Design and Synthesis of New Thiozolidinone Derivatives as Potential Antibacterial and Antifungal Agents

Vinay Mahyavanshi, Sunil I. Marjadi*

Department of Chemistry, KBS College, Vapi–396 195, India.
*Email: dr.marjadi@yahoo.in

Received: 3 January 2011; Accepted: 18 April 2011

Abstract
Some new 2-acetamido-N-(4-oxo-2-substitutedphenyl thiazolidin-3-yl)-3-(2-oxocyclopentyl) propanamide (4a-n) were prepared. The structures of the synthesized compounds were assigned on the basis of elemental analysis, IR, 1H NMR and 13C NMR spectral data. All the products were screened against various strains of bacteria and fungi.

Keywords: Antibacterial; Antifungal; One pot synthesis; Thiozolidinone.

1. Introduction
Sulfur-nitrogen containing heterocycles have wide application in medicinal chemistry. During the past few decades, interest has been rapidly growing in gaining insight into the properties and transformations of these heterocycles. Thiozolidinone have been found to possess a large number of biological activities viz. antimicrobial [1], antitumor [2], anticonvulsants [3], anti-inflammatory [4], antiviral [5], sulfur containing heterocycle like 4-thiazolidinone is an importance class of drug with important biological activities such as anti-HIV [6], fungicidal [7], antitubercular [8] and antibacterial [9-11].

The present work deals with the synthesis of the title compounds starting from methyl 2-acetamido-3-(2-oxocyclopentyl) propanoate, followed by their antimicrobial screening.

2. Experimental
2.1. General
Laboratory Chemicals were supplied by Rankem India Ltd. and Fisher Scientific Ltd. Melting points were determined by the open tube capillary method and are uncorrected. The purity of the compounds was determined by thin layer chromatography (TLC) plates (silica gel G) in the solvent system toluene: acetone (50:50). The spots were observed by exposure to iodine vapours or by UV light. The IR spectra were obtained on a Perkin-Elmer 1720 FT-IR spectrometer (KBr pellets). The 1H and 13C NMR spectra were recorded on a Bruker Avance II 400 spectrometer using TMS as the internal standard in CDCl3. Elemental analysis of the newly synthesized compounds were carried out on Carlo Erba 1108 analyzer.
2. 2. Preparation of 2-acetamido-3-(2-oxocyclopentyl) propanehydrazide (2)

A mixture of methyl 2-acetamido-3-(2-oxocyclopentyl) propanoate (1, 0.1 mole) and hydrazine hydrate (0.1 mole) in Methanol (30 mL) was refluxed for about 6 h. After TLC completed cooling the reaction mass and under vacuum distilled out methanol completely and added DM water and adjust pH 4.0 by using 10% acetic acid solution. Separated aqueous layer and adjusted pH 9.0 to 9.5 by using 10% sodium carbonate solution. Product Extracted by used MDC and under vacuum distilled out MDC completely to get colorless oil. Yield 70%. (Eluent: toluene/acetone 5:5).

2. 3. General preparation of the compounds (4a-n)

A mixture of 2-acetamido-3-(2-oxocyclopentyl) propanehydrazide (2) (0.1 mole) and appropriate aldehyde 3a–n (1.2 mole) in 30 mL of Toluene was taken in a round bottom flask with containing Dean-Stark water separator apparatus and was heated up to reflux temperature under constant stirring for 1 h; after one h, thioglycolic acid (0.15 mole) was added and the mass was further refluxed for 6 h and after then cooled to 30 °C. The whole mass was treated with saturated solution of NaHCO₃ and Toluene was evaporated. The product thus obtained was recrystallized from alcohol to get the pure crystals of 4a-n.

![Thiozolidinone 4a-n](image-url)

Fig. 1. Thiozolidinone 4a-n.

