Research Article

Synthesis, Antimicrobial, and Anti-HIV1 Activity of Quinazoline-4(3H)-one Derivatives

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The present investigation aims to synthesize 11 compounds of quinazoline-1 derivatives and to test their antimicrobial and anti-HIV1 activities. A quick-witted method was developed for the synthesis of novel substituted quinazolinone derivatives by summarizing diverse diamines with benzoxazine reactions, and it demonstrated the benefits of typical reactions, handy operation, and outstanding product yields. These compounds were confirmed by elemental analysis, IR, ¹H NMR, ¹³C NMR, and mass spectra. Then antimicrobial and anti-HIV1 activities of the compounds were tested *in-vitro*. It was found that compounds 7–11 possessed a wide range of anti microbial and anti-HIV1 activity.

1. Introduction

In spite of the fact that the chemistry quinazolinones have mesmerized the attention of researchers for a long time [1–3], the number of competent approaches to the synthesis of their derivatives containing functional groups is inadequate [4, 5]. The quinazolinone skeleton appears in many alkaloids, most commonly in the form of 4-(3H)-quinazolinone [6]. The quinazolinone moiety is an important pharmacophore showing many types of pharmacological activities. The quinazolinones are considered to be a potent structure for drug developments [7–9]. This has recently inspired the development of a new ring synthesis method. Several successful attempts have been made and recorded in the literature demonstrating promising outcomes [10–12]. The present investigation is a continuation of our earlier [13] study on quinazolinone derivatives.

2. Result and Discussion

2.1. Chemistry. In the present investigation, an attempt was made to synthesize quinazolinone derivatives through a multistep process. For this purpose, the required 3(2-aminophenyl)-2-methyl quinazolin-4(3H)-one (1) was prepared

according to the literature procedure [14, 15], the condensation reaction between benzoxazine and o-phenylene diamine using acetic acid. Formation of the product was confirmed by the formation of intellectual band at 1607 cm⁻¹ (C=N stretching) along with a peak reading at 1699 cm⁻¹ (C=O) in IR spectra. Benzoxazine [16] was converted to 3(2-aminophenyl)-2-methyl quinazolin-4(3H)-one (1) by nucleophilic substitution reaction with o-phenylenediamine along with appearance of new peak near 3398.5 cm⁻¹ (NH₂ stretching) and 3317.09 cm⁻¹ (N–H stretching) which also helped in assigning structure of (1). When (1) was treated with benzoyl chloride [17, 18] in presence of pyridine as a base, nucleophilic reaction took place at the o-phenylenediamine site of molecule, and, as a result, quinazolinone ring was formed, to yield a new heterocyclic compound (2). New band was observed in the IR spectra at 3087.40 cm⁻¹ and a singlet in ¹H NMR at δ 2.1 (CH₃) for methylene protons and a singlet at 8.1–8.19 (1H, s, CO–NH C–H) for NH proton in accordance with the structure of quinazolinone ring. 3–6 compounds were condensed with different aromatic acid chloride derivatives. When compound (2) was treated with phosphorus pentachloride, an intermediate compound was obtained and then further treated with sodium azide which yielded a compound tetrazole moiety (7–11). The bands were observed in IR protons,

TABLE 1: Antibacterial activity of the quinazolinone compounds at different concentrations.

S. no.	Name of the organisms	Zone of inhibition in mm										STD
		7		8		9		10		11		
		50 μ g	150 μ g	50 μ g	150 μ g	50 μ g	150 μ g	50 μ g	150 μ g	50 μ g	150 μ g	
(1)	<i>Staphylococcus aureus</i>	12	17	11	12	25	20	14	18	16	23	30
(2)	<i>Escherichia coli</i>	16	19	23	26	20	24	27	29	20	25	38
(3)	<i>Pseudomonas aureus</i>	20	21	12	14	12	16	17	20	23	28	40
(4)	<i>Bacillus subtilis</i>	16	20	14	13	13	18	15	19	21	23	35

Standard (STD)—ciprofloxacin 5 μ g/disc for bacteria. Solvent control (Sc)—DMSO.

7.82 (17H, Ar-H, and N=C=O) and 8.57 (CH, Ar-H), respectively, and confirmed the synthesis of final compounds (7–11). The peak values of 1600 cm^{-1} (C=N of tetrazole), 1240 cm^{-1} (tetrazole moiety) compounds at δ 2.4 (CH₃) for methylene protons were discovered in ¹H NMR analysis.

