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NOVEL 6-IODO-3H-QUINAZOLIN-4-ONE DERIVATIVES: CLASS OF PHARMACEUTICAL ACTIVE SCAFFOLD

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ABSTRACT

Quinazolinone, a hetetocyclic compound, has been extensively studied and used in certain specific biological activities. 3H-quinazolin-4 one and its derivative constitute an important class of fused heterocycles that are found in more than 200 naturally occurring alkaloids. With passage of time newer and more complex variants of quinazolinone structure are being discovered. Novel scaffold of 3H-quinazolin-4 one was synthesized by the base catalysed cyclisation of cromenamodo with 3:5-dinitrophenyl hydrazine hydrate. The overall reaction was conventional multistep process. The structure of synthesized compounds was confirmed on the basis of elemental analysis, IR and NMR spectra results. The pharmacological studies of title compounds were screened for s.aureus, b.subtilis gram positive bacteria, E. coli, P.aeruginosa gram negative bacteria and A.niger, C. albican plant pathogens for antifungal activity in vitro by disc diffusion method. The strength of synthesized compounds was compared with standard drug.

KEYWORDS: Pharmacological, Quinoline, In Vitro, 3H-Quinazolin-4-one.

INTRODUCTION

Quinazolinone derivatives are the emerging pharmacophore, which has drawn a growing interest in the area of drug designing. 3H-quinazolin-4 one and its nitrogen containing precursors had diversified biological properties. One of the most frequently encountered heterocycles in medicinal chemistry is 3H-quinazolin-4 one with pyrazoline and its analogs have widespread applications as a potential anti-inflammatory, anticancer and analgesics agent[1, 2, 3] in field of medicinal chemistry. Moreover, a large number of 3H-quinazolin-4 ones derivatives have been reported as a potential antifungal and antimicrobial agents[4, 5, 6].

Pyrazoline derivatives of 3H-quinazolin-4 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 [7] and CNS depressant agent[8]. The halogenated derivatives of quinazolin-4(3H) ones possess potential antihyperlipidemic activity and have no significant toxic side effect at the sub lethal drop level 2 mg/kg [9]. In addition 3H-quinazolin-4 one bearing quinoline moiety reported to potential anticonvulsant[10] and HIV-1 integrate inhibitors[11].

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. The targeted molecules screened for antibacterial and antifungal activities in vitro by disc diffusion method.