2. 3. 1. 2-acetamido-N-(2-(4-hydroxyphenyl)-4-oxothiazolidin-3-yl)-3-(2-oxocyclopentyl) propanamide (4a)

Yield 65%; m.p. 100-102 °C, IR (KBr, cm⁻¹) 3483 (-OH), 1734 (C=O thiozolidinone), 1654 (CONH), 625 (C=S-C), ¹H NMR 2.02 (s, 3H, NHCOCH₃), 2.01-2.11 (m, 6H,-CH₂ (Cyclopentane), 3.40 (dd, 1H, -CH), 8.01 (s, 1H, -NH-C=O), 5.93 (s, 1H, N-CH
2. 3. 2. 2-acetamido-N-(2-(4-methoxyphenyl) -4 -oxothiazolidin-3-yl)-3-(2-oxocyclopentyl) propanamide (4b)

Yield 65%; m.p. 150 °C, IR (KBr, cm⁻¹) 3484 (-OH), 1735 (C=O thiazolidinone), 1647 (CONH), 626 (C-S-C), 1H NMR 2.01 (s, 3H, NHCOC₃), 2.00-2.13 (m, 6H, -CH₂ (Cyclopentane), 3.41 (dd, 1H, -CH), 8.04 (s, 1H, -NH-C=O), 5.95 (s, 1H, N-CH thiazolidinone), 6.63-6.98 (m, 8H, Ar-H), 13C NMR 218.6 (C=O, cyclopentane) 168.84 (C=O, thiazolidinone), 57.19 (CHS, thiazolidinone); 114.0 -159.0 (Aromatic), 13C NMR 55.5 (O-CH₃), 218.4 (C=O, cyclopentane) 168.80 (C=O, thiazolidinone), 57.30 (CHS, thiazolidinone); 114.0 -159.0 (Aromatic), Anal. Calcd for C₁₉H₂₃N₅O₂S: C, 57.26; H, 6.01; N, 10.02; found C, 57.22; H, 5.99; N, 10.00.

2. 3. 3. 2-acetamido-N-(4-oxo-2-phenyl thia-lidin-3-yl)-3-(2-oxocyclopentyl) propanamide (4c)

Yield 63%; m.p. 133 °C, IR (KBr, cm⁻¹) 3471 (-OH), 1735 (C=O thiazolidinone), 1654 (CONH), 625 (C-S-C), 1H NMR 2.02-2.12 (m, 6H, -CH₂ (Cyclopentane), 3.44 (dd, 1H, -CH), 8.02 (s, 1H, -NH-C=O), 5.92 (s, 1H, N-CH thiazolidinone), 6.63-6.98 (m, 8H, Ar-H), 13C NMR 218.6 (C=O, cyclopentane) 168.84 (C=O, thiazolidinone), 57.19 (CHS, thiazolidinone); 114.0 -159.0 (Aromatic), 13C NMR (50 MHz; CDCl₃) δ: 218.4 (C=O, cyclopentane), 168.56 (C=O, thiazolidinone), 57.32 (CHS, thiazolidinone); 115.0 -160.0 (Aromatic), Anal. Calcd for C₁₉H₂₃N₅O₂S: C, 58.59; H, 5.95; N, 10.79; found C, 58.56; H, 5.93; N, 10.76.

2. 3. 4. 2-acetamido-N- (2-(2,3-dichlorophenyl) -4-oxothiazolidin-3-yl)-3-(2-oxocyclopentyl) propanamide (4d)

