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Original Article

Synthesis and Antimicrobial Evaluation of New (4-Oxo-thiazolidinyl)quinazolin-4(3*H*)ones of 2-[(2,6-Dichlorophenyl)amino]phenylacetic acid

Navin B.Patel* and Virendra N.Patel

Department of Chemistry, Veer Narmad South Gujarat University, SURAT-395007, India.

Abstract

Synthesis of 2-[2-(2,6-dichlorophenyl)amino]phenylmethyl-3-[4-(2-substitutedphenyl-4-oxo-thiazolidinyl)aryl]-6-bromo quinazolin-4(3*H*)ones $\mathbf{VI}_{a-j}$ have been achieved from the starting material 2-[(2,6-dichlorophenyl)amino] phenylacetic acid **I** to benzoxazine **III,** Further reaction with *p*-phenylindiamine and substituted aromatic aldehyde gave 2-[2-(2,6-dichlorophenyl)amino]phenyl methyl-3-(4-aminoaryl)-6-bromo quinazolin-4(3*H*)-ones **IV** and 2-[2-(2,6-dichlorophenyl)amino]phenylmethyl-3-[4-(2-substituted arylidene)aryl]-6-bromo quinazolin-4(3*H*)ones $\mathbf{V}_{a-j}$ respectively**.** $\mathbf{V}_{a-j}$ on cyclization with thioglycolic acid gave $\mathbf{VI}_{a-j}$. All the synthesized compounds have been characterized on the basis of elemental analysis, IR and ^1H-NMR spectral data. They were screened for antibacterial and antifungal activity at two concentrations and compared with the standard drugs penicillin-G, ampicillin, and amoxicillin. The compounds containing 4-OCH_3 and 3, 4, 5-$(OCH_3)_3$ showed good activity, compared with the standard drugs.

Keywords: Quinazolinone; Thiazolidinone; P-Phenylenediamine; Antibacterial; Antifungal.

Introduction

Quinazolinones are an important class of fused heterocycles, enjoying considerable interest on account of their diverse range of biological activity, such as antimicrobial, antihypertensive, CNS depressants, anti-inflammatory,and potent hypotensive activity in anesthetized rabbits and in conscious spontaneously hypertensive rats. They have also been screened for their analgesic,and acrogenic activities and those compounds, which showed a promising anti-inflammatory activity, were also screened for their cyclo-oxygenase assay (1-3).

Non-steroidal anti-inflammatory drugs (NSAIDs) are widely used for the treatment of pain, fever and inflammation, particularly arthritis. Among the most popular NSAIDs, 2-[(2,6-dichlorophenyl) amino]phenyl acetic acid has been approved in 120 countries since its introduction 25 years ago and is ranked 30thamong the top 200 drug with respect to new prescriptions and in the United States alone (4). Schiff base (arylidene) possesses a variety of activities viz. anticancer, antifungal and hypotensive (5-6). Thiazolidine is an importance class of drugs with several types of biological activity such as anti-HIV, anthelmintic, anti-inflammatory and anti-convulsant properties (7-10).A combination of two or more biologically active moiety could increase or decrease the activity. Keeping this aspects, we thought to extend our previous work on quinazolinone frame work with various substituted aryl acetamides and substituted aryl amines (11, 12).We prepared 2-[2-(2,6-

* Corresponding author:
E-mail: drnavin@satyam.net.in

dichlorophenyl)amino]phenylmethyl-3-[4-(2-substitutedphenyl-4-oxo-thiazolidinyl)aryl]-6-bromo quinazolin-4(3*H*)ones **VI**$_{a-j}$ via 2-[2-(2,6-dichlorophenyl)amino]phenylmethyl-3-[4-(2-substitutedarylidene)aryl]-6-bromo quinazolin-4(3*H*)ones **V**$_{a-j}$ and studied their antimicrobial activities.

Experimental

Melting points were determined in open capillaries and were left uncorrected. The IR spectra were recorded on Perkin-Elmer-843 spectrometer, using KBr pallets. ^{1}*H*-NMR spectra were scanned on Bruker DPX-200 FT-NMR spectrometer at 300 MHz, using TMS as the internal standard and $CDCl_3$ as solvent (chemical shift in δ ppm). The compounds gave satisfactory C and N analysis. Samples were routinely purified by crystallization from ethanol: benzene (1:3) and checked by TLC.