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

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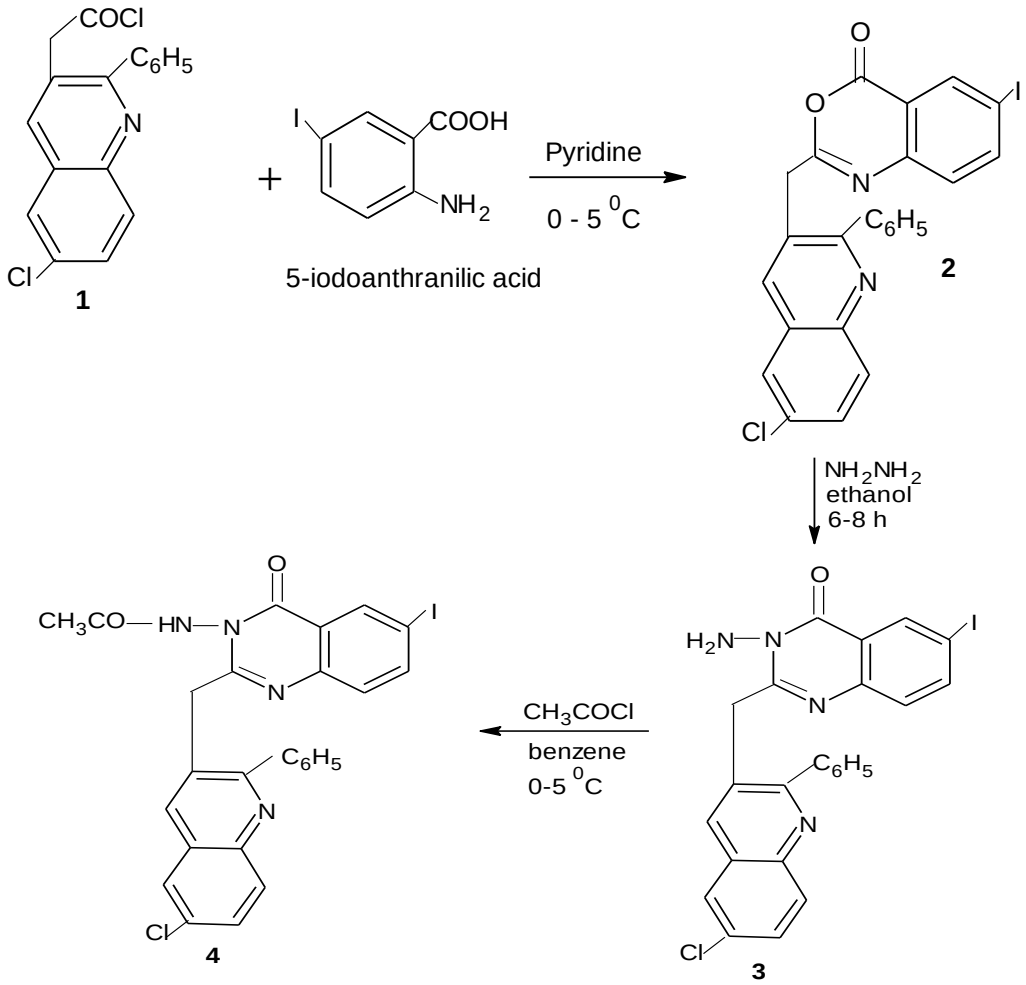
cm^{-1}. ^1H NMR and ^{13}C NMR spectra were recorded on Bruker Advance II 400 NMR spectrometer using $CDCl_3$ as a solvent. The chemical shifts were reported in (δ ppm) downfield using tetra methyl silane as internal standard. Elemental analyses of newly synthesized compounds were carried out on Carlo 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 [12].

Scheme I Synthetic Pathway for Target Molecule



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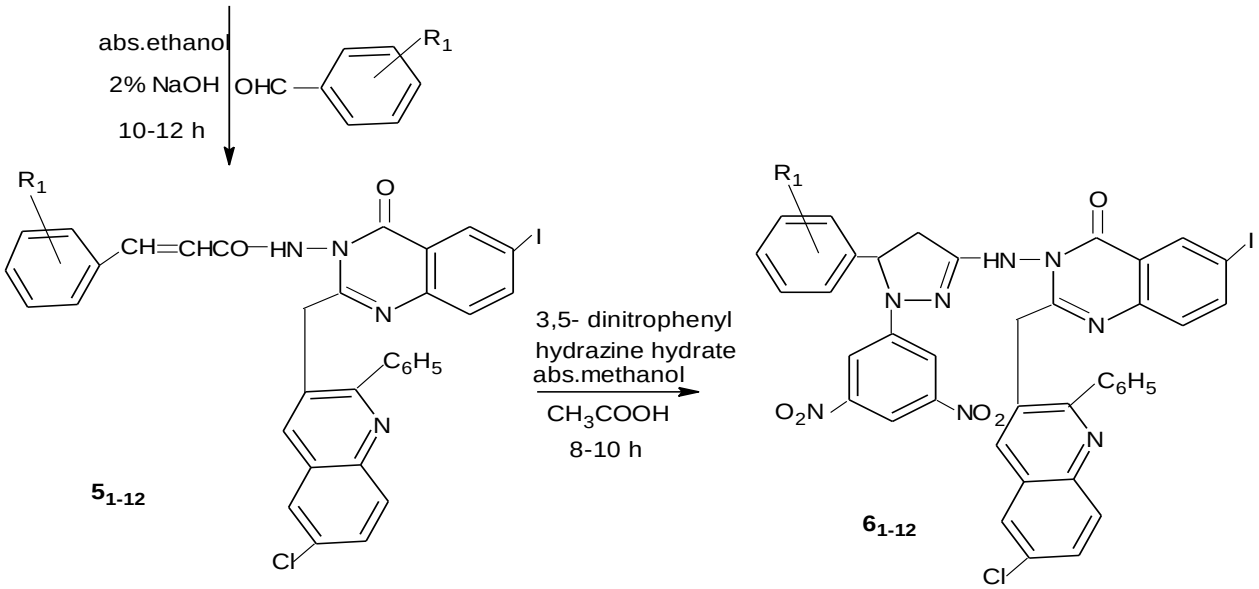

