# SUMMARY OF PROJECT

**Principal Investigator : Dr. Gamanbhai G. Barat**

**File No. : 47-296/12(WRO) Date : 25-02-2013**

## 1. Literature Survey

Pyrazole nucleus is an important pharmacophore in medicinal chemistry, since a large number of its derivatives possess useful biological properties. 4(3*H*)-Quinazolinones have emerged as an important class of nitrogenated heterocyclic that have attached synthetic interest because of they possess good pharmacological and therapeutic properties, along with quinolin moiety played vital role in the medicinal chemistry. Quinazolin-4(3H) one possess pyrazoline moiety with the widespread applications in medicinal chemistry as antibacterial (Gupta, et al. 2008), antifungal (Bartroli, et al. 1998), analgesics, anti-imflammatory (Alafeefy, et al. 2007), anticonvulsant (Ozdemir, et al. 2008) agent. Quinolin derivatives are found to possess antimalarial, anti-imflammatory, antituberclosis and anti-breast cancer (A. Shi, et al. 2008) activity.

Encourage by the literature reports and to assess the pharmacological properties of such class of compounds it was thought to construct the quinolin nucleus linked with quinazolinone with pyrazoline moiety, which enhanced the biological activity. In the light of these findings leads to synthesize the new chemical entities incorporating the quinolin and pyrazoline with quinazolin-4(3H) ones may prove to be useful to the biological activity point of view.

## 2. OBJECTIVES OF PROJECT

(a) There are many methods are available for preparation of quinazolin-4(3H) ones from the chalcones it is new developed method and cheaper also, more over there are three biologically active moieties in the title synthesized compounds enhanced their microbial activities.

(b) Chalcone is very important intermediate obtained by this method is useful for preparation of various biologically active heterocycles.

(c) Chalcones and their rigid analogues represent an important class of small molecules having antimicrobial activity. Therefore, in this study the synthesis and antimicrobial activity of new 6-iodopyrazolylquinazolinone-4(3H) ones were described as rigid chalcone analogues.

(d) Screening results of the title compounds of the project shows very good antimicrobial activity against gram positive, gram negative bacteria and fungi species also. These results lead on the focusing of further better research on these molecules and to studies are undergoing to explore the scope of the various biological activities.

(e) Title compounds of the projects possess very good antimicrobial activity and least toxic and more potent. Hence, synthesized compound have better future in various field of medicinal chemistry.

(f) The research work useful to society, nation and new avenue of research for the better future.

## 3. Method development

Method developed for the synthetic route of target molecule for project summarized in Scheme I and scheme II described in experimental section of copy book of project.

All reagents and solvents were purchased from Merck chemicals and further purified before use.

## 4. Characterization of Synthesized compounds

Synthesized compounds were characterized by physical and spectroscopic techniques, viz. elemental analysis, IR, $^{1}H$ NMR and $^{13}C$ NMR spectra. IR spectra were recorded on Perkin-Elmer 1300 FTIR spectrophotometer using KBr powder. $^{1}H$ NMR and $^{13}C$ NMR spectra of the synthesized compounds were recorded in $CDCl_3$ on a Bruker spectrometer at 400 MHz and 75 MHz respectively, chemical shift recorded in $\delta$ ppm. TMS used as internal standard. The purity of compounds was checked by TLC on silica gel G plates and spot visualization was done by exposing to iodine vapour. Elemental analyses of newly sysnthesized compounds were carried out on Carlo Ebra 1108 analyzer and the result were varying within ± 0.04 % of the calculated values.

## 5. Antimicrobial Screening results

### (i) Cup Plate Method

The *in vitro* antimicrobial activity of synthesized compounds was carried out by cup plate method. 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.

### (ii) Measurement of 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 anti bacterial activity at two different concentrations 100 and 50 μg/ml, Penicillin-G was used as standard, where as zone of inhibition measured for anti fungal activity also at two different concentrations 20 and 10 μg/ml and Fluconazole was used as a standard.

**(iii) 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.

**(iv) Potency**

Potency of newly synthesized compounds were calculated by the following equation and compared the strength of synthesized compounds with standard drug.

Potency P = {antilog(D/B x I ) }x M x F

Where,

F = dilution factor  M = value of $S_H$ =1 unit / ml = 100 %

I = log $S_H$ / $S_L$  D = ( $U_H$+ $U_L$) – ($S_H$+$S_L$)

B = ( $U_H$ - $U_L$) + ($S_H$-$S_L$)

$S_H$ =Zone of inhibition of standard at high concentration.

$S_L$ = Zone of inhibition of standard at low concentration.

$U_H$ =Zone of inhibition of unknown at high concentration.

$U_L$ = Zone of inhibition of unknown at low concentration.

## 6. CONCLUSION

From the screening results of the synthesized compound of series :I and Series: II compound **6a(R= 2-Cl), 6b (R=3-Cl)** and **6c (R=3-Cl)** showed very good activity against Gram positive compared to standard. Compounds **6i(R= 3-$NO_2$)** and **6j((R= 4-$NO_2$)** showed very good activity against Gram negative bacteria compared to standard. Compound **6a(R= -H), 6k(R= 2-$OCH_3$)** and **6l ((R= 4-$OCH_3$)** showed very good anti-fungal activities compared to standard. Remaining compound of the series shows moderate or week activities against the microorganisms in vitro.

## 7. APPLICATION

In the present study the derivatives of quinazolin-4(3H) ones were synthesized by well organized method. All synthesized compounds were screened for their antimicrobial activity, due to active pharmacophore, promising results were obtained. Results were also useful to focus for further studies undergoing to explore the scope of varieties of biological activity.

## 8. PUBLICATION

1. N. B. Patel and G. G. Barat, " Synthesis and Pharmacological Aspects of Some Novel Nitrogen Containing Heterocycles With 6-Iodo Quinazolin-4(3H) Ones", Journal of Applicable Chemistry, Vol. 3, no.3, pp.1084-1093, May 2014.

2. G. G. Barat and N. B. Patel, " Synthesis, Structural Elucidation and in vitro Antimicrobial Studies of Some Novel Pyrazolylquinazolin-4(3H) Ones Bearing Quinoline Moiety", International Journal of Scientific Research, Vol. 3, no.11, pp.441-445, Nov. 2014.

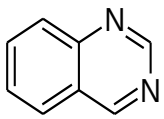
**RESEARCH DOCUMENTS AND MONOGRAPH**

## INDEX

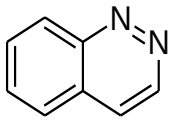
# 1. INTRODUCTION AND LITERATURE REVIEW

## 1.1. Literature survey of 4(3*H*)-quinazolinone

The name quinazoline (chinazolin) is today universally used to denote the 1,3- benzodiazine ring system **(I).** Widdige first proposed it in 1887 on observing that compound was isomeric with the known cinnoline **(II)** and quinaxaline **(III)** derivatives.




**(I)**

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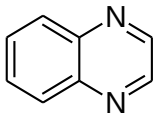
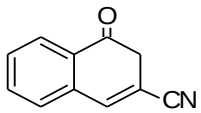


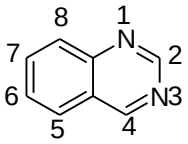

**(III)**



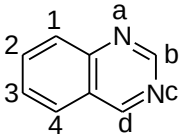

**(IV)**

Quinazoline also known as 1,3- diazanaphthalene was prepared by Gabriel in 1903 although, the first derivatives was synthesized by, Griess 34- years earlier.Other name of quinazoline such as phenmiazine, benzo -1,3 –diazine,and 5,6- benzo –pyrimidine have occasionally been used.

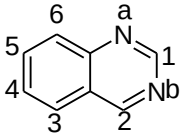
The presently accepted numbering (VI) was first adopted by Paal and Buch in 1889, as suggested by L. Knorr, & designate individual atoms of a ring with numbers. The position was designated as shown.



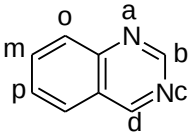

**(V)**




**(VI)**




**(VII)**




**(VIII)**

Compounds containing the quinazoline nucleus fall into three distinct classes on the basis of their physical and chemical properties and their means and ease of preparation.

1. Quinazoline
2. Hydrogenated quinazoline
3. Hydroxy quinazoline or quinazolinone

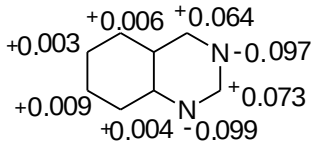
The first simplest class of quinazolines comprised those, which are unsubstituted in the heterocyclic ring. They may or may not be substituent in the benzene ring and not in the heterocyclic ring they are termed Bz-substituted quinazolines**[1].**

The presence of a fused benzene ring alters the properties of the pyrimidine ring considerably. The two nitrogen atoms are not equivalent, and the marked polarization of the 3,4 – double bond is reflected in the reaction of quinazoline.

The properties of substituted quinazoline depends largely on :

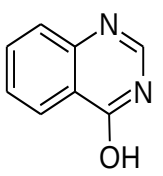
a. the nature of the substituents
b. whether they are in the pyrimidine ring or in the benzene ring
c. whether or not complete conjugation is present in the pyrimidine ring.

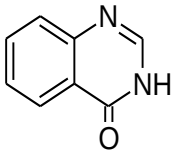
Theoretical treatment by Brown has led electron density diagram for quinazoline (IX). These values were obtained by molecular orbital calculations using uniform parameters. They are self – consistent and give dipolemoments in agreement with experiment **[2].**




(IX)

Quinazoline having a hydroxyl group 2 or 4 position are tautomeric with the its corresponding keto- dihydroquinazolines. Thus 4 – hydroxyquinazoline, tautomeric with 4 – keto – 3, 4 – dihydroquinazoline, is commonly named 4(3)- quinazolone or simply 4 – quinazolone. It was further simplify that 4 – hydroxyquinazoline **(**XI**)** and 4 –quinazoline or 4(3) – quinazoline (XII) is a tautomeric mixture of the lactum and the lactim form.

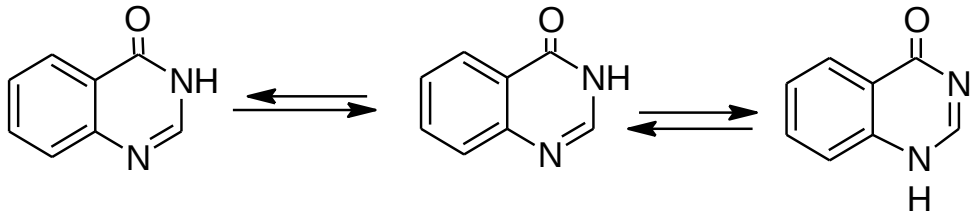



(XI) (XII)

Because of tautomerism, the quinazolones are high melting insoluble solids, extremely stable to heat, light and air and resistant to chemical oxidation, reduction, hydrolysis and substitution on the benzene ring. They are readily soluble in alkali and form stable salts**[1].**

The ultra violet spectrum of 4 –hydroxyquinazoline when compared with that of 4 – hydro xyquinazoline, 3-methyl -4-(3*H*) quinazolinone and 1-methyl - 4 (1*H*) quinazolinone indicate that (XIII) (XIV) and) (XV) are present. The lactum form (XV) is least fevered and (XIV) the most fevered.



(XIII) (XIV) (XV)

The *chemical abstact* nomenclature is adopted for N-1 and N-3 derivatives of hydroxy quinozolines, i.e. 3- and 1- methyl derivatives are written as 3- methyl – 4 (3*H*) quinazolinone and 1- methyl – 4 (1*H*) quinazolinone respectively. These compounds form the largest group of known quinazoline derivatives**[2].**

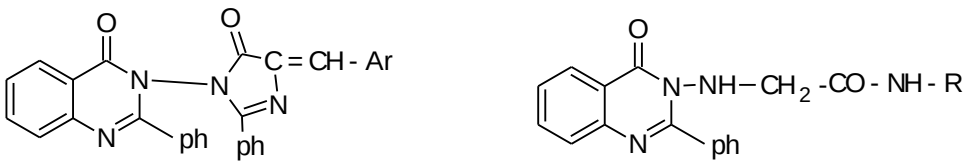
In contrast to the limited method of preparation of the most quinazoline derivatives , there are many synthesis known for 4-quinazolinones, majority of these proceed from anthranilic acid as the original starting compound. The most common synthesis of 4 –quinazolones was first described by V. Niementowski in 1895 **[1].**

The V. Niementowski reaction has been carried out with a variety of substituted anthranilic acid to give the corrosponding Bz- substituted 4 – quinazolones**[1].**

Mayer and Wagner subjected the reaction to a detail mechanistic examination and established that it proceed in discrete steps and the steps indicated several possibilities in terms of yield improvement in the reaction and alternative starting materials for the quinazolone sysnthesis **[3].** Later on Patel & Patel**[4]** studied V. Niementowski reaction . They modified Niementowski reaction mechanism, which has increased its applicability. Anthranilic acid is heat with excess of formamide at 120 $^0$C, water is expelled and a nearly quantitative conversion of 4 – quinazolone is achieved.

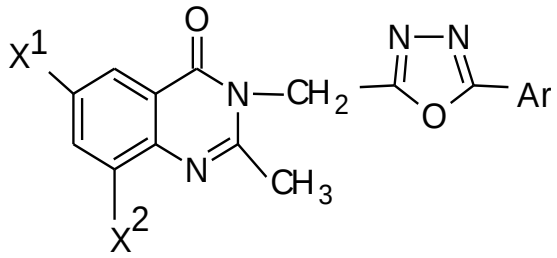
A method of wide applicability for the preparation of 4 - quinazolone involves the direct synthesis and isolation of the desired N – acylanthranilamides, when heated above their melting points, these loss water with formation of the quinazoline ring.

Desai and his co- workers**[5, 6]** synthesized 3-(4,5-dihydro – 4-arylidine-5 – oxo – 2 – phenyl – 1*H*- imidazol -1- yl) – 2 –phenyl 4 – (3*H*) – oxoquinazoline(XVI), [2- phenyl – 4(3*H*) – oxo – 3 –quinazolinylamino] – *N*- substituted – aryl acetamides (XVII) and tasted for their anti bacterial, antitubercular, anticancer and anti –HIV activity.



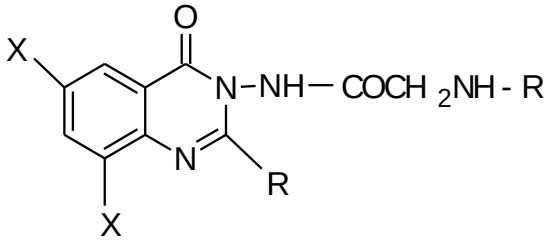
(XVI) (XVII)

Rao et al. **[7]** synthesized 3 –( 5 – aryl-1,3,4 – oxadiazol -2 – yl- methyl) – 2 – methyl -4 (3*H*)-quinazolinones(XVIII) some of these were found to be good analgesics and anti-inflammatory agents.



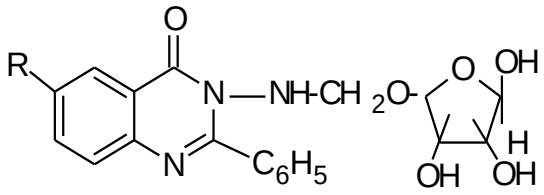
(XVIII)

Gupta et al. **[8]** reported 6,8 – disubstituted- 3 – ( substituted acetamido) – 2 – methyl -4-(3*H*) -quinazolinones(XIX) were found to effect 100 % clearance of worms. Different types of quinazolinone derivatives exhibited potent anathematic activity**.**



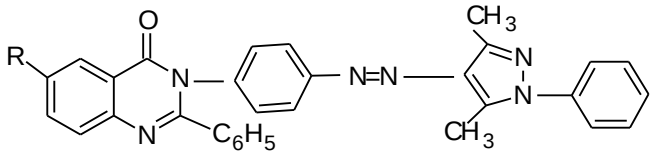
(XIX)

Mohamed and co-workers**[9]** synthesized 6-substituted -3-amino-2-phenyl-4(3*H*) –quinazolinone with D-ribose and L-arabinose**(XX),**found to potential anti-inflammatory and analgesics activity.



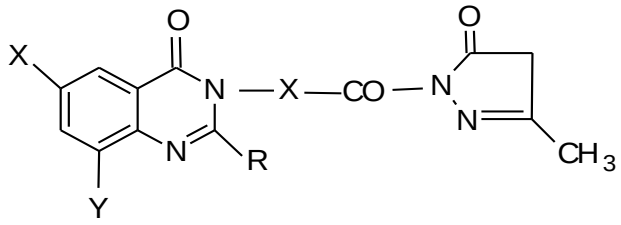
(XX)

Demetrio Raffa et al. **[10]** synthesized 6-chloro-2-phenyl-3-(heteroaryl)-4(3*H*) -quinazolinone(XXI)and found to possess powerful cytotoxic activity and inhibitory effects.



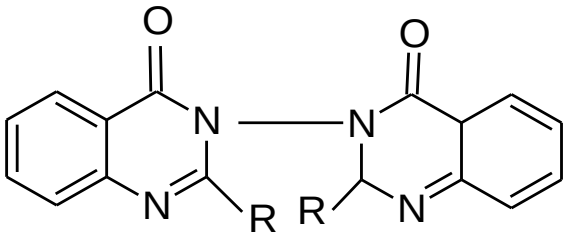
(XXI)

J. panda and his co-workers**[11]** synthesized 6,8-disubstituted 2- (phenyl /methyl)-3-[4-(3-methyl -5- pyrazolinone-1-yl- carbonyl)phenyl/methyl/benzyl]-4(3*H*)-qunazolinone(XXII),found potential antibacterial and anti-fungal activity.



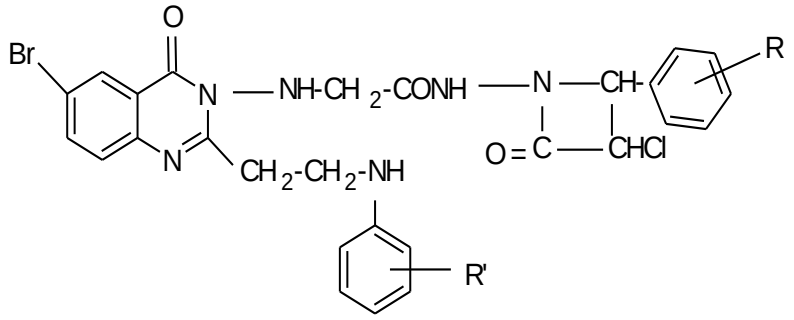
(XXII)

A.A.S.Wasfy[**12**] synthesized novel 2,2-disubstituted -3,3 – biquinazolin-4(3*H*)-one(XXIII) and reported their antibacterial and antifungal activity.It shows significant gram positive and gram negative antibacterial activity.



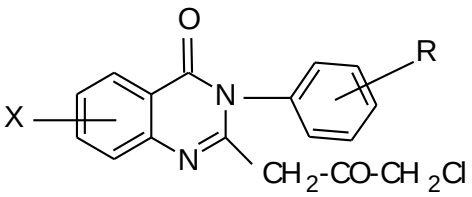
(XXIII)

Ashokkumar and his co-workers **[13]** synthesized 3-[2’-(substituted aryl)-3’-chloro-4’-oxo-1’-azetidinyl]amino acetyl amino-2-[(substituted phenyl)amino ethyl]-2-methyl -6-bromo quinazolin-4(3*H*)-ones(XXIV)and found potential hypertensive agents.

