

## Synthesis characterization and pharmacological activity of novel thiazolidin – 4 one analogues

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### ABSTRACT

A new series of 4-oxo-thiazolidines (3a<sub>1</sub>-3a<sub>6</sub>) were prepared by reacting Sulphadiazine with substituted aldehydes in alcohol medium in presence of strong base. The resulted Schiff's base undergoes cyclization with mercapto acetic acid and mercapto succinic acid to yield 4-oxo-thiazolidines (3b<sub>1</sub>-3b<sub>6</sub>). The structure of the final synthesized compounds were confirmed by IR, <sup>1</sup>H-NMR and MASS spectral technique. The title compounds were screened for their analgesic, anticonvulsant and antibacterial activities.

**Key words:** 4-oxo-thiazolidines, Schiff's base, Analgesic activity, Anticonvulsant activity, Antimicrobial activity.

### INTRODUCTION

4-oxo-thiazolidone is an important heterocyclic compound, has been the subject of study in the recent year. It plays a vital role owing to their wide range of biological & pharmacological activities. These are well known compounds that were found to possess various biological activities like antibacterial<sup>1</sup>, antifungal<sup>2</sup>, antitubercular<sup>3</sup>, anthelmintic<sup>4</sup>, antiviral & malarial<sup>5</sup>, properties. It was also found that they possess analgesic, anti-inflammatory, anticonvulsant<sup>6</sup>, and antioxidant<sup>7</sup>, antiparkinsonian activities<sup>8</sup>,

Bacterial infections have increased dramatically in recent years. Bacteria have been the cause of some of the most deadly disease and widespread epidemics in human civilization. Bacterial disease such as tuberculosis, typhus, plague, diphtheria, typhoid fever, cholera, dysentery, and pneumonia have taken a high toll on humanity.

Epilepsy is the most frequent neurologic affection characterized by excessive temporary neuronal discharge. The overall prevalence of the

disease is 0.5-1.0% of the population and up to 50 million people worldwide. Many patients with epilepsy do not respond well to currently available antiepileptic drugs (AED) such as phenytoin, carbamazepine, diazepam, Phenobarbital. Ethusoximide, valproate, valroceamide, vigabatrin, gabapentin, zonisamide, topiramate, tiagabine, felbamate, retigabine, lamotrigine, and levetiracetam which are effective towards only 50-80% of the patients and present some undesirable side effect such as vertigo, ataxia, headache, hirsutism, hepato toxicity, gastrointestinal, and cardiovascular side effects.

This study seeks to synthesize a series of novel thiazole derivatives that contain the sydnonyl moiety, with the aim of obtaining new biologically active compound. In view of the continued interest in the development of simpler and more convenient synthetic routes for preparing heterocyclic systems.

The main synthetic routes to 1,3-thiazolidin-4-ones involve three components (an aldehyde, an amine and mercaptoacetic acid), either in a one – or a two –step process. 1 the reaction

proceed by initial formation of an imine, which undergoes attack by the sulfur nucleophile, followed by intramolecular cyclization on elimination of water. The most common protocol to remove the water is by azeotropic distillation, but use of chemical drying agents (Scavengers) such as DCC has been demonstrated.

## MATERIAL AND METHODS

The title compounds melting points were taken by open capillary tubes and were uncorrected. The purity of compounds was checked by TLC on silica gel G plates using methanol: chloroform (1:9) and acetone, chloroform (1:1) as solvent system. IR spectra were recorded using KBR plates on shimadzu 8000 series spectrophotometer H<sup>1</sup>, NMR spectra on a various EM-200, advance 200MHz spectrophotometer using DMSO as solvent 4 TMS as internal standard (chemical shift values expressed in PPM) and mass spectra on Jeol SX 102(FAB) mass spectrophotometer.

