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# 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, $^{1}$H NMR, $^{13}$C 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*, *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-disubstitued quinazolin-4(3H)-ones were reported to possess anti-HIV[1-3], anticancer[4-6] antibacterial[7], antifungal[8], analgesics[9], anti-inflammatory agent[10], antiparasitic[11], enzyme inhibitory agent[12] and rheumatic arthritis[13]. Several scientists elucidated 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 agents[14,15]. 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 work[16-20] and synthesized new series of quinazolinonyl chalcones 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[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 get 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[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(3*H*)-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$^{o}$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$^{o}$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-dibromo quinazolin-4(3H)-one (5a)

A solution of 2-[2-(2,6-dichlorophenyl)amino]phenyl methyl-3-acetamido-6,8-dibromoquinazolin-4(3*H*)-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,

1H, -N-NH), 6.34-7.91 (m, 14H, Ar-H), 2.61 (s, 2H, -$CH_2$), 6.80 (D, 1H, COCH=), 8.62 (d, 1H, =CH-Ar).

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 acryl amido)-6,8-dibromoquinazolin-4(3*H*)-one (6.71 g, 0.01 mol) in methanol, phenylhydrazine hydrate (99%) (2.56.0 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). $^1$H NMR: δ ppm; 9.78 (S, 1H, -NH), 8.34 (S, 1H, -N-NH), 3.61 (S, 2H, -$CH_2$), 3.06 (d, 1 Ha), 48 (d, 1Hb), 6.53 (t, 1Hx), 6.43-7.95 (m, 19H, Ar-H). $^{13}$C NMR: 30.7 (-$CH_2$), 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 –$COCH_3$), 1566 (CH=CH), 1317 (C-N), 779 (C-Cl), 613 (C-Br). $^1$H 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, -$CH_2$), 6.80 (d, 1H, COCH=), 8.62 (d, 1H, =CH-Ar), 10.34 (s, 1H, -OH). $^{13}$C NMR: 30.5 (-$CH_2$), 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 –$COCH_3$), 1575 (CH=CH), 1317 (C-N), 780 (C-Cl), 616 (C-Br). $^1$H 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, -$CH_2$), 6.82 (d, 1H, COCH=), 8.61 (d, 1H, =CH-Ar), 10.38 (s, 1H, -OH). $^{13}$C NMR: 30.5 (-$CH_2$), 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 acryl amido]-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 $–COCH_3$), 1572 (CH=CH), 1319 (C-N), 780 (C-Cl), 615 (C-Br). $^1$H 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, $-CH_2$), 6.80 (d, 1H, COCH=), 8.62 (d, 1H, =CH-Ar), 10.35 (s, 1H, -OH). $^{13}$C NMR: 30.6 ($-CH_2$), 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 acryl amido]-6,8-dibromoquinazolin-4(3H)-one**

IR (KBr) : ($cm^{-1}$); 3365 (NH), 3061, 2857 (C-H), 1729 (C=O), 1613 (C=O of $–COCH_3$), 1578 (CH=CH), 1314 (C-N), 781 (C-Cl), 617 (C-Br). $^1$H 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, $-CH_2$), 6.82 (d, 1H, COCH=), 8.61 (d, 1H, =CH-Ar), $^{13}$C NMR: 29.6 ($-CH_2$), 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 acryl amido]-6,8-dibromoquinazolin-4(3H)-one**

IR (KBr) : ($cm^{-1}$); 3413 (NH), 3067, 2853 (C-H), 1729 (C=O), 1615 (C=O of $–COCH_3$), 1578 (CH=CH), 1318 (C-N), 779 (C-Cl), 616 (C-Br). $^1$H 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, $-CH_2$), 6.80 (d, 1H, COCH=), 8.60 (d, 1H, =CH-Ar), $^{13}$C NMR: 31.3 ($-CH_2$), 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 acryl amido]-6,8-dibromoquinazolin-4(3H)-one**

