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SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF SOME N'-(SUBSTITUTED BENZYLIDENE)-2-(7-BROMO-PHENYLQUINAZOLIN-4-YLOXY) ACETOHYDRAZIDE DERIVATIVES

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Keywords:

Acetohydrazide, Quinazoline, Quinazoline, Hydrazide derivatives, Antimicrobial activity, Antifungal activity

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ABSTRACT: Quinoline or 1-aza-naphthalene or benzo [b] pyridine is a weak tertiary base. In the study, the synthesis of compounds and their antimicrobial activity which is not done earlier and is quite significant. An attempt has been made for the synthesis of N'-(substituted benzylidene)-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(3H)-one derivative (2). The esterification product of quinazolin-4(3H)-one derivative, when reacted with hydrazine-hydrate gave (7-bromo-2-phenylquinazolin-4yloxy) acetohydrazide (4). The sub stituted benzaldehyde on reaction with 7-Bromo-2-phenylquinazoline-4yloxyacetohydrazide (4) yielded N'-(sub stituted benzylidene)-2-(7-bromo-2-phenyl quinazolin-4-yloxy) acetohydrazide (5-15). Primarily the structures of all synthesized compounds were confirmed from Melting point and TLC methods and then spectral analysis IR, 1H NMR and mass spectra. All synthesized derivative compounds were evaluated for their in vitro antimicrobial activities using the disc diffusion technique. It was found that all the synthesized compounds exhibit antimicrobial activity and that compounds 7, 11, 13 and 14 have a broad spectrum of activity at 50 µg/ml.

INTRODUCTION: Quinazoline is the main six-membered heterocyclic ring system reported for the wide range of their biological activities like antibacterial [1, 2], antifungal [3, 6] antimicrobial [7, 8] anti-inflammatory [9, 11]. Antimalarial [12, 14], anti-HIV [15], antituberculosis [16, 17].

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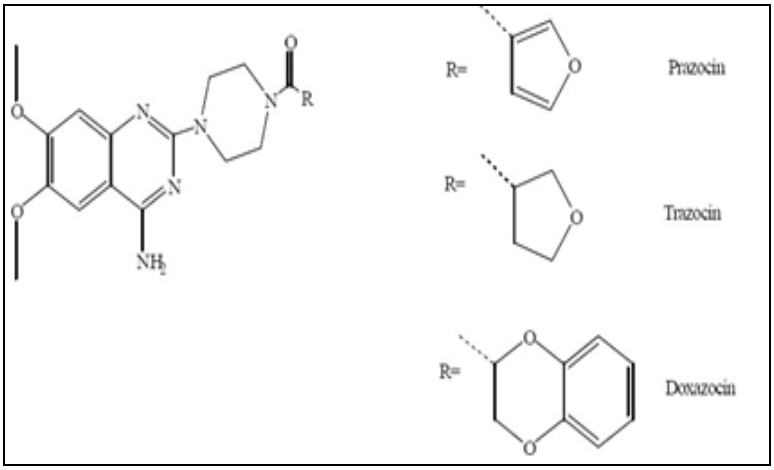
Quinazoline is also effective in the treatment of filarial-type diseases like river blindness [18] (caused filarial nematode Onchocerca volvulus). The other most important activities were also reported for anti-convulsant [19], antihypertensive [20], sedative-hypnotic [21, 24], anticancer [25, 26].

Several approved drugs have quinazoline structures in the market, such as prazosin hydrochloride (Antihypertensive), doxazosinemesy late, and terazosine hydrochloride for regulation of blood pressure. Bacterial resistance to existing drugs is a growing problem in the world. In the last few decades, 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 positions with chloro, nitro, 3, 4, 5 trimethoxy, fluoro and hydroxy groups to correlate the electronic effect of such substituents on the magnitude of the antimicrobial activity. The literature review prompted us to synthesize some newer quinazoline derivatives for better efficacy at a lower concentration. In the present study, newly synthesized compounds N'-(N-substituted benzylidene)-2-(7-bromo-2 phenyl quinazolin-4yloxy) acetohydrazide (5-15) showed potent antimicrobial activity. The N'-(N-substituted benzylidene)-2-(7-bromo-2-phenylquinazolin-4yloxy) acetohydra zide derivatives were synthesized by long chain of reactions of 7-bromo-2-phenylquinazolin-4-yloxy acetohydrazide with different reactants. And compounds 7, 11, 13, 14, showed potent activity towards microbes.



