Research Paper

Volume : 3 | Issue : 11 | November 2014 • ISSN No 2277 - 8179

Synthesis, Structural Elucidation and in vitro Antimicrobial Studies of Some Novel Pyrazolylquinazolin-4(3H) Ones Bearing Quinoline Moiety

Pharmaceutical chemistry

KEYWORDS : Antimicrobial, pyrazoline, quinoline, quinazolin-4(3H) one.

Dr. Gaman G. Barat — Department of Chemistry, Arts, Science and Commerce College, Pilvai-382850, Gujarat, India

Navin B. Patel — Department of Chemistry, Veer Narmad South Gujarat University, Surat-395007, Gujarat, India

ABSTRACT

A new series of 6-iodo quinazolin-4(3H) ones bearing pyrazoline and quinoline moieties 6a-l were synthesized by the cyclisation of acrylamide 5a-l with phenyl hydrazine hydrate. The overall reaction was carried out by base catalyzed multistep process. The structural confirmations of the synthesized compounds were carried out on the basis of elemental analysis as well as IR and NMR spectra results. All the synthesized compounds were screened for in vitro antimicrobial activity.

INTRODUCTION

Quinoline nucleus is an important pharmacophore in medicinal chemistry, since a large number of its derivatives possess useful biological properties. 4(3H)-Quinazolinones have emerged as an important class of nitrogenated heterocyclic that attached with pyrazoline moiety have synthetic interest because of they possess good pharmacological and therapeutic properties, along with quinoline moiety played vital role in the medicinal chemistry. The large number of synthetic compounds of quinazolin-4(3H) with pyrazoline and quinoline nucleus used for analgesics[1], ant-inflammatory, anticancer[2-3],HIV-1 integrase inhibitor[4], cardiovascular, anticancer[5], anti-bacterial, antifungal[6-8], antimicrobial[9-10], antidepressant, anticonvulsant[11-12], antimalarial[13] ,antitubercular[14] in medicinal chemistry. The exploration for new biologically active heterocyclic analogues and continues to be an area of intention research in medicinal chemistry. In the light of these findings, the synthesis of new chemical entities incorporating the quinoline and pyrazoles with quinazolinones may prove to be useful frame of the biological activity point of view.

MATERIAL AND METHOD

All reagents and solvents were purchased from Merck chemicals and further purified before use. 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 melting points of all synthesized compounds were taken in open capillary tube and are uncorrected. 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. 1H NMR and 13C NMR spectra were recorded on Bruker Advance II 400 NMR spectrometer using deutero CDCl3 as a solvent. The chemical shifts were reported in (δ ppm) downfield using tetra methyl silane as internal standard. Elemental analyses of newly sysnthesized compounds were carried out on Carlo Ebra 1108 analyzer.3-(6-chloro-2-phenylquinolin) acetyl chloride 1 was synthesized by literature procedure (Furniss et al., 1989).

Synthesis of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl–6-iodo-3, 1-benzoxazin-4(3H) one 2

To 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 5-iodo anthranilic acid (2.63 g, 0.01 mol) and stirred well for 1 h. to keep the temperature between 0-5 ^{0}C. Further reaction mixture was stirred 1h. at room temperature. A pasty mass thus obtained which washed thoroughly with sodium bicarbonate (5 %) to remove unreacted acid. A solid separated was filtered, dried and recrystalised from methanol.

M.P. : 162 ^{0}C. Yeild : 79 % IR (KBr) : 3069,2861 (C-H), 1721 (C=O), 1618 (C=N),1327(C-N),1236(C-O-C), 778(C-Cl),506(C-I).Anal. (%) for $C_{24}H_{14}N_2O_2ICl$ Calcd; C, 54.90; H, 2.66; N, 5.33; Found; C, 54.93; H, 2.67; N, 5.35.

Synthesis of 3-Amino-2-[3-(6-chloro-2-phenyl)quinolin-3-yl] methyl–6-iodoquinazolin–4(3H) one 3

To a mixture of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl–6-iodo-3,1-benzoxazin-4(3H) one (5.245 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 slowly poured onto crushed acidic (HCl, 25ml) ice cold water with occasional stirring. The product thus obtained was filtered and washed several times with water, dried and recrystalized from ethanol.

M.P.:145 ^{0}C. Yield: 74 % IR (KBr) : 3407(NH), 3063, 2866(C-H), 1720(C=O), 1616(C=N), 1325(C-N), 781(C-Cl), 511(C-I). 1HNMR($CDCl_3$): 2.2(s, 2H, -N-NH_2), 6.36-7.93(m, 12H, Ar-H), 3.62(s, 2H, -CH_2). Anal. (%) for $C_{24}H_{16}N_4OICl$ Calcd; C, 53.48; H, 2.97; N,10.40; Found; C, 53.49; H, 2.99; N, 10.42.