IR (KBr) : ($cm^{-1}$) 3369 (NH), 3061, 2859 (C-H), 1731 (C=O), 1615 (C=O of $–COCH_3$), 1576 (CH=CH), 1316 (C-N), 782 (C-Cl), 618 (C-Br). $^1$H 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, $-CH_2$), 6.83 (d, 1H, COCH=), 8.62 (d, 1H, =CH-Ar), $^{13}$C NMR: 30.6 ($-CH_2$), 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 acryl amido]-6,8-dibromoquinazolin-4(3H)-one**

IR (KBr) : ($cm^{-1}$) 3416 (NH), 3066, 2856 (C-H), 1727 (C=O), 1617 (C=O of $–COCH_3$),

1578 (CH=CH), 1319 (C-N), 1567, 1363 (-$NO_2$) 779 (C-Cl), 617 (C-Br). $^1$H 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, -$CH_2$), 6.81 (d, 1H, COCH=), 8.64 (d, 1H, =CH-Ar), $^{13}$C NMR: 30.5 (-$CH_2$), 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 acryl amido]-6,8-dibromoquinazolin-4(3H)-one**

IR (KBr) : (cm$^{-1}$) 3411 (NH), 3071, 2856 (C-H), 1728 (C=O), 1615 (C=O of –$COCH_3$), 1576 (CH=CH), 1317 (C-N), 1550, 1356 (-$NO_2$) 785 (C-Cl), 613 (C-Br). $^1$H 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, -$CH_2$), 6.80 (d, 1H, COCH=), 8.62 (d, 1H, =CH-Ar), $^{13}$C NMR: 30.4 (-$CH_2$), 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 acryl amido]-6,8-dibromoquinazolin-4(3H)-one**

IR (KBr):(cm$^{-1}$) 3411 (NH), 3059,2853 (C-H), 1727 (C=O), 1613 (C=O of –$COCH_3$), 1574 (CH=CH), 1561, 1359 (-$NO_2$), 1319 (C-N), 783 (C-Cl), 617 (C-Br). $^1$H 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, -$CH_2$), 6.81 (d, 1H, COCH=), 8.59 (d, 1H, =CH-Ar), $^{13}$C NMR: 30.6 (-$CH_2$), 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 acryl amido]-6,8-dibromoquinazolin-4(3H)-one**

IR (KBr) : (cm$^{-1}$) 3379 (NH), 3066, 2859 (C-H), 1727 (C=O), 1614 (C=O of –$COCH_3$), 1578 (CH=CH), 1317 (C-N), 780 (C-Cl), 613 (C-Br). $^1$H 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, -$CH_2$), 6.81 (d, 1H, COCH=), 8.62 (d, 1H, =CH-Ar), 2.83 (s, 6H, -$CH_3$), $^{13}$C NMR: 31.2 (-$CH_2$), 36.2, 41.6 (CH=CH), 46.2 (N-$CH_3$) 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 acryl amido]-6,8-dibromoquinazolin-4(3H)-one**

IR (KBr) : (cm$^{-1}$) 3411 (NH), 3061, 2857 (C-H), 1722 (C=O), 1613 (C=O) of –$COCH_3$), 1574 (CH=CH), 1317 (C-N), 1242, 1107 (C-O-C), 781 (C-Cl), 605 (C-Br). $^1$H 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, -$CH_2$), 6.81 (d, 1H, COCH=), 8.61 (d, 1H, =CH-Ar), 3.79 (s, 3H, -$OCH_3$), $^{13}$C NMR:

30.2 (-$CH_2$), 36.8, 41.7 (CH=CH), 59.4 (-$OCH_3$) 161.1 (immine –C), 162.0 (> C = O), 173.1 (immine arom-C) 109.14-143.17 (arom-24C).