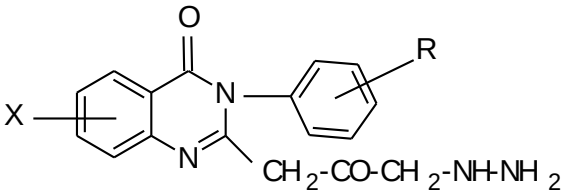


(XXIV)

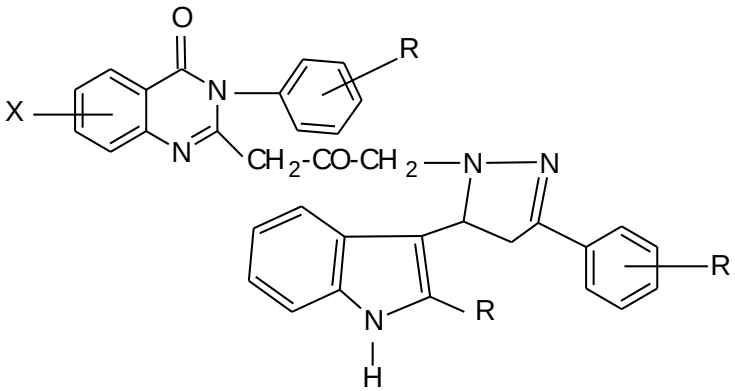
Ashokkumar and his co-workers**[14]**synthesized 2-(w-chloroacetonyl)-3-substituted phenyl-6-halo/ 6,8-dihaloquinazolin-4(3*H*)-ones(XXV), 2-(w-hydrazino acetonyl)-3-substituted phenyl-6-halo / 6,8-dihalo quinazolin-4(3*H*)-ones(XXVI) and 1-[3'-substituted phenyl- 6-halo / 6,8-dihalo quinazolin-4(3*H*)-one -2-acetonyl]-3'-aryl-5'-(2-substituted indol-3-yl)-$\Delta^2$ pyrazoline (XXVII) and reported their anti-inflammatory,analgesics,ulcerogenic and cyclooxegenase activity.



(XXV)

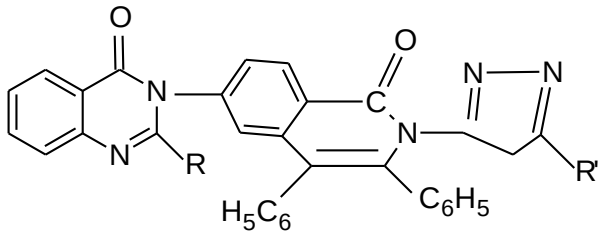


(XXVI)



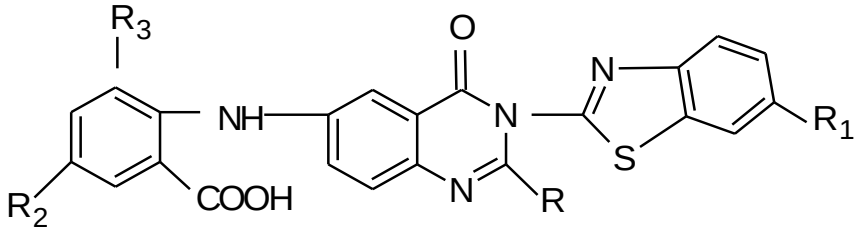
(XXVII)

Pandey and his co-workers**[15]** synthesized 2-aryl-[5'-aralkyl-1',3',4'-thiadiazolyl-{2'-(3",4"-diphenyl-1"-oxo-isoquinazolinyl}]-4(3H)-ones(XXVIII)and found potential antifungal and antiviral activity.




(XXVIII)

Rohit D. Patel and his co-workers**[16]** synthesized 6,8-dihalo derivatives of quinazolinone (XXIX) and reported their anti bacterial activity.They found potential activity against Baccilus sereus, S.aureus and B.subtilis gram positive bacteria.

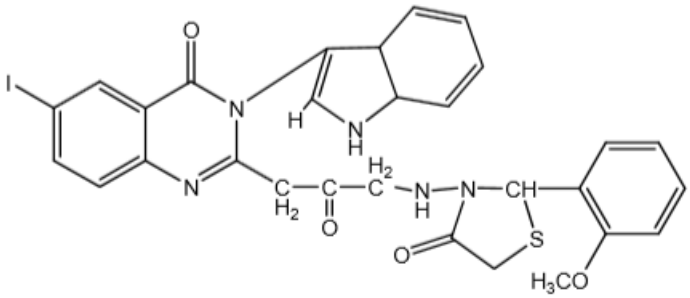



(XXIX)

4(3*H*)-Quinazolinone are well-known building block agent and have a broad spectrum of variety of biological activities. Their derivatives exhibit anti-inflammatory, sedative activity and antifungal activity. 4(3*H*)-Quinazolinone were identified as selective COX-2 inhibitors; antibacterial, antitubercular, anticancer and anti –HIV activity **[17]**. 6-iodo and 6,8- dibromo quinazolin 4-(3*H*)-one derivatives are reported as treatment of non diabetic and diabetic hyper cholesterolemic and have no significant toxic side effects at the drop sub lethal dose levels (2 mg / kg) **[18]**.

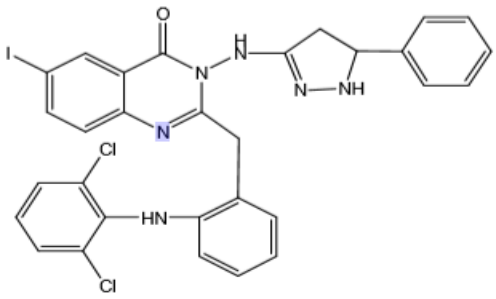
Kumar et al**[19]** synthesized various 2-(substituted phenylmethylene imino) amino acetyl methylene-3-(2'-substitutedindol-3'-yl)-halosubstituted-4(3H) quinazolinone and 2-(substituted

phenylamino methylene acetyl-4'-oxo-1'-thiazolidinyl-3-(2"-substitutedindol-3"-yl) 4 (3H)-quinazolinones(XXX) and reported that exhibited good anti-inflammatory activity.



(XXX)

Patel et al**[20]** synthesized a series of new 2-[2-(2,6-dichlorophenyl) amino] phenyl methyl-3- (5-substitutedphenyl)-1,5-dihydro-1H-pyrazol-3-yl-amino]-6-iodoquinazolin-4(3H) ones (XXXI) were tested for theirantibacterial activityin vitroby measuring zone of inhibition in mm by cup-platemethod against different strains like two Gram positive bacteria viz.Staphylcoccus aureus, Bacillus subtilisand two Gram negative bacteria viz.Escherichia coli, Certiumat two different concentration100 µg/mL and 50 µg /ML



(XXXI)

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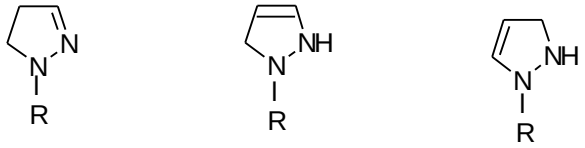
### 1.3 Literature survey of pyrazoline

Knorr in 1883 suggested the name pyrazole [**1]** to unsaturated five membered ring containing adjacent nitrogen atoms. The dihydropyrazole is termed as pyrazoline**[2**].

(I) (II)

Substituted pyrazolines exhibit tautomerism. The tautomers (IIa) and (IIb) are termed as $\Delta^1$ pyrazolines and $\Delta^2$ - pyrazolines respectively which are more stable than (IIc) tautomer. No evidence have been reported for the stability of tautomer (IIc).

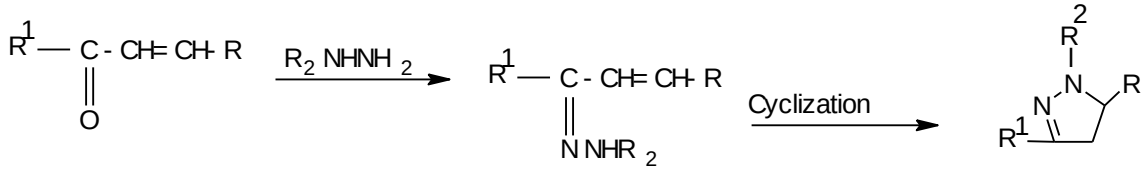


**(IIa)** **(IIb)** **(IIc)**

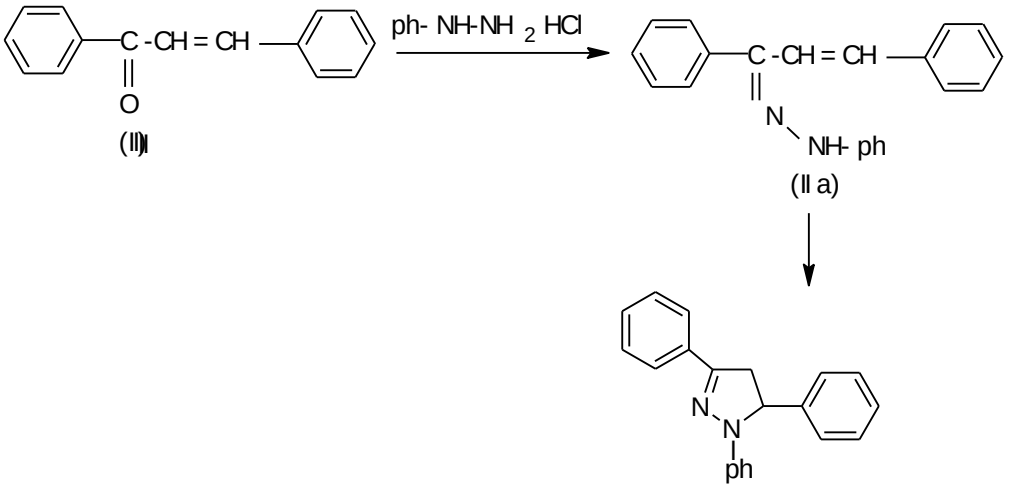
Since four decaded, pyrazole ring has attached much attention that showing diver : properties which has become fairly accessible. A number of pyrazole derivatives have been recently appeared as anaesthetics besides the basis of numerous dyes and drugs[**2,3**].

Recently, pyrazolines found for their use as an effective bleaching agents, as luminiscents, fluorescents[**4-8]** and as oxidized forms in the development of cine films[**9**]. Where as pyrazolines were formerly regarded only as intermidiatesin the synthesis of pyrazoles.

The convenient method for the synthesis of pyrazolines is the action of hydrazine or phenyl hydrazine on α , ß- unsaturated carbonyl compounds like chalcones, flavanones. In such reactions hydrazones, or phenyl hydrazones are formed as intermediates which can subsequently be cyclised to pyrazolines **[10]** on treatment with reagent like acetic acid or alcohol containing a little HCl **[11**]. However , acetic acid gives good yields rather than the yields with alcohol containing a little HCl. The rate of cyclization of hydrazones to pyrazolines varies with the substituent $R_1$ in the order $R_1$ = PH > Me > H**[12,13]**




The pyrazolines (IIb), **[14,15**] was prepared by heating phenyl hydrazones(IIa).

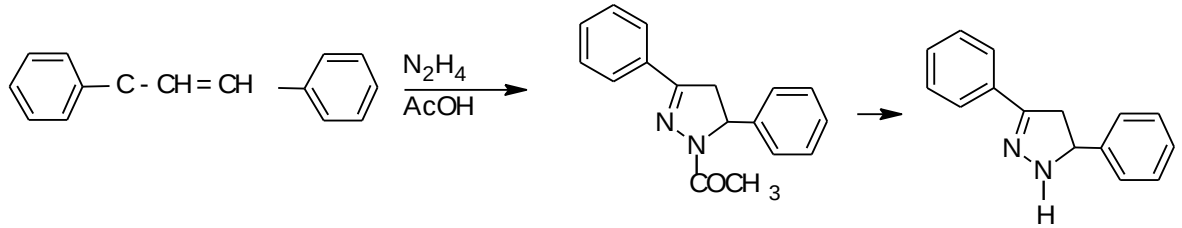



**(IIb)**

The phenyl hydrazones has not been isolated in many cases. It has been found, that the phenyl hydrazone becomes more liable due to the presence of electron releasing groups like hydroxyl, alkoxy or amino on either phenyl ring of benzal acetophenone **[16-18**]. Where as stabilization of phenyl hydrazone is done by electron withdrawing groups[**16-21**].

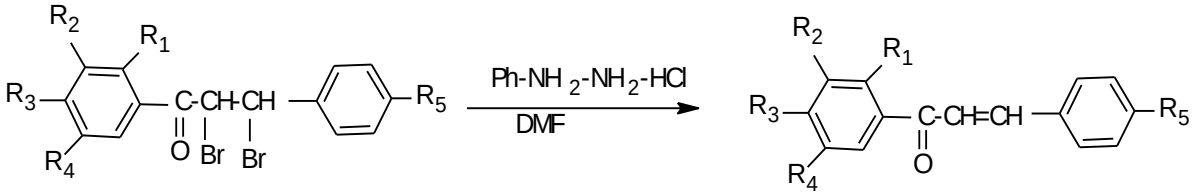
Unsymmetrically substituted dibenzalacetophenone gives the pyrazolines directly and in this reaction there is no formation of intermediate called hydrazone**[21,22].**

Excess quantity of hydrazine in acetic acid when reacted with benzalacetophenone at reflux temperature yields N- acetyl pyrazoline(3a) which can immediately be converted to 3, 5 – diphenyl pyrazoline(3b)[**23**].

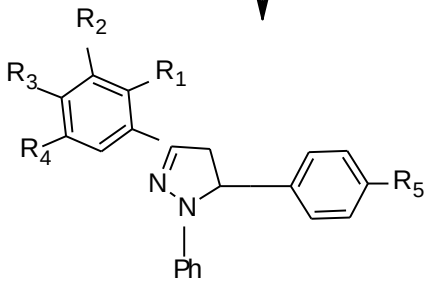



(III) (IIIa) (IIIb)

The mechanism for the formation of pyrazolines from α , ß- unsaturated ketones (IV) by 1,2 – addition of phenyl hydrazine through an adduct intermediate was suggested by Aubaguac et al**[24].**The synthesis of 3,5-diaryl-1-phenyl pyrazolines(IVa) from chalcone dibromide (IV) and phenyl hydrazine hydrochloride in DMF has been reported by Joshi and Vadodkar**[25].**

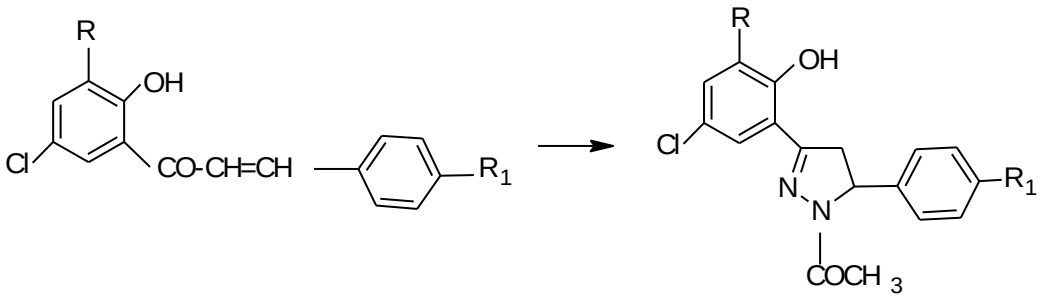



(IV)



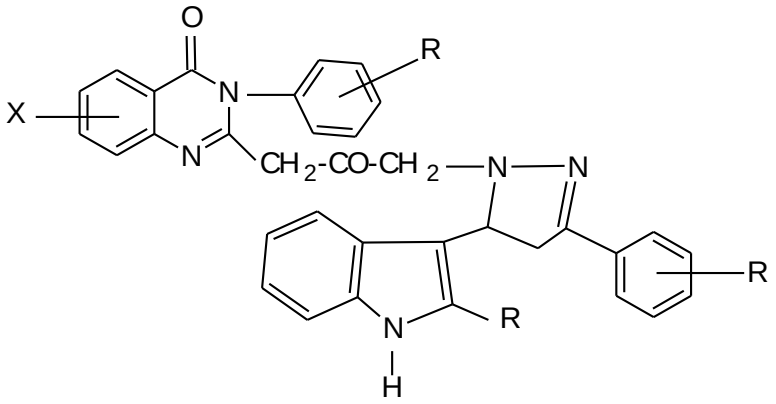

(IVa)

Uthale et al**[26]** synthesized 1-acetyl -3,5-diaryl- $\Delta^2$ -pyrazolines(V) by the action of 2- hydroxyl chalcones(VI) with semicarbazide hydrochloride in alcoholic medium has been observed in literature.



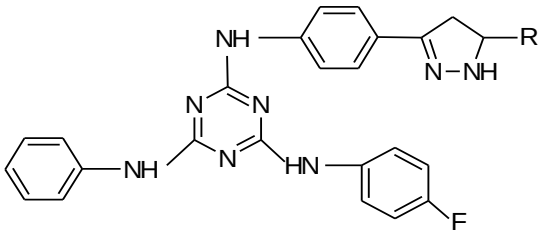

(V) (VI)

Ashokkumar and his co-workers**[27]**synthesized 1-[3'-substituted phenyl- 6-halo / 6,8-dihalo quinazolin-4(3*H*)-one -2-acetonyl]-3'-aryl-5'-(2-substituted indol-3-yl) $-\Delta^2$ – pyrazoline (VII) and reported their anti-inflammatory, analgesics, ulcerogenic and cyclooxegenase activity.



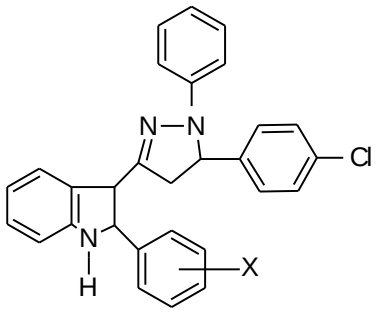

(VII)

Anjanee Solankee and Indrajit Thakor**[28]** synthesized 2-phenyl amino-4[4'-floro phenyl amino]-6-[4'-{5"-(3"-chloro phenyl)pyrazoline-3"-yl}phenyl amino-5-triazine(VIII)and found good antibacterial activity against S.paratyphi-A, S.aureno,E.coli and B.subtilis.It shows significant antifungal activity against A.flavas.



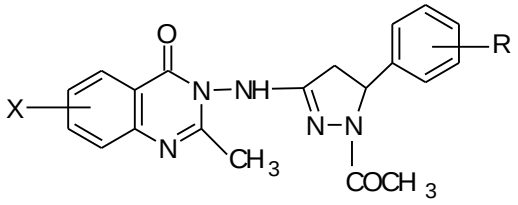
(VIII)

Vijai Nath Pathak**[29]**and his co-workers synthesized 4,5-dihydro-3-(2-arylindol-3-yl)-5-(4-chlorophenyl)-N1-phenyl pyrazolines(IX)and reported their antibacterial and antifungal activity.It shows higher activity against A.niger at various concentration.



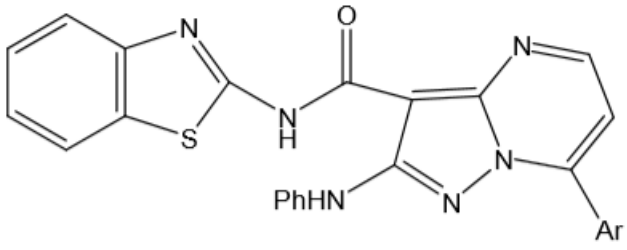

(IX)

Archna et al**[30]**synthesized 1-acetyl-5-substituted-3-[3'-amino-2'-methyl-6'-monosubstituted quinazolin-4(3*H*)-only]-2-pyrazolines(X)and reported their anti-convulsant activity.The potent compounds were investigated for their acute toxicity.



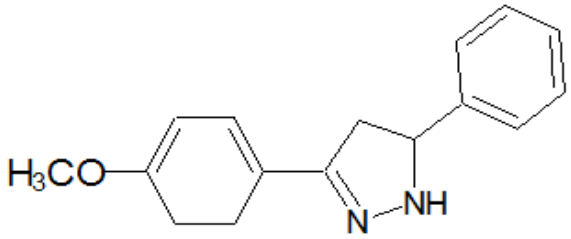

(X)

Samir Bondock et al**[31]**2010synthesized a series of substituted pyrazole derivatives. The given compound (XI) was found to exhibit the most potent in vitro antifungal activity with MICs (6.25µ/ml) against A. fumigates and F. Oxysporumcomparab; e with Chloroamphenicol.



