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Synthesis and Charecterization of new 6-bromo-3-(2-(ethyl(methyl)amino) ethyl) -2-thioxo-2,3-dihydroquinazolin-4 (1H) –one derivatives and Evaluation of their Anti Microbial Activity.

P.Chaitanya[a], Guguloth Ravi[b*],S.Damodhar[a],A.RavinderNath[a]
[a]Department of Pharmacy and Biotechnology,University college Technology,
Osmania University,Hyderabad-500007,Telangana State,India.
.[b*]Department of Pharmaceutical Chemistry,Telangana University,
Nizamabad-503322,Telangana State,India.
*Corresponding author E_mail:drraviguguloth@gmail.com.

Abstract: ***Synthesis of new 6-bromo-3-(2-(ethyl(methyl)amino)ethyl)-2-thioxo-2,3-dihydroquinazolin-4(1H)-one derivatives has been prepared reaction in between 6-bromo-3-(2-(ethyl(methyl)amino)ethyl)-2-thioxo-2,3-dihydroquinazolin-4(1H)-one (III-30 a-h) and Potasium peramanganate in presence of Alc.KOH, Charecterized by ^{1}H-NMR, CMR, IR, Mass and elemental analysis also Evaluated their Anti Microbial Activity.***

Key Words:6-bromo-3-(2-(ethyl(methyl)amino)ethyl)-2-thioxo-2,3-dihydroquinazolin-4(1H)-one derivatives, 6-bromo-3-(2-(ethyl(methyl)amino)ethyl)-2-thioxo-2,3-dihydroquinazolin-4(1H)-one, Anti Microbial Activity.

1. INTRODUCTION

Quinazolinone is a bicycle compound consisting of a Pyrimidine system fused at 2, 3 position with benzene ring Quinazoline is considered as an important chemical synthesis of various physiological significance and pharmacological utility.These rings are exhibits like non-typeable.Haemophilus influenzae[1]. It is a multiscale response to stress required for repair and regeneration after injury[2]. Many pathophysiological pathways like cytokines, interlukin, NF-kB, protein kinases (Adenosine Monophosphate-activated protein Kinase- AMPK), tyrosine kinases and various immunological responses regulate and mediate the process of inflammation [3-6]. During inflammation, NF-kB has a proapoptotic role in neutrophils which may represent an important anti-inflammatory mechanism during acute inflammation [7-9]. In the process of inflammation, prostaglandin synthesis is a vital step where cyclooxygenase 2 (COX-2) enzyme is one of the two key enzymes. In the second step, COX reduces PGG2 to PGH2 [10, 11]. COX is majorlyinvolved in the process of inflammation and is the targeted protein for most of the NSAIDs (non-steroidal anti-inflammatory drugs). It is also found to be key protein in various physiological processes like gastric secretions [12], gastro intestinal motility and in other pathological conditions like inflammation, arthritis and colon cancer [13]. Quinazolinone derivatives were previously reported as inhibitors of various enzymes involved in process of inflammation (COX, prostaglandin E2) [14,15], allergic reactions (Histamine H_3 receptor inhibition) [16], and also in tumor suppressing process through interacting with DNA, tubulin and thus acting as anticancer agents [17, 18]. Some series of quinazolinone derivatives were also shown to have remarkable antimicrobial and antifungal properties[19-23].In addition molecules with quinazolinone scaffold acts as regulators of calcium and sodium at cellular membranes by inhibiting sodium/calcium exchange process [24].

2.METERIALS AND METHOD

In this experiment all reagents are used analytical reagent grade obtained from Sigma-Aldrich, Merck, SD fine and avira chemicals. With using standard procedures we purified Water, methanol, acetone, ether etc. 6-bromo-3-(2-(ethyl(methyl)amino)ethyl)-2-thioxo-2,3-dihydroquinazolin-4(1H)-one derivatives ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker 400 MHz NMR instrument using tetra methyl silane (TMS) as internal standard

compound and coupling constants (*J*) are reported in Hz units.VG AUTOSPEC mass spectrometer. Electronic spectra of all compounds were recorded on Schimadzu UV–Vis 1601 spectrophotometer. ESI mass spectra were Melting points of the ligands and metal complexes decomposition temperature were determined on Polmon instrument (Model No. MP-102). IR spectra of the compounds were recorded using KBr pellets in the range 4000–600 cm ^{1} on Perkin-Elmer Infrared model 337. The percentage composition of C, H, N of the compounds were determined by using micro analytical techniques on Perkin Elmer 240C (USA) elemental analyzer. All reactions were monitored by thin-layer chromatography (TLC) on pre-coated silica gel F254 plates from Merck, and compounds visualized either by exposure to UV light. Chromatographic columns 60–120 mesh silica gel for separations were used. Elemental analyses (C, H, N) determined by means of a Perkin–Elmer 240 C,H,N and O elemental analyzer, were within ± 0.4% of Perkin–Elmer theory.

