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ANTIMICROBIAL *IN VITRO* PHARMACOLOGICAL STUDIES OF SOME PYRAZOLYL QUINAZOLIN-4(3H) ONE DERIVATIVES

Gaman G. Barat*

Department of Chemistry, Arts, Science and Commerce College, Pilvai-382850, Gujarat, India.

***Corresponding Author: Dr. Gaman G. Barat**

Department of Chemistry, Arts, Science and Commerce College, Pilvai-382850, Gujarat, India.

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ABSTRACT

Some pyrazolylquinazolin-4(3H) one derivatives were synthesized by the base catalysed cyclisation of acrylamide with 3:5-dinitrophenyl hydrazine hydrate. The overall reaction was carried out by multistep process. The structural confirmation of the synthesized compounds was carried out on the basis of elemental analysis, IR and NMR spectra results. The title compounds were screened for antibacterial and antifungal pharmacological studies *in vitro* by cup plate method. The potency of synthesized compounds focus on the strength compared with standard drug.

KEYWORDS: Antibacterial, Antifungal, Acrylamide, Quinazolin-4(3H) one.

INTRODUCTION

Heterocyclic derivatives are pharmaceutically very important class of compounds which were developed better result in the medicinal chemistry. Quinazolin-4(3H) one and its nitrogen containing precursors had diversified biological properties. Quinazolin-4(3H) one with its pyrazoline analogs has extensively used as anti-inflammatory, anticancer].[1,2,3] Moreover, a large number of Quinazolin-4(3H) ones derivatives have been reported as a potential against alziemer disease and analgesics agents.[4] Quinazolin-4(3H) one with pyrazole moiety have been reported as a very good antifungal and antimicrobial agents.[5,6] In addition triquinazolinone derivatives and quinazolin-4(3H) one bearing quinoline moiety reported to anti-hyperglycemic[7] activity and HIV-1 integrate inhibitors.[8]

Pyrazoline derivatives of quinazolin-4(3H) one have important therapeutic properties, among many derivatives are biologically active scaffold and important constituent of many pharmaceutical product and used as a Cox-II inhibitor.[9,10] Some precursor of quinazolin-4(3H) one has reported to anti convulsant activity and CNS depressant agent.[11,12]

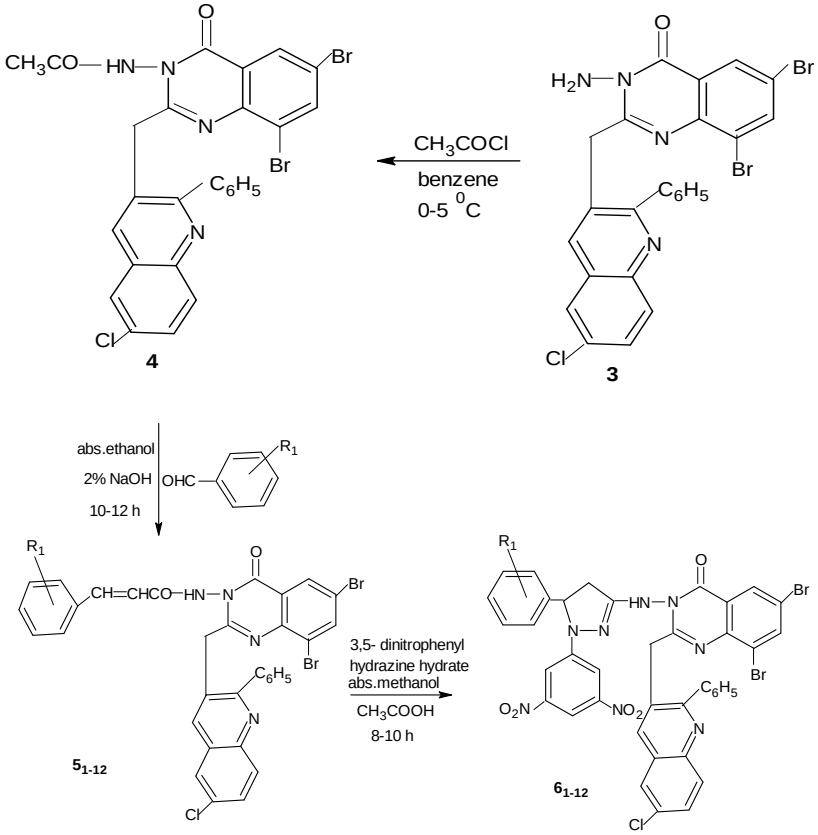
Encourage by the wide spectrum of therapeutic activities exhibited and literature survey of quinazoline derivatives revealed that in this study, we have synthesized quinazolin-4(3H) one incorporating two heterocyclic moieties pyrazoline at C-3 and quinoline at C-2 respectively and studied its antibacterial and antifungal activities. The potency (Edwin and Marion 1945) of these compounds was calculated and compare with standard drugs to observe the strength of these compounds.