MATERIALS AND METHODS: Melting point ranges of newly synthesized compounds were determined by the closed capillary method using the electrothermal melting point apparatus and were uncorrected. IR spectrum of compounds in KBr pellets was recorded on an FTIR-8400S spectrophotometer (SHIMADZU) using KBr disc, and ^{1}HNMR 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 was performed on a Perkin-Elmer 240 elemental analyzer for C, H, O, N and halogens and agreed with the proposed structures within ±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 a mobile phase. The spots were visualized by exposure to iodine vapors.

RESULTS AND DISCUSSION: The starting material, oxazine-4-one (1) was prepared from the reaction of 4-bromoanthranilic acid and benzoyl chloride in solvent ethanol for continuous heating 7 hrs. Then an intermediate quinazolin-4(3H)-one (2) compound was prepared by oxazine-4-one on reaction with formamide. And this quinazolin-4(3H)-one gave another intermediate compound quinazpline-4- yloxy [aceate] (3) by the reaction of ethylchloro acetate in the solvent of acetone on water-bath. Conversely, hydrazinolysis of compound 3 afforded 2-(7-bromo-2-phenylquinazolin-4-yloxy) acetohydrazide (4). Compound 4 was allowed to react with certain aromatic aldehydes to give the corresponding quinazolinehydrazides (5-15) the title compounds. The structures of the newly synthesized compounds were confirmed by the different microanalysis as well as spectral analysis. For the confirmation of the title structure, IR, 1HNMR, Mass and elemental analysis was 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 whereas 1672.53 cm-1of C=O and 1581.52 cm^{-1} for the C=N of quinazoline ring. The ^{1}HNMR spectrum has been shown singlet at δ2.13 ppm corresponding to =C-H, singlet of three protons appeared at δ3.24 which was assigned to protons of -OCH_3 group, two proton singlet appeared at δ4.23 ppm was assigned to protons of CH_2 group, ten proton multiplet appeared between δ6.54-8.62 ppm indicated aromatic protons and singlet appeared at δ11.69 was assigned to N-H proton which was disappeared on D2O exchange. The mass spectrum revealed a molecular ion peak at m/z 550.05 [M^{+2}] +.

Elemental analyses 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. The antimicrobial activity for title synthesized compounds was obtained against gram-positive and gram-negative bacterial strains and fungal strains.

The zone of inhibition was measured and compared against the standard. All these novel synthesized compounds have been shown mild to moderate antibacterial and antifungal activity when compared with the standard at the different concentrations, where 50 µg/ml was the good concentration for all the antimicrobial activity. Compounds no 7, 11, 13 and 14 showed potent activity towards microbes **Fig. 2** and **Fig. 3.**

CONCLUSION: In this research, we successfully synthesized and confirmed the chemical structure of new quinazoline hydrazide of n'-(substituted benzylidene)-2-(7-bromo-2-phenyl quinazolin-4-yloxy) aceto hydrazides. The obtained compounds were in vitro screened against a panel of bacterial and fungal strains. The result reflects that newly synthesized compounds showed potent activity towards all strains.

Experimental: The title compound was prepared by the following lowering steps according to scheme **Fig. 1.**

Step 1: 7-Bromo-2-Phenyl-4h-Benzo (1, 3) Oxazin-4-One (1): A cold solution of 4-Bromoanthranilic acid (12 gm, 0.05 mol) in ethanol (45 ml) and (23.22 ml, 0.2 mol) benzolyl chloride was stirred for 7 h at room temperature. Then the reaction mixture was poured into crushed ice. The solid was obtained. The separated solid was filtered, dried, and recrystallized from ethanol to give compound 1; Yield 68.9%; M.P. 225-227 °C [27].

