

Original Research Article

## Synthesis of Possible Anti-Cancer and Anti-Mycobacterial Fluoro Substituted Sulphonamide Benzothiazoles Comprising Potent Thiazolidinone

Jagtap VA<sup>\*1</sup>, Gautam DT<sup>1</sup>, Mule VS<sup>1</sup>, Gandhi SM<sup>1</sup>, Jayachandran E<sup>2</sup><sup>1</sup>Dept. of Pharmaceutical Chemistry, Yashwantrao Bhonsale College of Pharmacy, Sawantwadi – 416 510, Dist: Sindhudurg (M. S.), India<sup>2</sup>PG Dept. of Pharmaceutical Chemistry, S. C. S. College of Pharmacy, Harapanahalli – 583 131, Dist: Davangere (K. S.), India

### \*Corresponding Author:

Jagtap VA

Email: [drvajagtap@gmail.com](mailto:drvajagtap@gmail.com)

**Abstract:** In the present study, a series of *N*-[6-fluoro-7-substituted-1,3-benzothiazol-2-yl]-4-[2-(3-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide and *N*-[6-fluoro-7-substituted-1,3-benzothiazol-2-yl]-4-[2-(4-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide derivatives were synthesized in good yields and characterized by FTIR, <sup>1</sup>HNMR, mass spectral and elemental analyses. All synthesized compounds were evaluated for their preliminary in vitro anti-mycobacterial activity against Mycobacterium tuberculosis H37 Rv strain by tube dilution assay method. Some selected synthesized compounds were also evaluated for cytostatic activities against malignant human cell lines: cervical (HeLa), bone marrow (K-562) and kidney cell (HEK-293).

**Keywords:** Fluorobenzothiazole, Sulphonamido, Thiazolidinone, Anti-mycobacterial activity, Anti-cancer activity

### INTRODUCTION

Emergences of multi drug resistant-TB synergized with other immune-compressive diseases have increased the life threatening capacities of the disease [1-2]. One third of the world's population is thought to have been infected with *M. tuberculosis* [3-4]. Therefore, there is an urgent need for novel anti-mycobacterial agents with a different mode of action. Literature study reveals that 2-substituted benzothiazole derivatives have anti-mycobacterial [5-10], anti-cancer [11-17] and other broad spectrum of biological activities. More recently, sulphonamides have been found to be potent cysteine protease inhibitors, which could possibly extent their therapeutic application to include conditions such as alzheimer's disease, arthritis and cancer. As a class the sulfa drugs have a variable history of application for the treatment of bacterial infections [18-19]. Benzothiazole with sulphonyl group were reported to possess anti-mycobacterial [20], cytotoxic activity [21]. Based on the above observations we have synthesized some Fluoro substituted sulphonamide benzothiazoles. In addition to this we have incorporated a potent thiazolidinone heterocycle. Thiazolidinones are well known heterocyclic compounds for their known activities such as anti-mycobacterial [22], anti-cancer [23], anti-HIV [24], and antimicrobial [25]. It was to be found that incorporation of thiazolidinone moiety into sulphonamidobenzothiazole scaffold enhances its

activity. Thus in the present investigation, 24 different derivatives of *N*-[6-fluoro-7-substituted-1,3-benzothiazol-2-yl]-4-[2-(3-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide and *N*-[6-fluoro-7-substituted-1,3-benzothiazol-2-yl]-4-[2-(4-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide derivatives were synthesized and evaluated for their anti-mycobacterial and anti-cancer activity.

### MATERIAL AND METHODS

#### General

All commercial reagents and chemicals were used without further purification. Reactions were monitored by TLC. Melting points were determined by open capillary method and are uncorrected. The infrared spectra were recorded by a Fourier transform infrared (FTIR) spectrometer Bruker Vertex 70 equipped with an attenuated total reflection (ATR) accessory with a diamond crystal. <sup>1</sup>HNMR spectra were recorded on Bruker AM 400 instrument (at 400 MHz) using tetramethyl silane (TMS) as an internal standard and DMSO-*d*<sub>6</sub> as a solvent. The <sup>1</sup>HNMR chemical shift values ( $\delta$ ) are expressed in ppm referred to tetramethyl silane (TMS) and coupling constants (*J*) in Hz. Precoated Merck Silica Gel 60F-254 plates were used for thin layer chromatography (TLC) and the spots were detected under UV light (254 nm). Elemental analyses were carried out using FLASH EA 1112 CHN analyzer

from Thermo Finnigen, Italy and values were within  $\pm$  0.4 % of the calculated.

The synthetic route of targeted compounds *N*-[6-fluoro-7-substituted-1,3-benzothiazol-2-yl]-4-[2-(3-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide derivatives **6 (a-l)** and *N*-[6-fluoro-7-substituted-1,3-benzothiazol-2-yl]-4-[2-(4-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide derivatives **6 (m-x)** were done from schiff's base illustrated in Figure 1.

### Synthesis

It has been found that reaction of commercially available compound (**1**) with *p*-acetamido benzene sulphonyl chloride in presence of pyridine and acetic anhydride in ethanol produced the condensed derivative (**2**) in 80% yield. Compound **2** hydrolyzed by boiling in 80% acetic acid give product (**3**) in 74 % yield. Compound (**3**) with two different aromatic aldehydes viz. 3-nitro benzaldehyde and 4-nitrobenzaldehyde in presence of ethanol and 2-3 drops of hydrochloric acid yields Schiff's bases **4 (a-b)**. Schiff's bases on further treatment of 2-thioglycolic acid in presence of 1,4-dioxane and sodium bicarbonate yields compound **5 (a-b)**. Compound **5 (a-b)** on treatment with equimolar quantities of various aromatic amines in presence of dimethyl formamide yields target compounds **6 (a-x)**. Physical and analytical of all target compounds is given in Table I.

### Chemistry

Specific examples presented below illustrate general synthetic procedure.

#### 7-Chloro-6-fluoro-1,3-benzothiazol-2-amine (1)

4-fluoro-3-chloro-aniline (0.01 mol) was treated with potassium thiocyanate (0.08 mol) in presence of cool glacial acetic acid (20 ml) bromine (1.6 ml) and ammonia to get yellow solid compound **1**. (51.02%) m.p. 212 °c (d); Anal. calcd. for C<sub>7</sub>H<sub>4</sub>ClFN<sub>2</sub>S: C 41.53 H 2.04 N 13.85 Found C 41.30 H 2.01 N 13.82.