Synthesis of 2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl-3-acetamido-6-iodoquinazolin-4(3H)-one 4

To a solution of 3-Amino-2-[3-(6-chloro-2-phenyl)quinolin-3-yl] methyl–6-iodoquinazolin–4(3H) one (5.385 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, from the time interval of 1 h. with constant stirring, after addition was complete 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 ^{0}C. Yeild : 69 % IR(KBr): 3409(NH), 3064,2862(C-H),1723(C=O), 1638(C=O of –$COCH_3$), 1323(C-N), 776(C-Cl), 507(C-I). 1H-NMR($CDCl_3$) : 2.13(s, 1H, -N-NH-), 6.36- 7.93(m, 12H, Ar-H), 2.73(s, 3H, -$COCH_3$), 3.62(s, 2H, -CH_2). Anal. (%) for $C_{26}H_{18}N_4O_2ICl$ Calcd; C, 53.74; H, 3.10; N, 9.64; Found; C, 53.76; H, 3.11; N, 9.66.

Synthesis of 2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl-3-substituted phenyl acryl amido-6-iodoquinazolin-4(3H)-one 5a

A solution of 2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl-3-acetamido-6-iodoquinazolin-4(3H)-one (5.805g, 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 obtained was filtered, washed with water and recrystalized from methanol.

M.P.: 137 ^{0}C. Yeild: 76 % IR(KBr) : 3407(NH), 3062, 2859(C-H), 1721(C =O), 1642(C=O of –$COCH_3$), 1578 (CH=CH), 1319(C-N), 780(C-Cl), 510(C-I).1H-NMR($CDCl_3$) : 2.11(s, 1H, -N-NH), 6.36-7.93(m, 17H, Ar-H), 3.63(s, 2H, -CH_2), 6.80(d, 1H, COCH=), 8.61(d,

1H, =CH-Ar). Anal; (%) $C_{33}H_{22}N_4O_2ICl$ Calcd; C, 59.23; H, 3.29; N, 8.37; Found; C, 59.24; H, 3.30; N, 8.39.

The remaining 5b-l compounds were prepared by the above mention similar method.

Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-[(2-chloro) phenyl acryl amido]-6-iodoquinazolin-4(3H)-one (5b)

M.P.: 131-133 ^{0}C. Yeild: 70 % IR(KBr) : 3387(NH), 3061, 2861(C-H), 1728(C =O), 1638(C=O of –$COCH_3$), 1579 (CH=CH), 1317(C-N), 779(C-Cl), 509(C-I). 1H NMR($CDCl_3$) : 2.13(s, 1H, -N-NH), 6.36- 7.93(m, 16H, Ar-H), 3.63 (s, 2H, -CH_2), 6.81(d, 1H, COCH=), 8.62(d, 1H, =CH-Ar). 13C NMR: 29.6(-CH_2), 36.2, 41.5(CH=CH), 160.8 (immine>C=O), 162.1 (>C=O), 173.2(immine aromatic-C), 109.23-143.21(aromatic-27C). Anal; (%) $C_{33}H_{21}N_4O_2ICl_2$ Calcd; C, 56.33; H, 2.99; N,7.96; Found; C, 56.34; H, 3.01; N, 7.97.

Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-[(3-chloro) phenyl acryl amido]-6-iodoquinazolin-4(3H)-one (5c)

M.P.: 124-125 ^{0}C. Yeild: 72 % IR(KBr) : 3391(NH), 3062, 2861(C-H), 1727(C =O), 1639(C=O of –$COCH_3$), 1579 (CH=CH), 1316(C-N), 781(C-Cl), 506(C-I). 1H NMR($CDCl_3$) : 2.12(s, 1H, -N-NH), 6.36- 7.93(m, 16H, Ar-H), 3.61 (s, 2H, -CH_2), 6.81(d, 1H, COCH=), 8.60(d, 1H, =CH-Ar). 13C NMR: 31.2(-CH_2), 36.6, 41.2(CH=CH), 161.2(immine>C=O), 162.3(>C=O), 173.1(immine aromatic-C), 109.23-143.21(aromatic-27C). Anal; (%) $C_{33}H_{21}N_4O_2ICl_2$ Calcd; C, 56.33; H, 2.99; N,7.96; Found; C, 56.35; H, 3.02; N, 7.98.

Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-[(4-chloro) phenyl acryl amido]-6-iodoquinazolin-4(3H)-one (5d)

M.P.: 127-129 ^{0}C. Yeild: 72 % IR(KBr) : 3398(NH), 3063, 2858(C-H), 1729(C =O), 1637(C=O of –$COCH_3$), 1576(CH=CH), 1317(C-N), 780(C-Cl), 511(C-I). 1H NMR($CDCl_3$) :2.13(s, 1H, -N-NH), 6.36- 7.93(m, 16H, Ar-H), 3.62(s, 2H, -CH_2), 6.82(d, 1H, COCH=), 8.61(d, 1H, =CH-Ar). 13C NMR: 31.6(-CH_2), 36.4, 41.3(CH=CH), 161.1 (immine >C=O), 162.1(>C=O), 173.2(immine aromatic-C), 109.23-143.21(aromatic-27C). Anal; (%) $C_{33}H_{21}N_4O_2ICl_2$ Calcd; C, 56.33; H, 2.99; N,7.96; Found; C, 56.35; H, 3.01; N, 7.97.