2-[2-(2,6-Dichlorophenyl)amino]phenylmethyl-3-[4-(2-ubstitutedphenyl-4-oxo-thiazolidinyl)aryl]-6-bromo quinazolin-4(3*H*)ones **VI**$_{a-j}$ were synthesized by the following synthetic route. Acid **I** on reaction with thionyl chloride gave the corresponding acid chloride **II**, that on cyclization with 5-bromo anthranilic acid gave **III**, which on treatment with *p*-phenylindiamine gave **IV** in good yield. Then, **IV** on reaction with substituted aromatic aldehydes converted to 2-[2-(2,6-dichlorophenyl)amino]phenylmethyl-3-[4-(2-substitutedarylidene)aryl]-6-bromo quinazolin-4(3*H*)ones **V**$_{a-j}$, which on cyclization with thioglycolic acid gave 2-[2-(2,6-dichlorophenyl)amino]phenylmethyl-3-[4-(2-substitutedphenyl-4-oxo-thiazolidinyl)aryl]-6-bromo quinazolin-4(3*H*)ones **VI**$_{a-j}$. Structure of compounds **V**$_{a-j}$ and **VI**$_{a-j}$ was established on the basis of elemental and spectral data. The bands of methyl and methylene stretching vibrations were observed near 2926 & 2853 cm^{-1}, broad band of N-H stretching at 3450-3350 cm^{-1}, bands of C=O stretching vibrations at 1700-1660 cm^{-1} and 1725-1738 cm^{-1} (quinazolinone), A strong absorption band near 1640-1580 cm^{-1} indicated the presence of –N=CH- (Schiff base).The C=O stretching of thiazolidin ring was observed at 1760-1755 cm^{-1}. ^{1}*H* NMR spectra of all synthesized compounds showed a singlet of –N=CH- at 6.00, a singlet of –CH_2-S- at 3.65. The multiplets of aromatic rings were observed in the range of 6.60-7.85 δ ppm.

2-[(2,6-Dichlorophenyl)amino]phenylacetyl chloride II

2-[(2,6-Dichlorophenyl)amino]phenylacetic acid **I** (0.01 mol) was dissolved in dry benzene (50 ml). To this solution thionyl chloride (0.01 mol) was added dropwise in 1 h, with occasional stirring. The reaction mixture was refluxed on water bath for 2 h and protected from humidity with calcium chloride guard tube. When evolution of HCl and SO_2 ceased, the excess of thionyl chloride was removed by distillation with benzene.

2-*[2-(2,6-Dichlorophenyl)amino]phenylmethyl-6-bromo-3,1-benzoxazin-4(H)one III*

2-[(2,6-Dichlorophenyl)amino]phenylacetyl chloride **II** (0.01mol) dissolved in pyridine (60 ml). To this solution 5-bromo anthranilic acid (0.01 mol) in pyridine was added dropwise at 0-5 °C in 1h, stirred for 2h and further refluxed for 1h on an oil bath. The reaction mixture was poured into ice-cold water containing concentrated. HCl.The separated solid was filtered, washed and recrystalized from ethanol. M.P.- 200 °C, Yield-60%, **IR (KBr):**ν_{max} (cm^{-1}) 3445 (NH Secondary), 2925, 2842 (C-H), 1672 (C=O), 1615 (C=N); 1310 (C-N), 1140 (C-O-C), 785 (C-Cl), 615 (C-Br); **^{1}*H*-NMR** (chemical shift in δ ppm) -NH- (1H, s, 9.45), Ar-H (10H, m, 6.25-7.63), -CH_2- (2H, s, 3.70).