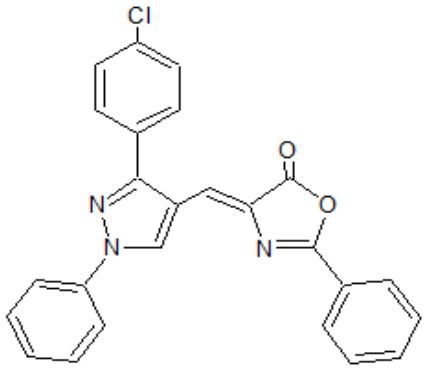
(XI)

Giuseppe Cocconcelli et al**[32]** have described the parallel synthesis of aryl azoles. Here substituted phenyl hydrazine is made to react with α, β-unsaturated ketones, which leads to regioselective formation of 4, 5-dihydro-1-H-pyrazole(XII) and acetic acid was used as catalyst. Compound posseses good neuroprotective activity.




(XII)

Argade N. D. et al**[33]** have reported the conventional microwave assistance Synthesis of pyrazole containing 2, 4-disubstituted oxazol-5-one(XIII) as a new class of antimicrobial agents. Compared to the conventional method, the microwave-assisted synthesis demonstrates several advantages, in terms of reaction time and overall yield. Compounds with electron withdrawing groups showed good antibacterial and antifungal activities.




(XIII)

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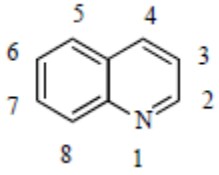
### 1.5 Literature survey of Quinoline

Quinoline (1-azanaphthalene) is a heterocyclic aromatic nitrogen compound characterized by a double-ring structure that contains a benzene ring fused to pyridine at two adjacent carbon atoms (Fig. **1**) [1]. Quinoline derivatives have been the intense research interest for many years since the quinoline structure is found in a large number of natural products as well as in numerous commercial products such as pharmaceuticals, fragrances, and dyes. Inparticular, quinoline alkaloids are found in many different plants including Berberidaceae, Fumariaceae, Papavaraceae and Rutaceae[2-6]. A number of these compounds are planar aromatic heterocyclesthat have shown cytotoxic activity by inhibiting topoisomeraseII [6].



Quinoline compounds are widely used as "parental" compounds to synthesize molecules with medical benefits, especially with anti-malarial and anti-microbial activities [7, 8]. The quinoline ring system containing drugs such as quinine, chloroquine, mefloquine, and amodiaquine are used as efficient drugs for the treatment of malaria [9]. In addition, certain quinoline-based compounds showeffective anticancer activity (reviewed in [10]. This broad spectrum of biological and biochemical activities has been further facilitated by the synthetic versatility of quinoline, which allows creatinga large number of structurally diverse derivatives. Recent studies have shown that quinoline and its analogs can inhibit tyrosine kinases, protea some, tubulin polymerization and DNA repair. In this review, we summarize our knowledge on quinoline and its analogs with respect to their biological activities, mechanisms of action, structure-activity relationship (SAR), and selective and specific activity against various cancer drug targets. We will also focus our review on *in vitro* and *in vivo* anticancer activities of quinoline ring-based analogs in the context of cancer drug development and refinement.

Quinoline based fused heterocyclic compounds have been reported various biological activities such as Anti-mycobacterial, Anti-convulsant, Anti-inflammatory, Anti-viral and Anti-microbial activities. Hence there is a need for synthesis of compounds containing quinoline ring and thione group in hope of getting compounds with better biological and pharmacological activity**[11-17]**.

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## 2. EXPERIMENTAL

### 2.1. Method and material

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. 2-(2-phenylamino) phenyl 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(3*H*) one 2**

To the 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 each small portion of 5-iodo anthranilic acid (2.63 g, 0.01 mol) was added portion wise and were stirred for 1 h. to maintain temperature 0-5 $^0$C. Further reaction mixture was stirred 1h at room temperature. A pasty mass thus obtained which was washed thoroughly with sodium bicarbonate (5 %) to remove unreacted acid. A solid separated was filtered, dried and recrystalised from methanol.

**Synthesis of 3-Amino-2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl–6-iodoquinazolin–4(3*H*) 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(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 obtained was filtered and washed several times with water. The crushed product was dried and recrystallized from ethanol.

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

To a solution of **3-Amino-2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl–6-iodoquinazolin–4(3*H*) 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 completion of addition 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**.**

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

A solution of **2--[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl-3-acetamido-6-iodoquinazolin-4(3*H*)-one (**5.805g, 0.01 mol) in absolute ethanol (50 ml) and added 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 with water and recrystalized from methanol.

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

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

IR(KBr) : 3367(NH), 3061, 2855(C-H), 1727(C =O), 1613(C=O of –$COCH_3$), 1579 (CH=CH), 1314(C-N), 781(C-Cl), 511(C-I).$^1$H NMR($CDCl_3$) **:** 2.13(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).$^{13}$C NMR: 29.5(-$CH_2$), 36.1, 41.6(CH=CH),160.9 (immine>C=O), 162.1(>C=O),173.1 (immine aromatic-C), 109.20-143.16(aromatic-27C).

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

IR(KBr) : 3371(NH), 3065, 2858(C-H), 1729(C =O), 1615(C=O of –$COCH_3$), 1577 (CH=CH), 1316(C-N), 779(C-Cl), 509(C-I).$^1$H NMR($CDCl_3$) **:** 2.11(s, 1H, -N-NH), 6.39- 7.93(m, 16H, Ar-H), 3.61 (s, 2H, -$CH_2$), 6.81(d, 1H, COCH=), 8.61(d, 1H, =CH-Ar).$^{13}$C NMR: 31.3(-$CH_2$), 36.5, 41.1(CH=CH), 161.3(immine>C=O), 162.3(>C=O), 173.2(immine aromatic-C), 109.13-143.17(aromatic-27C).

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

IR(KBr) : 3368(NH), 3063, 2856(C-H), 1727(C =O), 1617(C=O of $–COCH_3$), 1578(CH=CH), 1317(C-N), 781(C-Cl), 513(C-I).$^1$H NMR($CDCl_3$) **:**2.11(s, 1H, -N-NH), 6.37- 7.96(m, 16H, Ar-H), 3.63(s, 2H, $-CH_2$), 6.81(d, 1H, COCH=), 8.62(d, 1H, =CH-Ar).$^{13}$C NMR: 30.6($-CH_2$),36.2, 41.3(CH=CH),161.4(immine>C=O),162.0(>C=O), 173.1(immine aromatic-C),109.17-143.21 (aromatic-27C).

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

IR(KBr) : 3549(-OH),3413(NH), 3061, 2854(C-H), 1719(C =O), 1619(C=O of $–COCH_3$), 1572 (CH=CH), 1319(C-N), 779(C-Cl), 507(C-I).$^1$H NMR(CDCl3) **:**2.11(s, 1H, -N-NH), 6.34-7.91(m, 16H, Ar-H), 3.62 (s, 2H, $-CH_2$), 6.80(d, 1H, COCH=), 8.61(d, 1H, =CH-Ar), 10.36(s, 1H,-OH).$^{13}$C NMR: 30.7($-CH_2$), 36.3, 41.4(CH=CH),160.9(immine>C=O),162.1(>C=O), 173.1 (immine aromatic-C), 109.3-143.4(aromatic-27C)

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

IR(KBr) : 3552(-OH),3416(NH), 3067, 2852(C-H), 1721(C =O), 1615(C=O of $–COCH_3$), 1574 (CH=CH), 1318(C-N), 780(C-Cl), 510(C-I).$^1$H NMR($CDCl_3$) **:**2.17(s, 1H, -N-NH), 6.36-7.96(m, 16H, Ar-H), 3.63 (s, 2H, $-CH_2$), 6.82(d, 1H, COCH=), 8.61(d, 1H, =CH-Ar),10.38(s, 1H,-OH).$^{13}$C NMR :30.8($-CH_2$), 37.5, 42.7(CH=CH),161.2(immine>C=O),162.2(>C=O), 173.3 (immine aromatic-C), 109.21-143.27(aromatic-27C)

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

IR(KBr) : 3557(-OH),3411(NH), 3064, 2854(C-H), 1720(C =O), 1613(C=O of $–COCH_3$), 1571(CH=CH), 1319(C-N), 782(C-Cl), 509(C-I).$^1$H NMR($CDCl_3$) **:**2.11(s, 1H, -N-NH), 6.35-7.93(m, 16H, Ar-H), 3.62 (s, 2H, $-CH_2$), 6.80(d, 1H, COCH=), 8.61(d, 1H, =CH-Ar), 10.36(s, 1H,-OH).$^{13}$C NMR : 30.7($-CH_2$), 36.5,41.5(CH=CH),161.1(immine>C=O),162.3(>C=O), 173.1(immine aromatic-C), 108.78-143.24(aromatic-27C).

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

IR(KBr) : 3413(NH), 3061, 2852(C-H), 1721(C =O), 1614(C=O of $-COCH_3$), 1572(CH=CH), 1317(C-N),1565,1367($-NO_2$) 779(C-Cl), 507(C-I).$^1$H 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).$^{13}$C 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).

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

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).$^1$H 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).$^{13}$C NMR : 30.6($-CH_2$),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).

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

IR(KBr) : 3415(NH), 3059, 2857(C-H), 1724(C =O), 1613(C=O of $-COCH_3$), 1572 (CH=CH),1563,1366($-NO_2$),1317(C-N), 778(C-Cl), 507(C-I).$^1$H NMR($CDCl_3$) **:**2.16(s, 1H, -N-NH), 6.39- 7.94(m, 16H, Ar-H), 3.62 (s, 2H, $-CH_2$), 6.81(d, 1H, COCH=), 8.60(d, 1H, =CH-Ar). $^{13}$C NMR : 30.4($-CH_2$),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).

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

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).$^1$H-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,$-OCH_3$).$^{13}$C NMR: 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).

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

**IR(KBr)** : 3409(NH), 3063, 2859(C-H), 1721(C =O), 1615(C=O of –COCH3), 1575(CH=CH), 1317(C-N),1245,1108(C-O-C),778(C-Cl), 509(C-I).$^{1}$H 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,-$OCH_3$).$^{13}$C NMR: 30.6(-$CH_2$), 36.6,42.4 (CH=CH),59.7(-$OCH_3$),161.1 (immine> C=O), 162.3(>C=O), 173.2(immine aromatic-C), 109.21-143.20(aromatic-27C).

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

To a solution of 2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl-3-substituted phenyl acryl amido-6-iodoquinazolin-4(3*H*)-one (6.685 g, 0.01 mol) in methanol, add hydrazine hydrate(99 %) (1.0 g, 0.02 mol) and few drops of glacial acetic acid. The reaction mixture was refluxed for 8-10 h., distilled and cooled. The separated solid was filtered, washed with water and recrystallized from methanol.

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

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

IR(KBr):3368(N-H),3059,2861(C-H),1729(C=O),1616(C=N), 1315(C-N), 782(C-Cl), 509(C-I).

$^{1}$H NMR($CDCl_3$):2.13(d,1H,=N-NH),8.28(s,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,16H,Ar-H). $^{13}$C NMR: 30.4(-$CH_2$), 36.2, 41.5, 160.7(immine pyrazol-C),162.2(>C=O),173.1(immine aromatic-C), 108.92-143.25(aromatic-27C).

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

IR(KBr): 3371(N-H),3061, 2856(C-H),1731 (C=O),1614(C=N),1318(C-N),780(C-Cl),511(C-I).

$^{1}$H NMR($CDCl_3$):2.16(d,1H,=N-NH),8.30(s,1H,-N-NH),3.64(s,2H,-$CH_2$),3.06(d,1Ha), 3.51(d, 1Hb), 6.57(t,1Hx), 6.43-7.96(m,16H,Ar-H).$^{13}$C NMR: 31.3(-$CH_2$),36.4, 41.3,161.3(immine pyrazol-C),162.1(>C=O),173.3(immine aromatic-C), 109.13-143.17(aromatic-27C).

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

IR(KBr):3367(N-H),3060,2866(C-H),1735(C=O),1616(C=N),1317(C-N), 782(C-Cl),510(C-I). $^{1}$H NMR($CDCl_3$):2.18(d,1H,=N-NH),8.32(s,1H,-N-NH),3.61(s,2H,-$CH_2$), 3.05(d,1Ha), 3.48 (d,1Hb),6.53(t,1Hx), 6.44-7.95(m,16H,Ar-H).$^{13}$C NMR : 31.6(-$CH_2$),36.2, 41.5,161.2 (immine pyrazol-C),162.2(>C=O),172.9(immine aromatic-C), 109.17-143.21(aromatic-27C).

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

IR(KBr):3548(O-H),3415(N-H),3063,2856 (C-H),1733(C=O),1614(C=N),1316 (C-N), 780(C-Cl),511(C-I). $^{1}$H NMR($CDCl_3$):2.14(d,1H,=N-NH),8.32(s,1H,-N-NH),3.62(s,2H,-$CH_2$), 3.06 (d,1Ha), 3.45(d, 1Hb),6.52(t,1Hx), 6.44-7.96(m,16H,Ar-H),10.39(s,1H,-OH).$^{13}$C NMR: 30.6(-$CH_2$), 36.4, 41.5,160.8(pyrazol-C), 162.1(>C=O),172.9(immine aromatic-C) 109.23-143.21(aromatic-27C).

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

IR(KBr):3549(O-H),3409(N-H),3067,2855(C-H),1731(C=O),1617(C=N),1314(C-N), 782(C-Cl),508(C-I).$^{1}$H NMR($CDCl_3$):2.16(d,1H,=N-NH),8.34(s,1H,-N-NH),3.63(s,2H,-$CH_2$), 3.05 (d,1Ha), 3.46(d,1Hb),6.51(t,1Hx), 6.43-7.96(m,16H,Ar-H),10.35(s,1H,-OH).$^{13}$C NMR:30.7(-$CH_2$), 36.5, 41.9,161.2(immine pyrazol-C),162.3(>C=O),172.7(immine aromatic-C) 109.15-143.19(aromatic-27C).

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

IR(KBr):3553(O-H),3411(N-H),3061,2856 (C-H),1725(C=O), 1614(C=N),1316(C-N), 778(C-Cl), 513(C-I). $^{1}$H NMR($CDCl_3$):2.17(d,1H,=N-NH),8.36(s,1H,-N-NH),3.61(s,2H,-$CH_2$), 3.06

(d,1Ha), 3.46(d, 1Hb),6.52(t,1Hx), 6.44-7.96(m,16H,Ar-H), 10.34(s,1H,-OH).$^{13}$C NMR: 30.6(-$CH_2$), 36.3,41.6,161.1(immine pyrazol-C),162.1(>C=O),173.1(immine aromatic-C), 109.17-143.16(aromatic-27C).

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

IR(KBr): 3415(N-H),3063,2856(C-H),1728(C=O),1615(C=N),1564,1363(-$NO_2$), 1318(C-N), 781(C-Cl),510(C-I).$^1$H NMR($CDCl_3$):2.16(d,1H,=N-NH),8.32(s,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,16H,Ar-H).$^{13}$C NMR : 30.5(-$CH_2$), 36.5, 42.2,161.6(immine pyrazol-C),162.1(>C=O),173.1(immine aromatic-C), 109.19-143.16 (aromatic-27C).

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

IR(KBr):3411(NH),3065,2854(C-H),1729(C=O),1613(C=N),1565,1361(-$NO_2$),1316(C-N),779 (C-Cl),513(C-I).$^1$H NMR($CDCl_3$):2.17(d,1H,=N-NH),8.33(s,1H,-N-NH),3.61(s,2H,-$CH_2$), 3.06 (d,1Ha), 3.46(d, 1Hb),6.52(t,1Hx), 6.43-7.96(m,16H,Ar-H). $^{13}$C NMR : 30.4(-$CH_2$),36.1, 41.8, 160.9(immine pyrazol-C),162.3(>C=O),172.9(immine aromatic-C), 109.19-143.16(aromatic-27C).

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

IR(KBr):3415(NH),3060,2855(C-H),1726(C=O),1615(C=N),1563,1359(-$NO_2$),1318(C-N), 783 (C-Cl),516(C-I).$^1$H NMR($CDCl_3$):2.18(d,1H,=N-NH),8.31(s,1H,-N-NH),3.63(s,2H,-$CH_2$), 3.05 (d,1Ha), 3.48(d,1Hb),6.53(t,1Hx), 6.43-7.96(m,16H,Ar-H).$^{13}$C NMR: 30.6(-$CH_2$),36.2, 42.3, 161.2 (immine pyrazol-C),162.3(>C=O),173.1(immine aromatic-C), 109.19-143.11(aromatic-27C).

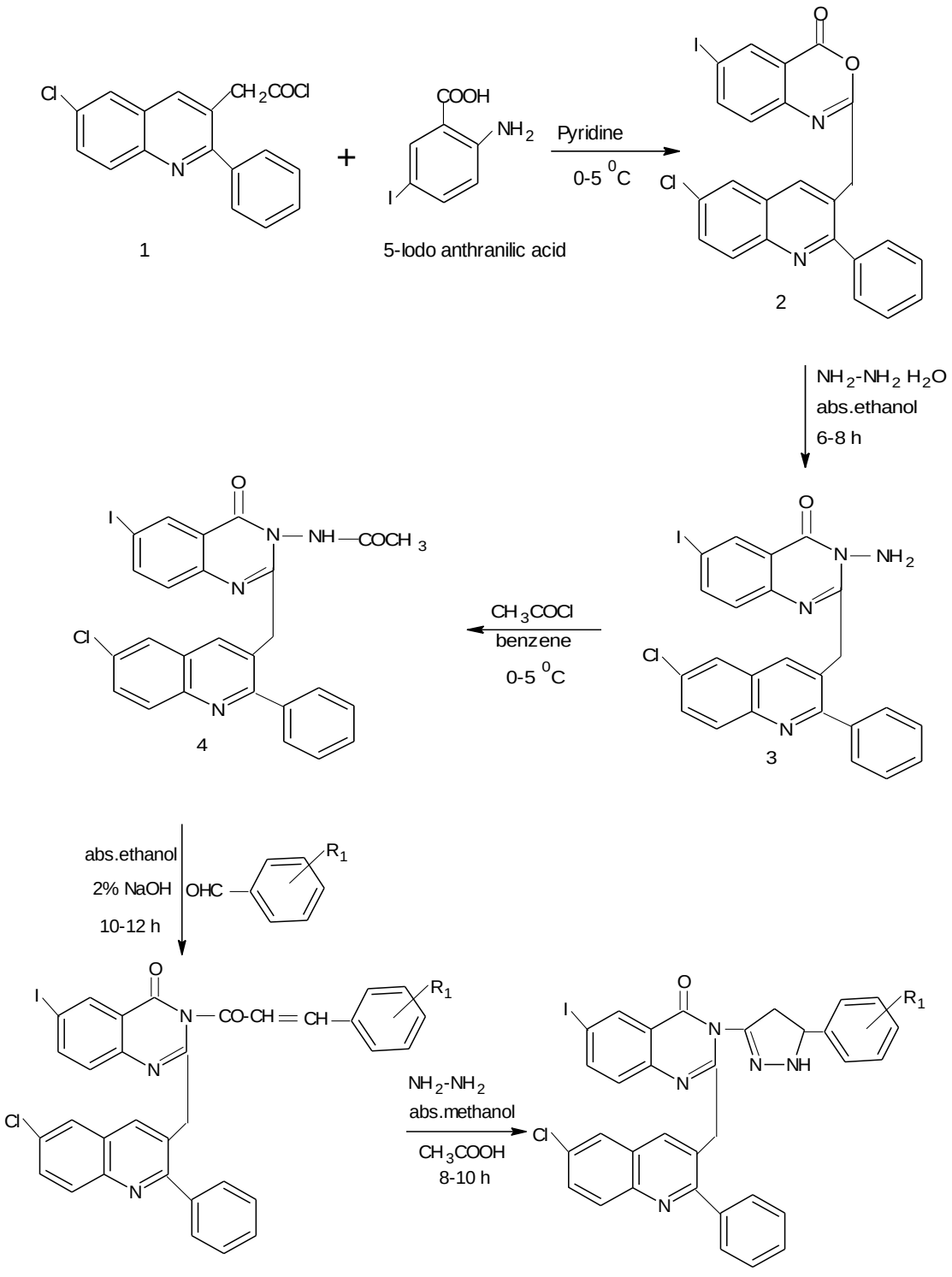
**Spectral data of 6k: 2-[3-(6-chloro-2-phenyl) quinolin-3-yl]methyl-3–[5-(2-methoxy) phenyl-4,5-dihydro-1*H*-pyrazol-3-yl amino]-6-iodo quinazolin-4(3*H*)-one**

IR(KBr):3408(N-H),3065,2859 (C-H),1730 (C=O), 1611 (C=N),1319 (C-N),1241,1109(C-O-C), 784(C-Cl), 502(C-I). $^{1}$H NMR($CDCl_3$):2.16(d,1H,=N-NH),8.30(s,1H,-N-NH),3.62(s,2H,-$CH_2$), 3.05(d,1Ha), 3.46(d, 1Hb),6.51(t,1Hx), 6.43-7.96(m,16H,Ar-H), 3.81(s,3H,-$OCH_3$).$^{13}$C NMR : 31.3(-$CH_2$),36.4, 42.4,161.1(immine pyrazol-C),162.0(>C=O),173.3(immine aromatic-C),58.3(-$OCH_3$),109.14-143.17(aromatic-27C).

