Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2013, 5(7):1-6

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Synthesis and antimicrobial activity of new Schiff base containing 4-oxo-thiazolidines and their spectral characterisation

A. N. Solankee* and R. B. Patel

Department of Chemistry, B. K. M. Science College, Valsad-396001
(Affilated to The Veer Narmad South Gujarat University, Surat). India

---

ABSTRACT

*A series of Schiff bases **(2a-e)** have been prepared by the condensation of 5-bromofuran-2-carboxyhydrazide **(1)** with different aromatic and heterocyclic aldehydes. The synthesis of various 2-(substituted phenyl)-3-(5'-bromofuran-2'-carboxamido) – thiazolidine-4-ones **(3a-e)** by cyclocondensation reaction between schiff bases **(2a-e)** and thioglycolic acid. Cyclocondensation of schiff bases **(2a-e)** with thiolactic acid resulted 2-(susbstituted phenyl)-3-(5'-bromofuran-2'-carboxamido)–5-methyl thiazolidine - 4 - ones **(4a-e)**. The structures of all the synthesised compounds were confirmed by their elemental analysis and IR, ^{1}H NMR spectral data. All the synthesised compounds have been screened for their antimicrobial activity.*

Keywords : Hydrazones, 4-Oxo-thiazolidines, Thioglycolic acid, Thiolactic acid, Spectral data, Antimicrobial activity.

INTRODUCTION

Azomethine group (–C=N–) containing compounds typically known as Schiff bases have been synthesised by the condensation of primary amines with active carbonyls. Schiff bases form a significant class of compounds in medicinal and pharmaceutical chemistry with several biological applications that include antibacterial, antifungal [1-6] and antitumor activity [7,8]. 4-Oxo-thiazolidinones are synthesised either by cyclisation of acyclic compounds or by interconversation among appropriately substituted thiazolidine derivatives. The 4-oxo-thiazolidine ring system comprises the broad spectrum for a number of biologically active compounds. In recent years, 4-oxo-thiazolidine are the most extensively investigated class of compounds, which exhibit various biological activities, such as antimicrobial, anti-inflammatory, anti-HIV, anti-toxoplasma, gondii, antitubercular, antioxidant, and analgesic [9–17]. Different method for the preparation of 4-oxo-thiazolidines have been reported [18-19]. In continuation of our works on 4-thiazolidinone derivatives [20-23], we have undertaken the synthesis of 4-oxo-thiazolidines of type **(3a-e)** by the condensation of schiff-bases **(2a-e)** with thioglycolic acid. Cyclocondensation of schiff-bases **(2a-e)** with thiolactic yielded 4-oxo-thiazolidines of type **(4a-e)**. All the synthesised compounds were confirmed on the basis of their spectral data and physical data.

EXPERIMENTAL SECTION

All the melting points were determined in an open capillary and are uncorrected. The IR spectra were recorded on Perkin-Elmer spectrum BX series FT-IR spectrophotometer. ^{1}H NMR spectra on a Varian Gemini 400 MHz spectrometer with $CDCl_3$ as a solvent and TMS as internal reference. The chemical shifts are expressed in part per million (ppm) downfield from the internal standard and signals are quoted as *s* (singlet), *d* (doublet) and *m* (multiplate). Thin Layer Chromatography (TLC) analytical separation was conducted with Silica Gel 60 F-254 (Merck) plates of 0.25mm thickness eluted with visualized with UV (254nm) or iodine to check the purity of the synthesised compounds. Elemental analyses were carried out on a Perkin-Elmer series ii 2400 equipment.