#### *N*-[4-[(7-Chloro-6-fluoro-1,3-benzothiazol-2-yl)sulfamoyl]phenyl]acetamide (2)

To a suspension of compound (**1**) (0.013 mol), pyridine (4 ml) and acetic anhydride (20 ml), *p*-acetamido benzene sulphonyl chloride (0.01 mol) was added and refluxed in water bath for 2 h. After cooling of reaction mixture in ice cold water the precipitated solid obtained was filtered and recrystallised from dil ethanol (80%). (60.15 %.) m.p. 221°c (d); Anal. calcd. for C<sub>15</sub>H<sub>11</sub>ClFN<sub>3</sub>O<sub>3</sub>S<sub>2</sub>, C, 45.10; H, 2.84; N, 10.55 Found C, 45.06; H, 2.80; N, 10.53.

#### 4-Amino-*N*-(7-chloro-6-fluoro-1,3-benzothiazol-2-yl)benzenesulphonamide (3)

The compound (**2**) (0.01 mol) hydrolyzed by boiling in 50 ml of 80% acetic acid for 4 to 5 h and the

contents were poured onto crushed ice. The obtained hydrolyzed derivatives were filtered at suction and dried. (76.12%) m.p. 189°c (d); Anal. calcd. for C<sub>13</sub>H<sub>6</sub>ClFN<sub>3</sub>O<sub>2</sub>S<sub>2</sub>, C, 43.64; H, 2.45; N, 11.47; Found C, 43.62; H, 2.41; N, 11.43.

#### *N*-(7-Chloro-6-fluoro-1,3-benzothiazol-2-yl)-4-[(E)-(3-nitrophenyl)methyleneamino]benzenesulphonamide (4a)

0.01 mol of compound (**3**) with 0.015 mol solution of 3-nitro benzaldehyde, added 20 ml ethanol and 3-4 drops of HCl and refluxed for 2-3 h. Solution cooled and poured into crushed ice. Recrystallised with benzene and ethanol. (80.15%) m.p.195°c (d); Anal. calcd. for C<sub>20</sub>H<sub>12</sub>ClFN<sub>4</sub>O<sub>4</sub>S<sub>2</sub>, C, 48.95; H, 2.55; N, 11.34; Found C, 48.91; H, 2.51; N, 11.30.

#### *N*-(7-Chloro-6-fluoro-1,3-benzothiazol-2-yl)-4-[(E)-(4-nitrophenyl)methyleneamino]benzenesulphonamide (4b)

0.01 mol of compound (**3**) with 0.015 mol solution of 4-nitro benzaldehyde, added 20 ml ethanol and 3-4 drops of HCl and refluxed for 2-3 h. Solution cooled and poured into crushed ice. Recrystallised with benzene and ethanol. (78.15%) m.p.190°c (d); Anal. calcd. for C<sub>20</sub>H<sub>12</sub>ClFN<sub>4</sub>O<sub>4</sub>S<sub>2</sub>, C, 48.95; H, 2.55; N, 11.34; Found C, 48.93; H, 2.53; N, 11.32.

#### *N*-(7-Chloro-6-fluoro-1,3-benzothiazol-2-yl)-4-[2-(3-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide (5a).

To a solution of Schiff's base (**4a**) (0.01 mol) added 1,4-dioxane (50ml) and 2-thioglycolic acid (0.025 mol) refluxed for 12 h. After reflux cooled and triturated with 10% sodium bicarbonate solution. The product was recrystallised from benzene and ethanol. (72.21%) m.p. 234°c (d); Anal. calcd. for C<sub>22</sub>H<sub>14</sub>ClFN<sub>4</sub>O<sub>5</sub>S<sub>3</sub>; C, 46.86; H, 2.55; N, 9.90; Found C, 46.82; H, 2.52; N, 9.88.

#### *N*-(7-Chloro-6-fluoro-1,3-benzothiazol-2-yl)-4-[2-(4-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide (5b).

To a solution of Schiff's base (**4b**) (0.01 mol) added 1,4-dioxane (50ml) and 2-thioglycolic acid (0.025 mol) refluxed for 12 h. After reflux cooled and triturated with 10% sodium bicarbonate solution. The product was recrystallised from benzene and ethanol. (78.00%) m.p. 245°c (d); Anal. calcd. for C<sub>22</sub>H<sub>14</sub>ClFN<sub>4</sub>O<sub>5</sub>S<sub>3</sub>; C, 46.86; H, 2.55; N, 9.90; Found C, 46.81; H, 2.53; N, 9.87.

#### *N*-[6-Fluoro-7-(2-nitroanilino)-1,3-benzothiazol-2-yl]-4-[2-(3-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide (6a)

Compound (**5a**) (0.01 mol) was treated with equimolar quantity of 2-nitroaniline refluxed for 2 h in presence of DMF, recrystallised from alcohol and benzene. (72.00%) m.p. 180°c (d); IR (cm<sup>-1</sup>):ν = 3385,

3080, 1815, 1450, 1397, 1380, 1300, 1193, 1190, 720; <sup>1</sup>HNMR (400 MHz, DMSO-*d*<sub>6</sub>), δ (ppm) 6.5-7.9 (m, Ar-H), 5.3 (s, NH), FAB-MS m/z 668 [M+1]<sup>+</sup>; Anal. calcd. for C<sub>28</sub>H<sub>19</sub>FN<sub>5</sub>O<sub>5</sub>S<sub>3</sub> C, 50.44; H, 2.96; N, 12.61; Found C, 50.41; H, 2.93; N, 12.64.

***N*-[6-Fluoro-7-(3-nitroanilino)-1,3-benzothiazol-2-yl]-4-[2-(3-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide (6b)**

Compound (5a) (0.01 mol) was treated with equimolar quantity of 3-nitroaniline refluxed for 2 h in presence of DMF, recrystallised from alcohol and benzene. (78.00%) m.p. 132°C (d); IR (cm<sup>-1</sup>):ν = 3400, 3100, 1830, 1435, 1385, 1295, 1280, 1200, 725; <sup>1</sup>HNMR (400 MHz, DMSO-*d*<sub>6</sub>), δ (ppm) 6.6-7.6 (m, Ar-H), 5.1 (s, NH), FAB-MS m/z 668 [M+1]<sup>+</sup>; Anal. calcd. for C<sub>28</sub>H<sub>19</sub>FN<sub>5</sub>O<sub>5</sub>S<sub>3</sub> C, 50.44; H, 2.96; N, 12.61; Found C, 50.41; H, 2.93; N, 12.64.