### Preparation 4-(arylidineamine) –N-pyrimidin-2-yl benzene sulphonamide: (2<sub>a1</sub>-2<sub>a6</sub>)

Equimolar mixture of sulfadiazine (0.01mol) and substituted benzaldehyde (0.01 mol) dissolved in ethanol few drops of 20% KOH 10M and 100mg of PISA was added. The reaction mixture was refluxed for 18-20 hrs. the reaction mixture was then poured into crushed ice. Then the solution was acidified with 10% HCL to get solid and it was filtered. The obtained product was recrystallized from ethanol and their physical data are given.

**2<sub>a1</sub>** IR (KBr) cm<sup>-1</sup> 3231 (NH), 3060(-CH, aromatic) 1632 (C=N) 1580 (N=CH). <sup>1</sup>H NMR:10.0 (s,NH) 8.6(s,CH),6.5-8.4(m,Ar H).

**2<sub>a2</sub>** IR (KBr) cm<sup>-1</sup> 3351 (NH), 3098(-CH, aromatic) 1625 (C=N) 1595 (N=CH). <sup>1</sup>H NMR:10.1 (s,NH) 8.9(s,CH),6.5-8.5(m,Ar H).

**2<sub>a3</sub>** IR (KBr) cm<sup>-1</sup> 3215 (NH), 3011(-CH, aromatic) 1625 (C=N) 1578 (N=CH). <sup>1</sup>H NMR:11.2 (s,NH) 10.0(s,OH),8.9(s,CH),6.6-8.5(m,Ar H).

**2<sub>a4</sub>** IR (KBr) cm<sup>-1</sup> 3345 (NH), 3110(-CH, aromatic) 1640 (C=N) 1550 (N=CH). <sup>1</sup>H NMR:11.2 (s,NH) 10.1(s,OH),8.8(s,CH),6.5-8.5(m,Ar H).

**2<sub>a5</sub>** IR (KBr) cm<sup>-1</sup> 3325 (NH), 3100(-CH, aromatic) 1680 (C=N) 1562 (N=CH). <sup>1</sup>H NMR:10.0 (s,NH) 8.9(s,CH),6.6-8.6(m,Ar H),3.9(s,CH<sub>3</sub>).

**2<sub>a6</sub>** IR (KBr) cm<sup>-1</sup> 3340 (NH), 3025(-CH, aromatic) 1659 (C=N) 1556 (N=CH). <sup>1</sup>H NMR:10.0 (s,NH) 8.8(s,CH),6.5-8.5(m,Ar H).

Preparation of 4-oxa Thiazolidine Derivatives : Equimolar quantity of Schiff bases and mercapto acetic acid or mercapto succinic acid were refluxed for 10 to 12 hours on 50 ml THF using anhydrous zinc chloride as catalyst the reaction mixture was concentrated by evaporation and triturated with 20% sodium bicarbonate 10 M to remove unreacted acid and solution thus obtained was filtered and recrystallized by appropriate solvent to give 4-oxathiazolidine derivative. Physical data is given in Table 1 and 2.

**3<sub>a1</sub>** IR (KBr) cm<sup>-1</sup> 3740(NH), 3057 (-CH, aromatic), 2845 (C=C), 1746 (C=O), 1367 (C-N) 688 (C-S). <sup>1</sup>H NMR:ä 10.0(s,NH), 6.4(s, CH<sub>2</sub>),3.9(s, CH<sub>2</sub>), 6.5-7.5(m,Ar-H), 8.8(m.pyrAr-H). Mass (m/z) = M+412.

**3<sub>a2</sub>** IR (KBr) cm<sup>-1</sup> 3735(NH), 3157 (-CH, aromatic), 2815 (C=C), 1754 (C=O), 1354 (C-N) 688 (C-S). <sup>1</sup>H NMR:ä 10.1(s,NH), 6.5(s, CH<sub>2</sub>),4.0(s, CH<sub>2</sub>), 6.5-7.8(m,Ar-H), 8.5(m.pyr Ar-H). Mass (m/z) = M+446.