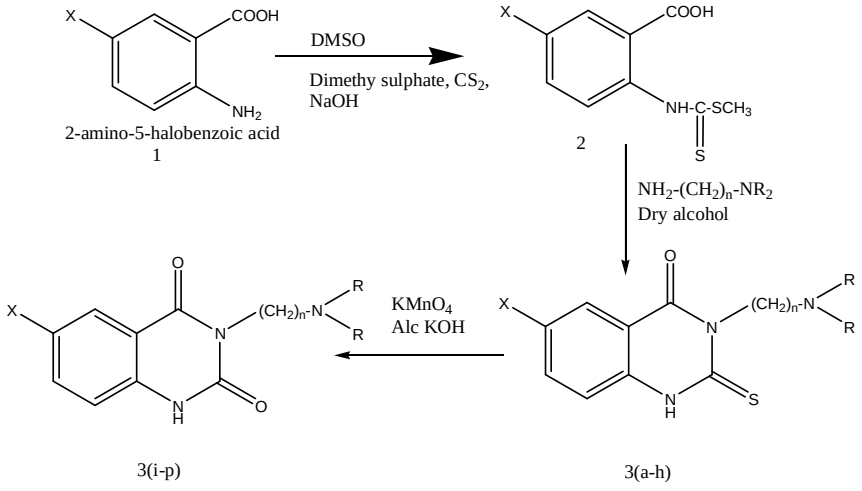
3. EXPERIMENTAL:

3.1.General procedure for the synthesis of 3-bromo-2-(methyl thio carbano thionyl)benzoic acid. (2):

The compound (2) has been prepared from mono bromo or iodo anthranilic acid by reacting with DMSO, KOH and carbon disulfide by a known procedure[26]. The product good yielded a yellow color and characterized by ^{1}H-NMR,CMR,IR,Mass and elemental analysis.

IR (cm^{-1}) ν_{max}:3441,3358,3041,2952,1708,1642,1575,783,586, **^{1}H NMR (DMSO-d$_6$, 300 MHz)δ:**1,98(s,1H,SCH_3),3.6(s,1H,-NH),7.4-7.9(m,*J*=8.3Hz,3H,Ar-H,),10.8(s,1H,-COOH). **^{13}CNMR(DMSO-d$_6$,75MHz)δ:** 21.0,119.0,122.7,128.6,132.2,137.2,140.9, 169.4, 199.9. **Mass:***m/z*305(M^+),307(M+2), ***Anal*.Calcd.** for **$C_9H_8NO_2S_2Br$:** C,72.13;H,8.28;N, 14.37;S,8.12. Found: C, 72.78; H, 9.05; N, 15.18;S,7.12. Yield: 74% , M.P: 148^{0}C.

Scheme-I



Compound-3:

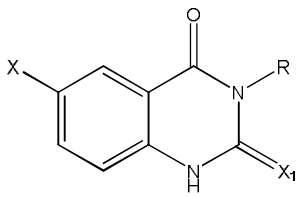


Table-1

Compound	X	X 1	R	Molecular Formula	Molecular weight	Melting point	Yield (%)
3a	Br	S	$-(CH_2)_3-N-(CH_3)_2$	$C_{13}H_{16}N_3BrSO$	342	150-152	65
3b	Br	S	$-(CH_2)_3-N-(C_2H_5)_2$	$C_{15}H_{20}N_3BrSO$	370	159-161	70
3c	Br	S	$-(CH_2)_2-N-(C_2H_5)_2$	$C_{14}H_{18}N_3BrSO$	356	150-152	68
3d	Br	S	$-(CH_2)_2-N-(CH_3)_2$	$C_{12}H_{14}N_3BrSO$	328	148-150	70
3e	I	S	$-(CH_2)_3-N-(CH_3)_2$	$C_{13}H_{16}N_3ISO$	389	200-203	78
3f	I	S	$-(CH_2)_2-N-(C_2H_5)_2$	$C_{14}H_{18}N_3ISO$	403	188-190	72
3g	I	S	$-(CH_2)_3-N-(C_2H_5)_2$	$C_{15}H_{20}N_3ISO$	417	203-205	70
3h	I	S	$-(CH_2)_2-N-(CH_3)_2$	$C_{12}H_{14}N_3ISO$	375	179-181	79
3i	Br	O	$-(CH_2)_3-N-(CH_3)_2$	$C_{13}H_{16}N_3BrO_2$	326	136-137	74
3j	Br	O	$-(CH_2)_3-N-(C_2H_5)_2$	$C_{15}H_{20}N_3BrO_2$	354	129-132	79
3k	Br	O	$-(CH_2)_2-N-(C_2H_5)_2$	$C_{14}H_{18}N_3BrO_2$	340	134-136	82
3l	Br	O	$-(CH_2)_2-N-(CH_3)_2$	$C_{12}H_{14}N_3BrO_2$	312	131-133	70
3m	I	O	$-(CH_2)_3-N-(CH_3)_2$	$C_{13}H_{16}N_3IO_2$	373	176-178	75
3n	I	O	$-(CH_2)_2-N-(C_2H_5)_2$	$C_{14}H_{18}N_3IO_2$	387	165-167	74
3o	I	O	$-(CH_2)_3-N-(C_2H_5)_2$	$C_{15}H_{20}N_3IO_2$	401	143-145	70
3p	I	O	$-(CH_2)_2-N-(CH_3)_2$	$C_{12}H_{14}N_3IO_2$	359	155-157	74

3.2. General procedure for the synthesis 6-bromo-3-(2-(ethyl(methyl)amino)ethyl)-2-thioxo-2,3-dihydroquinazolin-4(1H)-one (3a-h):