Preparation of N-(2',3'-dimethoxybenzylidene)-5–bromofuran-2-carbonyl hydrazones (2a).
5-Bromofuran-2-carbohydrazide **(1)** (0.01 mol) and 2,3- dimethoxybenzaldehyde (0.01 mol) in dry toluene (50 mL) were refluxed on water bath using Dean-Stark water separator for 4-5 h. The progress of the reaction was monitored on TLC plate. Excess of toluene was then distilled off and the product separated out was recrystallized from alcohol to give (**2a).**

Similarly, the remaining compounds **(2b-e)** were prepared by this method. Their physical data are given in **Table-1.**

Compound (2a) : IR (KBr) cm^{-1}; 1660 (>C=O, -CONH str), 1570 (-N=CH str), 1246 (C-O-C str), 625 (C-Br str). ^1H NMR (DMSO) δ ppm ; 3.40 (3H, *s*, o-OCH_3), 3.74 (3H, *s*, m-OCH_3), 6.30-7.81 (5H, *m*, Ar-H and –CH of furan ring), 8.1(1H, *s*, N=CH), 9.3 (1H, s, -CONH). ^{13}C NMR ($CDCl_3$) δ ; 56.1 (1), 61.3 (1), 112.8 (1), 115.7 (1), 116.3 (1), 117.6 (1), 117.9 (1), 122.6 (1), 124.0 (1), 146.3 (1), 149.7 (1), 150.9 (1), 153.5 (1), 166.3 (1).

Compound (2b) : IR (KBr) cm^{-1}; 1656 (>C=O, -CONH str), 1564 (-N=CH str), 1253 (C-O-C str), 632 (C-Br str). ^1H NMR (DMSO) δ ppm ; 3.47 (3H, *s*, m-OCH_3), 3.79 (3H, *s*, p-OCH_3), 6.50-7.81 (5H, *m*, Ar-H and –CH of furan ring), 8.5(1H, *s*, N=CH), 9.7 (1H, s, -CONH). ^{13}C NMR ($CDCl_3$) δ ; 56.3 (1), 61.6 (1), 112.8. (1), 115.9 (1), 116.5 (1), 117.6 (1), 117.9 (1), 122.6 (1), 124.4 (1), 146.3 (1), 149.4 (1), 150.5 (1), 153.6 (1), 166.2 (1).

Compound (2c) : IR (KBr) cm^{-1}; 1662 (>C=O, -CONH str), 1573 (-N=CH str), 1248 (C-O-C str), 629 (C-Br str). ^1H NMR (DMSO) δ ppm ; 6.30-7.81 (6H, *m*, Ar-H and –CH of furan ring), 8.1(1H, *s*, N=CH), 9.3 (1H, s, -CONH). ^{13}C NMR ($CDCl_3$) δ ; 112.8 (1), 115.7 (1), 122.6 (1), 122.8 (2), 129.8 (2), 146.3 (1), 146.9(2), 149.7 (1), 166.3 (1).

Compound (2d) : IR (KBr) cm^{-1}; 1672 (>C=O, -CONH str), 1567 (-N=CH str), 1267 (C-O-C str), 654 (C-Br str). ^1H NMR (DMSO) δ ppm ; 6.8-7.7 (6H, *m*, Ar-H and –CH of furan ring), 8.4 (1H, *s*, N=CH), 9.1 (1H, s, -CONH). ^{13}C NMR ($CDCl_3$) δ ; 112.4 (1), 115.7 (1), 122.8 (1), 122.9 (2), 129.3 (2), 146.7 (1), 146.2 (2), 149.3 (1), 166.6 (1).

Compound (2e) : IR (KBr) cm^{-1}; 1666 (>C=O, -CONH str), 1575 (-N=CH str), 1250 (C-O-C str), 632 (C-Br str). ^1H NMR (DMSO) δ ppm ; 2.82 (2H, *q*, -CH_2), 3.36 (3H, *t*, -CH_3), 6.39-7.76 (6H, *m*, Ar-H and –CH of furan ring), 8.2 (1H, *s*, N=CH), 9.6 (1H, s, -CONH). ^{13}C NMR ($CDCl_3$) δ ; 14.5 (1), 28.2 (1), 112.9 (1), 115.8 (1), 122.9 (1), 122.8 (2), 129.8 (2), 146.1 (1), 146.9(2), 149.8 (1), 166.3 (1).