**3<sub>a3</sub>** IR (KBr) cm<sup>-1</sup> 3723(NH), 3127 (-CH, aromatic), 2821 (C=C), 1726 (C=O), 1321 (C-N) 667 (C-S). <sup>1</sup>H NMR:ä 10.5(s,NH), 6.5(s, CH<sub>2</sub>),4.2(s, CH<sub>2</sub>), 6.5-7.9(m,Ar-H), 8.6(m.pyr Ar-H). Mass (m/z) = M+446.

**3<sub>a4</sub>**

IR (KBr)  $\text{cm}^{-1}$  3740(NH), 3352(OH), 3076 (-CH, aromatic), 2740 (C=C), 1764 (C=O), 1354 (C-N) 681 (C-S).  $^1\text{H NMR}$ : $\delta$  10.1(s,NH), 9.8(s, OH), 6.5 (s, CH), 4.0(s,  $\text{CH}_2$ ), 6.5-7.8(m, Ar-H), 8.5(m, pyr Ar-H). Mass (m/z) = M+428.

**3<sub>a5</sub>**

IR (KBr)  $\text{cm}^{-1}$  3740(NH), 3450(OH), 3147 (-CH, aromatic), 2745 (C=C), 1736 (C=O), 1343 (C-N) 687 (C-S).  $^1\text{H NMR}$ : $\delta$  10.0(s,NH), 9.6(s, OH), 6.5 (s, CH), 4.1(s,  $\text{CH}_2$ ), 6.6-8.0(m, Ar-H), 8.5(m, pyr Ar-H). Mass (m/z) = M+428.

**3<sub>a6</sub>**

IR (KBr)  $\text{cm}^{-1}$  3625(NH), 3155 (-CH, aromatic), 2825 (C=C), 1726 (C=O), 1325 (C-N) 678 (C-S).  $^1\text{H NMR}$ : $\delta$  10.1(s,NH), 10.1(s, NH), 8.5(m, Ar-H), 6.6-8.0(m, Ar-H), 4.0(s, CH), 3.8(s,  $\text{CH}_2$ ),. Mass (m/z) = M+442.

**3<sub>b1</sub>**

IR (KBr)  $\text{cm}^{-1}$  3625(NH), 3155 (-CH, aromatic), 2815 (C=C), 1746 (C=O), 1695(C=O, -COOH), 1335 (C-N) 678 (C-S).  $^1\text{H NMR}$ : $\delta$  12.1(s,NH), 10.0(s, COOH), 8.5(m, Pyr Ar-H), 6.5-8.5(m, Ar-H), 3.0(t, CH), 2.8(d,  $\text{CH}_2$ ),. Mass (m/z) = M+470.

**3<sub>b2</sub>**

IR (KBr)  $\text{cm}^{-1}$  3652(NH), 3125 (-CH, aromatic), 2785 (C=C), 1726 (C=O), 1700(C=O, -COOH), 1345 (C-N) 680 (C-S).  $^1\text{H NMR}$ : $\delta$  12.2(s,NH), 10.0(s, COOH), 8.5(m, Pyr Ar-H), 6.5-7.9(m, Ar-H), 3.0(t, CH), 2.9(d,  $\text{CH}_2$ ),. Mass (m/z) = M+505.

**3<sub>b3</sub>**

IR (KBr)  $\text{cm}^{-1}$  3725(NH), 3055 (-CH, aromatic), 2855 (C=C), 1762 (C=O), 1685(C=O, -COOH), 1342 (C-N) 685 (C-S).  $^1\text{H NMR}$ : $\delta$  12.3(s,NH), 10.0(s, COOH), 8.6(m, Pyr Ar-H), 6.6-8.9(m, Ar-H), 3.0(t, CH), 2.9(d,  $\text{CH}_2$ ),. Mass (m/z) = M+505.

**3<sub>b4</sub>**

IR (KBr)  $\text{cm}^{-1}$  3625(NH), 3451 (OH), 3105(-CH, aromatic), 2855 (C=C), 1730 (C=O), 1701(C=O, -COOH), 1353 (C-N) 658 (C-S).  $^1\text{H NMR}$ : $\delta$  12.5(s,NH), 10.1(s, COOH), 9.8(s, OH) 8.5(m, Pyr

Ar-H), 6.5-7.1(m, Ar-H), 3.0(t, CH), 2.8(d,  $\text{CH}_2$ ),. Mass (m/z) = M+486.