R₁ = H, 2-Cl, 3-Cl, 4-Cl, 2-OH, 3-OH, 4-OH, 2-NO₂, 3-NO₂, 4-NO₂, 2-OCH₃, 4-OCH₃

EXPERIMENTAL SECTION

2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl–6-iodo-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 5-iodo anthranilic acid (2.53 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.

Yeild: 79% M.P.:162-163 ^{0}C. IR(KBr): 3073, 2861(C-H), 1725(C=O), 1616(C=N), 1327(C-N), 1238 (C-O-C), 782(C-Cl), 538(C-I). Anal. (%) for $C_{24}H_{14}N_2O_2ICl$ Calcd; C, 54.90; H, 2.66; N, 5.33; Found; C, 54.91; H, 2.68; N, 5.34.

3-Amino-2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl–6-iodo-3H-quinazolin–4 one 3

To a mixture of 2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl–6-iodo-3,1-benzoxazin-4(3*H*) one (5.245 g, 0.01 mol) and hydrazine hydrate(99 %) (0.50 g, 0.01mol) in 25.0 ml pyridine was heated at 180-200 ^{0}C in an oil bath for 5-6 h. The oily mass was 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.

Yeild**:** 74 % M.P**.:** 145-146 ^{0}C. IR(KBr): 3407(NH), 3069, 2863(C-H), 1718(C=O), 1614 (C=N), 1325(C-N), 779(C-Cl), 540(C-I). ^{1}HNMR(400 MHz, $CDCl_3$)**:** 3.62(s, 2H, -CH_2), 5.74(s, 2H, -NH_2), 6.42-7.96(m, 12H, Ar-H). Anal. (%) for $C_{24}H_{16}N_4OICl$ Calcd; C, 53.48; H, 2.97; N,10.39; Found; C, 53.49; H, 2.98; N, 10.41.

2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl-3-acetamido-6-iodo-3H-quinazolin-4 one 4

To a solution of 3-Amino-2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl–6-iodo-3H-quinazolin-4 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, 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.

Yeild**:** 69 % M.P**.:** 173-174 ^{0}C. IR(KBr): 3408(NH), 3062,2861(C-H),1721(C=O), 1640(C=O of –$COCH_3$), 1323(C-N), 774(C-Cl), 537(C-I). ^{1}H-NMR(400 MHz, $CDCl_3$) **:** 2.24(s, 3H, -$COCH_3$), 3.63(s, 2H, -CH_2), 6.42-7.96 (m, 12H, Ar-H), 9.15(s, 1H, -NH). 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, 9.65.

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

To a solution of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl]methyl-3-acetamido-6-iodo-3H-quinazolin-4 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 thus obtained was filtered, washed with water and recrystalized from methanol.

