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Research Paper

Synthesis, Characterization and Antimicrobial Activity of some newer Quinazoline Derivatives

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In the present investigation an attempt has been made for the synthesis of *N*'-(substitutedbenzylidene)-2-(7-bromo-2-phenylquinazolin-4-yloxy)acetohydrazide (5-15). The titled compounds were prepared by the reaction of bromoanthranilic acid with benzoyl chloride which gave oxazine-4-one derivative (1), which on reaction with formamide gave quinazolin-4(3*H*)-one derivative (2). The esterification product of quinazolin-4(3*H*)-one derivative, when reacted with hydrazine-hydrate gave (7-bromo-2-phenylquinazolin-4yloxy)acetohydrazide (4). The substituted benzaldehyde on reaction with 7-Bromo-2-phenylquinazoline-4yloxyacetohydrazide (4) yielded *N*'-(substitutedbenzylidene)-2-(7-bromo-2-phenylquinazolin-4-yloxy)acetohydrazide (5-15) All the newly synthesized quinazoline derivatives (5-15) were screened for antibacterial and antifungal activity.

Key words : Acetohydrazide, Quinazoline, Antimicrobial activity, antibacterial, antifungal.

INTRODUCTION

In the past 40 years emphasis has shifted to develop new molecules and semi-synthetic derivatives of older antibiotics with more desirable properties or differing spectrum of activity. Quinazoline, a nitrogenous heterocycle, proved to possess a multitude of biological potency including antimicrobial activity. The quinazoline moiety is a very useful and framework in medicinal chemistry. The ring was substituted at various position with chloro, nitro, 3, 4, 5 trimethoxy, fluoro and hydroxy groups to correlate the electronic effect of such substituent's on the magnitude of the antimicrobial activity. It was found that the biological versatility of quinazoline has shown anti-microbial[1-2], anti-inflammatory[3], anti-convulsant[4], antitubercular[5], antihypertensive[6], antifungal[7-8], sedative hypnotic[9-12], anticancer[13-14] antimalarial[15-16] and many other therapeutic activity. Among these compounds, some compounds are identified as well known drugs for antihypertensive and diuretics like Prazosin (Antihypertensive), Alfuzosin (Antihypertensive) and Bunazosin (Antihypertensive). Search for more effective agents are carrying on by the continuous study.

The literature review prompted us to synthesize some newer quinazoline

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derivative for better efficacy at lower concentration. In the present study newly synthesized compounds *N'*-(*N*-substitutedbenzylidene)-2-(7-bromo-2-phenylquinazolin-4yloxy) acetohydrazide (5-15) showed potent antimicrobial activity. The *N'*-(*N*-substituted benzylidene)-2-(7-bromo-2-phenylquinazo -lin-4yloxy)acetohydrazide derivatives were synthesized by the long chain of reactions of 7-bromo-2-phenylquinazolin-4-yloxy acetohydrazide with different reactants. The newly synthesized compounds were screened against Gram negative bacteria (*E. coli, P. aeurginosa*), Gram positive bacteria (*S. aureus, B. subtilis*) and fungi (*C. albicans, A. niger*).