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

IR(KBr): 3405(N-H),3066,2861(C-H),1729(C=O),1613(C=N),1317(C-N),1243,1108 (C-O-C), 786(C-Cl), 507(C-I).$^{1}$H NMR($CDCl_3$):2.17(d,1H,=N-NH),8.32(s,1H,-N-NH),3.61(s,2H,-$CH_2$), 3.06(d,1Ha), 3.46(d, 1Hb),6.52(t,1Hx), 6.43-7.96(m,16H,Ar-H), 3.80(s,3H,-$OCH_3$).$^{13}$CNMR: 31.2(-$CH_2$), 36.5,42.6,161.3(immine pyrazol-C),162.1(>C=O),173.2(immine aromatic-C),58.2(-$OCH_3$),109.14-143.17(aromatic-27C).

**2.2. Scheme I**




**5a-l** **6a-l**

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

**2.3. Synthetic method: II**

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

**Synthesis of 3-Amino-2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl–6-iodoquinazolin–4(3*H*) 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(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 recrystalised from ethanol.

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

To a solution of 3-Amino-2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl–6-iodoquinazolin–4(3*H*) 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 36uinazoline36d from methanol.

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

A solution of 2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl-3-acetamido-6-iodoquinazolin-4(3*H*)-one **(**5.805g, 0.01 mol) in absolute ethanol (50 ml) and add 37uinazoline37 (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 37uinazoline37d 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).$^1$H-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(3*H*)-one (5b)**

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). $^1$H 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). $^{13}$C 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).

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

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). $^1$H 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). $^{13}$C 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).

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

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). $^1$H 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). $^{13}$C 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).

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

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). $^1$H 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). $^{13}$C 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).

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

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). $^1$H 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).$^{13}$C NMR: 31.1($-CH_2$), 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).

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

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). $^1$H NMR($CDCl_3$)**:** 2.12(s, 1H, -N-NH),6.36-7.93(m,16H, Ar-H),3.62 (s, 2H, $-CH_2$), 6.81(d, 1H, COCH=), 8.61(d, 1H, =CH-Ar), 10.37(s,1H,-OH).$^{13}$C 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).

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

IR(KBr) : 3413(NH), 3061, 2852(C-H), 1721(C =O), 1614(C=O of $-COCH_3$), 1572(CH=CH), 1317(C-N),1565,1367($-NO_2$) 779(C-Cl), 507(C-I). $^1$H 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). $^{13}$C

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).

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

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). $^1$H 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).$^{13}$CNMR:30.6(-$CH_2$),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).

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

IR(KBr) : 3415(NH), 3059, 2857(C-H), 1724(C =O), 1613(C=O of –$COCH_3$), 1572 (CH=CH),1563,1366(-$NO_2$),1317(C-N), 778(C-Cl), 507(C-I). $^1$H NMR($CDCl_3$)**:** 2.16(s, 1H, -N-NH), 6.39- 7.94(m, 16H, Ar-H), 3.62 (s, 2H, -$CH_2$), 6.81(d, 1H, COCH=), 8.60(d, 1H, =CH-Ar).$^{13}$CNMR:30.4(-$CH_2$),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).

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

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).$^1$H-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,-$OCH_3$).$^{13}$CNMR: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).

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

IR(KBr) : 3409(NH), 3063, 2859(C-H), 1721(C =O), 1615(C=O of –COCH3), 1575(CH=CH), 1317(C-N),1245,1108(C-O-C),778(C-Cl), 509(C-I). $^1$H 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,-$OCH_3$).$^{13}$C NMR: 30.6(-$CH_2$), 36.6,42.4(CH=CH),59.7(-$OCH_3$),161.1(immine >C=O),162.3 (>C=O), 173.2(immine aromatic-C), 109.21-143.20(aromatic-27C).

**Synthesis of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3–(1, 5-diphenyl-4,5-dihydro-1*H*-pyrazol-3-yl amino)-6-iodo 40uinazoline-4(3*H*)-one 6a**

To a solution of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3-substituted phenyl acryl amido-6-iodoquinazolin-4(3*H*)-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 40uinazoline40d from methanol.

IR(KBr): 3369(N-H),3063,2857(C-H),1725(C=O),1616(C=N), 1319(C-N),780(C-Cl),507(C-I). $^1$H 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). $^{13}$C NMR: 30.6(-$CH_2$), 36.4, 41.1, 161.3(pyrazol-C), 162.2 (>C=O), 173.1(immine aromatic-C) 109.21-143.20(aromatic-33C).

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-1*H*-pyrazol-3-yl amino]-6-iodo 40uinazoline-4(3*H*)-one(6b)**

IR(KBr):3368(N-H),3059,2861(C-H),1729(C=O),1616(C=N), 1315(C-N), 782(C-Cl), 509(C-I). $^1$H NMR($CDCl_3$): 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).$^{13}$C 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).

**Spectral data of 6c: 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3–[5-(3-chloro) phenyl-1-phenyl-4, 5-dihydro-1*H*-pyrazol-3-yl amino]-6-iodo 40uinazoline-4(3*H*)-one (6c)**

IR(KBr): 3371(N-H),3061, 2856(C-H),1731 (C=O),1614(C=N), 1318(C-N), 780(C-Cl),511(C-I). $^1$HNMR($CDCl_3$):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). $^{13}$C 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).

**Spectral data of 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 40uinazoline-4(3*H*)-one(6d)**

IR(KBr):3367(N-H),3061,2863(C-H),1729(C=O),1616(C=N),1319(C-N), 782(C-Cl),510(C-I). $^{1}$H 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).$^{13}$C NMR: 31.5(-$CH_2$), 36.2, 41.5, 161.2 (immine pyrazol-C),162.2(>C=O),172.9(immine aromatic-C), 109.21-143.20(aromatic-33C).

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3–[5-(2-hydroxy) phenyl-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl amino]-6-iodo 41uinazoline-4(3*H*)-one(6e)**

(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).$^{1}$H 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). $^{13}$C 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).

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3–[5-(3-hydroxy) phenyl-1-phenyl-4, 5-dihydro-1*H*-pyrazol-3-yl amino]-6-iodo 41uinazoline-4(3*H*)-one (6f)**

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). $^{1}$H NMR($CDCl_3$): 2.17(d,1H,=N-NH),3.63 (s,2H,-$CH_2$), 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). $^{13}$C NMR: 30.7(-$CH_2$), 36.4, 41.6, 161.2 (immine pyrazol-C), 162.3(>C=O), 173.1 (immine aromatic-C)109.21-143.20 (aromatic-33C).

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3–[5-(4-hydroxy) phenyl-1-phenyl-4, 5-dihydro-1*H*-pyrazol-3-yl amino]-6-iodo 41uinazoline-4(3*H*)-one (6g)**

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). $^{1}$H 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). $^{13}$C 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).

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3–[5-(2-nitro) phenyl-1-phenyl-4, 5-dihydro-1*H*-pyrazol-3-yl amino]-6-iodo 41uinazoline-4(3*H*)-one(6h)**

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).$^{1}$H 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).$^{13}$C 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).

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3–[5-(3-nitro) phenyl-1-phenyl-4, 5-dihydro -1*H*-pyrazol-3-yl amino]-6-iodo 42uinazoline-4(3*H*)-one (6i)**

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). $^1$H 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). $^{13}$C NMR: 30.9(-$CH_2$), 36.5, 41.6, 161.2 (immine pyrazol-C), 162.1(>C=O),172.9(immine aromatic-C), 109.21-143.20 (aromatic-33C).

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3–[5-(4-nitro) phenyl-1-phenyl-4, 5-dihydro-1*H*-pyrazol-3-yl amino]-6-iodo 42uinazoline-4(3*H*)-one (6j)**

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). $^1$H 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). $^{13}$C 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).

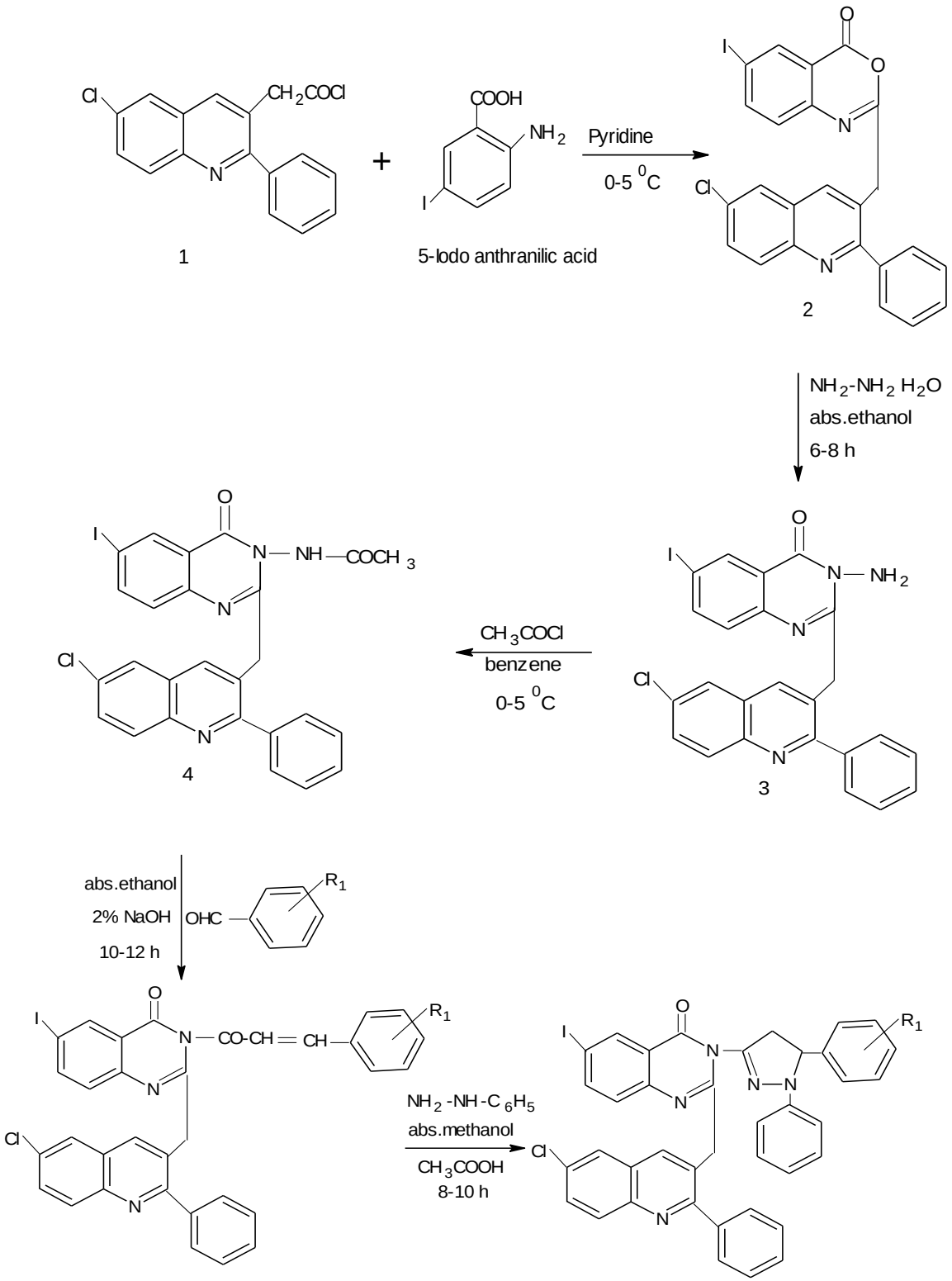
**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3–[5-(2-methoxy) phenyl-1-phenyl-4, 5-dihydro-1*H*-pyrazol-3-yl amino]-6-iodo 42uinazoline-4(3*H*)-one(6k)**

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). $^1$H 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), 3.82(s,3H,-$OCH_3$).$^{13}$C 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).

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3–[5-(4-methoxy) phenyl-1-phenyl-4, 5-dihydro-1*H*-pyrazol-3-yl amino]-6-iodo 42uinazoline-4(3*H*)-one(6l)**

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).$^1$H 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,-$OCH_3$). $^{13}$C 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).

**2.4. Scheme-II**




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

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# 3. CHARACTERISATION

### 3.1. Method

The IR spectra of the synthesized compounds were recorded on Perkin-Elmer 1300 FTIR spectrophotometer using KBr pellets and frequencies are recorded in $cm^{-1}$. $^{1}H$ NMR and $^{13}C$ NMR spectra were recorded on Bruker Advance II 400 NMR spectrometer using deutero $CDCl_3$ as a solvent. The chemical shifts were reported in (δ ppm) downfield using tetra methyl silane as internal standard. Elemental analyses of newly synthesized compounds were carried out on Carlo Ebra 1108 analyzer.

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 $^{1}H$ 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 $^{1}H$ 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 $^{1}H$ NMR spectra of compounds 6a-j 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 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 $^{13}C$ 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.

Physical data of the synthesized compounds scheme : I summarized in the table:1 and scheme :II in the table :2. Synthetic route of scheme: I also confirmed by the IR, $^{1}H$ NMR and $^{13}C$ NMR spectra (Fig: 1-8).

### 3.2. Physical and spectral results

**Table: 1 Physical characterization of compound 6a-l scheme:I**

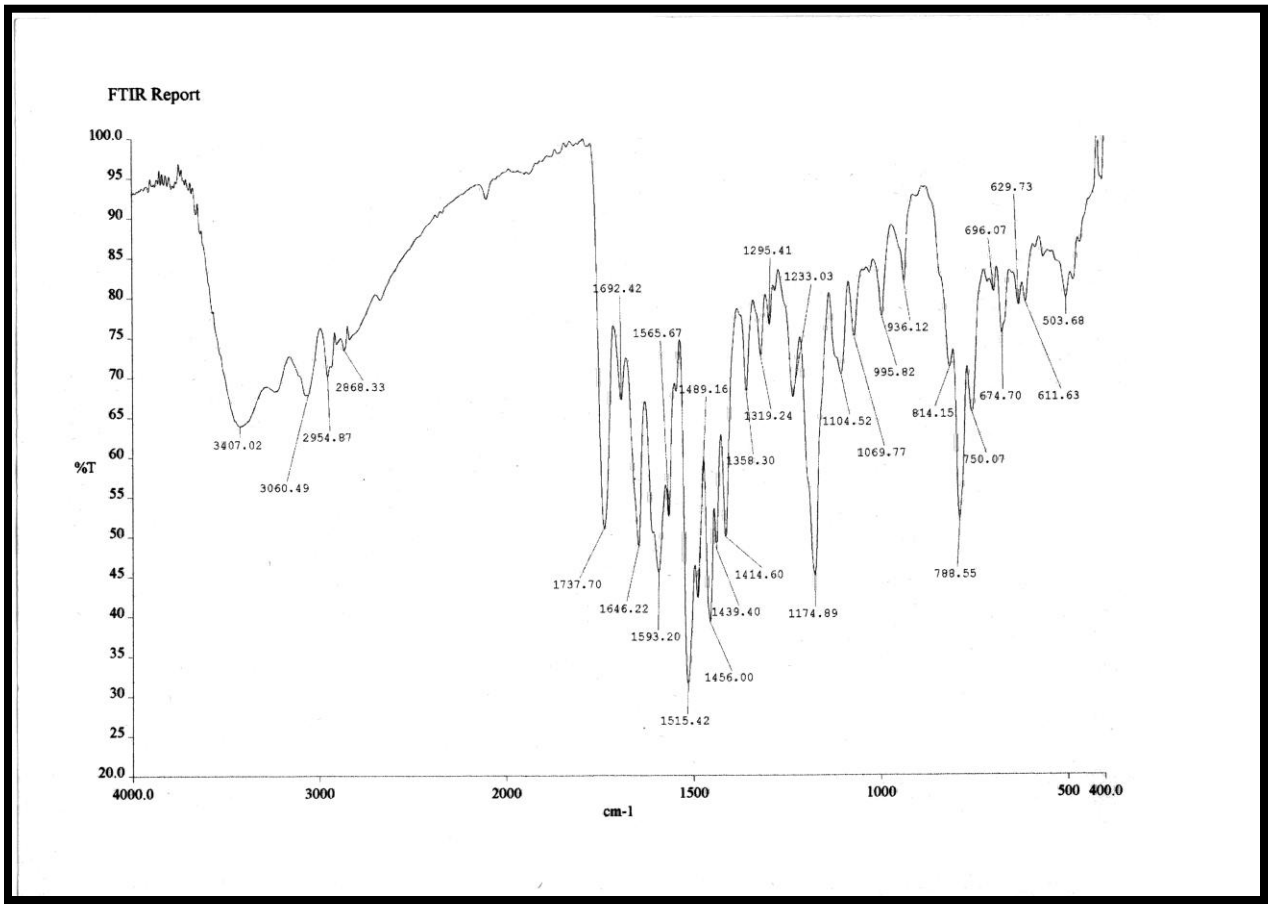
| Cpd. No. | $R_1$ | Molecular Formula | M.P. $^{0}C$ | Yield % | Elemental analysis % | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | C | | H | | N | |
| | | | | | *Calcd* | *Found* | *Calcd* | *Found* | *Calcd* | *Found* |
| 6a | H | $C_{33}H_{24}N_6OICl$ | 141-143 | 78 | 58.02 | 58.05 | 3.51 | 3.50 | 12.30 | 12.31 |
| 6b | 2-Cl | $C_{33}H_{23}N_6OICl_2$ | 135-137 | 68 | 55.23 | 55.25 | 3.20 | 3.22 | 11.71 | 11.73 |
| 6c | 3-Cl | $C_{33}H_{23}N_6OICl_2$ | 123-124 | 72 | 55.23 | 55.26 | 3.20 | 3.24 | 11.71 | 11.75 |
| 6d | 4-Cl | $C_{33}H_{23}N_6OICl_2$ | 132-133 | 75 | 55.23 | 55.24 | 3.20 | 3.21 | 11.71 | 11.74 |
| 6e | 2-OH | $C_{33}H_{24}N_6O_2ICl$ | 152-153 | 70 | 56.69 | 56.63 | 3.43 | 3.45 | 12.02 | 12.05 |
| 6f | 3-OH | $C_{33}H_{24}N_6O_2ICl$ | 157-159 | 69 | 56.69 | 56.70 | 3.43 | 3.47 | 12.02 | 12.03 |
| 6g | 4-OH | $C_{33}H_{24}N_6O_2ICl$ | 163-165 | 72 | 56.69 | 56.67 | 3.43 | 3.46 | 12.02 | 12.06 |
| 6h | 2-$NO_2$ | $C_{33}H_{23}N_7O_3ICl$ | 173-175 | 67 | 54.43 | 54.47 | 3.16 | 3.20 | 13.47 | 13.48 |
| 6i | 3-$NO_2$ | $C_{33}H_{23}N_7O_3ICl$ | 184-186 | 65 | 54.43 | 54.41 | 3.16 | 3.19 | 13.47 | 13.51 |
| 6j | 4-$NO_2$ | $C_{33}H_{23}N_7O_3ICl$ | 195-197 | 69 | 54.43 | 54.45 | 3.16 | 3.17 | 13.47 | 13.45 |
| 6k | 2-$OCH_3$ | $C_{34}H_{26}N_6O_2ICl$ | 144-145 | 71 | 57.26 | 57.29 | 3.64 | 3.66 | 11.79 | 11.80 |
| 6l | 4-$OCH_3$ | $C_{34}H_{26}N_6O_2ICl$ | 147-149 | 74 | 57.26 | 57.24 | 3.64 | 3.67 | 11.79 | 11.82 |

