Acta Poloniae Pharmaceutica – Drug Research, Vol. 67 No. 3 pp. 267–275, 2010 ISSN 0001-6837
Polish Pharmaceutical Society

SYNTHESIS AND MICROBIAL STUDIES OF (4-OXO-THIAZOLIDINYL) SULFONAMIDES BEARING QUINAZOLIN-4(3*H*)ONES

NAVIN B. PATEL*, VIRENDRA N. PATEL, HEMANT R. PATEL, FAIYAZ M. SHAIKH and JAYMIN C. PATEL

Department of Chemistry, Veer Narmad South Gujarat University, Surat-395 007, India

Abstract: 2-[(2,6-Dichlorophenyl)amino]phenylacetic acid (**A**) on reaction with thionyl chloride gave corresponding acid chloride (**B**). A series of (4-oxo-thiazolidinyl)sulfonamides of quinazolin-4(3*H*)ones (**4a-l**) were prepared from Schiff bases (**3a-l**) of 2-[2-(2,6-dichlorophenyl)amino]phenylmethyl-3-[(4-aminophenyl)sulfonamido-1-yl]quinazolin-4(3*H*)one (**D**) and substituted aromatic aldehyde. Newly synthesized compounds have been examined on the basis of elemental analysis, IR, ^{1}H NMR and ^{13}C NMR spectra. Antibacterial activity (minimum inhibitory concentration – MIC) against Gram-positive *(S. aureus* & *S. pyogeneus*) and Gram-negative (*P. aeruginosa* and *E. coli*) bacteria, as well as antifungal acivities (MIC) against *C. albicans, A. niger* and *A. clavatus* were determined by broth dilution method. Some of the compounds were endowed with a remarkable antibacterial as well as antifungal acivities.

Keywords*:* quinazolinone, Schiff base, thiazolidinone, microbial studies

In continuation of our previous work on quinazolinone molecular system by incorporating different substituted amines, acetamide, thiazolidinone and azetidinone on third position of quinazolinone and studies of their antimicrobial activities (1-5), we initiated to forward this work by synthesis of several new compounds of quinazolin-4(3*H*)ones by receiving (4-oxo-thiazolidinyl)sulfonamides.

Quinazolinones and the derivatives thereof are now known to have a wide range of biological properties, e.g. antiviral, anticonvulsant, antitubercular, antimicrobial and antitumor activities (6-11).

Sulfonamides, which have been clinically used for many years, have been found to possess a large number of different biological activities including anticonvulsant, anticancer, antifungal, antitumor and antimicrobial activity (12-16).

Schiff's bases have biological importance and possess variety of activities viz. anticonvulsant, antimicrobial, antimycobacterial, anticancer, antitumor, antimalarial and antitubercular activities (17-23).

Sulfur containing heterocycles, like 4-thiazolidinone, form an important class of drugs with several types of biological activities such as antifungal, anti-HIV, anticonvulsant, antibacterial and anti-inflammatory (24-27).

