SYNTHESIS AND ANTITUBERCULAR ACTIVITY OF 4-OXO-THIAZOLIDINE DERIVATIVES OF 2-AMINO-5-NITROTHIAZOLE

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ABSTRACT. New series of \( N\{3-(2\text{-amino-5-nitrothiazolyl})\text{-propyl}\}2\text{-}(\text{substituted phenyl})\text{-4-oxo-5-}\text{(substituted benzylidene)-1,3-thiazolidine-carboxamide}, \( 5(a-j) \) have been synthesized from 2-amino-5-nitrothiazole as a starting material. The structure of all the synthesized compounds were confirmed by chemical and spectral analyses such as IR, \(^1\)H NMR, \(^{13}\)C NMR and FAB-Mass. All the final synthesized compounds \( 5(a-j) \) were screened for their antibacterial and antifungal activities against some selected bacteria and fungi with their MIC values and antitubercular activity screened against \( M.\text{tuberculosis} \).

KEY WORDS: Synthesis, 2-Amino-5-nitrothiazole, Thiazolidinone, Antimicrobial, Antitubercular

INTRODUCTION

Molecules containing thiazole ring systems are widely studied because of its low toxicity. Thiazole moiety is the key pharmacophore for the synthesis of several biological important molecules. Thiazole containing derivatives plays an important role in biological activity of many compounds such as antimicrobial activity [1, 2], anti-inflammatory [3], antitumor activities [4], antiarrhythmic and anticoagulant activities [5]. We also knows that imine derivatives possess potent activities including antibacterial [6, 7], antifungal [8, 9] and antitubercular [10] activities. Thiazolidine-4-ones are an important subunit of heterocyclic compounds having valuable biological activities. The thiazolidinones and correlated motifs have high biological relevance since the discovery. They are present in both natural products and pharmaceutical compounds. Some synthesized thiazolidinone derivatives possess antimicrobial [11-14], antidiabetic agents [15], antiviral [16], anti-inflammatory [17] activities.

In the present study, we have synthesized new series of biologically active thiazolidine derivatives. We have described the synthesis of a new series of \( N\{3-(2\text{-amino-5-nitrothiazolyl})\text{-propyl}\}2\text{-}(\text{substituted phenyl})\text{-4-oxo-5-}\text{(substituted benzylidene)-1,3-thiazolidine-carboxamide}, \) compounds \( 5(a-j) \) and other intermediate of the series compound \( 1, 2, 3(a-j), 4(a-j) \) (Scheme 1). The structure of all the synthesized compounds were confirmed by chemical and spectral analyses such as IR, \(^1\)H NMR, \(^{13}\)C NMR and FAB-Mass. All the final synthesized compounds \( 5(a-j) \) were screened for their antibacterial and antifungal activities against some selected bacteria and fungi with their MIC values and antitubercular activity screened against \( M.\text{tuberculosis} \).

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Scheme 1. Synthesis of compounds 1, 2, 3(a-j), 4(a-j) and 5(a-j).

<table>
<thead>
<tr>
<th>Compound</th>
<th>Ar = Ar₁</th>
<th>Compound</th>
<th>Ar = Ar₁</th>
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<td>3f, 4f, 5f</td>
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<tr>
<td>3b, 4b, 5b</td>
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<tr>
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<td>3e, 4e, 5e</td>
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<td>3j, 4j, 5j</td>
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</table>
RESULTS AND DISCUSSION

Synthesis

The reaction of 1-bromo-3-chloro-propane with 2-amino-5-nitrothiazole to afford a product compound 1 [18]. Spectroscopic analyses of compound 1 showed absorption peaks for N-CH and C-Cl at 1313 cm⁻¹ and 727 cm⁻¹ in the IR spectrum which confirms the formation of compound 1. Compound 1 on the reaction with urea yielded compound 2 [19]. IR spectrum of compound 2 showed three absorption peaks for NH, NH₂ and CO at 3387, 3452 cm⁻¹ and 1662 cm⁻¹ respectively while absorption of C-Cl disappeared. This is clearly indicated that compound 1 gives the substitution reaction with urea. This fact was also supported by ¹H and ¹³C NMR spectra because two signals appeared in the ¹H NMR spectrum for NH at δ 5.67 and 5.97 ppm, respectively. The formation of compound 2 was fully supported by a CO group which gives a signal at δ 163.3 ppm in the ¹³C NMR spectrum. All the facts together are strong evidence for the synthesis of compound 2. Compound 2 gives the condensation reaction with substituted benzaldehydes furnished compounds 3(a-j) [20] which were confirmed by IR, ¹H NMR and ¹³C NMR spectra. In the IR spectra an absorption found in the range of 1555-1573 cm⁻¹ for N=C while a strong signal appeared in the range of δ 8.02-8.20 and δ 147.4-151.6 ppm in the ¹H NMR and ¹³C NMR spectra respectively for N=CH of compounds 3(a-j). The facts also supported by the disappearance of NH₂ proton in the ¹H NMR spectrum of compound 2. Compounds 3(a-j) on reaction with thioglycolic acid in the presence of ZnCl₂ furnished compounds 4(a-j). Compounds 4(a-j) showed a characteristic absorption of the cyclic carbonyl group (cyclic CO) in the range of 1739-1755 cm⁻¹ in the IR spectra. The ¹H NMR spectra of compounds 4(a-j) aroused our attention and clearly indicate the presence of the active methylene group (-CH₂-) in the thiazolidine ring in the range of δ 3.20-3.38 ppm. ¹³C NMR spectra of compounds 4(a-j) also supported the fact that cyclic carbonyl group (cyclic CO) present and a signal appeared in the range of δ 170.3-173.7 ppm. All these facts also supported by the two evidences that are (a) disappearance of N=CH proton and (b) appearance of N-CH proton in the range of δ 5.18-5.37 ppm in the ¹H NMR spectra of compounds 4(a-j). Compounds 4(a-j) underwent the Knoevenagel condensation reaction with several selected series of substituted benzaldehydes in the presence of C₂H₅ONa to afford the compounds 5(a-j). In the ¹H NMR spectra of compounds 5(a-j), we found the disappearance of two methylene protons of compounds 4(a-j) and an appearance of a new signal for C=CH in the range of δ 6.45-6.73 ppm in the ¹H NMR and two new signals for C=CH and C=CH appeared in the range of δ 135.9-141.7 and δ 140.2-143.8 ppm respectively in the ¹³C NMR spectra of compounds 5(a-j). All these facts clearly confirmed the synthesis of all 1, 2, 3(a-j), 4(a-j) and 5(a-j) products.

Biological significance

The results of all described activities (antibacterial, antifungal and antitubercular) are summarized in Tables 1. The results of the antimicrobial screening data revealed that all final compounds of the series compounds 5(a-j) showed considerable and varied activity against the selected microorganism. A new series of N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(substituted phenyl)-4-oxo-5-(substituted benzyldiene)-1,3-thiazolidine-carboxamide, compounds 5(a-j) were synthesized and screened for their antimicrobial and antitubercular activities data (as shown in Table 1) revealed that all the synthesized compounds 5(a-j) have a structure activity relationship (SAR) because activities of compounds varies with substitution. Nitro group containing compounds (5h, 5i and 5j) showed higher activity than chloro (5c, 5d) and bromo group containing compounds (5e, 5f). On the basis of SAR, we concluded that the sequence of the activity is following...
The investigation of antimicrobial (antibacterial, antifungal and antitubercular) data revealed that the compounds (5c), (5d), (5e), (5f), (5i) and (5j) displayed high activity in the series, the compounds (5b) and (5g) showed moderate activity and rest compounds showed less activity against all the strains compared with standard drugs.

Table 1. Antibacterial, antifungal and antitubercular activities of compounds 5(a–j).