**Table: 2 Physical characterization of compound 6a-l scheme:II**

| Cpd. No. | $R_1$ | Molecular Formula | M.P. $^0$C | Yield % | Elemental analysis % | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | C | | H | | N | |
| | | | | | *Calcd* | *Found* | *Calcd* | *Found* | *Calcd* | *Found* |
| 6a | H | $C_{39}H_{28}N_6OICl$ | 147-149 | 73 | 61.70 | 61.72 | 3.69 | 3.70 | 11.07 | 11.09 |
| 6b | 2-Cl | $C_{39}H_{27}N_6OICl_2$ | 140-141 | 68 | 59.01 | 59.03 | 3.40 | 3.41 | 10.59 | 10.61 |
| 6c | 3-Cl | $C_{39}H_{27}N_6OICl_2$ | 128-130 | 70 | 59.01 | 59.02 | 3.40 | 3.43 | 10.59 | 10.60 |
| 6d | 4-Cl | $C_{39}H_{27}N_6OICl_2$ | 132-133 | 75 | 59.01 | 59.03 | 3.40 | 3.42 | 10.59 | 10.62 |
| 6e | 2-OH | $C_{39}H_{28}N_6O_2ICl$ | 156-158 | 71 | 60.42 | 60.43 | 3.61 | 3.63 | 10.84 | 10.85 |
| 6f | 3-OH | $C_{39}H_{28}N_6O_2ICl$ | 163-165 | 65 | 60.42 | 60.45 | 3.61 | 3.62 | 10.84 | 10.87 |
| 6g | 4-OH | $C_{39}H_{28}N_6O_2ICl$ | 168-170 | 69 | 60.42 | 60.44 | 3.61 | 3.61 | 10.84 | 10.86 |
| 6h | 2-$NO_2$ | $C_{39}H_{27}N_7O_3ICl$ | 180-181 | 66 | 58.24 | 58.27 | 3.36 | 3.37 | 12.19 | 12.21 |
| 6i | 3-$NO_2$ | $C_{39}H_{27}N_7O_3ICl$ | 189-190 | 64 | 58.24 | 58.25 | 3.36 | 3.39 | 12.19 | 12.20 |
| 6j | 4-$NO_2$ | $C_{39}H_{27}N_7O_3ICl$ | 201-203 | 70 | 58.24 | 58.26 | 3.36 | 3.38 | 12.19 | 12.22 |
| 6k | 2-$OCH_3$ | $C_{40}H_{30}N_6O_2ICl$ | 150-151 | 73 | 60.87 | 60.90 | 3.80 | 3.81 | 10.65 | 10.67 |
| 6l | 4-$OCH_3$ | $C_{40}H_{30}N_6O_2ICl$ | 153-155 | 73 | 60.87 | 60.88 | 3.80 | 3.82 | 10.65 | 10.66 |

# Fig:1 IR Spectrum

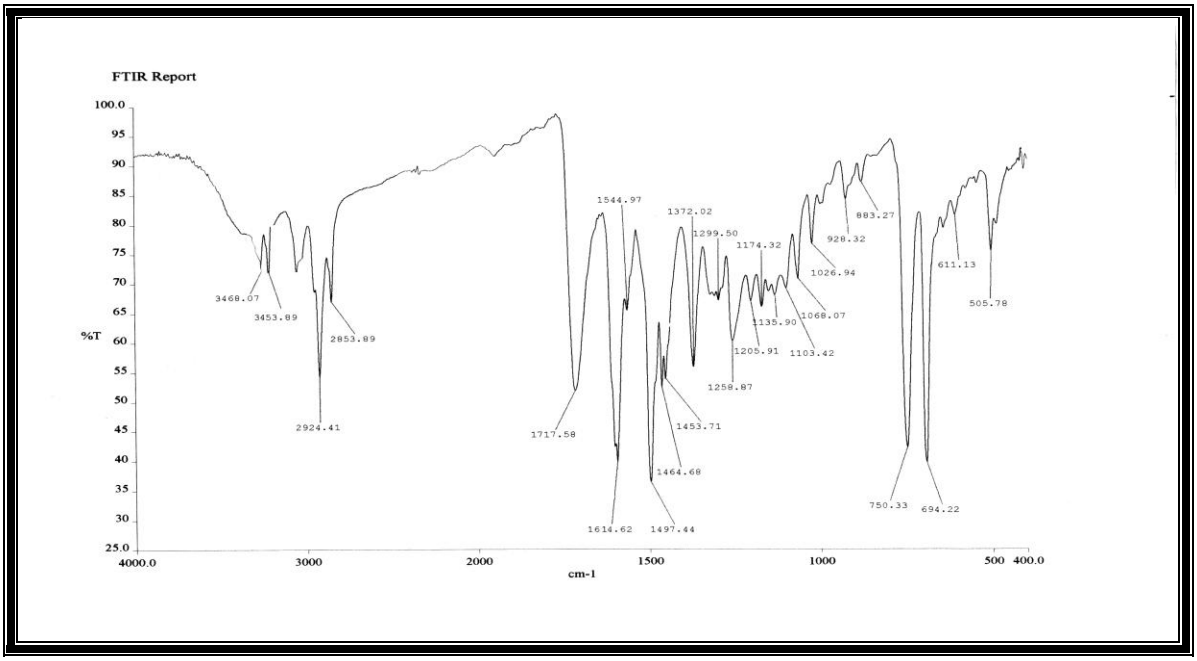
**2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl–6-iodo-3, 1-benzoxazin-4(3*H*) one**




**IR(cm$^{-1}$):**3060,2868(C-H),1737(C=O),1616(C=N),1319(C-N),1233(C-O-C),789(C-Cl), 503(C-I)

# Fig:2 IR Spectrum

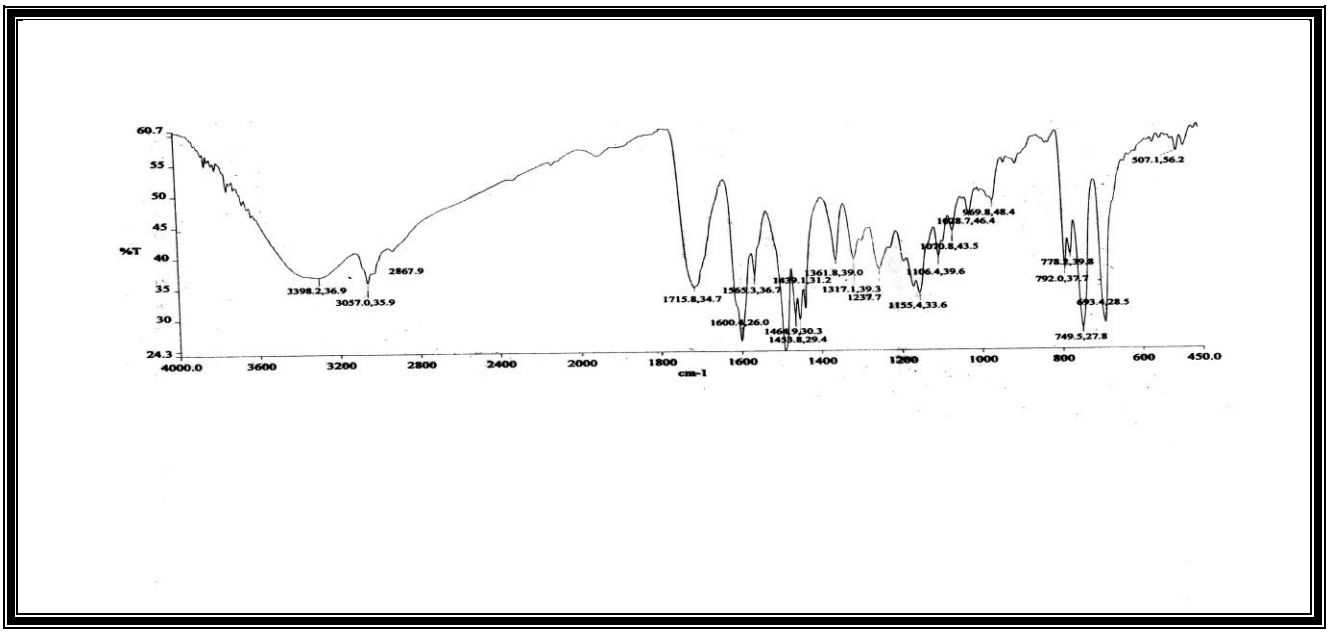
**3-Amino-2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl–6-iodoquinazolin–4(3*H*) one**




**IR(cm$^{-1}$) :**3468(-$NH_2$), 3068, 2853(C-H), 1717(C=O), 1614(C=N), 750(NH-Wag), 783(C-Cl), 506(C-I).

# Fig:3 IR Spectrum

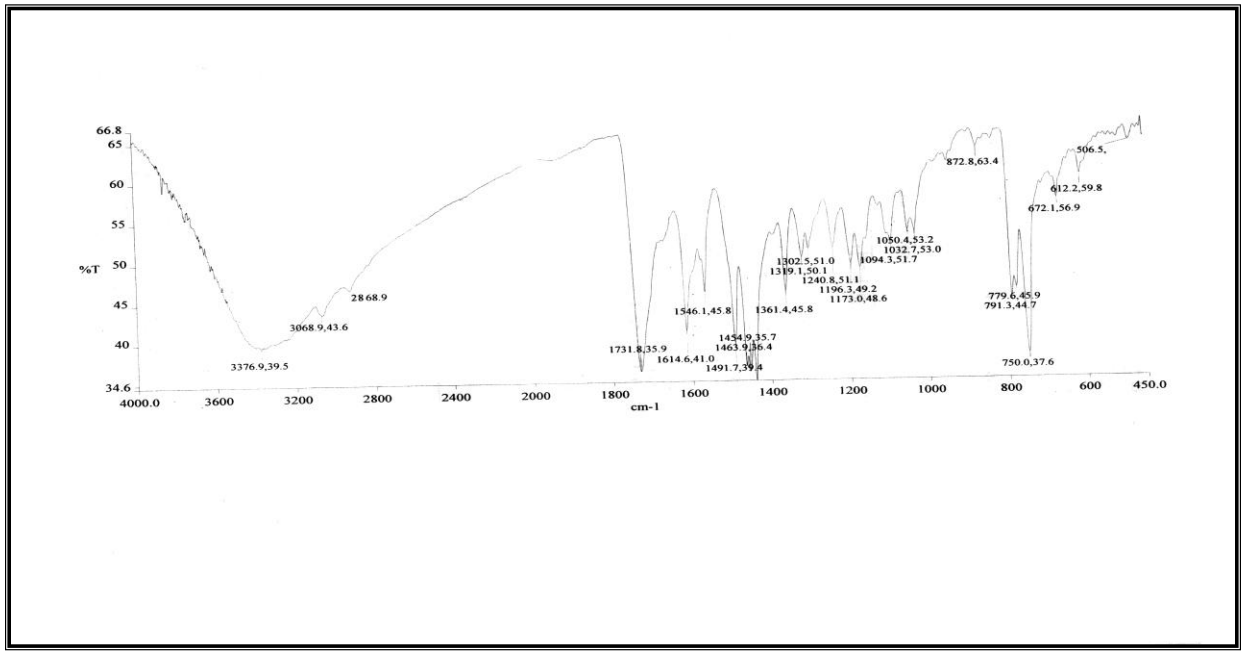
**2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl-3-acetamido-6-iodoquinazolin-4(3*H*)-one**




**IR($cm^{-1}$) :** 3398 (NH), 3057, 2867 (C-H), 1715 (C=O), 1634 (C=O of $–COCH_3$), 1319 (C-N), 750 (NH-Wag), 778(C-Cl), 507(C-I).

# Fig: 4 IR Spectrum

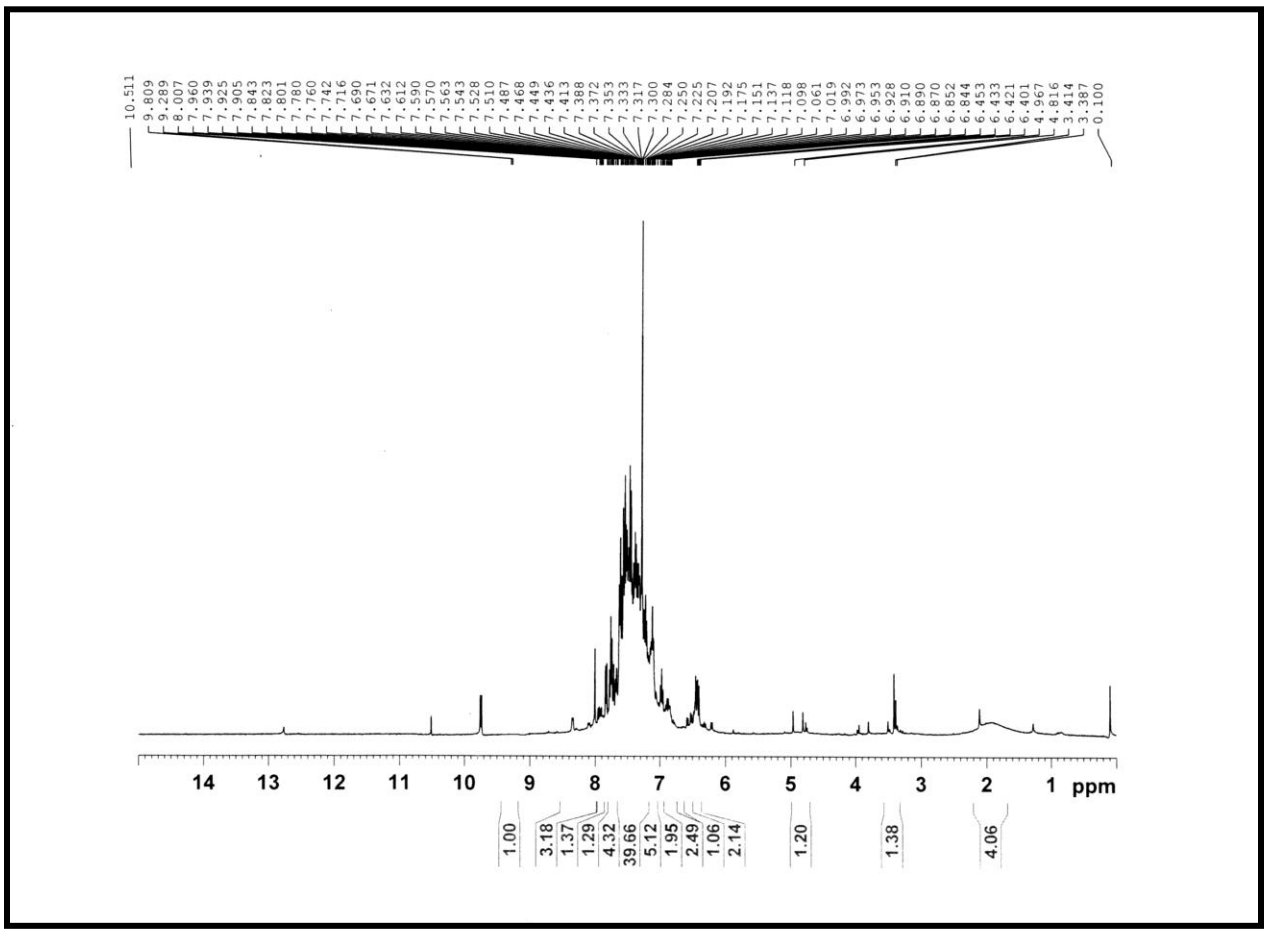
**2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl-3-substituted phenyl acryl amido-6-iodoquinazolin-4(3*H*)-one**




**IR(cm$^{-1}$) :**3376(NH), 3068, 2868(C-H), 1731(C=O), 1634(C=O of –$COCH_3$), 1566(CH=CH), 1319(C-N),750(NH-Wag), 782(C-Cl), 506(C-I).

# Fig:5 $^{1}$H NMR Spectrum

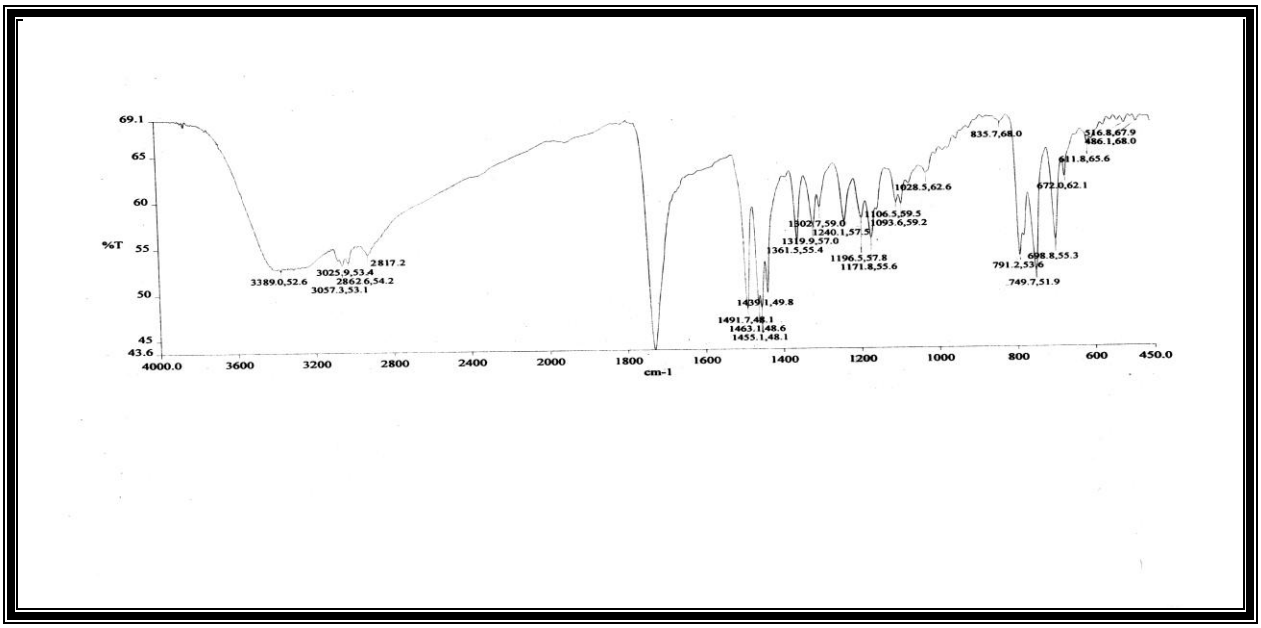
**2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl-3-substituted phenyl acryl amido-6-iodoquinazolin-4(3*H*)-one**




**$^{1}$H-NMR($CDCl_3$) :** 2.11(s, 1H, -N-NH), 6.34- 7.91(m, 17H, Ar-H), 3.61 (s, 2H, -$CH_2$), 6.81(d, 1H, COCH=), 8.61(d, 1H, =CH-Ar).

# Fig:6 IR Spectrum

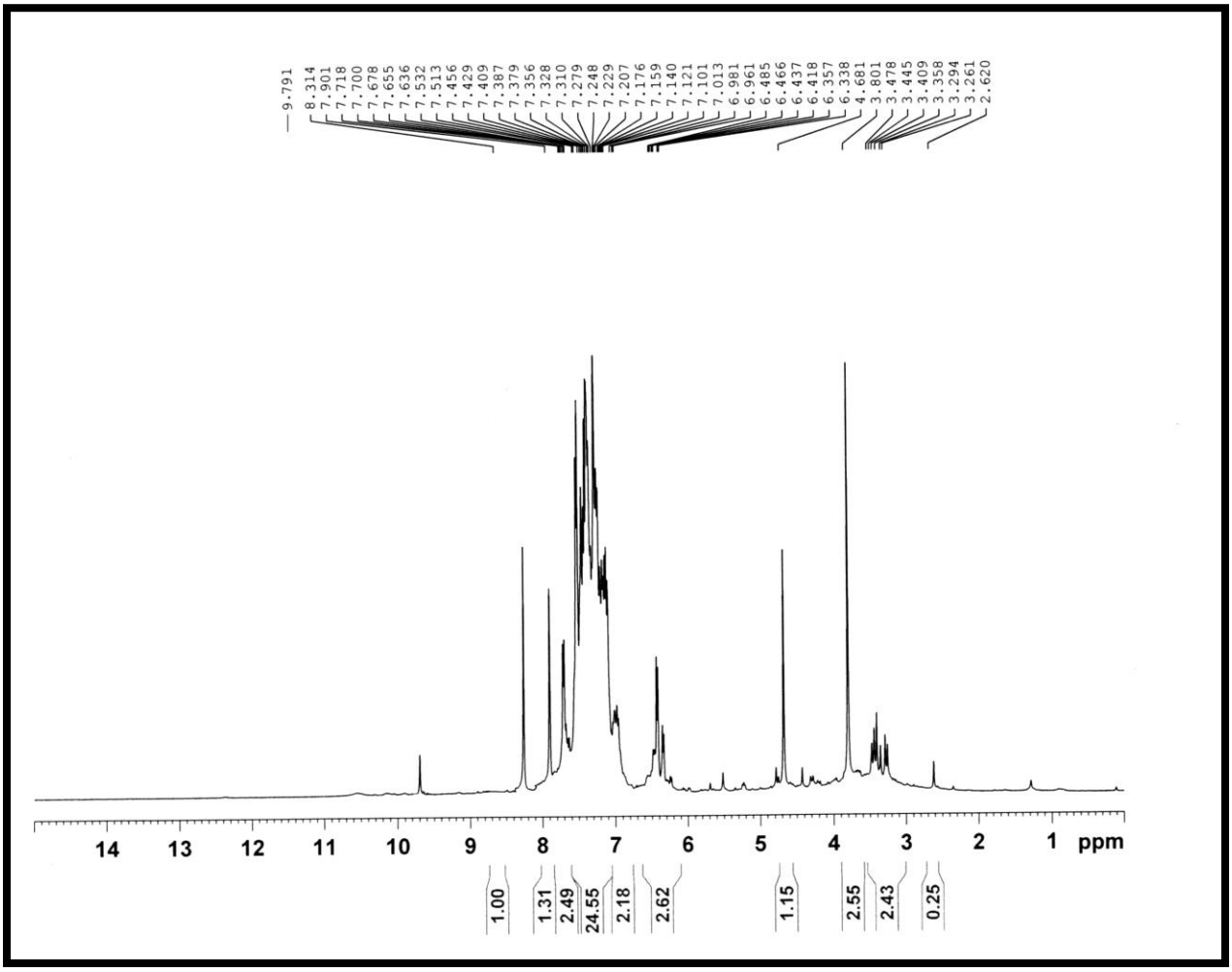
**2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl-3–(5-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl amino)-6-iodo quinazolin-4(3*H*)-one**




**IR(cm$^{-1}$) :**3389(NH), 3057, 2862(C-H), 1731(C=O), 1614(C=N), 1546,1361(N=O), 1319(C-N), 750(NH-Wag), 779(C-Cl), 506(C-I).

# Fig:7 $^{1}$H NMR Spectrum

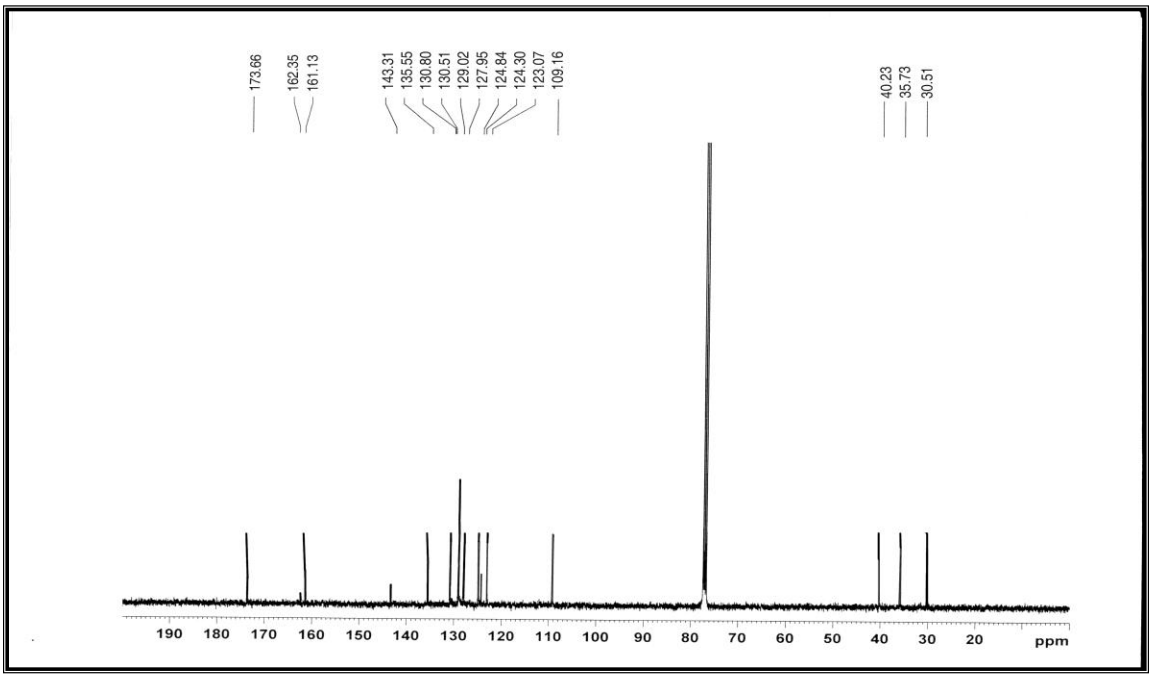
**2-[3-(6-chloro-2-phenyl) quinolin-3-yl]methyl-3–(5-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl amino)-6-iodo quinazolin-4(3*H*)-one**




**$^{1}$H NMR($CDCl_3$)**:2.17(d,1H,=N-NH),8.32(s,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,17H,Ar-H).

## Fig: 8 $^{13}$C NMR Spectrum

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




**$^{13}$C NMR (δ ppm):** 30.51 (Methylene –$CH_2$), 35.73, 40.23 (Pyrazol–C), 109.16-143.31 (Aromatic Carbon), 161.13 (Immine – C), 162.35 ( > C = O),173.66 (Immine Aromatic- C)

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# 4. RESULT AND DISCUSSION

## 4.1. Antimicrobial activity

The *in vitro* antimicrobial activity of compounds 6a-j 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, 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. Penicillin-G and fluconazole were used as standard drugs.

**Cup plate Method**

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.

**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 for the comparison and result is recorded as under.

**4.2. Potency**

Potency is the dose of drug required to produce a specific effect of given intensity as compared to standard reference. Potency is a comparative rather than an absolute expression of drug activity. Drug potency depends on both affinity and efficacy. Thus, two agonists can be equipotent, but have different intrinsic efficacies with compensating differences in affinity.

Potency of newly synthesized compounds were calculated by the following equation

$$\text{Potency } P = \{\text{antilog}(D/B \times I)\} \times M \times F$$

Where,

F = dilution factor

M = value of $S_H$ =1 unit / ml = 100 %

$I = \log S_H / S_L$

$D = (U_H + U_L) - (S_H + S_L)$

$B = (U_H - U_L) + (S_H - S_L)$

$S_H$ =Zone of inhibition of standard at high concentration.

$S_L$ = Zone of inhibition of standard at low concentration.

$U_H$ =Zone of inhibition of unknown at high concentration.

$U_L$ = Zone of inhibition of unknown at low concentration.

Screening results of antimicrobial activity of series(I) and series (II) summarized in table:3, 4, 5 and 6 respectively.

### 4.3. Screening results

**Table: 3 Anti-bacterial activity of compound 6a-l (series:I)**

| 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 | 10 | 08 | 41.44 | 11 | 09 | 43.86 | 10 | 08 | 41.44 | 11 | 09 | 43.86 |
| **6b** | **2-Cl** | **18** | **14** | **68.69** | **19** | **17** | **68.29** | 15 | 12 | 52.44 | 13 | 11 | 49.15 |
| **6c** | **3-Cl** | **16** | **13** | **60.81** | **16** | **12** | **62.87** | 14 | 11 | 55.05 | 15 | 12 | 52.44 |
| **6d** | **4-Cl** | **19** | **16** | **70.60** | **20** | **17** | **73.48** | 15 | 13 | 54.00 | 16 | 13 | 59.84 |
| 6e | 2-OH | 11 | 09 | 43.86 | 12 | 10 | 46.40 | 11 | 09 | 43.86 | 12 | 10 | 46.40 |
| 6f | 3-OH | 11 | 08 | 47.42 | 12 | 10 | 46.40 | 11 | 09 | 43.86 | 12 | 10 | 46.40 |
| 6g | 4-OH | 12 | 10 | 46.40 | 13 | 11 | 49.15 | 12 | 10 | 46.40 | 13 | 11 | 49.15 |
| 6h | 2-$NO_2$ | 15 | 13 | 55.05 | 16 | 13 | 59.84 | 16 | 13 | 59.84 | **17** | **14** | **62.99** |
| 6i | 3-$NO_2$ | 14 | 11 | 54.96 | 14 | 11 | 54.96 | **16** | **14** | **61.69** | **18** | **15** | **66.29** |
| 6j | 4-$NO_2$ | 15 | 12 | 52.44 | 15 | 13 | 54.00 | 14 | 11 | 55.05 | 16 | 13 | 59.84 |
| 6k | 2-$OCH_3$ | 11 | 08 | 41.44 | 12 | 10 | 46.40 | 11 | 08 | 47.42 | 13 | 11 | 49.15 |
| 6l | 4-$OCH_3$ | 13 | 11 | 49.15 | **13** | **11** | 49.15 | 11 | 08 | 47.42 | 13 | 11 | 49.15 |
| **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: 4 Antifungal activity of compound 6a-l(Series:I)**

| 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** | **13** | **70.13** | **17** | **14** | **68.92** |
| 6b | 2-Cl | 11 | 08 | 50.90 | 12 | 09 | 53.75 |
| 6c | 3-Cl | 11 | 09 | 47.09 | 12 | 10 | 49.89 |
| 6d | 4-Cl | 12 | 09 | 53.75 | 13 | 11 | 52.86 |
| 6e | 2-OH | 15 | 13 | 59.36 | 14 | 12 | 56.03 |
| 6f | 3-OH | 14 | 12 | 56.03 | 14 | 12 | 56.03 |
| 6g | 4-OH | 14 | 11 | 59.36 | 14 | 11 | 59.36 |
| 6h | 2-$NO_2$ | 12 | 10 | 49.89 | 10 | 08 | 38.19 |
| 6i | 3-$NO_2$ | 09 | 07 | 41.93 | 11 | 10 | 36.91 |
| 6j | 4-$NO_2$ | 11 | 09 | 47.09 | 11 | 09 | 40.53 |
| 6k | 2-$OCH_3$ | **15** | **12** | **62.38** | **15** | **13** | **59.36** |
| 6l | 4-$OCH_3$ | **16** | **13** | **65.88** | **16** | **13** | **65.88** |
| **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.

**Table: 5 Anti-bacterial activity of compound 6a-l(Series:II)**

| 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: 6 Antifungal activity of compound 6a-l(Series:II)**

| 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.

### 4.4. Conclusion

From the screening results of the synthesized compound of series :I and Series: II compound **6a(R= 2-Cl), 6b (R=3-Cl)** and **6c (R=3-Cl)** showed very good activity against Gram positive compared to standard. Compounds **6i(R= 3-$NO_2$)** and **6j((R= 4-$NO_2$)** showed very good activity against Gram negative bacteria compared to standard. Compound **6a(R= -H), 6k(R= 2-$OCH_3$)** and **6l ((R= 4-$OCH_3$)** showed very good anti-fungal activities compared to standard. Remaining compound of the series shows moderate or week activities against the microorganisms in vitro.

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# Synthesis and Pharmacological Aspects of Some Novel Nitrogen Containing Heterocycles With 6-Iodo Quinazolin-4(3H) Ones

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## ABSTRACT

*Several 6-iodo quinazolin-4(3H) ones **6a-l** were synthesized by the cyclization of acrylamide 5**a-l** with hydrazine hydrate. The overall reaction was carried out by multistep process. The base catalyzed cyclization of acid chloride **1** with 5-iodo anthranilic acid yielded benzoxazinone **2**, which on reaction with hydrazine hydrate to afforded amino quinazolin-4(3H) one **3**. The structural confirmation of the synthesized compounds was carried out on the basis of elemental analysis as well as IR and NMR spectra results. The title compounds were evaluated for antibacterial and antifungal activity in vitro.*

**Keywords:** Acryl amide, Antimicrobial activity, Quinolin, Quinazolin-4(3H) one.

## INTRODUCTION

Quinolin nucleus is an important pharmacophore in medicinal chemistry, since a large number of its derivatives possess useful biological properties. 4(3*H*)-quinazolinones have emerged as an important class of nitrogenated heterocyclic that have attached synthetic interest because of they possess good pharmacological and therapeutic properties, along with quinolin moiety played vital role in the medicinal chemistry. The large number of synthetic compounds with pyrazoline and quinolin nucleus used for antibacterial[1-2], antimycobacterial[3], analgesics[4], antifungal[5-6], anticonvulsant[7], rheumatic arthritis[8], antinociceptive[9], anxiolytic activity[10] ,anti-inflammatory and anti-breast cancer agent[11]. A Quinazolinones system possess pyrazoline moiety at C-3 positions to yield the potential anti-tumor and antidiabetic activities[12]. Its halogenated derivatives possess potential antihyperlipidemic activity[13] and have no significant toxic side effects at the drop sub lethal dose level (2mg/kg). There are broad spectrum of therapeutic values of pyrazoline with 4(3H)-Quinazolinones for the pharmacological activity [14-20]. In the light of these findings, the synthesis of new chemical entities incorporating the quinolin and pyrazoles with quinazolinones may prove to be useful from the biological activity point of view.

## MATERIALS AND METHODS

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 $^{13}C$ NMR spectra were recorded on Bruker Advance II 400 NMR spectrometer using deutero $CDCl_3$ as a solvent. The chemical shift are 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 providing satisfactory results. The purities of all the compounds were checked by TLC on Merck silica gel 60 F 254 using toluene : ethylacetate (8:2) as mobile phase, and spots were visualized under UV radiation. The reagent grade chemicals were purchased from commercial sources and further purified before use. 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(3*H*) one 2:** To the 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 each small portion of 5-iodo anthranilic acid (2.63 g, 0.01 mol) was added portion wise and were stirred for 1 h. to maintain temperature 0-5 $^0$C. Furthere reaction mixture was stirred 1h at room temperature. A pasty mass thus obtained which was washed thoroughly with sodium bicarbonate (5 %) to remove unreacted acid. A solid separated was filtered, dried and recrystallized from methanol. M.P.: 162 $^0$C. Yeild : 79 % IR(KBr):3071,2859(C-H),1723(C=O),1616(C=N),1325(C-N),1237(C-O-C), 781(C-Cl),504(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(3*H*) 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(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 obtained was filtered and washed several times with water. The crushed product was dried and recrystallized from ethanol. M.P. **:**145 $^0$C. Yeild **:** 74 % IR(KBr) : 3405(NH), 3068, 2865(C-H), 1719(C=O), 1614(C=N), 1323(C-N), 778(C-Cl), 508(C-I). $^1$HNMR($CDCl_3$)**:** 2.1(s, 2H, -N-$NH_2$), 6.37-7.94(m, 12H, Ar-H), 2.72(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(3*H*)-one 4 :** To a solution of 3-Amino-2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl–6-iodoquinazolin–4(3*H*) 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 completion of addition 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 recrystallized from methanol. M.P. **:**173 $^0$C. Yeild **:** 69 % IR(KBr): 3405(NH), 3063,2860(C-H),1723(C=O), 1642(C=O of –$COCH_3$), 1321(C-N), 779(C-Cl), 513(C-I). $^1$H-NMR($CDCl_3$) **:** 2.12(s, 1H, -N-NH-), 6.33- 7.96(m, 12H, Ar-H), 2.72(s, 3H, -$CH_3$), 2.62(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(3*H*)-one 5a :** A solution of 2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl-3-acetamido-6-iodoquinazolin-4(3*H*)-one **(**5.805g, 0.01 mol) in absolute ethanol (50 ml) and added 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 with water and recrystallized from methanol. M.P.**:** 137 $^0$C. Yeild**:** 76 % IR(KBr) : 3409(NH), 3061, 2857(C-H), 1718(C =O), 1651(C=O of –$COCH_3$), 1577 (CH=CH), 1317(C-N), 780(C-Cl), 511(C-I).$^1$H-NMR($CDCl_3$) **:** 2.11(s, 1H, -N-NH), 6.34- 7.91(m, 17H, Ar-H), 2.61 (s, 2H, -CH2),