Yield 69%; m.p. 141 °C; IR (KBr, cm⁻¹) 3481 (-OH), 1737 (C=O thiazolidinone), 1648 (CONH), 620 (C-S-C), 1H NMR 2.02 (s, 3H, NHCOC₃), 2.04-2.15 (m, 6H, -CH₂ (Cyclopentane), 3.42 (dd, 1H, -CH), 8.04 (s, 1H, -NH-C=O), 5.91 (s, 1H, N-CH thiazolidinone), 6.66-6.98 (m, 8H, Ar-H), 13C NMR 218.6 (C=O, cyclopentane) 168.84 (C=O, thiazolidinone), 57.19 (CHS, thiazolidinone); 114.0 -159.0 (Aromatic), 13C NMR (50 MHz; CDCl₃) δ: 218.51 (C=O, cyclopentane), 168.60 (C=O, thiazolidinone), 47.29 (CHS, thiazolidinone); 115.0 -160.0 (Aromatic), Anal. Calcd for C₁₉H₂₃N₅O₂S: C, 49.79; H, 4.62; N, 9.17; found C, 49.76; H, 4.60; N, 9.15.

2. 3. 5. 2-acetamido-N- (2- (2, 3, 4-tri-methoxyphenyl)- 4- oxothiazolidin-3-yl) -3-(2-oxocyclopentyl) propanamide (4e)

Yield 62%; m.p. 178 °C, IR (KBr, cm⁻¹) 3471 (-OH), 1730 (C=O thiazolidinone), 1655 (CONH), 623 (C-S-C), 1H NMR 2.03 (s, 3H, NHCOC₃), 2.02-2.15 (m, 6H, -CH₂ (Cyclopentane), 3.39 (dd, 1H, -CH), 8.00 (s, 1H, -NH-C=O), 5.92 (s, 1H, N-CH thiazolidinone), 6.65-6.96 (m, 8H, Ar-H), 13C NMR 218.6 (C=O, cyclopentane) 168.84 (C=O, thiazolidinone), 57.19 (CHS, thiazolidinone); 114.0 -159.0 (Aromatic), 13C NMR (50 MHz; CDCl₃) δ: 55.90 (O-CH₃), 218.55 (C=O, cyclopentane), 168.81 (C=O, thiazolidinone), 47.25 (CHS, thiazolidinone); 115.0 -160.0 (Aromatic), Anal. Calcd for C₂₂H₂₅N₅O₃S: C, 55.10; H, 6.10; N, 8.76; found C, 55.09; H, 6.08; N, 8.74.

2. 3. 6. 2-acetamido-N- (2- (2-chlorophenyl)-4- oxothiazolidin-3 -yl)-3-(2-oxocyclopentyl) propanamide (4f)

Yield 65%; m.p. 118 °C; IR (KBr, cm⁻¹) 3449 (-OH), 1718 (C=O thiazolidinone), 1654
2. 3. 7. 2-acetamido-N-(2-(4-nitrophenyl)-4-oxothiazolidin-3-yl)-3-(2-oxocyclopentyl) propanamide (4g)

Yield (64%); m.p. 130 °C, IR (KBr, cm⁻¹) 3471 (-OH), 1735 (C=O thiazolidine), 1661 (CONH), 627 (C=S-C), 1H NMR 2.00 (s, 3H, NHCOC₃), 2.05-2.16 (m, 6H,-CH₂ (Cyclopentane), 3.39 (dd, 1H,-CH), 8.02 (s, 1H,-NH-C=O), 5.97 (s, 1H, N-CH thiazolidine), 6.62-6.98 (m, 8H, Ar-H), 13C NMR 218.6 (C=O, cyclopentane) 168.84 (C=O, thiazolidine), 57.19 (CHS, thiazolidine); 114.0 -159.0 (Aromatic), 13C NMR (50 MHz; CDCl₃) δ: 55.90 (O-CH₃), 218.51 (C=O, cyclopentane), 168.85 (C=O, thiazolidine), 57.91 (CHS, thiazolidine); 115.0 -157.50 (Aromatic), Anal. Calcd for C₂₃H₂₉N₃O₅S: C, 55.10; H, 6.10; N, 8.76; found C, 55.08; H, 6.07; N, 8.74.