Step 2: 7-Bromo-2-Phenylquinazolin-4(3h)-One (2): A mixture of 7-Bromo-2-phenyl-4H-benzo (1,3) oxazin-4-one1 (8.56 gm, 0.02 mol) and formamide (13.5 gm, 11.94 ml, 0.3 mol) was fused in an oil bath at 150 °C for 8 h and poured into water. The solid obtained was filtered, dried and recrystallized with ethanol to give compound 2; Yield 75.92%; M.P. 180-182 °C [28].

Step 3: Ethyl 2-(7-Bromo-2-Phenylquinazolin-4-Yloxy) Acetate (3): A mixture containing 7-Bromo-2-phenylquinazolin-4(3H)-one-2 (6.96 gm, 0.01 mol) was dissolve in10 ml of acetone in a 100 ml of round bottom flask to this ethylchloroacetate (1.22 gm, 1.06 ml, 0.01 mol) was refluxed for 36 h. The separated solid is filtered, dried and recrystallised with ethanol to give compound 3; Yield 55.42%; M.P. 142-143 °C [29].

Step 4: 2-(7-Bromo-2-Phenylquinazolin-4-Yloxy) Acetohydrazide (4): A mixture containing Ethyl2-(7-bromo-2-phenylquinazolin-4-yloxy)acetate (3) (4.2 gm, 0.01 mol) and hydrazine hydrate (0.50 gm, 0.56 ml, 0.01 mol) in ethanol was taken in round bottom flask and refluxed for a period of 8 hrs. The product was found in solid form, filtrate out this and wash with water and recrystallized from absolute ethanol to give compound 4; Yield 55.47%; M.P. 235-236 °C [30].

Step 5: General Method For The Synthesis Of N'-(Substituted Benzylidene)-2-(7-Bromo-2 Phenyl Quinazolin-4-Yloxy) Acetohydrazide (5-15): A mixture of 2-(7-Bromo-2-phenylquinazolin-4yl-oxy) acetohydrazide (4) (0.002 mol) and substituted benzaldehyde (0.002 mol) was refluxed in alcohol for 6-8 h. The reaction mixture was cooled and poured into cold water. The residue was filtered, dried, and recrystallized with ethanol, a mixture to give compound 5-15 [31].

N'-(4-Chlorobenzylidene)-2-(7-Bromo-2-Phenyl Quinazolin-4-Yloxy) Acetohydrazide (5): Yield: 45.17%; M.P. 225-227 °C; Elemental Analysis: Calcd for $C_{23}H_{16}BrC_lN_4O_2$: 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}; 1H NMR (DMSO-d6): 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, NHD2O exchangeable) ppm; ESI full mass-MS: m/z- 494.0 $[M^{+2}]$+.

N'-(3, 4, 5-Trimethoxybenzylidene)-2-(7-Bromo-Phenyl Quinazolin-4-Yloxy) Acetohydrazide (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 %; 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} ;1HNMR (DMSO-d6): 2.13 ppm (s, 1H, N=C-H), 3.24 (s, 3H, OCH3), 4.23 (s, 2H, CH_2), 6.54-8.62 (m, 10H, Ar-H), 11.69 ppm (s, 1H, NH, D2O exchangeable);ESI full mass-MS: m/z 550.05 $[M^{+2}]$+.

N'-(3-Nitrobenzyli Dene) -2-(7-Bromo-2-Phenyl Quinazolin -4-Yloxy) Aceto Hydrazide (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. Mono substituted), 748.35 (C-H def. o-disubstituted) cm^{-1} ; 1HNMR (DMSO-d6): 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, D2O exchangeable); ESI full mass-MS: m/z 505.04 $[M^{+2}]$+.

N'-(2-Chloro Benzyli Dene)-2-(7-Bromo-2-Phenyl Quinazolin-4-Yloxy) Acetohydrazide (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. Mono substituted), 746.76 (C-H def. o-disubstituted), 628.75 (C-Cl str.) cm-1; 1HNMR (DMSO-d6): 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, D2O exchangeable);ESI full mass-MS: m/z 494.01 $[M^{+2}]$+.