The appropriate dialkyl amino alkyl amine (0.012 moles) and 2-methyl dithio amido-5-halo-1-benzophenone (3-II; 0.01 moles) were taken in dry alcohol (15 ml) and refluxed for 8 h. The course of the reaction was monitored every hour with the help of TLC. Completion of reaction was confirmed by filter paper soaked in sodium nitroprusside solution failing to turn pink when exposed at the top of the condenser. Reflux was continued till the unpleasant smell disappeared. Contents of the reaction mixture were concentrated under reduced pressure and poured onto crushed ice. The final compound was filtered dried and purified by recrystallization from chloroform. Using the above procedure eight such 3-[(N, N-dialkyl amino) alkyl-2-thio-6-halo-quinazolin-4 (3H)-ones (3a-h) were prepared and characterized by ^{1}H-NMR,CMR,IR,Mass and elemental analysis.

3.2.a.6-bromo-3-(2-(ethyl(methyl)amino)ethyl)-2-thioxo-2,3-dihydroquinazolin-4(1H)-one.

IR (cm^{-1}) ν_{max}:3350,3078,2978,1650,1420,1370,682, **^{1}H NMR (DMSO-d_6, 300 MHz) δ:** 1,01(t,3H,CH_3),2.27(s,3H,CH_3),2.40(q,2H,CH_2), 2.66(t,2H,CH_2),3.55(t,2H,CH_2),3.8 (s,1H,NH),6.53(d,*J*=7.4 Hz,1H,Ar-H),7.43(d, *J* = 7.6 Hz, 1H,Ar-H),7.87(s,*J*=8.2 Hz,1H,Ar-H),**^{13}C NMR (DMSO-d_6,75 MHz) δ:** 13.1,26.2,43.1,51.7,57.0, 119.2,126.8,130.4,134.0, 138.1,143.4,161.5,176.4,**Mass:** *m/z* 342 (M^+),344(M+2), ***Anal.* Calcd.** for **$C_{13}H_{16}N_3OSBr$:** C, 68.15; H, 9.13; N, 12.31;S,4.12. Found: C, 65.15; H, 8.12; N, 13.15; S, 5.23. Yield: 65%, M.P: 150-152^{0}C.

3.2.b.6-bromo-3-(3-(diethylamino)propyl)-2-thioxo-2,3-dihydroquinazolin-4(1H)-one

IR (cm^{-1}) ν_{max}:3315,3010,2968,1687,1413,1368,690, **^{1}H NMR (DMSO-d_6, 300 MHz) δ:** 1,10(t,6H,CH_3),2.35(q,4H,CH_2), 2.66(t,4H,CH_2), 3.55(m,2H,CH_2),3.9(s,1H,NH),6.55 (d,*J*=7.4 Hz,1H,Ar-H),7.40(d, *J* = 7.6 Hz, 1H,Ar-H),7.87(s,*J*=8.2 Hz,1H,Ar-H),**^{13}C NMR (DMSO-d_6,75MHz)δ:**12.8,25.4,32.1,44.1,52.7,58.0,118.2,125.8,129.4,133.2,136.2,144.6, 162.5,178.2,**Mass:** *m/z*312 (M^+),314(M+2), ***Anal.* Calcd.** for **$C_{15}H_{20}N_3OSBr$**: C, 72.13; H, 8.28;N, 14.37;S,8.12. Found: C, 72.78; H, 9.05; N, 15.18; S, 7.12. Yield: 70%, M.P: 159-161^{0}C.

3.2.c.6-bromo-3-(2-(diethylamino)ethyl)-2-thioxo-2,3-dihydroquinazolin-4(1H)-one
IR (cm^{-1}) ν_{max}: 3355, 3090, 2988,1701,1460,1392,710, **^{1}H NMR (DMSO-d_6, 300 MHz) δ:** 1,15(t,6H,CH_3),2.45(q,4H,CH_2),2.68(t,2H,CH_2),3.58(t,2H,CH_2),3.85(s,1H,NH),6.8(d,*J*=7.4H z,1H,Ar-H), 7.45(d, *J* = 7.6 Hz, 1H,Ar-H),7.90(s,*J*=8.2 Hz,1H,Ar-H),**^{13}C NMR (DMSO-d_6,75 MHz) δ:** 15.1,28.2,44.1,54.7,58.0, 121.2,128.8,132.4,136.0, 139.1,145.4,163.5, 178.4. **Mass:***m/z*356(M^+),358(M+2), ***Anal.*Calcd.**for**$C_9H_8NO_2S_2Br$:** C, 68.25; H, 6.67; N, 12.14; S, 4.75. Found: C, 69.12; H, 8.15; N, 10.23; S, 8.45. Yield: 68%, M.P: 150-158^{0}C.

