SYNTHESIS OF CHALCONE CONTAINING PYRAZOLYL
QUINAZOLIN-4(3H) ONES AND THEIR IN VITRO
MICROBIAL STUDIES

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ABSTRACT

A series of 2-[2-(2, 6-dichlorophenyl)amino]phenyl methyl-3-[(5-substituted phenyl-1-phenyl)-5-
hydro-1H-pyrazol-3-yl-amino]-6,8-dibromoquinazolin-4(3H)-ones were synthesized from 2-[2-(2, 6-
dichlorophenyl)amino]phenyl methyl-3-substituted phenyl acryl amido-6,8-dibromoquinazolin-4(3H)-
ones with phenylhydrazine hydrate in the presence of glacial acetic acid. Their chemical structures were
assigned by spectral analysis (FT-IR, 1H NMR, 13C NMR). All the compounds were screened for in vitro
antimicrobial activity and some of them exhibited promising results against S. aureus, B. subtilis, E. coli,
C. Certium, A. niger and C. albicans.

Key words: Quinazoline, Pyrazoline, Chalcone, Antibacterial, Antifungal.

INTRODUCTION

Quinazolin-4(3H)-one is a versatile lead molecule for the design of potential
bioactive agents, 2, 3-disubstituted quinazolin-4(3H)-ones were reported to possess anti-
HIV1-3, anticancer4-6 antibacterial7, antifungal8, analgesics9, anti-inflammatory agent10,
antiparasitic11, enzyme inhibitory agent12 and rheumatic arthritis13. Several scientists
elicited that quinazolinone system possessed variable sites at C-2 and C-3 positions,
which can be modified by the introduction of different heterocyclic moieties viz. pyrazol and
oxazole to yield potential anticonvulsant agents14,15. In order to see the effect of
incorporation of pyrazoline moiety in quanazoline nucleus at C-3 position on convulsions
produced by maximal electro shock in albino rats. Keeping this observation in view, we
have continued our previous work16-20 and synthesized new series of quinazolinonyl
chalones and quinazolinonyl pyrazolines to get more active compounds.

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A classical synthesis of these compounds involves base-catalyzed condensation of quinazolinone and aromatic aldehyde to give chalcone, which undergoes a subsequent cyclisation reaction with phenylhydrazine affording 3-pyrazoline\textsuperscript{21}.

**EXPERIMENTAL**

Melting points of all synthesized compounds were taken in open capillaries and are uncorrected. IR spectra were recorded on Perkin-Elmer 1300 FTIR spectrophotometer. $^1$H NMR and $^{13}$C NMR spectra were recorded in CDCl$_3$ using TMS as internal standard on a Bruker spectrometer at 400 MHz and 75 MHz, respectively (chemical shift in δ ppm). Purity of all compounds was checked by TLC on silica gel G plates and the spots were located by keeping the plates in iodine vapour. All the compounds were analyzed for carbon, hydrogen and nitrogen and the results were within ± 0.04% of the calculated values. The compounds (1) to (3) were synthesized by reported methods\textsuperscript{10,16-20,28}.

2-[2-(2,6-Dichlorophenyl)amino]phenylmethyl-3-acetamido-6,8-dibromoquinazolin-4(3H)-one (4)

To a solution of 3-amino 2-[2-, 6-dichlorophenyl)amino]phenyl methyl-6,8-di bromoquinazolin-4(3H)-one (5.41 g, 0.01 mol) in dry benzene (50 mL, acetyl chloride (0.785 g, 0.01 mol) was added drop by drop at 0-5°C for 1 h with constant stirring. After completion of addition, the reaction mixture was kept over night. 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.: 193-195°C, Yield: 69 %. Elemental analysis: % C = 47.41 (47.36), % H = 2.83 (2.74), % N = 9.71 (9.60). IR (KBr): (cm$^{-1}$) 3407 (NH), 3062, 2859 (C-H), 1727 (C=O), 1645(C=O of –COOCH$_3$), 1320 (C-N), 783 (C-Cl), 613 (C-Br). $^1$H-NMR: δ ppm ; 9.78 (s, 1H, -NH-), 2.12 (s, 1H, -N-NH-), 6.34-7.96 (m, 9H, Ar-H), 2.70 (s, 3H, -CH$_3$), 2.71 (s, 2H, -CH$_2$).