6.81(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(3*H*)-one (5b) :** M.P.**:** 131-133 $^0$C. Yeild**:** 70 % IR(KBr) : 3367(NH), 3061, 2855(C-H), 1727(C =O), 1613(C=O of –$COCH_3$), 1579 (CH=CH), 1314(C-N), 781(C-Cl), 511(C-I). $^1$H NMR($CDCl_3$) **:** 2.13(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). $^{13}$C NMR: 29.5(-$CH_2$), 36.1, 41.6(CH=CH), 160.9 (immine>C=O), 162.1 (>C=O), 173.1(immine aromatic-C), 109.20-143.16(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(3*H*)-one (5c) :** M.P.**:** 134-135 $^0$C. Yeild**:** 72 % IR(KBr) : 3371(NH), 3065, 2858(C-H), 1729(C =O), 1615(C=O of –$COCH_3$), 1577 (CH=CH), 1316(C-N), 779(C-Cl), 509(C-I). $^1$H NMR($CDCl_3$) **:** 2.11(s, 1H, -N-NH), 6.39- 7.93(m, 16H, Ar-H), 3.61 (s, 2H, -$CH_2$), 6.81(d, 1H, COCH=), 8.61(d, 1H, =CH-Ar). $^{13}$C NMR: 31.3(-$CH_2$), 36.5, 41.1(CH=CH), 161.3(immine>C=O), 162.3(>C=O), 173.2(immine aromatic-C), 109.13-143.17(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(3*H*)-one (5d) :** M.P.**:** 127-129 $^0$C. Yeild**:** 72 % IR(KBr) : 3368(NH), 3063, 2856(C-H), 1727(C =O), 1617(C=O of –$COCH_3$), 1578(CH=CH), 1317(C-N), 781(C-Cl), 513(C-I). $^1$H NMR($CDCl_3$) **:**2.11(s, 1H, -N-NH), 6.37- 7.96(m, 16H, Ar-H), 3.63(s, 2H, -$CH_2$), 6.81(d, 1H, COCH=), 8.62(d, 1H, =CH-Ar). $^{13}$C NMR: 30.6(-$CH_2$), 36.2, 41.3(CH=CH), 161.4 (immine >C=O),162.0(>C=O), 173.1(immine aromatic-C), 109.17-143.21(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(3*H*)-one (5e) :** M.P.**:** 146-148 $^0$C. Yeild**:** 71 % IR (KBr) : 3549(-OH),3413(NH), 3061, 2854(C-H), 1719(C =O), 1619(C=O of –$COCH_3$), 1572 (CH=CH), 1319(C-N), 779(C-Cl), 507(C-I). $^1$H NMR($CDCl_3$) **:**2.11(s, 1H, -N-NH),6.34- 7.91(m,16H, Ar-H),3.62 (s, 2H, -$CH_2$), 6.80(d, 1H, COCH=), 8.61(d, 1H, =CH-Ar), 10.36(s, 1H,-OH). $^{13}$C NMR: 30.7(-$CH_2$), 36.3, 41.4(CH=CH),160.9 (immine>C=O),162.1 (>C=O), 173.1(immine aromatic-C), 109.3-143.4(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(3*H*)-one (5f) :** M.P.**:**151-153 $^0$C. Yeild**: 6**7 % IR(KBr) : 3552(-OH),3416(NH), 3067, 2852(C-H), 1721(C =O), 1615(C=O of –$COCH_3$), 1574 (CH=CH), 1318(C-N), 780(C-Cl), 510(C-I). $^1$H NMR($CDCl_3$) **:**2.17(s, 1H, -N-NH), 6.36- 7.96(m, 16H, Ar-H), 3.63 (s, 2H, -$CH_2$), 6.82(d, 1H, COCH=), 8.61(d, 1H, =CH-Ar),10.38(s,1H,-OH).$^{13}$C NMR: 30.8(-$CH_2$), 37.5, 42.7(CH=CH), 161.2 (immine>C=O),162.2 (>C=O), 173.3(immine aromatic-C), 109.21-143.27(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(3*H*)-one (5g) :** M.P.**:** 157-159 $^0$C. Yeild**:**70 % IR(KBr): 3557(-OH),3411(NH), 3064, 2854(C-H), 1720(C =O), 1613(C=O of –$COCH_3$), 1571(CH=CH), 1319(C-N), 782(C-Cl), 509(C-I). $^1$H NMR($CDCl_3$)**:** 2.11(s, 1H, -N-NH),6.35- 7.93(m,16H, Ar-H),3.62 (s, 2H, -$CH_2$), 6.80(d, 1H, COCH=), 8.61(d, 1H, =CH-Ar), 10.36(s,1H,-OH).$^{13}$C NMR: 30.7(-$CH_2$), 36.5,41.5 (CH=CH), 161.1

(immine>C=O),162.3(>C=O),173.1 (immine aromatic-C), 108.78-143.24 (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, 3.21; 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(3*H*)-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 –$COCH_3$), 1572(CH=CH), 1317(C-N),1565,1367(-$NO_2$) 779(C-Cl), 507(C-I). $^1$H 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). $^{13}$C 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(3*H*)-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). $^1$H 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).$^{13}$CNMR:30.6(-$CH_2$), 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(3*H*)-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 –$COCH_3$), 1572 (CH=CH),1563,1366(-$NO_2$),1317(C-N), 778(C-Cl), 507(C-I). $^1$H NMR($CDCl_3$)**:** 2.16(s, 1H, -N-NH), 6.39- 7.94(m, 16H, Ar-H), 3.62 (s, 2H, -$CH_2$), 6.81(d, 1H, COCH=), 8.60(d, 1H, =CH-Ar).$^{13}$CNMR:30.4(-$CH_2$), 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(3*H*)-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).$^1$H-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,-$OCH_3$).$^{13}$CNMR: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(3*H*)-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 –COCH3), 1575(CH=CH), 1317(C-N),1245,1108(C-O-C),778(C-Cl), 509(C-I). $^1$H 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,-$OCH_3$).$^{13}$C NMR: 30.6(-$CH_2$), 36.6,42.4(CH=CH),59.7(-$OCH_3$),161.1(immine >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–(5-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl amino)-6-iodo quinazolin-4(3*H*)-one 6a :** To a solution of 2-[3-(6-chloro-2-phenyl)quinolin-3-yl]methyl-3-substituted phenyl acryl amido-6-iodoquinazolin-4(3*H*)-one (6.685 g, 0.01 mol) in methanol, add hydrazine hydrate(99 %) (1.0 g, 0.02 mol) and few drops of glacial acetic acid. The reaction mixture was refluxed for 8-10 h., distilled and cooled. The separated solid was filtered, washed with water and recrystallized from methanol. M.P.**:** 141-143 $^0$C. Yeild**:** 78 % IR(KBr): 3369(N-H),3063,2857(C-H),1725(C=O),1616(C=N), 1319(C-N),780(C-Cl),507(C-I).$^1$H NMR($CDCl_3$): 2.17(d,1H,=N-NH), 8.32(s,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,17H,Ar-H). $^{13}$C

NMR: 30.6(-$CH_2$), 36.4, 41.1, 161.3( pyrazol-C), 162.2 (>C=O), 173.1(immine aromatic-C) 109.1-143.2(aromatic-27C). Anal; (%) $C_{34}H_{24}N_6OICl$ Calcd; C, 58.02; H, 3.51; N,12.30; Found; C, 58.04; H, 3.54; N, 12.32.

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-4,5-dihydro-1*H*-pyrazol-3-yl amino]-6-iodo quinazolin-4(3*H*)-one(6b) :** M.P.**:** 135-137 $^0$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). $^1$H NMR($CDCl_3$): 2.13(d,1H,=N-NH),8.28(s,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,16H,Ar-H).$^{13}$C NMR: 30.4(-$CH_2$), 36.2, 41.5, 160.7 (immine pyrazol-C),162.2 (>C=O),173.1(immine aromatic-C), 108.92-143.25(aromatic-27C). Anal; (%) $C_{33}H_{23}N_6OICl_2$ Calcd; C, 55.23; H, 3.20; N,11.71; Found; C, 55.24; H, 3.22; N, 11.73.

**Spectral data of 6c: 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3–[5-(3-chloro) phenyl-4,5-dihydro-1*H*-pyrazol-3-yl amino]-6-iodo quinazolin-4(3*H*)-one(6c) :** M.P.**:** 123-124 $^0$C. Yeild**:** 72 % IR(KBr): 3371(N-H),3061, 2856(C-H),1731 (C=O),1614(C=N), 1318(C-N), 780(C-Cl),511(C-I). $^1$H NMR($CDCl_3$):2.16(d,1H,=N-NH),8.30(s,1H,-N-NH),3.64(s,2H,-$CH_2$), 3.06 (d,1Ha), 3.51(d,1Hb), 6.57 (t,1Hx), 6.43-7.96(m,16H,Ar-H). $^{13}$C NMR: 31.3(-$CH_2$), 36.4, 41.3,161.3 (immine pyrazol-C),162.1 (>C=O),173.3(immine aromatic-C), 109.13-143.17(aromatic-27C). Anal; (%) $C_{33}H_{23}N_6OICl_2$ Calcd; C, 55.23; H, 3.20; N,11.71; Found; C, 55.25; H, 3.21; N, 11.72.

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl] methyl-3–[5-(4-chloro) phenyl-4,5-dihydro-1*H*-pyrazol-3-yl amino]-6-iodo quinazolin-4(3*H*)-one(6d) :** M.P.**:**132-133 $^0$C. Yeild**:** 75 % IR(KBr):3367(N-H),3060,2866(C-H),1735(C=O),1616(C=N),1317(C-N), 782(C-Cl),510(C-I). $^1$H NMR ($CDCl_3$): 2.18 (d,1H,=N-NH),8.32 (s,1H,-N-NH),3.61(s,2H,-$CH_2$), 3.05 (d,1Ha), 3.48(d,1Hb), 6.53(t,1Hx), 6.44-7.95(m,16H,Ar-H).$^{13}$C NMR: 31.6(-$CH_2$), 36.2, 41.5, 161.2 (immine pyrazol-C),162.2 (>C=O),172.9(immine aromatic-C), 109.17-143.21(aromatic-27C). Anal; (%) $C_{33}H_{23}N_6OICl_2$ Calcd; C, 55.23; H, 3.20; N,11.71; Found; C, 55.26; H, 3.22; N, 11.73.

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl]methyl-3–[5-(2-hydroxy)phenyl-4,5-dihydro-1*H*-pyrazol-3-yl amino]-6-iodo quinazolin-4(3*H*)-one(6e) :** M.P.**:**152-153 $^0$C.Yeild**:** 70 % IR(KBr):3548(O-H),3415(N-H),3063,2856 (C-H),1733(C=O),1614 (C=N), (C-N), 780(C-Cl),511(C-I).$^1$H NMR($CDCl_3$): 2.14(d,1H,=N-NH), 8.32(s,1H,-N-NH), 3.62(s,2H,-$CH_2$), 3.06(d,1Ha), 3.45(d,1Hb), 6.52(t,1Hx), 6.44-7.96(m,16H,Ar-H),10.39(s,1H,-OH). $^{13}$C NMR: 30.6(-$CH_2$), 36.4, 41.5,160.8(pyrazol-C), 162.1(>C=O),172.9(immine aromatic-C) 109.23-143.21(aromatic-27C). Anal; (%) $C_{33}H_{24}N_6O_2ICl$ Calcd; C, 56.69; H, 3.43; N,12.02; Found; C, 56.70; H, 3.45; N, 12.03.

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl]methyl-3–[5-(3-hydroxy)phenyl-4,5-dihydro-1*H*-pyrazol-3-yl amino]-6-iodo quinazolin-4(3*H*)-one(6f) :** M.P.**:** 157-159 $^0$C.Yeild**:** 69 %IR(KBr): 3549(O-H), 3409(N-H), 3067,2855(C-H), 1731(C=O), 1617 (C=N),1314(C-N), 782(C-Cl),508(C-I). $^1$H NMR($CDCl_3$): 2.16(d,1H,=N-NH), 8.34(s,1H,-N-NH), 3.63 (s,2H,-$CH_2$), 3.05(d,1Ha), 3.46 (d,1Hb), 6.51(t,1Hx), 6.43-7.96(m,16H,Ar-H),10.35(s,1H,-OH). $^{13}$C NMR: 30.7(-$CH_2$), 36.5, 41.9,161.2 (immine pyrazol-C), 162.3(>C=O),172.7 (immine aromatic-C) 109.15-143.19 (aromatic-27C). Anal; (%) $C_{33}H_{24}N_6O_2ICl$ Calcd; C, 56.69; H, 3.43; N,12.02; Found; C, 56.71; H, 3.44; N, 12.05.

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl]methyl-3–[5-(4-hydroxy)phenyl-4,5-dihydro-1*H*-pyrazol-3-yl amino]-6-iodo quinazolin-4(3*H*)-one(6g) :** M.P.: 163-165 $^0$C.Yield: 72 % IR(KBr): 3553(O-H), 3411(N-H), 3061,2856 (C-H),1725(C=O), 1614 (C=N),1316(C-N), 778(C-Cl), 513(C-I). $^1$H NMR($CDCl_3$): 2.17(d,1H,=N-NH), 8.36(s,1H,-N-NH), 3.61 (s,2H,-$CH_2$), 3.06(d,1Ha), 3.46(d,1Hb), 6.52(t,1Hx), 6.44-7.96(m,16H,Ar-H), 10.34(s,1H,-OH). $^{13}$C NMR: 30.6(-$CH_2$), 36.3,41.6,161.1(immine

pyrazol-C),162.1(>C=O),173.1(immine aromatic-C), 109.17-143.16(aromatic-27C). Anal; (%) $C_{33}H_{24}N_6O_2ICl$ Calcd; C, 56.69; H, 3.43; N,12.02; Found; C, 56.71; H, 3.45; N, 12.04.

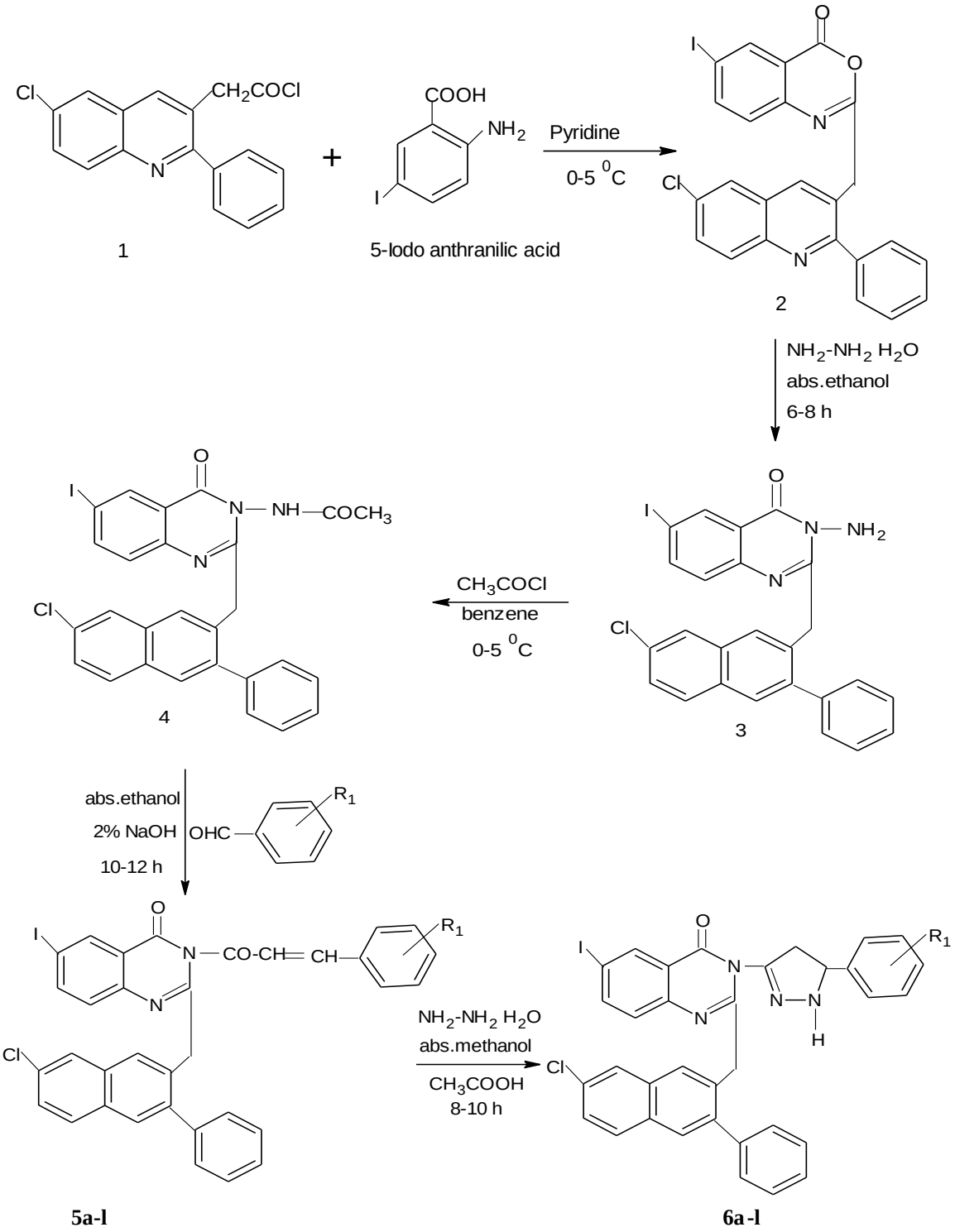
**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl]methyl-3–[5-(2-nitro)phenyl-4,5-dihydro-1*H*-pyrazol-3-yl amino]-6-iodo quinazolin-4(3*H*)-one(6h) :** M.P.**:** 173-175 $^0$C.Yeild**:** 67 % IR(KBr): 3415(N-H),3063,2856(C-H),1728(C=O),1615(C=N), 1564, 1363(-$NO_2$), 1318(C-N),781(C-Cl),510(C-I).$^1$H NMR($CDCl_3$): 2.16(d,1H,=N-NH), 8.32(s,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,16H,Ar-H).13C NMR : 30.5(-$CH_2$), 36.5,42.2,161.6(immine pyrazol-C),162.1(>C=O),173.1(immine aromatic-C), 109.19-143.16(aromatic-27C). Anal; (%) $C_{33}H_{23}N_7O_3ICl$ Calcd; C, 54.43; H, 3.16; N,13.47; Found; C, 54.45; H, 3.17; N, 13.48.

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl]methyl-3–[5-(3-nitro)phenyl-4,5-dihydro -1*H*-pyrazol-3-yl amino]-6-iodo quinazolin-4(3*H*)-one(6i) :** M.P.**:** 184-186 $^0$C.Yeild**:** 65 % IR(KBr):3411(NH),3065,2854(C-H),1729(C=O),1613(C=N),1565, 1361(-$NO_2$),1316(C-N), 779(C-Cl),513 (C-I). $^1$H NMR($CDCl_3$): 2.17(d,1H,=N-NH), 8.33(s,1H,-N-NH), 3.61 (s,2H,-$CH_2$), 3.06(d,1Ha), 3.46 (d,1Hb),6.52(t,1Hx), 6.43-7.96(m,16H,Ar-H). $^{13}$C NMR: 30.4(-$CH_2$),36.1, 41.8,160.9(immine pyrazol-C),162.3(>C=O),172.9(immine aromatic-C), 109.19-143.16 (aromatic-27C). Anal; (%) $C_{33}H_{23}N_7O_3ICl$ Calcd; C, 54.43; H, 3.16; N,13.47; Found; C, 54.44; H, 3.18; N, 13.49.

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl]methyl-3–[5-(4-nitro)phenyl-4,5-dihydro-1*H*-pyrazol-3-yl amino]-6-iodo quinazolin-4(3*H*)-one(6j) :** M.P.**:** 195-197 $^0$C.Yeild**:** 69 % IR (KBr): 3415(NH), 3060,2855(C-H), 1726(C=O),1615(C=N), 1563, 1359(-$NO_2$),1318(C-N), 783(C-Cl),516(C-I). $^1$H NMR($CDCl_3$): 2.18(d,1H,=N-NH), 8.31(s,1H,-N-NH), 3.63(s,2H,-$CH_2$), 3.05(d,1Ha), 3.48 (d,1Hb),6.53(t,1Hx), 6.43-7.96(m,16H,Ar-H). $^{13}$C NMR: 30.6(-$CH_2$), 36.2, 42.3,161.2(immine pyrazol-C),162.3(>C=O),173.1(immine aromatic-C), 109.19-143.11 (aromatic-27C). Anal; (%) $C_{33}H_{23}N_7O_3ICl$ Calcd; C, 54.43; H, 3.16; N,13.47; Found; C, 54.45; H, 3.19; N, 13.48.