2. 3. 9. 2-acetamido-N-(4-oxo-2-(3-phenoxyphe-nyl) thiazolidin-3-yl)-3-(2-oxocyclo-pentyl) propanamide (4i)

Yield 66%; m.p. 105 °C; IR (KBr, cm⁻¹) 3477 (-OH), 1734 (C=O thiazolidine), 1654 (CONH), 620 (C=S-C), 1H NMR 2.03 (s, 3H, NHCOC₃), 2.00-2.14 (m, 6H,-CH₂ (Cyclopentane), 3.39 (dd, 1H,-CH), 8.01 (s, 1H,-NH-C=O), 5.93 (s, 1H, N-CH thiazolidine), 6.65-6.96 (m, 8H, Ar-H), 13C NMR 218.6 (C=O, cyclopentane) 168.84 (C=O, thiazolidine), 57.19 (CHS, thiazolidine); 114.0 -159.0 (Aromatic), 13C NMR (50 MHz; CDCl₃) δ: 218.49 (C=O, cyclopentane), 168.81 (C=O, thiazolidine), 57.62 (CHS, thiazolidine); 117.0 -157.00 (Aromatic), Anal. Calcd for C₂₃H₂₉N₃O₅S: C, 62.35; H, 5.65; N, 8.73; found C, 62.34; H, 5.63; N, 8.70.

2. 3. 10. 2-acetamido-N- (2-(4-(dimethyl amino) phenyl) -4- oxothiazolidin-3-yl) -3-(2-oxocyclopentyl) propanamide (4j)

Yield 61%; m.p. 120°C; IR (KBr, cm⁻¹) 3475 (-OH), 1718 (C=O thiazolidine), 1654 (CONH), 622 (C=S-C), 1H NMR 1.99 (s, 3H, NHCOC₃), 2.05-2.16 (m, 6H,-CH₂ (Cyclopentane), 3.39 (dd, 1H,-CH), 8.00 (s, 1H,-NH-C=O), 5.92 (s, 1H, N-CH thiazolidine), 6.65-6.97 (m, 8H, Ar-H), 13C NMR 218.6 (C=O, cyclopentane) 168.84 (C=O, thiazolidine), 57.19 (CHS, thiazolidine); 114.0 -159.0 (Aromatic), 13C NMR (50 MHz; CDCl₃) δ: 218.56 (C=O, cyclopentane), 168.85 (C=O, thiazolidine), 57.31 (CHS, thiazolidine); 114.0 -148.00 (Aromatic), Anal. Calcd for C₂₁H₂₈N₃O₅S: C, 58.31; H, 6.52; N, 12.95; found C, 58.29; H, 6.50; N, 12.93.
2.3.11. 2-acetamido-N- (2-(4-hydroxy-3-methoxyphenyl) -4-oxothiazolidin -3-yl)-3- (2-oxocyclopentyl) propanamide (4k)
Yield 71%; m.p. 174 °C; IR (KBr, cm⁻¹): 3475 (-OH), 1718 (C=O thiazolidinone), 1654 (CONH), 622 (C=S-C), 1H NMR 2.02 (s, 3H, NHCOCH₃), 2.01 - 2.12 (m, 6H, -CH₂ (Cyclopentane), 3.38 (dd, 1H, -CH), 8.01 (s, 1H, -NH-C=O), 5.95 (s, 1H, N-CH₃(=S)), 6.64-6.95 (m, 8H, Ar-H), 13C NMR 218.6 (C=O, cyclopentane) 168.84 (C=O, thiazolidinone), 57.19 (CHS, thiazolidinone); 114.0 -159.0 (Aromatic), 13C NMR (50 MHz; CDCl₃) δ: 56.21 (O-CH₃), 218.51 (C=O, cyclopentane), 168.80 (C=O, thiazolidinone), 57.61 (CHS, thiazolidinone); 114.0 -151.00 (Aromatic), Anal. Calcd for C₃₄H₂₅N₃O₆S: C, 55.16; H, 5.79; N, 9.65; found C, 55.14; H, 5.77; N, 9.63.