2-[2-(2,6-Dichlorophenyl)amino]phenylmethyl-3-(phenyl acrylamido)-6,8-dibromoquinazolin-4(3H)-one (5a)

A solution of 2-[2-(2,6-dichlorophenyl)amino]phenyl methyl-3-acetamido-6,8-dibromoquinazolin-4(3H)-one (5.82 g, 0.01 mol) in absolute ethanol (50 mL) and 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 and recrystalized from methanol, Yield: 71 %. Elemental analysis: % C = 53.71 (53.66), % H = 3.02 (2.98), % N = 8.41 (8.34). IR (KBr) (cm$^{-1}$); 3411(NH), 3061, 2852 (C-H), 1719 (C=O), 1653 (C=O of –COCH$_3$), 1576 (CH=CH), 1316 (C-N), 779 (C-Cl), 611 (C-Br). $^1$H NMR; δ ppm; 9.78 (s, 1H, -NH-), 2.11 (s,
The remaining compounds (5b-m) were prepared by the similar method.

**2-[2-(2,6-Dichlorophenyl)amino]phenyl methyl-3-(1,5-diphenyl-5-hydro-1H-pyrazol-3-yl amino)-6,8-dibromo quinazolin-4(3H)-one (6a)**

To a solution of 2-[2-(2,6-dichlorophenyl)amino]phenyl methyl-3-phenyl acrylamido)-6,8-dibromoquinazolin-4(3H)-one (6.71 g, 0.01 mol) in methanol, phenylhydrazine hydrate (99%) (2.5-6.0 g, 0.02 mol) and few drops of glacial acetic acid were added. The reaction mixture was refluxed for 8-10 h., distilled and cooled. The separated solid was filtered, washed and recrystallized from methanol. IR (KBr) (cm⁻¹); 3413 (N-H), 3092, 2855 (C-H), 1732 (C = O), 1613 (C = N), 1317 (C-N), 782 (C-Cl), 612 (C-Br). ¹H NMR: δ ppm; 9.78 (S, 1H, -NH), 8.34 (S, 1H, -N-NH), 3.61 (S, 2H, -CH₂), 3.06 (d, 1 Ha), 48 (d, 1Hb), 6.53 (t, 1Hx), 6.43-7.95 (m, 19H, Ar-H). ¹³C NMR: 30.7 (CH₂), 36.3, 42.2, 161.3 (pyra-C), 162.3 (> C = O), 173.2 (immine arom-C) 109.1-143.2 (arom-30C).

The remaining compounds (6b-m) were prepared by the similar method.

**5b: 2-[2-(2,6-Dichlorophenyl)amino]phenyl methyl-3-[2-hydroxy) phenyl acryl amido]-6,8-dibromoquinazolin-4(3H)-one**

IR (KBr) : (cm⁻¹): 3547 (-OH), 3411 (NH), 3061, 2852 (C-H), 1719 (C=O), 1617 (C=O) of –COCH₃, 1566 (CH=CH), 1317 (C-N), 779 (C-Cl), 613 (C-Br). ¹H NMR : δ ppm; 9.78 (s, 1H, -NH-), 2.11 (s, 1H, -N-NH), 6.34-7.91 (m, 13 H, Ar-H), 3.63 (s, 2H, -CH₂), 6.80 (d, 1H, COCH=), 8.62 (d, 1H, =CH-Ar), 10.34 (s, 1H, -OH). ¹³C NMR: 30.5 (-CH₂), 36.4, 1.6 (CH=CH), 160.8 (immine –C), 162.1 (> C = O), 173.1 (immine arom-C) 109.3-143.4 (arom-24C).

**5c: 2-[2-(2,6-Dichlorophenyl)amino]phenyl methyl-3-[3-hydroxy) phenyl acryl amido]-6,8-dibromoquinazolin-4(3H)-one**

IR (KBr) : (cm⁻¹): 3551 (-OH), 3413 (NH), 3071, 2852 (C-H), 1729 (C=O), 1613 (C=O) of –COCH₃, 1575 (CH=CH), 1317 (C-N), 780 (C-Cl), 616 (C-Br). ¹H NMR : δ ppm; 9.77 (s, 1H, -NH-), 2.17 (s, 1H, -N-NH), 6.34-7.91 (m, 13 H, Ar-H), 3.61 (s, 2H, -CH₂), 6.82 (d, 1H, COCH=), 8.61 (d, 1H, =CH-Ar), 10.38 (s, 1H, -OH). ¹³C NMR: 30.5 (-CH₂), 37.5, 42.9 (CH=CH), 161.2 (immine –C), 162.1 (> C = O), 173.2 (immine arom-C) 109.21-143.27 (arom-24C).
(5d): 2-[2-(2,6-Dichlorophenyl)amino]phenyl methyl-3-[(4-hydroxy) phenyl acrylamido]-6,8-dibromoquinazolin-4(3H)-one

IR (KBr) : (cm⁻¹): 3557 (-OH), 3367 (NH), 3064, 2852 (C-H), 1719 (C=O), 1611 (C=O of –COCH₃), 1572 (CH=CH), 1319 (C-N), 780 (C-Cl), 615 (C-Br). ¹H NMR : 9.78 (s, 1H, -NH), 2.11 (s, 1H, -N-NH), 6.34-7.91 (m, 13 H, Ar-H), 3.65 (s, 2H, -CH₂), 6.80 (d, 1H, COCH=), 8.62 (d, 1H, =CH-Ar), 10.35 (s, 1H, -OH). ¹³C NMR: 30.6 (-CH₂), 36.5, 41.6 (CH=CH), 161.3 (immine –C), 162.1 (> C = O), 173.1 (immine arom-C) 108.77-143.23 (arom-24C).