Yeild**:** 76 % M.P.**:** 137-138 ^{0}C. 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),539(C-I).^{1}H-NMR(400 MHz, $CDCl_3$)**:** 3.63(s, 2H, -CH_2), 6.42- 7.96(m, 17H, Ar-H), 6.77(d, 1H, J=16.6Hz, =CHCO), 7.62(d, 1H, J=16.6Hz, =CH-Ar), 9.15(s, 1H, -NH). Anal; (%) $C_{33}H_{22}N_4O_2ICl$ Calcd; C, 59.23; H, 3.29; N, 8.37; Found; C, 59.24; H, 3.31; N, 8.38.
The remaining **$5_{2\text{-}12}$** 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-iodo-3H-quinazolin-4 one 6_1

To a solution of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-substituted phenyl acryl amido-6-iodo-3H-quinazolin-4 one (6.685 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.
Yeild**:** 73% M.P.**:**127-128 ^{0}C. 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), 541(C-I). ^{1}HNMR (400 MHz, $CDCl_3$): 3.02 (dd,1H, J_{ab}= 17.4 Hz, J_{ax}= 5.6 Hz, Ha), 3.45 (dd,1H, J_{ba} = 17.4 Hz, J_{bx} = 12.2 Hz, Hb),3.62 (s,2H,-CH_2), 5.47(dd,1H, J_{xb} = 12.2 Hz, J_{xa} = 5.6 Hz, Hx), 6.42-7.96 (m,20H,Ar-H), 9.15 (d,1H,-NH). ^{13}C NMR(100 MHz, $CDCl_3$): 31.4(CH_2-C), 36.5, 41.1, 161.2(pyrazol-3C), 162.2 (C=O,C), 173.1(Immine-C) 109.21-143.20(Ar-33C). Anal; (%) $C_{39}H_{26}N_8O_5ICl$ Calcd; C, 55.15; H, 3.06; N,13.19; Found; C, 55.17; H, 3.07; N, 13.20.
The remaining **$6_{2\text{-}12}$** 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-iodo-3H-quinazolin-4 one 6_2

Yeild **:** 75 % M.P.**:** 182-183 ^{0}C. 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), 534 (C-I). ^{1}HNMR (400 MHz, $CDCl_3$): 3.04 (dd,1H, J_{ab}= 17.4 Hz, J_{ax}= 5.6 Hz, Ha), 3.49 (dd,1H, J_{ba} = 17.4 Hz, J_{bx} = 12.2 Hz, Hb),3.62 (s,2H,-CH_2), 5.47(dd,1H, J_{xb} = 12.2 Hz, J_{xa} = 5.6 Hz, Hx), 6.42-7.96 (m,19H,Ar-H), 9.15 (d,1H,-NH). ^{13}C NMR(100 MHz, $CDCl_3$): 31.3(CH_2-C), 36.4, 41.6, 160.9(pyrazol-3C), 162.2 (C=O,C), 173.1(Immine-C) 109.21-143.20(Ar-33C). Anal; (%) $C_{39}H_{25}N_8O_5ICl_2$ Calcd; C, 53.00; H, 2.83; N,12.68; Found; C, 53.01; H, 2.83; N, 12.69.

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-iodo-3H-quinazolin-4 one 6_3

Yeild**:** 70 % M.P.**:** 150-151 ^{0}C. 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),529(C-I). ^{1}HNMR (400 MHz, $CDCl_3$): 3.02 (dd,1H, J_{ab}= 17.4 Hz, J_{ax}= 5.6 Hz, Ha), 3.45 (dd,1H, J_{ba} = 17.4 Hz, J_{bx} = 12.2 Hz, Hb),3.62 (s,2H,-CH_2), 5.49(dd,1H, J_{xb} = 12.0 Hz, J_{xa} = 5.6 Hz, Hx), 6.42-7.96 (m,19H,Ar-H), 9.15 (d,1H,-NH). ^{13}C NMR (100 MHz, $CDCl_3$): 31.6(CH_2-C), 36.7, 41.3, 161.1(pyrazol-3C), 162.1 (C=O,C), 173.1(Immine-C) 109.21-143.20(Ar-33C). Anal; (%) $C_{39}H_{25}N_8O_5ICl_2$ Calcd; C, 53.00; H, 2.83; N,12.68; Found; C, 53.02; H, 2.84; N, 12.69.