2-[2-(2,6-Dichlorophenyl)amino)]phenylmethyl-3-(4-aminoaryl)-6-bromo quinazolin-4(3H)ones IV

2-[2-(2,6-Dichlorophenyl)amino]phenylmethyl-6-bromo-3,1-benzoxazin-4-(*H*)one **III** (0.476 g, 0.001 mol) and *p*-phenylindiamine (0.108 g, 0.001 mol) were dissolved in pyridine (40 ml), heated on an oil bath at 180-200°C for 5-6h and poured into ice-cold water containing concentrated. HCl. The separated solid was filtered, washed and recrystalized from ethanol. Yield-55%, M.P.- 210 °C; **IR (KBr):**ν_{max} (cm^{-1}) 3505 (NH_2 Primary), 3440 (NH Secondary), 2920, 2845 (C-H), 1665 (C=O), 1610 (C=N); 1324 (C-N), 1140 (C-O-C), 620 (C-Br); **^{1}*H*-**

NMR (chemical shift in δ ppm) -NH- (1H, s, 9.55), Ar-H (14H, m, 6.30-7.60), $-NH_2$ (2H, s, 5.75), $-CH_2-$ (2H, s, 3.65).

2-[2-(2,6-Dichlorophenyl)amino]phenylmethyl-3-[4-(4-hydroxyarylidene) aryl]-6-bromo quinazolin-4(3H)ones V_d

2-[2-(2,6-Dichlorophenyl)amino]phenyl methyl-3-(4-aminoaryl)-6-bromo quinazolin-4(3*H*)ones **IV** (0.001 mol) and 4-hydroxy benzaldehyde (0.001 mol) were dissolved in absolute ethanol (40 ml),by the addition of a few drops of glacial acetic acid . The reaction mixture was refluxed for 6h on a water bath and poured into ice cold water. The separated solid was filtered, washed and recrystalized from ethanol.

Similarly, other derivatives were prepared by the same method.

2-[2-(2,6-Dichlorophenyl)amino]phenylmethyl-3-[4-(4-hydroxyphenyl-4-oxo-thiazolidinyl)aryl]-6-bromo quinazolin-4(3H)ones VI_d

2-[2-(2,6-dichlorophenyl)amino]phenylmethyl-3-[4-(4-hydroxyarylidene) aryl]-6-bromo quinazolin-4(3*H*)ones $\mathbf{V_d}$ (0.001 mol) were dissolved in dry DMF (50 ml), containing a pinch of anhydrous $ZnCl_2$ and thioglycolic acid (0.002 mol) and refluxed for 8h. Excess of solvent was distilled off and the residual reaction mixture cooled and poured into ice cold water. The separated solid was filtered, washed and recrystalized from ethanol.

