3398(N-H),3062, 2859(C-H),1725 (C=O), 1614 (C=N), 1320(C-N), 778(C-Cl) 618(C-Br). ^{1}H NMR($CDCl_3$): 3.09 (d,1Ha), 3.41 (d,1Hb), 6.45(t,1Hx), 3.63 (s, 2H, -CH_2), 8.17(s, 1H, -N–NH), 9.86 (s, 1H, - NH), 6.42-7.96(m, 20H, Ar- H). ^{13}C NMR: 30.4 (CH_2-C), 35.6, 40.3, 160.1 (pyrazole-3C),109.21-143.20 (Ar-30C),162.1(C=O,C),173.6(immine-C). $C_{36}H_{27}N_6OBr_2Cl$ anal % calcd : C 57.25, H 3.57, N 11.13 found C 57.27 H 3.58 N 11.14.

2-(2-phenyl amino) phenyl methyl -3-[5-(3-chlorophenyl)-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl-amino]-6,8-dibromoquinazolin-4(3*H*)-one 6_6

M.P.: 132-133 ^{0}C Yeild: 72 % IR(KBr): 3409 (N-H), 3064, 2856 (C-H),1727(C=O), 1617(C=N),1322(C-N),781(C-Cl),611(C-Br).^{1}HNMR($CDCl_3$):3.06 (d,1Ha), 3.42(d,1Hb), 6.49(t,1Hx), 3.61 (s, 2H, -CH_2), 8.16(s, 1H, -N–NH), 9.84 (s, 1H, -NH), 6.42-7.96(m, 20H, Ar- H). ^{13}C NMR: 30.4 (CH_2-C), 35.6, 40.4, 161.1(pyrazole-3C), 109.21-143.20 (Ar-30C), 162.2 (C=O,C), 173.0 (immine-C). $C_{36}H_{27}N_6OBr_2Cl$ anal % calcd : C 57.25, H 3.57, N 11.13 found C 57.26 H 3.59 N 11.14.

2-(2-phenyl amino) phenyl methyl -3-[5-(4-chloro phenyl)-1-phenyl-4, 5-dihydro-1*H*-pyrazol-3-yl-amino-6,8-dibromoquinazolin-4(3*H*)-one 6_7

M.P.: 146-147 ^{0}C Yeild: 66 % IR(KBr):3408(N-H),3066,2880(C-H), 1730 (C=O), 1609(C=N),1319(C-N),768(C-Cl),615(C-Br).^{1}HNMR($CDCl_3$):3.09(d,1Ha), 3.44 (d,1Hb), 6.45(t,1Hx), 3.62 (s, 2H, -CH_2), 8.17(s, 1H, -N–NH), 9.89 (s, 1H, -NH), 6.42-7.96(m, 20H, Ar- H). ^{13}C NMR: 30.5(CH_2-C), 35.5, 40.4, 161.1 (pyrazole-3C), 109.21 -143.20 (Ar-30C), 162.2 (C = O,C), 173.2 (immine-C). $C_{36}H_{27}N_6OBr_2Cl$ anal % calcd : C 57.25, H 3.57, N 11.13 found C 57.26 H 3.58 N 11.14.

2-(2-phenyl amino) phenyl methyl -3-[5-(2-nitrophenyl)-1-phenyl-4, 5-dihydro-1*H*-pyrazol-3-yl-amino]-6,8-dibromoquinazolin-4(3*H*)-one 6_8

M.P.: 159-160 ^{0}C Yeild : 67 % IR(KBr): 3370(N-H), 3065, 2861(C-H),1727(C=O), 1613(C=N),1543, 1361(-NO_2), 1321(C-N), 617(C-Br). ^{1}HNMR($CDCl_3$): 3.10(d,1Ha), 3.45 (d,1Hb), 6.47(t,1Hx), 3.60 (s, 2H, -CH_2),8.19(s, 1H, -N–NH), 9.85 (s, 1H, - NH), 6.42-7.96(m,20H, Ar- H). ^{13}C NMR: 30.4 (CH_2-C), 35.7, 41.4, 160.9 (pyrazole–3C), 109.21-143.20(Ar-30C), 162.0(C=O,C), 173.5 (immine-C). $C_{36}H_{27}N_7O_3Br_2$ anal % calcd : C 56.47, H 3.52, N 12.81 found C 56.49 H 3.54 N 12.82.