***N*-[6-Fluoro-7-(4-nitroanilino)-1,3-benzothiazol-2-yl]-4-[2-(3-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide (6c)**

Compound (5a) (0.01 mol) was treated with equimolar quantity of 4-nitroaniline refluxed for 2 h in presence of DMF, recrystallised from alcohol and benzene. (83.00%) m.p. 97°C (d); IR (cm<sup>-1</sup>):ν = 3390, 3090, 1830, 1440, 1390, 1285, 1210, 1195, 718; <sup>1</sup>HNMR (400 MHz, DMSO-*d*<sub>6</sub>), δ (ppm) 6.7-7.4 (m, Ar-H), 5.2 (s, NH), FAB-MS m/z 668 [M+1]<sup>+</sup>; Anal. calcd. for C<sub>28</sub>H<sub>19</sub>FN<sub>5</sub>O<sub>5</sub>S<sub>3</sub> C, 50.44; H, 2.96; N, 12.61; Found C, 50.41; H, 2.93; N, 12.64.

***N*-[6-Fluoro-7-(2-chloroanilino)-1,3-benzothiazol-2-yl]-4-[2-(3-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide (6d)**

Compound (5a) (0.01 mol) was treated with equimolar quantity of 2-chloroaniline refluxed for 2 h in presence of DMF, recrystallised from alcohol and benzene. (88.00%) m.p. 170°C (d); IR (cm<sup>-1</sup>):ν = 3128, 3369, 1825, 1607, 1290, 1282, 1607, 1197, 1182; <sup>1</sup>HNMR (400 MHz, DMSO-*d*<sub>6</sub>), δ (ppm) 6.5-7.2 (m, Ar-H), 5.2 (s, NH), FAB-MS m/z 657 [M+1]<sup>+</sup>; Anal. calcd. for C<sub>28</sub>H<sub>19</sub>ClFN<sub>5</sub>O<sub>5</sub>S<sub>3</sub> C, 51.31; H, 2.96; N, 10.73; Found C, 51.34; H, 2.93; N, 10.71.

***N*-[6-Fluoro-7-(3-chloroanilino)-1,3-benzothiazol-2-yl]-4-[2-(3-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide (6e)**

Compound (5a) (0.01 mol) was treated with equimolar quantity of 3-chloroaniline refluxed for 2 h in presence of DMF, recrystallised from alcohol and benzene. (70.00%) m.p. 125°C (d); IR (cm<sup>-1</sup>):ν = 3315, 3228, 1820, 1699, 1555, 1296, 1295, 1385, 1195, 1184; <sup>1</sup>HNMR (400 MHz, DMSO-*d*<sub>6</sub>), δ (ppm) 6.2-7.2 (m, Ar-H), 5.5 (s, NH), FAB-MS m/z 657 [M+1]<sup>+</sup>; Anal. calcd. for C<sub>28</sub>H<sub>19</sub>ClFN<sub>5</sub>O<sub>5</sub>S<sub>3</sub> C, 51.31; H, 2.96; N, 10.73; Found C, 51.32; H, 2.92; N, 10.74.

***N*-[6-Fluoro-7-(4-chloroanilino)-1,3-benzothiazol-2-yl]-4-[2-(3-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide (6f)**

Compound (5a) (0.01 mol) was treated with equimolar quantity of 4-chloroaniline refluxed for 2 h in presence of DMF, recrystallised from alcohol and benzene. (80.00%) m.p. 82°C (d); IR (cm<sup>-1</sup>):ν = 3452, 3201, 1825, 1690, 1512, 1397, 1390, 1300, 1297, 1172; <sup>1</sup>HNMR (400 MHz, DMSO-*d*<sub>6</sub>), δ (ppm) 6.4-7.1 (m, Ar-H), 5.6 (s, NH), FAB-MS m/z 657 [M+1]<sup>+</sup>; Anal. calcd. for C<sub>28</sub>H<sub>19</sub>ClFN<sub>5</sub>O<sub>5</sub>S<sub>3</sub> C, 51.31; H, 2.96; N, 10.73; Found C, 51.35; H, 2.99; N, 10.76.

**4-[[6-Fluoro-2-[[4-[2-(3-nitrophenyl)-4-oxo-thiazolidin-3-yl]phenyl]sulfonylamino]-1,3-benzothiazol-7-yl]amino]benzoic acid (6g)**

Compound (5a) (0.01 mol) was treated with equimolar quantity of 4-amino benzoic acid refluxed for 2 h in presence of DMF, recrystallised from alcohol and benzene. (89.00%) m.p. 90°C (d); IR (cm<sup>-1</sup>):ν = 3200, 3110, 1820, 1550, 1380, 1397, 1390, 1310, 1195, 1184; <sup>1</sup>HNMR (400 MHz, DMSO-*d*<sub>6</sub>), δ (ppm) 6.2-7.4 (m, Ar-H), 5.5 (s, NH), FAB-MS m/z 668 [M+1]<sup>+</sup>; Anal. calcd. for C<sub>29</sub>H<sub>20</sub>FN<sub>5</sub>O<sub>7</sub>S<sub>3</sub> C, 52.34; H, 3.00; N, 10.55; Found C, 52.30; H, 2.99; N, 10.54.

***N*-[6-Fluoro-7-(anilino)-1,3-benzothiazol-2-yl]-4-[2-(3-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide (6h)**

Compound (5a) (0.01 mol) was treated with equimolar quantity of aniline refluxed for 2 h in presence of DMF, recrystallised from alcohol and benzene. (80.00%) m.p. 72°C (d); IR (cm<sup>-1</sup>):ν = 3370, 3100, 1825, 1600, 1380, 1295, 1249, 1170; <sup>1</sup>HNMR (400 MHz, DMSO-*d*<sub>6</sub>), δ (ppm) 6.3-7.4 (m, Ar-H), 5.8 (s, NH), FAB-MS m/z 622 [M+1]<sup>+</sup>; Anal. calcd. for C<sub>28</sub>H<sub>20</sub>FN<sub>5</sub>O<sub>5</sub>S<sub>3</sub> C, 54.10; H, 3.20; N, 11.34; Found C, 54.11; H, 3.16; N, 11.30.