2.2. Biological Evaluation

2.2.1. Report on Antimicrobial Activity of the Given Compounds. The antimicrobial activity for the given compounds was carried out by Disc Diffusion Technique (Indian Pharmacopoeia 1996, Volume II A-105). The test microorganisms of Gram-positive *Staphylococcus aureus* and Gram-negative *Escherichia coli*, *Pseudomonas aereus*, and *Bacillus subtilis* were obtained from National Chemical Laboratory (NCL), Pune, and maintained by periodical subculturing on nutrient agar medium. The effect produced by the sample was compared with that produced by the positive control (reference standard ciprofloxacin 5 μ g/disc for bacteria).

2.2.2. Anti-HIV1 Screening

(1) Cell Culture. The MT-4 cells were grown in RPMI 1640 Dutch Modification (DM) medium, supplemented with 10% (v/v) heat-inactivated fetal calf serum (FCS), 2 Mm L-glutamine, 0.1% sodium bicarbonate, and 20 μ g/mL gentamycin (equal compete medium). The cells were maintained at 37°C in a humidified atmosphere of 5% CO₂ in air. Every 3–4 days and always 2 days before starting the experiment, cells were seeded at 3×10^5 cells/mL. At regular time intervals, the MT-4 cells were analyzed for the presence of mycoplasma and consistently found to be mycoplasma free.

(2) Virus. HIV1 (strain HTLV-IIIB/LAI) was obtained from the culture supernatant of HIV1 infected MT-4 cells lines. The virus titer of the supernatant was determined in MT-4 cells. The virus stocks were stored at 37°C until used.

The present protection achieved by the compound in HIV-infected cells was calculated by the following formula:

$$\frac{(\text{OD}_T)_{\text{HIV}} - (\text{OD}_C)_{\text{HIV}}}{(\text{OD}_C)_{\text{MOCK}} - (\text{OD}_C)_{\text{HIV}}} \text{ expressed in } \%, \quad (1)$$

where (OD_T)_{HIV} is the optical density measured with a given concentration of the test compound in HIV-infected cells; (OD_C)_{HIV} is the optical density measured for the control untreated HIV-infected cells; (OD_C)_{MOCK} is the optical

TABLE 2: Anti-HIV1 Activity of compounds.

Entry	Strain	IC ₅₀ (μ g/mL) ^a	CC ₅₀ (μ g/mL) ^b
7	III _B	>48.9	48.9
8	III _B	>37.5	37.5
9	III _B	>0.456	0.456
10	III _B	>0.482	0.482
11	III _B	>35.1	35.1
AZT	III _B	0.0012	65.9

^aEffective concentration of compounds, achieving 50% protection of MT-4 cells against cytopathic effect of HIV.

^bCytotoxic concentration of compounds, required to reduce the viability of mock infected MT-4 cells by 50%.

density measured for the control untreated HIV-infected cells. The dose achieving 50% protection according to the above formula was defined as the 50% effective concentration (EC₅₀).

3. Conclusion

The present research work demonstrated a genuine and convenient method for synthesizing 3-(2-aminophenyl)-2-methyl quinazolin-4(3H) one, N-[(2-(2-methyl-4-oxoquinazolin-3(4H)-1) phenyl)] benzamide, and 2-methyl-3-[(2-(5-phenyl-1H-tetrazol-1-yl) phenyl)]-quinazolin-4(3H)-one. The solvent using method for the condensation step was proved to be more proficient and ecofriendly than the traditional procedures. The condensation reaction took place at relatively high temperatures. This method also simplified the handling of the reactions and yielded quinazolin-4(3H)-one derivative. This procedure was simple and low cost. The reactions scheme exhibited moderate activity and valuable contribution to the existing methodologies. The compounds exhibited considerable antibacterial and anti-HIV activities (Tables 1 and 2).

4. Experimental

4.1. General Methods. Melting points were uncorrected and recorded on an REMI Series, Lab India Instrument. TLC analysis was done using precoated silica gel plates, and visualization was done using iodine. IR spectra were recorded in KBr on Shimadzu FT-IR spectrometer. ¹H and ¹³C-NMR spectra were recorded on a Bruker (AC 400 MHz) using TMS as an internal standard. Elemental analysis was carried out

on a Perkin-Elmer series-II CHNS/O Analyzer 2400. All the chemicals were obtained from Aldrich, and all the solvents used were of commercial grade only.