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-iodo-3H-quinazolin-4 one 6_4

Yeild**:** 76% M.P.**:**169-170 ^{0}C. 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),538(C-I). ^{1}HNMR (400 MHz, $CDCl_3$): 3.05 (dd,1H, J_{ab}= 17.8 Hz, J_{ax}= 5.4 Hz, Ha), 3.48 (dd,1H, J_{ba} = 17.8 Hz, J_{bx} = 11.8 Hz, Hb),3.62 (s,2H,-CH_2), 5.47(dd, 1H, J_{xb} = 11.8 Hz, J_{xa} = 5.6 Hz, Hx), 6.42-7.96 (m,19H, Ar-H), 9.15 (d,1H,-NH). ^{13}C NMR (100 MHz, $CDCl_3$): 31.5(CH_2-C), 36.3, 41.5,161.2(pyrazol-3C),162.2(C=O,C), 173.1 (Immine-C) 109.21-143.20(Ar-33C). Anal; (%) $C_{39}H_{25}N_8O_5ICl_2$ Calcd; C, 53.00; H, 2.83; N,12.68; Found; C, 53.01; H, 2.84; N, 12.69.

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-iodo-3H-quinazolin-4 one 6_5

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Yeild**:** 65% M.P.**:**143-144 ^{0}C. 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),536(C-I). ^{1}HNMR (400 MHz, $CDCl_3$): 3.03 (dd,1H, J_{ab}= 17.6 Hz, J_{ax}= 5.4 Hz, Ha), 3.46 (dd,1H, J_{ba} = 17.6 Hz, J_{bx} = 11.8 Hz, Hb),3.62 (s,2H,-CH_2), 5.51(dd,1H, J_{xb} = 11.8 Hz, J_{xa} = 5.4 Hz, Hx), 6.42-7.96 (m,19H,Ar-H), 9.15 (d,1H,-NH), 10.38(s,1H,-OH). ^{13}C NMR(100 MHz, $CDCl_3$): 31.4(CH_2-C), 36.4, 41.3, 161.1(pyrazol-3C), 162.1 (C=O,C), 173.1(Immine-C) 109.21-143.20(Ar-33C). Anal; (%) $C_{39}H_{26}N_8O_6ICl$ Calcd; C, 54.13; H, 3.00; N,12.95; Found; C, 54.15; H, 3.01; N, 12.96.

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-iodo-3H-quinazolin-4 one 6_6

Yeild**:** 72 % M.P.**:** 131-132 ^{0}C. 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),539(C-I). ^{1}HNMR (400 MHz, $CDCl_3$): 3.05 (dd,1H, J_{ab}= 17.8 Hz, J_{ax}= 5.6 Hz, Ha), 3.48 (dd,1H, J_{ba} = 17.8 Hz, J_{bx} = 12.4 Hz, Hb),3.62 (s,2H,-CH_2), 5.52(dd,1H, J_{xb} = 12.4 Hz, J_{xa} = 5.6 Hz, Hx), 6.42-7.96 (m,19H,Ar-H), 9.15 (d,1H,-NH), 10.39(s,1H,-OH). ^{13}C NMR (100 MHz, $CDCl_3$): 31.5(CH_2-C), 36.4, 41.6, 161.2(pyrazol-3C), 162.2 (C=O,C), 173.1(Immine-C) 109.21-143.20(Ar-33C). Anal; (%) $C_{39}H_{26}N_8O_6ICl$ Calcd; C, 54.13; H, 3.00; N,12.95; Found; C, 54.14; H, 3.01; N, 12.96.

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-iodo-3H-quinazolin-4 one 6_7

Yeild**:** 67 % M.P.: 148-149 ^{0}C. 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), 535(C-I). ^{1}HNMR (400 MHz, $CDCl_3$): 3.07 (dd,1H, J_{ab}= 17.6 Hz, J_{ax}= 5.4 Hz, Ha), 3.50 (dd,1H, J_{ba} = 17.6 Hz, J_{bx} = 12.0 Hz, Hb),3.62 (s,2H,-CH_2), 5.52(dd,1H, J_{xb} = 12.0 Hz, J_{xa} = 5.4 Hz, Hx), 6.42-7.96 (m,19H,Ar-H), 9.15 (d,1H,-NH), 10.38(s,1H,-OH). ^{13}C NMR(100 MHz, $CDCl_3$): 31.4(CH_2-C), 36.5, 41.4, 161.1(pyrazol-3C), 162.1 (C=O,C), 173.3(Immine-C) 109.21-143.20(Ar-33C). Anal; (%) $C_{39}H_{26}N_8O_6ICl$ Calcd; C, 54.13; H, 3.00; N,12.95; Found; C, 54.13; H, 3.02; N, 12.97.

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-iodo-3H-quinazolin-4 one 6_8

Yeild**:** 77 % M.P.**:** 179-180 ^{0}C. 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),542(C-I). ^{1}HNMR (400 MHz, $CDCl_3$): 3.01 (dd,1H, J_{ab}= 17.0 Hz, J_{ax}= 5.2 Hz, Ha), 3.46 (dd,1H, J_{ba} = 17.6 Hz, J_{bx} = 11.8 Hz, Hb),3.62 (s,2H,-CH_2), 5.51(dd,1H, J_{xb} = 11.8 Hz, J_{xa} = 5.4 Hz, Hx), 6.42-7.96 (m,19H,Ar-H), 9.15 (d,1H,-NH). ^{13}C NMR(100 MHz, $CDCl_3$): 31.5(CH_2-C), 36.3, 41.7, 161.4(pyrazol-3C), 162.2 (C=O,C), 173.1(Immine-C) 109.21-143.20(Ar-33C). Anal; (%) $C_{39}H_{25}N_9O_7ICl$ Calcd; C, 52.37; H, 2.79; N,14.10; Found; C, 52.38; H, 2.81; N, 14.11.

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-iodo-3H-quinazolin-4 one 6_9

Yeild**:** 74 % M.P.**:** 171-172 ^{0}C. IR(KBr):3371(NH),3062,2857(C-H),1725(C=O),1616 (C=N), 1566, 1361(-NO_2),1319(C-N), 779(C-Cl),537(C-I). ^{1}HNMR (400 MHz, $CDCl_3$): 3.03 (dd,1H, J_{ab}= 17.4 Hz, J_{ax}= 5.6 Hz, Ha), 3.50 (dd,1H, J_{ba} = 17.4 Hz, J_{bx} = 12.2 Hz, Hb),3.62 (s,2H,-CH_2), 5.52(dd,1H, J_{xb} = 12.2 Hz, J_{xa} = 5.6 Hz, Hx), 6.42-7.96 (m,19H,Ar-H), 9.15 (d,1H,-NH). ^{13}C NMR(100 MHz, $CDCl_3$): 31.4(CH_2-C), 36.5, 41.6, 161.3(pyrazol-3C), 162.2 (C=O,C), 172.9(Immine-C) 109.21-143.20(Ar-33C). Anal; (%) $C_{39}H_{25}N_9O_7ICl$ Calcd; C, 52.37; H, 2.79; N,14.10; Found; C, 52.37; H, 2.80; N, 14.12.