MATERIAL AND METHOD

General Instrumentation

The reagent grade chemicals were purchased from commercial sources and further purified before use. The melting points of all synthesized compounds were taken in open capillary tube and are uncorrected. The purities of all synthesized compounds were checked by TLC on Merck silica gel 60 F 254 using toluene: ethyl acetate (8:2) as mobile phase and spots were visualized under UV radiation. The IR spectra of the synthesized compounds were recorded on Perkin-Elmer 1300 FTIR spectrophotometer using KBr pellets and frequencies are recorded in cm^{-1}. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker Advance II 400 NMR spectrometer using deutero $CDCl_3$ as a solvent. The chemical shifts were reported in (δ ppm) downfield using tetra methyl silane as internal standard. Elemental analyses of newly synthesized compounds were carried out on Carlo Ebra 1108 analyzer. Microanalysis of compounds was within ±0.4% of theoretical values and the spectral data (Elemental analysis, IR, and NMR) were compatible with the assigned structures. 3-(6-chloro-2-phenylquinolin) acetyl chloride **1** was synthesized by literature procedure.[13]

Scheme I Synthetic Pathway for Target Molecule



R_1 = H, 2-Cl, 3-Cl, 4-Cl, 2-OH, 3-OH, 4-OH, 2-NO_2, 3-NO_2, 4-NO_2, 2-OCH_3, 4-OCH_3

EXPERIMENTAL SECTION

2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl–6,8-dibromo-3,1-benzoxazin-4(3*H*) 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^{0}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^{0}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 recrystalised from methanol.

M.P.:162-163^{0}C.Yeild: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 $C_{24}H_{13}N_2O_2Br_2Cl$ Calcd; C, 51.75; H, 2.33; N, 5.03; Found; C, 51.77; H, 2.34; N, 5.05.

3-Amino-2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl–6,8-dibromoquinazolin–4(3*H*) one 3

To a mixture of 2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl–6,8-dibromo-3,1-benzoxazin-4(3*H*) 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^{0}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 recrystalized from ethanol.

M.P.**:** 145^{0}C. Yeild**:** 74% IR(KBr): 3407(NH), 3069, 2863(C-H), 1718(C=O), 1614(C=N), 1325(C-N), 779(C-Cl), 580(C-Br). ^{1}HNMR($CDCl_3$)**:** 2.11(s, 2H, -N-NH_2), 6.42-7.96(m, 11H, Ar-H), 2.62(s, 2H, -CH_2). Anal. (%) for $C_{24}H_{15}N_4OBr_2Cl$ Calcd; C, 50.48; H, 2.62; N,9.81; Found; C, 50.49; H, 2.64; N, 9.83.

2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl-3-acetamido-6,8-dibromoquinazolin-4(3*H*) one 4

To a solution of 3-Amino-2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl–6,8-dibromo quinazolin –4(3*H*) 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^{0}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 recrystalized from methanol.