2.3.12. 2-acetamido- N- (2- (3-bromo-4- methoxyphenyl) -4-oxothiazolidin-3-yl) -3- (2-oxocyclopentyl) propanamide (4l)
Yield 70%; m.p. 146 °C; IR (KBr, cm⁻¹): 3475 (-OH), 1718 (C=O thiazolidinone), 1654 (CONH), 622 (C=S-C), 1H NMR 2.02 (s, 3H, NHCOCH₃), 2.01-2.11 (m, 6H, -CH₂ (Cyclopentane), 3.40 (dd, 1H, -CH), 8.01 (s, 1H, -NH-C=O), 5.93 (s, 1H, N-CH₃(thiazolidinone), 6.65-6.96 (m, 8H, Ar-H), 13C NMR 218.6 (C=O, cyclopentane) 168.84 (C=O, thiazolidinone), 57.19 (CHS, thiazolidinone); 114.0 -159.0 (Aromatic), 13C NMR (50 MHz; CDCl₃) δ: 56.21 (O-CH₃), 218.56 (C=O, cyclopentane), 168.87 (C=O, thiazolidinone), 56.61 (CHS, thiazolidinone); 114.0 -155.00 (Aromatic), Anal. Calcd for C₃₂H₂₄BrN₃O₆S: C, 48.20; H, 4.85; N, 8.43; found C, 48.18; H, 4.83; N, 8.40.

2.3.13. 2-acetamido-N-(2-(2-nitrophenyl)-4-oxothiazolidin-3-yl)-3- (2-oxocyclopentyl) propanamide (4m)
Yield 67%; m.p. 119 °C; IR (KBr, cm⁻¹): 3475 (-OH), 1718 (C=O thiazolidinone), 1654 (CONH), 622 (C=S-C), 1H NMR 2.01 (s, 3H, NHCOCH₃), 2.01-2.10 (m, 6H, -CH₂ (Cyclopentane), 3.39 (dd, 1H, -CH), 8.01 (s, 1H, -NH-C=O), 5.93 (s, 1H, N-CH₃(thiazolidinone), 6.65-6.96 (m, 8H, Ar-H), 13C NMR 218.6 (C=O, cyclopentane) 168.84 (C=O, thiazolidinone), 57.19 (CHS, thiazolidinone); 114.0 -159.0 (Aromatic), 13C NMR (50 MHz; CDCl₃) δ: 218.51 (C=O, cyclopentane), 168.81 (C=O, thiazolidinone), 48.91 (CHS, thiazolidinone); 121.0 -149.00 (Aromatic), Anal. Calcd for C₁₉H₁₂₂N₄O₆S: C, 52.52; H, 5.10; N, 12.90; found C, 52.50; H, 5.08; N, 12.87.

2.3.14. 2-acetamido-N-(2-(3-chlorophenyl)-4-oxothiazolidin-3-yl) -3- (2-oxocyclopentyl) propanamide (4n)
Yield 72%; m.p. 181 °C; IR (KBr, cm⁻¹): 3475 (-OH), 1718 (C=O thiazolidinone), 1654 (CONH), 622 (C=S-C), 1H NMR 2.02 (s, 3H, NHCOCH₃), 2.01-2.11 (m, 6H, -CH₂ (Cyclopentane), 3.39 (dd, 1H, -CH), 8.01 (s, 1H, -NH-C=O), 5.93 (s, 1H, N-CH₃(thiazolidinone), 6.65-6.95 (m, 8H, Ar-H), 13C NMR 218.6 (C=O, cyclopentane) 168.84 (C=O, thiazolidinone), 57.19 (CHS, thiazolidinone); 114.0 -159.0 (Aromatic), 13C NMR (50 MHz; CDCl₃) δ: 218.59 (C=O, cyclopentane), 168.84 (C=O, thiazolidinone), 48.91 (CHS, thiazolidinone); 121.0 -149.00 (Aromatic), Anal. Calcd for C₁₉H₁₂₂N₄O₆S: C, 52.52; H, 5.10; N, 12.90; found C, 52.50; H, 5.08; N, 12.87.