**3<sub>b5</sub>**

IR (KBr)  $\text{cm}^{-1}$  3645(NH), 3330 (C=O), 3075(-CH, aromatic), 2735 (C=C), 1756 (C=O), 1690(C=O, -COOH), 1395 (C-N) 624 (C-S).  $^1\text{H NMR}$ : $\delta$  12.5(s,NH), 10.1(s, COOH), 9.8(s, OH) 8.5(m, Pyr Ar-H), 6.5-7.1(m, Ar-H), 3.0(t, CH), 2.8(d,  $\text{CH}_2$ ),. Mass (m/z) = M+486.

**3<sub>b6</sub>**

IR (KBr)  $\text{cm}^{-1}$  3325(NH), 3105 (-CH, aromatic), 2852 (C=C), 1761 (C=O), 1705(C=O, -COOH), 1325 (C-N) 678 (C-S).  $^1\text{H NMR}$ : $\delta$  12.2(s,NH), 10.1(s, COOH), 8.5(m, Pyr Ar-H), 6.5-7.9(m, Ar-H), 3.9(s,  $\text{OCH}_3$ ) 3.1(t, CH), 2.7(d,  $\text{CH}_2$ ),. Mass (m/z) = M+500.

#### Acute toxicity studies<sup>9</sup>

The acute toxicity of synthesized compounds was determined by using albino mice of either sex (20-30g). maintained under standard husbandary conditions. The animals were fasted overnight prior to the experiment and fixed dose (OECD) guideline No. 425) method of (CPCSEA) was adopted for toxicity studies. Effective dose ( $\text{ED}_{50}$  Therapeutic dose) is taken as 1/10<sup>th</sup> of lethal dose.

#### Analgesic Acitivity<sup>10</sup>

The analgesic activity of all the synthesized compounds was carried out by Eddy's hot plate method using albino mices of either sex (20-30 g). animals were deprived of food for 18hrs. prior to experiment (the first group was control group and received standard pentazocine drug (10 mg/kg I.P) and the remaining groups reward the compounds under investigation at 200 mg/kg P.O).

All the synthesized compounds (at 200mg/kg P.O) concentration were subjected to the determination of analgesic activity and compared the basal reaction time in seconds at different at different time intervals against the drug pentazoline (10 g/kg) and gum acacia (2%) was used as control. The results are shown in Table 3.

#### Anticonvulsant Activity<sup>11</sup>

The anticonvulsant activity of all the

synthesized compounds was carried out by MES induced convulsions method using albino mice of either (20-30 g). animals were deprived of food for 18hrs. prior to experiment (the first group was control group and received standard pentazocine drug (10 mg/kg I.P) and the remaining groups reward the compounds under investigation at 200 mg/kg P.O).

A 60mA current was delivered transauricularly for 0.2 sec in mice via small alligator clips attached to cornea. For recording various parameters. Mice were placed in a rectangular plastic cage with an open top, permitting full view of animals motor response to seizure in the pilot study of various phases of convulsions. The following parameters were recorded during 30min. test session. Tonic flexion, Tonic extension, Clonus convulsions, Percent protection. The values were expressed as mean $\pm$ SEM from 6 animals. The result were subjected to statistical analysis by using ANOVA followed by Tukey-Kramer test to calculate the significance difference if any among the groups  $p < 0.05$  was considered as significant. The result are shown in Table 4.

#### Antibacterial Activity<sup>12</sup>

Antibacterial Activity of all synthesized compound was determined by the disc diffusion method against the gram +ve organisms. Bacillus subtilis and Bacillus pumitis and gram -ve organisms E-coli, Pseudomonas aeruginosa at 100 mg/ml concentration. The bacteria were subcultured on nutrient agar medium. The petridishes were

incubated at 37°C for 24hrs. Std. anitbacteria drug ampicillin at 100mg/ml conc. Was also increased under similar conditions. The result are shown in Table 5.