3.2.d.6-bromo-3-(2-(dimethylamino)ethyl)-2-thioxo-2,3-dihydroquinazolin-4(1H)-one
IR (cm^{-1}) ν_{max}:3398,3100,2985,1721,1430,1385,721, **^{1}H NMR (DMSO-d_6, 300 MHz) δ:** 1,5(s,3H,CH_3),2.30(s,3H,CH_3),2.30(t,2H,CH_2),2.50(t,2H,CH_2),4.0(s,1H,NH),6.6(d,*J*=7.4 Hz,1H,Ar-H),7.41(d, *J* = 7.6 Hz, 1H,Ar-H),7.81(s,*J*=8.2 Hz,1H,Ar-H),**^{13}C NMR (DMSO-d_6,75 MHz) δ:** 14.2,25.1,42.5,52.6,58.0, 120.2,127.8,129.4,138.2, 139.1,144.4,162.5,172.4, **Mass:** *m/z* 328 (M^+),330(M+2),***Anal.* Calcd.** For **$C_{12}H_{14}N_3OSBr$:**C, 63.15; H, 9.26; N, 10.12;S,7.56. Found: C, 64.48; H, 8.10; N, 12.10;S,8.16. Yield: 70% , M.P: 148-150^{0}C.

3.2.e. 3-(2-(ethyl(methyl)amino)ethyl)-6-iodo-2-thioxo-2,3-dihydroquinazolin-4(1H)-one
IR (cm^{-1}) ν_{max}:3332,3081,2962,1720,1435,1365,732, **^{1}H NMR (DMSO-d_6, 300 MHz) δ:** 1,5(t,3H,CH_3),2.18(s,3H,CH_3),2.35(q,2H,CH_2),2.54(t,2H,CH_2),3.21(t,2H,CH_2),4.1(s,1H,NH), 6.62(d,*J*=7.4 Hz,1H,Ar-H),7.41(d, *J* = 7.6 Hz, 1H,Ar-H),7.80(s,*J*=8.2 Hz,1H,Ar-H),**^{13}C NMR (DMSO-d_6,75 MHz) δ:** 15.4,24.2,40.1,49.7,55.0, 117.2,124.8,128.4,132.2, 136.1, 143.5,160.5,172.3,**Mass:** *m/z* 389 (M^+),***Anal.* Calcd.** for **$C_{13}H_{16}N_3OSI$:** C, 69.14; H, 9.12; N, 12.15;S,9.34. Found: C, 68.12; H, 8.12; N, 14.20;S,8.12. Yield: 78% , M.P: 200-202^{0}C.

3.2.f. 3-(3-(diethylamino)propyl)-6-iodo-2-thioxo-2,3-dihydroquinazolin-4(1H)-one
IR (cm^{-1}) ν_{max}:3321,3023,2961,1738,1432,1327,752, **^{1}H NMR (DMSO-d_6, 300 MHz) δ:** 1,35(t,6H,CH_3),2.39(q,4H,CH_2),2.52(t,2H,CH_2),2.62(t,2H,CH_2),3.50(M,2H,CH_2),4.2(s,1H,N H),6.41(d,*J*=7.4 Hz,1H,Ar-H),7.23(d, *J* = 7.6 Hz, 1H,Ar-H),7.87(s,*J*=8.2 Hz,1H,Ar-H),**^{13}C NMR (DMSO-d_6,75 MHz) δ:**14.6,27.2,44.1,52.7,58.2, 121.2,128.8,132.4,135.0, 140.1, 144.4,162.5,172.4,**Mass:** *m/z* 403 (M^+),***Anal.* Calcd.** for **$C_{14}H_{18}N_3OSI$:** C, 76.16; H, 8.78; N, 6.37;S,7.12. Found: C, 68.78; H, 8.6; N, 12.11;S,8.42. Yield: 72% , M.P: 188-190^{0}C.

3.2.g. 3-(2-(diethylamino)ethyl)-6-iodo-2-thioxo-2,3-dihydroquinazolin-4(1H)-one
IR (cm^{-1}) ν_{max}:3402,3092,2962,1702,1432,1385,723, **^{1}H NMR (DMSO-d_6, 300 MHz) δ:** 1,3(t,6H,CH_3), 2.20(q,4H,CH_2), 2.54(t,2H,CH_2), 2.87(t,2H,CH_2),4.1(s,1H,NH),6.82(d,*J*=7.4 Hz,1H,Ar-H),7.21(d, *J* = 7.6 Hz, 1H,Ar-H),7.61(s,*J*=8.2Hz,1H,Ar-H).**^{13}CNMR(DMSO-d_6,75MHz)δ:**14.5,30.2,38.1,46.7,51.0, 112.3,118.8,128.2,128.1, 132.1,138.4,158.2,168.4, **Mass:** *m/z* 417 (M^+),***Anal.* Calcd.** for $C_{15}H_{20}N_3OSI$: C, 62.13; H, 6.28; N, 8.37;S,9.12. Found: C, 62.78; H, 8.05; N, 9.18;S,8.12. Yield: 74% , M.P: 203-205^{0}C.