M.P.**:** 173^{0}C. Yeild**:** 69% IR(KBr): 3407(NH), 3063,2864(C-H),1721(C=O), 1640(C=O of –$COCH_3$), 1323(C-N), 774(C-Cl), 576(C-I). ^{1}H-NMR($CDCl_3$)**:** 2.12(s, 1H, -N-NH-), 6.42- 7.96 (m, 11H, Ar-H), 2.73(s, 3H, -$COCH_3$), 2.63(s, 2H, -CH_2). Anal. (%) for $C_{26}H_{17}N_4O_2Br_2Cl$ Calcd; C, 50.93; H, 2.77; N, 9.14; Found; C, 50.94; H, 2.79; N, 9.16.

2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl-3-substituted phenyl acryl amido-6,8-dibromo quinazolin-4(3*H*)-one 5_1

To a solution of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl]methyl-3-acetamido-6,8-dibromo quinazolin-4(3*H*)-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 recrystalized from methanol.

M.P.**:** 151^{0}C. Yeild**:** 74% IR(KBr): 3409(NH), 3062, 2859(C-H), 1719(C =O), 1641(C=O of –$COCH_3$), 1578 (CH=CH), 1318(C-N), 778(C-Cl), 579(C-Br).^{1}H-NMR($CDCl_3$)**:** 2.11(s, 1H, -N-NH), 6.42- 7.96(m, 16H, Ar-H), 2.63(s, 2H, -CH_2), 6.81(d, 1H, COCH=), 8.61(d, 1H, =CH-Ar). Anal; (%) $C_{33}H_{21}N_4O_2Br_2Cl$ Calcd; C, 56.53; H, 2.99; N, 7.99; Found; C, 56.54; H, 3.01; N, 8.02.

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

2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3–[1-(3,5-dinitrophenyl)-5-phenyl-4, 5-dihydro-1*H*-pyrazol-3-yl amino]-6,8-dibromoquinazolin-4(3*H*)-one 6_1

To a solution of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-substituted phenyl acryl amido-6, 8-dibromoquinazolin-4(3*H*)-one (7.005 g, 0.01 mol) in methanol, add 3:5-dinitrophenyl hydrazine hydrate (99%) (4.36g, 0.02mol) and few drops of glacial acetic acid. The reaction mixture was refluxed for 8-10 h., distilled the excess methanol and cooled. Thus the solid separated was filtered, washed with water and recrystalized from methanol.

M.P.**:**147-148^{0}C. Yeild**:** 76% IR(KBr):3372(N-H),3063,2858(C-H),1728(C=O),1616(C=N), 1566, 1361(-NO_2),1319 (C-N),779(C-Cl), 581(C-Br). ^{1}HNMR($CDCl_3$): 2.13 (d,1H,=N-NH), 3.62 (s,2H,-CH_2),3.06 (d,1Ha), 3.45 (d,1Hb), 6.51(t,1Hx), 6.42-7.96 (m,19H,Ar-H). ^{13}C NMR: 31.4(-CH_2), 36.5, 41.1, 161.2(pyrazol-C), 162.2 (>C=O), 173.1(immine aromatic-C) 109.21-143.20(aromatic-33C). Anal; (%) $C_{39}H_{25}N_8O_5Br_2Cl$ Calcd; C, 53.15; H, 2.83; N,12.72; Found; C, 53.17; H, 2.84; N, 12.73.

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

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

M.P.**:** 173-174^{0}C. Yeild**:** 74% IR(KBr):3368(N-H),3062,2860(C-H),1727(C=O),1616(C=N), 1564, 1362(-NO_2) 1318(C-N), 780 (C-Cl), 574 (C-Br). ^{1}H NMR($CDCl_3$): 2.12(d,1H,=N-NH), 3.63(s,2H,-CH_2), 3.05 (d,1Ha), 3.47(d,1Hb), 6.52(t,1Hx), 6.42-7.96(m,18H,Ar-H).^{13}C NMR: 31.3(-CH_2), 36.4, 41.6, 160.9 (immine pyrazol-C),162.2 (>C=O),173.1(immine aromatic-C), 109.21-143.20(aromatic-33C). Anal; (%) $C_{39}H_{24}N_8O_5Br_2Cl_2$ Calcd; C, 51.14; H, 2.62; N,12.24; Found; C, 51.16; H, 2.63; N, 12.25.