***N*-[6-Fluoro-7-(morpholino)-1,3-benzothiazol-2-yl]-4-[2-(3-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide (6i)**

Compound (5a) (0.01 mol) was treated with equimolar quantity of morpholine refluxed for 2 h in presence of DMF, recrystallised from alcohol and benzene. (67.00%) m.p. 145°C (d); IR (cm<sup>-1</sup>):ν = 3350, 3095, 1835, 1597, 1395, 1300, 1295, 1280; <sup>1</sup>HNMR (400 MHz, DMSO-*d*<sub>6</sub>), δ (ppm) 6.5-7.2 (m, Ar-H), 5.4 (s, NH), FAB-MS m/z 616 [M+1]<sup>+</sup>; Anal. calcd. for C<sub>26</sub>H<sub>22</sub>FN<sub>5</sub>O<sub>6</sub>S<sub>3</sub> C, 50.77; H, 3.61; N, 11.44; Found C, 50.73; H, 3.59; N, 11.41.

***N*-[6-Fluoro-7-(piperazino)-1,3-benzothiazol-2-yl]-4-[2-(3-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide (6j)**

Compound (5a) (0.01 mol) was treated with equimolar quantity of piperazino refluxed for 2 h in presence of DMF, recrystallised from alcohol and

benzene. (72.00%) m.p. 110°C (d); IR (cm<sup>-1</sup>):ν = 3400, 3080, 1820, 1540, 1385, 1295, 1195, 1170; <sup>1</sup>HNMR (400 MHz, DMSO-*d*<sub>6</sub>), δ (ppm) 6.3-7.0 (m, Ar-H), 5.2 (s, NH), FAB-MS m/z 615 [M+1]<sup>+</sup>; Anal. calcd. for C<sub>26</sub>H<sub>23</sub>FN<sub>6</sub>O<sub>5</sub>S<sub>3</sub> C, 50.87; H, 3.81; N, 13.71; Found C, 50.86; H, 3.80; N, 13.68.

**N-[6-Fluoro-7-(N,N-diphenylamino)-1,3-benzothiazol-2-yl]-4-[2-(3-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide (6k)**

Compound (5a) (0.01 mol) was treated with equimolar quantity of N,N-diphenylamine refluxed for 2 h in presence of DMF, recrystallised from alcohol and benzene. (68.00%) m.p. 280°C (d); IR (cm<sup>-1</sup>):ν = 3406, 3101, 1823, 1616, 1390, 1290, 1249, 1170; <sup>1</sup>HNMR (400 MHz, DMSO-*d*<sub>6</sub>), δ (ppm) 6.1-7.1 (m, Ar-H), 5.1 (s, NH), FAB-MS m/z 698 [M+1]<sup>+</sup>; Anal. calcd. for C<sub>34</sub>H<sub>24</sub>FN<sub>5</sub>O<sub>5</sub>S<sub>3</sub> C, 58.50; H, 3.51; N, 10.08; Found C, 58.49; H, 3.52; N, 10.10.

**N-[6-fluoro-7-(N,N-dimethylamino)-1,3-benzothiazol-2-yl]-4-[2-(3-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide (6l)**

Compound (5a) (0.01 mol) was treated with equimolar quantity of N,N-dimethylamine refluxed for 2 h in presence of DMF, recrystallised from alcohol and benzene. (68.00%) m.p. 280°C (d); IR (cm<sup>-1</sup>):ν = 3406, 3101, 1823, 1616, 1390, 1290, 1249, 1170; <sup>1</sup>HNMR (400 MHz, DMSO-*d*<sub>6</sub>), δ (ppm) 6.3-7.4 (m, Ar-H), 5.4 (s, NH), FAB-MS m/z 574 [M+1]<sup>+</sup>; Anal. calcd. for C<sub>24</sub>H<sub>20</sub>FN<sub>5</sub>O<sub>5</sub>S<sub>3</sub> C, 50.35; H, 3.51; N, 12.21; Found C, 50.31; H, 3.52; N, 12.20.

**N-[6-fluoro-7-(2-nitroanilino)-1,3-benzothiazol-2-yl]-4-[2-(4-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide (6m)**

Compound (5b) (0.01 mol) was treated with equimolar quantity of 2-nitroaniline refluxed for 2 h in presence of DMF, recrystallised from alcohol and benzene. (78.00%) m.p. 110°C (d); IR (cm<sup>-1</sup>):ν = 3300, 3100, 1822, 1456, 1334, 1200, 725; <sup>1</sup>HNMR (400 MHz, DMSO-*d*<sub>6</sub>), δ (ppm) 7.7-8.7 (m, Ar-H), 9.0 (s, NH), FAB-MS m/z 668 [M+1]<sup>+</sup>; Anal. calcd. for C<sub>28</sub>H<sub>19</sub>FN<sub>6</sub>O<sub>7</sub>S<sub>3</sub> C, 50.44; H, 2.96; N, 12.61; Found C, 50.41; H, 2.93; N, 12.64.

**N-[6-fluoro-7-(3-nitroanilino)-1,3-benzothiazol-2-yl]-4-[2-(4-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide (6n)**

Compound (5b) (0.01 mol) was treated with equimolar quantity of 3-nitroaniline refluxed for 2 h in presence of DMF, recrystallised from alcohol and benzene. (89.00%) m.p. 156°C (d); IR (cm<sup>-1</sup>):ν = 3423, 3200, 1856, 1434, 1390, 1295, 1290, 1297, 778; <sup>1</sup>HNMR (400 MHz, DMSO-*d*<sub>6</sub>), δ (ppm) 6.8-7.2 (m, Ar-H), 8.3 (s, NH), FAB-MS m/z 668 [M+1]<sup>+</sup>; Anal. calcd. for C<sub>28</sub>H<sub>19</sub>FN<sub>6</sub>O<sub>7</sub>S<sub>3</sub> C, 50.44; H, 2.96; N, 12.61; Found C, 50.41; H, 2.93; N, 12.64.