Preparation of 2-(2',3'-dimethoxyphenyl)-3-(5'-bromofuran-2'-carboxamido)– thiazolidine- 4 - one (3a)
Compound **(2a)** (0.01 mole) and thioglycolic acid (0.012 mole, 1.104g) in dry toluene (80 ml) were refluxed on water bath for 10-12 h using Dean-Stark water separator. The progress of the reaction was monitored on TLC plate. Excess of toluene was then distilled off and the resulting viscous liquid was treated with saturated $NaHCO_3$ solution to remove unreacted thioglycolic acid. The product separated out was washed with water, dried and recrystallised from alcohol.

Similarly, the remaining compounds **(3b-e)** were prepared by this method. Their physical data are given in **Table-1.**

Compound (3a) IR (KBr) cm^{-1}; 1673 (>C=O, -CONH str), 1680 (>C=O, thiazolidine ring), 1249 (C-O-C str), 709 (C-S-C str), 620 (C-Br str). ^1H NMR ($CDCl_3$) δ ppm ; 3.5-3.7 (2H, *q*, -CH_2), 3.85 (3H, *s*, o-OCH_3), 3.92 (3H, *s*, m-OCH_3), 5.9 (1H, s, -CH-Ar), 6.45 -7.20 (5H, m, Ar-H and -CH furan ring), 8.0 (1H, s, -CONH). ^{13}C NMR ($CDCl_3$) δ ; 35.6 (1), 56.1 (1), 56.7 (1), 64.6 (1), 112.3 (1), 112.8 (1), 113.8 (1), 115.7(1), 122.0 (1), 122.6 (1), 132.5 (1), 148.2 (1), 149.7 (1), 149.9(1), 157.1 (1), 168.8 (1).

Compound (3b) IR (KBr) cm^{-1}; 1666 (>C=O, -CONH str), 1687 (>C=O, thiazolidine ring), 1232 (C-O-C str), 787 (C-S-C str), 629 (C-Br str). ^1H NMR ($CDCl_3$) δ ppm; 3.52-3.69 (2H, *q*, -CH_2), 3.78 (3H, *s*, m-OCH_3), 3.86 (3H, *s*, p-OCH_3), 5.67 (1H, s, -CH-Ar), 6.54 -7.34 (5H, m, Ar-H and -CH furan ring), 8.3 (1H, s, -CONH). ^{13}C NMR ($CDCl_3$) δ ; 35.6 (1), 56.0 (2), 64.5 (1), 112.1 (1), 112.7 (1), 113.7 (1), 115.1 (1), 122.9 (1), 122.1 (1), 132.7 (1), 148.8 (1), 149.3 (1), 149.3 (1), 157.1 (1), 168.1 (1).

Compound (3c) IR (KBr) cm^{-1}; 1637 (>C=O, -CONH str), 1689 (>C=O, thiazolidine ring), 1271 (C-O-C str), 757 (C-S-C str), 661 (C-Br str). ^1H NMR ($CDCl_3$) δ ppm; 3.49-3.72 (2H, *q*, -CH_2), 5.92 (1H, s, -CH-Ar), 6.45 -7.14 (6H, m, Ar-H and -CH furan ring), 8.7 (1H, s, -CONH). ^{13}C NMR ($CDCl_3$) δ ; 35.6 (1), 64.6 (1), 112.8 (1), 115.7 (1), 121.5 (1), 122.6 (1), 130.9 (2), 131.5 (2), 149.3 (1), 138.2 (1), 157.1 (1), 168.8 (1).

Compound (3d) IR (KBr) cm^{-1}; 1685 (>C=O, -CONH str), 1697 (>C=O, thiazolidine ring), 1264 (C-O-C str), 711 (C-S-C str), 646 (C-Br str). ^1H NMR ($CDCl_3$) δ ppm; 3.51-3.73 (2H, *q*, -CH_2), 5.94 (1H, s, -CH-Ar), 6.41 -7.19 (6H,

m, Ar-H and -CH furan ring), 8.4 (1H, s, -CONH). ^{13}C NMR ($CDCl_3$) δ ; 35.7 (1), 64.3 (1), 112.2 (1), 115.1 (1), 121.8 (1), 122.6 (1), 130.9 (2), 131.5 (2), 149.1 (1), 138.6 (1), 157.7 (1), 168.2 (1).