EXPERIMENTAL

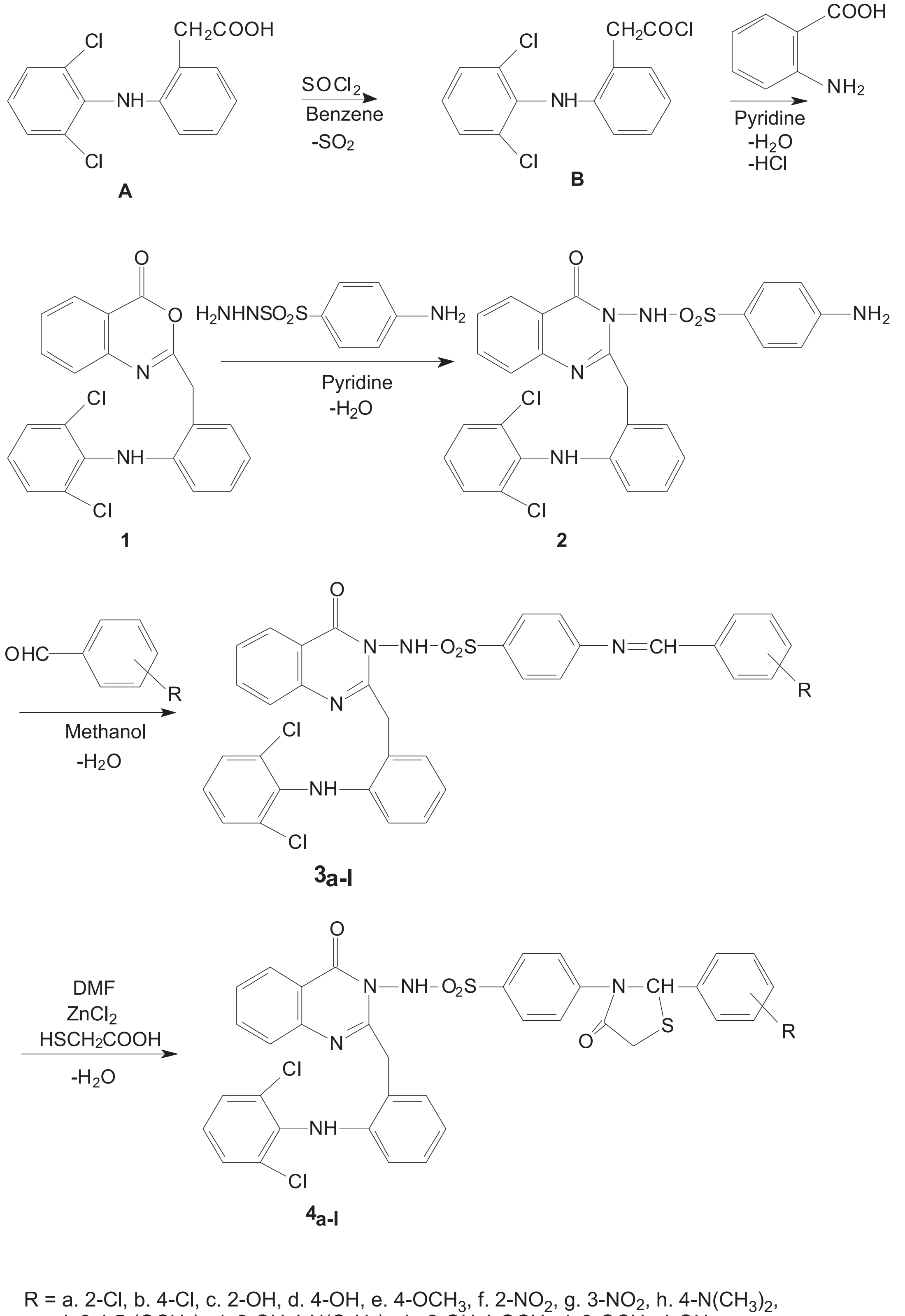
Chemistry

All commercial reagents and solvents were used without purification. Reactions were monitored by TLC performed on silica gel plates (Merck); the spots were located by UV (254 nm) or iodine. Melting points (uncorrected) were measured in open capillary tubes on a Gallenkamp-5 apparatus. The IR spectra were recorded on Perkin-Elmer-843 spectrometer using KBr pellets. ^{1}H NMR and ^{13}C NMR spectra were recorded on BRUKER AVANCE II 400 NMR spectrometer in $CDCl_3$, chemical shifts (d) were expressed in ppm relative to tetramethylsilane used as an internal standard. 2-[(2,6-Dichlorophenyl)amino] phenylacetyl chloride (29) and 4-aminobenzenesulfonyl hydrazide (30-32) have been prepared by reported methods.

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

To a stirred solution of anthranilic acid (1.37 g, 0.01 mol) in pyridine (60 mL), 2-[(2,6-dichlorophenyl)amino]phenylacetyl chloride (**B**, 0.01 mol) was added dropwise, keeping the temperature 0-5°C for 1 h. Reaction mixture was stirred for another 1 h at room temperature and then refluxed for 2 h. The

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



R = a. 2-Cl, b. 4-Cl, c. 2-OH, d. 4-OH, e. 4-OCH_3, f. 2-NO_2, g. 3-NO_2, h. 4-$N(CH_3)_2$, i. 3,4,5-$(OCH_3)_3$, j. 2-OH 4-$N(C_2H_5)_2$, k. 2-OH 4-OCH_3, l. 3-OCH_3 4-OH

Scheme 1.

Table 1. Physical and analytical data of the synthesized compounds **3a-l** and **4a-l**.

Compd.	R	Molecular formula	M. p. (°C)	Yield %	C, H, N analysis calculated (found)		
					%C	%H	%N
3a	2-Cl	$C_{34}H_{24}O_3N_5SCl_3$	138.7-139.5	62	59.70 (59.63)	3.51 (3.43)	10.16 (10.09)
3b	4-Cl	$C_{34}H_{24}O_3N_5SCl_3$	158.2-159.1	67	59.70 (59.63)	3.51 (3.43)	10.16 (10.09)
3c	2-OH	$C_{34}H_{25}O_4NSCl_2$	146.1-147.3	72	60.90 (60.82)	3.76 (3.70)	10.44 (10.38)
3d	4-OH	$C_{34}H_{25}O_4NSCl_2$	167.2-168.4	74	60.90 (60.82)	3.76 (3.70)	10.44 (10.38)