Spectral data of 2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl-3-[(2-hydroxy)phenyl acryl amido]-6-iodoquinazolin-4(3H)-one (5e)

M.P.: 146-148 ^{0}C. Yeild: 71 % IR (KBr) : 3541(-OH),3381(NH), 3061, 2856(C-H), 1731(C =O), 1639(C=O of –$COCH_3$), 1578 (CH=CH), 1318(C-N), 776(C-Cl), 507(C-I). 1H NMR($CDCl_3$) :2.11(s, 1H, -N-NH),6.36- 7.93(m,16H, Ar-H),3.63 (s, 2H, -CH_2), 6.81(d, 1H, COCH=), 8.60(d, 1H, =CH-Ar), 10.38(s, 1H,-OH). 13C NMR: 30.9(-CH_2), 36.3, 41.5(CH=CH), 160.8 (immine >C=O), 162.2 (>C=O), 173.1(immine aromatic-C), 109.23-143.21(aromatic-27C). Anal; (%) $C_{33}H_{22}N_4O_3ICl$ Calcd; C, 57.85; H, 3.21; N,8.18; Found; C, 57.86; H, 3.23; N, 8.19.

Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-[(3-hydroxy) phenyl acryl amido]-6-iodoquinazolin-4(3H)-one (5f)

M.P.:151-153 ^{0}C. Yeild: 67 % IR(KBr) : 3549(-OH),3392(NH), 3064, 2859(C-H), 1733(C =O), 1638(C=O of –$COCH_3$), 1576 (CH=CH), 1319(C-N), 778(C-Cl), 509(C-I). 1H NMR($CDCl_3$) :2.13(s, 1H, -N-NH), 6.36- 7.93(m, 16H, Ar-H), 3.61 (s, 2H, -CH_2), 6.83(d, 1H, COCH=), 8.61(d, 1H, =CH-Ar),10.39(s,1H,-OH).13C NMR: 31.1(-CH2), 36.5, 41.7(CH=CH),161.2(immine >C=O),162.3 (>C=O), 173.1(immine aromatic-C), 109.23-143.21(aromatic-27C). Anal; (%) $C_{33}H_{22}N_4O_3ICl$ Calcd; C, 57.85; H, 3.21; N,8.18; Found; C, 57.87; H, 3.23; N, 8.20.

Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-[(4-hydroxy) phenyl acryl amido]-6-iodoquinazolin-4(3H)-one (5g)

M.P.: 157-159 ^{0}C. Yeild:70 % IR(KBr): 3551(-OH),3395(NH), 3063, 2857(C-H), 1735(C =O), 1638(C=O of –$COCH_3$), 1578(CH=CH), 1320(C-N), 781(C-Cl), 511(C-I). 1H NMR($CDCl_3$): 2.12(s, 1H, -N-NH),6.36- 7.93(m,16H, Ar-H),3.62 (s, 2H, -CH2), 6.81(d, 1H, COCH=), 8.61(d, 1H, =CH-Ar), 10.37(s,1H,-OH).13C NMR: 30.9(-CH_2),36.7,41.6(CH=CH),161.1(immine >C=O),162.4(>C=O),173.1 (immine aromatic-C), 109.23-143.21(aromatic-27C). Anal; (%) C33H22N4O3ICl Calcd; C, 57.85; H, 3.21; N,8.18; Found; C, 57.86; H, 3.21; N, 8.20.

Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-[(2-nitro) phenyl acryl amido]-6-iodoquinazolin-4(3H)-one (5h)

M.P.: 169-171 ^{0}C. Yeild: 68 % IR(KBr) : 3413(NH), 3061, 2852(C-H), 1721(C =O), 1614(C=O of –COCH3), 1572(CH=CH), 1317(C-N),1565,1367(-NO_2) 779(C-Cl), 507(C-I). 1H NMR($CDCl_3$): 2.15(s, 1H, -N-NH), 6.36- 7.91(m, 16H, Ar-H), 3.61 (s, 2H, -CH_2), 6.81(d, 1H, COCH=), 8.62(d, 1H, =CH-Ar). 13C NMR:30.5(-CH_2),36.6,42.3(CH=CH),161.4(immine >C=O),162.1(>C=O),173.2(immine aromatic-C), 108.89-143.13(aromatic-27C). Anal; (%) $C_{33}H_{21}N_5O_4ICl$ Calcd; C, 55.50; H, 2.94; N,9.81; Found; C, 55.53; H, 2.96; N, 9.83.

Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-[(3-nitro) phenyl acryl amido]-6-iodoquinazolin-4(3H)-one (5i)

M.P.: 174-176 ^{0}C. Yeild: 66 % IR(KBr) : 3411(NH), 3063, 2854(C-H), 1723(C =O), 1615(C=O of –$COCH_3$), 1574(CH=CH), 1319(C-N),1561,1363(-NO_2), 781(C-Cl), 509(C-I). 1H NMR($CDCl_3$): 2.17(s, 1H, -N-NH), 6.37- 7.92(m, 16H, Ar-H), 3.63(s, 2H, -CH_2), 6.80(d, 1H, COCH=), 8.61(d, 1H, =CH-Ar).13CNMR:30.6(-CH2),36.4,42.2(CH=CH),161.1(immine>C=O),162.0(>C=O),173.3(immine aromatic-C), 109.13-143.14(aromatic-27C). Anal; (%) $C_{33}H_{21}N_5O_4ICl$ Calcd; C, 55.50; H, 2.94; N,9.81; Found; C, 55.51; H, 2.95; N, 9.82.

Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-[(4-nitro) phenyl acryl amido]-6-iodoquinazolin-4(3H)-one (5j)

M.P.: 181-182 ^{0}C. Yeild: 70 % IR(KBr) : 3415(NH), 3059, 2857(C-H), 1724(C =O), 1613(C=O of –COCH3), 1572 (CH=CH),1563,1366(-NO2),1317(C-N), 778(C-Cl), 507(C-I). 1H NMR(CDCl3): 2.16(s, 1H, -N-NH), 6.39- 7.94(m, 16H, Ar-H), 3.62 (s, 2H, -CH2), 6.81(d, 1H, COCH=), 8.60(d, 1H, =CH-Ar).13CNMR:30.4(-CH2),36.3,42.3(CH=CH),161.2(immine>C=O),162.1(>C=O),173.2 (immine aromatic-C),109.19-143.13(aromatic-27C). Anal; (%) $C_{33}H_{21}N_5O_4ICl$ Calcd; C, 55.50; H, 2.94; N, 9.81; Found; C, 55.53; H, 2.96; N, 9.84.

Spectral data of 2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl-3-[(2-methoxy)phenyl acryl amido]-6-iodoquinazolin-4(3H)-one (5k)

M.P.:141-143 ^{0}C. Yeild: 72 % IR(KBr) : 3412(NH), 3061, 2856(C-H), 1723(C =O), 1614(C=O of –$COCH_3$),1573(CH=CH),1319(C-N),1243,1109(C-O-C),781(C-Cl),509(C-I).1H-NMR($CDCl_3$): 2.15(s, 1H, -N-NH),6.38- 7.91(m,16H, Ar-H), 3.63 (s, 2H, -CH_2),6.80(d,1H, COCH=),8.62(d,1H, =CH-Ar), 3.77(s,3H,-OCH3).13CNMR:30.5(-CH_2),36.5,41.9(CH=CH), 59.5(-OCH_3)161.3(immine >C=O), 162.2 (>C=O),173.1(immine aromatic-C),109.17-143.21(aromatic-27C). Anal;(%) $C_{34}H_{24}N_4O_3ICl$ Calcd; C, 58.41; H, 3.43; N,8.01; Found; C, 58.43; H, 3.45; N, 8.03.

Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-[(4-methoxy) phenyl acryl amido]-6-iodoquinazolin-4(3H)-one (5l)

M.P.: 149-151 ^{0}C. Yeild: 75 % IR(KBr) : 3409(NH), 3063, 2859(C-H), 1721(C =O), 1615(C=O of –$COCH_3$), 1575(CH=CH), 1317(C-N),1245,1108(C-O-C),778(C-Cl), 509(C-I). 1H NMR($CDCl_3$): 2.16(s, 1H, -N-NH), 6.39- 7.93(m, 16H, Ar-H), 3.62 (s, 2H, -CH_2), 6.81(d, 1H, COCH=), 8.62(d, 1H, =CH-Ar), 3.80(s,3H,-OCH_3).13C NMR: 30.6(-CH_2), 36.6,42.4(CH=CH),59.7(-OCH_3),161.1(immine

Volume : 3 | Issue : 11 | November 2014 • ISSN No 2277 - 8179

>C=O),162.3 (>C=O), 173.2(immine aromatic-C), 109.21-143.20(aromatic-27C). Anal; (%) $C_{34}H_{24}N_4O_3ICl$ Calcd; C, 58.41; H, 3.43; N,8.01; Found; C, 58.42; H, 3.44; N, 8.04.

Synthesis of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3–(1, 5-diphenyl-4,5-dihydro-1H-pyrazol-3-yl amino)-6-iodo quinazolin-4(3H)-one 6a

To a solution of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-substituted phenyl acryl amido-6-iodoquinazolin-4(3H)-one (6.685 g, 0.01 mol) in methanol, add phenyl hydrazine hydrate (99 %) (2.16g, 0.02 mol)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.: 147-149 ^{0}C. Yeild: 73 % IR(KBr): 3369(N-H),3063,2857(C-H),1725(C=O),1616(C=N), 1319(C-N),780(C-Cl),507(C-I).1H NMR($CDCl_3$): 2.17(d,1H,=N-NH),3.61(s,2H,-CH_2),3.06 (d,1Ha), 3.47(d,1Hb), 6.53(t,1Hx), 6.43-7.95(m,22H,Ar-H). 13C NMR: 30.6(-CH2), 36.4, 41.1, 161.3(pyrazol-C), 162.2 (>C=O), 173.1(immine aromatic-C) 109.21-143.20(aromatic-33C). Anal; (%) $C_{39}H_{28}N_6OICl$ Calcd; C, 61.70; H, 3.69; N,11.07; Found; C, 61.72; H, 3.70; N, 11.09.

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

Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3–[5-(2-chloro) phenyl-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl amino]-6-iodo quinazolin-4(3H)-one(6b)

M.P.: 140-141 ^{0}C. Yeild: 68 % IR(KBr):3368(N-H),3059,2861(C-H),1729(C=O),1616(C=N), 1315(C-N), 782(C-Cl), 509(C-I). 1H NMR(CDCl3): 2.13(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,21H,Ar-H).13C NMR: 30.4(-CH_2), 36.2, 41.5, 160.7 (immine pyrazol-C),162.2(>C=O),173.1(immine aromatic-C), 109.21-143.20(aromatic-33C). Anal; (%) $C_{39}H_{27}N_6OICl_2$ Calcd; C, 59.01; H, 3.40; N,10.59; Found; C, 59.03; H, 3.41; N, 10.61.