Compound (3e) IR (KBr) cm^{-1}; 1677 (>C=O, -CONH str), 1687 (>C=O, thiazolidine ring), 1248 (C-O-C str), 707 (C-S-C str), 627 (C-Br str). ^{1}H NMR ($CDCl_3$) δ ppm; 2.82 (2H, *q*, -CH_2), 3.36 (3H, *t*, -CH_3), 3.50-3.70 (2H, *q*, -CH_2), 5.9 (1H, s, -CH-Ar), 6.45 -7.20 (6H, m, Ar-H and -CH furan ring), 8.0 (1H, s, -CONH). ^{13}C NMR ($CDCl_3$) δ ; 15.5 (1), 28.2 (1), 35.6 (1), 64.6 (1), 112.8 (1), 115.7 (1), 121.5 (1), 122.6 (1), 130.9 (2), 131.5 (2), 149.6 (1), 138.2 (1), 157.1 (1), 168.8 (1).

Preparation of 2-(2',3'-dimethoxyphenyl)-3-(5'-bromofuran-2'-carboxamido)– 5- methyl-thiazolidine-4 - ones (4a)

Compound **(2a)** (0.01 mole) and thioglycolic acid (0.012 mole, 1.104g) in dry toluene (80 ml) were refluxed on water bath for 10-12 h using Dean-Stark water separator. The progress of the reaction was monitored on TLC plate. Excess of toluene was then distilled off and the resulting viscous liquid was treated with saturated $NaHCO_3$ solution to remove unreacted thioglycolic acid. The product separated out was washed with water, dried and recrystallised from alcohol.

Similarly, the remaining compounds **(4b-e)** were prepared by this method. Their physical data are given in **Table-1.**

Compound (4a) IR (KBr) cm^{-1}; 1673 (>C=O, -CONH str), 1685 (>C=O, thiazolidine ring), 1249 (C-O-C str), 709 (C-S-C str), 620 (C-Br str). ^{1}H NMR ($CDCl_3$) δ ppm; 1.63 (3H, *d*, -CH_3), 3.72 (3H, *s*, o-OCH_3), 3.89 (3H, *s*, m-OCH_3), 5.89 (1H, s, -CH-Ar), 6.35 - 7.60 (5H, m, Ar-H and -CH furan ring), 8.2 (1H, s, -CONH). ^{13}C NMR ($CDCl_3$) δ ; 20.6 (1), 35.7 (1), 56.2 (1), 56.8 (1), 64.5 (1), 112.3 (1), 112.8 (1), 113.9 (1), 115.8 (1), 122.0 (1), 122.3 (1), 132.5 (1), 148.2 (1), 149.6 (1), 149.8 (1), 157.1 (1), 168.4 (1).

Compound (4b) IR (KBr) cm^{-1}; 1653 (>C=O, -CONH str), 1692 (>C=O, thiazolidine ring), 1244 (C-O-C str), 751 (C-S-C str), 688 (C-Br str). ^{1}H NMR ($CDCl_3$) δ ppm; 1.87 (3H, *d*, -CH_3), 3.78 (3H, *s*, m-OCH_3), 3.93 (3H, *s*, p-OCH_3), 5.85 (1H, s, -CH-Ar), 6.39 - 7.34 (5H, m, Ar-H and -CH furan ring), 8.5 (1H, s, -CONH). ^{13}C NMR ($CDCl_3$) δ ; 20.8 (1), 35.2 (1), 56.5 (1), 56.8 (1), 64.2 (1), 112.7 (1), 112.3 (1), 113.1 (1), 115.1 (1), 122.3 (1), 122.9 (1), 132.4 (1), 148.8 (1), 149.5 (1), 149.7 (1), 157.5 (1), 168.8 (1).