4.2. Synthesis of 3-(2-Aminophenyl)-2-methyl Quinazolin-4(3H) One (1) [12]. An equimolar (0.01 mole) mixture of 2-methyl-3, 1-benzoxazin-4-one and o-phenylenediamine (0.1 mole) was refluxed for 13 h in the presence of glacial acetic acid (10 mL). The residue was recrystallized from ethanol and purified by column chromatography to give 1.

Compound (1): Yield: (74%); m.p. 218°C; Anal. Calcd for $C_{15}H_{13}N_3O$: C, 71.70; H, 5.21; N, 16.72; O, 6.37; Found: C, 71.74; H, 5.17; N, 16.75; O, 6.32; IR (KBr, cm^{-1}): 3390.5 (s, NH_2), 3310 (s, N-H), 3095 (s, C-H), 1671.3 (C=O), 1600.48 (s, C=N); 1H NMR (400 MHz, DMSO- d_6 , δ/ppm): 8.2 (1H, s, CO-NH C-H), 7.33–7.04 (m, Ar-H), 6.26 (C-H), 2.14 (CH_3); ^{13}C NMR (100 MHz, DMSO- d_6 , δ/ppm): 161 (Cl-amide), 155.5 (C-2), 148.2 (N=C), 145.3 (C-8a), 134.5 (C-4''), 127.3 (C-8), 117.2 (C-1''), 24.3 (CH_3); MS (m/z , (relative abundance, %)): 251.0294 (0.10) 237.2923, 235.

4.3. Synthesis of [N-(2-(2-Methyl-4-oxoquinazolin-3(4H)-yl) Phenyl)] Benzamide (2) [12]. The title compound 2 was prepared by using 3-(2-aminophenyl)-2-methyl quinazolin-4(3H) one (1; 0.01 mole) of an equivalent amount of benzoyl chloride (0.1 mole) which was refluxed with pyridine (40 mL) for 11 h. The reaction mixture was cooled, treated with cold ice, and neutralized with conc. HCl. The separated solid was filtered and washed with ice cold water. The residue was recrystallized from ethanol and purified by column chromatography.

Compound (2): Yield: (67%); m.p. 171°C; Anal. Calcd for $C_{22}H_{17}N_3O_2$: C, 74.35; H, 4.82; N, 11.82; O, 9.00; Found: C, 74.30; H, 4.81; N, 11.80; O, 9.02; IR (KBr, cm^{-1}): 3471.83 (s, N-H 1° amine), 3303 (s, N-H), 3080.40 (s, C-H), 1680.78 (s, C=O), 1609 (s, C=N), 1530 (C=C aromatic amine), 1270.21 (C-N str 1° aromatic amine), 1170 (s, C-N); 1H NMR (400 MHz, DMSO- d_6 , δ/ppm): 10.11 (N-H 2° amide), 8.5–8.3 (Ar-CH), 7.84–7.70 (13H, m, Ar-H), 2.13 (CH_3); ^{13}C NMR (100 MHz, DMSO- d_6 , δ/ppm): 161.5 (Cl-amide), 165.5 (C-2), 155.5 (C-4), 150 (C-8a), 135.5 (C-1), 130 (C-5), 128.6 (C-6), 127.8 (C-8), 122.6 (C-4a), 24.1 (CH_3); MS (m/z , (relative abundance, %)): 355.3978 (0.13), 341.4112, 329.0529.

4.4. Synthesis of 4-Fluoro-[N-(2-(2-methyl-4-oxoquinazolin-3(4H)-yl) Phenyl)] Benzamide (3) [12]. The title compound 3 was prepared by using 3-(2-aminophenyl)-2-methyl quinazolin-4(3H) one (1; 0.01 mole) of an equivalent amount of 4-fluorobenzoyl chloride (0.1 mole) by the general procedure. The separated solid was filtered and washed with ice cold water. The residue was recrystallized from ethanol and purified by column chromatography.