3.2.h. 3-(2-(dimethylamino)ethyl)-6-iodo-2-thioxo-2,3-dihydroquinazolin-4(1H)-one
IR (cm^{-1}) ν_{max}:3410,3102,2998,1705,1445,1385,722,**^{1}H NMR (DMSO-d_6, 300 MHz) δ:** 1,12(s,6H,CH_3),1.27(t,2H,CH_2),2.40(t,2H,CH_2), 2.52(t,2H,CH_2),3.7(s,1H,NH),6.63(d,*J*=7.4 Hz,1H,Ar-H),7.34(d, *J* = 7.6 Hz, 1H,Ar-H),7.48(s,*J*=8.2 Hz,1H,Ar-H),**^{13}C NMR (DMSO-d_6,75 MHz) δ:** 20.1,27.2,44.1,50.7,55.0, 125.2,128.8,129.4,132.0, 136.1,140.4,158.5,172.4, **Mass:** *m/z* 375 (M^+).***Anal.* Calcd.** for **$C_{12}H_{14}N_3OSI$:**C, 67.13; H, 9.28; N, 12.37;S,9.12. Found: C, 68.78; H, 10.05; N, 12.18;S,8.12. Yield: 79% , M.P: 179-181^{0}C.

3.3. General procedure for the synthesis of 6-bromo-3-(2-(ethyl (methyl) amino) ethyl) quinazoline-2,4(1H,3H)-dione (3 i-p)

The appropriate of 3-[(N, N-dialkyl amino) alkyl-2-thio-6-halo-quinazolin-4 (3H)-ones (3 a-h ; 0.01 mole) and alcoholic KOH (15 ml) were refluxed together for 2 h. Potassium permanganate (1 g) was added in small quantities continuously. The refluxing was continued for 30 m after the complete addition of potassium permanganate. The course of the reaction was monitored by TLC. The excess solvent from the reaction mixture was removed under vacuum distillation. The product that separated out was recrystallized from methanol to get the product in good yields. Using the above procedure eight such 3-[(N, N-dialkyl amino) alkyl-2-oxo-6-halo-quinazolin-4 (3H)-ones (3 i-p) were prepared and characterized by ^{1}H-NMR,CMR,IR,Mass and elemental analysis.

3.3.i. 6-bromo-3-(2-(ethyl(methyl)amino)ethyl)quinazoline-2,4(1H,3H)-dione

IR (cm^{-1}) ν_{max}:3352, 3120, 2982, 2690,2324,1735,1625,1562,1215,1003,746, **^{1}H NMR (DMSO-d$_6$, 300 MHz) δ:** 1,90(s,3H,CH_3),2.30(q,3H,CH_3),2.56(t,3H,CH_3), 2.81(t,2H,CH_2),3.23(t,2H,CH_2),4.22(s,1H,NH),7.25-7.89(m,*J*=7.4 Hz,3H,Ar-H),**^{13}C NMR (DMSO-d$_6$,75 MHz) δ:** 13.1,43.1, 49.1, 51.7, 52.3, 118.8, 123.9, 125.5, 131.2, 135.3, 136.9, 151.5, 59.5, **Mass:** *m/z* 326 (M^+), 328(M+2), ***Anal*. Calcd.** for **$C_{13}H_{16}N_3O_2Br$:** C, 74.13; H, 7.28; N, 11.27; S,7.12. Found: C, 71.28; H, 8.05; N, 13.18; S, 8.12. Yield: 74%, M.P: 136-138^{0}C.

3.3.j. 6-bromo-3-(3-(diethylamino)propyl)quinazoline-2,4(1H,3H)-dione

IR (cm^{-1}) ν_{max}:3352, 3120, 2982, 2690,2324,1735,1625,1562,1215,1003,746, **^{1}H NMR (DMSO-d$_6$, 300 MHz) δ:** 1,90(s,3H,CH_3),2.30(q,3H,CH_3),2.56(t,3H,CH_3), 2.81(t,2H,CH_2),3.23(t,2H,CH_2),4.22(s,1H,NH),7.25-7.89(m,*J*=7.4 Hz,3H,Ar-H),**^{13}C NMR (DMSO-d$_6$,75 MHz) δ:** 13.1,43.1,49.1,51.7,52.3,118.8,123.9, 125.5,131.2,135.3,136.9, 151.5, 159.5,**Mass:** *m/z* 354 (M^+),356(M+2),***Anal*. Calcd.** for **$C_{15}H_{20}N_3O_2Br$:** C, 71.14; H, 7.52; N, 11.30. Found: C, 69.78; H, 6.05; N, 12.18. Yield: 79% , M.P: 129-131^{0}C.

3.3.k. 6-bromo-3-(2-(diethylamino)ethyl)quinazoline-2,4(1H,3H)-dione

IR (cm^{-1}) ν_{max}:3346, 3118, 2972, 2670,2344,1755,1603, 1590,1542,1210,986,725, **^{1}H NMR (DMSO-d$_6$, 300 MHz) δ:** 1,85(t,6H,CH_3),2.25(q,2H,CH_2),2.43(t,3H,CH_2),2.78(t,2H,CH_2), 4.12(s,1H,NH),7.23-7.819(m,*J*=7.4 Hz,3H,Ar-H),**^{13}C NMR (DMSO-d$_6$,75 MHz) δ:** 16.5,40.1,42.1,45.7,49.3,112.8,120.9, 122.5,136.2,140.3,143.9,154.5,160.5,**Mass:** *m/z* 340 (M^+),342(M+2),***Anal*. Calcd.** for **$C_{14}H_{18}N_3O_2Br$:** C, 62.16; H, 9.88; N, 10.27. Found: C, 61.78; H, 8.25; N, 12.19. Yield: 82% , M.P: 134-136^{0}C.