Compound (4c) IR (KBr) cm^{-1}; 1664 (>C=O, -CONH str), 1699 (>C=O, thiazolidine ring), 1278 (C-O-C str), 781 (C-S-C str), 671 (C-Br str). ^{1}H NMR ($CDCl_3$) δ ppm; 1.98 (3H, *d*, -CH_3), 5.56 (1H, s, -CH-Ar), 6.32 - 7.30 (6H, m, Ar-H and -CH furan ring), 8.43 (1H, s, -CONH). ^{13}C NMR ($CDCl_3$) δ ; 20.8 (1), 35.6 (1), 64.6 (1), 112.8 (1), 115.7 (1), 121.5 (1), 122.6 (1), 130.6 (2), 131.5 (2), 149.2 (1), 138.9 (1), 157.1 (1), 168.4 (1).

Compound (4d) IR (KBr) cm^{-1}; 1655 (>C=O, -CONH str), 1692 (>C=O, thiazolidine ring), 1247 (C-O-C str), 757 (C-S-C str), 686 (C-Br str). ^{1}H NMR ($CDCl_3$) δ ppm; 1.89 (3H, *d*, -CH_3), 5.83 (1H, s, -CH-Ar), 6.40 - 7.21 (6H, m, Ar-H and -CH furan ring), 8.45 (1H, s, -CONH). ^{13}C NMR ($CDCl_3$) δ ; 20.8 (1), 35.4 (1), 64.3 (1), 112.9 (1), 115.1 (1), 121.8 (1), 122.7 (1), 130.9 (2), 131.5 (2), 149.5 (1), 138.4 (1), 157.3 (1), 168.2 (1).

Compound (4e) IR (KBr) cm^{-1}; 1611 (>C=O, -CONH str), 1698 (>C=O, thiazolidine ring), 1222 (C-O-C str), 734 (C-S-C str), 699 (C-Br str). ^{1}H NMR ($CDCl_3$) δ ppm; 1.87 (3H, *d*, -CH_3), 2.32 (2H, *q*, -CH_2), 3.21 (3H, *t*, -CH_3), 5.84 (1H, s, -CH-Ar), 6.39 - 7.11 (6H, m, Ar-H and -CH furan ring), 8.0 (1H, s, -CONH). ^{13}C NMR ($CDCl_3$) δ ;15.5 (1), 20.8 (1), 28.2 (1), 35.6 (1), 64.6 (1), 112.8 (1), 115.7 (1), 121.5 (1), 122.6 (1), 130.9 (2), 131.5 (2), 149.6 (1), 138.2 (1), 157.1 (1), 168.8 (1).

RESULTS AND DISCUSSION

Minimum inhibitory concentration (MIC) of all the synthesised compounds have been screened by Broth dilution method against four different strains, viz. Gram positive bacteria (*S. aureus* MTCC 96 and *S. pyogenes* MTCC 442) and Gram negative bacteria (*E.coli* MTCC 443 and *P. aeruginosa* MTCC 1688) and compared with standard drug Ampicillin. Antifungal activity against *C. albicans* MTCC 227, *A. niger* MTCC 282 and *A. clavatus* MTCC 1323 organisms was determined by same method and compared with standard drug Griseofulvin.

Antibacterial activity

In Gram positive bacterial strains compounds **2b, 2d, 2e, 3a, 3c, 4b** and **4d** showed good to very good activity (25 – 150 µg/ml) against *S. aureus* ; where as compounds **3b** and **3d** showed very good activity (62.5 – 100 µg/ml) against *S. pyogenes* compared with Ampicillin. In Gram negative bacterial compounds **2b, 2d, 2e, 3a, 3c, 4b** and **4d** showed very good activity (25 – 125 µg/ml) against *E. coli* ; compounds **2b, 2c, 2d, 2e** and **4b** showed good

activity (50 – 100 µg/ml) against *P. aeruginosa*. All others compounds show moderately active or less active against all bacterial strains.