2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3–[5-(3-chloro) phenyl-1-(3,5-dinitrophenyl)-4,5-dihydro-1*H*-pyrazol-3-yl amino]-6,8-dibromoquinazolin-4(3*H*)-one 6_3

M.P.**:** 162-163^{0}C. Yeild**:** 78% IR(KBr): 3372(N-H),3061, 2859(C-H),1729 (C=O),1616(C=N), 1566, 1361(-NO_2),1317(C-N),782 (C-Cl),575 (C-Br). ^{1}HNMR($CDCl_3$):2.13(d,1H,=N-NH), 3.63 (s,2H,-CH_2), 3.06 (d,1Ha), 3.48 (d,1Hb), 6.54(t,1Hx), 6.42-7.96(m,18H,Ar-H). ^{13}C NMR: 31.6(-CH_2), 36.7, 41.3, 161.1 (immine pyrazol-C),162.1(>C=O),173.1(immine aromatic-C), 109.21-143.20(aromatic-33C). Anal; (%) $C_{39}H_{24}N_8O_5Br_2Cl_2$ Calcd; C, 51.14; H, 2.62; N,12.24; Found; C, 51.15; H, 2.64; N, 12.25.

2-[3-(6-chloro-2-phenyl) quinolin-3-yl] 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_4

M.P.**:**178-179^{0}C. Yeild**:** 76% IR(KBr):3369(N-H),3062,2861(C-H),1727(C=O),1616(C=N), 1566, 1361(-NO_2),1319(C-N), 781(C-Cl),578(C-Br). ^{1}HNMR ($CDCl_3$): 2.13 (d,1H,=N-NH), 3.63(s,2H,-CH_2), 3.07 (d,1Ha), 3.48(d,1Hb), 6.55(t,1Hx), 6.42-7.96(m,18H,Ar-H).^{13}C NMR: 31.5(-CH_2), 36.3, 41.5, 161.2 (immine pyrazol-C),162.2(>C=O),173.1(immine aromatic-C), 109.21-143.20(aromatic-33C). Anal; (%) $C_{39}H_{24}N_8O_5Br_2Cl_2$ Calcd; C, 51.14; H, 2.62; N,12.24; Found; C, 51.16; H, 2.63; N, 12.26.

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

M.P.**:**155-156^{0}C.Yeild**:** 73% IR(KBr): 3543(O-H),3369(N-H),3063,2861(C-H),1729(C=O), 1616(C=N), 1565, 1361(-NO_2), 1318(C-N), 780 (C-Cl),576 (C-Br). ^{1}H NMR ($CDCl_3$): 2.12 (d,1H,=N-NH), 3.62(s,2H,-CH_2), 3.06(d,1Ha), 3.48(d,1Hb),6.54(t,1Hx), 6.42-7.96(m,18H,Ar-H),10.38(s,1H,-OH). ^{13}C NMR: 31.4(-CH_2), 36.4, 41.3, 161.1(pyrazol-C), 162.1(>C=O), 173.1 (immine aromatic-C) 109.21-143.20(aromatic-33C). Anal; (%) $C_{39}H_{25}N_8O_6Br_2Cl$ Calcd; C, 52.20; H, 2.78; N,12.49; Found; C, 52.21; H, 2.79; N, 12.51.