3.3.l. 6-bromo-3-(2-(dimethylamino)ethyl)quinazoline-2,4(1H,3H)-dione

IR (cm^{-1}) ν_{max}:3234, 3185, 2962, 2673,2290,1755,1655, 1615,1552,1280,950,726, **^{1}H NMR (DMSO-d$_6$, 300 MHz) δ:** 1,24(s,6H,CH_3),2.81(t,2H,CH_2), 3.12(t,2H,CH_2), 4.10(s,1H,NH), 7.10-7.63(m,*J*=7.4 Hz,3H,Ar-H),**^{13}C NMR(DMSO-d$_6$,75MHz) δ:** 10.2,41.1,46.2, 50.3,51.3,114.8,121.9,122.5,128.2,130.3,140.9,149.5,162.5,**Mass:** *m/z* 312 (M^+),314(M+2),***Anal*. Calcd.** for **$C_{12}H_{14}N_3O_2Br$:** C, 61.14; H, 9.12; N, 10.23. Found: C, 60.78; H, 8.98; N, 10.18. Yield: 70% , M.P: 131-133^{0}C.

3.3.m. 3-(2-(ethyl(methyl)amino)ethyl)-6-iodoquinazoline-2,4(1H,3H)-dione

IR (cm^{-1}) ν_{max}:3422, 3098, 2922, 2602,2295,1756,1595, 1575,1562,1195,1020,698, **^{1}H NMR (DMSO-d$_6$, 300 MHz) δ:** 1,32(t,3H,CH_3), 2.01(q,3H,CH_2), 2.06 (s,3H,CH_3), 2.79(t,2H,CH_2),3.13(t,2H,CH_2),4.10(s,1H,NH),7.10-7.53(m,*J*=7.4 Hz,3H,Ar-H),**^{13}C NMR (DMSO-d$_6$,75 MHz) δ:** 10.2, 40.1, 43.4, 48.7, 51.3, 114.8, 121.9, 123.5, 130.9, 132.3, 138.2,

154.6, 158.6,**Mass:** *m/z* 372 (M^+), ***Anal.*** **Calcd.** for $\mathbf{C_{13}H_{16}N_3O_2I}$**:** C, 58.14; H, 9.21; N, 11.37. Found: C, 57.78; H, 9.05; N, 10.18. Yield: 75% , M.P: 372-374^{0}C.

3.3.n. 3-(3-(diethylamino)propyl)-6-iodoquinazoline-2,4(1H,3H)-dione

IR (cm^{-1}) ν_{max}:3398, 3113, 2968, 2598,2328,1695,1665,1612,1543,1205,974,698, **^{1}H NMR (DMSO-d_6, 300 MHz) δ:** 1,2(t,6H,CH_3),2.1(q,4H,CH_2),2.3(t,2H,CH_2), 2.62(m,2H,CH_2), 3.10(t,2H,CH_2),4.12(s,1H,NH),7.10-7.65(m,*J*=7.4 Hz,3H,Ar-H),**^{13}C NMR (DMSO-d_6,75 MHz) δ:**10.3,35.2,43.4,47.3.7,50.3,112.4,121.5, 124.3,129.4,132.5,134.2,149.5,162.5,**Mass:** *m/z* 372 (M^+),***Anal.*** **Calcd.** for $\mathbf{C_{15}H_{20}N_3O_2I}$**:** C, 56.19; H, 7.28; N, 12.72; S. Found: C, 57.23; H, 8.12; N, 11.20. Yield: 74%, M.P: 165-167^{0}C.

3.3.o. 3-(2-(diethylamino)ethyl)-6-iodoquinazoline-2,4(1H,3H)-dione

IR (cm^{-1}) ν_{max}:3402, 3170, 2902, 2670,2421,1765,1675, 1605,1552,1205,1005,684, **^{1}H NMR (DMSO-d_6, 300 MHz) δ:** 1,56 (t,6H,CH_3), 2.15 (q,4H,CH_2), 2.3(t,2H,CH_2), 2.5(t,2H,CH_2), 4.10(s,1H,NH),7.05-7.65(m,*J*=7.4 Hz,3H,Ar-H),**^{13}C NMR (DMSO-d_6,75 MHz) δ:** 11.6, 32.2, 41.1, 45.7, 48.3, 128.8,132.9, 134.5, 136.2, 140.3,141.9, 165.5, 168.5, **Mass:** *m/z* 387 (M^+),***Anal.*** **Calcd.** for $\mathbf{C_{14}H_{18}N_3O_2I}$**:** C, 52.13; H, 9.28; N, 9.37. Found: C, 51.78; H, 8.86; N, 10.18. Yield: 70%, M.P: 143-145^{0}C.

3.3.p. 3-(2-(dimethylamino)ethyl)-6-iodoquinazoline-2,4(1H,3H)-dione

IR (cm^{-1}) ν_{max}:3405, 3190, 2962, 2592,2124,1745,1685,1615,1422,1285,1113,678, **^{1}H NMR (DMSO-d_6,300 MHz) δ:**1,5(s,6H,CH_3),2.56(t,3H,CH_2), 2.71(t,2H,CH_2),4.15(s,1H,NH),7.32-7.6(m,*J*=7.4Hz,3H,Ar-H),**^{13}C-NMR(DMSO-d_6,75MHz) δ:**14.1,38.1, 43.2,48.7,49.3, 112.8, 118.9,123.5,128.2,133.3,138.9, 164.5,167.5, **Mass:** *m/z* 359 (M^+).***Anal.*** **Calcd.** for $\mathbf{C_{12}H_{14}N_3O_2I}$**:** C, 52.18; H, 9.48; N, 10.42. Found: C, 53.78; H, 8.02; N, 10.18. Yield: 74%, M.P: 155-157^{0}C.