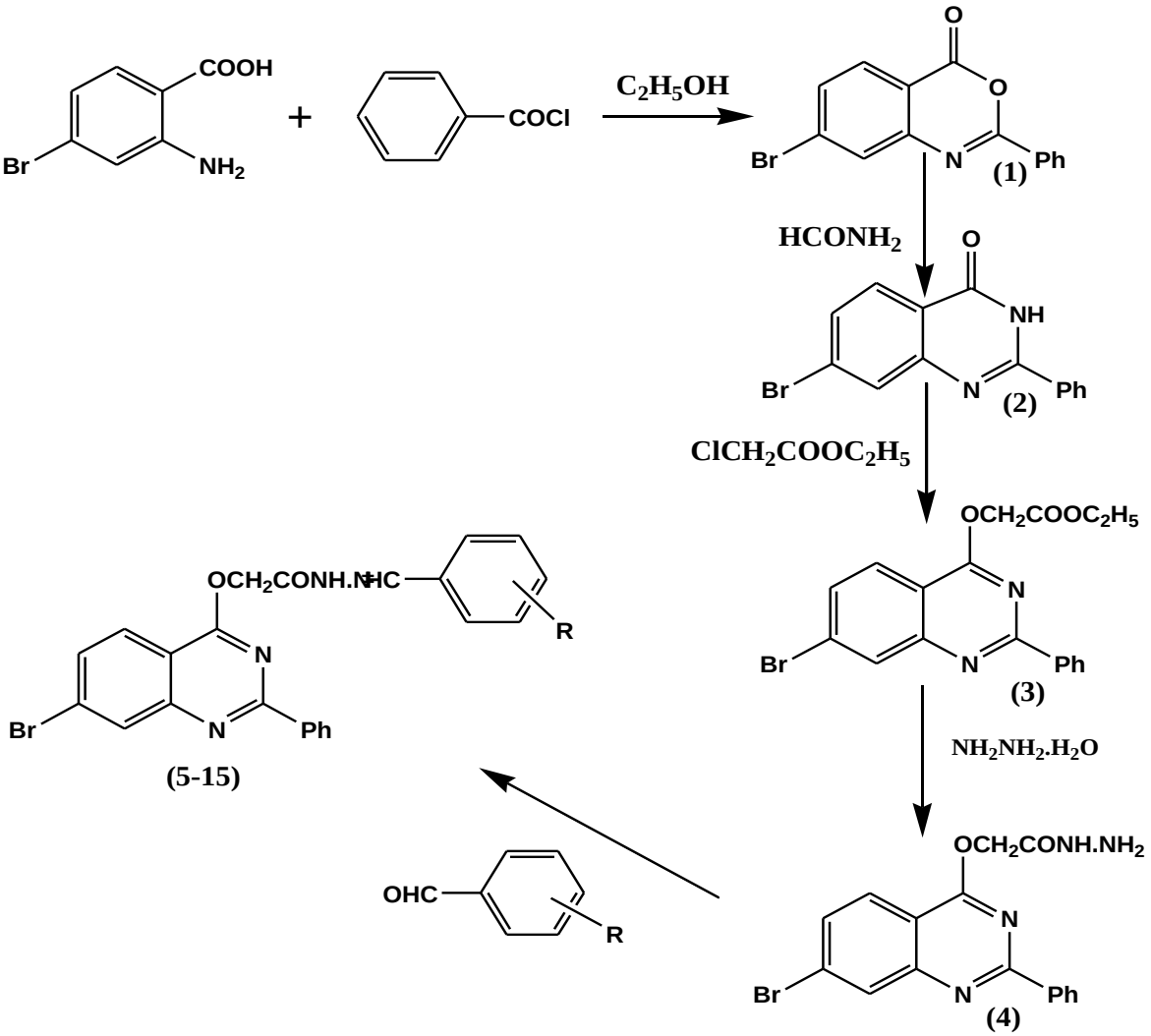
Results and discussion

In the present work the quinazoline derivatives are synthesized by the multisteps process. These newly synthesized quinazoline derivatives *N'*-(substitutedbenzylidene)-2-(7-bromo-2-phenylquinazolin-4-yloxy)acetohydrazide **(5-15)** are synthesized by the reaction of 7-Bromo-2-phenylquinazoline-4-yloxy aceto hydrazide (4) with substituted benzaldehyde. These 7-bromo-2-phenylquinazolin-4yloxy aceto -hydrazide were prepared by the reaction between ester of quinazolin-4(3*H*)-one derivative with hydrazine hydrate. The intermediate compound oxazine-4-one on reaction with formamide gave quinazolin-4(3*H*)-one intermediate. The structure of the newly synthesized compounds were confirmed by the different microanalysis as well as spectral analysis. For the confirmation of the title structure, IR, ^{1}H NMR, Mass and elemental analysis were performed. For the discussion point, we discussed compound no. (**6)** because in the spectra all the peaks were very sharp. **IR spectra** showed absorption band at 3325.16 cm^{-1} for the presence of –NH where as 1672.53 cm^{-1} of C=O and 1581.52 cm^{-1} for the C=N of quinazoline ring. **^{1}H NMR** spectrum has been shown singlet at δ 2.13 ppm corresponding to =C-H, A singlet of three proton appeared at δ 3.24 which was assigned to protons of OCH_3 group, Two proton singlet appeared at δ 4.23 ppm was assigned to protons of CH_2 group, Ten proton multiplet appeared between δ 6.54-8.62 ppm indicated aromatic protons and singlet appeared at δ 11.69 was assigned to N-H proton which disappeared on D_2O exchange. The mass spectrum revealed a molecular ion peak at m/z 550.05 $[M+2]^+$.

Elemental analysis of the synthesized titled compounds were correlated with the theoretical values with practical values. The difference of these values was found to be within ± 0.02% which is desirable. All these novel synthesized compounds have been shown mild to moderate anti bacterial as well as antifungal activity, when they were compared with standard at the different concentration, where the bacterial as well as antifungal activity, was the good concentration for all the antimicrobial activity. The compound no when they were compared with standard

at bacterial as well as antifungal activity, when they were compared with standard at the different concentration, where the different concentration, where the 50µg/ml **7, 11, 13** and **14** showed potent activity towards microbes.