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2-(2-phenyl amino) phenyl methyl -3-[5-(3-nitro phenyl)-1-phenyl-4, 5-dihydro-1*H*-pyrazol-3-yl-amino]-6,8-dibromoquinazolin-4(3*H*)-one 6$_9$

M.P.: 173-174 ^{0}C Yeild: 71 % IR (KBr):3377(NH), 3066, 2861(C-H), 1730(C=O), 1614(C=N), 1541, 1359(-NO_2), 1319(C-N), 615(C-Br). ^{1}H NMR($CDCl_3$): 3.06(d,1Ha), 3.45(d,1Hb), 6.47(t,1Hx), 3.62 (s, 2H, -CH_2),8.17(s, 1H, -N –NH), 9.84 (s, 1H, - NH), 6.42-7.96(m,20H, Ar- H).^{13}C NMR: 31.4 (CH_2-C), 34.7, 41.3, 161.1 (pyrazole–3C), 109.21-143.20(Ar-30C), 162.1(C=O,C), 173.5 (immine-C). $C_{36}H_{27}N_7O_3Br_2$ anal % calcd : C 56.47, H 3.52, N 12.81 found C 56.48 H 3.54 N 12.83.

2-(2-phenyl amino) phenyl methyl -3-[5-(4-nitrophenyl)-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl-amino]-6,8-dibromoquinazolin-4(3*H*)-one 6$_{10}$

M.P.: 191-192 ^{0}C Yeild: 68 % IR(KBr): 3375(NH), 3067, 2857(C-H),1731(C=O), 1615(C=N),1539,1363(-NO_2),1318(C-N), 611(C-Br). ^{1}H NMR($CDCl_3$): 3.07(d,1Ha), 3.43(d,1Hb), 6.45 (t,1Hx), 3.63 (s, 2H, -CH_2),8.16(s, 1H, N –NH), 9.86 (s, 1H, - NH), 6.42-7.96 (m,20H, Ar- H). ^{13}C NMR: 30.5(CH_2-C), 35.6, 41.3, 161.1 (pyrazole–3C), 109.21-143.20(Ar-30C),162.0 (C=O,C), 173.5 (Immine-C). $C_{36}H_{27}N_7O_3Br_2$ anal % calcd : C 56.47, H 3.52, N 12.81 found C 56.48 H 3.53 N 12.82.

2-(2-phenyl amino) phenyl methyl -3-[5-(2-methoxy phenyl)-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl-amino]-6,8-dibromoquinazoline-4(3*H*)-one 6$_{11}$

M.P.: 119-120 ^{0}C Yeild : 74 % IR(KBr):3389 (N-H),3057,2861 (C-H), 1719 (C=O), 1613 (C=N),1319 (C-N), 1243, 1107(C-O-C), 615(C-Br). ^{1}H NMR($CDCl_3$): 3.07(d,1Ha), 3.41(d,1Hb), 6.49(t,1Hx), 3.62 (s, 2H, -CH_2), 3.81(s, 3H, -OCH_3), 8.19(s, 1H, -N –NH), 9.86 (s, 1H, - NH), 6.42-7.96(m,20H, Ar- H). ^{13}C NMR: 30.4(CH_2-C), 35.6, 40.3, 160.9 (pyrazole–3C), 62.3(OCH_3-C) 109.21-143.20(Ar-30C), 162.1(C=O,C),173.5 (immine-C). $C_{37}H_{30}N_6O_2Br_2$ anal % calcd : C 59.20, H 4.00, N 11.20 found C 59.21 H 4.02 N 11.22.

2-(2-phenyl amino) phenyl methyl -3-[5-(4-methoxy phenyl)-1-phenyl-4, 5-dihydro-1*H*-pyrazol-3-yl-amino]-6,8-dibromoquinazolin-4(3*H*)-one 6$_{12}$

M.P.: 139-140 ^{0}C Yeild: 71 % IR(KBr): 3398(N-H), 3057, 2865(C-H),1718(C=O), 1610(C=N),1318(C-N),1239,1105 (C-O-C), 611(C-Br). ^{1}H NMR($CDCl_3$): 3.09(d,1Ha), 3.45(d,1Hb), 6.43 (t,1Hx), 3.63 (s, 2H, -CH_2), 3.80(s, 3H, -OCH_3), 8.17(s, 1H, -N –NH), 9.86 (s, 1H, - NH), 6.42-7.96 (m,20H, Ar- H).^{13}C NMR: 30.4(CH_2-C), 35.7, 40.3, 161.1 (pyrazole-3C), 62.3(OCH_3-C) 109.21-143.20(Ar-30C),162.3 (C=O,C), 173.6(immine-C). $C_{37}H_{30}N_6O_2Br_2$ anal % calcd : C 59.20, H 4.00, N 11.20 found C 59.21 H 4.01 N 11.21.