<table>
<thead>
<tr>
<th>Comp.</th>
<th>Antibacterial activity</th>
<th>Antifungal activity</th>
<th>Antitubercular activity</th>
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<tbody>
<tr>
<td></td>
<td>B. subtilis</td>
<td>E. coli</td>
<td>S. aureus</td>
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<td>5j</td>
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<td>3.75</td>
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</tbody>
</table>

The MIC values of standard streptomycin for all bacterial strain and griseofulvin for all fungal strain were in the range of 2.50-3.25 and 6.25-12.50 µg/mL, respectively. Isoniazid and rifampicin were used as standards, MIC values in the range of 1.25-2.50 µg/mL for M. tuberculosis.

CONCLUSION

The present research study reports the successful synthesis of a new series of \(N\)-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(substituted phenyl)-4-oxo-5-(substituted benzylidene)-1,3-thiazolidine-carboxamide, compounds 5(a–j). Antimicrobial and antitubercular activities of newly synthesized compounds bearing thiazolidine moiety, revealed that all tested compounds showed moderate to good antibacterial, antifungal and antitubercular activities against selected microbial strains.

EXPERIMENTAL

Melting points were taken in open capillaries and are uncorrected. Progress of reaction was monitored by silica gel-G coated TLC plates in MeOH:CHCl\(_3\) system (1:9). The spot was visualized by exposing dry plate in iodine vapours. IR spectra were recorded in KBr disc on a Schimadzu 8201 PC FTIR spectrophotometer (\(\nu_{\text{max}}\) in cm\(^{-1}\)) and \(^1H\) and \(^{13}C\) NMR spectra were measured on a Brucker DRX-300 spectrometer in CDCl\(_3\) at 300 and 75 MHz respectively using TMS as an internal standard. All chemical shifts were reported on \(\delta\) scales. The FAB mass spectra were recorded on a Jeol SX–102 mass spectrometer. Elemental analyses were performed on a Carlo Erba–1108 analyzer. The analytical data of all the compounds were highly satisfactory. For column chromatographic purification of the products, Merck silica Gel 60 (230-400 Mesh) was used. The reagent grade chemicals were purchased from the commercial sources and further purified before use.
Synthesis and antitubercular activity of 4-oxo-thiazolidine derivatives

Synthesis of 1-(3-chloropropyl)-2-amino-5-nitrothiazole, compound 1

2-Amino-5-nitrothiazole (0.345 mol) and 1-bromo-3-chloropropane (0.345 mol) in methanol (100 mL) were stirred on a magnetic stirrer for about 6.5 h at room temperature. The completion of the reaction was monitored by silica gel-G coated TLC plates. After the completion of the reaction the product was filtered and purified over a silica gel packed column chromatography using CHCl₃:CH₃OH (8:2 v/v) system as eluant (120 mL). The purified product was dried under vacuo and recrystallized from ethanol at room temperature to yield compound 1 (Figure 1).

\[
\begin{align*}
\text{O} & \quad \text{N} \\
\text{S} & \quad \text{N} \\
\text{4} & \quad \text{7} \\
\text{5} & \quad \text{8} \\
\text{6} & \quad \text{9} \\
\end{align*}
\]

Figure 1. Structure of compound 1.

1-(3-Chloropropyl)-2-amino-5-nitrothiazole (1). Yield: 62%; m.p. 173-175 °C; IR (cm⁻¹): 727 (C-Cl), 881 (C-S), 968 (C-NO), 1313 (N-CH₂), 1362, 1532 (NO₂), 1559 (C=c), 1436, 2832, 2897 (CH₂), 3009 (CH-Ar), 3388 (NH); ¹H NMR (300 MHz, CDCl₃, TMS) δ: 1.91-1.95 (m, 2H, H-8), 3.27 (t, J 7.35 Hz, 2H, H-9), 3.85-3.89 (m, 2H, H-7), 7.71 (s, 1H, H-4), 7.83 (br. s, 1H, H-6); ¹³C NMR (75 MHz, CDCl₃, TMS) δ: 34.4 (C-8), 41.7 (C-9), 45.9 (C-7), 134.2 (C-4), 137.8 (C-5), 166.5 (C-2); FAB-Mass (m/z): 221 [M⁺]; anal. calc. for C₆H₈N₃O₂SCl: C 32.51, H 3.63, N 18.95; found: C 32.49, H 3.59, N 18.87%.

Synthesis of N-[3-(2-amino-5-nitrothiazolyl)-propyl]-urea, compound 2

Compound 1 (0.2256 mol) and urea (0.2256 mol) in methanol (100 mL) were stirred on a magnetic stirrer for about 6.5 h at room temperature. The completion of the reaction was monitored by silica gel-G coated TLC plates. After the completion of the reaction the product was filtered and purified over a silica gel packed column chromatography using CHCl₃:CH₃OH (8:2 v/v) system as eluant (120 mL). The purified product was dried under vacuo and recrystallized from ethanol at room temperature to yield compound 2 (Figure 2).

\[
\begin{align*}
\text{N} & \quad \text{O} \\
\text{S} & \quad \text{N} \\
\text{2} & \quad \text{3} \\
\end{align*}
\]

Figure 2. Structure of compound 2.

N-[3-(2-amino-5-nitrothiazolyl)-propyl]-urea (2). Yield: 70%; m.p. 153-155 °C; IR (cm⁻¹): 879 (C=S), 966 (C-NO), 1324 (N-CH₂), 1360, 1533 (NO₂), 1559 (C=c), 1662 (C=O), 1432, 2885, 2918 (CH₂), 3021 (CH-Ar), 3387 (NH), 3452 (NH₃); ¹H NMR (300 MHz, CDCl₃, TMS) δ: 2.08-2.12 (m, 2H, H-8), 3.19-3.24 (m, 2H, H-9), 3.82-3.90 (m, 2H, H-7), 5.67 (s, 1H, H-1'), 5.97 (br s, 2H, H-3'), 7.65 (s, 1H, H-4), 7.80 (br. s, 1H, H-6); ¹³C NMR (75 MHz, CDCl₃, TMS) δ: 33.4 (C-8), 38.6 (C-9), 44.1 (C-7), 133.8 (C-4), 138.5 (C-5), 163.4 (C-2'), 165.3 (C-2); FAB-

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Mass (m/z): 245 [M⁺]; anal. calc. for C₇H₁₁N₅O₃S: C 34.28, H 4.52, N 28.55; found: C 34.25, H 4.48, N 28.51%.

**Synthesis of N-[3-(1H-2-amino-5-nitrothiazolyl)-propyl]-N’-{(phenyl)-methylidene}-urea, compound 3a**

Compound 2 (0.0330 mol) and benzaldehyde (0.0330 mol) in methanol (100 mL) in the presence of 2-4 drops of glacial acetic acid were first stirred on a magnetic stirrer for about 2 h followed by reflux on a steam bath for about 3.5 h. The completion of the reaction was monitored by silica gel-G coated TLC plates. The product was filtered and cooled at room temperature. The filtered product was purified over a silica gel packed column chromatography using CH₃OH:CHCl₃ (7:3 v/v) as eluent (75 mL). The purified product was dried under vacuo and recrystallized from ethanol at room temperature to furnish compound 3a (Figure 3).

![Figure 3. Structure of compounds 3(a-j).](image-url)

Compounds 3 (b-j) have also been synthesized by using similar method as above.

**N-[3-(2-amino-5-nitrothiazolyl)-propyl]-N’-{(phenyl)-methylidene}-urea (3a).** Yield: 62%; m.p. 148-149 °C; IR (cm⁻¹): 856 (C-S), 961 (C-NO), 1329 (N-CH₂), 1356, 1531 (NO₂), 1547 (C=O), 1661 (C=O), 1427, 2878, 2912 (CH₃), 3016 (CH-Ar), 3382 (NH); ¹H NMR (300 MHz, CDCl₃, TMS) δ: 2.02-2.07 (m, 2H, H-8), 3.20-3.25 (m, 2H, H-9), 3.80-3.85 (m, 2H, H-7), 5.60 (s, 1H, H-1’), 7.24 (s, 1H, H-4), 7.89 (s, 1H, H-6), 8.02 (s, 1H, H-10), 6.75-7.84 (m, 5H, Ar-H); ¹³C NMR (75 MHz, CDCl₃, TMS) δ: 28.2 (C-8), 36.5 (C-9), 42.4 (C-7), 126.7 (C-12 and C-16), 128.4 (C-14), 129.3 (C-13 and C-15), 130.7 (C-4), 136.6 (C-5), 137.2 (C-11), 147.4 (C-10), 160.5 (C-2’), 168.8 (C-2); FAB-Mass (m/z): 333 [M⁺]; anal. calc. for C₁₄H₁₅N₅O₃S: C 50.44, H 4.53, N 21.00; found: C 50.35, H 4.55, N 20.95%.

**N-[3-(2-amino-5-nitrothiazolyl)-propyl]-N’-{(4-chlorophenyl)-methylidene}-urea (3b).** Yield: 62%; m.p. 178-179 °C; IR (cm⁻¹): 744 (C-Cl), 870 (C-S), 968 (C-NO), 1329 (C=O), 1356, 1531 (NO₂), 1547 (C=O), 1661 (C=O), 1427, 2878, 2912 (CH₃), 3016 (CH-Ar), 3382 (NH); ¹H NMR (300 MHz, CDCl₃, TMS) δ: 2.11-2.15 (m, 2H, H-8), 3.22-3.27 (m, 2H, H-9), 3.83-3.88 (m, 2H, H-7), 5.64 (s, 1H, H-1’), 7.89 (s, 1H, H-4), 7.98 (s, 1H, H-6), 8.13 (s, 1H, H-10), 6.94-7.65 (m, 4H, Ar-H); ¹³C NMR (75 MHz, CDCl₃, TMS) δ: 28.2 (C-8), 40.1 (C-9), 43.2 (C-7), 126.6 (C-12 and C-16), 128.9 (C-14), 129.6 (C-13 and C-15), 130.9 (C-4), 135.2 (C-5), 141.4 (C-11), 147.7 (C-10), 160.2 (C-2’), 168.4 (C-2); FAB-Mass (m/z): 367 [M⁺]; anal. calc. for C₁₄H₁₄N₅O₃SCl: C 45.71, H 3.83, N 19.04; found: C 45.60, H 3.81, N 19.01%.

**N-[3-(2-amino-5-nitrothiazolyl)-propyl]-N’-{(3-chlorophenyl)-methylidene}-urea (3c).** Yield: 62%; m.p. 174-175 °C; IR (cm⁻¹): 745 (C=Cl), 866 (C-S), 977 (C-NO), 1336 (N=O₂), 1360, 1536 (NO₂), 1550 (C=N), 1667 (C=O), 1434, 2892, 2930 (CH₃), 3026 (CH=Ar), 3386 (NH); ¹H NMR (300 MHz, CDCl₃, TMS) δ: 2.11-2.15 (m, 2H, H-8), 3.28-3.32 (m, 2H, H-9), 3.84-3.89 (m, 2H, H-7), 5.72 (s, 1H, H-1’), 7.30 (s, 1H, H-4), 7.95 (s, 1H, H-6), 8.14 (s, 1H, H-10).

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N-[3-(2-amino-5-nitrothiazolyl)-propyl]-N'-[2-chlorophenyl]-methylidene]-urea (3d)

Yield: 62%; m.p. 172-173 °C; IR (cm⁻¹): 747 (C-Cl), 860 (C-S), 962 (C-NO), 1330 (N=CH), 1358, 1534 (NO₂), 1549 (C=C), 1663 (C=O), 1428, 2880, 2913 (CH₂), 3017 (CH-Ar), 3384 (NH); ¹H NMR (300 MHz, CDCl₃, TMS) δ: 2.08-2.12 (m, 2H, H-8), 3.30-3.35 (m, 2H, H-9), 3.82-3.86 (m, 2H, H-7), 5.70 (s, 1H, H-1'), 7.31 (s, 1H, H-4), 7.91 (s, 1H, H-6), 8.18 (s, 1H, H-10), 6.86-7.84 (m, 4H, Ar-H); ¹³C NMR (75 MHz, CDCl₃, TMS) δ: 31.8 (C-8), 37.2 (C-9), 42.6 (C-7), 43.5 (C-5), 125.8 (C-12), 126.6 (C-16), 129.7 (C-14), 130.4 (C-13), 132.5 (C-15), 134.5 (C-4), 138.2 (C-11), 138.9 (C-5), 151.6 (C-10), 162.4 (C-2'), 169.3 (C-2), (Ar); FAB-Mass (m/z): 367 [M⁺]; anal. calc. for C₁₇H₁₄N₄O₂S: C 57.12, H 3.90, N 21.81%; found: C 57.08, H 3.85, N 21.77%.

N-[3-(2-amino-5-nitrothiazolyl)-propyl]-N'-[4-bromophenyl]-methylidene]-urea (3e)

Yield: 62%; m.p. 169-170 °C; IR (cm⁻¹): 634 (C-Br), 858 (C-S), 970 (C-NO), 1335 (N=CH), 1370, 1537 (NO₂), 1551 (C=C), 1674 (C=O), 1440, 2886, 2921 (CH₂), 3019 (CH-Ar), 3387 (NH); ¹H NMR (300 MHz, CDCl₃, TMS) δ: 2.07-2.12 (m, 2H, H-8), 3.29-3.34 (m, 2H, H-9), 3.81-3.85 (m, 2H, H-7), 5.73 (s, 1H, H-1'), 7.28 (s, 1H, H-4), 7.91 (s, 1H, H-6), 8.20 (s, 1H, H-10), 6.70-7.85 (m, 4H, Ar-H); ¹³C NMR (75 MHz, CDCl₃, TMS) δ: 29.3 (C-8), 36.8 (C-9), 42.6 (C-7), 128.6 (C-12 and C-16), 130.5 (C-14), 131.2 (C-13 and C-15), 132.2 (C-4), 136.3 (C-5), 138.8 (C-11), 150.7 (C-10), 162.1 (C-2'), 170.4 (C-2); FAB-Mass (m/z): 412 [M⁺]; anal. calc. for C₁₇H₁₂BrN₄O₂S: C 54.78, H 3.42, N 21.81%; found: C 54.73, H 3.47, N 21.76%.

N-[3-(2-amino-5-nitrothiazolyl)-propyl]-N'-[3-bromophenyl]-methylidene]-urea (3f)

Yield: 62%; m.p. 159-160 °C; IR (cm⁻¹): 643 (C-Br), 860 (C-S), 963 (C-NO), 1337 (N=CH), 1374, 1540 (NO₂), 1554 (C=C), 1671 (C=O), 1432, 2888, 2922 (CH₂), 3025 (CH-Ar), 3388 (NH); ¹H NMR (300 MHz, CDCl₃, TMS) δ: 2.10-2.17 (m, 2H, H-8), 3.30-3.36 (m, 2H, H-9), 3.87-3.92 (m, 2H, H-7), 5.67 (s, 1H, H-1'), 7.39 (s, 1H, H-4), 7.99 (s, 1H, H-6), 8.16 (s, 1H, H-10), 6.69-7.81 (m, 4H, Ar-H); ¹³C NMR (75 MHz, CDCl₃, TMS) δ: 30.3 (C-8), 39.6 (C-9), 43.5 (C-7), 128.3 (C-12), 128.4 (C-16), 129.4 (C-14), 130.3 (C-13), 131.7 (C-15), 133.4 (C-4), 137.1 (C-5), 141.9 (C-11), 151.2 (C-10), 161.3 (C-2'), 169.8 (C-2); FAB-Mass (m/z): 367 [M⁺]; anal. calc. for C₁₇H₁₂BrN₄O₂S: C 54.78, H 3.42, N 21.81%; found: C 54.73, H 3.47, N 21.76%.

Synthesis and antitubercular activity of 4-oxo-thiazolidine derivatives

Yield: 62%; m.p. 170-171 °C; IR (cm⁻¹): 31.8 (C-8), 37.2 (C-9), 45.4 (C-7), 128.3 (C-12), 128.7 (C-16), 130.8 (C-14), 131.6 (C-13), 132.7 (C-4), 133.8 (C-15), 136.4 (C-5), 139.4 (C-11), 148.6 (C-10), 161.9 (C-2'), 170.7 (C-2); FAB-Mass (m/z): 412 [M⁺]; anal. calc. for C₁₇H₁₂BrN₄O₂S: C 54.78, H 3.42, N 21.81%; found: C 54.73, H 3.47, N 21.76%.

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Ar-H; $^{13}$C NMR (75 MHz, CDCl$_3$, TMS) $\delta$: 29.8 (C-8), 40.4 (C-9), 44.5 (C-7), 129.8 (C-12 and C-16), 131.2 (C-14), 132.7 (C-13 and C-15), 134.8 (C-4), 138.6 (C-5), 140.3 (C-11), 150.7 (C-10), 160.4 (C-2'), 171.3 (C-2); FAB-Mass (m/z): 378 [M$^+$]; anal. calc. for C$_{14}$H$_{14}$N$_6$O$_5$S: C 44.44, H 3.72, N 22.21; found: C 44.40, H 3.69, N 22.19%.

N-[3-(2-amino-5-nitrothiazolyl)-propyl]-N'-(3-nitrophenyl)-methylidene-urea (3i). Yield: 62%; m.p. 165-166 °C; IR (cm$^{-1}$): 859 (C-S), 972 (C-NO), 1338 (N-CH$_2$), 1371, 1545 (NO$_2$), 1557 (C=C), 1665 (C=O), 1431, 2894, 2927 (CH$_2$), 3030 (CH-Ar), 3394 (NH); $^1$H NMR (300 MHz, CDCl$_3$, TMS) $\delta$: 2.11-2.15 (m, 2H, H-8), 3.29-3.33 (m, 2H, H-9), 3.85-3.89 (m, 2H, H-7), 5.66 (s, 1H, H-1'), 7.33 (s, 1H, H-4), 7.92 (s, 1H, H-6), 8.15 (s, 1H, H-10), 6.78-7.86 (m, 4H, Ar-H); $^{13}$C NMR (75 MHz, CDCl$_3$, TMS) $\delta$: 30.7 (C-8), 38.3 (C-9), 45.8 (C-7), 131.4 (C-4), 130.5 (C-12), 130.9 (C-16), 133.4 (C-13), 134.1 (C-15), 136.9 (C-5), 137.5 (C-11), 149.2 (C-10), 163.6 (C-2’), 172.7 (C-2); FAB-Mass (m/z): 378 [M$^+$]; anal. calc. for C$_{14}$H$_{14}$N$_6$O$_5$S: C 44.44, H 3.72, N 22.21; found: C 44.38, H 3.66, N 22.17%.

N-[3-(2-amino-5-nitrothiazolyl)-propyl]-N’-(2-nitrophenyl)-methylidene-urea (3j). Yield: 62%; m.p. 162-163 °C; IR (cm$^{-1}$): 864 (C-S), 976 (C-NO), 1341, 1541 (NO$_2$), 1553 (C=C), 1669 (C=O), 1438, 2890, 2924 (CH$_2$), 3028 (CH-Ar), 3397 (NH); $^1$H NMR (300 MHz, CDCl$_3$, TMS) $\delta$: 2.15-2.19 (m, 2H, H-8), 3.20-3.26 (m, 2H, H-9), 3.87-3.93 (m, 2H, H-7), 5.68 (s, 1H, H-1’), 7.36 (s, 1H, H-4), 7.96 (s, 1H, H-6), 8.10 (s, 1H, H-10), 6.80-7.90 (m, 4H, Ar-H); $^{13}$C NMR (75 MHz, CDCl$_3$, TMS) $\delta$: 30.7 (C-8), 39.7 (C-9), 44.5 (C-7), 131.8 (C-4), 130.5 (C-12), 131.6 (C-16), 132.4 (C-13), 134.5 (C-15), 137.3 (C-5), 139.7 (C-11), 149.9 (C-10), 163.2 (C-2’), 172.1 (C-2); FAB-Mass (m/z): 378 [M$^+$]; anal. calc. for C$_{14}$H$_{14}$N$_6$O$_5$S: C 44.44, H 3.72, N 22.21; found: C 44.35, H 3.70, N 22.18%.

Synthesis of N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(phenyl)-4-oxo-1,3-thiazolidine-carboxamide, compound 4a.

The compound 3a (0.015 mol) and thioglycolic acid (0.015 mol) in methanol (50 mL) in the presence of ZnCl$_2$ (0.015 mol) were allowed to react at room temperature. The reaction mixture was first stirred on a magnetic stirrer for about 2 h followed by reflux on a steam bath for about 4 h. The product was filtered and cooled at room temperature. The completion of the reaction was monitored by silica gel-G coated TLC plates. The filtered product was purified over a silica gel packed column chromatography using CH$_3$OH:CHCl$_3$ (7:3 v/v) as eluent (80 mL). The purified product was dried under vacuo and recrystallized from ethanol at room temperature to furnish compound 4a (Figure 4).

Figure 4. Structure of compounds 4(a-j).
Compounds 4 (b-j) have also been synthesized by using similar method as above.

N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(phenyl)-4-oxo-1,3-thiazolidine-carboxamide (4a). Yield: 64%; m.p. 159-160 °C; IR (cm⁻¹): 698 (C-S-C), 1012 (C-NO), 1338 (N-CH₂), 1378, 1545 (NO₂), 1565 (C=C), 1657 (C=O), 1739 (CO cyclic), 1426, 2833, 2914 (CH₃), 2950 (CH₂), 3052 (CH=Ar), 3372 (NH); ¹H NMR (300 MHz, CDCl₃, TMS) δ: 2.13-2.15 (m, 2H, H-8), 3.20 (2H, H-5''), 3.34-3.37 (m, 2H, H-9), 3.95-3.99 (m, 2H, H-7), 5.18 (s, 1H, H-2'''), 5.70 (s, 1H, H-1'), 7.85 (s, 1H, H-4), 7.97 (s, 1H, H-6), 6.66-7.72 (m, 5H, Ar-H); ¹³C NMR (75 MHz, CDCl₃, TMS) δ: 30.2 (C-8), 34.3 (C-5'''), 38.0 (C-9), 45.6 (C-7), 61.2 (C-2''), 128.4 (C-11 and C-16), 129.7 (C-15), 130.5 (C-12 and C-14), 133.5 (C-4), 137.3 (C-5), 139.2 (C-10), 162.4 (C-2'), 169.6 (C-2), 170.3 (C-4''); FAB-Mass (m/z): 407 [M⁺]; anal. calc. for C₁₅H₁₇N₂O₅S: C 47.16, H 4.20, N 17.18%; found: C 47.12, H 4.18, N 17.16%.

N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(4-bromophenyl)-4-oxo-1,3-thiazolidine-carboxamide (4d). Yield: 61%; m.p. 185-187 °C; IR (cm⁻¹): 682 (C-S-C), 734 (C=C), 867 (C-S), 972 (C-NO), 1339 (N-CH₂), 1369, 1540 (NO₂), 1556 (C=C), 1671 (C=O), 1755 (CO cyclic), 1440, 2894, 2924 (CH₃), 2963 (S-CH₂), 3025 (CH=Ar), 3393 (NH); ¹H NMR (300 MHz, CDCl₃, TMS) δ: 2.13-2.18 (m, 2H, H-8), 3.26 (2H, H-5''), 3.32-3.37 (m, 2H, H-9), 3.94-3.98 (m, 2H, H-7), 5.22 (s, 1H, H-2'''), 5.73 (s, 1H, H-1'), 7.90 (s, 1H, H-4), 7.99 (s, 1H, H-6), 6.82-7.85 (m, 4H, Ar-H); ¹³C NMR (75 MHz, CDCl₃, TMS) δ: 31.8 (C-8), 34.8 (C-5'''), 40.5 (C-9), 45.9 (C-7), 61.5 (C-2''), 129.1 (C-11 and C-16), 130.5 (C-15), 130.9 (C-12 and C-14), 134.4 (C-4), 138.6 (C-10), 139.8 (C-5), 162.8 (C-2'), 170.5 (C-2), 170.7 (C-4'''); FAB-Mass (m/z): 442 [M⁺]; anal. calc. for C₁₆H₁₅BrN₂O₄S: C 43.48, H 3.64, N 15.84%; found: C 43.44, H 3.56, N 15.78%.

N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(3-chlorophenyl)-4-oxo-1,3-thiazolidine-carboxamide (4c). Yield: 65; m.p. 180-181 °C; IR (cm⁻¹): 679 (C-S-C), 745 (C=C), 868 (C-S), 975 (C-NO), 1339 (N-CH₂), 1369, 1540 (NO₂), 1557 (C=C), 1674 (C=O), 1752 (CO cyclic), 1442, 2892, 2925 (CH₃), 2966 (S-CH₂), 3030 (CH=Ar), 3394 (NH); ¹H NMR (300 MHz, CDCl₃, TMS) δ: 2.13-2.19 (m, 2H, H-8), 3.26 (2H, H-5''), 3.38-3.42 (m, 2H, H-9), 4.01-4.06 (m, 2H, H-7), 5.24 (s, 1H, H-2'''), 5.76 (s, 1H, H-1'), 7.86 (s, 1H, H-4), 8.05 (s, 1H, H-6), 6.64-7.76 (m, 4H, Ar-H); ¹³C NMR (75 MHz, CDCl₃, TMS) δ: 31.2 (C-8), 35.3 (C-5'''), 39.2 (C-9), 46.3 (C-7), 65.6 (C-2''), 128.7 (C-11), 129.3 (C-16), 130.9 (C-15), 131.5 (C-12), 132.9 (C-14), 136.7 (C-4), 138.6 (C-5), 140.5 (C-10), 162.4 (C-2'), 172.1 (C-2), 171.3 (C-4''); FAB-Mass (m/z): 442 [M⁺]; anal. calc. for C₁₅H₁₅ClN₂O₄S: C 43.48, H 3.64, N 15.84%; found: C 43.45, H 3.58, N 15.77%.

N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(2-chlorophenyl)-4-oxo-1,3-thiazolidine-carboxamide (4d). Yield: 64; m.p. 182-183 °C; IR (cm⁻¹): 681 (C-S-C), 750 (C=C), 871 (C-S), 976 (C-NO), 1341 (N-CH₂), 1374, 1546 (NO₂), 1554 (C=C), 1677 (C=O), 1746 (CO cyclic), 1443, 2890, 2931 (CH₃), 2968 (S-CH₂), 3026 (CH=Ar), 3395 (NH); ¹H NMR (300 MHz, CDCl₃, TMS) δ: 2.16-2.20 (m, 2H, H-8), 3.27 (2H, H-5''), 3.37-3.43 (m, 2H, H-9), 4.03-4.08 (m, 2H, H-7), 5.32 (s, 1H, H-2'''), 5.79 (s, 1H, H-1'), 7.91 (s, 1H, H-4), 8.07 (s, 1H, H-6), 6.66-7.72 (m, 4H, Ar-H); ¹³C NMR (75 MHz, CDCl₃, TMS) δ: 30.5 (C-8), 37.2 (C-5'''), 40.1 (C-9), 46.0 (C-7), 64.4 (C-2''), 137.2 (C-4'), 130.3 (C-11), 130.8 (C-16), 131.5 (C-15), 131.7 (C-12), 132.6 (C-14), 140.2 (C-10), 141.1 (C-5), 164.6 (C-2'), 171.5 (C-2), 173.7 (C-4''); FAB-Mass (m/z): 442 [M⁺]; anal. calc. for C₁₅H₁₅ClN₂O₄S: C 43.48, H 3.64, N 15.84; found: C 43.43, H 3.57, N 15.74%.

N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(4-bromophenyl)-4-oxo-1,3-thiazolidine-carboxamide (4e). Yield: 67%; m.p. 176-177 °C; IR (cm⁻¹): 652 (C-Br), 678 (C-S-C), 869 (C-S), 982 (C-NO), 1340 (N-CH₂), 1366, 1547 (NO₂), 1557 (C=C), 1680 (C=O), 1747 (CO cyclic), 1445, 2893, 2926 (CH₃), 2969 (S-CH₂), 3027 (CH=Ar), 3397 (NH); ¹H NMR (300 MHz, CDCl₃, Bull. Chem. Soc. Ethiop. 2013, 27(2).
N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(3-bromophenyl)-4-oxo-1,3-thiazolidine-carboxamide (4f). Yield: 68%; m.p. 174-175 ºC; IR (cm\(^{-1}\)): 646 (C-Br), 678 (C-S-C), 870 (C=S), 977 (C-NO), 1342 (N-CH\(_2\)), 1367, 1542 (NO\(_2\)), 1555 (C=C), 1750 (CO cyclic), 1443, 2897, 2927 (CH\(_3\)), 2964 (S-CH\(_3\)), 3028 (CH-Ar), 3392 (NH); \(^1\)H NMR (300 MHz, CDCl\(_3\)), TMS: \(2.15-2.20\) (m, 2H, H-8), 3.38 (s, 2H, H-5\(^\prime\)), 3.41-3.46 (m, 2H, H-9), 3.99-4.04 (m, 2H, H-7), 5.19 (s, 1H, H-1\(^\prime\)), 5.83 (s, 1H, H-1\(^\prime\)), 7.98 (s, 1H, H-4), 8.15 (s, 1H, H-6), 6.79-7.81 (m, 4H, Ar-H); \(^1\)C NMR (75 MHz, CDCl\(_3\)), TMS: \(32.7 (C-8), 37.6 (C-5\(^\prime\)), 41.7 (C-9), 47.5 (C-7), 64.9 (C-2\(^\prime\)), 103.7 (C-11 and C-16), 131.3 (C-15), 132.6 (C-12 and C-14), 137.5 (C-4), 141.4 (C-10), 141.6 (C-5), 165.4 (C-2\(^\prime\)), 170.9 (C-2), 171.8 (C-4\(^\prime\)); FAB-Mass (m/z): 486 [M\(^+\)]; anal. calc. for \(C_{16}H_{16}NO_5S\): Br: C 39.51, H 3.31, N 14.39; found: C 39.47, H 3.28, N 14.36%.

N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(4-bromophenyl)-4-oxo-1,3-thiazolidine-carboxamide (4g). Yield: 62%; m.p. 179-180 ºC; IR (cm\(^{-1}\)): 645 (C-Br), 676 (C-S-C), 872 (C=S), 980 (C-NO), 1343 (N-CH\(_2\)), 1370, 1548 (NO\(_2\)), 1570 (C=C), 1762 (C=O), 1438, 2889, 2930 (CH\(_3\)), 2965 (S-CH\(_3\)), 3032 (CH-Ar), 3394 (NH); \(^1\)H NMR (300 MHz, CDCl\(_3\)), TMS: \(2.19-2.25\) (m, 2H, H-8), 3.30 (s, 2H, H-5\(^\prime\)), 3.44-3.49 (m, 2H, H-9), 4.10-4.16 (m, 2H, H-7), 5.20 (s, 1H, H-2\(^\prime\)), 5.77 (s, 1H, H-1\(^\prime\)), 7.87 (s, 1H, H-4), 8.00 (s, 1H, H-6), 6.70-7.62 (m, 4H, Ar-H); \(^1\)C NMR (75 MHz, CDCl\(_3\)), TMS: \(33.4 (C-8), 36.8 (C-5\(^\prime\)), 39.6 (C-9), 49.7 (C-7), 63.3 (C-2\(^\prime\)), 131.4 (C-11), 131.9 (C-15), 132.5 (C-13), 133.6 (C-14), 136.1 (C-4), 137.4 (C-5), 163.6 (C-2\(^\prime\)), 143.7 (C-10), 172.1 (C-2), 173.3 (C-4\(^\prime\)); FAB-Mass (m/z): 486 [M\(^+\)]; anal. calc. for \(C_{16}H_{16}NO_5S\): Br: C 39.51, H 3.31, N 14.39; found: C 39.45, H 3.27, N 14.36%.

N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(4-nitrophenyl)-4-oxo-1,3-thiazolidine-carboxamide (4h). Yield: 65%; m.p. 181-182 ºC; IR (cm\(^{-1}\)): 677 (C-S-C), 875 (C=S), 981 (C-NO), 1340 (N-CH\(_2\)), 1368, 1534 (NO\(_2\)), 1572 (C=C), 1765 (C=O), 1754 (CO cyclic), 1439, 2891, 2932 (CH\(_3\)), 2971 (S-CH\(_3\)), 3033 (CH-Ar), 3390 (NH); \(^1\)H NMR (300 MHz, CDCl\(_3\)), TMS: \(2.22-2.27\) (m, 2H, H-8), 3.32 (s, 2H, H-5\(^\prime\)), 3.44-3.48 (m, 2H, H-9), 3.97-4.03 (m, 2H, H-7), 5.24 (s, 1H, H-2\(^\prime\)), 5.78 (s, 1H, H-1\(^\prime\)), 7.93 (s, 1H, H-4), 8.03 (s, 1H, H-6), 6.65-7.70 (m, 4H, Ar-H); \(^1\)C NMR (75 MHz, CDCl\(_3\)), TMS: \(33.4 (C-8), 36.2 (C-5\(^\prime\)), 41.5 (C-9), 48.8 (C-7), 63.7 (C-2\(^\prime\)), 132.1 (C-11 and C-16), 133.0 (C-15), 133.7 (C-12 and C-14), 135.7 (C-4), 139.2 (C-5), 141.7 (C-10), 164.1 (C-2\(^\prime\)), 171.8 (C-2), 172.4 (C-4\(^\prime\)); (Ar): FAB-Mass (m/z): 452 [M\(^+\)]; anal. calc. for \(C_{16}H_{16}NO_5S\): C 42.47, H 3.56, N 18.57; found: C 42.45, H 3.53, N 18.54%.

N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(3-nitrophenyl)-4-oxo-1,3-thiazolidine-carboxamide (4i). Yield: 66%; m.p. 177-178 ºC; IR (cm\(^{-1}\)): 676 (C-S-C), 874 (C=S), 978 (C-NO), 1345 (N-CH\(_2\)), 1371, 1545 (NO\(_2\)), 1568 (C=C), 1676 (C=O), 1749 (CO cyclic), 1440, 2896, 2929 (CH\(_3\)), 2967 (S-CH\(_3\)), 3034 (CH-Ar), 3396 (NH); \(^1\)H NMR (300 MHz, CDCl\(_3\)), TMS: \(2.11-2.15\) (m, 2H, H-8), 3.28 (s, 2H, H-5\(^\prime\)), 3.32-3.39 (m, 2H, H-9), 4.09-4.13 (m, 2H, H-7), 5.31 (s, 1H, H-1\(^\prime\)), 5.80 (s, 1H, H-1\(^\prime\)), 7.95 (s, 1H, H-4), 8.06 (s, 1H, H-6), 6.80-7.86 (m, 4H, Ar-H); \(^1\)C NMR (75 MHz, CDCl\(_3\)), TMS: \(34.6 (C-8), 38.1 (C-5\(^\prime\)), 42.7 (C-9), 46.5 (C-7), 62.2 (C-2\(^\prime\)), 132.8 (C-11), 133.5 (C-16), 134.2 (C-15), 134.8 (C-12), 135.2 (C-4), 135.7 (C-14), 140.7 (C-5), 142.2 (C-10), 165.7 (C-2\(^\prime\)), 172.4 (C-2), 172.7 (C-4\(^\prime\)); FAB-Mass (m/z): 452 [M\(^+\)]; anal. calc. for \(C_{16}H_{16}NO_5S\): C 42.47, H 3.56, N 18.57; found: C 42.41, H 3.52, N 18.54%.

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Synthesis and antitubercular activity of 4-oxo-thiazolidine derivatives

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N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(2-nitrophenyl)-4-oxo-1,3-thiazolidine-carboxamide (4j). Yield: 63%; m.p. 181-183 °C; IR (cm\(^{-1}\)): 674 (C-S-C), 869 (C-S), 978 (C-NO), 1344 (N-CH\(_2\)), 1372, 1541 (NO\(_2\)), 1569 (C=C), 1679 (C=O), 1750 (CO cyclic), 1441, 2899, 2932 (CH\(_3\)), 2970 (S-CH\(_3\)), 3035 (CH-Ar), 3398 (NH); \(^1\)H NMR (300 MHz, CDCl\(_3\), TMS) \(\delta\): 2.13-2.19 (m, 2H, H-8), 3.35 (s, 2H, H-5\(^{-}\)), 3.40-3.44 (m, 2H, H-9), 4.15-4.19 (m, 2H, H-7), 5.37 (s, 1H, H-2\(^{-}\)), 5.84 (s, 1H, H-1\(^{\prime}\)), 7.97 (s, 1H, H-4), 8.11 (s, 1H, H-6), 6.75-7.89 (m, 4H, Ar-H); \(^1\)C NMR (75 MHz, CDCl\(_3\), TMS) \(\delta\): 34.1 (C-8), 38.6 (C-5\(^{-}\)), 47.6 (C-7), 65.1 (C-2\(^{-}\)), 130.5 (C-11), 131.2 (C-16), 132.1 (C-15), 133.7 (C-4), 134.2 (C-12), 134.9 (C-14), 138.4 (C-5), 143.3 (C-10), 163.3 (C-2\(^{-}\)), 172.9 (C-4\(^{-}\)); FAB-Mass (m/z): 452 [M\(^{+}\)]; anal. calc. for C\(_{16}\)H\(_{16}\)N\(_{6}\)O\(_6\)S\(_2\): C 42.47, H 3.56, N 18.57; found: C 42.41, H 3.49, N 18.52%.

Synthesis of N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(phenyl)-4-oxo-5-(benzylidene)-1,3-thiazolidine-carboxamide, compound 5a

The compound 4a (0.009 mol) and benzaldehyde (0.009 mol) in ethanol (50 mL) in the presence of CH\(_3\)CHONa (0.009 mol) were allowed to react at room temperature. The reaction mixture was first stirred on a magnetic stirrer for about 2 h followed by reflux on a steam bath for about 5.5 h. The completion of the reaction was monitored by silica gel-G coated TLC plates. The product was filtered and cooled at room temperature. The filtered product was purified over a silica gel packed column chromatography using CH\(_3\)OH:CHCl\(_3\) (7:3 v/v) as eluent (80 mL). The purified product was dried under vacuo and recrystallized from acetone at room temperature to furnish compound 5a (Figure 5).

![Structure of compounds 5(a-j)](image)

Figure 5. Structure of compounds 5(a-j).

Compounds 5 (b-j) have also been synthesized by using similar method as above.

N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(substitutedphenyl)-4-oxo-5-(benzylidene)-1,3-thiazolidine-carboxamide (5a). Yield: 60%; m.p. 155-156 °C; IR (cm\(^{-1}\)): 872 (C-S), 977 (C-NO), 1345 (N-CH\(_3\)), 1371, 1542 (NO\(_2\)), 1567 (C=C), 1675 (C=O), 1750 (CO cyclic), 1441, 2899, 2926 (CH\(_3\)), 2966 (C=CH), 3027 (CH-Ar), 3393 (NH); \(^1\)H NMR (300 MHz, CDCl\(_3\), TMS) \(\delta\): 2.06-2.09 (m, 2H, H-8), 3.35-3.39 (m, 2H, H-9), 3.97-4.02 (m, 2H, H-7), 5.22 (s, 1H, H-2\(^{-}\)), 5.76 (s, 1H, H-1\(^{\prime}\)), 6.45 (s, 1H, H-16), 7.80 (s, 1H, H-4), 8.05 (s, 1H, H-6), 6.65-7.78 (m, 10H, Ar-H); \(^1\)C NMR (75 MHz, CDCl\(_3\), TMS) \(\delta\): 31.2 (C-8), 39.5 (C-9), 46.2 (C-7), 62.4 (C-2\(^{-}\)), 128.4 (C-18 and C-22), 129.1 (C-11 and C-15), 129.6 (C-13), 130.1 (C-20), 130.1 (C-19 and C-21), 132.7 (C-12 and C-14), 134.6 (C-4), 136.2 (C-16), 138.2 (C-17), 139.6 (C-5), 140.6
(C-10), 141.5 (C-5"), 163.5 (C-2"), 169.7 (C-2), 172.7 (C-4"); FAB-Mass (m/z): 495 [M⁺]. anal. calc. for C₂H₅NiO₂S₂C: C 55.74, H 4.27, N 14.13; found: C 55.71, H 4.25, N 14.09%.

N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(4-chlorophenyl)-4-oxo-5-(4-chlorobenzylidene)-1,3-thiazolidine-carboxamide (5b). Yield: 64%; m.p. 180-181 ºC; IR (cm⁻¹): 752 (C-Cl), 876 (C=S), 979 (C-NO), 1350 (N=O), 1570 (C=C), 1677 (C=O), 1752 (CO cyclic), 1443, 2854, 2930 (CH₃), 2969 (C=CH), 3028 (CH-Ar), 3397 (NH); ¹³C NMR (300 MHz, CDCl₃, TMS) δ: 2.11-2.14 (m, 2H, H-8), 3.41-3.47 (m, 2H, H-9), 3.98-4.03 (m, 2H, H-7), 5.25 (s, 1H, H-2"), 5.81 (s, 1H, H-1"), 6.51 (s, 1H, H-16), 7.83 (s, 1H, H-4), 8.06 (s, 1H, H-6), 6.67-7.80 (m, 8H, Ar-H); ¹⁹F NMR (75 MHz, CDCl₃, TMS) δ: 31.8 (C-8), 40.2 (C-9), 49.5 (C-7), 62.9 (C-2"), 130.1 (C-1 and C-22), 131.3 (C-11 and C-15), 131.5 (C-19 and C-21), 132.1 (C-13), 133.9 (C-20), 134.1 (C-12 and C-14), 137.6 (C-4), 139.7 (C-16), 138.1 (C-5), 138.8 (C-17), 142.3 (C-10), 142.5 (C-5"), 167.4 (C-2"), 172.7 (C-2), 172.6 (C-4"); (Ar): FAB-Mass (m/z): 564 [M⁺]; anal. calc. for C₂H₅NiO₂S₂Cl: C 48.94, H 3.39, N 12.40; found: C 48.91, H 3.32, N 12.38%.

N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(3-chlorophenyl)-4-oxo-5-(3-chlorobenzylidene)-1,3-thiazolidine-carboxamide (5e). Yield: 63%; m.p. 177-178 ºC; IR (cm⁻¹): 755 (C-Cl), 875 (C=S), 992 (C-NO), 1348 (N=O), 1735 (C=C), 1755 (CO cyclic), 1445, 2847, 2932 (CH₃), 2976 (C=CH), 3030 (CH-Ar), 3398 (NH); ¹³C NMR (300 MHz, CDCl₃, TMS) δ: 2.19-2.24 (m, 2H, H-8), 3.32-3.36 (m, 2H, H-9), 4.02-4.07 (m, 2H, H-7), 5.27 (s, 1H, H-2"), 5.87 (s, 1H, H-1"), 6.53 (s, 1H, H-16), 7.87 (s, 1H, H-4), 8.09 (s, 1H, H-6), 6.71-7.82 (m, 8H, Ar-H); ¹⁹F NMR (75 MHz, CDCl₃, TMS) δ: 32.6 (C-8), 39.4 (C-9), 49.0 (C-7), 63.6 (C-2"), 135.7 (C-4), 139.6 (C-5), 167.5 (C-2"), 173.1 (C-2), 131.2 (C-11), 131.6 (C-15), 130.5 (C-18), 131.3 (C-22), 132.0 (C-19), 132.5 (C-21), 132.8 (C-13), 133.3 (C-20), 134.2 (C-12), 134.9 (C-14), 137.5 (C-16), 138.7 (C-17), 142.9 (C-10), 143.1 (C-5"), 173.8 (C-4"); FAB-Mass (m/z): 564 [M⁺]; anal. calc. for C₂H₅NiO₂S₂Cl: C 48.94, H 3.39, N 12.40; found: C 48.89, H 3.32, N 12.35%.

N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(2-chlorophenyl)-4-oxo-5-(2-chlorobenzylidene)-1,3-thiazolidine-carboxamide (5d). Yield: 61%; m.p. 178-180 ºC; IR (cm⁻¹): 747 (C-Cl), 885 (C=S), 978 (C-NO), 1360 (N=O), 1576 (C=C), 1681 (C=O), 1757 (CO cyclic), 1446, 2845, 2935 (CH₃), 2972 (C=CH), 3029 (CH-Ar), 3395 (NH); ¹³C NMR (300 MHz, CDCl₃, TMS) δ: 2.15-2.19 (m, 2H, H-8), 3.43-3.48 (m, 2H, H-9), 4.02-4.07 (m, 2H, H-7), 5.28 (s, 1H, H-2"), 5.96 (s, 1H, H-1"), 6.57 (s, 1H, H-16), 7.92 (s, 1H, H-4), 8.21 (s, 1H, H-6), 6.75-7.64 (m, 8H, Ar-H); ¹⁹F NMR (75 MHz, CDCl₃, TMS) δ: 35.4 (C-8), 43.7 (C-9), 48.5 (C-7), 63.6 (C-2"), 128.5 (C-18), 128.9 (C-22), 129.8 (C-11), 130.3 (C-15), 130.9 (C-13), 131.1 (C-20), 132.7 (C-12), 132.2 (C-19 and C-21), 133.6 (C-14), 135.5 (C-4), 137.6 (C-16), 139.1 (C-5), 140.5 (C-17), 141.4 (C-10), 143.2 (C-5"), 166.7 (C-2"), 169.3 (C-2), 173.8 (C-4"); (Ar): FAB-Mass (m/z): 564 [M⁺]; anal. calc. for C₂H₅NiO₂S₂Cl: C 48.94, H 3.39, N 12.40; found: C 48.88, H 3.36, N 12.36%.

N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(4-bromophenyl)-4-oxo-5-(4-bromobenzylidene)-1,3-thiazolidine-carboxamide (5e). Yield: 66%; m.p. 169-171 ºC; IR (cm⁻¹): 656 (C-Br), 877 (C=S), 983 (C-NO), 1346 (N=O), 1373, 1557 (NO₂), 1581 (C=O), 1684 (C=O), 1761 (CO cyclic), 1455, 2837, 2937 (CH₃), 2973 (C=CH), 3040 (CH-Ar), 3399 (NH); ¹³C NMR (300 MHz, CDCl₃, TMS) δ: 2.12-2.17 (m, 2H, H-8), 3.48-3.54 (m, 2H, H-9), 4.02-4.09 (m, 2H, H-7), 5.40 (s, 1H, H-2"), 5.99 (s, 1H, H-1"), 6.60 (s, 1H, H-16), 7.85 (s, 1H, H-4), 8.12 (s, 1H, H-6), 6.77-7.75 (m, 8H, Ar-H); ¹⁹F NMR (75 MHz, CDCl₃, TMS) δ: 35.3 (C-8), 43.3 (C-9), 47.4 (C-7), 64.2 (C-2"), 130.3 (C-18 and C-22), 131.1 (C-11 and C-15), 132.8 (C-13), 133.4 (C-20),

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133.5 (C-12 and C-14), 134.8 (C-19 and C-21), 138.1 (C-4), 138.7 (C-16), 140.7 (C-5), 141.1 (C-10), 141.6 (C-17), 142.9 (C-5"), 163.6 (C-2"'), 170.2 (C-2), 174.4 (C-4"'); (Ar); FAB-Mass (m/z): 653 [M⁺]; anal. calc. for C₁₅H₁₅N₂O₂S₂Br₂: C 42.28, H 2.93, N 10.71; found: C 42.25, H 2.87, N 10.69%.

N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(3-bromophenyl)-4-oxo-5-(3-bromobenzylidene)-1,3-thiazolidine-carboxamide (5f). Yield: 60%; m.p. 166-167 °C; IR (cm⁻¹): 649 (C-Br), 885 (C-S), 987 (C-NO), 1348 (N-CH₃), 1374, 1556 (NO₂), 1578 (C=C), 1685 (C=O), 1763 (CO cyclic), 1442, 2830, 2918 (CH₃), 2975 (C=CH), 3031 (CH-Ar), 3400 (NH); ¹H NMR (300 MHz, CDCl₃, TMS) δ: 2.08-2.13 (m, 2H, H-8), 3.35-3.39 (m, 2H, H-9), 4.08-4.12 (m, 2H, H-7), 5.31 (s, 1H, H-2"'), 5.85 (s, 1H, H-1'), 6.64 (s, 1H, H-16), 7.84 (s, 1H, H-4), 8.15 (s, 1H, H-6), 6.68-7.72 (m, 8H, Ar-H); ¹³C NMR (75 MHz, CDCl₃, TMS) δ: 34.5 (C-8), 42.2 (C-9), 48.4 (C-7), 64.3 (C-2"'), 128.8 (C-18), 129.1 (C-11), 129.8 (C-15), 130.4 (C-22), 130.7 (C-13), 131.1 (C-12), 132.5 (C-12), 132.9 (C-14), 134.1 (C-19), 134.9 (C-21), 135.2 (C-16), 138.3 (C-4), 140.1 (C-5), 138.6 (C-10), 140.8 (C-17), 143.3 (C-5"), 165.3 (C-2"'), 173.2 (C-2), 174.7 (C-4"'); (Ar); IR: FAB-Mass (m/z): 653 [M⁺]; anal. calc. for C₁₅H₁₅N₂O₂S₂Br₂: C 42.28, H 2.93, N 10.71; found: C 42.22, H 2.87, N 10.66%.

N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(3-bromophenyl)-4-oxo-5-(3-bromobenzylidene)-1,3-thiazolidine-carboxamide (5g). Yield: 62%; m.p. 165-167 °C; IR (cm⁻¹): 652 (C-Br), 881 (C-S), 980 (C-NO), 1357 (N-CH₃), 1381, 1548 (NO₂), 1582 (C=C), 1680 (C=O), 1770 (CO cyclic), 1453, 2843, 2940 (CH₃), 2974 (C=CH), 3034 (CH-Ar), 3401 (NH); ¹H NMR (300 MHz, CDCl₃, TMS) δ: 2.14-2.19 (m, 2H, H-8), 3.41-3.46 (m, 2H, H-9), 4.11-4.18 (m, 2H, H-7), 5.34 (s, 1H, H-2"'), 5.80 (s, 1H, H-1'), 6.68 (s, 1H, H-16), 7.77 (s, 1H, H-4), 8.17 (s, 1H, H-6), 6.72-7.76 (m, 8H, Ar-H); ¹³C NMR (75 MHz, CDCl₃, TMS) δ: 32.2 (C-8), 41.9 (C-9), 47.8 (C-7), 65.0 (C-2"'), 128.7 (C-15), 129.7 (C-18), 130.5 (C-22), 130.6 (C-11), 131.4 (C-13), 132.5 (C-20), 132.7 (C-14), 133.9 (C-12), 134.0 (C-19), 134.5 (C-21), 135.0 (C-16), 136.9 (C-4), 138.2 (C-10), 140.0 (C-17), 140.2 (C-5"), 141.8 (C-5), 164.0 (C-2"'), 170.7 (C-2), 175.8 (C-4"'); (Ar); FAB-Mass (m/z): 653 [M⁺]; anal. calc. for C₁₅H₁₅N₂O₂S₂Br₂: C 42.28, H 2.93, N 10.71; found: C 42.21, H 2.87, N 10.65%.

N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(4-nitrophenyl)-4-oxo-5-(4-nitrobenzylidene)-1,3-thiazolidine-carboxamide (5h). Yield: 65%; m.p. 170-172 °C; IR (cm⁻¹): 874 (C-S), 987 (C-NO), 1353 (N-CH₃), 1376, 1544 (NO₂), 1587 (C=C), 1679 (C=O), 1765 (CO cyclic), 1447, 2848, 2929 (CH₃), 2977 (C=CH), 3038 (CH-Ar), 3396 (NH); ¹H NMR (300 MHz, CDCl₃, TMS) δ: 2.21-2.26 (m, 2H, H-8), 3.42-3.47 (m, 2H, H-9), 4.13-4.18 (m, 2H, H-7), 5.36 (s, 1H, H-2"'), 5.79 (s, 1H, H-1'), 6.71 (s, 1H, H-16), 7.95 (s, 1H, H-4), 8.08 (s, 1H, H-6), 6.72-7.74 (m, 8H, Ar-H); ¹³C NMR (75 MHz, CDCl₃, TMS) δ: 33.5 (C-8), 40.5 (C-9), 49.6 (C-7), 65.4 (C-2"'), 128.1 (C-18 and C-22), 129.2 (C-11 and C-15), 130.3 (C-13), 131.0 (C-20), 132.6 (C-12 and C-14), 135.9 (C-19 and C-21), 136.1 (C-4), 138.2 (C-17), 140.1 (C-10), 141.7 (C-16), 141.9 (C-5), 143.8 (C-5"'), 166.5 (C-2"'), 172.4 (C-2), 175.6 (C-4"'); FAB-Mass (m/z): 586 [M⁺]; anal. calc. for C₁₅H₁₃N₂O₂S₂: C 47.17, H 3.27, N 16.74; found: C 47.14, H 3.25, N 16.71%.

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N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(2-nitrophenyl)-4-oxo-5-(2-nitrobenzylidene)-1,3-thiazolidine-carboxamide (5j). Yield: 63%; m.p. 166-168 °C; IR (cm⁻¹): 880 (C=S), 996 (C-NO), 1356 (CH₂), 2967 (C-H), 3274 (N-H); ¹H NMR (300 MHz, CDCl₃, TMS) δ: 2.19-2.25 (m, 2H, H-8), 3.42-3.47 (m, 2H, H-9), 4.12-4.16 (m, 2H, H-7), 5.28 (s, 1H, H-2"), 5.80 (s, 1H, H-1'), 6.76 (s, 1H, H-16), 7.81 (s, 1H, H-4), 8.19 (s, 1H, H-6), 6.69-7.71 (m, 8H, Ar-H); ¹³C NMR (75 MHz, CDCl₃, TMS) δ: 34.9 (C-8), 42.6 (C-7), 62.1 (C-2"), 127.5 (C-22), 128.7 (C-18), 129.9 (C-15), 130.8 (C-11), 131.1 (C-13), 132.7 (C-20), 133.0 (C-12), 133.8 (C-14), 134.8 (C-4), 135.1 (C-19), 135.6 (C-21), 137.9 (C-16), 138.7 (C-5), 139.1 (C-10), 139.6 (C-17), 143.1 (C-5"), 164.3 (C-2"), 171.6 (C-2'), 176.5 (C-4"); FAB-Mass (m/z): 586 [M⁺]; anal. calc. for C₂₃H₁₉N₇O₈S₂: C 47.17, H 3.27, N 16.74; found: C 47.14, H 3.23, N 16.71%.

Invitro study (antibacterial, antifungal and antitubercular activities)

The antibacterial, antifungal and antitubercular activity of compound 5(a-j) has been assayed in vitro against selected bacteria, B. subtilis, E. coli, S. aureus fungi A. niger, A. flavus, C. albicans and M. tuberculosis H37Rv strain, respectively. MIC values of compounds 5(a-j) were determined using filter paper disc diffusion method (antibacterial and antifungal activities) and L. J. medium (conventional) method (antitubercular activity). Streptomycin and griseofulvin used as standard for antibacterial and antifungal activities respectively and for antitubercular activity, isoniazid and rifampicin were taken as standards. All standards were also screened under the similar condition for comparison. Results of given activities of above compounds are given in Table 1.

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