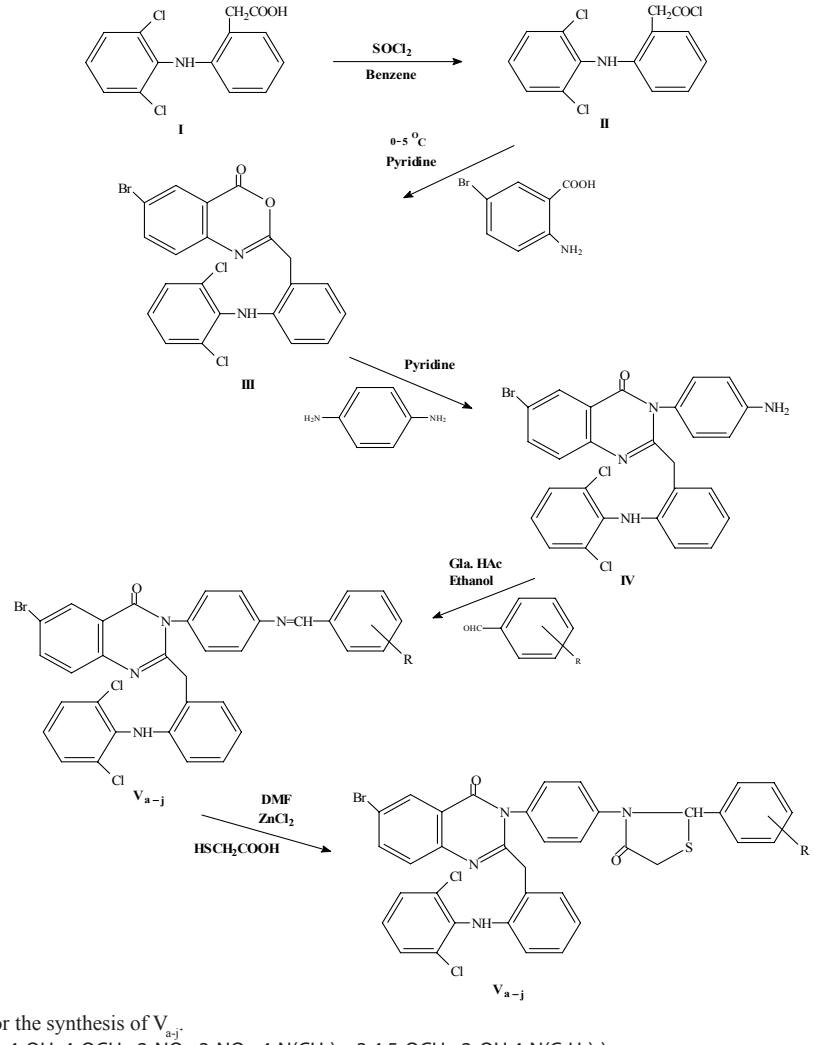

Figure 1. Scheme for the synthesis of V_{a-j}.
(R = 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH_3, 2-NO_2, 3-NO_2, 4-$N(CH_3)_2$, 3,4,5-OCH_3, 2-OH 4-$N(C_2H_5)_2$).

Table 1. Characterization data of compounds V_{a-j} and VI_{a-j}.

Compound	R	M.P (°C)	Yield (%)	Crystalization solvent	Mol. Formula	Found(Calcd) %		
						C	H	N
V_a	2-Cl	144-145	60	Ethanol	$C_{34}H_{22}ON_4BrCl_3$	59.18 59.26	3.12 3.19	8.07 8.13
V_b	4-Cl	163-164	62	Ethanol	$C_{34}H_{22}ON_4BrCl_3$	59.18 59.26	3.12 3.19	8.07 8.13
V_c	2-OH	154-155	58	Ethanol	$C_{34}H_{23}ON_4BrCl_2$	60.80 60.89	3.35 3.43	8.27 8.36
V_d	4-OH	164-165	61	Ethanol	$C_{34}H_{23}ON_4BrCl_2$	60.80 60.89	3.35 3.43	8.27 8.36
Ve	4-OCH_3	159-160	63	Ethanol	$C_{35}H_{26}O_2N_4BrCl_2$	61.23 61.31	3.73 3.79	8.09 8.17
V_f	2-NO_2	175-176	62	Ethanol	$C_{34}H_{22}O_3N_5BrCl_2$	58.27 58.36	3.08 3.15	9.96 10.01
V_g	3-NO_2	166-167	60	Ethanol	$C_{34}H_{22}O_3N_5BrCl_29$	58.27 58.36	3.08 3.15	9.96 10.01
V_h	4-$N(CH_3)_2$	180-181	64	Ethanol	$C_{36}H_{28}ON_5BrCl_2$	61.89 61.98	3.95 4.02	9.98 10.04
V_i	3,4,5-$(OCH_3)_3$	150-151	61	Ethanol	$C_{37}H_{29}O_4N_4BrCl_2$	59.61 59.68	4.82 3.90	7.44 7.53
V_j	2-OH,4- $N(C_2H_5)_2$	142-143	65	Ethanol	$C_{38}H_{32}O_2N_5BrCl_2$	61.47 61.54	4.25 4.32	9.37 9.45
VI_a	2-Cl	157-158	55	Ethanol	$C_{36}H_{24}O_2N_4SBrCl_3$	56.47 56.65	3.08 3.15	7.27 7.34
VI_b	4-Cl	178-179	57	Ethanol	$C_{36}H_{24}O_2N_4SBrCl_3$	56.47 56.65	3.08 3.15	7.27 7.34
VI_c	2-OH	170-171	53	Ethanol	$C_{36}H_{25}O_3N_4SBrCl_2$	57.98 58.06	3.28 3.36	7.46 7.52
VI_d	4-OH	179-180	55	Ethanol	$C_{36}H_{25}O_3N_4SBrCl_2$	57.98 58.06	3.28 3.36	7.46 7.52
VI_e	4-OCH_3	172-173	57	Ethanol	$C_{37}H_{28}O_3N_4SBrCl_2$	58.40 58.49	3.61 3.68	7.29 7.37
VI_f	2-NO_2	185-186	56	Ethanol	$C_{36}H_{24}O_4N_5SBrCl_2$	55.81 55.88	3.02 3.10	8.99 9.05
VI_g	3-NO_2	171-176	54	Ethanol	$C_{36}H_{24}O_4N_5SBrCl_2$	55.81 55.88	3.02 3.10	8.99 9.05
VI_h	4-$N(CH_3)_2$	193-194	57	Ethanol	$C_{38}H_{30}O_2N_5SBrCl_2$	59.09 59.14	3.81 3.89	9.00 9.07
VI_i	3,4,5-$(OCH_3)_3$	165-166	56	Ethanol	$C_{39}H_{31}O_5N_4SBrCl_2$	57.15 57.21	3.70 3.78	6.77 6.84
VI_j	2-OH,4-$N(C_2H_5)_2$	158-159	58	Ethanol	$C_{40}H_{34}O_3N_5SBrCl_2$	58.80 58.89	4.09 4.17	8.51 8.58