N'-(3-Methoxy Benzyli Dene)-2-(7-Bromo-2-Phenyl Quinazolin-4-Yloxy) Acetohydrazide (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. Mono substituted), 773.04 (C-H def. m-disubstituted) cm^{-1}; 1HNMR (DMSO-d6): 2.33 ppm (s, 1H, N=C-H), 3.67 (s, 1H, OCH3), 4.51 (s, 2H, CH_2), 6.80-7.69 (m, 12H, Ar-H), 8.42 ppm (s, 1H, NH, D2O exchangeable); ESI full mass-MS: m/z477.06 $[M^{+2}]$+.

N'-(2-Hydroxy Benzyli Dene)-2-(7-Bromo-2-Phenyl Quinazolin-4-Yloxy) Acetohydrazide (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. Mono substituted), 753.92 (C-H def. o-disubstituted) cm^{-1}.1HNMR (DMSO-d6): 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 D2O), 8.46 ppm (s, 1H, NH, D2O exchangeable); ESI full mass-MS: m/z 463.04 $[M^{+2}]$+.

N'-(4-Fluro Benzylidene) -2-(7-Bromo-2-Phenyl Quinazolin-4-Yloxy) Acetohydrazide (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. Mono substituted), 823.55 (aliphatic C-H str. of N=CH-), 817.35 (C-H def. p-disubstituted) cm^{-1}; 1HNMR (DMSO-d6): 2.47 ppm (s, 1H, N=C-H), 4.67 (s, 2H, CH2), 6.59-8.34 (m, 12H, Ar-H), 8.47 ppm (s, 1H, NH, D2O exchangeable); ESI full mass-MS: m/z (%) 478.09 $[M^{+2}]$+.

N'-(4-Hydroxy Benzylidene) -2-(7-Bromo-2-Phenyl Quinazolin-4-Yloxy) Acetohydrazide (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. Mono substituted) cm-1; 1HNMR (DMSO-d6): 2.51 ppm (s, 1H, N=C-H), 4.16 (s, 2H, CH_2),5.23 (s, 1H, OH, exchangeable with D2O), 6.60-7.86 (m, 12H, Ar-H), 8.84 ppm (s, 1H, NH, D2O exchangeable); ESI full mass-MS: m/z 476.05 $[M^{+1}]$+.

N'-(2-Nitro Benzylidene) -2-(7-Bromo-2-Phenyl Quinazolin-4-Yloxy) Acetohydrazide (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 mono substituted), 753.16 (C-H def. o-disubstituted) cm^{-1}; 1HNMR (DMSO-d6): 2.34 ppm (s, 1H, N=C-H), 4.35 (s, 2H, CH2), 6.82-7.65 (m, 12H, Ar-H), 8.71 ppm (s, 1H, NH, D2O exchangeable);ESI full mass-MS: m/z 494.01 $[M^{+2}]$+.

N'-(4-Nitro Benzylidene) -2-(7-Bromo-2-Phenyl Quinazolin-4-Yloxy) Acetohydrazide (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. mono substituted), 734.83 (C-H def.o-disubstituted) cm^{-1}; 1HNMR (DMSO-d6): 2.42 ppm (s, 1H, N=C-H), 4.72 (s, 2H, CH2), 6.63-7.83 (m, 12H, Ar-H), 8.32 ppm (s, 1H, NH, D2O exchangeable);ESI full mass-MS: m/z505.04 $[M^{+1}]$+.

N'-(3-Chloro Benzylidene)- 2-(7-Bromo-2-Phenyl Quinazolin-4-Yloxy) Acetohydrazide (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. mono substituted), 707.66 (C-H def. m-disubstituted), 658.80 (C-Cl str.) cm^{-1}; 1HNMR (DMSO-d6): 2.39 ppm (s, 1H, N=C-H), 4.24 (s, 2H, CH2), 6.67-7.63 (m, 12H, Ar-H), 8.62 ppm (s, 1H, NH, D2O exchangeable); ESI full mass-MS: m/z 300 $[M^{+2}]$+ **Table 1.**

Antimicrobial Activity: The preliminary antibacterial and antifungal activities were obtained for synthesized compounds against various bacteria and fungi, namely: *Staphylococcus aureus* (Gram-positive bacteria). *Bacillus subtilis* (Gram-positive spore-forming bacteria). *Pseudomonas aeruginosa* (Gram-negative, aerobic bacteria). *Escherichia coil* (Gram-negative bacteria). *Aspergillus niger* (representative of fungi) *Candida albicans* (representative of fungi).