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

IR (KBr) : ($cm^{-1}$) 3401 (NH), 3068, 2861 (C-H), 1721 (C=O), 1613 (C=O of –$COCH_3$), 1577 (CH=CH), 1319 (C-N), 1245, 1107 (C-O-C), 783 (C-Cl), 609 (C-Br). $^1$H NMR : δ ppm; 9.78 (s, 1H, -NH-), 2.17 (s, 1H, -N-NH), 6.38-7.95 (m, 13 H, Ar-H), 3.63 (s, 2H, -$CH_2$), 6.82 (d, 1H, COCH=), 8.61 (d, 1H, =CH-Ar), 3.80 (s, 3H, -$OCH_3$), $^{13}$C NMR: 30.7 (-$CH_2$), 36.5, 42.6 (CH=CH), 58.7 (-$OCH_3$) 161.3 (immine –C), 162.0 (> C = O), 173.2 (immine arom-C) 109.17-143.19 (arom-24C).

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

IR (KBr) : ($cm^{-1}$) 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). $^1$H NMR : δ 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). $^{13}$C NMR: 30.5 (-$CH_2$), 36.4, 42.6, 160.9 (pyra–C), 162.1 (> C = O), 1649 (immine arom-C) 109.3-143.4 (arom-30C).

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

IR (KBr) : ($cm^{-1}$) 3369 (O-H), 3077, 2854 (C-H), 1730 (C=O), 1614 (C=N), 1313 (C-N), 789 (C-Cl), 613 (C-Br). $^1$H NMR : δ 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). $^{13}$C NMR: 31.5 (-$CH_2$), 36.5, 42.9, 161.2 (immine pyra–C), 162.3 (> C = O), 172.9 (immine arom-C) 109.12-143.15 (arom-30C).

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

IR (KBr) : ($cm^{-1}$) 3533 (O-H), 3362, 2854 (C-H), 1725 (C=O), 1616 (C=N), 1321 (C-N), 782 (C-Cl), 615 (C-Br). $^1$H NMR : δ 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). $^{13}$C NMR: 30.6 (-$CH_2$), 36.5, 43.6, 161.3 (immine pyra–C), 162.1 (> C = O), 173.1 (immine arom-C) 109.17-143.13 (arom-30C).

**(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 : δ 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 : δ 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 : δ 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 : δ 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 : δ ppm; 9.77 (s, 1H, -NH-),

8.33 (s, 1H, -N-NH), 3.61 (s, 2H, -$CH_2$), 3.06 (d, 1Ha), 3.48 (d, 1Hb, 6.54 (t, 1Hx), 6.43-7.96 (m, 18H, Ar-H), $^{13}$C NMR: 30.4 (-$CH_2$), 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-1-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 (-$NO_2$), 1319 (C-N), 788 (C-Cl), 612 (C-Br). $^1$H NMR : δ ppm; 9.77 (s, 1H, -NH-), 8.33 (s, 1H, -N-NH), 3.61 (s, 2H, -$CH_2$), 3.05 (d, 1Ha), 3.48 (d, 1Hb, 6.52 (t, 1Hx), 6.43-7.96 (m, 18H, Ar-H), $^{13}$C NMR: 30.6 (-$CH_2$), 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-1-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). $^1$H NMR : δ ppm; 9.79 (s, 1H, -NH-), 8.36 (s, 1H, -N-NH), 3.66 (s, 2H, -$CH_2$), 3.05 (d, 1Ha), 3.45 (d, 1Hb, 6.43 (t, 1Hx), 6.46-7.94 (m, 18H, Ar-H), 2.85 (s, 6H, -$CH_3$). $^{13}$C NMR: 29.05 (-$CH_2$), 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-$CH_3$).