Similarly, the other thiazolidinone derivatives were prepared by the same method. The characterization data, IR spectral data, ^1H-NMR spectral data and antimicrobial activity of all

Table 2. IR spectral data.

Compound	IR(cm^{-1})
V_a	3442 (NH), 2920, 2846 (C-H), 1680 (C=O), 1625 (-N=CH-), 1610 (C=N), 1320 (C-N), 765 (C-Cl), 625 (C-Br)
V_b	3445 (NH), 2925, 2852 (C-H), 1685 (C=O), 1638 (-N=CH-), 1614 (C=N), 1322 (C-N), 770 (C-Cl), 622 (C-Br)
V_c	3440 (NH), 3255 (O-H), 2914, 2842 (C-H), 1686 (C=O), 1610 (C=N); 1634 (-N=CH-), 1324 (C-N),780 (C-Cl), 630 (C-Br)
V_d	3438 (NH), 3252 (O-H), 2915, 2845 (C-H), 1675 (C=O), 1605 (C=N); 1630 (-N=CH-), 1322 (C-N),785 (C-Cl), 620 (C-Br)
Ve	3430 (NH), 2925, 2840 (C-H), 1668 (C=O), 1635 (-N=CH-), 1612 (C=N), 1318 (C-N), 1015, 1210 (C-O-C), 770 (C-Cl), 628 (C-Br)
V_f	3440 (NH), 2920, 2845 (C-H), 1675 (C=O) 1628 (-N=CH-), 1610 (C=N), 1375, 1555 (-NO_2 sym, asym), 1320 (C-N), 775 (C-Cl), 624 (C-Br)
V_g	3448 (NH), 2926, 2842 (C-H), 1679 (C=O) 1632 (-N=CH-), 1615 (C=N), 1370, 1552 (-NO_2 sym, asym), 1322 (C-N), 783 (C-Cl) , 626 (C-Br)
V_h	3446 (NH), 2925, 2845 (C-H), 1684 (C=O), 1628 (-N=CH-), 1610 (C=N), 1320 (C-N),765 (C-Cl), 629 (C-Br)
V_i	3447 (NH), 2935, 2842 (C-H), 1690 (C=O), 1640 (-N=CH-), 1614 (C=N), 1322 (C-N), 1012, 1215 (C-O-C), 775 (C-Cl) , 632 (C-Br)
V_j	3448 (NH), 2925, 2856 (C-H), 1685 (C=O), 1628 (-N=CH-), 1616 (C=N), 1315 (C-N), 782 (C-Cl), 623 (C-Br)
VI_a	3436 (NH), 2925, 2840 (C-H), 1735 (C=O of Thiazolidinone), 1680 (C=O), 1620 (C=N), 1310 (C-N), 765 (C-Cl), 625 (C-Br)
VI_b	3438 (NH), 2935, 2849 (C-H), 1730 (C=O of Thiazolidinone), 1682 (C=O), 1624 (C=N), 1315 (C-N), 770 (C-Cl), 628 (C-Br)
VI_c	3435 (NH), 3255 (O-H), 2920, 2845 (C-H), 1730 (C=O of Thiazolidinone), 1675 (C=O), 1615 (C=N), 1325 (C-N), 770 (C-Cl), 630 (C-Br)
VI_d	3440 (NH), 3254 (O-H), 2926, 2850 (C-H), 1729 (C=O of Thiazolidinone), 1680 (C=O), 1620 (C=N), 1322 (C-N), 772 (C-Cl), 624 (C-Br)
VI_e	3435 (NH); 2928, 2842 (C-H); 1742 (C=O of Thiazolidinone), 1685 (C=O); 1615 (C=N), 1312 (C-N); 1018, 1210 (C-O-C), 780 (C-Cl), 620 (C-Br)
VI_f	3438 (NH), 2914, 2830 (C-H), 1736 (C=O of Thiazolidinone), 1684 (C=O), 1620 (C=N), 1360, 1554 (-NO_2 sym, asym), 1317 (C-N), 769 (C-Cl), 626 (C-Br)
VI_g	3435 (NH), 2910, 2828 (C-H), 1738 (C=O of Thiazolidinone), 1672 (C=O), 1615 (C=N), 1365, 1550 (-NO_2 sym, asym), 1315 (C-N), 762 (C-Cl), 625 (C-Br)
VI_h	3444 (NH); 3248 (O-H), 2921, 2850 (C-H), 1745 (C=O of Thiazolidinone), 1685 (C=O), 1616 (C=N); 1324 (C-N); 783 (C-Cl) , 628 (C-Br)
VI_i	3435 (NH); 2925, 2840 (C-H); 1740 (C=O of Thiazolidinone), 1675 (C=O); 1605 (C=N), 1315 (C-N); 1020, 1205 (C-O-C), 785 (C-Cl), 623 (C-Br)