3e	4-OCH_3	$C_{35}H_{27}O_4N_5SCl_2$	147.0-147.9	69	61.41 (61.33)	3.98 (3.93)	10.23 (10.15)
3f	2-NO_2	$C_{34}H_{24}O_5N_6SCl_2$	134.8-135.3	79	58.37 (58.29)	3.46 (3.38)	12.01 (11.96)
3g	3-NO_2	$C_{34}H_{24}O_5N_6SCl_2$	178.9-179.5	71	58.37 (58.29)	3.46 (3.38)	12.01 (11.96)
3h	4-$N(CH_3)_2$	$C_{36}H_{30}O_3N_6SCl_2$	153.8-154.7	65	61.98 (61.91)	4.33 (3.26)	10.05 (12.00)
3i	3,4,5-$(OCH_3)_3$	$C_{37}H_{31}O_6N_5SCl_2$	184.7-185.5	70	59.68 (59.62)	4.20 (4.15)	9.40 (9.33)
3j	2-OH, 4-$N(C_2H_5)_2$	$C_{38}H_{34}O_4N_6SCl_2$	144.6-145.7	78	61.54 (61.47)	4.62 (4.56)	11.33 (11.26)
3k	2-OH, 4-OCH_3	$C_{35}H_{27}O_5N_5SCl_2$	169.3-170.2	68	60.00 (59.04)	3.88 (3.81)	10.00 (9.94)
3l	3-OCH_3, 4-OH	$C_{35}H_{27}O_5N_5SCl_2$	133.6-135.2	75	60.00 (59.02)	3.88 (3.79)	10.00 (9.92)
4a	2-Cl	$C_{36}H_{25}O_4N_5S_2BrCl_3$	149.1-150.3	69	51.35 (51.28)	2.99 (2.90)	8.32 (8.27)
4b	4-Cl	$C_{36}H_{25}O_4N_5S_2BrCl_3$	170.3-171.6	67	51.35 (51.28)	2.99 (2.90)	8.32 (8.27)
4c	2-OH	$C_{36}H_{26}O_5N_5S_2BrCl_2$	190.0-191.4	69	52.50 (52.43)	3.18 (3.11)	8.50 (8.43)
4d	4-OH	$C_{36}H_{26}O_5N_5S_2BrCl_2$	163.4-164.7	70	52.50 (52.43)	3.18 (3.11)	8.50 (8.43)
4e	4-OCH_3	$C_{37}H_{28}O_5N_5S_2BrCl_2$	158.0-159.2	78	53.06 (53.00)	3.37 (3.32)	8.36 (8.30)
4f	2-NO_2	$C_{36}H_{25}O_6N_6S_2BrCl_2$	168.3-169.5	75	50.72 (50.66)	2.96 (2.89)	9.86 (9.79)
4g	3-NO_2	$C_{36}H_{25}O_6N_6S_2BrCl_2$	164.7-165.9	74	50.72 (50.66)	2.96 (2.89)	9.86 (9.79)
4h	4-$N(CH_3)_2$	$C_{38}H_{31}O_4N_6S_2BrCl_2$	169.0-170.3	80	53.66 (53.59)	3.67 (3.60)	9.88 (9.81)
4i	3,4,5-$(OCH_3)_3$	$C_{39}H_{32}O_7N_5S_2BrCl_2$	159.3-160.2	68	52.18 (52.13)	3.59 (3.52)	7.80 (7.73)
4j	2-OH, 4-$N(C_2H_5)_2$	$C_{40}H_{35}O_5N_6S_2BrCl_2$	176.7-177.9	79	53.70 (53.62)	3.94 (3.87)	9.39 (9.32)
4k	2-OH, 4-OCH_3	$C_{37}H_{28}O_6N_5S_2BrCl_2$	150.0-151.6	80	52.06 (52.00)	3.31 (3.26)	8.20 (8.13)
4l	3-OCH_3, 4-OH	$C_{37}H_{28}O_6N_5S_2BrCl_2$	151.2-152.8	70	52.06 (51.99)	3.31 (3.26)	8.20 (8.13)