Antifungal activity

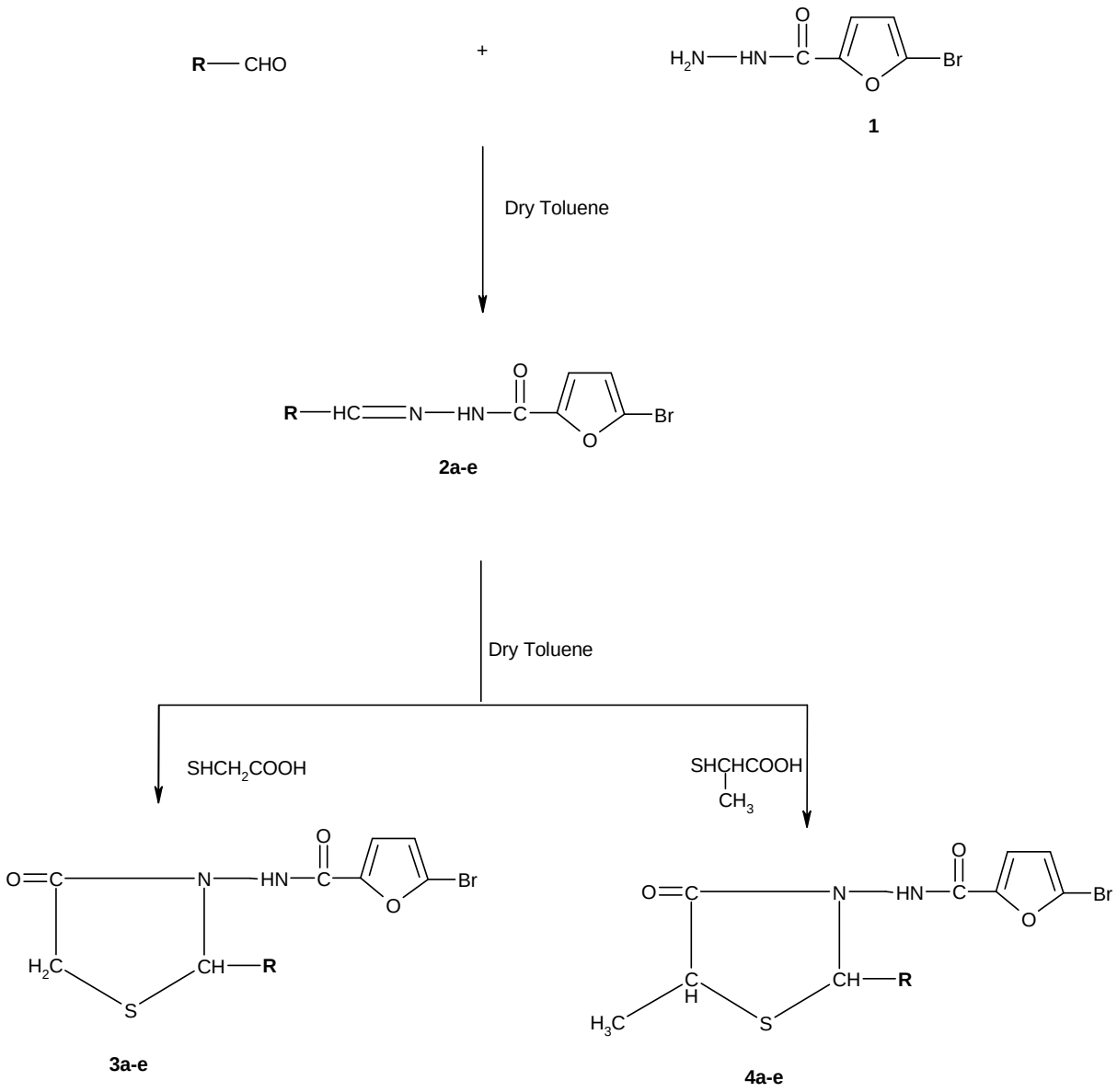
From the screening results **(Table – 2)**, compound **4b** showed very good activity against *C. albicans*, while compounds **2b, 3d, 4d** and **4e** showed good activity against *C. albicans* compared with Griseofulvin. Rest of the compounds show moderately active or less active against all bacterial strains.