SCHEME



R = 4-Cl, 3,4,5-OCH_3, 3-NO_2, 2-Cl, 3-OCH_3, 2-OH, 4-F, 4-OH, 2-NO_2, 4-NO_2, 3-Cl

Antimicrobial activity

The antimicrobial activities were performed by disc diffusion method. The sample was dissolved in DMF at different concentration of 25, 50, 100µg/ml. Antibacterial activity against (gram positive) *S. aureus*, *B.sutilis* and (gram negative bacteria) *P.aeureginosa*, *E. coli*. Antifungal activity was carried out against *A. niger and C. albicans* under aseptic conditions. Ciprofloxacin and Fluconazole were used as standard drug for antibacterial and antifungal activity. The zone of inihibition was compared with

standard drug after 24 hrs of incubation at 25°C for antibacterial activity and 48 hrs at 32°C for antifungal activity. Among of them the newly synthesized compound 6 and 9 have shown potential activity against bacteria *S. aureus* and *B.sutilis* similarly compound 8, 14 and 11 have shown mild to moderate activity against bacteria *P.aeureginosa*, *E. coli*. The compounds 7, 9, 10, 11, 14 and 15 exhibited good activity against *A. niger* and *C. albicans*. Results are tabulated in Table 2.

EXPERIMENTAL

Melting point ranges of newly synthesized compounds were determined by close capillary method using the electro thermal melting point apparatus and were uncorrected. IR spectrum of compounds in KBr pellets were recorded on a FTIR-8400S spectrophotometer (SHIMADZU) using KBr disc and ^{1}H NMR spectra were recorded in DMSO on a Bruker Advance (400 MHz) NMR spectrophotometer using TMS as internal standard and spectra on a MS (ESI) (SHIMADZU-2010 AT, software class VP). Mass spectra of the compounds were recorded on Micro mass quarto II EIMS. Microanalysis were performed on a Perkin-Elmer 240 elemental analyzer for C,H,O,N and halogens and agreed with the proposed structures with in ±0.4% of the theoretical values. Thin layer chromatographic analysis of the intermediates and title compounds were performed on silica gel G coated glass plates. Ethanol:Ethylacetate (4:6) was used as mobile phase. The spots were visualized by exposure to iodine vapours.

7-Bromo-2-phenyl-4*H*-benzo (1, 3) oxazin-4-one (1)

A cold solution of 4-Bromoanthranilic acid (12.gm, 0.05mol) in ethanol (45ml) and

Table1. Physical data of the synthesized compounds

Comp.No	R	Molecular Formula	Molecular weight	Rf-value	Melting point (°C)	% yield
5	4-Cl	$C_{25}H_{16}BrClN_4O_2$	495.76	0.85	225-227	45.17
6	3,4,5 OCH_3	$C_{26}H_{23}BrN_4O_5$	551.39	0.82	180-182	45.92
7	3-NO_2	$C_{25}H_{11}BrN_5O_4$	535.37	0.87	215-217	46.78
8	2-Cl	$C_{25}H_{21}BrClN_4O_2$	495.76	0.88	213-215	35.08
9	3-OCH_3	$C_{26}H_{24}BrN_4O_3$	520.41	0.75	211-213	21.57
10	2-OH	$C_{25}H_{22}BrN_4O_3$	506.37	0.86	210-212	30.20
11	4-F	$C_{23}H_{16}BrFN_4O_2$	449.35	0.80	209-211	39.27
12	4-OH	$C_{23}H_{17}BrN_4O_3$	477.31	0.81	178-180	42.13
13	2-NO_2	$C_{23}H_{16}BrN_5O_4$	506.31	0.78	186-188	18.15
14	4-NO_2	$C_{23}H_{16}BrN_5O_4$	506.31	0.73	190-192	51.17
15	3-Cl	$C_{25}H_{16}BrClN_4O_2$	495.76	0.83	175-177	43.15

(23.22ml, 0.2mol) benzolyl chloride was stirred for 7 hrs at room temperature. Then the reaction mixture was poured to crushed ice. The solid was obtained. The separated solid was filtered, dried and recrystallised from ethanol to gave compound **1; Yield** 68.9%**; m.p.** 225-227°C.[17]

7-Bromo-2-phenylquinazolin-4(3H)-one (2)

A mixture of 7-Bromo-2-phenyl-4*H*-benzo(1,3)oxazin-4-one **1** (8.56gm, 0.02mol) and formamide (13.5gm, 11.94ml, 0.3mol) was fused in an oil bath at 150°C for 8 hrs and poured into water. The solid obtained was filtered, dried and recrystallized with ethanol to gave compound **2; Yield** 75.92%**; m.p.** 180-182°C.[18]