Table 2. IR spectral data of compounds **3a-l** and **4a-l**.

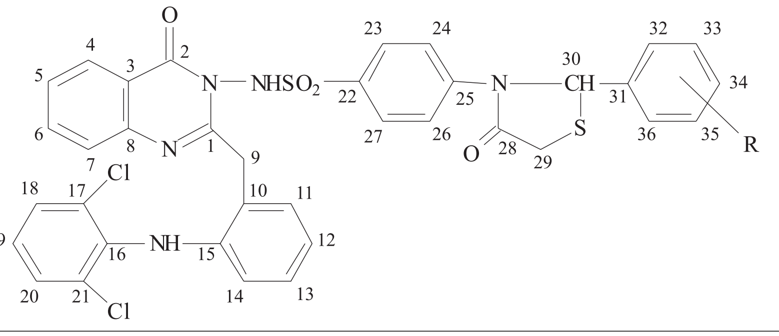
Compd. No.	IR spectral data
3a	3430 (NH), 2920, 2841 (CH), 1686 (C=O of qui.*), 1636 (N=CH), 1614 (C=N), 1360, 1154 (S=O), 1325 (C-N), 783 (C-Cl), 748 (NH)
3b	3428 (NH), 2920, 2845 (CH), 1675 (C=O of qui.), 1635 (N=CH), 1605 (C=N), 1340, 1160 (S=O), 1308 (C-N), 785 (C-Cl), 740 (NH)
3c	3436 (NH), 3255 (OH), 2925, 2852 (CH), 1669 (C=O of qui.), 1632 (N=CH), 1610 (C=N), 1342, 1158 (S=O), 1316 (C-N), 762 (C-Cl),748 (NH)
3d	3432 (NH), 3250 (OH), 2923, 2842 (CH), 1680 (C=O of qui.), 1635 (N=CH), 1608 (C=N), 1350, 1158 (S=O), 1325 (C-N), 789 (C-Cl), 743 (NH)
3e	3435 (NH), 2924, 2850 (CH), 1672 (C=O of qui.), 1637 (N=CH), 1607 (C=N), 1355, 1160 (S=O), 1320 (C-N), 1204, 1108 (C-O-C), 787 (C-Cl), 740 (NH)
3f	3432 (NH), 2918, 2843 (CH), 1675 (C=O of qui.), 1634 (N=CH), 1612 (C=N), 1546, 1360 (N=O), 1345, 1256 (S=O), 1318 (C-N), 785 (C-Cl), 745 (NH)
3g	3435 (NH), 2928, 2843 (CH), 1682 (C=O of qui.), 1628 (N=CH), 1602 (C=N), 1550, 1362 (N=O), 1338, 1154 (S=O), 1315 (C-N), 782 (C-Cl), 746 (NH)
3h	3425 (NH), 2912, 2832 (CH), 1680 (C=O of qui.), 1632 (N=CH), 1612 (C=N), 1355, 1164 (S=O), 1322 (C-N), 786 (C-Cl), 742 (NH)
3i	3433 (NH), 2920, 2845 (CH), 1675 (C=O of qui.), 1630 (N=CH), 1610 (C=N), 1350, 1162 (S=O), 1320 (C-N), 1210, 1114 (C-O-C), 785 (C-Cl), 750 (NH)
3j	3438 (NH), 3258 (OH), 2922, 2850 (CH), 1679 (C=O of qui.), 1636 (N=CH), 1605 (C=N), 1358, 1165 (S=O), 1315 (C-N), 784 (C-Cl), 749 (NH)
3k	3435 (NH), 3253 (OH), 2920, 2845 (CH), 1675 (C=O of qui.), 1630 (N=CH), 1610 (C=N), 1350, 1162 (S=O), 1320 (C-N), 1200, 1104 (C-O-C), 785 (C-Cl), 750 (NH)
3l	3430 (NH), 3256 (OH), 2928, 2848 (CH), 1670 (C=O of qui.), 1634 (N=CH), 1612 (C=N), 1353, 1147 (S=O), 1325 (C-N), 1210, 1106 (C-O-C), 782 (C-Cl), 745 (NH)
4a	3424 (NH), 2922, 2839 (CH), 1761 (C=O of thia.**), 1682 (C=O of qui.), 1610 (C=N), 1362, 1150 (S=O), 1323 (C-N), 785 (C-Cl), 744 (NH)
4b	3425 (NH), 2927, 2843 (CH), 1750 (C=O of thia.),1672 (C=O of qui.), 1600 (C=N), 1345, 1156 (S=O), 1312 (C-N), 776 (C-Cl), 740 (NH)
4c	3429 (NH), 3250 (OH), 2924, 2887 (CH), 1752 (C=O of thia.),1670 (C=O of qui.), 1613 (C=N), 1340, 1155 (S=O), 1313 (C-N), 760 (C-Cl),745 (NH)
4d	3430 (NH), 3255 (OH), 2927, 2848 (CH), 1744 (C=O of thia.),1682 (C=O of qui.), 1614 (C=N), 1339, 1153 (S=O), 1327 (C-N), 780 (C-Cl), 741 (NH)
4e	3436 (NH), 2926, 2858 (CH), 1748 (C=O of thia.),1670 (C=O of qui.), 1610 (C=N), 1345, 1152 (S=O), 1326 (C-N), 1200, 1105 (C-O-C), 780 (C-Cl), 742 (NH)
4f	3437 (NH), 2915, 2840 (CH), 1758 (C=O of thia.),1672 (C=O of qui.), 1616 (C=N), 1545, 13654 (N=O), 1340, 1257 (S=O), 1313 (C-N), 774 (C-Cl), 743 (NH)
4g	3432 (NH), 2930, 2837 (CH), 1764 (C=O of thia.),1680 (C=O of qui.), 1605 (C=N), 1554, 1362 (N=O), 1333, 1150 (S=O), 1312 (C-N), 780 (C-Cl), 744 (NH)
4h	3435 (NH), 2915, 2836 (CH), 1752 (C=O of thia.),1678 (C=O of qui.), 1614 (C=N), 1350, 1154 (S=O), 1320 (C-N), 779 (C-Cl), 740 (NH)
4i	3430 (NH), 2927, 2835 (CH), 1755 (C=O of thia.),1670 (C=O of qui.), 1613 (C=N), 1348, 1152 (S=O), 1315 (C-N), 1210, 1110 (C-O-C), 780 (C-Cl), 746 (NH)
4j	3434 (NH), 3247 (OH), 2926, 2854 (CH), 1748 (C=O of thia.),1676 (C=O of qui.), 1608 (C=N), 1353, 1159 (S=O), 1310 (C-N), 776 (C-Cl), 750 (NH)
4k	3433 (NH), 3258 (OH), 2924, 2842 (CH), 1753 (C=O of thia.),1674 (C=O of qui.), 1612 (C=N), 1347, 1154 (S=O), 1322 (C-N), 1210, 1106 (C-O-C), 780 (C-Cl), 752 (NH)
4l	3437 (NH), 3243 (OH), 2920, 2845 (CH), 1750 (C=O of thia.),1678 (C=O of qui.), 1611 (C=N), 1350, 1144 (S=O), 1328 (C-N), 1214, 1112 (C-O-C), 785 (C-Cl), 745 (NH)

*qui. = quinazolinone, **thia. = 4-oxo-thiazolidine

Table 3. ^{1}H NMR spectral data of **3a-l** and **4a-l**.

Compd. No.	^{1}H NMR spectral data
3a	3.70 (s, 2H, -CH_2-), 5.62 (s, 1H, -N=CH-), 9.38 (s, 1H, -NH-), 9.80 (s, 1H, -SO_2NH-), 6.35-7.96 (m, 18H, Ar-H)
3b	3.67 (s, 2H, -CH_2-), 5.55 (s, 1H, -N=CH-), 9.32 (s, 1H, -NH-), 9.75 (s, 1H, -SO_2NH-), 6.37-7.98 (m, 18H, Ar-H)
3c	3.69 (s, 2H, -CH_2-), 4.92 (s, 1H, -OH), 5.56 (s, 1H, -N=CH-), 9.40 (s, 1H, -NH-), 9.78 (s, 1H, -SO_2NH-), 6.35-7.94 (m, 18H, Ar-H)
3d	3.72 (s, 2H, -CH_2-), 4.98 (s, 1H, -OH), 5.63 (s, 1H, -N=CH-), 9.35 (s, 1H, -NH-), 9.74 (s, 1H, -SO_2NH-), 6.39-7.96 (m, 18H, Ar-H)
3e	3.30 (s, 3H, -OCH_3), 3.65 (s, 2H, -CH_2-), 5.58 (s, 1H, -N=CH-), 9.32 (s, 1H, -NH-), 9.77 (s, 1H, -SO_2NH-), 6.34-7.93 (m, 19H, Ar-H)
3f	3.75 (s, 2H, -CH_2-), 5.59 (s, 1H, -N=CH-), 9.38 (s, 1H, -NH-), 9.74 (s, 1H, -SO_2NH-), 6.36-7.97 (m, 18H, Ar-H)
3g	3.72 (s, 2H, -CH_2-), 5.60 (s, 1H, -N=CH-), 9.36 (s, 1H, -NH-), 9.76 (s, 1H, -SO_2NH-), 6.38-7.94 (m, 18H, Ar-H)
3h	3.10 (s, 6H, -N-CH_3), 3.69 (s, 2H, -CH_2-), 5.63 (s, 1H, -N=CH-), 9.39 (s, 1H, -NH-), 9.75 (s, 1H, -SO_2NH-), 6.40-7.98 (m, 18H, Ar-H)
3i	3.32 (s, 3H, -OCH_3), 3.76 (s, 2H, -CH_2-), 5.57 (s, 1H, -N=CH-), 9.28 (s, 1H, -NH-), 9.78 (s, 1H, -SO_2NH-), 6.36-7.95 (m, 16H, Ar-H)
3j	1.35 (t, 6H, -CH_3), 2.82 (q, 4H, -N-CH_2-), 3.64 (s, 2H, -CH_2-), 4.96 (s, 1H, -OH), 5.61 (s, 1H, -N=CH-), 9.37 (s, 1H, -NH-), 9.69 (s, 1H, -SO_2NH-), 6.37-7.98 (m, 17H, Ar-H)
3k	3.34 (s, 3H, -OCH_3), 3.68 (s, 2H, -CH_2-), 4.99 (s, 1H, -OH), 5.65 (s, 1H, -N=CH-), 9.34 (s, 1H, -NH-), 9.80 (s, 1H, -SO_2NH-), 6.35-7.94 (m, 17H, Ar-H)
3l	3.37 (s, 3H, -OCH_3), 3.67 (s, 2H, -CH_2-), 4.94 (s, 1H, -OH), 5.66 (s, 1H, -N=CH-), 9.30 (s, 1H, -NH-), 9.75 (s, 1H, -SO_2NH-), 6.39-7.99 (m, 17H, Ar-H)
4a	3.72 (s, 2H, -CH_2-), 3.96 (s, 2H, -CH_2-S-), 5.23 (s, 1H, >CH-S-), 9.35 (s, 1H, -NH-), 9.84 (s, 1H, -SO_2NH-), 6.35-7.96 (m, 18H, Ar-H)
4b	3.67 (s, 2H, -CH_2-), 3.97 (s, 2H, -CH_2-S-), 5.21 (s, 1H, >CH-S-), 9.30 (s, 1H, -NH-), 9.70 (s, 1H, -SO_2NH-), 6.38-7.99 (m, 18H, Ar-H)
4c	3.70 (s, 2H, -CH_2-), 3.95 (s, 2H, -CH_2-S-), 5.24 (s, 1H, >CH-S-), 4.90 (s, 1H, -OH), 9.44 (s, 1H, -NH-), 9.76 (s, 1H, -SO_2NH-), 6.37-7.94 (m, 18H, Ar-H)
4d	3.75 (s, 2H, -CH_2-), 3.98 (s, 2H, -CH_2-S-), 5.18 (s, 1H, >CH-S-), 4.95 (s, 1H, -OH), 9.34 (s, 1H, -NH-), 9.76 (s, 1H, -SO_2NH-), 6.37-7.94 (m, 18H, Ar-H)
4e	3.32 (s, 3H, -OCH_3), 3.67 (s, 2H, -CH_2-), 3.97 (s, 2H, -CH_2-S-), 5.19 (s, 1H, >CH-S-), 9.30 (s, 1H, -NH-), 9.79 (s, 1H, -SO_2NH-), 6.36-7.95 (m, 18H, Ar-H)
4f	3.77 (s, 2H, -CH_2-), 3.96 (s, 2H, -CH_2-S-), 5.23 (s, 1H, >CH-S-), 9.36 (s, 1H, -NH-), 9.72 (s, 1H, -SO_2NH-), 6.38-7.99 (m, 18H, Ar-H)
4g	3.74 (s, 2H, -CH_2-), 3.97 (s, 2H, -CH_2-S-), 5.22 (s, 1H, >CH-S-), 9.37 (s, 1H, -NH-), 9.78 (s, 1H, -SO_2NH-), 6.35-7.98 (m, 18H, Ar-H)
4h	3.12 (s, 6H, -N-CH_3), 3.67 (s, 2H, -CH_2-), 3.97 (s, 2H, -CH_2-S-), 5.16 (s, 1H, >CH-S-), 9.32 (s, 1H, -NH-), 9.78 (s, 1H, -SO_2NH-), 6.36-7.94 (m, 18H, Ar-H)
4i	3.30 (s, 3H, -OCH_3), 3.75 (s, 2H, -CH_2-), 3.95 (s, 2H, -CH_2-S-), 5.19 (s, 1H, >CH-S-), 9.34 (s, 1H, -NH-), 9.82 (s, 1H, -SO_2NH-), 6.38-7.95 (m, 16H, Ar-H)
4j	1.32 (t, 6H, -CH_3), 2.80 (q, 4H, -N-CH_2-), 3.62 (s, 2H, -CH_2-), 3.97 (s, 2H, -CH_2-S-), 5.25 (s, 1H, >CH-S-), 4.92 (s, 1H, -OH), 9.35 (s, 1H, -NH-), 9.71 (s, 1H, -SO_2NH-), 6.36-7.97 (m, 16H, Ar-H)
4k	3.33 (s, 3H, -OCH_3), 3.65 (s, 2H, -CH_2-), 3.94 (s, 2H, -CH_2-S-), 5.22 (s, 1H, >CH-S-), 4.96 (s, 1H, -OH), 9.35 (s, 1H, -NH-), 9.83 (s, 1H, -SO_2NH-), 6.38-7.97 (m, 17H, Ar-H)
4l	3.35 (s, 3H, -OCH_3), 3.67 (s, 2H, -CH_2-), 3.96 (s, 2H, -CH_2-S-), 5.18 (s, 1H, >CH-S-), 4.97 (s, 1H, -OH), 9.33 (s, 1H, -NH-), 9.78 (s, 1H, -SO_2NH-), 6.38-7.96 (m, 17H, Ar-H)

Table 4. ^{13}C NMR spectral data of **4a-l**.