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

M.P.**:** 142-143^{0}C. Yeild**:** 79% IR(KBr): 3547(O-H), 3371(N-H), 3061,2863(C-H), 1729(C=O), 1616 (C=N), 1566, 1361(-NO_2),1319(C-N), 781(C-Cl),579(C-Br). ^{1}H NMR($CDCl_3$): 2.13 (d,1H,=N-NH),3.63 (s,2H,-CH_2), 3.07(d,1Ha), 3.45(d,1Hb),6.52(t,1Hx), 6.42-7.96(m,18H,Ar-H), 10.39(s,1H,-OH). ^{13}C NMR: 31.5(-

CH_2), 36.4, 41.6, 161.2 (immine pyrazol-C), 162.2(>C=O), 173.1(immine aromatic-C), 109.21-143.20 (aromatic-33C). Anal; (%) $C_{39}H_{25}N_8O_6Br_2Cl$ Calcd; C, 52.20; H, 2.78; N,12.49; Found; C, 52.21; H, 2.79; N, 12.51.

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

M.P.: 160-161^{0}C. Yield: 72% IR(KBr): 3546(O-H), 3369(N-H), 3062,2861 (C-H),1727(C=O), 1616 (C=N), 1566, 1361(-NO_2),1319(C-N), 778(C-Cl), 576(C-Br). ^{1}H NMR($CDCl_3$): 2.13 (d,1H,=N-NH),3.62 (s,2H,-CH_2), 3.06(d,1Ha), 3.46(d,1Hb),6.52(t,1Hx), 6.42-7.96(m,18H,Ar-H), 10.38(s,1H,-OH). ^{13}C NMR: 31.4(-CH_2), 36.5, 41.4, 161.1(immine pyrazol-C), 162.1(>C=O), 173.3(immine aromatic-C), 109.21-143.20(aromatic-33C). Anal; (%) $C_{39}H_{25}N_8O_6Br_2Cl$ Calcd; C, 52.20; H, 2.78; N,12.49; Found; C, 52.21; H, 2.79; N, 12.51.

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

M.P.**:** 191-192^{0}C. Yeild**:** 74% IR(KBr): 3375(N-H), 3063,2859(C-H),1729(C=O),1616(C=N), 1567, 1361(-NO_2), 1317(C-N),783(C-Cl), 579(C-Br).^{1}H NMR($CDCl_3$): 2.13(d,1H,=N-NH), 3.62 (s,2H,-CH_2), 3.07(d,1Ha), 3.46(d,1Hb), 6.53(t,1Hx),6.42-7.96(m,18H,Ar-H). ^{13}CNMR:31.5(-CH_2), 36.3, 41.7, 161.4 (immine pyrazol-C), 162.2(>C=O),173.1(immine aromatic-C), 109.21-143.20 (aromatic-33C). Anal; (%) $C_{39}H_{24}N_9O_7Br_2Cl$ Calcd; C, 50.56; H, 2.59; N,13.61; Found; C, 50.58; H, 2.60; N, 13.63.

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

M.P.**:** 182-183^{0}C.Yeild**:** 71% IR(KBr): 3371(NH),3062,2857(C-H),1725(C=O),1616 (C=N), 1566, 1361(-NO_2),1319(C-N), 779(C-Cl),577(C-Br). ^{1}H NMR($CDCl_3$): 2.13(d,1H,=N-NH),3.63 (s,2H,-CH_2), 3.06(d,1Ha),3.46(d,1Hb), 6.52(t,1Hx), 6.42-7.96 (m,18H,Ar-H).^{13}C NMR:31.4(-CH_2), 36.5, 41.6,161.2 (immine pyrazol-C), 162.1(>C=O),172.9(immine aromatic-C), 109.21-143.20 (aromatic-33C). Anal; (%) $C_{39}H_{24}N_9O_7Br_2Cl$ Calcd; C, 50.56; H, 2.59; N,13.61; Found; C, 50.57; H, 2.61; N, 13.62.

2-[3-(6-chloro-2-phenyl) quinolin-3-yl]methyl-3–[5-(4-nitro)phenyl-1-(3,5-dinitro phenyl)-4,5-dihydro-1*H*-pyrazol-3-yl amino]-6,8-dibromoquinazolin-4(3*H*)-one 6_{10}

M.P.**:** 204-205^{0}C.Yeild**:** 77% IR (KBr):3373(NH), 3061, 2859(C-H), 1726(C=O), 1616(C=N), 1565, 1361(-NO_2), 1319(C-N), 781(C-Cl), 576(C-Br). ^{1}H NMR($CDCl_3$):2.13(d,1H,=N-NH), 3.63 (s,2H,-CH_2), 3.07(d,1Ha), 3.46(d,1Hb),6.53(t,1Hx),6.42-7.96(m,18H,Ar-H).^{13}CNMR: 31.5(-CH_2), 36.3, 41.5, 161.1 (immine pyrazol-C),162.3(>C=O),173.1(immine aromatic-C), 109.21-143.20 (aromatic-33C). Anal; (%) $C_{39}H_{24}N_9O_7Br_2Cl$ Calcd; C, 50.56; H, 2.59; N,13.61; Found; C, 50.57; H, 2.60; N, 13.62.

2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3–[5-(2-methoxy)phenyl-1-(3,5-dinitro phenyl)-4,5-dihydro-1*H*-pyrazol-3-yl amino]-6,8-dibromoquinazolin-4(3*H*)-one 6_{11}

M.P.**:**167-168^{0}C. Yeild**:** 75% IR(KBr): 3368(N-H), 3063,2861 (C-H), 1729 (C=O), 1617 (C=N), 1566,1361(-NO_2),1319 (C-N),1244, 1109(C-O-C),779(C-Cl), 578(C-Br). ^{1}H NMR($CDCl_3$): 2.13 (d,1H,=N-NH), 3.63(s,2H,-CH_2), 3.07(d,1Ha), 3.46(d,1Hb), 6.53(t,1Hx), 6.42-7.96 (m,18H,Ar-H), 3.83(s,3H,-OCH_3).^{13}C NMR:31.5(-CH_2), 36.4,41.5,161.1(imminepyrazol-C), 162.0(>C=O), 173.1 (immine aromatic-C),58.2(-OCH_3), 109.21-143.20(aromatic-33C). Anal; (%) $C_{40}H_{27}N_8O_6Br_2Cl$ Calcd; C, 52.71; H, 2.96; N,12.30; Found; C, 52.72; H, 2.98; N, 12.31.

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

M.P.**:**175-176^{0}C. Yeild**:**72% IR(KBr): 3371(N-H), 3063, 2861(C-H), 1728(C=O), 1616 (C=N), 1566,1361(-NO_2), 1317(C-N),1242,1108(C-O-C),778(C-Cl),577(C-Br). ^{1}H NMR ($CDCl_3$):2.13 (d,1H,=N-NH), 3.63(s,2H,-CH_2), 3.06(d,1Ha), 3.47(d,1Hb),6.53(t,1Hx),6.42-7.96(m,18H,Ar-H), 3.81(s,3H,-OCH_3).^{13}C NMR:31.5(-CH_2), 36.5,41.6,161.3(imminepyrazol-C),162.1(>C=O), 173.2 (immine aromatic-C),58.1(-OCH_3),109.21-143.20(aromatic-33C). Anal; (%) $C_{40}H_{27}N_8O_6Br_2Cl$ Calcd; C, 52.71; H, 2.96; N,12.30; Found; C, 52.73; H, 2.98; N, 12.32.

Determination of Antimicrobial Activity

Cup plate Method

The *in vitro* antimicrobial activity of synthesized compounds was carried out by cup-plate method.[14,15] 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.

Bacterial and Plant Pathogenic Stains Used

The *in vitro* antimicrobial activity of synthesized compounds was screened against two gram positive bacteria(Staphylococcus aureus ATCC 9144 and Bacillus Subtilis ATCC 6633) and two gram negative bacteria(Escherichia coli ATCC 25922 and Pseudomonas

aeruginosa ATCC 9027), whereas two plant pathogens for antifungal activity was tested against Candida albicans ATCC 10231 and Aspergillus niger ATCC 6275.