Spectral data of 6c: 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3–[5-(3-chloro) phenyl-1-phenyl-4, 5-dihydro-1H-pyrazol-3-yl amino]-6-iodo quinazolin-4(3H)-one (6c)

M.P.: 128-130 ^{0}C. Yeild: 70 % IR(KBr): 3371(N-H),3061, 2856(C-H),1731 (C=O),1614(C=N), 1318(C-N), 780(C-Cl),511(C-I).1HNMR($CDCl_3$):2.16(d,1H,=N-NH),3.63(s,2H,-CH_2), 3.06 (d,1Ha), 3.51(d,1Hb), 6.57(t,1Hx), 6.43-7.96(m,21H,Ar-H). 13C NMR: 31.3(-CH_2), 36.4, 41.3, 161.3 (immine pyrazol-C), 162.1(>C=O), 173.3(immine aromatic-C), 109.21-143.20(aromatic-33C). Anal; (%) $C_{39}H_{27}N_6OICl_2$ Calcd; C, 59.01; H, 3.40; N,10.59; Found; C, 59.02; H, 3.43; N, 10.60.

Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3–[5-(4-chloro) phenyl-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl amino]-6-iodo quinazolin-4(3H)-one(6d)

M.P.:135-136 ^{0}C. Yeild: 71 % IR(KBr):3367(N-H),3061,2863(C-H),1729(C=O),1616(C=N),1319(C-N), 782(C-Cl),510(C-I). 1H NMR ($CDCl_3$): 2.17 (d,1H,=N-NH), 3.62(s,2H,-CH_2), 3.07 (d,1Ha), 3.48(d,1Hb), 6.55(t,1Hx), 6.43-7.96(m,21H,Ar-H).13C NMR: 31.5(-CH2), 36.2, 41.5, 161.2 (immine pyrazol-C),162.2(>C=O),172.9(immine aromatic-C), 109.21-143.20(aromatic-33C). Anal; (%) $C_{39}H_{27}N_6OICl_2$ Calcd; C, 59.01; H, 3.40; N,10.59; Found; C, 59.03; H, 3.42; N, 10.62.

Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3–[5-(2-hydroxy) phenyl-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl amino]-6-iodo quinazolin-4(3H)-one(6e)

M.P.:156-158 ^{0}C.Yeild: 71 % IR(KBr):3541(O-H),3389(N-H),3063,2857 (C-H),1731(C=O),1614 (C=N), 1316(C-N), 780(C-Cl),511(C-I).1H NMR($CDCl_3$): 2.16(d,1H,=N-NH), 3.62(s,2H,-CH_2), 3.06(d,1Ha), 3.46(d,1Hb),6.52(t,1Hx), 6.43-7.96(m,21H,Ar-H),10.37(s,1H,-OH). 13C NMR: 30.9(-CH_2), 36.4, 41.3, 160.9(pyrazol-C), 162.1(>C=O), 173.0(immine aromatic-C) 109.21-143.20(aromatic-33C). Anal; (%) $C_{39}H_{28}N_6O_2ICl$ Calcd; C, 60.42; H, 3.61; N,10.84; Found; C, 60.43; H, 3.63; N, 10.85.

Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3–[5-(3-hydroxy) phenyl-1-phenyl-4, 5-dihydro-1H-pyrazol-3-yl amino]-6-iodo quinazolin-4(3H)-one (6f)

M.P.: 163-165 ^{0}C.Yeild: 65 %IR(KBr): 3549(O-H), 3391(N-H), 3061,2859(C-H), 1733(C=O), 1617 (C=N),1314(C-N), 781(C-Cl),509(C-I). 1H NMR($CDCl_3$): 2.17(d,1H,=N-NH),3.63 (s,2H,-CH2), 3.08(d,1Ha), 3.45(d,1Hb),6.53(t,1Hx), 6.43-7.96(m,21H,Ar-H),10.39(s,1H,-OH). 13C NMR: 30.7(-CH2), 36.4, 41.6, 161.2 (immine pyrazol-C), 162.3(>C=O), 173.1 (immine aromatic-C)109.21-143.20 (aromatic-33C). Anal; (%) $C_{39}H_{28}N_6O_2ICl$ Calcd; C, 60.42; H, 3.61; N,10.84; Found; C, 60.45; H, 3.62; N, 10.87.

Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3–[5-(4-hydroxy) phenyl-1-phenyl-4, 5-dihydro-1H-pyrazol-3-yl amino]-6-iodo quinazolin-4(3H)-one (6g)

M.P.: 168-170 ^{0}C.Yeild: 69 % IR(KBr): 3546(O-H), 3393(N-H), 3061,2857 (C-H),1729(C=O), 1614 (C=N),1317(C-N), 778(C-Cl), 511(C-I). 1H NMR($CDCl_3$): 2.16(d,1H,=N-NH),3.62 (s,2H,-CH_2), 3.06(d,1Ha), 3.44(d,1Hb),6.50(t,1Hx), 6.43-7.96(m,21H,Ar-H), 10.36(s,1H,-OH). 13C NMR: 30.6(-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; (%) $C_{39}H_{28}N_6O_2ICl$ Calcd; C, 60.42; H, 3.61; N,10.84; Found; C, 60.44; H, 3.61; N, 10.86.

Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3–[5-(2-nitro) phenyl-1-phenyl-4, 5-dihydro-1H-pyrazol-3-yl amino]-6-iodo quinazolin-4(3H)-one(6h)

M.P.: 180-181 ^{0}C.Yeild: 66 % IR(KBr): 3413(N-H),3063,2856(C-H),1727(C=O),1616(C=N), 1566, 1362(-NO_2), 1317(C-N),781(C-Cl),509(C-I).1H NMR($CDCl_3$): 2.16(d,1H,=N-NH),3.62(s,2H,-CH_2), 3.07(d,1Ha), 3.46(d,1Hb),6.53(t,1Hx), 6.43-7.96(m,21H,Ar-H).13C NMR : 30.7(-CH_2), 36.2,41.7,161.4 (immine pyrazol-C),162.3(>C=O),173.1(immine aromatic-C), 109.21-143.20(aromatic-33C). Anal; (%) $C_{39}H_{27}N_7O_3ICl$ Calcd; C, 58.24; H, 3.36; N,12.19; Found; C, 58.27; H, 3.37; N, 12.21.

Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3–[5-(3-nitro) phenyl-1-phenyl-4, 5-dihydro -1H-pyrazol-3-yl amino]-6-iodo quinazolin-4(3H)-one (6i)

M.P.: 189-190 ^{0}C.Yeild: 64 % IR (KBr):3409(NH), 3062, 2857(C-H), 1725(C=O),1614(C=N),1565, 1361(-NO_2),1316(C-N), 779(C-Cl),511(C-I). 1H NMR($CDCl_3$): 2.17(d,1H,=N-NH),3.61 (s,2H,-CH_2), 3.06(d,1Ha), 3.45(d,1Hb),6.51(t,1Hx), 6.43-7.96(m,21H,Ar-H). 13C NMR: 30.9(-CH2), 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; (%) $C_{39}H_{27}N_7O_3ICl$ Calcd; C, 58.24; H, 3.36; N,12.19; Found; C, 58.25; H, 3.39; N, 12.20.

Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3–[5-(4-nitro) phenyl-1-phenyl-4, 5-dihydro-1H-pyrazol-3-yl amino]-6-iodo quinazolin-4(3H)-one (6j)

M.P.: 201-203 ^{0}C.Yeild: 70 % IR (KBr):3411(NH), 3061, 2859(C-H), 1728(C=O), 1615(C=N), 1563, 1362(-NO_2), 1317(C-N), 781(C-Cl), 510(C-I). 1H NMR($CDCl_3$): 2.16(d,1H,=N-NH), 3.63(s,2H,-CH_2), 3.07(d,1Ha), 3.46(d,1Hb),6.53(t,1Hx), 6.43-7.96(m,21H,Ar-H). 13C NMR: 30.8(CH_2), 36.2, 41.3,161.1 (immine pyrazol-C),162.3(>C=O),173.1(immine aromatic-C), 109.21-143.20 (aromatic-33C). Anal; (%) $C_{39}H_{27}N_7O_3ICl$ Calcd; C, 58.24; H, 3.36; N,12.19; Found; C, 58.26; H, 3.38; N, 12.22.

Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3–[5-(2-methoxy) phenyl-1-phenyl-4, 5-dihydro-1H-pyrazol-3-yl amino]-6-iodo quinazolin-4(3H)-one(6k)

M.P.: 150-151 ^{0}C. Yeild: 73 % IR(KBr): 3408 (N-H),3063,2857 (C-H), 1730 (C=O), 1617 (C=N),1319 (C-N), 1243, 1109(C-O-C), 779(C-Cl), 508(C-I). 1H NMR(CDCl3):2.16(d,1H,=N-NH), 3.62(s,2H,-CH_2),

3.06(d,1Ha), 3.46(d,1Hb), 6.52(t,1Hx), 6.43-7.96 (m,21H,Ar-H), 3.82(s,3H,-OCH_3).13C NMR : 30.9(-CH_2),36.4, 41.5,161.1(immine pyrazol-C),162.0(>C=O), 173.1 (immine aromatic-C),58.2(-OCH_3), 109.21-143.20(aromatic-33C). Anal; (%) $C_{40}H_{30}N_6O_2ICl$ Calcd; C, 60.87; H, 3.80; N,10.65; Found; C, 60.90; H, 3.81; N, 10.67.

Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3–[5-(4-methoxy) phenyl-1-phenyl-4, 5-dihydro-1H-pyrazol-3-yl amino]-6-iodo quinazolin-4(3H)-one(6l)

M.P.:153-155 ^{0}C. Yeild: 74 % IR (KBr): 3411(N-H), 3064, 2861 (C-H), 1728(C=O), 1616(C=N), 1317 (C-N), 1241,1108 (C-O-C), 778(C-Cl), 507(C-I).1H NMR($CDCl_3$):2.17(d,1H,=N-NH) , 3.63(s,2H,-CH_2), 3.06(d,1Ha), 3.47(d,1Hb),6.53(t,1Hx), 6.43-7.96(m,21H,Ar-H), 3.81(s,3H,-OCH_3). 13C NMR: 30.8(-CH_2), 36.5, 41.6,161.3 (immine pyrazol-C),162.1(>C=O), 173.2 (immine aromatic-C),58.1(-OCH_3), 109.21-143.20(aromatic-33C). Anal; (%) $C_{40}H_{30}N_6O_2ICl$ Calcd; C, 60.87; H, 3.80; N,10.65; Found; C, 60.88; H, 3.82; N, 10.66.

RESULT AND DISCUSSION

The title compound 6-iodoquinazolin-4(3H) one bearing pyrazoline and quinoline moieties 6a-l was synthesized according to the described procedure in scheme-I. The IR spectra showing strong stretching vibration at 1723 and 1649 cm-1 indicates the presence of C=O group of quinazolinone and acetamide respectively. This was further confirming by 1H NMR spectra which showed singlet at δ 2.73 ppm equivalent to three protons of acetamide group. The acetamido quinazolin-4(3H) one 4 on based catalyzed condensation with aromatic aldehydes yielded acrylamide 5a-l which showed CH=CH stretching at1578 cm-1 in IR spectrum while 1H NMR spectra showed doublet of these protons at δ 6.80 and δ 8.60 ppm with coupling constant J = 16.0-16.6 Hz. Further cyclization of acrylamide 5a-l with phenyl hydrazine yielded the desired compounds 6-iodoquinazolin-4(3H) one bearing pyrazoline and quinoline moieties 6a-l. The IR spectra of compounds 6a-l showed C=O and C=N stretching of quinazolinone at 1725 and 1616 cm-1 respectively. The 1H NMR spectra of compounds 6a-j indicates that the –CH_2 protons of the pyrazoline ring resonated as a pair of doublet of doublets (Ha and Hb) because of germinal 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 position 4 of pyrazoline 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 13C 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 ACTIVITY

The in vitro antimicrobial activity of compounds 6a-l was carried out by cup-plate method (Barry 1976). Antibacterial activity 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), by measuring the zone of inhibition on agar plates at two different concentrations 100 and 50 µg/ml, penicillin-G were used as a standard, whereas antifungal activity was tested by measuring the zone of inhibition on agar plates with two fungal species, Candida albicans ATCC 10231 and Aspergillus niger ATCC 6275, at two different concentrations 20 and 10 µg/ml, fluconazole were used as a standard. In vitro screening results of synthesized compounds mentioned in table 1 and table 2.

Table: 1 Anti-bacterial activity of compound 6a-l

Compd	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 %
6a	H	12	10	46.40	13	11	49.15	11	09	43.86	12	10	46.40
6b	2-Cl	18	16	64.54	19	17	68.41	15	13	54.16	16	14	57.41
6c	3-Cl	17	14	62.99	18	15	66.43	15	12	52.44	15	13	54.16
6d	4-Cl	19	16	70.60	20	17	73.48	16	14	57.41	16	14	59.84
6e	2-OH	12	10	46.40	13	11	49.15	12	10	46.40	13	11	49.15
6f	3-OH	13	11	49.15	15	12	52.44	12	10	46.40	13	11	49.15
6g	4-OH	12	10	46.40	13	11	49.15	13	11	49.15	15	12	52.44
6h	2-NO_2	15	13	54.16	16	13	59.84	17	14	62.99	18	15	66.29
6i	3-NO_2	14	12	51.09	15	13	54.16	16	13	59.84	16	14	61.69
6j	4-NO_2	16	14	57.41	17	15	60.87	18	15	66.43	19	17	68.41
6k	2-OCH_3	13	11	49.15	15	12	52.44	15	12	52.44	15	13	54.16
6l	4-OCH_3	15	12	52.44	16	14	57.41	15	13	54.16	16	14	57.41
Penicillin - G		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 6a-l

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 %
6a	H	17	14	68.76	18	15	72.24
6b	2-Cl	14	12	56.03	14	12	56.03
6c	3-Cl	11	08	50.90	13	11	52.86
6d	4-Cl	14	11	59.36	14	11	59.39
6e	2-OH	12	09	47.75	14	11	59.39
6f	3-OH	12	10	49.89	13	11	52.86
6g	4-OH	13	11	52.86	14	12	56.03
6h	2-NO_2	11	09	47.09	12	10	49.89
6i	3-NO_2	09	07	41.93	10	08	44.43
6j	4-NO_2	12	10	49.89	13	11	52.86
6k	2-OCH_3	15	12	62.38	16	13	65.57
6l	4-OCH_3	16	13	65.88	17	15	66.67
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.

CONCLUSIONS

The title compound pyrazolylquinazolin-4(3H) ones bearing quinoline moiety 6a-l were synthesized by well organized method. The active pharmacophore present in newly synthesized compounds possessed good antibacterial and antifungal activity in vitro. Phenyl nucleus containing chloro group on ortho, meta and para position were active inhibitor against gram positive bacteria, whereas nitro precursor showed very good activity against gram negative bacteria compared to standard. Phenyl nucleus, 2-methoxy and 4- methoxy substituted compounds showed very good antifungal activity. These results lead

to identification of potentially active antibacterial and anti-fungal inhibitor and improvement of further research on these molecules.