4a	163.0 (C_1), 159.5 (C_2), 121.0 (C_3), 127.6 (C_4), 125.2 (C_5), 133.0 (C_6), 123.4 (C_7), 143.2 (C_8), 173.7 (C_{28}), 35.7 (C_{29}), 58.8 (C_{30}) 30.0-160.3 (C_9-C_{27} & C_{31}-C_{35})
4b	163.4 (C_1), 158.0 (C_2), 120.2 (C_3), 127.4 (C_4), 125.0(C_5), 133.5 (C_6), 123.0 (C_7), 143.0 (C_8), 172.6 (C_{28}), 35.0 (C_{29}), 58.0 (C_{30}) 30.7-160.5 (C_9-C_{27} & C_{31}-C_{35})
4c	163.8 (C_1), 157.4 (C_2), 120.5 (C_3), 127.2 (C_4), 125.4(C_5), 133.2 (C_6), 123.6 (C_7), 143.5 (C_8), 172.2 (C_{28}), 35.4 (C_{29}), 58.2 (C_{30}) 30.5-160.3 (C_9-C_{27} & C_{31}-C_{35})
4d	162.8 (C_1), 158.8 (C_2), 120.8 (C_3), 128.4 (C_4), 125.4(C_5), 133.4 (C_6), 123.1 (C_7), 143.2 (C_8), 172.0 (C_{28}), 35.7 (C_{29}), 58.7 (C_{30}) 31.3-159.7 (C_9-C_{27} & C_{31}-C_{35})
4e	163.5 (C_1), 160.2 (C_2), 121.8 (C_3), 127.0 (C_4), 125.2(C_5), 133.8 (C_6), 123.8 (C_7), 144.5 (C_8), 172.8 172.8 (C_{28}), 35.2 (C_{29}), 58.4 (C_{30}) 31.0-159.5 (C_9-C_{27} & C_{31}-C_{35})
4f	162.6 (C_1), 157.5 (C_2), 121.5 (C_3), 128.7 (C_4), 124.5(C_5), 133.3 (C_6), 123.4 (C_7), 144.0 (C_8), 173.4 (C_{28}), 35.8 (C_{29}), 58.5 (C_{30}) 30.4-159.9 (C_9-C_{27} & C_{31}-C_{35})
4g	164.3 (C_1), 158.7 (C_2), 121.2 (C_3), 128.0 (C_4), 124.8(C_5), 133.6 (C_6), 123.0 (C_7), 144.8 (C_8), 172.2 (C_{28}), 35.0 (C_{29}), 57.8 (C_{30}) 29.8-160.3 (C_9-C_{27} & C_{31}-C_{35})
4h	162.3 (C_1), 158.4 (C_2), 120.7 (C_3), 128.2 (C_4), 124.7(C_5), 133.8 (C_6), 123.5 (C_7), 143.9 (C_8), 172.9 (C_{28}), 35.3 (C_{29}), 58.4 (C_{30}) 30.6-161.2(C_9-C_{27} & C_{31}-C_{35})
4i	164.5 (C_1), 158.8 (C_2), 120.6 (C_3), 127.0 (C_4), 124.8(C_5), 133.2 (C_6), 123.9 (C_7), 144.4 (C_8), 172.7 (C_{28}), 35.6 (C_{29}), 58.3 (C_{30}) 31.3-160.3 (C_9-C_{27} & C_{31}-C_{35})
4j	164.0 (C_1), 157.3 (C_2), 122.0 (C_3), 127.5 (C_4), 124.5(C_5), 132.9 (C_6), 124.0 (C_7), 144.2 (C_8), 172.4 (C_{28}), 35.9 (C_{29}), 57.6 (C_{30}) 31.1-160.0 (C_9-C_{27} & C_{31}-C_{35})
4k	163.4 (C_1), 157.0 (C_2), 121.7 (C_3), 128.4 (C_4), 124.0(C_5), 132.7 (C_6), 123.3 (C_7), 143.7 (C_8), 172.8 (C_{28}), 34.6 (C_{29}), 57.9 (C_{30}) 29.4-159.5 (C_9-C_{27} & C_{31}-C_{35})
4l	163.8 (C_1), 157.9 (C_2), 121.4 (C_3), 128.0 (C_4), 125.0(C_5), 133.3 (C_6), 123.0 (C_7), 144.0 (C_8), 173.0 (C_{28}), 34.9 (C_{29}), 57.5 (C_{30}) 29.9-159.8 (C_9-C_{27} & C_{31}-C_{35})

reaction mixture was neutralized with cooled diluted HCl solution. A solid obtained was filtered, washed with water and recrystallized from ethanol.Yield 62%; m.p. 128.3-129.7°C; IR (KBr, cm^{-1}): 3445 (NH), 2925, 2842 (C-H), 1672 (C=O, cyclic), 1615 (C=N), 1310 (C-N), 785 (C-Cl); ^{1}H NMR ($CDCl_3$, δ, ppm): 3.70 (s, 2H, $-CH_2-$), 6.25-7.63 (m, 10H, Ar-H) 9.45 (s, 1H, -NH-).