Ethyl 2-(7-bromo-2-phenylquinazolin-4-yloxy)acetate (3)

A mixture containing 7-Bromo-2-phenylquinazolin-4(3*H*)-one **2** (6.96gm, 0.01mol) was dissolve in10ml of acetone in a 100ml of round bottom flask to this ethylchloroacetate (1.22gm, 1.06ml, 0.01mol) was refluxed for 36 hrs. The separated solid filtered, dried and recrystallised with ethanol to gave compound **3; Yield** 55.42%**; m.p.** 142-143°C.[19]

2-(7-Bromo-2-phenylquinazolin-4-yloxy) acetohydrazide (4)

A mixture containing Ethyl 2-(7-bromo-2-phenylquinazolin-4-yloxy)acetate **3** (4.2gm, 0.01mol) and hydrazine hydrate (0.50gm, 0.56ml, 0.01mol) in ethanol was taken in r.b.f. and refluxed for a period of 8 hrs. The product was found in solid form filtrate out this and wash with water and recrystallised from absolute ethanol to gave compound **4; Yield** 55.47%**; m.p.** 235-236°C.[20]

Table-2 Antimicrobial activity of synthesized compounds (5-15)

Comp. No	Antibacterial activity at 50µg/ml				Antifungal activity at 50µg/ml	
	S. aureus	*E. coli*	*B. subtilis*	*P. aeruginosa*	*A. niger*	*C. albicans*
5	18.23	12.25	11.13	16.74	17.32	14.37
6	10.12	12.12	16.16	9.09	10.35	12.02
7	15.13	11.44	13.71	15.32	20.53	14.50
8	11.24	8.24	11.02	16.27	11.20	6.34
9	15.56	11.75	15.10	14.57	14.36	13.78
10	16.67	10.25	14.34	10.78	16.65	10.89
11	16.45	11.89	10.17	14.05	15.67	11.04
12	14.67	12.36	12.32	8.07	17.95	9.56
13	15.78	12.46	14.32	13.56	19.78	15.36
14	15.38	12.67	13.37	14.37	19.19	14.80
15	11.34	6.46	12.14	11.27	18.06	13.70
Standard*	17.23	13.01	15.30	17.56	21.29	16.03

General method for the synthesis of *N*'-(Substitutedbenzylidene)-2-(7-bromo-2-phenylquinazolin-4-yloxy) acetohydrazide (5-15)

A mixture of 2-(7-Bromo-2-phenylquinazolin-4yl-oxy)acetohydrazide **4** (0.002mol) and substitutedbenzaldehyde (0.002mol) was refluxed in alcohal for 6-8 hrs. The reaction mixture was cooled, and poured into cold water. The residue was filtered, dried and recrystallized with ethanol, mixture to gave compound **5-15.**[21]

***N*'-(4-Chlorobenzylidene)-2-(7-bromo-2-phenylquinazolin-4-yloxy) acetohydrazi-de (5)**

Yield 45.17%**; m.p.** 225-227°C**; Elemental Analysis:** Calcd for $C_{23}H_{16}BrClN_4O_2$: C, 55.72; H, 3.25; N, 11.30; Cl, 7.15; Br, 16.12. Found: C, 55.70; H, 3.22; N, 11.28; Cl, 7.13; Br, 16.09 %**; FTIR (KBr):** 3315.68 (N-H str.), 3064.68 (Ar C-H str.), 1657.82 (C=O str.), 1538.07 (C=N str.), 1566.09 (Ar C-C str.), 1292.23 (C-N str.), 1033.77 (C-Br str.), 890.91 (aliphatic C-H str. of N=CH-), 887.19 (C-H def. monosubstituted), 829.33 (C-H def. *p*-disubstituted), 707.83 (C-Cl str.) cm^{-1} **; ^{1}H NMR (DMSO-d_6):** δ 3.21 ppm (s, 1H, N=C-H), 4.12 (s, 2H, CH_2), 6.82-8.91 (m, 12H, Ar-H), 11.24 ppm (s, 1H, NH D_2O exchangeable) ppm**; ESI full mass-MS: m/z** 494.01 $[M+2]^+$.

***N*'-(3,4,5-Trimethoxybenzylidene)-2-(7-bromo-phenylquinazolin-4-yloxy) aceto hydrazide (6)**

Yield 45.92%**; m.p.** 180-182°C**; Elemental Analysis:** Calcd for $C_{26}H_{23}BrN_4O_5$: C, 56.63; H, 4.20; N, 10.16; Br, 14.49. Found: C, 56.61; H, 4.17; N, 10.14; Br, 14.47 %**;**

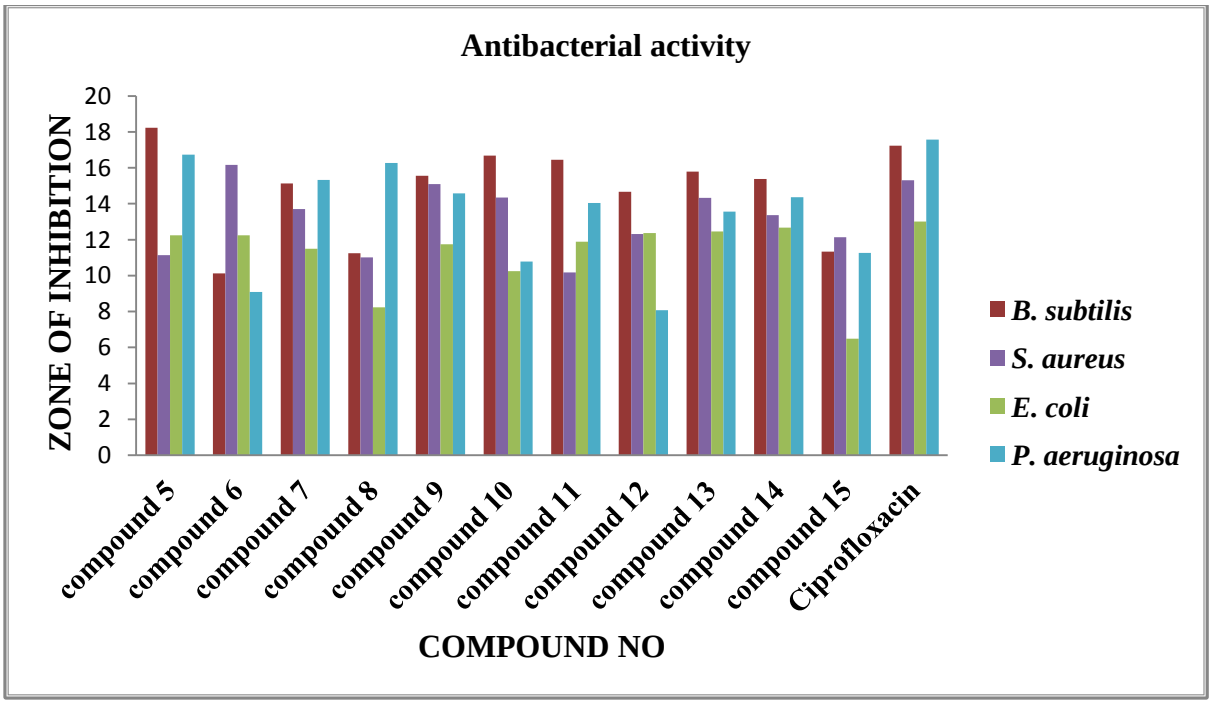


Fig. 1: Comparison of antibacterial study with different bacterial strain at 50µg/ml