Table -1 Characterisation data of compounds (2a-e), (3a-e) and (4a-e)

Compouds	R	M. F.	m.p. °C	Elemental Analysis		
				% C Found (Calcd)	% N Found (Calcd)	% H Found (Calcd)
2a	2,3-Dimethoxyphenyl	$C_{14}H_{13}BrN_2O_4$	158	47.61 (47.60)	7.93 (7.90)	3.71 (3.69)
2b	2,5-Dimethoxyphenyl	$C_{13}H_{11}BrN_2O_4$	203	47.61 (47.58)	7.93 (7.91)	3.71 (3.67)
2c	4-Fluorophenyl	$C_{12}H_8BrFN_2O_2$	138	46.33 (46.30)	9.00 (8.98)	2.59 (2.57)
2d	4-Bromophenyl	$C_{12}H_8Br_2N_2O_2$	196	38.74 (38.72)	7.53 (7.51)	2.17 (2.15)
2e	4-Ethylphenyl	$C_{14}H_{13}BrN_2O_2$	96	52.36 (52.33)	8.72 (8.70)	4.08 (4.07)
3[a]	2,3-Dimethoxyphenyl	$C_{16}H_{15}BrN_2O_5S$	141	44.98 (44.95)	6.56 (6.53)	3.54 (3.52)
3b	2,5-Dimethoxyphenyl	$C_{16}H_{15}BrN_2O_5S$	198	44.98 (44.97)	6.56 (6.52)	3.54 (3.51)
3c	4-Fluorophenyl	$C_{14}H_{10}BrFN_2O_3S$	185	43.65 (43.62)	7.27 (7.25)	2.62 (2.60)
3d	4-Bromophenyl	$C_{14}H_{10}Br_2N_2O_3S$	179	37.69 (37.66)	6.28 (6.26)	2.26 (2.24)
3e	4-Ethylphenyl	$C_{15}H_{13}BrN_2O_3S$	175	48.62 (48.60)	7.09 (7.07)	3.82 (3.80)
4a	3,4-Dimethoxyphenyl	$C_{17}H_{17}BrN_2O_5S$	180	46.27 (46.24)	6.35 (6.32)	3.38 (3.36)
4b	2,5-Dimethoxyphenyl	$C_{17}H_{17}BrN_2O_5S$	132	46.27 (46.25)	6.35 (6.34)	3.38 (3.35)
4c	4-Fluorophenyl	$C_{15}H_{12}BrFN_2O_3S$	218	45.13 (45.10)	7.02 (7.00)	3.03 (3.01)
4d	4-Bromophenyl	$C_{15}H_{12}Br_2N_2O_3S$	151	39.15 (39.12)	6.09 (6.06)	2.63 (2.62)
4e	4-Ethylphenyl	$C_{17}H_{17}BrN_2O_3S$	118	49.89 (49.87)	6.84 (6.82)	4.19 (4.17)

Table 2 – Antibacterial and antifungal activity data of compounds (2a-e), (3a-e) and (4a-e)

Compounds	Minimal bactericidal concentration µg/ml				Minimal fungicidal concentration µg/ml		
	Gram positive		Gram negative				
	S.aureus MTCC-96	*S.pyogenus* MTCC-442	*E. coli* MTCC-443	*P. aerug* MTCC-1688	*C. albicans*MTCC-227	*A. niger* MTCC-282	*A. clavatus*MTCC-1323
2a	125	125	200	125	1000	>1000	>1000
2b	500	250	100	100	500	>1000	>1000
2c	500	250	200	100	>1000	>1000	>1000
2d	200	250	125	100	>1000	500	500
2e	125	200	100	100	1000	>1000	>1000
3a	250	250	125	250	>1000	1000	1000
3b	100	62.5	200	200	>1000	>1000	>1000
3c	500	500	125	250	1000	>1000	>1000
3d	100	100	200	250	500	1000	1000
3e	200	200	200	125	1000	250	500
4a	250	250	200	200	500	1000	1000
4b	200	200	62.5	100	200	500	500
4c	500	250	500	500	1000	1000	1000
4d	250	250	100	125	1000	>1000	>1000
4e	250	250	250	250	500	1000	1000
Ampicillin	250	100	100	100	-	-	-
Griseofulvin	-	-	-		500	100	100



SCHEME - 1

CONCLUSION

Compound having methoxy group have exhibited more antimicrobial activity. These results suggest that the 4-oxo-thiazolidine derivatives have excellent scope for further development as commercial antimicrobial agents. All the newly synthesised compounds showed moderate to mild antimicrobial activity. These findings concluded that the titled compounds have the property to kill the microbes in some extent when compared with standard drug.