2-[2-(2,6-Dichlorophenyl)amino]phenylmethyl-3-[(4-aminophenyl)sulfonamido-1-yl] quinazolin-4(3H)one (**2**) (33)

A mixture of **1** (3.97 g, 0.01 mol) and 4-aminobenzenesulfonyl hydrazide (1.87 g, 0.01 mol) was dissolved in 50 mL of pyridine. The reaction mixture was reflux for 5-6 h, cooled and poured into ice-cold water containing concentrated HCl. The separated solid was filtered, washed and recrystallized from ethanol. IR (KBr) cm^{-1}: 3505 (NH_2), 3440 (NH), 2920, 2845 (C-H), 1665 (C=O of quinazolinone), 1610 (C=N); 1324 (C-N); ^{1}H NMR ($CDCl_3$, δ, ppm) = 3.65 (s, 2H, $-CH_2-$), 5.75 (s, 2H, $-NH_2$), Ar-H (15H, m, 6.30-7.60), 9.22 (s, 1H, -NH-), 9.55 (s, 1H, $-SO_2NH-$).

Table 5. Antimicrobial activity of **3a-l** and **4a-l**

Compd.	Minimal bactericidal concentration mg/mL				Minimal fungicidal concentration mg/mL		
	Gram negative		Gram positive				
	E. coli	*P. aeruginosa*	*S. aureus*	*S. pyogenus*	*C. albicans*	*A. niger*	*A. clavatus*
3a	125	125	500	1000	1000	1000	> 1000
3b	500	500	100	500	1000	1000	> 1000
3c	125	500	100	1000	> 1000	> 1000	500
3d	500	500	500	500	500	> 1000	> 1000
3e	500	500	500	500	500	> 1000	> 1000
3f	500	200	200	1000	> 1000	> 1000	> 1000
3g	500	500	500	250	> 1000	> 1000	> 1000
3h	500	500	500	500	> 1000	> 1000	> 1000
3i	500	500	500	250	> 1000	> 1000	> 1000
3j	50	125	50	250	> 1000	> 1000	> 1000
3k	250	50	100	125	> 1000	> 1000	> 1000
3l	200	125	100	250	200	200	500
4a	500	250	500	250	200	1000	1000
4b	250	100	250	500	500	500	1000
4c	500	62.5	500	500	250	500	500
4d	250	500	250	500	500	1000	1000
4e	500	250	250	500	1000	1000	1000
4f	500	250	500	250	1000	> 1000	> 1000
4g	125	62.5	250	500	500	1000	1000
4h	200	250	500	500	500	1000	1000
4i	250	250	250	250	1000	1000	1000
4j	62.5	100	62.5	125	1000	1000	1000
4k	250	500	500	100	1000	> 1000	> 1000
4l	250	250	500	500	1000	> 1000	> 1000
Gent.	0.05	1	0.25	0.5	-	-	-
Amp.	100	100	250	100	-	-	-
Chlor.	50	50	50	50	-	-	-
Cipr.	25	25	50	50	-	-	-
Norf.	10	10	10	10	-	-	-
Nys.	-	-	-	-	100	100	100
Gris.	-	-	-	-	500	100	100

Gent. = gentamycin, Amp = ampicillin, Chlor. = chloramphenicol, Cipr. = ciprofloxacin, Norf. = norfloxacin, Nys. = nystatin, Gris. = griseofulvin

2-[2-(2,6-Dichlorophenyl)amino]phenylmethyl-3-{[4-(N- arylidene) phenyl]sulfonamido-1-yl}quinazolin-4(3H)ones **(3)**

A mixture of **2** (2.83 g, 0.005 mol) and the respective benzaldehyde (0.005 mol) was dissolved in 40 mL of absolute ethanol and a few drops of glacial acetic acid were added. A mixture was refluxed for 5-6 h on water bath, then poured into ice-cold water, and the separated solid was filtered, washed and recrystallized from ethanol.

2-[2-(2,6-Dichlorophenyl)amino]phenylmethyl-3-{4-[2-(aryl)-4-oxo-thiazolidin-3-yl]phenylsulfonamido-1-yl}quinazolin-4(3H)ones **(4)**

A solution of **3** (0.002 mol) in 50 mL of dry DMF, containing a pinch of anhydrous $ZnCl_2$ and thioglycolic acid (0.004 mol) was refluxed for 8-9 h. An excess of solvent was distilled off and the residual reaction mixture was cooled and poured into ice-cold water. The separated solid was filtered, washed and recrystallized from ethanol.

The physical properties, IR spectral data, ^1H NMR spectral data, ^{13}C NMR spectral data and antimicrobial activity of all the synthesized compounds are given in Table 1, 2, 3, 4 and 5, respectively.

RESULTS AND DISCUSSION

Minimum inhibitory concentration (MIC) of all the synthesized compounds have been screened by broth dilution method (28) against four different strains, viz. two Gram positive bacteria (*S. aureus* and *S. pyogenes* and two Gram negative bacteria (*E. coli* and *P. aeruginosa*) and compared with standard drugs: gentamycin, ampicillin, chloramphenicol, ciprofloxacin and norfloxacin. Antifungal activity against *C. albicans*, *A. niger* and *A. clavatus* organisms was determined by same method and compared with standard drugs: nystatin and greseofulvin. We have synthesized 12 4-oxo-thiazolidinyl sulfonamides of quinazolin-4(3*H*)ones *via* 12 Schiff bases from which some showed very good activity against Gram positive and Gram negative bacteria.

Antibacterial activity

From screening results of the substituted Schiff bases attached at position-3 of 2-substituted quinazolin-4(3*H*)ones, compound **3j** possesses very good activity compared with ampicillin against *E. coli*. When it was cyclized with thioglycolic acid, it gave 4-thiazolidinone **4j** which showed as good activity as Schiff base **3j**.

Compound **3k** possesses very good activity against *P. aeruginosa*, while **4c** and **4g** showed very good activity compared with ampicillin against *P. aeruginosa*. Both compounds **3j** and **4j** also showed excellent activity against *S. aureus*.

Moderate activity was observed for compound **3k** against *S. pyogenes*, *w*hereas 4-thiazolidinone **4j** demonstrated good activity with ampicillin.