(5e): 2-[2-(2,6-Dichlorophenyl)amino]phenyl methyl-3-[(2-hydroxy) phenyl acrylamido]-6,8-dibromoquinazolin-4(3H)-one

IR (KBr) : (cm⁻¹); 3365 (NH), 3061, 2857 (C-H), 1729 (C=O), 1613 (C=O of –COCH₃), 1578 (CH=CH), 1314 (C-N), 781 (C-Cl), 617 (C-Br). ¹H NMR : δ ppm; 9.78 (s, 1H, -NH), 2.13 (s, 1H, -N-NH), 6.38-7.91 (m, 13 H, Ar-H), 3.63 (s, 2H, -CH₂), 6.82 (d, 1H, COCH=), 8.61 (d, 1H, =CH-Ar), ¹³C NMR: 29.6 (-CH₂), 36.0, 41.5 (CH=CH), 160.9 (immine –C), 162.3 (> C = O), 173.1 (immine arom-C) 109.22-143.15 (arom-24C).

(5f): 2-[2-(2,6-Dichlorophenyl)amino]phenyl methyl-3-[(3-hydroxy) phenyl acrylamido]-6,8-dibromoquinazolin-4(3H)-one

IR (KBr) : (cm⁻¹); 3413 (NH), 3067, 2853 (C-H), 1729 (C=O), 1615 (C=O of –COCH₃), 1578 (CH=CH), 1318 (C-N), 779 (C-Cl), 616 (C-Br). ¹H NMR : δ ppm; 9.79 (s, 1H, -NH), 2.11 (s, 1H, -N-NH), 6.39-7.93 (m, 13 H, Ar-H), 3.63 (s, 2H, -CH₂), 6.80 (d, 1H, COCH=), 8.60 (d, 1H, =CH-Ar), ¹³C NMR: 31.3 (-CH₂), 36.5, 41.1 (CH=CH), 161.3 (immine –C), 162.1 (> C = O), 173.2 (immine arom-C) 109.13-143.17 (arom-24C).

(5g): 2-[2-(2,6-Dichlorophenyl)amino]phenyl methyl-3-[(4-hydroxy) phenyl acrylamido]-6,8-dibromoquinazolin-4(3H)-one

IR (KBr) : (cm⁻¹) 3369 (NH), 3061, 2859 (C-H), 1731 (C=O), 1615 (C=O of –COCH₃), 1576 (CH=CH), 1316 (C-N), 782 (C-Cl), 618 (C-Br). ¹H NMR : 9.78 (s, 1H, -NH-), 2.11 (s, 1H, -N-NH), 6.39-7.94 (m, 13 H, Ar-H), 3.65 (s, 2H, -CH₂), 6.83 (d, 1H, COCH=), 8.62 (d, 1H, =CH-Ar), ¹³C NMR: 30.6 (-CH₂), 36.2, 41.7 (CH=CH), 161.2 (immine –C), 162.0 (> C = O), 172.8 (immine arom-C) 109.17-143.21 (arom-24C).

(5h): 2-[2-(2,6-Dichlorophenyl)amino]phenyl methyl-3-[(4-hydroxy) phenyl acrylamido]-6,8-dibromoquinazolin-4(3H)-one

IR (KBr) : (cm⁻¹) 3416 (NH), 3066, 2856 (C-H), 1727 (C=O), 1617 (C=O of –COCH₃),
1578 (CH=CH), 1319 (C-N), 1567, 1363 (NO2) 779 (C-Cl), 617 (C-Br). ^1H NMR : δ ppm; 9.79 (s, 1H, -NH-), 2.15 (s, 1H, -N-NH), 6.39-7.93 (m, 13 H, Ar-H), 3.63 (s, 2H, -CH2), 6.81 (d, 1H, COCH=), 8.64 (d, 1H, =CH-Ar), 13C NMR: 30.5 (-CH2), 36.5, 42.2 (CH=CH), 161.1 (immine –C), 162.0 (> C = O), 173.1 (immine arom-C) 108.91-143.11 (arom-24C).

(5i): 2-[2-(2,6-Dichlorophenyl)amino]phenyl methyl-3-[(3-hydroxy) phenyl acrylamido]-6,8-dibromoquinazolin-4(3H)-one

IR (KBr) : (cm^-1) 3411 (NH), 3071, 2856 (C-H), 1728 (C=O), 1615 (C=O of –COCH3), 1576 (CH=CH), 1317 (C-N), 1550, 1356 (-NO2) 785 (C-Cl), 613 (C-Br). ^1H NMR : δ ppm; 9.78 (s, 1H, -NH-), 2.17 (s, 1H, -N-NH), 6.38-7.93 (m, 13 H, Ar-H), 3.61 (s, 2H, -CH2), 6.80 (d, 1H, COCH=), 8.62 (d, 1H, =CH-Ar), ^13C NMR: 30.4 (-CH2), 36.0, 41.6 (CH=CH), 160.9 (immine –C), 162.0 (> C = O), 172.9 (immine arom-C) 109.93-143.14 (arom-24C).

(5j): 2-[2-(2,6-Dichlorophenyl)amino]phenyl methyl-3-[(4-hydroxy) phenyl acrylamido]-6,8-dibromoquinazolin-4(3H)-one

IR (KBr): (cm^-1) 3411 (NH), 3059,2853 (C-H), 1727 (C=O), 1613 (C=O of –COCH3), 1574 (CH=CH), 1561, 1359 (-NO2), 1319 (C-N), 783 (C-Cl), 617 (C-Br). ^1H NMR : δ ppm; 9.79 (s, 1H, -NH-), 2.17 (s, 1H, -N-NH), 6.38-7.93 (m, 13 H, Ar-H), 3.64 (s, 2H, -CH2), 6.81 (d, 1H, COCH=), 8.59 (d, 1H, =CH-Ar), ^13C NMR: 30.6 (-CH2), 36.1, 42.7 (CH=CH), 61.2 (immine –C), 162.3 (> C = O), 173.1 (immine arom-C) 109.21-143.11 (arom-24C).

(5k): 2-[2-(2,6-Dichlorophenyl)amino]phenyl methyl-3-[(4-hydroxy) phenyl acrylamido]-6,8-dibromoquinazolin-4(3H)-one

IR (KBr): (cm^-1) 3379 (NH), 3066, 2859 (C-H), 1727 (C=O), 1614 (C=O of –COCH3), 1578 (CH=CH), 1317 (C-N), 780 (C-Cl), 613 (C-Br). ^1H NMR : δ ppm; 9.78 (s, 1H, -NH-), 2.17 (s, 1H, -N-NH), 6.39-7.93 (m, 13 H, Ar-H), 3.61 (s, 2H, -CH2), 6.81 (d, 1H, COCH=), 8.62 (d, 1H, =CH-Ar), 2.83 (s, 6H, -CH3), ^13C NMR: 31.2 (-CH2), 36.2, 41.6 (CH=CH), 46.2 (N-CH3) 160.9 (immine –C), 162.3 (> C = O), 172.8 (immine arom-C) 108.89-142.95 (arom-24C).

(5l): 2-[2-(2,6-Dichlorophenyl)amino]phenyl methyl-3-[(2-hydroxy) phenyl acrylamido]-6,8-dibromoquinazolin-4(3H)-one

IR (KBr) : (cm^-1) 3411 (NH), 3061, 2857 (C-H), 1722 (C=O), 1613 (C=O of –COCH3), 1574 (CH=CH), 1317 (C-N), 1242, 1107 (C-O-C), 781 (C-Cl), 605 (C-Br). ^1H NMR : δ ppm; 9.77 (s, 1H, -NH-), 2.14 (s, 1H, -N-NH), 6.39-7.93 (m, 13 H, Ar-H), 3.65 (s, 2H, -CH2), 6.81 (d, 1H, COCH=), 8.61 (d, 1H, =CH-Ar), 3.79 (s, 3H, -OCH3), ^13C NMR:
30.2 \((-\text{CH}_2\)), 36.8, 41.7 \((\text{CH} = \text{CH})\), 59.4 \((-\text{OCH}_3\)) 161.1 (immine \(-\text{C}\)), 162.0 (> C = O), 173.1 (immine arom-\text{C}) 109.14-143.17 (arom-2\text{C}).

\((5\text{m})\): \(2-\[2-(2,6\text{-Dichlorophenyl})\text{amino}\]phenyl methyl-3-[(4-hydroxy) phenyl acryl amido]-6,8-dibromoquinazolin-4(3\text{H})\)-one.

IR (KBr) : \((\text{cm}^{-1}\)) 3401 (NH), 3068, 2861 (C-H), 1721 (C=O), 1613 (C=O of \(-\text{COCH}_3\)), 1577 (\(\text{CH} = \text{CH}\)), 1319 (C-N), 1245, 1107 (C-O-C), 783 (C-Cl), 609 (C-Br). \(^1\text{H NMR :}\) \(\delta\) ppm; 9.78 (s, 1H, -NH-), 2.17 (s, 1H, -N-NH), 6.38-7.95 (m, 13H, Ar-H), 3.63 (s, 2H, -CH\(_2\)), 6.82 (d, 1H, COCH=), 8.61 (d, 1H, =CH-Ar), 3.80 (s, 3H, -OCH\(_3\)). \(^{13}\text{C NMR:}\) 30.7 \((-\text{CH}\(_2\)), 36.5, 42.6 (\text{CH}=\text{CH})\), 58.7 \((-\text{OCH}_3\)) 161.3 (immine \(-\text{C}\)), 162.0 (> C = O), 173.2 (immine arom-\text{C}) 109.17-143.19 (arom-2\text{C}).

\((6\text{b})\): \(2-\[2-(2,6\text{-Dichlorophenyl})\text{amino}\]phenyl methyl-3-\([5\text{-}(2\text{-hydroxy})\text{ phenyl acryl-1- phenyl-5-hydro-1H-pyrazol-3-yl-amino}]\)-6,8-dibromoquinazolin-4(3\text{H})\)-one

IR (KBr) : \((\text{cm}^{-1}\)) 3534 (O-H), 3361 (N-H), 3054, 2864 (C-H), 1732 (C=O), 1613 (C=N), 1329 (C-N), 782 (C-Cl), 620 (C-Br). \(^1\text{H NMR :}\) \(\delta\) ppm; 9.79 (s, 1H, -NH-), 8.31 (s, 1H, -N-NH), 3.59 (s, 2H, -CH\(_2\)), 3.05 (d, 1Ha), 3.46 (d, 1Hb, 6.51 (t, 1Hx), 6.43-7.95 (m, 18H, Ar-H),10.38 (s, 1H, -OH). \(^{13}\text{C NMR:}\) 30.5 \((-\text{CH}\(_2\)), 36.4, 42.6, 160.9 (pyra-\text{C}), 162.1 (> C = O), 1649 (immine arom-\text{C}) 109.3-143.4 (arom-30\text{C}).

\((6\text{c})\): \(2-\[2-(2,6\text{-Dichlorophenyl})\text{amino}\]phenyl methyl-3-\([5\text{-}(3\text{-hydroxy})\text{ phenyl acryl-1- phenyl-5-hydro-1H-pyrazol-3-yl-amino}]\)-6,8-dibromoquinazolin-4(3\text{H})\)-one

IR (KBr) : \((\text{cm}^{-1}\)) 3369 (O-H), 3077, 2854 (C-H), 1730 (C=O), 1614 (C=N), 1313 (C-N), 789 (C-Cl), 613 (C-Br). \(^1\text{H NMR :}\) \(\delta\) ppm; 9.79 (s, 1H, -NH-), 8.36 (s, 1H, -N-NH), 3.63 (s, 2H, -CH\(_2\)), 3.03 (d, 1Ha), 3.45 (d, 1Hb, 6.43 (t, 1Hx), 6.46-7.94 (m, 18H, Ar-H),10.31 (s, 1H, -OH). \(^{13}\text{C NMR:}\) 31.5 \((-\text{CH}\(_2\)), 36.5, 42.9, 161.2 (immine pyra-\text{C}), 162.3 (> C = O), 172.9 (immine arom-\text{C}) 109.12-143.15 (arom-30\text{C}).

\((6\text{d})\): \(2-\[2-(2,6\text{-Dichlorophenyl})\text{amino}\]phenyl methyl-3-\([5\text{-}(4\text{-hydroxy})\text{ phenyl acryl-1- phenyl-5-hydro-1H-pyrazol-3-yl-amino}]\)-6,8-dibromoquinazolin-4(3\text{H})\)-one

IR (KBr) : \((\text{cm}^{-1}\)) 3533 (O-H), 3362, 2854 (C-H), 1725 (C=O), 1616 (C=N), 1321 (C-N), 782 (C-Cl), 615 (C-Br). \(^1\text{H NMR :}\) \(\delta\) ppm; 9.78 (s, 1H, -NH-), 8.38 (s, 1H, -N-NH), 3.61 (s, 2H, -CH\(_2\)), 3.06 (d, 1Ha), 3.45 (d, 1Hb, 6.49 (t, 1Hx), 6.44-7.96 (m, 18H, Ar-H),10.34 (s, 1H, -OH). \(^{13}\text{C NMR:}\) 30.6 \((-\text{CH}\(_2\)), 36.5, 43.6, 161.3 (immine pyra-\text{C}), 162.1 (> C = O), 173.1 (immine arom-\text{C}) 109.17-143.13 (arom-30\text{C}).
(6e): 2-[2-(2,6-Dichlorophenyl)amino]phenyl methyl-3-[5-(2-chloro) phenyl-1-phenyl-5-hydro-1H-pyrazol-3-yl-amino]-6,8-dibromoquinazolin-4(3H)-one

IR (KBr): (cm\(^{-1}\)) 3361 (N-H), 3061, 2864 (C-H), 1732 (C=O), 1613 (C=N), 1312 (C-N), 782 (C-Cl), 619 (C-Br). \(^1\)H NMR: \(\delta\) ppm; 9.77 (s, 1H, -NH-), 8.28 (s, 1H, -N-NH), 3.62 (s, 2H, -CH\(_2\)), 3.05 (d, 1Ha), 3.48 (d, 1Hb, 6.49 (t, 1Hx), 6.44-7.96 (m, 18H, Ar-H), \(^{13}\)C NMR: 29.6 (-CH\(_2\)), 36.0, 42.5, 160.9 (immine pyra–C), 162.3 (> C = O), 173.1 (immine arom-C) 108.92-143.25 (arom-30C).

(6f): 2-[2-(2,6-Dichlorophenyl)amino]phenyl methyl-3-[5-(3-chloro) phenyl-1-phenyl-5-hydro-1H-pyrazol-3-yl-amino]-6,8-dibromoquinazolin-4(3H)-one

IR (KBr): (cm\(^{-1}\)) 3412 (N-H), 3061, 2855 (C-H), 1732 (C=O), 1614 (C=N), 1319 (C-N), 780 (C-Cl), 617 (C-Br). \(^1\)H NMR: \(\delta\) ppm; 9.79 (s, 1H, -NH-), 8.31 (s, 1H, -N-NH), 3.64 (s, 2H, -CH\(_2\)), 3.06 (d, 1Ha), 3.51 (d, 1Hb, 6.53 (t, 1Hx), 6.43-7.95 (m, 18H, Ar-H), \(^{13}\)C NMR: 31.3 (-CH\(_2\)), 36.5, 43.1, 161.3 (immine pyra–C), 162.3 (> C = O), 173.3 (immine arom-C) 109.13-143.17 (arom-30C).

(6g): 2-[2-(2,6-Dichlorophenyl)amino]phenyl methyl-3-[5-(4-chloro) phenyl-1-phenyl-5-hydro-1H-pyrazol-3-yl-amino]-6,8-dibromoquinazolin-4(3H)-one

IR (KBr): (cm\(^{-1}\)) 3367 (N-H), 3060, 2868 (C-H), 1737 (C=O), 1616 (C=N), 1319 (C-N), 781 (C-Cl), 612 (C-Br). \(^1\)H NMR: \(\delta\) ppm; 9.77 (s, 1H, -NH-), 8.30 (s, 1H, -N-NH), 3.61 (s, 2H, -CH\(_2\)), 3.06 (d, 1Ha), 3.48 (d, 1Hb, 6.51 (t, 1Hx), 6.44-7.95 (m, 18H, Ar-H), \(^{13}\)C NMR: 30.6 (-CH\(_2\)), 36.2, 42.7, 161.2 (immine pyra–C), 162.3 (> C = O), 172.8 (immine arom-C) 109.17-143.21 (arom-30C).

(6h): 2-[2-(2,6-Dichlorophenyl)amino]phenyl methyl-3-[5-(2-nitro) phenyl-1-phenyl-5-dihydro-1H-pyrazol-3-yl-amino]-6,8-dibromoquinazolin-4(3H)-one

IR (KBr): (cm\(^{-1}\)) 3411 (N-H), 3065, 2852 (C-H), 1730 (C=O), 1615 (C=N), 1546, 1351 (-NO\(_2\)), 1321 (C-N), 781 (C-Cl), 616 (C-Br). \(^1\)H NMR: \(\delta\) ppm; 9.79 (s, 1H, -NH-), 8.31 (s, 1H, -N-NH), 3.62 (s, 2H, -CH\(_2\)), 3.07 (d, 1Ha), 3.48 (d, 1Hb, 6.49 (t, 1Hx), 6.43-7.96 (m, 18H, Ar-H), \(^{13}\)C NMR: 30.5 (-CH\(_2\)), 36.6, 42.2, 161.6 (immine pyra–C), 162.1 (> C = O), 173.1 (immine arom-C) 108.91-143.11 (arom-30C).