Compound (3): Yield: (63%); m.p. 162°C; Anal. Calcd for $C_{22}H_{16}FN_3O_2$: C, 70.77; H, 4.32; N, 11.25; O, 8.57; F, 5.09; Found: C, 70.76; H, 4.36; N, 11.22; O, 8.51; F, 5.07; IR (KBr, cm^{-1}): 3474.97 (s, N-H 1° amine), 3264.19 (s, N-H), 3070 (s, Ar-C-H), 1680.71 (s, C=O), 1609.24 (s, C=N), 1530.08 (C=C aromatic amine), 1309.26 (s, C-N 1° aromatic amine), 1167.16

(s, C-N), 1102 (C-F); 1H NMR (400 MHz, DMSO- d_6 , δ/ppm): 10.29 (N-H 2° amide), 8.98 (1H, s, H-C=N-N), 8.18 (CH, F, (C=O)N), 7.87–7.98 (13H, m, Ar-H), 7.46 (F subt.), 7.24 (CH, NC=O), 2.15 (CH_3); ^{13}C NMR (100 MHz, DMSO- d_6 , δ/ppm): 161.5 (Cl-amide), 165.6 (H-C=N), 167.4 (=C(F), C-4''), 155.2 (C-2), 147.8 (C-8a), 134.3 (C-7), 131.4 (C-1''), 129.8 (C-2'), 128.4 (C-6), 127.6 (C-8), 122.6 (C-4a), 118.5 (C-3''), 24.1 (CH_3); MS (m/z , (relative abundance, %)): 375.2454 (0.13), 355.1354, 299.1021.

4.5. Synthesis of 4-Cyano-[N-(2-(2-methyl-4-oxoquinazolin-3(4H)-yl) Phenyl)] Benzamide (4) [13]. The title compound 4 was prepared by using 3-(2-aminophenyl)-2-methyl quinazolin-4(3H) one (1; 0.01 mole) of an equivalent amount of 4-cyanobenzoyl chloride (0.1 mole) by the general procedure. The separated solid was filtered and washed with ice cold water. The residue was recrystallized from ethanol and purified by column chromatography.

Compound (4): Yield: (66%); m.p. 165°C; Anal. Calcd for $C_{23}H_{16}N_4O_2$: C, 72.62; H, 4.24; N, 14.73; O, 8.41; Found: C, 72.60; H, 4.26; N, 14.77; O, 8.40; IR (KBr, cm^{-1}): 3505 (s, N-H 1° amine), 3310.17 (s, N-H), 3068.80 (s, Ar-C-H), 2278 (C≡N), 1679.16 (s, C=O), 1600.27 (s, C=N), 1540.46 (C=C aromatic amine), 1298.15 (s, C-N), 1177 (s, C-N); 1H NMR (400 MHz, DMSO- d_6 , δ/ppm): 10.29 (N-H 2° amide), 8.99 (1H, s, H-C=N-N), 8.13–8.45 (CH, CN, (C=O)N), 7.80–7.99 (13H, m, Ar-H), 7.27 (CH, NC=O), 2.15 (CH_3); ^{13}C NMR (100 MHz, DMSO- d_6 , δ/ppm): 161.5 (Cl-amide), 165.6 (H-C=N), 155.2 (C-2), 139.8 (C-8a), 132.9 (C-4), 130.9 (C-1''), 129.9 (C-2'), 128.8 ((C=O)-N, CN), 127.2 (C-8), 121.6 (C-4a), 118.5 (nitrile), 24.1 (CH_3); MS (m/z , (relative abundance, %)): 381.2336 (0.18), 367.1277, 355.1343, 305.1722 (0.06).

4.6. Synthesis of 4-Chloro-[N-(2-(2-methyl-4-oxoquinazolin-3(4H)-yl) Phenyl)] Benzamide (5) [13]. The title compound 5 was prepared by using 3-(2-aminophenyl)-2-methyl quinazolin-4(3H) one (1; 0.01 mole) of an equivalent amount of 4-chlorobenzoyl chloride (0.1 mole) by the general procedure. The separated solid was filtered and washed with ice cold water. The residue was recrystallized from ethanol and purified by column chromatography.