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-iodo-3H-quinazolin-4 one 6_{10}

Yeild**:** 71 % M.P.**:** 193-194 ^{0}C. IR (KBr):3373(NH), 3061, 2859(C-H), 1726(C=O), 1616(C=N), 1565, 1361(-NO_2),1319(C-N), 781(C-Cl), 536(C-I). ^{1}HNMR (400 MHz, $CDCl_3$): 3.02 (dd,1H, J_{ab}= 17.2 Hz, J_{ax}= 5.2 Hz, Ha), 3.47 (dd,1H, J_{ba} = 17.2 Hz, J_{bx} = 11.8 Hz, Hb),3.62 (s,2H,-CH_2), 5.48(dd,1H, J_{xb} = 11.8 Hz, J_{xa} = 5.2 Hz, Hx), 6.42-7.96 (m,19H,Ar-H), 9.15 (d,1H,-NH). ^{13}C NMR(100 MHz, $CDCl_3$): 31.5(CH_2-C), 36.3, 41.7, 161.2(pyrazol-3C), 162.3 (C=O,C), 173.1(Immine-C) 109.21-143.20(Ar-33C). Anal; (%) $C_{39}H_{25}N_9O_7ICl$ Calcd; C, 52.37; H, 2.79; N,14.10; Found; C, 52.38; H, 2.80; N, 14.12.

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-iodo-3H-quinazolin-4 one 6_{11}

Yeild**:** 68 % M.P.**:**158-159 ^{0}C. 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), 538(C-I). ^{1}HNMR (400 MHz, $CDCl_3$): 3.05 (dd,1H, J_{ab}= 17.8 Hz, J_{ax}= 5.6 Hz, Ha), 3.49 (dd,1H, J_{ba} = 17.8 Hz, J_{bx} = 12.2 Hz, Hb),3.62 (s,2H,-CH_2), 3.83(s,3H,-OCH_3),

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5.52(dd,1H, J_{xb} = 12.2 Hz, J_{xa} = 5.6 Hz, Hx), 6.42-7.96 (m,19H,Ar-H), 9.15 (d,1H,-NH). ^{13}C NMR(100 MHz, $CDCl_3$): 31.5(CH_2-C), 36.4, 41.7, 161.1(pyrazol-3C), 162.2 (C=O,C), 173.1(Immine-C) 109.21-143.20(Ar-33C). Anal; (%) $C_{40}H_{28}N_8O_6ICl$ Calcd; C, 54.63; H, 3.18; N,12.74; Found; C, 54.65; H, 3.18; N, 12.75.

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-iodo-3H-quinazolin-4 one 6_{12}
Yeild**:** 76 % M.P.**:** 166-167 ^{0}C. 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),534(C-I). ^{1}HNMR (400 MHz, $CDCl_3$): 3.01 (dd,1H, J_{ab}= 17.6 Hz, J_{ax}= 5.4 Hz, Ha), 3.49 (dd,1H, J_{ba} = 17.6 Hz, J_{bx} = 11.8 Hz, Hb),3.62 (s,2H,-CH_2), 3.81(s,3H,-OCH_3), 5.49(dd,1H, J_{xb} = 11.8 Hz, J_{xa} = 5.4 Hz, Hx), 6.42-7.96 (m,19H,Ar-H), 9.15 (d,1H,-NH). ^{13}C NMR (100 MHz, $CDCl_3$): 31.4(CH_2-C), 36.4, 41.6, 161.1(pyrazol-3C), 162.2 (C=O,C), 173.1(Immine-C) 109.21-143.20(Ar-33C). Anal; (%) $C_{40}H_{28}N_8O_6ICl$ Calcd; C, 54.63; H, 3.18; N,12.74; Found; C, 54.64; H, 3.19; N, 12.75.

DETERMINATION OF ANTIMICROBIAL ACTIVITY

Disc diffusion method
The *in vitro* antimicrobial activity of synthesized compounds was carried out by disc diffusion method[13,14]. 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 studies of target molecule 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 antifungal activity screened against two plant pathogens 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 ^{0}C for 24 h. After incubation period observed the plate for zone of inhibition around the cups. Measure the diameter of each zone in mm.