the synthesized compounds are given in s1-4, respectively.

Results and Discussion

Antibacterial and antifungal activity of all the synthesized compounds were screened against four different strain of two gram-positive bacteria (*Pseudomonas Sp.* & *B.subtilis*) and two gram-negative (*Ceretium* & *E.coli*) bacteria, for two different concentration of 100 µg/ml and 200 µg/ml, using the disk method (13). The growth of inhibition of bacteria was compared with the standard drug penicillin-G, ampicillin, and amoxicillin. These compounds were also tested for their antifungal activity against *C.albicans*,

Table 3. ^{1}H-NMR spectral data.

Compound	^{1}*H*-NMR (δ ppm)
V_a	-NH- (1H, s, 9.42), -N=CH- (1H, s, 6.21), C_5-H qui. (1H, d, 7.80), C_6-H qui. (1H, d, 7.40), C_8-H qui. (1H, s, 7.32), -CH_2- (2H, s, 3.77)
V_b	-NH- (1H, s, 9.47), -N=CH- (1H, s, 6.23), C_5-H qui. (1H, d, 7.82), C_6-H qui. (1H, d, 7.38), C_8-H qui. (1H, s, 7.30), -CH_2- (2H, s, 3.75)
V_c	NH- (1H, s, 9.38), -N=CH- (1H, s, 6.25), C_5-H qui. (1H, d, 7.78), C_6-H qui. (1H, d, 7.45), C_8-H qui. (1H, s, 7.35), -CH_2- (2H, s, 3.75), -OH (1H, s, 4.95)
V_d	NH- (1H, s, 9.36), -N=CH- (1H, s, 6.18), C_5-H qui. (1H, d, 7.76), C_6-H qui. (1H, d, 7.35), C_8-H qui. (1H, s, 7.26), -CH_2- (2H, s, 3.75), -OH (1H, s, 4.90)
V_e	-NH- (1H, s, 9.40), -N=CH- (1H, s, 6.15), C_5-H qui. (1H, d, 7.85), C_6-H qui. (1H, d, 7.48), C_8-H qui. (1H, s, 7.32), -CH_2- (2H, s, 3.78), -OCH_3 (3H, s, 3.62)
V_f	-NH- (1H, s, 9.45), -N=CH- (1H, s, 6.20), C_5-H qui. (1H, d, 7.88), C_6-H qui. (1H, d, 7.37), C_8-H qui. (1H, s, 7.29), -CH_2- (2H, s, 3.75)
V_g	-NH- (1H, s, 9.36), -N=CH- (1H, s, 6.14), C_5-H qui. (1H, d, 7.79), C_6-H qui. (1H, d, 7.42), C_8-H qui. (1H, s, 7.33), -CH_2- (2H, s, 3.69)
V_h	-NH- (1H, s, 9.47), -N=CH- (1H, s, 6.16), C_5-H qui. (1H, d, 7.90), C_6-H qui. (1H, d, 7.45), C_8-H qui. (1H, s, 7.30), -CH_2- (2H, s, 3.62) -$(CH_3)_2$ (6H, s, 2.84)
V_i	NH- (1H, s, 9.42), -N=CH- (1H, s, 6.15), C_5-H qui. (1H, d, 7.86), C_6-H qui. (1H, d, 7.36), C_8-H qui. (1H, s, 7.28), -CH_2- (2H, s, 3.78) -OCH_3 (9H, s, 3.56)