Compound (5): Yield: (61%); m.p. 174°C; Anal. Calcd for $C_{22}H_{16}ClN_3O_2$: C, 67.78; H, 4.14; N, 10.78; O, 8.21; Cl, 9.09; Found: C, 67.74; H, 4.18; N, 10.73; O, 8.20; Cl, 9.05; IR (KBr, cm^{-1}): 3471.92 (s, N-H 1° amine), 3296.43 (s, N-H), 3068.98 (s, Ar-C-H), 1677.70 (s, C=O), 1596.39 (s, C=N), 1535.61 (C=C aromatic amine), 1330.05 (C-N str 1° aromatic amine), 1170 (s, C-N), 752.46 (C-Cl); 1H NMR (400 MHz, DMSO- d_6 , δ/ppm): 10.29 (N-H 2° amide), 8.27–8.1 (Ar-CH), 7.84–7.99 (13H, m, Ar-H, Cl), 7.78 (Cl subt.), 7.40 (CH, NC=O), 2.14 (CH_3); ^{13}C NMR (100 MHz, DMSO- d_6 , δ/ppm): 161.4 (Cl-amide), 165.9 (H-C=N), 155 (C-2), 147.6 (C-8a), 140, 138.9, 134.8 (C-7), 132, 130.6 (C-2', Cl), 129.7 (C-3'), 127.9 (C-6), 126.8 (C-8), 120.9 (C-4a), 24.1 (CH_3); MS (m/z , (relative abundance, %)): 391.4036 (0.10), 377.0915, 355.2139, 329.1816.

4.7. Synthesis of [N-(2-(2-Methyl-4-oxoquinazolin-3(4H)-yl) Phenyl)]-4-nitrobenzamide (6) [13]. The title compound 6

was prepared by using 3-(2-aminophenyl)-2-methyl quinazolin-4(3H) one (1; 0.01 mole) of an equivalent amount of 4-nitrobenzoyl chloride (0.1 mole) by the general procedure. The separated solid was filtered and washed with ice cold water. The residue was recrystallized from ethanol and purified by column chromatography.

Compound (6): Yield: (74%); m.p. 245°C; Anal. Calcd for $C_{22}H_{16}N_4O_4$: C, 66.00; H, 4.03; N, 13.99; O, 15.98; Found: C, 66.09; H, 4.01; N, 13.95; O, 15.94; IR (KBr, cm^{-1}): 3501 (s, N-H 1° amine), 3319.26 (s, N-H), 3088.86 (s, Ar-C-H), 1690 (s, C=O), 1600.14 (s, C=N), 1499 (C=C aromatic amine), 1300.33 (C-N str 1° aromatic amine), 1345 (Ar-NO₂), 1180 (s, C-N); ¹H NMR (400 MHz, DMSO-d₆, δ /ppm): 10.28 (N-H 2° amide), 8.20–8.80 (s, H-C=N) (CH, (N=O)=O, (C=O)-N), 7.99 (H-8, m, Ar-H, Cl), 7.65 (H-4'/H-4''), 7.30 (CH, NC=O, H-7), 2.12 (CH₃); ¹³C NMR (100 MHz, DMSO-d₆, δ /ppm): 161.5 (Cl-amide), 167.5 (C-2), 157, 151.5 ((N=O)=O, (C=O)-N), 135 (=C-(NO₂), C-3''), 134 (C-1''), 131.2 (C-7), 129.9 (C-2'), 128.5 (C-6), 127.5 (C-8), 122.6 (C-4a), 116 (C-3''), 24.2 (CH₃); MS (m/z , (relative abundance, %)): 401.2235 (0.15), 399, 387.3.

4.8. Synthesis of 2-Methyl-3-(2-(5-phenyl-1H-tetrazol-1-yl) Phenyl) Quinazolin-4(3H)-one (7) [13]. The title compound 7 was prepared by using [N-(2-(2-methyl-4-oxoquinazolin-3(4H)-yl) phenyl)] benzamide (2; 0.01 mole) which was taken in a beaker, added to a known amount of PCl₅ (0.01 mole), and heated at 100°C until the evolution of HCl fumes ceased. The reaction mixtures contained some unreacted POCl₃ which was removed by distillation under reduced pressure. The resulting mixture was treated with ice cold solution of known weight of NaN₃ (0.02 moles); a known volume (40 mL) of acetone and known volume of sodium acetate were added. The reaction mixture was stirred for 30 h. The acetone was removed by distillation under reduced pressure. The resulting mixture was extracted with CHCl₃; then the organic layer was separated and evaporated; we got product. The product filtered and washed with ice cold water. The residue was recrystallized from benzene-pet-ether mixture and purified by column chromatography to give 7.