**N-[6-fluoro-7-(4-nitroanilino)-1,3-benzothiazol-2-yl]-4-[2-(4-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide (6o)**

Compound (5b) (0.01 mol) was treated with equimolar quantity of 4-nitroaniline refluxed for 2 h in presence of DMF, recrystallised from alcohol and benzene. (76.00%) m.p. 125°C (d); IR (cm<sup>-1</sup>):ν = 3345, 3100, 1876, 1456, 1400, 1287, 1231, 1200, 789; <sup>1</sup>HNMR (400 MHz, DMSO-*d*<sub>6</sub>), δ (ppm) 6.7-7.3 (m, Ar-H), 5.5 (s, NH), FAB-MS m/z 668 [M+1]<sup>+</sup>; Anal. calcd. for C<sub>28</sub>H<sub>19</sub>FN<sub>6</sub>O<sub>7</sub>S<sub>3</sub> C, 50.44; H, 2.96; N, 12.61; Found C, 50.41; H, 2.93; N, 12.64.

**N-[6-fluoro-7-(2-chloroanilino)-1,3-benzothiazol-2-yl]-4-[2-(4-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide (6p)**

Compound (5b) (0.01 mol) was treated with equimolar quantity of 2-chloroaniline refluxed for 2 h in presence of DMF, recrystallised from alcohol and benzene. (75.00%) m.p. 90°C (d); IR (cm<sup>-1</sup>):ν = 3372, 3200, 1825, 1708, 1359, 1295, 1278, 1200, 1190; <sup>1</sup>HNMR (400 MHz, DMSO-*d*<sub>6</sub>), δ (ppm) 6.6-7.2 (m, Ar-H), 5.7 (s, NH), FAB-MS m/z 657 [M+1]<sup>+</sup>; Anal. calcd. for C<sub>28</sub>H<sub>19</sub>ClFN<sub>5</sub>O<sub>5</sub>S<sub>3</sub> C, 51.31; H, 2.96; N, 10.73; Found C, 51.34; H, 2.93; N, 10.71.

**N-[6-fluoro-7-(3-chloroanilino)-1,3-benzothiazol-2-yl]-4-[2-(3-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide (6q)**

Compound (5b) (0.01 mol) was treated with equimolar quantity of 3-chloroaniline refluxed for 2 h in presence of DMF, recrystallised from alcohol and benzene. (82.00%) m.p. 115°C (d); IR (cm<sup>-1</sup>):ν = 3318, 3220, 1823, 1700, 1578, 1398, 1300, 1286, 1187; <sup>1</sup>HNMR (400 MHz, DMSO-*d*<sub>6</sub>), δ (ppm) 6.5-7.5 (m, Ar-H), 5.7 (s, NH), FAB-MS m/z 657 [M+1]<sup>+</sup>; Anal. calcd. for C<sub>28</sub>H<sub>19</sub>ClFN<sub>5</sub>O<sub>5</sub>S<sub>3</sub> C, 51.31; H, 2.96; N, 10.73; Found C, 51.32; H, 2.92; N, 10.74.

**N-[6-fluoro-7-(4-chloroanilino)-1,3-benzothiazol-2-yl]-4-[2-(4-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide (6r)**

Compound (5b) (0.01 mol) was treated with equimolar quantity of 4-chloroaniline refluxed for 2 h in presence of DMF, recrystallised from alcohol and benzene. (89.00%) m.p. 142°C (d); IR (cm<sup>-1</sup>):ν = 3400, 3301, 1825, 1698, 1562, 1399, 1385, 1309, 1289, 1183; <sup>1</sup>HNMR (400 MHz, DMSO-*d*<sub>6</sub>), δ (ppm) 6.2-7.2 (m, Ar-H), 5.8 (s, NH), FAB-MS m/z 657 [M+1]<sup>+</sup>; Anal. calcd. for C<sub>28</sub>H<sub>19</sub>ClFN<sub>5</sub>O<sub>5</sub>S<sub>3</sub> C, 51.31; H, 2.96; N, 10.73; Found C, 51.35; H, 2.99; N, 10.76.

**4-[[6-fluoro-2-[[4-[2-(4-nitrophenyl)-4-oxo-thiazolidin-3-yl]phenyl]sulfonylamino]-1,3-benzothiazol-7-yl]amino]benzoic acid (6s)**

Compound (5b) (0.01 mol) was treated with equimolar quantity of 4-amino benzoic acid refluxed for



2 h in presence of DMF, recrystallised from alcohol and benzene. (79.00%) m.p. 92°C (d); IR (cm<sup>-1</sup>):ν = 3208, 3200, 1827, 1600, 1380, 1329, 1200, 1198; <sup>1</sup>HNMR (400 MHz, DMSO-*d*<sub>6</sub>), δ (ppm) 6.1-7.4 (m, Ar-H), 5.1 (s, NH), FAB-MS m/z 668 [M+1]<sup>+</sup>; Anal. calcd. for C<sub>29</sub>H<sub>20</sub>FN<sub>5</sub>O<sub>7</sub>S<sub>3</sub> C, 52.34; H, 3.00; N, 10.55; Found C, 52.30; H, 2.99; N, 10.54.

**N-[6-fluoro-7-(anilino)-1,3-benzothiazol-2-yl]-4-[2-(4-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide (6t)**

Compound (5b) (0.01 mol) was treated with equimolar quantity of aniline refluxed for 2 h in presence of DMF, recrystallised from alcohol and benzene. (62.00%) m.p. 120°C (d); IR (cm<sup>-1</sup>):ν = 3380, 3298, 1825, 1640, 1390, 1323, 1289, 1170; <sup>1</sup>HNMR (400 MHz, DMSO-*d*<sub>6</sub>), δ (ppm) 6.3-7.3 (m, Ar-H), 5.1 (s, NH), FAB-MS m/z 622 [M+1]<sup>+</sup>; Anal. calcd. for C<sub>28</sub>H<sub>20</sub>FN<sub>5</sub>O<sub>5</sub>S<sub>3</sub> C, 54.10; H, 3.20; N, 11.34; Found C, 54.11; H, 3.16; N, 11.30.