V_j	-NH- (1H, s, 9.55), C_5-H qui. (1H, d, 7.82), C_6-H qui. (1H, d, 7.34), C_8-H qui. (1H, s, 7.25), -CH-Ar (1H, s, 6.23), -CH_2- (2H, s, 3.70), -N-CH_2- (4H, q, 2.88), -CH_3 (6H, t, 1.30)
VI_a	-NH- (1H, s, 9.45), C_5-H qui. (1H, d, 7.90), C_6-H qui. (1H, d, 7.40), C_8-H qui. (1H, s, 7.34),-CH-Ar (1H, s, 6.22), -CH_2-S- (2H, s, 3.74), -CH_2- (2H, s, 3.67)
VI_b	-NH- (1H, s, 9.50), C_5-H qui. (1H, d, 7.92), C_6-H qui. (1H, d, 7.42), C_8-H qui. (1H, s, 7.35), -CH-Ar (1H, s, 6.24), -CH_2-S- (2H, s, 3.76), -CH_2-(2H, s, 3.60)
VI_c	-NH- (1H, s, 9.47), C_5-H qui. (1H, d, 7.89), C_6-H qui. (1H, d, 7.45), C_8-H qui. (1H, s, 7.32), -CH-Ar (1H, s, 6.18), -CH_2-S- (2H, s, 3.70), -CH_2- (2H, s, 3.58), -OH (1H, s, 4.95)
VI_d	-NH- (1H, s, 9.36), C_5-H qui. (1H, d, 7.90), C_6-H qui. (1H, d, 7.40), C_8-H qui. (1H, s, 7.33), -CH-Ar (1H, s, 6.17), -CH_2-S- (2H, s, 3.72), -CH_2- (2H, s, 3.61), -OH (1H, s, 4.92)
VI_e	NH- (1H, s, 9.52), C_5-H qui. (1H, d, 7.90), C_6-H qui. (1H, d, 7.44), C_8-H qui. (1H, s, 7.30), -CH-Ar (1H, s, 6.21), -CH_2-S- (2H, s, 3.74), CH_2- (2H, s, 3.79), -$(OCH_3)_3$ (9H, s, 3.58)
VI_f	-NH- (1H, s, 9.38), C_5-H qui. (1H, d, 7.87), C_6-H qui. (1H, d, 7.40), C_8-H qui. (1H, s, 7.32), -CH-Ar (1H, s, 6.16), -CH_2-S- (2H, s, 3.), -CH_2- (2H, s, 3.69)
VI_g	-NH- (1H, s, 9.34), C_5-H qui. (1H, d, 7.90), C_6-H qui. (1H, d, 7.42), C_8-H qui. (1H, s, 7.30), -CH-Ar (1H, s, 6.24), -CH_2-S- (2H, s, 3.71), -CH_2- (2H, s, 3.55)
VI_h	NH- (1H, s, 9.47), C_5-H qui. (1H, d, 7.85), C_6-H qui. (1H, d, 7.36), C_8-H qui. (1H, s, 7.28), -CH-Ar (1H, s, 6.18), -CH_2-S- (2H, s, 3.74), -CH_2- (2H, s, 3.58) -$(CH_3)_2$ (6H, s, 2.82)
VI_i	-NH- (1H, s, 9.50), C_5-H qui. (1H, d, 7.86), C_6-H qui. (1H, d, 7.38), C_8-H qui. (1H, s, 7.30),-CH-Ar (1H, s, 6.20), -CH_2-S- (2H, s, 3.77), -CH_2- (2H, s, 3.62), -$(OCH_3)_3$ (9H, s, 3.60)
VI_j	-NH- (1H, s, 9.52),), C_5-H qui. (1H, d, 7.92), C_6-H qui. (1H, d, 7.40), C_8-H qui. (1H, s, 7.32), -CH-Ar (1H, s, 6.20), -CH_2-S- (2H, s, 3.75), -CH_2-(2H, s3.68), -N-CH_2- (4H, q, 2.94), -CH_3 (6H, t, 1.28)

using amphotericin-B as the standarddrug, and the cup-plate method (14) at the same concentration.