A solvent control was also run to know the activity of the blank . This was carried out in DMF at concentration of 0. 05 ml in similar manner and the zone of the inhibition of the bacterial growth were measured in diameter and it was 0.0 mm. The standard drugs were also screened under similar condition.
The zone of inhibition measured for antibacterial activity at concentrations 1 x 10^4µg/ml, Penicillin-G and Streptomycin were used as standard and zone of inhibition measured for anti fungal activity also at concentrations 1 x 10^4 µg/ml and Fluconazole was used as a standard.

RESULT AND DISCUSSION

The target molecule 6-iodo-3H-quinazolin-4 one incorporating heterocyclic moieties quinoline and pyrazoline **6_{1-12}** were synthesized and structure was confirmed by the spectral results. The IR spectra showing strong stretching vibration at 1728 and 1616 cm^{-1} indicates the presence of C=O group of quinazolinone and acetamide respectively. It was further confirming by ^{1}H NMR spectra which showed singlet at δ 2.24 ppm equivalent to three protons of acetamide group**(4)**. The acrylamide **5_{1-12}** which showed CH=CH stretching at1578 cm^{-1} in IR spectrum while ^{1}H NMR spectra showed doublet of these protons at δ 6.77 and δ 7.62 ppm with coupling constant *J* = 16.0-16.6 Hz. The IR spectra of compounds **6_{1-12}** showed C=O and C=N stretching of quinazolinone at 1725 and 1616 cm^{-1} respectively. The ^{1}H NMR spectra of compounds 6_{1-12} 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.

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Antimicrobial Assay

The *in vitro* antimicrobial screening results of synthesized compounds were recorded in the table **1.** The strength of synthesized compounds was compared with standard drug.

Table: 1 Antimicrobial activity of new synthesized compounds against the bacterial strains and plant pathogens tested based on disc diffusion techniques

Microorganism ATCC code	**Sample(Zone of inhibition in mm)**								
	1	**2**	**3**	**4**	**8**	**9**	**10**	**11**	**12**
S.aureus (9144)	12±0.56	21±2.31	18±1.63	**23±1.29**	12±0.49	14±1.29	12±1.15	NA	11±0.81
B.subtilis(6633)	NA	20±0.68	17±0.33	**22±0.72**	14±0.67	15±0.83	13±0.39	11±1.15	12±0.56
E.coli(25922)	NA	13±1.63	14±1.29	16±1.58	**25±0.81**	21±1.18	23±1.29	15±1.29	16±1.51
P.aeruginosa(9027)	NA	12±1.29	13±0.81	14±1.15	**22±0.57**	18±0.57	21±2.82	14±0.63	14±1.29
A.niger	**20±0.79**	NA	12±1.63	12±2.31	15±1.63	11±0.81	12±2.31	18±1.63	20±1.51
C.albicans	21±2.31	NA	NA	13±0.57	16±1.51	13±0.81	13±0.57	19±0.57	**22±0.57**

Standard used for Gram positive bacteria: Penicillin G (Zone of inhibition in mm) : 25±0.58
Standard used for Gram negative bacteria: Streptomycin (Zone of inhibition in mm) : 30±1.20
Standard used for antifungal activity: Fluconazole (Zone of inhibition in mm) : 23±0.58
Amount of sample: 80µl Concentration: 1 x 10^4 µg/ml

CONCLUSION

The title compound 6-iodoquinazolin-4(3H) ones derivatives **$6_{1\text{-}12}$** 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 compound **4** (R_1= 4-Cl) showed very good activity against gram positive bacteria while compound **8** (R_1= 2-NO_2) displayed very good activity against gram negative bacteria compared to standard. More over compound **1** ((R_1= -H) and compound **12** (R_1= 4-OCH_3) showed very good antifungal activities compared to standard. 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. Future investigation of quinazolinone structure could give some hopeful results in the field of medicinal chemistry.

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