Compound (7): Yield: (50%); m.p. 254°C; Anal. Calcd for $C_{22}H_{16}N_6O$: C, 69.46; H, 4.24; N, 22.09; O, 4.21; Found: C, 69.41; H, 4.29; N, 22.07; O, 4.20; IR (KBr, cm^{-1}): 3300 (s, N-H), 3060 (s, Ar-C-H), 1658 (s, C=N), 1600 (C=N, tetrazole), 1240 (tetrazole, N-N=N); ¹H NMR (400 MHz, DMSO-d₆, δ /ppm): 8.57, 8.6, 8.9, 9.5 (CH, Ar-H), 7.82 (17H, Ar-H, N=C=O), 7.70 (13H, Ar-H, (C=O)N), 2.4 (CH₃); ¹³C NMR (100 MHz, DMSO-d₆, δ /ppm): 161 (1-NH), 155.8 (C-2), 140–147.3 (C-8a), 135 (C-4'), 133, 131 (C-3'), 129 (C-6), 127.8 (C-2'), 125.6 (C-8), 123 (C-1''), 121.7 (C-4a), 24.9 (CH₃); MS (m/z , (relative abundance, %)): 381.2453 (0.31), 367.0372, 353.01347, 305.1032.

4.9. Synthesis of 3-(2-(5-(4-Fluorophenyl)-1H-tetrazol-1-yl) Phenyl)-2-methyl Quinazolin-4(3H)-one (8) [13]. The title compound 8 was prepared by using 4-fluoro-[N-(2-(2-methyl-4-oxoquinazolin-3(4H)-yl) phenyl)] benzamide (2; 0.01 mole) by the general procedure; the residue was recrystallized from

benzene-pet-ether mixture and purified by column chromatography.

Compound (8): Yield: (51%); m.p. 262°C; Anal. Calcd for $C_{22}H_{15}FN_6O$: C, 66.33; H, 3.80; N, 21.09; O, 4.02; F, 4.77; Found: C, 66.36; H, 3.83; N, 21.04; O, 4.01; IR (KBr, cm^{-1}): 3315.66 (N-H stretching), 3070.79 (aromatic C-H stretching), 1660.62 (C=N stretching), 1605 (C=N, tetrazole), 1107 (C-F), 1259 (tetrazole, N-N=N); ¹H NMR (400 MHz, DMSO-d₆, δ /ppm): 8.9 (H-5), 7.88 (F, C-Ar), 7.82 (17H, Ar-H, N=C=O), 7.70 (13H, Ar-H, (C=O)N), 7.37 (F, C-Ar), 2.3 (CH₃); ¹³C NMR (100 MHz, DMSO-d₆, δ /ppm): 164.4 (1-F, 1-Ar), 155.7 (C-2), 146.3 (C-8a), 135.9 (Cl, C-Ar), 130.6 (C-6), 129.2 (Cl, C-Ar), 128 (C-2'), 126.8, 125, 124.7 (F, 1-Ar), 121.6 (C-4a), 117.2 (CH₁-F), 25 (CH₃); MS (m/z , (relative abundance, %)): 399.3438 (0.24), 385.010, 381.1219, 371.1526, 323.0922.

4.10. Synthesis of 4-(1-(2-(2-Methyl-4-oxoquinazolin-3(4H)-yl) Phenyl)-1H-tetrazol-5-yl) Benzonitrile (9) [13]. The title compound 9 was prepared by using 4-cyano-[N-(2-(2-methyl-4-oxoquinazolin-3(4H)-yl) phenyl)] benzamide (2; 0.01 mole) by the general procedure; the residue was recrystallized from benzene-pet-ether mixture and purified by column chromatography.

Compound (9): Yield: (53%); m.p. 267°C; Anal. Calcd for $C_{23}H_{15}N_7O$: C, 68.14; H, 3.73; N, 24.18; O, 3.95; Found: C, 68.11; H, 3.76; N, 24.15; O, 3.98; IR (KBr, cm^{-1}): 3000 (s, N-H), 3083 (s, Ar-C-H), 1698.39 (s, C=O), 1610.62 (tetrazole), 1500.08 (C=C aromatic amine), 1307.59 (s, C-N 1° aromatic amine), 1280.84 (tetrazole, N-N=N), 1188.97 (s, C-N); ¹H NMR (400 MHz, DMSO-d₆, δ /ppm): 8.2–8.6 (CH, (C=O)N), 7.99 (CN, Ar-H), 2.3 (CH₃); ¹³C NMR (100 MHz, DMSO-d₆, δ /ppm): 161 (H-C=N), 155.7 (C-2), 139.8 (C-8a), 135.7 (CN, Ar-C), 130 (C-6), 129, 128.3 (Cl, C-Ar), 126.6 (C-8), 121.6 (C-4a), 119.2 (nitrile), 114 (CN), 25.5 (CH₃); MS (m/z , (relative abundance, %)): 405.3214 (0.32), 391.2133, 381.0310, 331.1377.