The antimicrobial activities were performed by disc diffusion method [32] under aseptic conditions. The sample was dissolved in DMF at different concentrations of 25, 50, 100 µg/ml. Ciprofloxacin and Fluconazole were used as standard drugs for antibacterial and antifungal activity. The zone of inhibition was compared with standard drug after 24 h of incubation at 25 °C for antibacterial activity

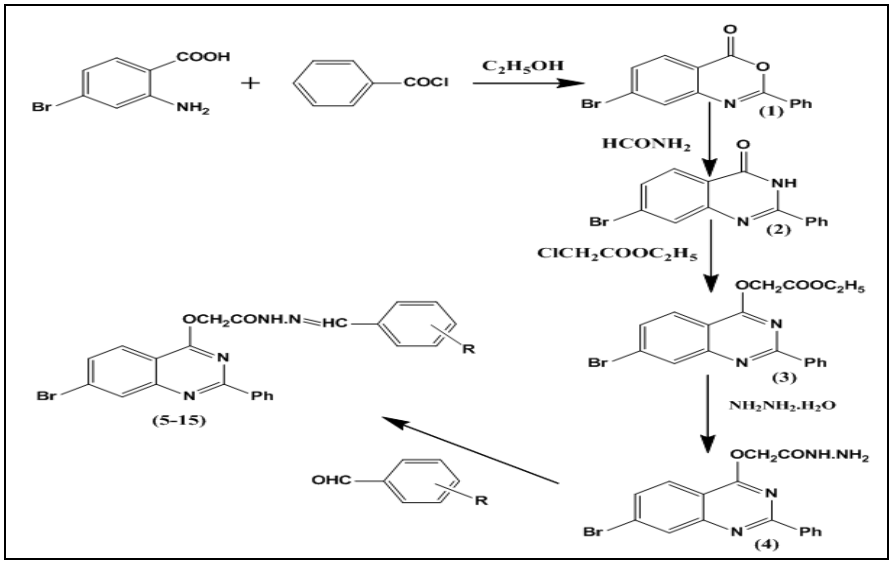
and 48 h at 32 °C for antifungal activity. Among them, the newly synthesized compounds 6 and 9 have shown potent activity against bacteria *S. aureus* and *B. sutilis* similarly, compounds 8, 14, and 11 have shown mild to moderate activity against bacteria *P. aeureginosa*, *E. coli*. The compounds 7, 9, 10, 11, 14 and 15 exhibited good activity against *A. niger* and *C. albicans*. Results are tabulated in **Table 2.** and compounds 12 and 13 were potent for other than *S. aureus* and *P. aeruginosa*.

TABLE 1: PHYSICAL DATA OF THE SYNTHESIZED COMPOUNDS

Comp. no.	R	Molecular Formula	Molecular Weight	R_f-value	Melting point (°C)	% yield
5	4-Cl	$C_{25}H_{16}BrClN_4O_2$	495.76	0.85	225-227	45.17
6	3,4,5OCH_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

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
Std: Ciprofloxacin /Fluconazole	17.23	13.01	15.30	17.56	21.29	16.03



5 R = 4-Cl, 6 R= 3, 4, 5-OCH_3, 7 R= 3-NO_2, 8 R= 2-Cl, 9R= 3-OCH_3, 10R= 2-OH, 11R= 4-F, 12, R=4-OH, 13 R= 2-NO_2, 14, R= 4-NO_2, 15R= 3-Cl

FIG. 1: PREPARATION OF N'-(SUBSTITUTED BENZYLIDENE)-2-(7-BROMO-2-PHENYLQUINAZOLIN-4-YLOXY) ACETOHYDRAZIDE.