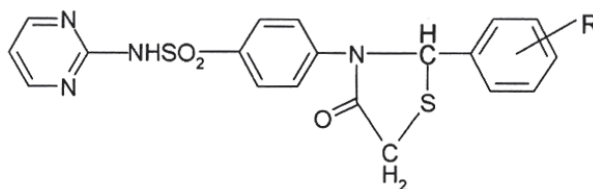
## RESULTS AND DISCUSSION

#### Analgesic Activity

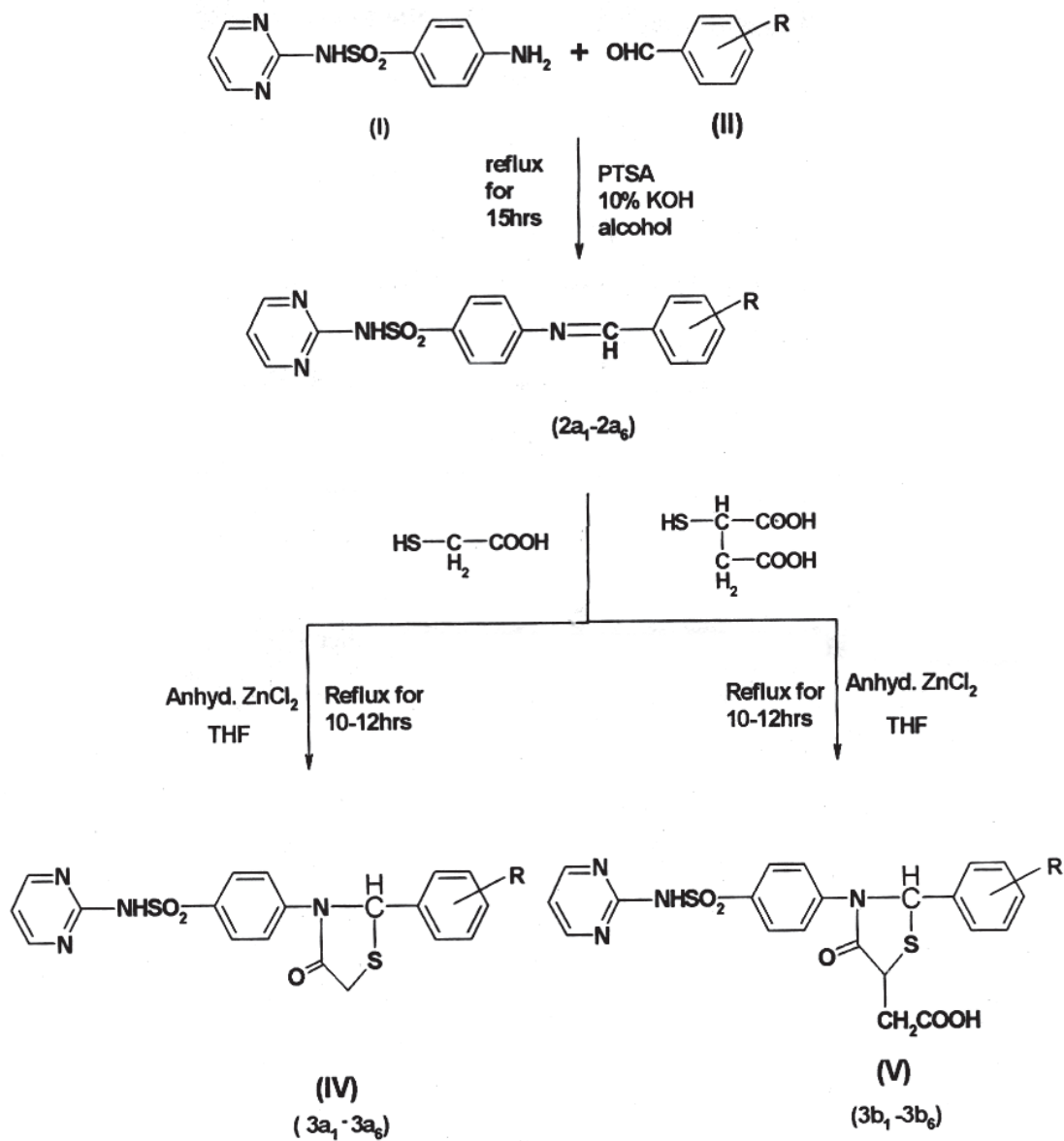
The synthesized 4-oxo-thioazolidine derivatives  $3_{a6}$ ,  $3_{a2}$ ,  $3_{b6}$ , were selected for the screening of analgesic activity at the dose of 200mg/kg using eddy's hot plate method in albino mice. The results are shown in Table No. III. The basal reaction time of compounds  $3_{a6}$ ,  $3_{a2}$ ,  $3_{b6}$ , and  $3_{b2}$  14.94, 14.71, 13.60 and 11.16 seconds respectively at 60 minutes, whereas of standard drug Pentazocine (10mg/kg) used was 13.87 seconds at 60 minutes. From the above data it is clear that former six compounds are having equipotent analgesic activity and later two compounds are moderate to less analgesic activity when compared to that of standard drug Pentazocine.