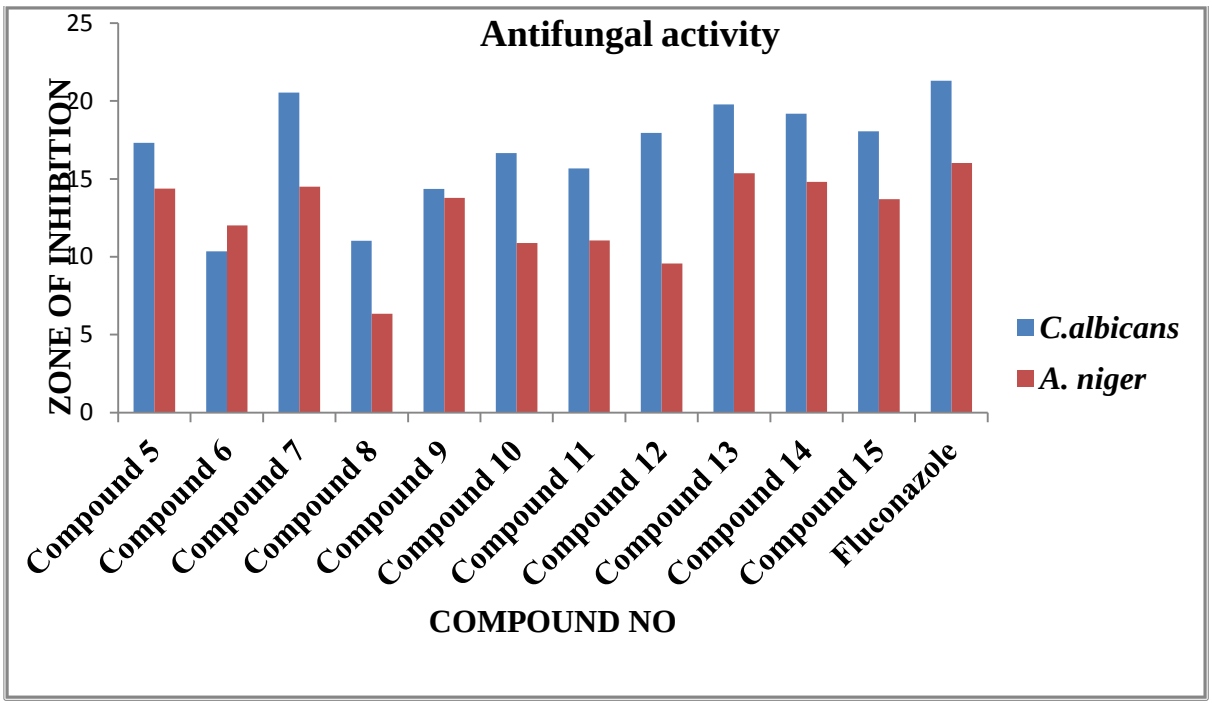


Fig. 2: Comparison of antifungal study with different fungal strain at 50µg/ml

FTIR (KBr): 3325.16 (N-H str.), 3066.61 (Ar C-H str.), 1672.53 (C=O str.), 1581.52 (C=N str.), 1575.73 (Ar C-C str.), 1271.47 (C-N str.), 1128.26 (C-O-C str.), 1068.49 (C-Br str.), 948.19 (aliphatic C-H str. of N=CH-), 833.19 (C-H def. *p*-disubstituted), 694.33 (C-H def. *m*-disubstituted) cm^{-1} **; ^{1}HNMR (DMSO-d_6):** δ 2.13 ppm (s, 1H, N=C-H), 3.24 (s, 3H, OCH_3), 4.23 (s, 2H, CH_2), 6.54-8.62 (m, 10H, Ar-H), 11.69 ppm (s, 1H, NH, D_2O exchangeable)**; ESI full mass-MS: m/z** 550.05 $[M+2]^+$.

***N*'-(3-Nitrobenzylidene)-2-(7-bromo-2-phenylquinazolin-4-yloxy)acetohydrazide (7)**

Yield 46.78%**; m.p.** 215-217°C**; Elemental Analysis:** Calcd for $C_{23}H_{16}BrN_5O_4$: C, 54.56; H, 3.19; N, 13.83; Br, 15.78. Found: C, 54.54; H, 3.17; N, 13.81; Br, 15.75 %**; FTIR (KBr):** 3365.72 (N-H str.), 3062.45 (Ar C-H str.), 1665.56 (C=O str.), 1577.66 (C=N str.), 1510.19 (Ar C-C str.), 1328.79 (C-NO_2 str.), 1342.43 (C-N str.), 1015.25 (C-Br str.), 830.33 (aliphatic C-H str. of N=CH-), 754.12 (C-H def. monosubstituted), 748.35 (C-H def. *o*-disubstituted) cm^{-1} **^{1}HNMR (DMSO-d_6):** δ 2.36 ppm (s, 1H, N=C-H), 4.35 (s, 2H, CH_2), 6.66-8.01 (m, 12H, Ar-H), 8.54 ppm (s, 1H, NH, D_2O exchangeable)**; ESI full mass-MS: m/z** 505.04 $[M+2]^+$**.**

***N*'-(2-Chlorobenzylidene)-2-(7-bromo-2-phenylquinazolin-4-yloxy)acetohydrazi--de (8)**

Yield 35.08%**; m.p.** 213-215°C**; Elemental Analysis:** Calcd for $C_{23}H_{16}BrClN_4O_2$: C, 55.72; H, 3.25; N,

11.30; Cl, 7.15; Br, 16.12. Found: C, 55.70; H, 3.22; N, 11.28; Cl, 7.13; Br,16.10 %**; FTIR (KBr):** 3372.34 (N-H str.), 3092.13 (Ar C-H str.), 1654.34 (C=O str.), 1565.34 (C=N str.), 1546.08 (Ar C-C str.), 1334.78 (C-N str.), 1108.99 (aliphatic C-H str. of N=CH-), 1024.67 (C-Br str.), 789.52 (C-H def. monosubstituted), 746.76 (C-H def. *o*-disubstituted), 628.75 (C-Cl str.) cm^{-1}**; ^{1}H NMR (DMSO-d_6):** δ 2.64 ppm (s, 1H, N=C-H), 4.82 (s, 2H, CH_2), 7.62-8.23 (m, 12H, Ar-H), 8.62 ppm (s, 1H, NH, D_2O exchangeable)**; ESI full mass-MS: m/z** 494.01 $[M+2]^+$.