**(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**

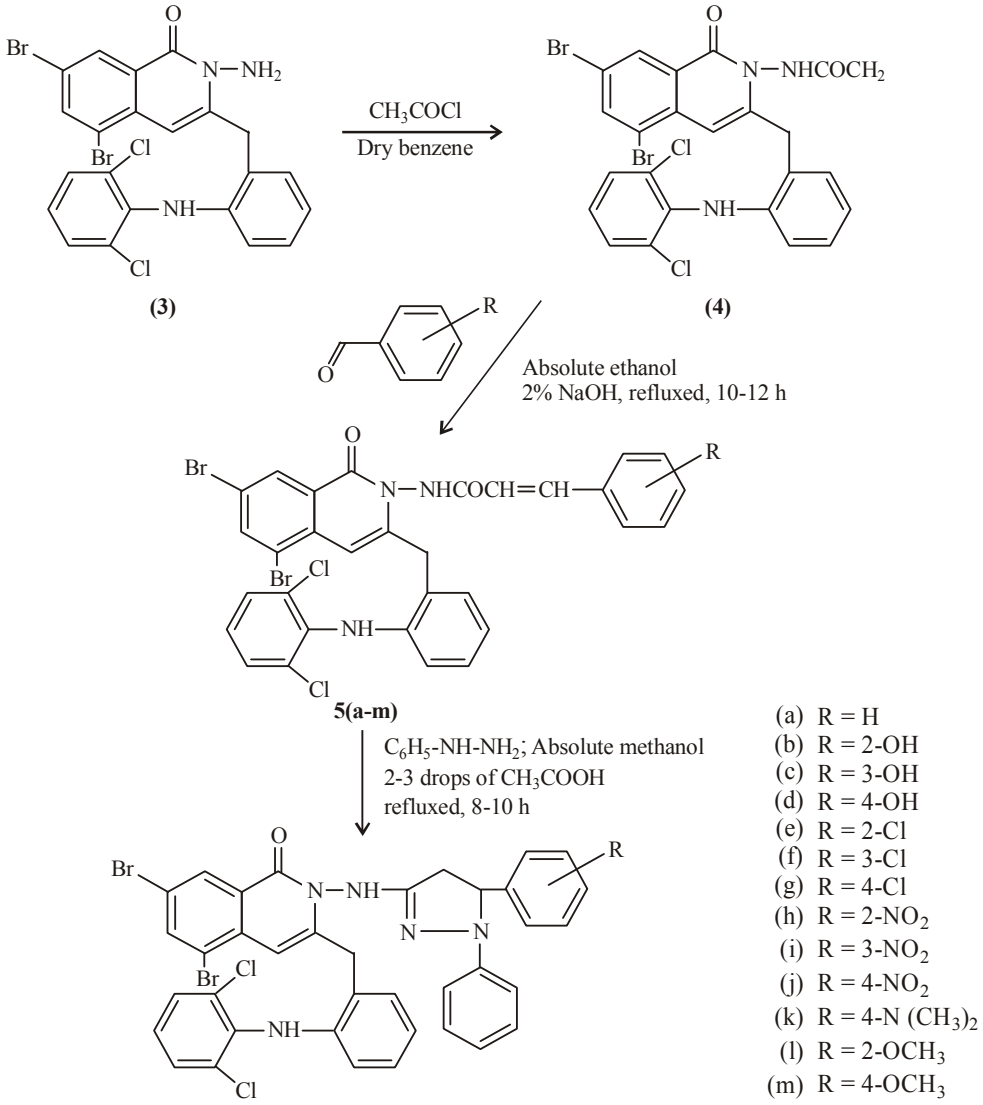
IR (KBr) : (cm$^{-1}$) 3406 (N-H), 3066, 2859 (C-H), 1730 (C=O), 1612 (C=N), 1319 (C-N), 1239, 1107 (C-O-C), 784 (C-Cl), 605 (C-Br). $^1$H NMR : δ ppm; 9.79 (s, 1H, -NH-), 8.29 (s, 1H, -N-NH), 3.64 (s, 2H, -$CH_2$), 3.05 (d, 1Ha), 3.48 (d, 1Hb, 6.53 (t, 1Hx), 6.43-7.96 (m, 18H, Ar-H), 3.80 (s, 6H, -$CH_3$). $^{13}$C NMR: 31.2 (-$CH_2$), 36.6, 42.7, 161.1 (immine pyra–C), 162.0 (> C = O), 173.3 (immine aromatic-C) 58.3 (-$OCH_3$), 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). $^1$H NMR : δ ppm; 9.78 (s, 1H, -NH-), 8.33 (s, 1H, -N-NH), 3.61 (s, 2H, -$CH_2$), 3.06 (d, 1Ha), 3.51 (d, 1Hb, 6.53 (t, 1Hx), 6.43-7.95 (m, 18H, Ar-H), 3.81 (s, 6H, -$CH_3$). $^{13}$C NMR: 30.2 (-$CH_2$), 36.5, 42.6, 161.3 (immine pyrazol–C), 162.3 (> C = O), 173.2 (immine aromatic-C) 59.2 (-$OCH_3$), 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 chlalcone, 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**