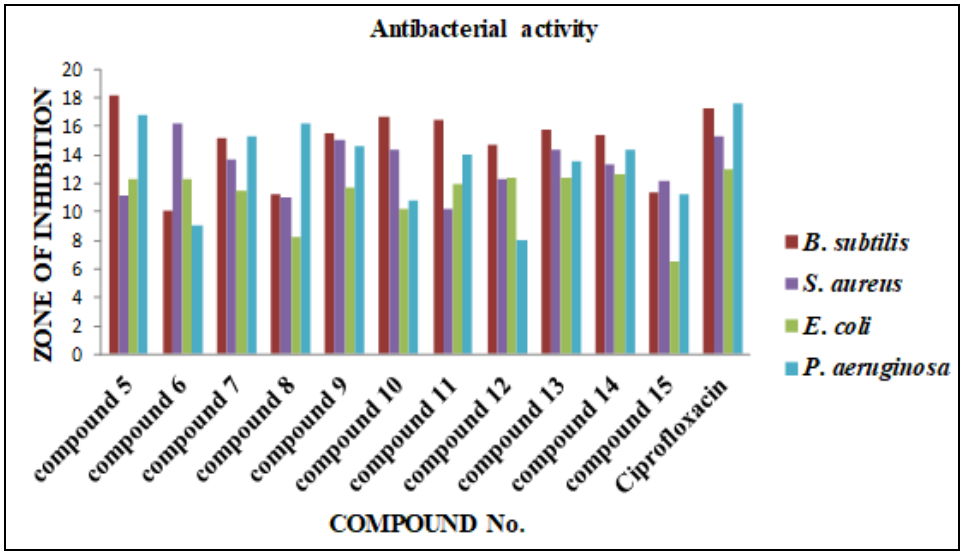


FIG. 2: COMPARISON ANTIBACTERIAL STUDY WITH DIFFERENT BACTERIAL STRAIN AT 50µG/ML

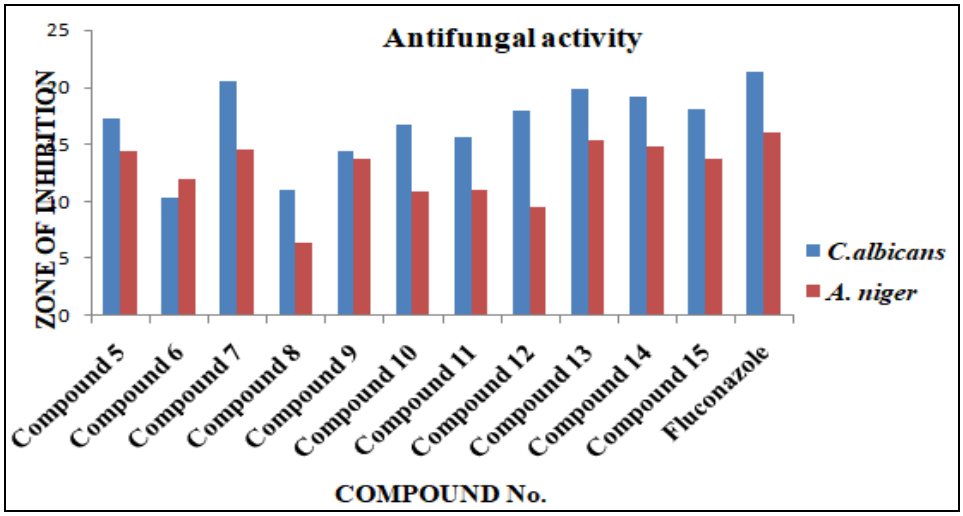


FIG. 3: COMPARISON ANTIFUNGAL STUDY WITH DIFFERENT FUNGAL STRAIN AT 50µG/ML

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REFERENCES:

1. Ghorab MM, Ismail ZH, Abdalla M and Radwan AA: Synthesis, antimicrobial evaluation and molecular modelling of novel sulfonamides carrying a biologically active quinazoline nucleus. Archives of Pharmacal Research 2013; 36: 660-70.
2. K Vijayakumar, Jafar AA and Thiruneelakandan G: Synthesis, antimicrobial and anti-hiv1 activity of quin-azoline-4(3h)-one derivative. J of App Chem 2013; 1-5.
3. Narasimhan B, Deep A,Kalavathy R, Mani V, Mishra RK, Bakar A and Majeed A: Synthesis, antimicrobial, anticancer evaluation and qsar studies of thiazolidin-4-ones clubbed with quinazolinone. Current Topics in Medicinal Chemistry 2013; 13: 1-13.
4. Al-Amiery AA, Kadhum AAH, Shamel M, Satar M, Khalid Y and Mohamad AB: Antioxidant and antimicrobial activities of novel quinazolinones. Medicinal Chemistry Research 2014; 23: 236-42.
5. Vashi RT, Patel SB and Kadiya HK: Synthesis, characterization and biological investigationson metal chelates of 2-[(8-hydroxyquinolinyl)-5-aminomethyl]-3-(4-. chlorophenyl)-3(h)-quinazolin-4-one. International Journal of Chem Tech Research 2010; 2: 1106-11.
6. Vashi RT, Shelat CD and Pate H: International J of Applied Biology and Pharma Tech 2010; 1: 883-89.
7. Kale AU, Kardile DP, Kalyane NV, Patel MR and Patel H: Synthesis and antimicrobial activity of some 2, 3-disubstituted quinazoline-4(3h)-ones. International J Pharm and Applied Sciences 2010; 1: 85-90.
8. Siddapa K, Reddy T, Mallikarjun M and Reddy CV: Synthesis, characterization and antimicrobial studies of 3[(2 hydroxy-quinolin-3-ylmethylene)-amino]-2-phenyl-3h-quinazolin-4-one and its metal (ii) complexes. European Journal of Chemistry 2008; 5: 155-62.
9. Fathallla OEMA, Kassem EMM, Ibrahem NM and Kamel MM: Synthesis of some new quinazolin-4-one derivatives and evaluation of their antimicrobial and anti-inflammatory effects .Acta Poloniae Pharmaceutica-Drug Research 2008; 65: 11-20.