3. Results and Discussion
3.1. Chemistry
One pot synthesis of 4-thiazolidinones from 2-acetamido-3-(2-oxocyclopentyl) propane-hydrazide (2) with different aromatic aldehyde (3a-n) in presence of Thioglycolic acid in Toluene has been described in scheme-1. All the synthesized compounds are confirmed from their characteristic IR, 1H NMR and 13C NMR spectroscopic data and elemental analyses as described in the experimental section.
3.2. Antimicrobial activity

The MICs of synthesized compounds were carried out by broth micro dilution method as described by EUCAST [12]. Antibacterial activity was screened against two gram positive (Staphylococcus aureus MTCC 96, Streptococcus pyogenes MTCC 443) and two gram negative (Escherichia coli MTCC 442, Pseudomonas aeruginosa MTCC 2488) bacteria, ampicillin was used as a standard antibacterial agent. Antifungal activity was screened against three fungal species Candida albicans MTCC 227, Aspergillus niger MTCC 282 and Aspergillus clavatus MTCC 1323, greseofulvin was used as a standard antifungal agent All MTCC cultures were collected from National Chemical Laboratory Pune (India).

3.2.1. Activity against E. coli

The maximum activity was shown by the compounds 4a, 4b, 4d, 4h, 4k and 4l the zone of inhibition was 18mm to 26mm, and the moderate activity was shown by the compound 4c the zone of inhibition was 10mm to 13mm and remaining compounds are less active compared to the standard drugs.

3.2.2. Activity against P. aeruginosa

The maximum activity was shown by the compounds 4a, 4b, 4n and 4m the zone of inhibition was 16mm to 21mm, and the moderate activity was shown by the compound 4e, 4f, 4g,4h and 4i the zone of inhibition was 12mm to 15mm and remaining compounds are less active compared to the standard drugs.

3.2.3. Activity against S. aureus

The maximum activity was shown by the compounds 4a, 4b, 4c, 4f, 4h and 4i the zone of inhibition was 15 mm to 18mm, and the moderate activity was shown by the compound 4d, 4e, 4j, 4l and 4n the zone of inhibition was 09mm to 14mm and remaining compounds are less active compared to the standard drugs.

3.3. Antifungal activity

3.3.1. Activity against C. albicans

The maximum activity was shown by the compounds 4b, 4d and 4f the zone of inhibition was 17mm to 21mm, and the moderate activity was shown by the compound 4g, 4h, 4i, 4j and 4e the zone of inhibition was 11mm to 14mm and remaining compounds are less active compared to the standard drugs.

3.3.2. Against A. niger

The maximum activity was shown by the compounds 4b the zone of inhibition was 22mm to 24mm, and the moderate activity was shown by the compound 4a, 4e and 4l the zone of inhibition was 15mm to 19mm and remaining compounds are less active compared to the standard drugs.

4. Conclusions

Thiozolidinone derivatives possessed very good activity against all four bacterial species. In the case of Thiozolidinone derivatives, compounds 4a, 4b, 4d, 4h, 4k and 4l are said to be active as Penicillin-G and Ampicillin when they were tested with E. coli. In the case of Thiozolidinone derivatives, Compound 4a and 4b are said to be active as Penicillin-G and Ampicillin when they were tested with P.aeruginosa. Compound 4m displayed excellent activity against P.aeruginosa. Compounds, 4b, 4c, 4f, 4h and 4i are said to be active as Penicillin-G and Ampicillin when they were tested with S. aureus. Compound 4g displayed excellent activity against S. aureus. Compounds 4b, 4d and 4f are said to be active as Griseofulvin when they were tested with C.albicans. Compound 4b displayed excellent activity against C.albicans. Compounds 4b are said to be active as Griseofulvin when they were tested with C.albicans. From the results, it is concluded that the Thiozolidinone derivatives showed good antibacterial activity rather than antifungal activity.
Table 1. Antimicrobial data of compounds 4a-n