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)**

| Compd. | R | Molecular Formaula | M.P. (°C) | Yield % | Elecmental analysis % | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | C | | H | | N | |
| | | | | | Calcd. | Found | Calcd. | Found | Calcd. | Found |
| **5a** | H | $C_{30}H_{20}N_4O_2Br_2Cl_2$ | 146-148 | 67 | 51.51 | 51.53 | 2.86 | 2.88 | 8.01 | 8.03 |
| **5b** | 2-OH | $C_{30}H_{20}N_4O_3Br_2Cl_2$ | 156-158 | 72 | 50.36 | 50.39 | 2.79 | 2.81 | 7.83 | 7.85 |
| **5c** | 3-OH | $C_{30}H_{20}N_4O_3Br_2Cl_2$ | 171.173 | 66 | 50.36 | 50.35 | 2.79 | 2.80 | 7.83 | 7.84 |
| **5d** | 4-OH | $C_{30}H_{20}N_4O_3Br_2Cl_2$ | 184-186 | 73 | 50.36 | 50.38 | 2.79 | 2.77 | 7.83 | 7.84 |
| **5e** | 2-Cl | $C_{30}H_{19}N_4O_2Br_2Cl_3$ | 145-147 | 72 | 49.09 | 49.12 | 2.59 | 2.62 | 7.63 | 7.65 |
| **5f** | 3-Cl | $C_{30}H_{19}N_4O_2Br_2Cl_3$ | 163-165 | 65 | 49.09 | 49.10 | 2.59 | 2.60 | 7.63 | 7.66 |
| **5g** | 4-Cl | $C_{30}H_{19}N_4O_2Br_2Cl_3$ | 176-178 | 69 | 49.09 | 49.11 | 2.59 | 2.61 | 7.63 | 7.64 |
| **5h** | 2-$NO_2$ | $C_{30}H_{19}N_5O_4Br_2Cl_2$ | 202-204 | 70 | 48.39 | 48.42 | 2.55 | 2.56 | 9.41 | 9.43 |
| **5i** | 3-$NO_2$ | $C_{30}H_{19}N_5O_4Br_2Cl_2$ | 227-229 | 68 | 48.39 | 48.40 | 2.55 | 2.57 | 9.41 | 9.40 |
| **5j** | 4-$NO_2$ | $C_{30}H_{19}N_5O_4Br_2Cl_2$ | 238-239 | 63 | 48.39 | 48.41 | 2.55 | 2.58 | 9.41 | 9.42 |
| **5k** | 4-$N(CH_3)_2$ | $C_{30}H_{20}N_5O_4Br_2Cl_2$ | 161-163 | 67 | 51.76 | 51.78 | 3.37 | 3.40 | 9.43 | 9.44 |
| **5l** | 2-$OCH_3$ | $C_{32}H_{25}N_5O_2Br_2Cl_2$ | 157-159 | 65 | 51.04 | 51.06 | 3.01 | 3.02 | 7.68 | 7.70 |
| **5m** | 4-$OCH_3$ | $C_{31}H_{20}N_4O_2Br_2Cl_2$ | 173-175 | 68 | 51.04 | 51.05 | 3.01 | 3.03 | 7.68 | 7.69 |
| **6a** | H | $C_{36}H_{22}N_4O_3Br_2Cl_2$ | 131-133 | 68 | 54.76 | 54.77 | 3.17 | 3.16 | 10.64 | 10.65 |
| **6b** | 2-OH | $C_{36}H_{26}N_6OBr_2Cl_2$ | 152-153 | 62 | 53.67 | 53.65 | 3.22 | 3.24 | 10.43 | 10.43 |
| **6c** | 3-OH | $C_{36}H_{26}N_6O_2Br_2Cl_2$ | 163-165 | 67 | 35.67 | 53.66 | 3.22 | 3.22 | 10.43 | 10.45 |
| **6d** | 4-OH | $C_{36}H_{26}N_6O_2Br_2Cl_2$ | 173-175 | 73 | 53.67 | 53.66 | 3.22 | 3.23 | 10.43 | 10.44 |
| **6e** | 2-Cl | $C_{36}H_{25}N_6O_2Br_2Cl_3$ | 139-141 | 69 | 52.47 | 52.48 | 3.03 | 3.05 | 10.20 | 10.21 |
| **6f** | 3-Cl | $C_{36}H_{25}N_4OBr_2Cl_3$ | 147-149 | 67 | 52.47 | 52.49 | 3.03 | 3.04 | 10.20 | 10.22 |
| **6g** | 4-Cl | $C_{36}H_{25}N_6OBr_2Cl_3$ | 159-161 | 65 | 52.47 | 52.48 | 3.03 | 3.02 | 10.20 | 10.21 |
| **6h** | 2-$NO_2$ | $C_{36}H_{25}N_7O_3Br_2Cl_2$ | 171-173 | 69 | 51.81 | 51.83 | 2.99 | 3.01 | 11.75 | 11.74 |