***N*'-(3-Methoxybenzylidene)-2-(7-bromo-2-phenylquinazolin-4-yloxy)acetohydra -zide (9)**

Yield 21.57%**; m.p.** 211-213°C**; Elemental Analysis:** Calcd for $C_{24}H_{19}BrN_4O_3$: C, 58.67; H, 3.90; N, 11.40; Br, 16.26. Found: C, 58.65; H, 3.88; N, 11.38; Br, 16.24 %**; FTIR (KBr):** 3384.23 (N-H str.), 3045.45 (Ar C-H str.), 1676.52 (C=O str.), 1545.37 (C=N str.), 1600.08 (Ar C-C str.), 1325.52 (C-N str.), 1193.85 (aliphatic C-H str. of N=CH-), 1072.31 (C-O-C str.), 1053.49 (C-Br str.), 883.34 (C-H def. monosubstituted), 773.04 (C-H def. *m*-disubstituted) cm^{-1}**; ^{1}H NMR (DMSO-d_6):** δ 2.33 ppm (s, 1H, N=C-H), 3.67 (s, 1H, OCH_3), 4.51 (s, 2H, CH_2), 6.80-7.69 (m, 12H, Ar-H), 8.42 ppm (s, 1H, NH, D_2O exchangeable)**; ESI full mass-MS: m/z** 477.06 $[M+2]^+$**.**

***N*'-(2-Hydroxybenzylidene)-2-(7-bromo-2-phenylquinazolin-4-yloxy)acetohydra -zide (10)**

Yield 30.20%**; m.p**. 210-212°C**; Elemental Analysis:** Calcd for $C_{23}H_{17}BrN_4O_3$: C, 57.88; H, 3.59; N, 11.74; Br, 16.74. Found: C, 57.86; H, 3.57; N, 11.71; Br, 16.72 %

FTIR (KBr):): 3512.62 (O-H str.), 3410.53 (N-H str.), 3062.86 (Ar C-H str.), 1652.02 (C=O str.), 1581.47 (C=N str.), 1510.16 (Ar C-C str.), 1308.76 (C-N str.), 1065.19 (C-Br str.), 886.19 (aliphatic C-H str. of N=CH-), 843.23 (C-H def. monosubstituted), 753.92 (C-H def. *o*-disubstituted) cm^{-1}**; ^{1}H NMR (DMSO-d_6):** δ 2.54 ppm (s, 1H, N=C-H), 4.20 (s, 2H, CH_2), 6.86-8.17 (m, 12H, Ar-H), 5.63 (s, 1H, OH, exchangeable with D_2O), 8.46 ppm (s, 1H, NH, D_2O exchangeable)**; ESI full mass-MS: m/z** 463.04 $[M+2]^+$.

***N*'-(4-Flurobenzylidene)-2-(7-bromo-2-phenylquinazolin-4-yloxy)acetohydra -zide (11)**

Yield 39.27%**; m.p.** 209-211°C**; Elemental Analysis:** Calcd for $C_{23}H_{16}BrFN_4O_2$: C, 57.64; H, 3.36; N, 11.69; F, 3.96 Br, 16.67. Found: C, 57.62; H, 3.34; N, 11.67; F, 3.94; Br, 16.65% **FTIR (KBr):** 3393.12 (N-H str.), 3050.76 (Ar C-H str.), 1681.54 (C=O str.), 1557.23 (C=N str.), 1560.33 (Ar C-C str.),

1334.65 (C-N str.), 1149.50 (C-F str.), 1022.29 (C-Br str.), 832.57 (C-H def. monosubstituted), 823.55 (aliphatic C-H str. of N=CH-), 817.35 (C-H def. *p*-disubstituted) cm^{-1}**; ^{1}H NMR (DMSO-d_6):** δ 2.47 ppm (s, 1H, N=C-H), 4.67 (s, 2H, CH_2), 6.59-8.34 (m, 12H, Ar-H), 8.47 ppm (s, 1H, NH, D_2O exchangeable)**; ESI full mass-MS: m/z (%)** 478.09 $[M+2]^+$.