**N-[6-fluoro-7-(morpholino)-1,3-benzothiazol-2-yl]-4-[2-(4-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide (6u)**

Compound (5b) (0.01 mol) was treated with equimolar quantity of morpholine refluxed for 2 h in presence of DMF, recrystallised from alcohol and benzene. (87.00%) m.p. 165°C (d); IR (cm<sup>-1</sup>):ν = 3370, 3100, 1840, 1597, 1345, 1309, 1300; <sup>1</sup>HNMR (400 MHz, DMSO-*d*<sub>6</sub>), δ (ppm) 6.3-7.2 (m, Ar-H), 5.2 (s, NH), FAB-MS m/z 616 [M+1]<sup>+</sup>; Anal. calcd. for C<sub>26</sub>H<sub>22</sub>FN<sub>5</sub>O<sub>6</sub>S<sub>3</sub> C, 50.77; H, 3.61; N, 11.44; Found C, 50.73; H, 3.59; N, 11.41.

**N-[6-fluoro-7-(piperazino)-1,3-benzothiazol-2-yl]-4-[2-(4-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide (6v)**

Compound (5b) (0.01 mol) was treated with equimolar quantity of piperazino refluxed for 2 h in presence of DMF, recrystallised from alcohol and benzene. (82.00%) m.p. 188°C (d); IR (cm<sup>-1</sup>):ν = 3390, 3100, 1890, 1560, 1385, 1300, 1209, 1150; <sup>1</sup>HNMR (400 MHz, DMSO-*d*<sub>6</sub>), δ (ppm) 6.1-7.0 (m, Ar-H), 5.2 (s, NH), FAB-MS m/z 615 [M+1]<sup>+</sup>; Anal. calcd. for C<sub>26</sub>H<sub>23</sub>FN<sub>6</sub>O<sub>5</sub>S<sub>3</sub> C, 50.87; H, 3.81; N, 13.71; Found C, 50.86; H, 3.80; N, 13.68.

**N-[6-fluoro-7-(N,N-diphenylamino)-1,3-benzothiazol-2-yl]-4-[2-(4-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide (6w)**

Compound (5b) (0.01 mol) was treated with equimolar quantity of N,N-diphenylamine refluxed for 2 h in presence of DMF, recrystallised from alcohol and benzene. (56.00%) m.p. 210°C (d); IR (cm<sup>-1</sup>):ν = 3306, 3120, 1867, 1623, 1395, 1289, 1250, 1200; <sup>1</sup>HNMR (400 MHz, DMSO-*d*<sub>6</sub>), δ (ppm) 6.0-7.0 (m, Ar-H), 5.6 (s, NH), FAB-MS m/z 698 [M+1]<sup>+</sup>; Anal. calcd. for

C<sub>34</sub>H<sub>24</sub>FN<sub>5</sub>O<sub>5</sub>S<sub>3</sub> C, 58.50; H, 3.51; N, 10.08; Found C, 58.49; H, 3.52; N, 10.10.

**N-[6-fluoro-7-(N,N-dimethylamino)-1,3-benzothiazol-2-yl]-4-[2-(4-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide (6x)**

Compound (5b) (0.01 mol) was treated with equimolar quantity of N,N-dimethylamine refluxed for 2 h in presence of DMF, recrystallised from alcohol and benzene. (76.00%) m.p. 156°C (d); IR (cm<sup>-1</sup>):ν = 3397, 3100, 1820, 1455, 1395, 1356, 1287, 1240; <sup>1</sup>HNMR (400 MHz, DMSO-*d*<sub>6</sub>), δ (ppm) 6.2-7.4 (m, Ar-H), 5.3 (s, NH), FAB-MS m/z 574 [M+1]<sup>+</sup>; Anal. calcd. for C<sub>24</sub>H<sub>20</sub>FN<sub>5</sub>O<sub>5</sub>S<sub>3</sub> C, 50.35; H, 3.51; N, 12.21; Found C, 50.31; H, 3.52; N, 12.20.

**Pharmacological activity**

**Anti-mycobacterial activity**

The entire test compounds were assayed in anti-mycobacterial activity was evaluated against H37Rv strain of M. tuberculosis (ATCC 27294). The MIC was determined by the test tube dilution technique using modified Kirchner's culture medium containing 0.5% sterilized horse serum for anti-mycobacterial activity. Rifampicin and isoniazid (INH) were used as reference standard for anti-mycobacterial activity. The stock solution (2-4 lg/mL) of test compounds was prepared in a mixture of sterile water and dimethyl formamide (8:2) solvent. The stock solution was sterilized by passing through a 0.2 mm polycarbonate sterile membrane (Nuclepore) filters. Further, the serial dilution of test compounds was carried out and the following concentration was used: 1000, 500, 250, 125, 62, 32, 16, 8, 4 and 1 lg/mL. Test compounds at various concentrations were added to culture medium in a sterilized borosilicate test tube and different bacterial strains were inoculated at 10<sup>6</sup> bacilli/mL concentration. The tubes were incubated at 37° for 14 and 21 days for anti-mycobacterial activity and then examined for the presence or absence of growth of the test organisms. All experiments were performed in triplicate. The MIC values were obtained from the lowest concentration of the test compound where the tubes remained clear, indicated that the bacterial growth was completely inhibited at this concentration.

**Anti-cancer activity**

**1. General**

Hela- Human cervix, K-562 – Human chronic myelogenous Leukemia bone marrow and HEK 293 – Human Kidney cells were centrifuged at 1000 rpm for 1 min. After centrifugation 2 ml supernatant of cells mixed with 200 µl of MEM medium in required number of wells using 96 well plates with 50 µl of cell line in each well. Into these wells 10µl, 20µl, and 30µl of testing compounds were added and Kept in CO<sub>2</sub> incubator at 37°C and 5% CO<sub>2</sub> for 72 h. After 72 h. observed whether lysis occur or not under inverted microscope. All the procedure was carried out under

aseptic conditions. MTT solution (10 mg in 10 ml of Hank's balanced solution) was used.