From analgesic activity evaluation data it is clear that compounds  $3_{a6}$ ,  $3_{a2}$ ,  $3_{b6}$ , shown very good analgesic. Activity whereas the compounds  $3_{b2}$  have shown less analgesic activity when compare to that of standard as well as other 4-oxo-thiazolidine derivatives. The poor activity of these compounds may be due to the presence of  $\text{CH}_2\text{COOH}$  group at 5<sup>th</sup> position of thiazolidinone nucleus, which made them less analgesic.

Table 1: Physical characterization data of compound ( $3a_1$ - $3a_6$ )



S. No	Compound Code	R	Melting point	Molecular formula	Molecular weight
1	$3a_1$	H	265°C-270°C	$\text{C}_{19}\text{H}_{16}\text{N}_4\text{O}_3\text{S}_2$	421
2	$3a_2$	2-Cl	245°C-247°C	$\text{C}_{19}\text{H}_{15}\text{ClN}_4\text{O}_3\text{S}_2$	446
3	$3a_3$	4-Cl	254°C-260°C	$\text{C}_{19}\text{H}_{15}\text{ClN}_4\text{O}_3\text{S}_2$	446
4	$3a_4$	2-OH	145°C-150°C	$\text{C}_{19}\text{H}_{16}\text{N}_4\text{O}_4\text{S}_2$	428
5	$3a_5$	4-OH	212°C-215°	$\text{C}_{19}\text{H}_{16}\text{N}_4\text{O}_4\text{S}_2$	428
6	$3a_6$	4- $\text{OCH}_3$	>300°	$\text{C}_{20}\text{H}_{18}\text{N}_4\text{O}_4\text{S}_2$	442



Scheme 1:

### Anticonvulsant activity

The 4-oxo-thiazolidine derivatives were selected and screened for the anticonvulsant activity at the dose of 200mg/kg using MES induced model in albino mice. The anticonvulsant activity data is given in table No. IV. The anticonvulsant activity result of the synthesized 4-oxo-thiazolidine was studied by considering 2 main parameters,

1. Lesser duration of tonic extensor phase,
2. Maximum protection of animals after 24hrs.

The compounds  $3_{a2}$ ,  $3_{a6}$ , and  $3_{b2}$  were exhibited significant anticonvulsant activity against electrically induced convulsion, they protected the animals up to 66.66% and the tonic extensor phase of these agents is 5,93,9.19, and 9.65 seconds respectively. Whereas rest of the compounds thought they showed good decrease in the tonic extensor phase Phenyl to in exerts its anticonvulsant action against generalized tonic seizures by preventing seizure spread.