Determination of Antimicrobial Activity

Disc Diffusion Method

The *in vitro* antimicrobial activity of synthesized compounds was carried out by disc diffusion method [12, 13]. The cup was bore in to the inoculated Petri dish. The cups were made (equidistance) by punching in to the agar surface with sterile cup borer and scooping out the punch part of the agar. After punching a bore, in to these cups were added 0. 01 ml portion of the test compound (0. 01 g dissolved in 10 ml DMF solvent) in solvent with the help of sterile syringe. The solution was allowed to defuse for about an hour in to the medium.

Measurement of the zone of Inhibition

After 2 h, for the diffusion of the substance in the agar medium and the plates were incubated at 37 ^{0}C for 24 h. After incubation period observed the plate for zone of inhibition around the cups. Measure the diameter of each zone in mm.

A solvent control was also run to know the activity of the blank . This was carried out in DMF at concentration of 0. 05 ml in similar manner and the zone of the inhibition of the bacterial growth were measured in diameter and it was 0.0 mm. The standard drugs were also screened under similar condition.

The zone of inhibition measured for anti bacterial activity at two different concentrations 100 and 50 µg/ml, Penicillin-G was used as standard, where as zone of inhibition measured for anti fungal activity also at two different concentrations 20 and 10 µg/ml and Fluconazole was used as a standard.

RESULT AND DISCUSSION

The title compounds of some precursors of quinazolin-4(3H) one incorporating pyrazoline moiety **6**$_{1\text{-}12}$ were synthesized and structure was confirmed by the spectral results. The IR spectra showing strong stretching vibration at 1729 and 1646 cm^{-1} indicates the presence of C=O group of quinazolinone and acetamide respectively. This was further confirming by ^{1}H NMR spectra which showed singlet at δ 2.73 ppm equivalent to three protons of

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acetamide group**(4)**. The acrylamide **5**$_{1\text{-}12}$ which showed CH=CH stretching at1578 cm^{-1} in IR spectrum while ^{1}H NMR spectra showed doublet of these protons at δ 6.81 and δ 8.61 ppm with coupling constant *J* = 16.0-16.6 Hz. The IR spectra of compounds **6**$_{1\text{-}12}$ showed C=O and C=N stretching of quinazolinone at 1725 and 1616 cm^{-1} respectively. The ^{1}H NMR spectra of compounds **6**$_{1\text{-}12}$ indicates that the –CH_2 protons of the pyrazoline ring resonated as a pair of doublet of doublets (Ha and Hb) because of geminal and vicinal coupling. The CH proton appeared as a doublet of doublet (Hx) because of vicinal coupling with the two magnetically nonequivalent protons of methylene group at C-4 of pyrazolin ring. The Ha proton which is cis to Hx resonates up field in the range δ 3.01-3.08 ppm as a doublet of doublet while Hb, the other proton which is trans to Hx resonates downfield in the range of δ 3.45-3.51 ppm as a doublet of doublet. The Hx proton which is vicinal to two methylene protons (Ha and Hb) resonates as a doublet of doublet in the range of δ 6.45-6.53 ppm. In ^{13}C NMR spectra, signals at δ 36.4 ppm, δ 41.1 ppm and δ 161.3 ppm confirms the presence of CH_2, CH and C=N of pyrazoline ring respectively, whereas C=O and C=N signals of quinazolinone ring are appear at around δ 162.2 and δ 173.1 ppm respectively.

Antimicrobial Assay

The *in vitro* antimicrobial screening results of synthesized compounds were recorded in the table **1** and **2**. Potency [14] was calculated from the screening results and compares the strength of synthesized compounds with standard drug.

Potency

Potency P = {antilog(D/B x I) }x M x F

Where,

F = dilution factor M = value of S_H =1 unit / ml = 100 %

I = log S_H / S_L D = (U_H+ U_L) – (S_H+S_L)

B = (U_H - U_L) + (S_H-S_L)

S_H =Zone of inhibition of standard at high concentration.

S_L = Zone of inhibition of standard at low concentration.

U_H =Zone of inhibition of unknown at high concentration.

U_L = Zone of inhibition of unknown at low concentration.