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl]methyl-3–[5-(2-methoxy)phenyl-4,5-dihydro-1*H*-pyrazol-3-yl amino]-6-iodo quinazolin-4(3*H*)-one(6k) :** M.P.**:** 144-145 $^0$C. Yeild**:** 71 % IR(KBr): 3408 (N-H),3065,2859 (C-H), 1730 (C=O), 1611 (C=N),1319 (C-N), 1241, 1109(C-O-C), 784(C-Cl), 502(C-I). $^1$H NMR($CDCl_3$):2.16(d,1H,=N-NH), 8.30(s,1H,-N-NH) 3.62(s,2H,-$CH_2$), 3.05(d,1Ha), 3.46(d,1Hb), 6.51(t,1Hx), 6.43-7.96 (m,16H,Ar-H), 3.81(s,3H,-$OCH_3$).$^{13}$C NMR : 31.3(-$CH_2$),36.4, 42.4,161.1(immine pyrazol-C),162.0(>C=O), 173.3 (immine aromatic-C),58.3(-$OCH_3$),109.14-143.17(aromatic-27C). Anal; (%) $C_{34}H_{26}N_6O_2ICl$ Calcd; C, 57.26; H, 3.64; N,11.79; Found; C, 57.28; H, 3.65; N, 11.80.

**Spectral data of 2-[3-(6-chloro-2-phenyl) quinolin-3-yl]methyl-3–[5-(4-methoxy)phenyl-4,5-dihydro-1*H*-pyrazol-3-yl amino]-6-iodo quinazolin-4(3*H*)-one(6l) :** M.P.**:**147-149 $^0$C. Yeild**:** 74 % IR (KBr): 3405(N-H), 3066, 2861 (C-H), 1729(C=O), 1613(C=N), 1317 (C-N), 1243,1108 (C-O-C), 786(C-Cl), 507(C-I).$^1$H NMR($CDCl_3$):2.17(d,1H,=N-NH) ,8.32 (s,1H,-N-NH), 3.61(s,2H,-$CH_2$), 3.06(d,1Ha), 3.46(d,1Hb),6.52(t,1Hx), 6.43-7.96(m,16H,Ar-H), 3.80(s,3H,-$OCH_3$). $^{13}$C NMR : 31.2(-$CH_2$), 36.5,42.6,161.3(immine pyrazol-C),162.1(>C=O), 173.2 (immine aromatic-C),58.2(-$OCH_3$),109.14-143.17(aromatic-27C). Anal; (%) $C_{34}H_{26}N_6O_2ICl$ Calcd; C, 57.26; H, 3.64; N,11.79; Found; C, 57.27; H, 3.66; N, 11.81.




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

**Scheme I**

## RESULTS AND DISCUSSION

The title compound pyrazolyl 6-iodoquinazolin-4(3H) ones **6a-l** was synthesized according to the described procedure in **scheme-I.** Based catalyzed cyclization of acid chloride **1** with 5- iodoanthranilic acid in pyridine at 0-5 $^0$C yielded benzoxazinone **2** which showed strong C=O stretching at 1734 cm$^{-1}$. The benzoxazinone **2** on condensation reaction with hydration hydrate and then acetylation with acetyl chloride afforded acetamido quinazolin-4(3H) one **4**. 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 $^1$H NMR spectra which showed singlet at δ 2.24 ppm equivalent to three protons of acetamide group. The acetamido quinazolin-4(3H) one **4** on based catalysed condensation with aromatic aldehydes yielded acrylamide 5a-j which showed CH=CH stretching at around 1576 cm$^{-1}$ in IR spectrum while $^1$H NMR spectra showed doublet of these protons at around δ 6.7 and δ 7.8 ppm with coupling constant *J*= 16.0-16.6 Hz. Further cyclization of acrylamide 5a-j with hydrazine hydrate yielded the desired compounds pyrazolyl 6-iodoquinazolin-4(3H) ones **6a-l**. The IR spectra of of compounds 6a-j showed C=O and C=N stretching of quinazolinone at around 1720 and 1610 cm$^{-1}$ respectively. The $^1$H NMR spectra of compounds 6a-j 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 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 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 5.45-5.52 ppm. In $^{13}$C NMR spectra, signals at around δ 36 ppm,δ 55 ppm and δ 161 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 and δ 168 ppm respectively.

## APPLICATIONS

### 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$^{-1}$, 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.

From the screening results compound **6d (R = 4-Cl), 6b (R = 2-Cl), and 6c(R = 3-Cl)** were active against gram positive bacteria, while compound **6i ($R_1$ = 3-$NO_2$)** were active against gram negative bacteria compared to penicillin-G. Compound **6a ($R_1$ = H), 6k($R_1$ = 2-$OCH_3$)** and **6l($R_1$ = 4-$OCH_3$)** showed very good antifungal activity compared to fluconazole.

In the present study the derivatives of quinazolin-4(3H) ones were synthesized and screened for their antimicrobial activity which have active pharmacophore and promising results were obtained. Results were also useful to further studies undergoing to explore the scope of varieties of biological activity.

**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 | 10 | 08 | 41.44 | 11 | 09 | 43.86 | 10 | 08 | 41.44 | 11 | 09 | 43.86 |
| **6b** | **2-Cl** | **18** | **14** | **68.69** | **19** | **17** | **68.29** | 15 | 12 | 52.44 | 13 | 11 | 49.15 |
| **6c** | **3-Cl** | **16** | **13** | **60.81** | **16** | **12** | **62.87** | 14 | 11 | 55.05 | 15 | 12 | 52.44 |
| **6d** | **4-Cl** | **19** | **16** | **70.60** | **20** | **17** | **73.48** | 15 | 13 | 54.00 | 16 | 13 | 59.84 |
| 6e | 2-OH | 11 | 09 | 43.86 | 12 | 10 | 46.40 | 11 | 09 | 43.86 | 12 | 10 | 46.40 |
| 6f | 3-OH | 11 | 08 | 47.42 | 12 | 10 | 46.40 | 11 | 09 | 43.86 | 12 | 10 | 46.40 |
| 6g | 4-OH | 12 | 10 | 46.40 | 13 | 11 | 49.15 | 12 | 10 | 46.40 | 13 | 11 | 49.15 |
| 6h | 2-$NO_2$ | 15 | 13 | 54.00 | 16 | 13 | 59.84 | 16 | 13 | 59.84 | **17** | **14** | **62.99** |
| 6i | 3-$NO_2$ | 14 | 11 | 55.05 | 14 | 11 | 54.96 | **16** | **14** | **61.69** | **18** | **15** | **66.29** |
| 6j | 4-$NO_2$ | 15 | 12 | 52.44 | 15 | 13 | 54.00 | 14 | 11 | 55.05 | 16 | 13 | 59.84 |
| 6k | 2-$OCH_3$ | 11 | 08 | 41.44 | 12 | 10 | 46.40 | 11 | 08 | 47.42 | 13 | 11 | 49.15 |
| 6l | 4-$OCH_3$ | 13 | 11 | 49.15 | 13 | 11 | 49.15 | 11 | 08 | 47.42 | 13 | 11 | 49.15 |
| **Penicillin-G** | | 27 | 22 | 100 | 27 | 22 | 100 | 27 | 22 | 100 | 27 | 22 | 100 |

$C_H$ Zone of inhibition at concentration 100 µg $mL^{-1}$, $C_L$ 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** | **13** | **70.13** | **17** | **14** | **68.92** |
| 6b | 2-Cl | 11 | 08 | 50.90 | 12 | 09 | 53.75 |
| 6c | 3-Cl | 11 | 09 | 47.09 | 12 | 10 | 49.89 |
| 6d | 4-Cl | 12 | 09 | 53.75 | 13 | 11 | 52.86 |
| 6e | 2-OH | 15 | 13 | 59.36 | 14 | 12 | 56.03 |
| 6f | 3-OH | 14 | 12 | 56.03 | 14 | 12 | 56.03 |
| 6g | 4-OH | 14 | 11 | 59.36 | 14 | 11 | 59.36 |
| 6h | 2-$NO_2$ | 12 | 10 | 49.89 | 10 | 08 | 38.19 |
| 6i | 3-$NO_2$ | 09 | 07 | 41.93 | 11 | 10 | 36.91 |
| 6j | 4-$NO_2$ | 11 | 09 | 47.09 | 11 | 09 | 40.53 |
| 6k | 2-$OCH_3$ | **15** | **12** | **62.38** | **15** | **13** | **59.36** |
| 6l | 4-$OCH_3$ | **16** | **13** | **65.88** | **16** | **13** | **65.88** |
| **Fluconazole** | | 25 | 21 | 100 | 25 | 21 | 100 |

$C_H$ Zone of inhibition at concentration 20 µg $mL^{-1}$, $C_L$ Zone of inhibition at concentration 10 µg $mL^{-1}$, potency of compound(%) as compared to fluconazole.

## CONCLUSIONS

The title compound pyrazolyl quinazolin-4(3H) ones bearing quinolin moiety 6a-l were comprehensively synthesized by well organized methods. In addition, some of the compounds possessed good antibacterial as well as antifungal activity in vitro. Phenyl nucleus containing chloro group on *ortho, para* position showed very good activity against gram positive bacteria compared to *meta* chloro containing compounds. On the other hand *meta* nitro group containing compounds displayed higher activity than *para* nitro group containing compound against gram nerative bacteria, while *ortho* nitro group containing compounds showed good activity against *P.aeruginosa* gram negative bacteria. Phenyl group, *ortho* and *para* methoxy substituted compounds showed very good antifungal activity compared to nitro, chloro and hydroxyl substituted compounds. Therefore, these results will give some idea about further research on this molecule.

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Research Paper

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# 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.

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## 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

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>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.

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Uploading Certificate

## CERTIFICATE

This is to certify that the Minor Research Project, entitled: **Synthesis and In Vitro Antimicrobial Studies of Chalcone Containing Quinazolin -4 (3H) Ones** awarded to (P. I. Name) **Dr. Gamanbhai G. Barat** has been completed and executive summary of the project has been uploaded on the college/university website, the URL link is **www.pilvaicollege.org/mrp/** This certificate is as per the requirement under prescribed Minor Research Project guidelines.

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Signature of the principal
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Principal
Shri U.P. Arts, Smt. [illegible] Science &
Shri V.L. Shah [illegible] College, Pilvai.

UNIVERSITY GRANTS COMMISION

WESTERN REGIONAL OFFICE

GANESHKHIND, PUNE - 411 007

PERFORMA FOR SUBMISSION OF INFORMATION AT THE TIME OF SENDING THE FINAL REPORT OF THE WORK DONE ON THE PROJECT

1. NAME AND ADDRESS OF THE PRINCIPAL INVESTIGATOR: Dr. Gamanbhai G. Barat

2. NAME AND ADDRESS OF THE INSTITUTION: Arts, Science and Commerce College, Pilvai

3. UGC APPROVAL NO AND DATE: File No. 47-296/12(WRO) Dt: 25 – 02 – 2013

4. DATE OF IMPLEMENTATION: 25 – 03 – 2013

5. TENURE OF THE PROJECT: 25 – 03 – 2013 to 24 – 03 – 2015

6. TOTAL GRANT ALLOTED : 85000/-

7. TOTAL GRANT RECEIVED: 62500/-

8. FINAL EXPENDITURE: 85493/-

9. TITLE OF THE PROJECT: Synthesis and In Vitro Antimicrobial Studies of Chalcone Containing Quinazolin -4(3H) Ones

10. OBJECTIVES OF THE PROJECT:

(a) There are many methods are available for preparation of quinazolin-4(3H) ones from the chalcones it is new developed method and cheaper also, more over there are three biologically active moieties in the title synthesized compounds enhanced their microbial activities.

(b) Chalcone is very important intermediate obtained by this method is useful for preparation of various biologically active heterocycles.

(c) Chalcones and their rigid analogues represent an important class of small molecules having antimicrobial activity. Therefore, in this study the synthesis and antimicrobial activity of new 6-iodopyrazolylquinazolinone-4(3H) ones were described as rigid chalcone analogues.

(d) Screening results of the title compounds of the project shows very good antimicrobial activity against gram positive, gram negative bacteria and fungi species also. These results lead on the focusing of further better research on these molecules and to studies are undergoing to explore the scope of the various biological activities.

(e) Title compounds of the projects possess very good antimicrobial activity and least toxic and more potent. Hence, synthesized compound have better future in various field of medicinal chemistry.

(f) The research work useful to society, nation and new avenue of research for the better future.

11. WHETHER OBJECTIVE WERE ACHIEVED:
(GIVE DETAILS)

Research work is going on some hypothesis, where results are some time inconsistent, however the objectives of the research work were successfully achieved. The target molecules were synthesized by classical method and relatively cheaper than the other classical method. Screening results of synthesized compounds were evaluated by cup-plate method for antibacterial and antifungal activity. Results were obtained in the promising range. The synthesized compounds are less toxic and more potent; hence it has better future in various field of medicinal chemistry.

12. ACHIEMENTS FROM THE PROJECT:

In the present study the derivatives of quinazolin-4(3H) ones were synthesized by well organized method. All synthesized compounds were screened for their antibacterial and antifungal activities by cup-plate method. The active pharmacophore present into the synthesized compounds, promising results were obtained. The synthesized compounds are less toxic and more potent; hence, results were very useful and focus for further studies undergoing to explore the scope of varieties of biological activity.

13. SUMMARY OF THE FINDING:
(IN 500 WORDS)

## Summary

### 1. Literature Survey

Pyrazole nucleus is an important pharmacophore in medicinal chemistry, since a large number of its derivatives possess useful biological properties. 4(3*H*)-Quinazolinones have emerged as an important class of nitrogenated heterocyclic that have attached synthetic interest because of they possess good pharmacological and therapeutic properties, along with quinolin moiety played vital role in the medicinal chemistry. Quinazolin-4(3H) one possess pyrazoline moiety with the widespread applications in medicinal chemistry as antibacterial (Gupta, et al. 2008), antifungal (Bartroli, et al. 1998), analgesics, anti-imflammatory (Alafeefy, et al. 2007), anticonvulsant (Ozdemir, et al. 2008) agent. Quinolin derivatives are found to possess antimalarial, anti-imflammatory, antituberclosis and anti-breast cancer (A. Shi, et al. 2008) activity.

Encourage by the literature reports and to assess the pharmacological properties of such class of compounds it was thought to construct the quinolin nucleus linked with quinazolinone with pyrazoline moiety, which enhanced the biological activity. In the light of these findings leads to synthesize the new chemical entities incorporating the quinolin and pyrazoline with quinazolin-4(3H) ones may prove to be useful to the biological activity point of view.

### 2. OBJECTIVES OF PROJECT

(a) There are many methods are available for preparation of quinazolin-4(3H) ones from the chalcones it is new developed method and cheaper also, more over there are three biologically active moieties in the title synthesized compounds enhanced their microbial activities.

(b) Chalcone is very important intermediate obtained by this method is useful for preparation of various biologically active heterocycles.

(c) Chalcones and their rigid analogues represent an important class of small molecules having antimicrobial activity. Therefore, in this study the synthesis and antimicrobial activity of new 6-iodopyrazolylquinazolinone-4(3H) ones were described as rigid chalcone analogues.

(d) Screening results of the title compounds of the project shows very good antimicrobial activity against gram positive, gram negative bacteria and fungi species also. These results lead on the focusing of further better research on these molecules and to studies are undergoing to explore the scope of the various biological activities.

(e) Title compounds of the projects possess very good antimicrobial activity and least toxic and more potent. Hence, synthesized compound have better future in various field of medicinal chemistry.

(f) The research work useful to society, nation and new avenue of research for the better future.

## 3. Method development

Method developed for the synthetic route of target molecule for project summarized in Scheme I and scheme II described in experimental section of copy book of project. All reagents and solvents were purchased from Merck chemicals and further purified before use.

## 4. Characterization of Synthesized compounds

Synthesized compounds were characterized by physical and spectroscopic techniques, viz. elemental analysis, IR, $^{1}H$ NMR and $^{13}C$ NMR spectra. IR spectra were recorded on Perkin-Elmer 1300 FTIR spectrophotometer using KBr powder. $^{1}H$ NMR and $^{13}C$ NMR spectra of the synthesized compounds were recorded in $CDCl_3$ on a Bruker spectrometer at 400 MHz and 75 MHz respectively, chemical shift recorded in $\delta$

ppm. TMS used as internal standard. The purity of compounds was checked by TLC on silica gel G plates and spot visualization was done by exposing to iodine vapour. Elemental analyses of newly sysnthesized compounds were carried out on Carlo Ebra 1108 analyzer and the result were varying within ± 0.04 % of the calculated values.

## 5. Antimicrobial Screening results

### (i) Cup Plate Method

The *in vitro* antimicrobial activity of synthesized compounds was carried out by cup plate method. 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.

### (ii) Measurement of 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 anti bacterial activity at two different concentrations 100 and 50 µg/ml, Penicillin-G was used as standard, where as zone of inhibition measured for anti fungal activity also at two different concentrations 20 and 10 µg/ml and Fluconazole was used as a standard.

### (iii) 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.

### (iv) Potency

Potency of newly synthesized compounds were calculated by the following equation and compared the strength of synthesized compounds with standard drug.

Potency $P = \{\text{antilog}(D/B \times I)\} \times M \times F$

Where,

$F$ = dilution factor

$M$ = value of $S_H$ =1 unit / ml = 100 %

$I = \log S_H / S_L$

$D = (U_H + U_L) - (S_H + S_L)$

$B = (U_H - U_L) + (S_H - S_L)$

$S_H$ =Zone of inhibition of standard at high concentration.

$S_L$ = Zone of inhibition of standard at low concentration.

$U_H$ =Zone of inhibition of unknown at high concentration.

$U_L$ = Zone of inhibition of unknown at low concentration.

## 6. CONCLUSION

From the screening results of the synthesized compound of series :I and Series: II compound **6a(R= 2-Cl), 6b (R=3-Cl)** and **6c (R=3-Cl)** showed very good activity against Gram positive compared to standard. Compounds **6i(R= 3-$NO_2$)** and **6j((R= 4-$NO_2$)** showed very good activity against Gram negative bacteria compared to standard. Compound **6a(R= -H), 6k(R= 2-$OCH_3$)** and **6l ((R= 4-$OCH_3$)** showed very good anti-fungal activities compared to standard. Remaining compound of the series shows moderate or week activities against the microorganisms in vitro.

## 7. APPLICATION

In the present study the derivatives of quinazolin-4(3H) ones were synthesized by well organized method. All synthesized compounds were screened for their antimicrobial activity, due to active pharmacophore, promising results were obtained. Results were also useful to focus for further studies undergoing to explore the scope of varieties of biological activity.

## 8. PUBLICATION


1. N. B. Patel and G. G. Barat, " Synthesis and Pharmacological Aspects of Some Novel Nitrogen Containing Heterocycles With 6-Iodo Quinazolin-4(3H) Ones", Journal of Applicable Chemistry, Vol. 3, no.3, pp.1084-1093, May 2014.

2. G. G. Barat and N. B. Patel, " Synthesis, Structural Elucidation and in vitro Antimicrobial Studies of Some Novel Pyrazolylquinazolin-4(3H) Ones Bearing Quinoline Moiety", International Journal of Scientific Research, Vol. 3, no.11, pp.441-445, Nov. 2014.


14. CONTRIBUTION TO THE SOCIETY:
(GIVE DETAILS)

Our research work was not limited only in the field of education and medicinal chemistry. However, it is useful to society also. Some direct and indirect support regarding with the research work, its benefit directly goes to the society. More over our research work also deal with medicinal chemistry, so our continuous effort to making good future of society.

15. NO. OF PUBLICATIONS OUT OF THE PROJECT: 02 (Title and journal included in summary)
(PLEASE ATTACHE RE-PRINTS)


1. N. B. Patel and G. G. Barat, " Synthesis and Pharmacological Aspects of Some Novel Nitrogen Containing Heterocycles With 6-Iodo Quinazolin-4(3H) Ones", Journal of Applicable Chemistry, Vol. 3, no.3, pp.1084-1093, May 2014.

2. G. G. Barat and N. B. Patel, " Synthesis, Structural Elucidation and in vitro Antimicrobial Studies of Some Novel Pyrazolylquinazolin-4(3H) Ones Bearing Quinoline Moiety", International Journal of Scientific Research, Vol. 3, no.11, pp.441-445, Nov. 2014.

(PRINCIPAL INVESTIGATOR)

(REGISTRAR/PRINCIPAL)

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Shri V.L. Shah Commerce College, Pilvai.