Acknowledgement
We are grateful to B. K. M. Science College, Valsad for providing research facilities, Atul Ltd. (Atul) for the IR spectral analysis and RSIC Punjab University for the ^{1}H NMR spectral analysis.

REFERENCE

[1] AA Abu-Hussen; *J. Coord Chem.*, **2006**, 59, 157.
[2] KM Sithambaram; PD Jagadesh; B Poojary; K Subramanya; *Bioorg. Med. Chem*., **2006**, 14, 7482.
[3] K Singh; MS Barwa; P Tyagi; *Eur. J. Med. Chem*., **2006**, 41, 1.

[4] P Pannerselvam; RR Nair; G Vijayalakshmi; EH Subramanian; SK Sridhar; *Eur. J. Med. Chem*., **2005**, 40, 225.
[5] SK Sridhar; M Saravan; A Ramesh; *Eur. J. Med. Chem*., **2001**, 36, 615.
[6] SN Pandeya; D Sriram; G Nath; E Declercq; *Eur. J. Pharmacol*., **1999**, 9, 25.
[7] R Mladenova; M Ignatova; N Manolova; T Petrova; I Rashkov; *Eur. Polym. J.*, **2002**, 38, 989.
[8] OM Walsh; MJ Meegan; RM Prendergast; TA Nakib; *Eur. J. Med. Chem*., **1996**,31, 989.
[9] AA Geronikaki; AA Lagunin; DI Hadjipavlou-Litina; PT Eleftheriou; DA Filimonov; VV Poroikov; I Alam; AK Saxena; *J Med Chem*., **2008**, 51, 1601.
[10] J Balzarini; B Orzeszko-Krzesinska; JK Maurin; A Orzeszko; *Eur J Med Chem*., **2009**, 44, 303.
[11] RP Tenorio; CS Carvalho; CS Pessanha; JG De Lima; AR De Faria; AJ Alves; EJ T. De Melo and AJ S. Goes; *Bioorg Med Chem Lett*., **2005**, 15, 2575.
[12] RM Abdel Rehman; *Boll. Chim. Fama*., **2001**, 140(6), 401.
[13] K Babaoglu; MA Page; VC Jones; MR Mcneil; C Dong; JH Nailsmith; And RE Lee; *Bioorg. Med. Chem. Letters*, **2003**, 13, 3227.
[14] MH Shih; and FY Ke; *Bioorg. Med. Chem.*, **2004**, 12**,** 4633.
[15] S Bondock; W Khalifa; and AA Fadda; *Eur. J. Med. Chem.*, **2007**, 42(7), 948, *Chem. Abstr.*, **2007**, 147, 257687z.
[16] JN Gadre; S Nair; and S Chitre; *Indian J. Chem.*, **2007**, 46B, 653.
[17] MG Vigorita; R Ottana; F Monforte; R Maccari; A Trovato; MT Monforte; MF Taviano; *Bioorg Med Chem Lett*., **2001**, 11, 2791.
[18] HR Hull; *J. Chem. Soc.*, **1957**, 4845.
[19] CL Patel; H Parekh; *J. Indian Chem. Soc*., **1988**, 65, 282.
[20] A Solankee; *J. Indian Chem. Soc*., **2011**, 88, 1.
[21] A Solankee; G Patel; R Patel; K Patel; *J. Inst. Chem*., **2011**, 83(6),176.
[22] A Solankee; K Patel; R Patel; *Adv. Appl. Sci. Res*., **2012**, 3(1), 117.
[23] A Solankee; K Patel; R Patel; *Arch. Appl. Sci. Res*., **2012**, 4(1),72.