<table>
<thead>
<tr>
<th>Compd.</th>
<th>E.coli 128µg/mL</th>
<th>P.aeruginosa 256µg/mL</th>
<th>S.aureus 512µg/mL</th>
<th>C.albicans 128µg/mL</th>
<th>A. niger 256µg/mL</th>
<th>C.albicans 512µg/mL</th>
<th>A. niger 256µg/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>4a</td>
<td>18</td>
<td>20</td>
<td>22</td>
<td>17</td>
<td>19</td>
<td>20</td>
<td>15</td>
</tr>
<tr>
<td>4b</td>
<td>18</td>
<td>19</td>
<td>21</td>
<td>17</td>
<td>19</td>
<td>20</td>
<td>19</td>
</tr>
<tr>
<td>4c</td>
<td>19</td>
<td>11</td>
<td>12</td>
<td>12</td>
<td>15</td>
<td>17</td>
<td>14</td>
</tr>
<tr>
<td>4d</td>
<td>19</td>
<td>19</td>
<td>20</td>
<td>13</td>
<td>16</td>
<td>19</td>
<td>15</td>
</tr>
<tr>
<td>4e</td>
<td>09</td>
<td>10</td>
<td>11</td>
<td>13</td>
<td>14</td>
<td>15</td>
<td>13</td>
</tr>
<tr>
<td>4f</td>
<td>09</td>
<td>11</td>
<td>12</td>
<td>13</td>
<td>14</td>
<td>15</td>
<td>13</td>
</tr>
<tr>
<td>4g</td>
<td>10</td>
<td>11</td>
<td>13</td>
<td>14</td>
<td>15</td>
<td>15</td>
<td>12</td>
</tr>
<tr>
<td>4h</td>
<td>19</td>
<td>20</td>
<td>22</td>
<td>12</td>
<td>13</td>
<td>15</td>
<td>11</td>
</tr>
<tr>
<td>4i</td>
<td>09</td>
<td>10</td>
<td>11</td>
<td>13</td>
<td>15</td>
<td>16</td>
<td>14</td>
</tr>
<tr>
<td>4j</td>
<td>10</td>
<td>12</td>
<td>14</td>
<td>12</td>
<td>14</td>
<td>17</td>
<td>13</td>
</tr>
<tr>
<td>4k</td>
<td>22</td>
<td>24</td>
<td>26</td>
<td>13</td>
<td>15</td>
<td>17</td>
<td>14</td>
</tr>
<tr>
<td>4l</td>
<td>18</td>
<td>20</td>
<td>21</td>
<td>15</td>
<td>17</td>
<td>19</td>
<td>14</td>
</tr>
<tr>
<td>4m</td>
<td>09</td>
<td>12</td>
<td>13</td>
<td>19</td>
<td>20</td>
<td>21</td>
<td>13</td>
</tr>
<tr>
<td>4n</td>
<td>07</td>
<td>11</td>
<td>13</td>
<td>08</td>
<td>10</td>
<td>10</td>
<td>09</td>
</tr>
</tbody>
</table>

Penicillin-G: 30 34 38 32 36 40 34 36 38 - - -
Ampicillin: 34 36 40 33 34 38 32 34 38 - - -
Griseofulvin: - - - - - - - 30 34 32 35

Acknowledgements
The authors are thankful to the management of KBS College, Vapi for facilities. We also wish to thank Aarti Health care for IR spectra, C.D.R.I., Lucknow for elemental analysis, and Center of excellence Vapi, for 1H NMR and 13C NMR spectral analysis.

References
[12] European Committee for Antimicrobial Susceptibility Testing (EUCAST) of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID).