Synthesis, Anti-Bacterial and Anti-biofilm Activity of New Iminothiazolidinones

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Authors’ contributions
This work was carried out in collaboration between both authors. Author KG designed the methodology, screened the biological activity and prepared the preliminary draft of the manuscript. Author RM has carried out the analysis study, interpretation of spectral data as well as experimental process including assistance in manuscript drafting. Both the authors read and approved final manuscript.

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ABSTRACT

Aim: Iminothiazolidinones are one of the important classes of heterocyclic compounds and they occupied unique position in medicinal chemistry due to their wide range of biological and pharmaceutical properties. In view this potential activity, it has been planned to synthesize a series of New Iminothiazolidinones on benzimidazole nucleus and to study their biological activity.

Methodology: Iminothiazolidinones and 1,1 dioxide- Iminothiazolidinones were synthesized with a simple and efficient method of cyclic condensation of aryl thiourea containing benzimidazole and thiazole with chloroacetic acid. This method requires mild reaction conditions, simple procedure and gives good yield.

Results: The structures of the synthesized compounds were assessed by Infrared, NMR and Mass spectroscopic methods. The synthesized compounds were screened for their antibacterial and biofilm inhibitory activities against selected multi drug resistant bacterial strains.

Conclusion: In accordance with the results obtained, growth inhibition was found significant with compounds 5d and 5e. Methicillin resistant Staphylococcus aureus (MRSA), Vancomycin resistant

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Enterococcus (VRE), and extended spectrum β-lactamase (ESBL) producing Klebsiella pneumoniae have shown varied susceptibility towards these compounds. The Biofilm inhibition Concentrations (BFIC) of compounds 5e and 5d are 3.22 ±0.56 and 6.58 ±1.5 µg/mL respectively were noted against MRSA.

Keywords: Benzimidazole; iminothiazolidinones; anti-bacterial activity and anti-biofilm activity.

1. INTRODUCTION

Benzimidazole is a very important class of heterocyclic compounds and it occupies unique position in the field of pharmaceutical chemistry [1-5]. Most of the heterocyclic compounds are natural products [6], they can act as antibiotics [7] and they find their application in pharmaceuticals enormously [8-10]. Thiazolidin-4-one derivatives have broad spectrum biological properties [11-13] and diverse chemical reactivity and so, they are playing a vital role in medicinal chemistry. Because of having imino group in their molecular framework [14-15], Imino-thiazolidin-4-ones exhibit various chemotherapeutic properties and hence, they have gained importance further. The molecules containing imino group are showing impressive biological activities. So, drawing inspiration from the above mentioned facts, this study has been taken up to highlight those features of the compounds.

Imino thiazolidinones are one of the important classes of heterocyclic compounds [16-17]. The derivatives of imino thiazolidinones are found to be possessing biological activities such as antibacterial [18], antihyperglycemic [19], anticancer [20] and antimicrobial [21]. Most of the drugs and pharmaceutical products are heterocyclic compounds and they are meeting biological and industrial requirements. So, it was felt appropriate to take up the study of synthesis of iminothiazolidinones linked with thiazole ring frame work in view of their potential biological activity.

2. MATERIALS AND METHODS

Melting points of the synthesized compounds were determined in open capillary tubes and were uncorrected. Reaction Progress was observed by TLC method. Bruker 300 MHz instrument was used for recording 1H NMR spectra in DMSO solvent using TMS as internal standard. Chemical shifts (δ) are expressed in ppm. Mass spectra were recorded by using Electrospray ionisation-Mass Spectrometry (ESI-MS). To record IR spectra, Perkin Elmer BX series FT-IR was used. Perkin Elmer 240 CHN analyzer was used for elemental analysis.

2.1 General Procedure for the Synthesis of 4-(1H-Benz [d] imidazo-2yl)-1, 3-Oxazol-2-Amine (2)

A mixture of urea (0.01m mol) and iodine (0.12 m mol) in isopropanol (20 ml) was taken and added with a solution of 2- acetyl benzimidazole (0.01m mol) in isopropanol (20 ml). The reaction mixture was refluxed for about 3 hours. The solvent was removed in vacuo after completion of the reaction (monitored by TLC). The solid was separated and washed with aqueous sodium bicarbonate solution. It was dried and followed by recrystallisation from ethanol to get the product (3) in a pure state.

Scheme:

![Scheme Image]

Fig. 1. Synthesis process

Ar = C₆H₅ (4a&5a), 4-CH₃C₆H₄ (4b&5b), 4-OCH₃ C₆H₄ (4c&5c), 4-NO₂ C₆H₅ (4d&5d), 4-Cl C₆H₅ (4e &5e)
2.2 General Procedure for Synthesis of 1-(4-(1H-benzo[d]imidazol-2-yl) thiazol-2-yl)-3-Phenythiourea (3)

A mixture of sodium hydride (0.5g, 20 m mol) and compound (2) (0.01mol) in Ethanol (80ml) was taken and refluxed for about 30 minutes and cooled. Refluxing was continued after adding arylisothiocyanates (0.01mol) for further 4 hours. The residue was taken after evaporating the solvent and dissolved in DCM (50 ml) and it was washed with dilute HCl. The organic phase was dried (over MgSO4) and the solvent was evaporated to get the desired compound (3).

2.3 General Procedure for the Synthesis of (4-(1H-benzo[d]imidazol-2-yl) thiazol-2-yl) imino)-3-Phenythiazolidin-4-one (4a)

A mixture of compound (3) [22] (1mmol) and chloroacetic acid (1mmol) was taken in absolute ethanol (20ml) and sodium acetate was added to it and refluxed for about 6.5 hours. Reaction progress was monitored by TLC. After the reaction was completed, it was concentrated, cooled and poured in crushed ice followed by filtration. The product was purified with column chromatography and the obtained solid was recrystallized from ethanol. Similar procedure was adopted for the preparation of remaining compounds 4 (b-e) with minor changes as per the reaction conditions.

Yield 72% m.p 175-178°C IR (KBr) 1780, 1725 cm−1, 1HNMR (DMSO d6, 300 MHz, ppm) 7.73-7.88 (m, 4H, Ar H), 7.10-7.41 (m,5H,Ar H), 6.65-6.78 (m,2H,Ar H), 6.92 (s,1H, CH Ar); 3.95 (s, 2H, CH2), MS, m/z (%), 305(M+) Anal. Calc. For C19H19NO2S2: C, 60.79; H, 3.49; N, 18.66%; Found: C, 60.05; H, 3.11; N, 18.15%.

2.4 4-(1H-benzo[d]imidazol-2-yl) thiazol-2-yl) imino)-3-(p-tolyl) Thiazolidin-4-One (4b)

Yield 70% m.p 176-188°C IR (KBr) 1780, 1725 cm−1, 1HNMR (DMSO d6, 300 MHz, ppm) 7.71-7.83 (m,4H,Ar H), 7.13-7.35 (m,5H,ArH), 6.52-6.71 (m,2H,Ar H), 11.40 (s,1H,NH), 6.84 (s,1H,CH Ar), 3.97 (s,2H,CH2), 2.53 (s,3H, CH3) MS, m/z (%), 389(M+) Anal. Calc. for C20H19NO2S2: C, 61.68; H, 3.88; N, 17.98% Found: C, 61.08; H,3.24; N,17.38%.

2.5 (4-(1H-benzo[d]imidazol-2-yl) thiazol-2-yl) imino)-3-(4-methoxyphenyl) Thiazolidin-4-One (4c)

Yield 68% m.p 181-183°C IR (KBr) 1780, 1725 cm−1, 1HNMR (DMSO d6, 300 MHz, ppm) 7.62-7.79 (m,4H,Ar H), 7.13-7.31 (m,5H,Ar H), 6.75-6.88(m,2H,Ar H), 11.45 (s,1H,NH), 6.96 (s,1H,CH Ar), 3.96 (s,2H,CH2), 3.53 (s,3H, CH3) MS, m/z (%), 405(M+) Anal. Calc. For C20H15NO2S2: C, 55.14; H, 2.28; N, 16.85%. Found: C, 58.88; H, 3.24; N, 16.85%.

2.6 (4-(1H-benzo[d]imidazol-2-yl) thiazol-2-yl) imino)-3-(4-nitrophenyl) Thiazolidin-4-One (4d)

Yield 65% m.p 173-175°C IR (KBr) 1780, 1725 cm−1, 1HNMR (DMSO d6, 300 MHz, ppm) 7.60-7.78 (m,4H,Ar H), 7.16-7.28 (m,5H,ArH), 6.71-6.85 (m,2H,Ar H), 11.08 (S,1H,NH), 6.71 (S,1H,CH Ar), 3.99 (s,2H, CH2)MS, m/z (%), 420 (M+) Anal. Calc. For C20H13NO2S2C: C, 54.28; H, 2.88; N, 19.99; (%) Found: C, 54.05; H, 2.41; N, 19.25 (%).

2.7 (4-(1H-benzo[d]imidazol-2-yl) thiazol-2-yl) imino)-3-(4-chlorophenyl) Thiazolidin-4-One (4e)

Yield 63% m.p 178-180°C IR (KBr) 1780, 1725 cm−1, 1HNMR (DMSO d6, 300 MHz, ppm) 7.66-7.81 (m,4H,Ar H), 7.14-7.32 (m,5H,ArH), 6.72-6.87(m,2H,Ar H), 10.51 (S,1H,NH),6.82 (s,1H,CH Ar), 3.96 (s,2H, CH2)MS, m/z (%), 409(M+), 410 (M+) Anal. Calc. For C20H12ClNO2S2C: C, 55.68; H, 2.95; Cl, 8.65; N, 17.09%; Found: C, 55.14; H, 2.28; N, 16.85%.

2.8 2-((4-(1H-benzo[d]imidazol-2-yl)thiazol-2-yl)imino)-3- Phenythiazolidin-4-One 1,1-dioxide

(5a)

An Ice cold solution of the compound 4 (1mmol) in glacial acetic acid (30 ml) was treated with 30% H2O2 (20 ml) in portions. The contents were allowed to attain laboratory temperature and then refluxed for 3.5 h. The reaction mixture was cooled and acetic acid was removed in vacuo. The residual portion was cooled, filtration and was further purified by recrystallisation using
water. The remaining compounds (5b-e) were prepared by similar procedure with minor change in reaction conditions.

Yield 72% m.p 175-178°C. IR (KBr) \( \lambda_{\text{max}} \) (cm\(^{-1}\))

3358 (NH), 1560 (C=O), 300 MHz, ppm), 7.67-7.81 (m, 4H, Ar H). 6.65-6.78 (m, 2H, Ar H), 6.92 (s, 1H, CH Ar); 3.95 (s, 2H, CH\(_2\)); MS, m/z(%) 375 (M\(^+\)) Anal. Calcd. For C\(_{19}\)H\(_{13}\)N\(_3\)O\(_5\)S\(_2\): C, 60.05; H, 3.11; N, 18.15%.

2.10 2-(4-(1H-benzodimidazol-2-yl)thiazol-2-yl)imino)-3-(p-tolyl)Thiazolidin-4-One 1,1-dioxide (5b)

Yield 70% m.p 176-188°C. IR (KBr) \( \lambda_{\text{max}} \) (cm\(^{-1}\))

3368 (NH), 3082 (C=H), 3010 (C=H), 6.84 (s, 1H, CH Ar), 3.97 (s, 2H, CH\(_2\)), 2.53 (s, 3H, CH\(_3\)); MS, m/z (%) 389 (M\(^+\)), Anal. Calcd. For C\(_{20}\)H\(_{15}\)N\(_2\)O\(_2\)S\(_2\): C, 61.68; H, 3.88; N, 17.98%.

Found: C, 61.08; H, 3.24; N, 17.38%.

2.11 2-(4-(1H-benzodimidazol-2-yl)thiazol-2-yl)imino)-3-(4-nitrophenyl)Thiazolidin-4-One 1,1-dioxide (5d)

Yield 65% m.p 173-175°C. IR (KBr) \( \lambda_{\text{max}} \) (cm\(^{-1}\))

3368 (NH), 3077 (C=H), 1532 (-NO\(_2\)) 1571 (C=N), 1663 (C=O). \(^1\)HNMR (DMSO \( d_6\), 300 MHz, ppm), 7.70-7.81 (m, 4H, Ar H), 7.67-7.78 (m, 2H, Ar H), 6.71-6.85 (m, 2H, Ar H), 11.08 (S, 1H, NH), 6.71 (s, 1H, CH Ar), 3.99 (s, 2H, CH\(_2\)); MS, m/z (%) 420 (M\(^+\)); Anal. Calcd. For C\(_{30}\)H\(_{17}\)N\(_2\)O\(_3\)S\(_2\): C, 54.28; H, 2.88; N, 19.99; (%) Found: C, 54.05; H, 2.41; N, 19.25 (%).

2.12 2-(4-(1H-benzodimidazol-2-yl)thiazol-2-yl)imino)-3-(4-chlorophenyl)Thiazolidin-4-One 1,1-dioxide (5e)

Yield 63% m.p 178-180°C. IR (KBr) \( \lambda_{\text{max}} \) (cm\(^{-1}\))

3368 (NH), 3078 (C=H), 1565 (C=N), 1652 (C=O), 783 (C=Cl): \(^1\)HNMR (DMSO \( d_6\), 300 MHz, ppm), 7.66-7.81 (m, 4H, Ar H), 6.72-6.87 (m, 2H, Ar H), 10.52 (s, 1H, NH), 6.82 (s, 1H, CH Ar), 7.96 (s, 2H, CH\(_2\)); MS, m/z (%) 409 (M\(^+\)), 410 (M\(^{+1}\)); Anal. Calcd. For C\(_{20}\)H\(_{15}\)ClN\(_2\)O\(_2\)S\(_2\): C, 55.68; H, 2.95; Cl, 8.85; N, 17.09; Found: C, 55.14; H, 2.28; N, 16.85%.

3. BIOLOGICAL ACTIVITY

3.1 Bacterial Strains

*Escherichia coli* (ATCC 8739), *Klebselie pneumoniae* (ATCC 13883), Methicillin-resistant *Staphylococcus aureus* (MRSA, NCTC 13616) were obtained from Kakatiya Medical College, Warangal Urban. MRSA was cultured and maintained on Mannitol Salt Agar medium, augmented with 7.5% sodium chloride. The other bacterial strains were maintained on Luria-Bertani (LB) medium (purchased from Hi-media Laboratories, Mumbai, India). All the bacterial cultures were incubated at 37°C for 24 hours. All strains were sub cultured on nutrient agar medium for bioassays examination. The cultures were grown and the turbidity was adjusted with sterile broth to obtain a half of MC Farland standard (1x108 - 5x108 cfu/ml). This was used as starting inoculum for the assay.

3.2 Growing a Bio-film

The ability of the selected compounds to prevent biofilm development or destruction of preformed biofilm was investigated by the standard method [23]. A 100 μl aliquot of standardized concentration of cultures with OD560 =0.05 (5x10\(^3\) CFU/ml) was added to individual flat-bottomed 96-well micro titre plates containing LB medium. The micro titre plate was incubated to develop a multilayer biofilm for about 24 hours (irreversible attachment phase) and 48 hours (mature biofilm) at 37°C. Compounds in different concentrations (1000-0 μg/ml) were added into 96-well micro titre plates and the plates were incubated further at 37°C for 24h. Wells with only...
media is served as negative control. The biofilm and biomass were assayed with crystal violet (CV) staining [24].

### 3.3 Crystal Violet Staining Assay

#### 3.3.1 Staining the biofilm

The cells were dumped by shaking and turning the plate briefly. The microtitre plates were washed gently and repeatedly for 3-4 times with sterile distilled water, air dried and then oven-dried at 60°C for 35-45min. This step removes unattached cells and media components that can be stained in the following step and mainly minimises the background staining of well. 125μl of 0.1% solution of crystal violet was added to each well and incubated at room temperature for 10-15min. The plates were rinsed 4-5 times with sterilised distilled water to get rid the plates of all excess cells and dye. At this stage, biofilm was observed as purple rings at the sidewall of the well. The plates were dried overnight and followed by quantitative assessment.

#### 3.3.2 Quantitative assessment of biofilm

A quantitative assessment of biofilm formation was done by adding 125 μl of 30% acetic acid to each well. The microtitre plate was incubated at room temperature for 10-15 min. A 125μl aliquot of the solubilised solution was transferred to a fresh and sterile microtitre plate and the absorbance was measured at 590nm using a micro plate reader [25]. The mean absorbance of the samples was determined, and the percentage inhibition of biofilm was determined using the equation below:

\[
\text{Percentage (%) of inhibition} = \frac{\text{OD Negative control} - \text{OD Experimental}}{\text{OD Negative control}} \times 100
\]

### 4. RESULTS AND DISCUSSION

The present study aims at synthesis of Iminothiazolidinones based on benzimidazole nucleus. Aryl thiourea and chloro acetic acid undergo dehydrohalogenation to gives imine, which cyclises to form hemiacetal later and it further undergoes dehydration to afford the compound imino thiazolidinone.

The chemical structures of title compounds 4 & 5 were established on the basis of spectroscopic analysis. The IR spectrum showed absorption bands in the range from 3355 to 3368 cm\(^{-1}\) for (NH) functions, 1562-1585 cm\(^{-1}\) for (C=N) function, C=S absorptions in the range from 1231-1275 cm\(^{-1}\), strong absorption in the range from 1165-1176 cm\(^{-1}\) for (SO\(_2\)), and C=O absorption band in the range of 1650-1663 cm\(^{-1}\). The \(^1\)H NMR spectra of test compounds have revealed the presence of singlet signals at 6.38 ppm for thiazole protons (CH), 11.45 ppm for NH proton, 4.05 ppm for CH\(_2\) (imino thiazolidinone) in addition to the aromatic protons as a multiplet in the range 6.52–8.45 ppm. The mass spectrum showed a corresponding molecular ion peak at m/z with respect to their molecular weights.

| Comp. | Conc. (µg/mL) | MRSA | VRE | K. pneumoniae | E. coli |
|-------|---------------|------|-----|---------------|--------|
| 4a    | 50            | 2.42±0.09 | --  | 4.35±0.12     | 4.2±0.18|
|       | 100           | 2.77±0.09 | --  | 7.17±0.12     | 5.6±0.14|
| 4b    | 50            | 5.52±0.09 | --  | 5.52±0.09     | 6.13±0.12|
|       | 100           | 8.62±0.12 | --  | 7.25±0.12     | 8.62±0.18|
| 4c    | 50            | 3.47±0.12 | --  | 7.12±0.09     | 4.17±0.23|
|       | 100           | 5.37±0.12 | --  | 10.0±0.17     | 6.42±0.17|
| 4d    | 50            | 5.62±0.09 | --  | 3.17±0.17     | 3.15±0.12|
|       | 100           | 8.2±0.18  | --  | 5.15±0.12     | 5.22±0.17|
| 4e    | 50            | 8.55±0.12 | 3.37±0.15 | 11.2±0.22 | 15.2±0.18|
|       | 100           | 11.1±0.23 | 5.55±0.17 | 13.2±0.16 | 20.4±0.29|
| Ampicillin | 50      | 3.67±0.12 | --  | 3.15±0.12 | 4.6±0.14|
|       | 100           | 5.17±0.17 | --  | 3.65±0.12 | 5.35±0.23|

Zone of inhibitions are represented as Mean±Standard deviation (SD). n=4
Table 2. Antibacterial activity of compound 5a-5e

| Comp. | Conc. (µg/mL) | MRSA | VRE | K. pneumoniae | E. coli |
|------|-------------|------|-----|---------------|--------|
| 5a   | 50          | 5.15±0.12 | --  | 7.25±0.25     | 9.27±0.22 |
|      | 100         | 6.57±0.15 | --  | 10.3±0.17     | 14.3±0.12 |
| 5b   | 50          | 17.2±0.28 | 12.6±0.15 | 15.3±0.20     | 19.2±0.20 |
|      | 100         | 22.6±0.14 | 16.4±0.12 | 19.5±0.24     | 24.3±0.26 |
| 5c   | 50          | 3.22±0.22 | --  | 3.35±0.26     | 8.3±0.21  |
|      | 100         | 5.22±0.17 | --  | 4.4±0.18      | 10.4±0.11 |
| 5d   | 50          | 14.2±0.17 | 9.57±0.09 | 14.4±0.33     | 18.5±0.21 |
|      | 100         | 19.3±0.14 | 14.7±0.17 | 18.45±0.19    | 22.4±0.12 |
| 5e   | 50          | 4.45±0.12 | --  | 5.55±0.28     | 6.25±0.12 |
|      | 100         | 5.3±0.25  | --  | 7.15±0.12     | 8.42±0.09 |
| Ampicillin | 75      | 19.2±0.18 | 155±0.31 | 17.5±0.12     | 21.3±0.23 |
|      | 100         | 23.3±0.27 | 21.3±0.15 | 21.6±0.12     | 27.3±0.2  |

Zone of inhibitions are represented as Mean ± Standard deviation (SD). n=4

Table 3. Minimum inhibitory concentration (MIC/µg/mL) compound 4a-4e and 5a-5e

| Comp. | MRSA | VRE | K. pneumoniae | E. coli |
|------|------|-----|---------------|--------|
| 4a   | 24.6 | --  | 27.8          | 22.4   |
| 4b   | 21.8 | --  | 24.6          | 23.5   |
| 4c   | 24.6 | --  | 19.0          | 29.2   |
| 4d   | 15.9 | --  | 20.1          | 18.1   |
| 4e   | 9.20 | 15.7| 6.44          | 15.2   |
| 5a   | 24.1 | --  | 25.4          | 17.6   |
| 5b   | 15.2 | 16.7| 15.5          | 14.9   |
| 5c   | 25.8 | --  | 30.3          | 19.4   |
| 5d   | 6.23 | 7.14| 6.25          | 3.62   |
| 5e   | 3.11 | 4.63| 3.25          | 2.95   |
| Std  | 2.99 | 2.40| 2.81          | 2.22   |

Fig. 2. Minimum inhibitory concentration (MIC/µg/mL) compound 4a-4e and 5a-5e

Table 4. Bio film inhibitory concentration (BIC/µg/mL) compounds 5d&5e

| Comp. | MRSA | VRE | K. pneumoniae | E. coli |
|------|------|-----|---------------|--------|
| 5d   | 8.23±0.5 | 7.56±0.11 | 6.25±0.5     | 6.62±1.5 |
| 5e   | 2.22±0.56 | 3.05±0.7 | 3.25±1.0     | 2.03±0.02 |
| Std  | 1.33±0.02 | 2.66±0.5 | 3.11±0.5     | 3.22±0.05 |

All the synthesized compounds have exhibited significant antibacterial activity against multidrug resistance pathogens. The activity was found to be concentration dependent. However, certain compounds tested have shown poor activity or did not exhibit the activity. Based on these results, the compounds 5d and 5e were found to be showing significant activity (p<0.01) in Minimum Inhibitory Concentration (MIC) 2.95, 3.62 µg/mL respectively against E. coli. In addition, these compounds were also found to exhibit significant activity (p<0.01) against Vancomycin resistant Enterococcus (VRE), Methicillin resistant Staphylococcus aureus.
(MRSA), and extended spectrum β-lactamase (ESBL) producing K. Pneumonia with MIC 3.11, 4.63 and 3.25, 6.23, 7.14 and 6.25, µg/mL respectively (Table 3 and Fig. 2). Ampicillin was taken as known reference drug and the results were compared with it. From the comparison of the results, it can be seen that compound 5e is highly competing with the standard in the inhibition of multidrug resistance bacteria (Tables 1, 2 and 3). Compounds 5d and 5e were further screened for their capability to inhibit the formation of biofilm in view of significant antibacterial activity of them. Compound 5 is found to be showing more biological activity due to the presence of sulfonyl group compared to compound 4 [26].

4.1 Anti-biofilm Activity

Anti-biofilm activity of the compounds 5d, 5e, at different concentrations (0-1000 µg/mL) were screened against multidrug resistance bacterial strains. As per Table 4, the biofilm inhibition concentration (BIC) is found to be significant with compound 5e. Compound 5e is exhibiting immense inhibition of 2.22±0.56 µg/mL (P<0.001) against MRSA. In addition, 5e is also found to be significant against E. coli and VRE with BIC 2.03±0.02 and 3.05±0.7 µg/mL (P<0.001) respectively, whereas, anti-biofilm activity of 5e against K. Pneumonia is also found to be high with BIC 3.25±1.0 (P<0.001). From the results obtained in the study, it is clear that the compound 5e is equally competent in the inhibition of biofilm with the reference drug Ampicillin against the bacterial strains (Table 4).

5. CONCLUSION

The present research study reported synthesis of new analogs of Imino thiazolidinones efficiently with different unsymmetrical thioureas by using chloroacetic acid. All the compounds were characterized by IR, NMR and Mass spectroscopic techniques and the synthesised compounds were screened for anti-bacterial activity by zone of inhibition and MIC. All the compounds have showed significant activity against the test organisms employed. Particularly, the compounds 5(a-e) were found to exhibit more activity than the compounds 4 (a-e) due to sulfonyl group present in the molecule. Antibiobfilm activity has been carried out for selected compounds (5d & 5e), because, these compounds are showing excellent antibacterial activity and also exhibiting excellent anti biofilm activity as compared to the standard drug.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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