Antifungal activity

Compound **3l** had very good activity against *C. albicans* compared with greseofulvin, while 4-thiazolidinones **4a**, **4c** and **4k** showed very good activity against *C. albicans*.

CONCLUSION

From the results of antibacterial and antifungal activity; it can be concluded that the compounds bearing -OH and $-OCH_3$ group are more potent than the remaining compounds. They showed comparatively good antibacterial as well as antifungal activity.

Acknowledgment

The authors thank Professor and Head, Department of Chemistry of Veer Narmad South Gujarat University, Surat for laboratory facilities. Also we wish to thank C.D.R.I., Lucknow for elemental analysis, S.A.I.F., Chandigarh for ^1H NMR & ^{13}C NMR spectral analysis and D. Rajani, Microcare Laboratory, Surat, for antimicrobial activity determinations.

REFERENCES

1. Patel N.B., Lilakar J.D.: Ind. J. Heterocycl. Chem. 11, 85 (2001).
2. Patel N.B., Chaudhari R.C.: J. Ind. Chem. Soc. 83, 838 (2006).
3. Patel N.B., Patel V.N.: Ind. J. Heterocycl. Chem. 16, 247 (2007).
4. Patel N.B., Patel V.N.: Iranian J. Pharm. Res. 6, 251 (2007).
5. Patel N.B., Patel J.C.: J. Saudi. Chem. Soc. 12, 121 (2008).
6. Saleh M.A., Abdel-Megged M.F., Abdo M.A., Abdel-Basset S.M.: Nucleosides Nucleotides Nucleic Acids 21, 93 (2002).
7. El-Hellby A.G.A., Wahab M.H.A.: Acta Pharm. 53, 127(2003).
8. Mosaad S.M., Mohammed K.I., Ahmed M.A., Abdel-Hamide S.G.J.: Appl. Sci. 4, 302 (2004).
9. El-Sayed R., Wasfy A.F.: J. Chin. Chem. Soc. 52, 129 (2005).
10. Al-Rashood S.T., Aboldahab I.A., Nagi M.N., Abouzeid L.A. et al.: Bioorg. Med. Chem. 14 8608 (2006).
11. El-Sayed B.S., Ghorab M.M., Saker H.M., Abd Rabo M.M.: Phosphorus Sulfur Silicon Relat. Elem.182, 65 (2007).
12. Masereel B., Rolin S, Francesco Abbate F., Scozzafava A, Supuran C.T.: J. Med. Chem. 45, 312 (2002).
13. Reddy N.S., Reddy M.M., Cosenza S., Gumireddy K. et al.: Bioorg. Med. Chem. Lett. 14, 4093 (2004).
14. Li X.-H., Yang X.-L., Ling Y., Zhi-Jin Fan Z.-J., Xiao-Mei Liang X.-M. Et al.: J. Agric. Food Chem. 53, 2202 (2005).

15. Hu L., Li Z-r., Li Y., Qu J., Ling Y.-H., Jiang J.-d., Boykin D.W.: J. Med. Chem. 49, 6273 (2006).
16. Accinelli C., Koskinen W.C., M. Becker J.M., Michael J. Sadowsky M.J.: Agric. Food Chem. 55, 2677 (2007).
17. Dimmock J.R., Vashishtha S.C., Stables J.P.: Eur. J. Med., Chem. 35, 241 (2000).
18. Vicini P., Zani F., Cozzini P., Doytchinova I.: Eur. J. Med. Chem. 37, 553 (2002).
19. Mamolo M.G., Falagiani V., Zampieri D., Vio L., Banfi E., Scialino G.: Farmaco 58, 631 (2003).
20. Savini L., Chiasserini L., Travagli V., Pellerano C., Novellino E., Cosentino S., Pisano M.B.: Eur. J. Med. Chem. 39, 113 (2004).
21. Cocco M.T., Congiu C., Lilliu V., Onnis V.: Bioorg. Med. Chem. 14 366 (2005).
22. Gemma S., Kukreja G., Fattorusso C., Persico M., Romano M. et al.: Bioorg. Med. Chem. Lett. 16, 5384 (2006).
23. Imramovsky A., Polanc S., Vinsova J., Kocevar M., Jampílek J., Reckova Z., Kaustova J.: Bioorg. Med. Chem. 15, 2551 (2007).
24. Liu H.-L., Li Z., Anthonsen T.: Molecules 5, 1055 (2000).
25. Barreca M.L., Balzarini J., Chimirri A., Clercq E.D., Luca L.D., Holtje H.D. et al.: J. Med. Chem. 45, 5410 (2002).
26. Sayyed M., Mokle S., Bokhare A., Mankar A., Surwase S., Bhusare S., Vibhutea Y.: ARKIVOC ii, 187 (2006).
27. Kumar A., Rajput C.S., Bhati S.K.: Bioorg. Med. Chem. 15, 3089 (2007).
28. Rattan A.: Antimicrobials in laboratory medicine, BI Churchill Livingstone. Pvt. Ltd., New Delhi 2000
29. Ahmed M., Sharma R., Nagda D.P., Jat J.L., Talesara G.L.: ARKIVOC xi, 66 (2006).
30. Chhajed M.R; Khedekar P.B; Mundhey A.S.: Ind. J. Heterocycl. Chem. 16, 259 (2007).
31. Myers A.G., Zheng B., Movassaghi M.: J. Org. Chem. 62, 7507 (1997).
32. Ahluwalia V.K., Aggarwal R.: Comprehensive Practical Organic Chemistry, Universities Press Ltd., Hyderabad 2000.
33. Shah B.R., Bhatt J.J., Patel H.H., Undavia N.K., Trivedi P.B., Desai N.C.: Ind. J. Chem. 34B, 201 (1995).

Received: 21. 10. 2009