4.ANTIBACTERIAL ACTIVITY:

The *in vitro* antibacterial activity *6-bromo-3-(2-(ethyl(methyl)amino)ethyl)-2-thioxo-2,3-dihydroquinazolin-4(1H)-one**(3a-j)*** and *6-bromo-3-(2-(ethyl(methyl)amino)ethyl)quinazoline-2,4(1H,3H)-dione**(3i-p)*** was assessed against three representative Gram-positive bacteria *viz. Bacillus subtilis*, *Bacillus sphaericus* and *Staphylo- coccus aureus*, and three Gram-negative bacteria *viz. Pseudomonas aeruginosa*, *Klebsiella aerogenes* and *Chromobacterium violaceum* by the broth dilution method recommended by National Committee for Clinical Laboratory Standards[27]**(Table 2).**

In the series of **30,31(a-p)**, the compounds **30b,30d,30f,30h** and **31j,31l,31n,31p** are found to be the most active against Gram-positive bacteria and the Gram-negative bacteria.

5.ANTIFUNGAL ACTIVITY

The compounds 3(a-p) were also screened for their antifungal activity against *Candida albicans* (*C.albicans*)(ATCC 10231), *Aspergillus fumigates(A.fumigatus)* (HIC 6094), *Trichophyton rubrum(T. rubrum)* (IFO 9185), and *Trichophyton mentagrophytes(T. mentagrophytes)* (IFO 40996) in dimethyl sulfoxide (DMSO) by disc difusion method. Amphotericin B was used as a standard drug and the mean inhibition zone (MZI) data were measured and compared with controls, the MZI values of the compounds screened are given in Table 4 & 5.Among the screened compounds, compound 30a,30c and 30g showed good antifungal activity. Remaining compounds showed moderate anti fungal activity against test compounds.

Table 2: Antibacterial activity of compounds 3(a-h).

Compd.	Minimum Inhibitory Concentration (MIC) in μg/mL					
	B. subtilis	*B. sphaericus*	*S. aureus*	*P. aeruginosa*	*K. aerogenes*	*C. violaceum*
3a	26	25	25	26	27	18
3b	31	28	28	32	33	27
3c	28	26	27	31	32	26
3d	30	27	28	34	34	27
3e	26	25	21	16	17	22
3f	32	28	29	34	33	28
3g	16	20	22	28	26	24
3h	32	28	28	33	33	26
SM	31	27	28	33	34	26

SM = Streptomycin.

Figure1:Graphical form of Anti-Bacterial Screening:

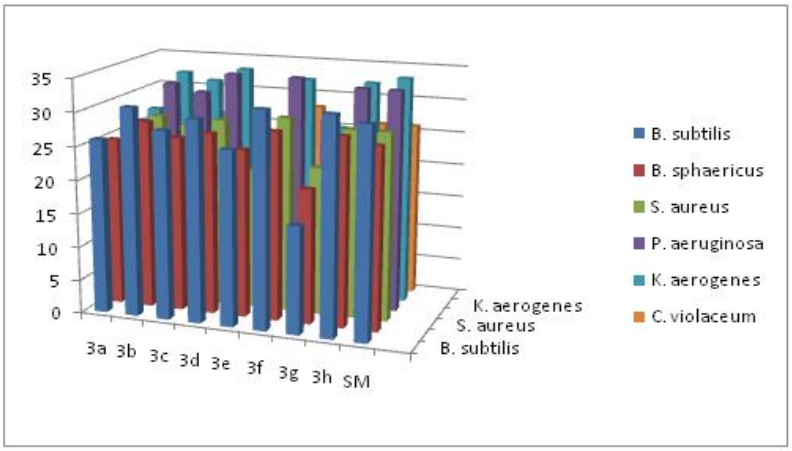


Table 3: Antibacterial activity of compounds 3(i-p).

Compd.	Minimum Inhibitory Concentration (MIC) in μg/mL					
	B. subtilis	*B. sphaericus*	*S. aureus*	*P. aeruginosa*	*K. aerogenes*	*C. violaceum*
3i	18	19	32	28	22	26
3j	32	29	33	29	29	30
3k	22	24	30	28	26	26
3l	33	30	36	31	30	30
3m	18	28	30	16	22	30
3n	34	30	32	31	29	28
3o	30	28	24	20	22	26
3p	32	28	32	28	28	28
SM	32	29	34	30	28	29

SM = Streptomycin.