4.11. Synthesis of 3-(2-(5-(4-Chlorophenyl)-1H-tetrazol-1-yl) Phenyl)-2-methyl Quinazolin-4(3H)-one (10) [13]. The title compound 10 was prepared by using 4-chloro-[N-(2-(2-methyl-4-oxoquinazolin-3(4H)-yl) phenyl)] benzamide (2; 0.01 mole) by the general procedure; the residue was recrystallized from benzene-pet-ether mixture and purified by column chromatography.

Compound (10): Yield: (50%); m.p. 278°C; Anal. Calcd for $C_{22}H_{15}ClN_6O$: C, 63.69; H, 3.64; N, 20.26; O, 3.86; Cl, 8.55; Found: C, 63.66; H, 3.67; N, 20.28; O, 3.88; Cl, 8.54; IR (KBr, cm^{-1}): 3290 (N-H stretching), 3066.24 (Ar-H stretching), 1655 (C=N stretching), 1600 (C=N, tetrazole), 1240 (tetrazole, N-N=N), 789 (C-Cl); ¹H NMR (400 MHz, DMSO-d₆, δ /ppm): 8.20, 8.46 (1-Cl, Ar-H), 7.82 (17H, Ar-H, N=C=O), 7.70 (13H, Ar-H, (C=O)N), 7.50 (Cl, C-Ar), 2.3 (CH₃); ¹³C NMR (100 MHz, DMSO-d₆, δ /ppm): 161 (1-NH), 155.7 (C-2), 148.3 (C-8a), 135.2 (Cl, C-Ar), 129–129.9 (C-6), 128.6–129 (Cl, C-Ar), 127 (C-2'), 126.4 (C-8), 121.6 C-4a), 25 (CH₃); MS (m/z , (relative abundance, %)): 417.2136 (0.80), 401.1726, 387.1813, 381.1511, 341.0947.

4.12. *Synthesis of 2-Methyl-3-(2-(5-(4-nitrophenyl)-1H-tetrazol-1-yl) Phenyl) Quinazolin-4(3H)-one (11) [13].* The title compound 11 was prepared by using [N-(2-(2-methyl-4-oxoquinazolin-3(4H)-yl) phenyl)]-4-nitrobenzamide (2; 0.01 mole) by the general procedure; the residue was recrystallized from benzene-pet-ether mixture and purified by column chromatography.

Compound (11): Yield: (52%); m.p. 280°C; Anal. Calcd for C₂₂H₁₅N₇O₃: C, 62.11; H, 3.55; N, 23.05; O, 11.28; Found: C, 62.16; H, 3.59; N, 23.09; O, 11.24; IR (KBr, cm⁻¹): 3292 (s, N-H), 3043.50 (s, C-H), 1700.52 (s, C=O), 1608.28 (C=N, tetrazole), 1507.07 (C=C aromatic amine), 1320 (s, C-N 1° aromatic amine), 1360 (Ar-NO₂), 1162 (s, C-N); ¹H NMR (400 MHz, DMSO-d₆, δ/ppm): 8.2–8.76 (NO₂), 7.90 (H-8, NC=O), 7.85 (CH, (C=O)N), 2.77 (CH₃). ¹³C NMR (100 MHz, DMSO-d₆, δ/ppm): 161 (C1-amide), 155.8 (C-2), 150.2 (C-8a), 140.6 (C-8a), 138.4 (NO₂), 129.7 (C-2'), 127.8 (CH, NO₂), 126.8 (C-8), 125.7 (NO₂, CH), 125.9 (N-C=O), 122.6 (C-4a), 25 (CH₃); MS (m/z, (relative abundance, %)): 425.1445 (0.16), 411.1235, 399.1528, 381.1412, 351.1177.

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