***N*'-(4-Hydroxybenzylidene)-2-(7-bromo-2-phenylquinazolin-4-yloxy)acetohydra -zide (12)**

Yield 42.13%**; m.p.** 178-180°C**; Elemental Analysis:** Calcd for $C_{23}H_{17}BrN_4O_3$: C, 57.88; H, 3.59; N, 11.74; Br, 16.74. Found: C, 57.86; H, 3.56; N, 11.71; Br, 16.72%**;**

FTIR (KBr): 3538.74 (O-H str.), 3396.61 (N-H str.), 3057.35 (Ar C-H str.), 1659.94 (C=O str.), 1571.08 (C=N str.), 1541.48 (Ar C-C str.), 1346.62 (C-N str.), 1052.34 (C-Br str.), 1034.16 (aliphatic C-H str. of N=CH-), 822.09 (C-H def. *p*-disubstituted) 806.45 (C-H def. monosubstituted) cm^{-1}**; ^{1}H NMR (DMSO-d_6):** δ 2.51 ppm (s, 1H, N=C-H), 4.16 (s, 2H, CH_2), 5.23 (s, 1H, OH, exchangeable with D_2O), 6.60-7.86 (m, 12H, Ar-H), 8.84 ppm (s, 1H, NH, D_2O exchangeable)**; ESI full mass-MS: m/z** 476.05 $[M+1]^+$.

***N*'-(2-Nitrobenzylidene)-2-(7-bromo-2-phenylquinazolin-4-yloxy)acetohydra -zide (13)**

Yield 18.15%**; m.p.** 186-188°C**; Elemental Analysis:** Calcd for $C_{23}H_{16}BrN_5O_4$: C, 54.56; H, 3.19; N, 13.83; Br, 15.78. Found: C, 54.56; H, 3.17; N, 13.81; Br, 15.75%

FTIR (KBr): 3381.43 (N-H str.), 3056.43 (Ar C-H str.), 1650.51 (C=O str.), 1568.41 (C=N str.), 1555.14 (Ar C-C str.), 1340.05 (C-NO_2 str.), 1299.67 (C-N str.), 1049.35 (C-Br str.), 836.53 (aliphatic C-H str. of N=CH-), 821.62 (C-H def. of monosubstituted), 753.16 (C-H def. *o*-disubstituted) cm^{-1} **^{1}HNMR (DMSO-d_6):** δ 2.34 ppm (s, 1H, N=C-H), 4.35 (s, 2H, CH_2), 6.82-7.65 (m, 12H, Ar-H), 8.71 ppm (s, 1H, NH, D_2O exchangeable)**; ESI full mass-MS: m/z** 494.01 $[M+2]^+$.

***N*'-(4-Nitrobenzylidene)-2-(7-bromo-2-phenylquinazolin-4-yloxy)acetohydra -zide (14)**

Yield 51.17% **m.p.** 190-192°C**; Elemental Analysis:** Calcd for $C_{23}H_{16}BrN_5O_4$: C, 54.56; H, 3.19; N, 13.83; Br, 15.78. Found: C, 54.56; H, 3.17; N, 13.81; Br, 15.75%**; FTIR (KBr):** 3380.43 (N-H str.), 3051.18 (Ar C-H str.), 1675.08 (C=O str.), 1575.73 (C=N str.), 1539.93 (Ar C-C str.), 1352.25 (C-NO_2 str.), 1283.13 (C-N str.), 1037.09 (C-Br str.), 972.64 (aliphatic C-H str. of N=CH), 815.08 (C-H def. monosubstituted), 734.83 (C-H def. *o*-disubstituted) cm^{-1}**; ^{1}H NMR (DMSO-d_6):** δ 2.42 ppm (s, 1H, N=C-H),

4.72 (s, 2H, CH_2), 6.63-7.83 (m, 12H, Ar-H), 8.32 ppm (s, 1H, NH, D_2O exchangeable)**; ESI full mass-MS: m/z** 505.04 $[M+1]^+$.

***N*'-(3-Chlorobenzylidene)-2-(7-bromo-2-phenylquinazolin-4-yloxy)acetohydra - zide (15)**

Yield 43.15%**; m.p.** 175-177°C**; Elemental Analysis:** Calcd for $C_{23}H_{16}BrClN_4O_2$: C, 55.72; H, 3.25; N, 11.30; Br, 16.12; Cl, 7.15. Found: C, 55.70; H, 3.22; N, 11.28; Br, 16.09; Cl, 7.13;% **; FTIR (KBr):** 3397.59 (N-H str.), 3022.08 (Ar C-H str.), 1658.53 (C=O str.), 1583.13 (C=N str.), 1539.42 (Ar C-C str.), 1314.33 (C-N str.), 1139.58 (aliphatic C-H str. of N=CH-), 1065.48 (C-Br str.), 815.43 (C-H def. monosubstituted), 707.66 (C-H def. *m*-disubstituted), 658.80 (C-Cl str.) cm^{-1}**; ^{1}H NMR (DMSO-d_6):** δ 2.39 ppm (s, 1H, N=C-H), 4.24 (s, 2H, CH_2), 6.67-7.63 (m, 12H, Ar-H), 8.62 ppm (s, 1H, NH, D_2O exchangeable)**; ESI full mass-MS: m/z** 300 $[M+2]^+$.

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