Cont...

| Compd. | R | Molecular Formaula | M.P. (°C) | Yield % | Elecmental analysis % | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | C | | H | | N | |
| | | | | | Calcd. | Found | Calcd. | Found | Calcd. | Found |
| **6j** | 4-$NO_2$ | $C_{36}H_{25}N_7O_3Br_2Cl_2$ | 203-205 | 63 | 51.81 | 51.80 | 2.99 | 3.01 | 11.75 | 11.75 |
| **6k** | 4-$N(CH_3)_2$ | $C_{38}H_{31}N_7OBr_2Cl_2$ | 149-151 | 68 | 54.82 | 54.83 | 3.72 | 3.74 | 11.77 | 11.78 |
| **6l** | 2-$OCH_3$ | $C_{37}H_{28}N_6O_2Br_2Cl_2$ | 139-141 | 63 | 54.22 | 54.23 | 3.41 | 3.42 | 10.25 | 10.26 |
| **6 m** | 4-$OCH_3$ | $C_{37}H_{28}N_6O_2Br_2Cl_2$ | 153-155 | 69 | 54.22 | 54.24 | 3.41 | 3.43 | 10.25 | 10.26 |

**Table 2: Antimicrobial assay of (6a-m)**

| Compd. | R | Antibacterial activity | | | | Fungicidal activity | |
|---|---|---|---|---|---|---|---|
| | | Zone of inhibition (mm) IZ (AI) | | | | Zone of inhibition (mm) IZ (AI) | |
| | | ***S. aureus*** | ***B. subtilis*** | ***E. coli*** | ***Certium*** | ***A. niger*** | ***C. albicans*** |
| **6a** | H | 22 (0.73)<br>19 (0.76) | 20 (0.74)<br>17 (0.81) | 12 (0.39)<br>10 (0.40) | 11 (0.39)<br>09 (0.39) | 15 (0.54)<br>13 (0.59) | 16 (0.62)<br>13 (0.62) |
| **6b** | 2-OH | 13 (0.43)<br>11 (0.44) | 20 (0.74)<br>17 (0.81) | 15 (0.48)<br>13 (0.52) | 14 (0.50)<br>12 (0.52) | 10 (0.36)<br>08 (0.36) | 11 (0.42)<br>09 (0.43) |
| **6c** | 3-OH | 12 (0.40)<br>10 (0.40) | 12 (0.44)<br>10 (0.47) | 15 (0.54)<br>13 (0.57) | 15 (0.54)<br>13 (0.57) | 13 (0.46)<br>11 (0.50) | 14 (0.54)<br>12 (0.57) |
| **6d** | 4-OH | 11 (0.36)<br>09 (0.36) | 11(0.41)0<br>9(0.43) | 13 (0.42)<br>11 (0.44) | 14 (0.50)<br>12 (0.52) | 09 (0.32)<br>07 (0.32) | 11 (0.42)<br>09 (0.43) |
| **6e** | 2-Cl | 10 (0.33)<br>08 (0.32) | 11(0.41)0<br>9(0.43) | 14 (0.45)<br>12 (0.48) | 12 (0.43)<br>10 (0.43) | 22 (0.79)<br>19 (0.86) | 23 (0.88)<br>19 (0.90) |
| **6f** | 3-Cl | 09(0.30)<br>07 (0.28) | 10(0.37)0<br>8(0.38) | 12 (0.39)<br>10 (0.40) | 12 (0.43)<br>10 (0.43) | 18 (0.64)<br>15 (0.68) | 20 (0.77)<br>17 (0.81) |
| **6g** | 4-Cl | 11(0.36)<br>09(0.36) | 12(0.44)1<br>0(0.47) | 11 (0.35)<br>09 (0.36) | 11 (0.39)<br>09 (0.39) | 19 (0.68)<br>16 (0.73) | 21 (0.81)<br>18 (0.86) |