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 37^0C 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 compound 6, 8-dibromoquinazolin-4(3H) one incorporating pyrazoline and quinoline moieties **$6_{1\text{-}12}$** 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 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 6a-l indicates that the $–CH_2$ protons of the pyrazoline ring resonated as a pair of doublet of doublets (H_a and H_b) 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.[16,17,18,19]

Antimicrobial Assay

The *in vitro* antimicrobial screening results of synthesized compounds were recorded in the table **1** and **2**. Potency[20] was calculated from the screening results and compares the strength of synthesized compounds with standard drug.

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

Compd No.	R_1	Zone of inhibition in (mm)											
		S. aureus ATCC9144			***B. subtilis*** ATCC6633			E.coli ATCC25922			P.aeruginosa ATCC9027		
		C_H	C_L	Pot%	C_H	C_L	Pot%	C_H	C_L	Pot%	C_H	C_L	Pot %
6_1	H	15	12	52.44	15	13	54.16	14	11	54.16	15	12	52.44
6_2	**2-Cl**	**20**	**18**	**72.52**	**20**	**17**	**73.58**	15	12	52.44	16	13	59.98
6_3	**3-Cl**	**19**	**17**	**68.41**	**19**	**16**	**69.92**	15	13	54.16	15	13	54.16
6_4	**4-Cl**	**22**	**19**	**81.51**	**23**	**20**	**85.76**	16	14	57.41	16	14	57.41
6_5	2-OH	13	11	49.15	15	13	54.16	13	11	49.15	15	12	52.44
6_6	3-OH	12	10	46.40	14	12	51.09	16	14	57.41	15	13	54.16
6_7	4-OH	15	13	54.16	16	14	57.41	14	11	54.16	16	14	57.41
6_8	2-NO_2	14	11	54.16	16	14	57.41	**19**	**16**	**69.92**	**21**	**19**	**76.90**
6_9	3-NO_2	15	12	52.44	15	13	54.16	**18**	**16**	**64.52**	**18**	**15**	**66.29**
6_{10}	4-NO_2	15	13	54.16	16	14	57.41	**21**	**18**	**77.45**	**22**	**19**	**81.51**
6_{11}	2-OCH_3	13	11	49.15	15	13	54.16	15	13	54.16	15	13	54.16
6_{12}	4-OCH_3	14	11	54.16	16	13	59.98	16	14	57.41	16	13	59.98
PenicillinG		27	22	100	27	22	100	27	22	100	27	22	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_{1-12}

Compd No.	R_1	Zone of inhibition in (mm)					
		C.albicans ATCC 10231			A.niger ATCC 6275		
		C_H	C_L	Pot%	C_H	C_L	Pot %
6_1	H	**20**	**16**	**80.48**	**21**	**18**	**84.05**
6_2	2-Cl	14	12	56.03	13	11	52.86
6_3	3-Cl	13	11	52.86	14	12	56.03
6_4	4-Cl	14	12	56.03	15	13	59.36
6_5	2-OH	13	11	52.86	13	11	52.86
6_6	3-OH	14	12	56.03	14	12	56.03
6_7	4-OH	15	13	59.36	15	13	59.36
6_8	2-NO_2	12	10	49.89	13	11	52.86
6_9	3-NO_2	13	11	52.86	14	12	56.03
6_{10}	4-NO_2	14	12	56.03	15	13	59.36
6_{11}	2-OCH_3	**17**	**15**	**66.67**	**17**	**14**	**68.92**
6_{12}	4-OCH_3	**18**	**16**	**70.63**	**19**	**17**	**74.85**
Fluconazole		25	21	100	25	21	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 compound 6, 8-dibromoquinazolin-4(3H) ones derivatives **6_{1-12}** were synthesized by well organized method. The active pharmacophore pyrazoline and quinoline present in a newly synthesized compounds possessed good antibacterial and antifungal activity *in vitro*. The chloro group in phenyl nucleus on *ortho, meta* and *para* position showed very good activity against gram positive bacteria while nitro analogues displayed very good activity against gram negative bacteria compared to standard. More over phenyl nucleus, *ortho* and *para* methoxy substituted phenyl compounds 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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