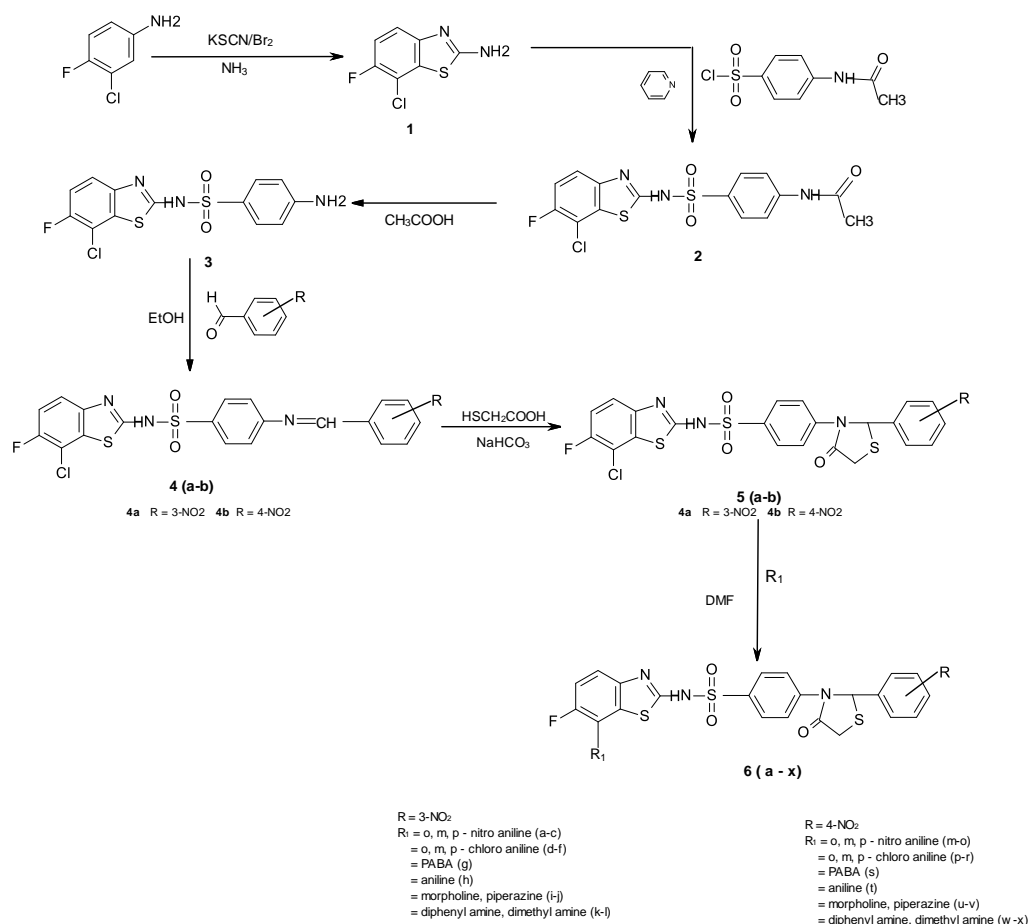
## 2. Cell culture

The cell line were maintained in 96 wells micro titer plate containing MEM (Minimum Essential medium) supplemented with 10% heat inactivated fetal calf serum (FCS), containing 5% of mixture of gentamycin, penicillin (100 Units/ml) and streptomycin (100µg/ml) in presence of 5% CO<sub>2</sub> at 37°C for 3-4 days. After 3-4 days removed the supernatant and replaced MEM media with Hank's balanced solution supplemented with gentamycin, penicillin and streptomycin and were incubated for overnight.

## 3. Cytotoxicity Assay

In vitro growth inhibition effect of test compounds were assessed by calorimetric or

spectrophotometric determination of conversion of MTT into "Formazan blue" by living cells. Supernatant removed from the plate added with fresh Hank's balanced salt solution and treated with different concentration of extract or compound appropriately diluted with DMSO. Control group contains only DMSO. After 24 h incubation at 37°C in a humidified atmosphere of 5% CO<sub>2</sub>, the medium were replaced with MTT solution (100µl, 1mg per ml in sterile Hank's balanced solution) for further 4 h incubation. The supernatant carefully aspirated, the precipitated crystals of "Formazan blue" were solubilised by adding DMSO (200µl) and optical density was measured at wavelength of 570nm. The result were represents the mean of three readings. Results are calculated by considering concentration at which the optical density of treated cells was reduced by 50% with respect to the untreated control.



**Fig-1: General scheme for synthesis of N-[6-fluoro-7-substituted-1,3-benzothiazol-2-yl]-4-[2-(3-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamides 6 (a-l) and N-[6-fluoro-7-substituted-1,3-benzothiazol-2-yl]-4-[2-(4-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamides 6 (m-x)**

## RESULTS

### Anti-mycobacterial activity

All the test compounds were assayed for in vitro anti-mycobacterial activity evaluated against H37

Rv strain of *M. tuberculosis* strain using standard protocol [26]. The minimum inhibitory concentration (MIC) was determined by the test tube dilution technique using modified Kirchner's culture medium

containing 0.5% sterilized horse serum for anti-mycobacterial activity. The MIC values were also tested for standard antibiotics rifampin and isoniazide (INH) to compare the anti-mycobacterial activity of test compounds. All experiments were performed in triplicate. The lowest concentration, which showed no visible growth, was taken as the end point i.e. minimum inhibitory concentration (MIC).

#### Anti-cancer activity [27-29]

In vitro cytotoxicity studies were carried out on human cells using Hela- Human cervix, K-562 – Human chronic myelogenous Leukemia bone marrow and HEK 293 – Human Kidney cells. Cell suspension ( $100 \mu\text{l} \times 10^6$  cells per ml) was transferred to each cell of a 96 well plates. Cell viability was determined after 24 h at  $37^\circ$  in a humidified 5%  $\text{CO}_2$  atmosphere by the Microculture Tetraolium Assay (MTT) method [30]. In vitro growth inhibition effect of test compounds were assessed by calorimetric or spectrophotometric determination of conversion of MTT into “Formazan blue” by living cells. DMSO was used as a control. The optical density were noted at 570 nm and compared with control. The results are expressed as % cell death at different concentrations.