Table: 1 Anti-bacterial activity of compound 6$_{1\text{-}12}$

Compd	R	Zone of inhibition in (mm)											
		S. aureus ATCC12228			***B. subtilis*** ATCC6633			**E.coli** ATCC11778			**Certium** ATCC27957		
		C_H	**C_L**	**Pot%**	**C_H**	**C_L**	**Pot%**	**C_H**	**C_L**	**Pot%**	**C_H**	**C_L**	**Pot %**
6_1	H	13	10	48.23	14	12	50.10	14	12	44.64	13	11	46.83
6_2	2-OH	14	11	50.47	14	11	52.61	16	13	52.46	15	13	52.40
6_3	3-OH	15	12	52.83	15	13	53.35	15	13	47.11	14	12	49.63
6_4	4-OH	14	11	50.47	13	11	47.05	16	13	52.46	15	13	52.40
6_5	**2-Cl**	**20**	**17**	**66.34**	**19**	**16**	**69.56**	17	14	55.02	15	12	55.43
6_6	**3-Cl**	**19**	**16**	**63.39**	**17**	**13**	**63.61**	16	13	52.46	15	13	52.40
6_7	**4-Cl**	**21**	**17**	**70.87**	**20**	**16**	**73.97**	17	14	55.02	14	12	49.63
6_8	2-NO_2	15	12	52.83	14	12	50.10	**22**	**19**	**69.87**	**19**	**16**	**67.47**
6_9	3-NO_2	13	10	48.23	15	12	55.69	**20**	**16**	**65.04**	**18**	**15**	**65.85**
6_{10}	4-NO_2	14	14	50.47	14	11	52.61	**23**	**19**	**74.00**	**20**	**16**	**73.99**
6_{11}	2-OCH_3	15	12	52.83	15	13	53.35	16	13	52.46	15	13	52.40
6_{12}	4-OCH_3	15	12	52.83	15	12	55.69	17	14	55.02	15	12	55.43
PenicillinG		30	25	100	27	21	100	31	25	100	28	23	100

C_H Zone of inhibition at concentration 100 µg/ml, C_L Zone of inhibition at concentration 50 µg/ml, potency of compound(%) as compared to penicillin-G.

Table: 2 Antifungal activity of compound 6$_{1\text{-}12}$

Compd	R	Zone of inhibition in (mm)

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No.		***C.albicans*** ATCC 10231			A.niger ATCC 16404		
		C_H	**C_L**	**Pot%**	**C_H**	**C_L**	**Pot %**
6_1	**H**	**20**	**17**	**76.62**	**20**	**16**	**71.35**
6_2	2-OH	13	11	49.60	12	10	43.08
6_3	3-OH	14	12	52.71	14	12	48.59
6_4	4-OH	14	12	52.71	15	12	54.08
6_5	2-Cl	12	10	46.68	11	09	40.53
6_6	3-Cl	14	12	52.71	12	10	43.08
6_7	4-Cl	13	11	49.60	14	12	48.59
6_8	2-NO_2	15	12	54.34	14	12	48.59
6_9	3-NO_2	15	12	54.34	15	12	54.08
6_{10}	4-NO_2	14	12	52.71	14	12	48.59
6_{11}	**2-OCH_3**	**18**	**16**	**67.26**	**19**	**16**	**66.90**
6_{12}	**4-OCH_3**	**19**	**16**	**72.59**	**19**	**15**	**68.42**
Fluconazole		26	21	100	28	22	100

C_H Zone of inhibition at concentration 20 µg/ml, C_L Zone of inhibition at concentration 10 µg/ml, potency of compound(%) as compared to fluconazole.

CONCLUSION

The title compounds 6, 8-dibromoquinazolin-4(3H) ones derivatives **$6_{1\text{-}12}$** were synthesized by well organized method. The active pharmacophore pyrazoline and quinazolin-4(3H) one present in a newly synthesized compounds possessed good antibacterial and antifungal activity *In Vitro*. The *chloro* group in phenyl nucleus at position R showed very good activity against gram positive bacteria but 4- Cl somewhat more potent than 2-Cl and 3-Cl, while nitro analogues displayed very good activity against gram negative bacteria compared to standard. More over phenyl nucleus, *ortho* and *para* methoxy substituted phenyl precursor showed very good antifungal activity. From these work, we were able to identify a few active molecules which are capable to inhibiting the growth of some bacteria and fungus species *In Vitro*.

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