Figure2:Graphical form of Anti-Bacterial Screening:

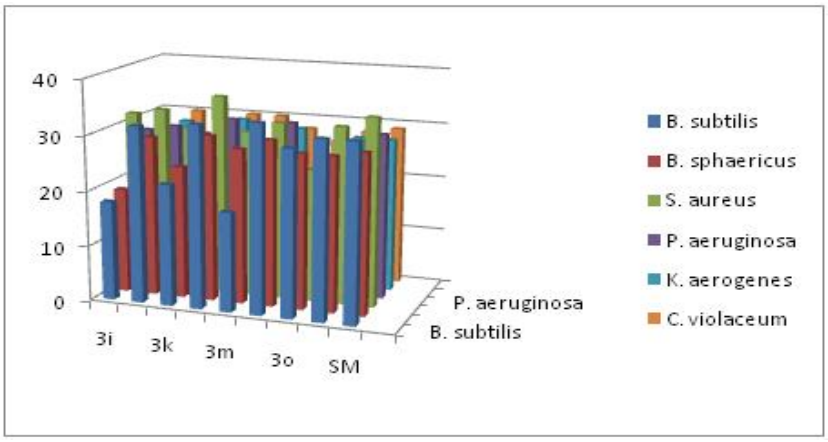


Table 4. Antifungal Activity of Compounds 3(a-h)

Compnd	Mean zone inhibition (MZI)[a] in 10 μg/mL			
	C. albicans	*A. fumigatus*	*T. rubrum*	*T. mentagropytes*
3a	26	21	16	18
3b	29	30	25	28
3c	26	26	26	29
3d	29	30	27	29
3e	29	18	22	22
3f	30	31	27	29
3g	16	18	22	21
3h	29	31	27	30
Amphotericin B	29	30	26	29

[a]Values are mean (n = 3).

Figure3:Graphical form of Anti-Fungal Screening:

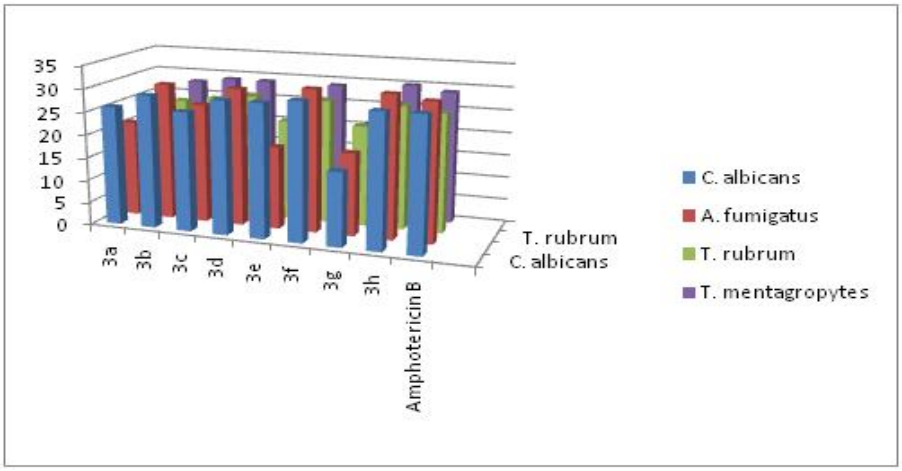
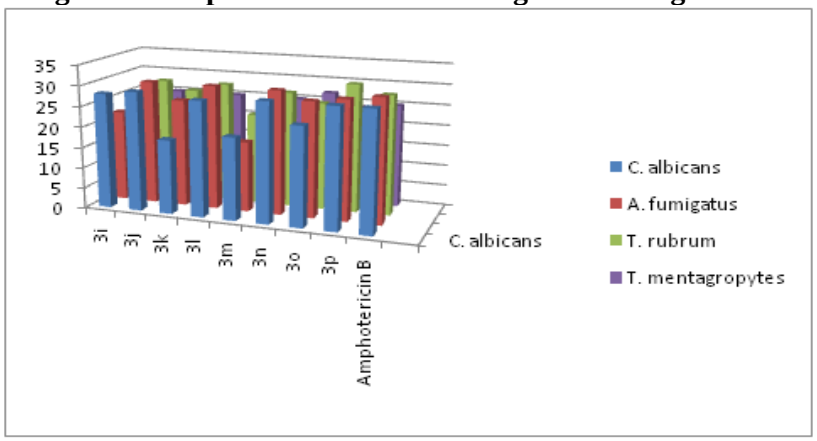


Table 5. Antifungal Activity of Compounds 3(i-p)

Compnd	Mean zone inhibition (MZI)[a] in 10 μg/mL			
	C. albicans	*A. fumigatus*	*T. rubrum*	*T. mentagropytes*
3i	28	22	21	20
3j	29	30	29	25
3k	18	26	27	22
3l	28	30	29	25
3m	20	17	22	20
3n	29	30	28	25
3o	24	28	26	27
3p	29	29	31	24
Amphotericin B	29	30	29	25

[a]Values are mean (n = 3).

Figure4 : Graphical form of Anti-Fungal Screening:



Inhibition zone in mm(indicates no inhibitory activity)

6. CONCLUSIONS

In conclusion, a series of quinazoline **30,31(a-p)** was prepared. The antibacterial activity of these compounds was evaluated against various bacteria. The compounds showed variable degree of antimicrobial activity. Among the screened compounds **30b,30d,30f,30h** and **31j,31l,31n,31p** were found to be the most active against all the microorganisms employed both for antibacterial and antifungal activity. With this set of analogues, we are now in a position to investigate the multiple biological activities of these compounds.

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