ACKNOWLEDGEMENT
The author is gratefully thanks to Head, Department of Chemistry, Arts, Science and Commerce College, Pilvai for providing laboratory facilities and also specially thanks to the UGC New Delhi for financial assistance.

REFERENCE

[1] Hosum, A.Saad; Nermen, A. Osman, and Ahmed, H. Moustafa; (2011), Synthesis and analgesics activity of some new pyrazole and triazole bearing 6,8-dibromo-2-methyl quinazolinone moiety; Molecule, 16,10187-10201; DOI: 10.3390/molecules 161210187. | [2] Chandrika, P M; Yakaiah, T; Rao, A R; Narsaiah, B; Reddy, N C; Sridhar, V; Rao, J V; (2008), Synthesis of novel disubstituted quinazolinone derivatives, their anti-inflammatory and anticancer activity against U 937 Leukemia cell lines; Eur. J. Med. Chem.; 43, 846-852. | [3] Rauf, A and Farshori, N, N; (2012), Microwave induced synthesis of aromatic heterocycles; Springer Briefs in Green Chemistry for Sustainability; DOI: 10.1007/978-94-007-1485-4-6,© The author(s) 2012. | [4] Liming, Hu; Song, Yan; Zaigang, Luo; Xiao, Han; Yujie, Wang; Zhanyang, Wang and Changchu, Zeng; (2012); Design practical synthesis and biological evaluation novel 6-(pyrazolyl methyl)-4- quinazolin-3-carboxylic acid derivatives as HIV-1 integrase inhibitors; Molecules; 17, 10652-10666; DOI: 10.3390/molecules 170910652. | [5] Suresh, K; Bawa, S; Gupta, H; (2009); Biological activity of quinoline derivatives; Mini review in Medicinal Chemistry; 9(14); 1648-1654; DOI: 10.2174/1389557097910/22247.(anticancer, cardiovascular, anti-inflammatory antimicrobial). | [6] Patel, N B; Patel, J C and Barat, G G; (2012); In vitro evaluation of the antibacterial and anti fungal activity of some new pyrazolylquinazolin-4(3H)-one derivatives; Med. Chem. Res.; 21, 229-238; DOI: 10.1007/600044-010-9530-z. | [7] Mohamed, M S; Kamel, M M; Kaseem, E M; Ahotaleb, N; Abd-El-Moez, S I; Ahmed, M F;(2010), Novel 6,8-dibromo-4(3H) quinazolinone derivatives of antibacterial and antifungal activities; Eur. J. Med. Chem.; 45(8),3313-3319; DOI: 10.1016/j.ejmech.2010.04.014.Epub 2010 Apr 20. | [8] Marti, Y; Singh, A K; Pathak, D; (2011), New 6-bromo-2-methyl-3-(substituted phenyl)-(3H)-quinazolin-4 ones with antibacterial and anti-inflammatory activities; Indian J. Pharm. Sci.; 73(3), 333-337; DOI: 10.4103/0250-474x.93512. | [9] Patel, N B; Barat, G G; (2010); In vitro microbial studies of pyrazolylquinazolin-4(3H) ones; Journal of Saudi Chemical Society; 14, 157-164; DOI: 10.1016/j.jscs.2010.02.016. | [10] Panneersalvam, P; Rather, B A; Ravi Shankar Reddy, D; Rameshkumar, N; (2009), Synthesis and antimicrobial screening of some Schiff bases of 3-amino-6,8-dibromo-2-phenyl quinazolin-4(3H) ones; Eur. J. Med. Chem.; 44(5), 2328-2333; DOI: 10.1016/j.ejmech.2008.04.010. Epub 2008 Apr 29. | [11] Amir, M; Ali, I; Hassan, M Z; (2013); Design and synthesis of some quinazolin-4(3H) ones as anticonvulsant and antidepressant agents; Arch Pharm Res.; 36(1), 61-68; DOI: 10.1007/s 12272-013-0004-y. | [12] Rahaman, T; Mohmad, A and Bahar,A; (2014); Synthesis of some 3:5-diphenyl-Δ1 –pyrazoline and 5-(2-furyl)- Δ1 –pyrazoline derivatives and their screening for antidepressant and anticonvulsant activity.; IJPSR International Journal of Pharmaceutical Sciences and Research.; 5,3228-3234; DOI: 10.13040 / IJPSR 0975-8232.5(8).3226-34 | [13] Tesfahunegn, R G;(2013); Synthesis, antileshmenial and antimalarial activity evaluation of novel 2,3- disubstituted quinazolinone-4(3H) ones bearing biologically active quinoline and pyrazoline moieties.; medicinal Chemistry and Computer Aided Drug Designing; 3,119; DOI: 10.4172/2161-0444 S1.008. | [14] Sivakumar, K K; Rajshekharan, A; Rao, B N; (2014); Synthesis SAR study and evaluation of Mannich and Schiff bases of pyrazol-5(4H)- one moiety containing 3-(Hydrazinyl)-2-phenyl quinazolin-4(3H) one; Indian J. Pharm. Sci.;75(4), 463-475; DOI: 10.4103/0250-474x.119832. | | |