10. Laddha SS, WadodKar SG and Meghal SK: Studies on some biologically active substituted 4(3H)-quinazolinones. Part 1. Synthesis, characterization and anti-inflammatory, antimicrobial activity of 6, 8-disubstituted 2-phenyl-3-[substituted-benzothia zol-2-yl]-4(3H)-quin azolinone. Arkivoc 2006; 11: 1-20.
11. Giri RS, Thaker HM, Giordano T, Williams J, Rogers D, Sudersanam V and Vasu KK: Design, synthesis and characterization of novel 2-(2,4-disubstituted-thiazole-5-yl)-3-aryl-3H-quinazoline-4-one derivatives as inhibitors of NF-kappaB and AP-1 mediated transcription activation and as potential anti-inflammatory agents. European Journal Medicinal Chemistry 2009; 44(5): 2184-89.
12. Lather V and Chowdary PVR: Synthesis and antimicrobial activity of n1- (arylidinehydrazidomethyl)-indoles, 2-(substituted aryl)-3-(n1-indolyl acetamidyl)-4-oxo-thiazolidines and 5-benzylidine derivatives of thiazolidinones. Indian Journal of Pharmaceutical Sciences 2003; 65: 576-79.
13. Chanda K, Datta MC and Vishwakarma JN: A facile one-pot synthetic route to substituted fused tetrahydraopyrimidines. Indian Journal of Chemistry 2006; 45: 1076-79.
14. Jiang S, Zeng Q, Gettayacamin M, Tungtaeng A, Wannaying S, Lim A, Hansukjariya P, Okunji CO, Zhu S and Fang D: Antimalarial Activities and Therapeutic Properties of
15. Febrifugine Analogs, Antimicrobial Agents and Chemotherapy 2005; 49(3): 1169-76.
16. Deetz MJ, Malerich JP, Beatty AM and Smith BD: One-step synthesis of 4(3H) quinazolinones. Tetrahedron Letters 2001; 42: 1851-54.
17. Khosropour AR, Iraj MB and Ghorbankhani H: Bi (TFA) 3-[nbp] Fecl4: A new, efficient and reusable promoter system for the synthesis of 4(3H)-quinazolinonederivatives. Tetrahedron Letter 2006; 47: 3561-64.
18. Nandy P, Vishalakshi MT and Bhat AR: Synthesis and antitubercular activity of mannich bases of -2-Methyl-3H-quinazolin-4-ones. Indian Journal of Heterocyclic Chemistry 2006; 15: 293-94.
19. Hübner Marc P, Gundersonb Emma, Vogel Ian, Christina A. Bulmanb and Limb KC: Short-course quinazoline drug treatments are effective in the Litomosoidessigmodontis and Brugiapahangijird models. IJP Drugs and Drug Resistance 2020; 12: 18-27.
20. Gopal N, Jagadeeswarant M and Saravanan VS: Synthesis and anticonvulsant activity of new 2-Substituted aryl/heteryl-3-(substituted arylidenimino)-6, 8-dibromo-1, 2, 3, 4-tetrahydroquinazolin-4(3H) –ones derivatives. Asian Journal of Chemistry 2006; 18: 2611-17.
21. Alagersamy V. and Pathak US: Synthesis and antihypertensive activity of novel 3-benzyl-2-substituted-3H-[1, 2, 4]triazolo [5,1-b] quinazoline-9-ones. Bioorganic & Medicinal Chemistry 2007; 15: 3457-62.
22. Pandey VK, Kumar A and Trivedi N: An investigation leading to preparation of tetrahydro-quinazoline derivatives involving ureidoalkylation and α-amidoalkylationreaction. Indian Journal of Chemistry 2008; 47: 1910-14.
23. Tiwari VK, Kale RR and Mishra BB: A facile one-pot MW approach for 3-Heteroaryl-2-thioxo-2, 3-dihydroquinazolin-4(1H)-ones. ARKIVOC 2008; 16: 27-36.
24. Sachar A and Sharma RL: Synthesis of some quinazoline based condensed heterocycles .Indian Journal of Heterocyclic Chemistry 2007; 16: 409-10.
25. Kashaw SK, Gupta V, Kashaw V and Jain NK: Anticonvulsant and sedative-hypnotic activity of some novel 3-[5-(4-substituted) phenyl-1, 3, 4-oxadiazole-2yl]-2-styrylquinazolin-4(3H)-ones. Medicinal Chemistry Research 2009; 12: 123-27.
26. Khodair I Ahmed, Alsafi A Mona and Nafie S Mohamed: Synthesis, molecular modeling and anti-cancer evaluation of a series of quinazoline derivatives. Carbohydrate Research 2019; 486: 1-13.
27. Li Baolin, Wang Wei, Zhang Yaling, Zhang Ying, Liu Juan, Chen Li and Zhao Lijun: Bioorganic & Medicinal Chemistry Letters 2017; 1-9.
28. Undavia NK, Trivedi PB, Shanishchara AP and Trivedi V: Synthesis and Antimicrobial Evaluation of 1-[4{4-(2-phenyl-4-oxa-3-quinazolinyl)phenyl}phenyl]-2-phenyl-4-aryl methane-5-oxa-imidazoles . Asian Journal of Chemistry 2004; 16: 1214-1216.
29. Sharada J, Kumari RY and Rao MK: Synthesis and biological activity of furoquinolines: 2-aroyl-4-methyl/4,6-dimethyl-3-phenyl-furo [3, 2-c] quinolones . Indian Journal of Pharmaceutical Sciences 1987; 49(1): 376-79.
30. El-Metwally AM, El-Hashash MA, Eissa AMF and El-Gohary AMF: Synthesis and biological evaluation of some new 4(3h)-quinazolinone derivatives as non-classical antifolate. Egyptian Journal of Chemistry 2010; 53(6): 777-90.
31. Pattan SR, Kale SH, Mali RA, Dengale SS, Pattan JS, Ghuge ND, Muluk RA and Dube SD: Synthesis and evaluation of some substituted 2-aminothiazole derivatives for their antitubercular, antimicrobial & antifungal activity. Indian Drugs 2012; 49: 24-32.
32. Demirbas N, Karaoglu SA, Demirbas A and Sancak K: Synthesis and antimicrobial activities of some new 1-(5-phenylamino-[1,3,4]thiadiazol-2-yl)methyl-5-oxo-[1,2,4] triazole and 1-(4-phenyl-5-thioxo-[1,2,4] triazol-3-yl)methyl-5-oxo- [1,2,4]triazole derivatives . European Journal of Medicinal Chemistry 2004; 39: 793-04.
33. Tendencia EA: Disk diffusion method. NCCLS publication, Second Edition 2004; 14-26.

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