Cont...

| Compd. | R | Antibacterial activity | | | | Fungicidal activity | |
|---|---|---|---|---|---|---|---|
| | | Zone of inhibition (mm) IZ (AI) | | | | Zone of inhibition (mm) IZ (AI) | |
| | | ***S. aureus*** | ***B. subtilis*** | ***E. coli*** | ***Certium*** | ***A. niger*** | ***C. albicans*** |
| **6h** | 2-$NO_2$ | 17 (0.57)<br>14 (0.56) | 16(0.59)1<br>3(0.62) | 18 (0.58)<br>15 (0.60) | 17 (0.61)<br>14 (0.61) | 15 (0.54)<br>13 (0.59) | 14 (0.54)<br>12 (0.57) |
| **6i** | 3-$NO_2$ | 15 (0.50)<br>13 (0.52) | 15(0.56)1<br>3(0.62) | 25 (0.81)<br>22 (0.88) | 24 (0.86)<br>20 (0.87) | 13 (0.46)<br>11 (0.50) | 13 (0.50)<br>11 (0.52) |
| **6j** | 4-$NO_2$ | 16 (0.53)<br>13 (0.52) | 16 (0.59)<br>13 (0.62) | 16 (0.52)<br>13 (0.52) | 17 (0.61)<br>14 (0.61) | 14 (0.50)<br>12 (0.55) | 16 (0.62)<br>13 (0.62) |
| **6k** | 4-$N(CH_3)_2$ | 13 (0.43)<br>11 (0.44) | 12 (0.44)<br>10 (0.47) | 13 (0.42)<br>11 (0.44) | 12 (0.43)<br>10 (0.43) | 15 (0.54)<br>13 (0.59) | 17 (0.65)<br>14 (0.67) |
| **6l** | 2-$OCH_3$ | 13 (0.43)<br>11 (0.44) | 13 (0.48)<br>11 (0.52) | 17 (0.55)<br>14 (0.56) | 16 (0.57)<br>13 (0.57) | 10 (0.36)<br>08 (0.36) | 12 (0.46)<br>10 (0.48) |
| **6m** | 4-$OCH_3$ | 14 (0.47)<br>12 (0.48) | 13 (0.48)<br>11 (0.52) | 18 (0.58)<br>15 (0.60) | 18 (0.64)<br>15 (0.65) | 09 (0.32)<br>07 (0.32) | 11 (0.42)<br>09 (0.43) |
| PEN | | 30<br>25 | 27<br>21 | 31<br>25 | 28<br>23 | FLU 28<br>22 | 26<br>21 |

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 (ii) 50 mg/mL

(FLU) Fluconazole (i) 20 mg/mL (ii) 10 mg/mL

## 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

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[27] 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.

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