Antibacterial activity

The screening results of antibacterial activities showed that the presence of bromo group at

Table 4. Antimicrobial Activity of compounds V_{a-j} and VI_{a-j}

Compounds	Antibacterial activity (zone of inhibition in MM.)								Antifungal Activity (zone of inhibition in MM.)	
	Gram -positive				Gram-negative					
	Pseudomonas sp.		*B.subtilis*		*Certium*		*E.coli*		*C.albicans*	
	100 µg/ml	200 µg/ml	100 µg/ml	200 µg/ml	100 µg/ml	200 µg/ml	100 µg/ml	200 µg/ml	100 µg/ml	200 µg/ml
V_a	5	8	4	7	4	8	4	9	1	2
V_b	6	10	5	9	5	12	6	11	2	3
V_c	2	4	3	5	3	7	3	7	1	2
V_d	4	7	5	7	4	6	4	9	2	3
Ve	7	12	10	13	9	10	8	11	4	6
V_f	4	7	6	8	5	10	3	5	1	2
V_g	3	6	3	5	4	7	2	4	_	1
V_h	_	2	_	1	_	1	_	2	_	_
V_i	6	11	8	14	9	14	7	10	4	7
V_j	_	_	_	1	_	_	_	1	_	1
VI_a	5	10	5	8	6	9	5	9	4	6
VI_b	7	10	7	9	8	11	9	13	3	5
VI_c	3	5	3	4	4	7	4	9	1	2
VI_d	4	7	5	8	5	9	6	10	2	3
VI_e	9	12	7	11	8	12	9	13	6	9
VI_f	4	7	6	9	5	8	4	7	2	3
VI_g	3	5	4	6	4	6	3	5	1	2
VI_h	_	_	1	3	_	2	_	1	_	_
VI_i	9	12	9	14	7	11	9	12	7	9
VI_j	_	1	_	2	_	1	_	_	_	_
Penicillin-G	14	26	15	25	13	22	14	25		
Ampicillin	15	26	17	30	18	31	18	29		
Amoxicillin	13	24	16	28	15	27	16	28		
Amphotericin-B									8	15

position-6 of the quinazoline ring,of compounds **V** bearing R= 4-OCH_3 and 3,4,5-$(OCH_3)_3$, showed good activity against *B.subtilis* at 100 µg/ml concentration. At 200 µg/ml concentration, compound **V** bearing R= 4-OCH_3 and 3, 4, 5-$(OCH_3)_3$ showed good activity against *Ceretium*, compared with the standard drug penicillin-G.

Compounds **VI** bearing R=4-OCH_3 and 3, 4, 5-$(OCH_3)_3$ showed good activity against *Pseudomonas Sp.* at 100 µg/ml concentration. At 200 µg/ml concentration, compound **VI** bearing R=4-OCH_3 and 3, 4, 5-$(OCH_3)_3$ showed good activity against *B. subtilis*, compared with the standard.

Compounds **VI** bearing R=4-Cl, 4-OCH_3, 3, 4, 5-$(OCH_3)_3$ showed good activity against *E.Coli* at 100 µg/ml concentration. At 200 µg/ml concentration, compound **VI** bearing R= 4-Cl, 4-OCH_3 and 3, 4, 5-$(OCH_3)_3$ showed good activity against *E.Coli,* compared with ampicillin.

Antifungal activity

In case of bromo group at position-6 of the main moiety, compound **VI** bearing R=4-OCH_3 and 3, 4, 5-$(OCH_3)_3$ showed good activity at 100 µg/ml concentration and at higher concentrations, compound **VI** bearing R=4-OCH_3 and 3, 4, 5-$(OCH_3)_3$ displayed moderate activity against

C.albicans , compared with Amphotericin-B.

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