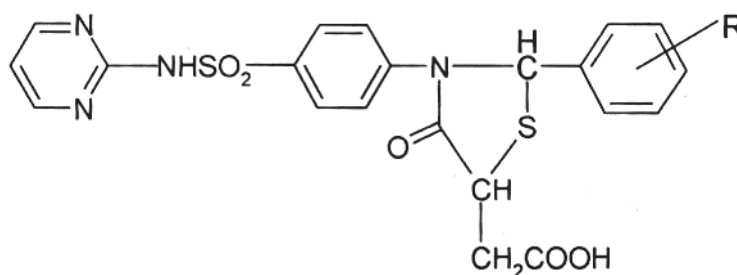
From anticonvulsant evaluation it was found that significant anticonvulsant activity of  $3_{a2}$ ,  $3_{a6}$ , and  $3_{b2}$  may be due to the presence of electron withdrawing groups at 2<sup>nd</sup> or 4<sup>th</sup> position of the phenyl ring. Which is attached to 2<sup>nd</sup> position of the thiazolidinone nucleus.

### Antibacterial Activity

The synthesized 12 compounds were screened for antibacterial activity studies at a concentration of 50µg/ml and 100µg/ml using DMSO as a control against *Staphylococcus aureus*, *Bacillus pumilus*, *Bacillus subtilis*, *Escherichia coli* and *Pseudomonas aeruginosa* by disk-diffusion method on nutrient agar media. Ampicillin was used as standard drugs for the comparison at the concentration 50µg/ml and 100µg/ml against Gram positive and gram – negative bacteria used for the study.

Data in the Table 5 clearly indicates that, none of the compound exhibits antibacterial activity. The zone of inhibition of all the synthesized compounds was between 7-10mm at 50µg/ml conc and 11-13mm at 100µg/ml conc. whereas the zone of inhibition of standard drug Ampicillin was 21-24mm at 50µg/ml conc. and 32-35mm at many studies have revealed that sulfanilamides are having very good antibacterial activity, but in the present study none of the synthesized compound exhibits such antibacterial activity, this may be due to the bulky substitution at N4 position of benzene sulfonamide, which may leads to the rigidity of the compounds and this may hinders the cleavage of molecule in physiological P<sup>H</sup>, which is a basic requirement for the activity of sulfonamides.

Table 2: Physical characterization data of compound (3b<sub>1</sub>-3b<sub>6</sub>)



S. No	Compound Code	R	Melting point	Molecular formula	Molecular weight
1	3b <sub>1</sub>	H	278°C-282°C	C <sub>21</sub> H <sub>18</sub> N <sub>4</sub> O <sub>5</sub> S <sub>2</sub>	470
2	3b <sub>2</sub>	2-Cl	262-265°C	C <sub>21</sub> H <sub>17</sub> ClN <sub>4</sub> O <sub>5</sub> S <sub>2</sub>	505
3	3b <sub>3</sub>	4-Cl	256°C-268°C	C <sub>21</sub> H <sub>17</sub> ClN <sub>4</sub> O <sub>5</sub> S <sub>2</sub>	505
4	3b <sub>4</sub>	2-OH	>300°C	C <sub>21</sub> H <sub>18</sub> N <sub>4</sub> O <sub>6</sub> S <sub>2</sub>	486
5	3b <sub>5</sub>	4-OH	223°C-227°C	C <sub>21</sub> H <sub>18</sub> N <sub>4</sub> O <sub>6</sub> S <sub>2</sub>	486
6	3b <sub>6</sub>	4-OCH <sub>3</sub>	292°C-296°C	C <sub>22</sub> H <sub>20</sub> N <sub>4</sub> O <sub>6</sub> S <sub>2</sub>	500