(6i): 2-[2-(2,6-Dichlorophenyl)amino]phenyl methyl-3-[5-(3-nitro) phenyl-1-phenyl-5-hydro-1H-pyrazol-3-yl-amino]-6,8-dibromoquinazolin-4(3H)-one

IR (KBr): (cm\(^{-1}\)) 3410 (N-H), 3075, 2854 (C-H), 1732 (C=O), 1613 (C=N), 1544, 1353 (-NO\(_2\)), 1317 (C-N), 791 (C-Cl), 613 (C-Br). \(^1\)H NMR: \(\delta\) ppm; 9.77 (s, 1H, -NH-),
8.33 (s, 1H, -N-NH), 3.61 (s, 2H, -CH₂), 3.06 (d, 1Ha), 3.48 (d, 1Hb, 6.54 (t, 1Hx), 6.43-7.96 (m, 18H, Ar-H), 1³C NMR: 30.4 (-CH₂), 36.0, 43.6, 160.9 (immine pyra–C), 162.0 (> C = O), 172.9 (immine aromatic-C) 109.13-143.14 (arom-30C).

(6j): 2-[2-(2,6-Dichlorophenyl)amino]phenyl methyl-3-[5-(4-nitro) phenyl-5-hydro-1H-pyrazol-3-yl-amino]-6,8-dibromoquinazolin-4(3H)-one

IR (KBr) : (cm⁻¹) 3409 (N-H), 3060, 2849 (C-H), 1737 (C=O), 1616 (C=N), 1545, 1356 (-NO₂), 1319 (C-N), 788 (C-Cl), 612 (C-Br). ¹H NMR : δ ppm; 9.77 (s, 1H, -NH-), 8.33 (s, 1H, -N-NH), 3.61 (s, 2H, -CH₂), 3.05 (d, 1Ha), 3.48 (d, 1Hb, 6.52 (t, 1Hx), 6.43-7.96 (m, 18H, Ar-H), 1³C NMR: 30.6 (-CH₂), 36.1, 42.7, 161.2 (immine pyra–C), 162.3 (> C = O), 73.1 (immine aromatic-C) 109.21-143.11 (arom-30C).

(6k): 2-[2-(2,6-Dichlorophenyl)amino]phenyl methyl-3-[5-(4-dimethylamino) phenyl-5-hydro-1H-pyrazol-3-yl-amino]-6,8-dibromoquinazolin-4(3H)-one

IR (KBr) : (cm⁻¹) 3377 (N-H), 3068, 2861 (C-H), 1731 (C=O), 1614 (C=N), 1319 (C-N), 781 (C-Cl), 611 (C-Br). ¹H NMR : δ ppm; 9.79 (s, 1H, -NH-), 8.36 (s, 1H, -N-NH), 3.66 (s, 2H, -CH₂), 3.05 (d, 1Ha), 3.45 (d, 1Hb, 6.43 (t, 1Hx), 6.46-7.94 (m, 18H, Ar-H), 2.85 (s, 6H, -CH₃). ¹³C NMR: 29.05 (-CH₂), 35.68, 43.15, 161.13 (immine pyra–C), 162.32 (> C = O), 173.62 (immine aromatic-C) 109.12-143.15 (arom-30C), 55.42 (N-CH₃).

(6l): 2-[2-(2,6-Dichlorophenyl)amino]phenyl methyl-3-[5-(2-methoxy) phenyl-1-phenyl-5-hydro-1H-pyrazol-3-yl-amino]-6,8-dibromoquinazolin-4(3H)-one

IR (KBr) : (cm⁻¹) 3406 (N-H), 3066, 2859 (C-H), 1730 (C=O), 1612 (C=N), 1319 (C-N), 1239, 1107 (C-O-C), 784 (C-Cl), 605 (C-Br). ¹H NMR : δ ppm; 9.79 (s, 1H, -NH-), 8.29 (s, 1H, -N-NH), 3.64 (s, 2H, -CH₂), 3.05 (d, 1Ha), 3.45 (d, 1Hb, 6.53 (t, 1Hx), 6.43-7.96 (m, 18H, Ar-H), 3.80 (s, 6H, -CH₃). ¹³C NMR: 31.2 (-CH₂), 36.6, 42.7, 161.1 (immine pyra–C), 162.0 (> C = O), 173.3 (immine aromatic-C) 58.3 (-OCH₃), 109.14-143.17 (aromatic-30C).

(6m): 2-[2-(2,6-Dichlorophenyl)amino]phenyl methyl-3-[5-(4-methoxy) phenyl-1-phenyl-5-hydro-1H-pyrazol-3-yl-amino]-6,8-dibromoquinazolin-4(3H)-one

IR (KBr) : (cm⁻¹) 3399 (N-H), 3069, 2861 (C-H), 1729 (C=O), 1611 (C=N), 1317 (C-N), 1241, 1105 (C-O-C), 787 (C-Cl), 607 (C-Br). ¹H NMR : δ ppm; 9.78 (s, 1H, -NH-), 8.33 (s, 1H, -N-NH), 3.61 (s, 2H, -CH₂), 3.06 (d, 1Ha), 3.51 (d, 1Hb, 6.53 (t, 1Hx), 6.43-7.95 (m, 18H, Ar-H), 3.81 (s, 6H, -CH₃). ¹³C NMR: 30.2 (-CH₂), 36.5, 42.6, 161.3 (immine pyrazol–C), 162.3 (> C = O), 173.2 (immine aromatic-C) 59.2 (-OCH₃), 109.12-143.15 (aromatic-30C).
RESULTS AND DISCUSSION

A mixture of 2-[2-(2,6-dichlorophenyl)amino]phenylmethyl-3-acetamido-6,8-dibromoquinazolin-4(3H)-one with different substituted aromatic aldehydes afforded chalcone. Quinazolinonyl chalcone, phenyl hydrazine and glacial acetic acid were heated to afford 2-[2-(2,6-dichlorophenyl)amino]phenylmethyl-3-[(5-substitutedphenyl-1-phenyl)-5-hydro-1H-pyrazol-3-yl-amino]-6, 8-dibromoquinazolin-4(3H)ones (Scheme 1).

![Scheme 1](image_url)
The physical and analytical data of compounds (5a-m) and (6a-m) are presented in Table 1 and 2, respectively. The compounds (1-4) were also characterized on the basis of their analytical and spectral data.22-24.

Table 1: Characterization data of compounds (5a-m) and (6a-m)

<table>
<thead>
<tr>
<th>Compd.</th>
<th>R</th>
<th>Molecular Formula</th>
<th>M.P. (°C)</th>
<th>Yield %</th>
<th>C</th>
<th>H</th>
<th>N</th>
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Table 2: Antimicrobial assay of (6a-m)

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<th>Compd</th>
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<th>Antibacterial activity</th>
<th>Fungicidal activity</th>
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<td></td>
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<td>Zone of inhibition (mm)</td>
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<tr>
<td></td>
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<td>S. aureus</td>
<td>B. subtilis</td>
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<td>6a</td>
<td>H</td>
<td>22 (0.73)</td>
<td>20 (0.74)</td>
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<td>2-OH</td>
<td>13 (0.43)</td>
<td>20 (0.74)</td>
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<td>6c</td>
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<td>6d</td>
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<td>10 (0.47)</td>
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<tr>
<td>6e</td>
<td>2-Cl</td>
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<td>11 (0.41)</td>
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<td>6f</td>
<td>3-Cl</td>
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Cont...
### Antibacterial activity

The synthesized compounds were tested for antibacterial *in vitro* activity against Gram positive *S. aureus*, *B. subtilis* and Gram negative *E. coli*, *certium* bacteria at two different concentrations 50 mg/mL and 100 mg/mL. Nutrient agar was used as culture medium by cup-plate method\(^{25,26}\). The zone of inhibition was measured in mm and compared with standard drug penicillin.

The compound *(6a)* showed significant antibacterial activity while *(6h)* and *(6j)* showed moderate activity against *S. aureus* and *B. subtilis*; *(6i)* showed significant activity

### Table: Antibacterial and Fungicidal Activity

<table>
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<th>Antibacterial activity</th>
<th>Fungicidal activity</th>
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<td>Zone of inhibition (mm) IZ (AI)</td>
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<td><em>B. subtilis</em></td>
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<td><strong>IZ (AI)</strong></td>
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<td>3 (0.62)</td>
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<tr>
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IZ = Inhibition area (Zone) excluding diameter of disc
A1 (Activity Index) = Inhibition area of sample/inhibition area of standard

(PEN) Penicillin concentration (i) 100 mg/mL (FLU) Fluconazole (i) 20 mg/mL
(PEN) Penicillin concentration (ii) 50 mg/mL (FLU) Fluconazole (ii) 10 mg/mL
against *E. coli* and *Certium* with penicillin. The compound (6h), (6j) and (6m) showed moderate activity against both Gram negative bacteria with penicillin.

**Antifungal activity**

The *in vitro* antifungal activity against fungi *A. niger* and *C. albicans* was carried out by employing agar disc diffusion method\(^2\) at two different concentration 20 mg/mL and 10 mg/mL. 0.05% DMF was used as a solvent control and sabouraud dextrose as culture media. Standard drug fluconazole was used for comparison.

The compound (6e), (6f), (6g) showed good activity, while (6a) exhibited moderate fungicidal activity against *A. niger* and *C. albicans* as compared to fluconazole. The screening results are shown in Table 2.

**ACKNOWLEDGEMENT**

The authors thank to Director ‘SICART’ V. V. Nagar, Gujarat for recording spectral data and also to Mrs. Anandita Mehta, Department of Microbiology, ATIRA, Ahmedabad for antimicrobial activity.

**REFERENCES**


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