Table 3: Analgesic activity data of 4-oxo-thizolidine derivatives

Treatment	No. of animals	Average weight of animals (grams)	Dose mg/kg	Basal reaction time (sec.) after										
				0 minutes	20 minutes	40 minutes	60 minutes	80 minutes	100 minutes	120 minutes	180 minutes			
Control (gum acacia)	6	34	-	3.9 ±0.367	4.12 ±0.473	4.12 ±0.553	4.22 ±0.503	4.27 ±0.324	3.88	5.20 ±0.647	-	-		
Standard (pentrazocine)	6	28	0.28	6.53 ±0.889	12.87 ±1.332	12.91 ±1.320	13.87 ±0.279	13.65 ±0.851	11.83	12.33 ±0.918	13.14	13.14		
3a <sub>6</sub> (Group III)	6	30.66	6.13	3.97 ±0.058	10.73 ±1.597	12.45 ±1.613	14.94 ±0.033	14.15 ±0.449	14.54	11.91 ±1.052	14.03	14.03		
3a <sub>2</sub> (Group IV)	6	29.33	5.86	5.49 ±0.416	11.66 ±1.889	14.66 ±0.210	14.71 ±10.181	13.39	14.09	11.79 ±1.028	10.49	10.49		
3a <sub>6</sub> (Group V)	6	32	6.4	5.62 ±0.158	12.13 ±1.813	13.40 ±1.008	13.60 ±0.593	13.16 ±1.164	13.16	12.97 ±0.028	12.19	12.19		
3b <sub>2</sub> (Group VII)	6	28	5.6	5.46 ±0.717	9.92 ±1.346	12.51 ±1.576	11.16 ±1.221	11.72	10.94	13.36 ±0.519	13.36	13.36		

Table 4: Anti-convulsant activity data of 4-oxo-thizolidine derivatives

Group No.	Treatment	Avg. wt	Avg. Dose (ml)	Latency (onset of clonus) (sec/30min) mean±SEM	Duration of tonic extensor (sec/30min) mean±SEM	% Production (24 hr)
I	Control (2% gum acacia)	26.75	0.26	3.62±0.036	13.35±0.018	12.5
II	Standard (Phenytoin, 25mg/kg p.o.)	22.25	0.22	10.25±0.036**	NO	100
III	Compound 3a <sub>6</sub> (200mg/kg p.o.)	28.00	0.33	11.83±0.450**	9.19±0.26**	66.66
IV	Compound 3b <sub>2</sub> (200mg/kg p.o.)	27.33	0.32	12.78±1.061**	9.65±0.191**	66.66
V	Compound (200mg/kg p.o.)	28.00	0.33	7.65±0.413**	5.93±0.810**	66.66
VI	Compound (200mg/kg p.o.)	26	0.30	7.67±0.602*	5.02±2.058**	
One way ANOVA			F	12.921	31.428	
			df	59	59	

n=6 Significance at P<0.05\*, <0.05\*, <0.001\*\*\* and ns-not significant



Table 5: Antibacterial activity of newly synthesized 4-oxo-thiazolidine derivatives

Sample Code	*Inhibition zone diameter in nm							
	B. subtilis		B. pumilis		E. coli		P. aureginosa	
	50µg	100µg	50µg	100µg	50µg	100µg	50µg	100µg
3a <sub>1</sub>	8	13	7	7	7	10	8	9
3a <sub>2</sub>	7	10	8	7	8	11	8	10
3a <sub>3</sub>	9	12	7	7	9	10	7	9
3a <sub>4</sub>	8	9	8	8	8	13	7	11
3a <sub>5</sub>	8	11	7	8	9	10	8	11
3a <sub>6</sub>	9	10	7	10	9	9	9	12
3b <sub>1</sub>	7	12	7	9	8	10	9	10
3b <sub>2</sub>	8	13	7	9	9	11	9	11
3b <sub>3</sub>	8	12	8	9	9	11	8	11
3b <sub>4</sub>	9	12	8	11	9	12	7	11
3b <sub>5</sub>	10	9	7	8	8	10	7	13
3b <sub>6</sub>	11	9	8	8	8	12	8	11
Ampicillin	22	34	21	32	22	35	24	34
DMSO	-	-	-	-	-	-	-	-

\*Average of triplicate±standard deviation

Note: '-'denotes no activity, 7-9 mm poor activity, 10-13 mm moderate activity

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