#### DISCUSSION

In present study, novel N-[6-fluoro-7-substituted-1,3-benzothiazol-2-yl]-4-[2-(3-nitrophenyl)-4-oxo-thiazolidin-3-yl]benzenesulphonamide derivatives **6 (a-l)** and N-[6-fluoro-7-substituted-1,3-benzothiazol-2-yl]-4-[2-(4-nitrophenyl)-4-oxo-

thiazolidin-3-yl]benzenesulphonamide derivatives **6 (m-x)** were synthesized and characterized using various analytical and spectral studies. All new compounds tested for their in vitro anti-mycobacterial activity using standard protocol. The MIC values of the test compounds are summarized in Table II. For comparison, the MICs of standard compounds rifampicin and isoniazide are also tabulated. The results revealed that the test compounds **6 (a-x)** exhibit remarkable anti-mycobacterial activities against H37Rv strain of *M. tuberculosis*. The MIC values are in the range of 13 – 27. Some selected three new synthesized compounds were screened for their anti-cancer activity using 3-cell line study. Percentage surviving cells were calculated using MTT assay method. Hela- Human cervix, K-562 – Human chronic myelogenous Leukemia bone marrow and HEK 293 – Human Kidney cells were used for 3-cell line study. All three viz. 6k, 6r and 6t showed lyses (cytotoxic) against Hela- Human cervix cell and also showed less surviving cell percentage in all  $10 \mu\text{l}$ ,  $20 \mu\text{l}$ , and  $30 \mu\text{l}$  concentration using MTT assay method. Compound 6k and 6r showed 50% lyses (active) and 50% less surviving cell percentage against K-562 and HEK 293 cells in  $30 \mu\text{l}$  concentration using MTT assay method. All 6k, 6r and 6t compounds in all concentrations except  $30 \mu\text{l}$  (compound B<sub>6</sub>) were found inactive in cytotoxic activity where no lyses found. Cytotoxicity of the compounds were compared with standard anti-cancer drugs viz. cisplatin and vincristine. Anticancer activity of test compounds is tabulated in Table III, IV and V.

**Table 1: Physical and analytical data of compounds**

Compound	R	R'	Molecular Formula	MP	Yield	Mass [M+1]
6a	3-Nitro	o-nitro aniline	$\text{C}_{28}\text{H}_{19}\text{FN}_6\text{O}_7\text{S}_3$	180	72	667
6b	3-Nitro	m-nitro aniline	$\text{C}_{28}\text{H}_{19}\text{FN}_6\text{O}_7\text{S}_3$	132	78	667
6c	3-Nitro	p-nitro aniline	$\text{C}_{28}\text{H}_{19}\text{FN}_6\text{O}_7\text{S}_3$	97	83	667
6d	3-Nitro	o-chloro aniline	$\text{C}_{28}\text{H}_{19}\text{ClFN}_5\text{O}_5\text{S}_3$	170	88	656
6e	3-Nitro	m- chloro aniline	$\text{C}_{28}\text{H}_{19}\text{ClFN}_5\text{O}_5\text{S}_3$	125	70	656
6f	3-Nitro	p- chloro aniline	$\text{C}_{28}\text{H}_{19}\text{ClFN}_5\text{O}_5\text{S}_3$	82	80	656
6g	3-Nitro	PABA	$\text{C}_{29}\text{H}_{20}\text{FN}_5\text{O}_7\text{S}_3$	90	89	667
6h	3-Nitro	Aniline	$\text{C}_{28}\text{H}_{20}\text{FN}_5\text{O}_5\text{S}_3$	80	72	622
6i	3-Nitro	N-morpholine	$\text{C}_{26}\text{H}_{22}\text{FN}_5\text{O}_6\text{S}_3$	145	67	616
6j	3-Nitro	N-piperazine	$\text{C}_{26}\text{H}_{23}\text{FN}_6\text{O}_5\text{S}_3$	110	72	615
6k	3-Nitro	N,N-diphenyl amine	$\text{C}_{34}\text{H}_{24}\text{FN}_5\text{O}_5\text{S}_3$	280	68	698
6l	3-Nitro	N,N-dimethyl amine	$\text{C}_{24}\text{H}_{20}\text{FN}_5\text{O}_5\text{S}_3$	101	74	574
6m	4-Nitro	o-nitro aniline	$\text{C}_{28}\text{H}_{19}\text{FN}_6\text{O}_7\text{S}_3$	110	78	667
6n	4-Nitro	m-nitro aniline	$\text{C}_{28}\text{H}_{19}\text{FN}_6\text{O}_7\text{S}_3$	156	89	667
6o	4-Nitro	p-nitro aniline	$\text{C}_{28}\text{H}_{19}\text{FN}_6\text{O}_7\text{S}_3$	125	76	667
6p	4-Nitro	o-chloro aniline	$\text{C}_{28}\text{H}_{19}\text{ClFN}_5\text{O}_5\text{S}_3$	90	75	656
6q	4-Nitro	m- chloro aniline	$\text{C}_{28}\text{H}_{19}\text{ClFN}_5\text{O}_5\text{S}_3$	115	82	656
6r	4-Nitro	p- chloro aniline	$\text{C}_{28}\text{H}_{19}\text{ClFN}_5\text{O}_5\text{S}_3$	142	89	656
6s	4-Nitro	PABA	$\text{C}_{29}\text{H}_{20}\text{FN}_5\text{O}_7\text{S}_3$	92	79	667
6t	4-Nitro	Aniline	$\text{C}_{28}\text{H}_{20}\text{FN}_5\text{O}_5\text{S}_3$	120	62	622
6u	4-Nitro	N-morpholine	$\text{C}_{26}\text{H}_{22}\text{FN}_5\text{O}_6\text{S}_3$	165	87	616
6v	4-Nitro	N-piperazine	$\text{C}_{26}\text{H}_{23}\text{FN}_6\text{O}_5\text{S}_3$	188	82	615
6w	4-Nitro	N,N-diphenyl amine	$\text{C}_{34}\text{H}_{24}\text{FN}_5\text{O}_5\text{S}_3$	210	56	698
6x	4-Nitro	N,N-dimethyl amine	$\text{C}_{24}\text{H}_{20}\text{FN}_5\text{O}_5\text{S}_3$	156	76	574

**Table 2: Anti-mycobacterial activity of test compounds**

Compounds	H37RV strain of <i>M. tuberculosis</i> 21 days MIC values
6a	23
6b	25
6c	24
6d	15
6e	13
6f	17
6g	21
6h	18
6i	14
6j	14
6k	14
6l	14
6m	20
6n	22
6o	27
6p	23
6q	22
6r	18
6s	20
6t	21
6u	20
6v	17
6w	16
6x	23
Rifampicin (Std 1)	0.25
Isoniazide (Std 2)	0.007

**Table 3: Anti-cancer activity of test compounds**

Compounds	Conc.	Human Cell Lines		
		HeLa	K – 562	HEK – 293
6k	10 µl	Lyses	No Lyses	No Lyses
	20 µl	Lyses	No Lyses	No Lyses
	30 µl	Lyses	No Lyses	Lyses
6r	10 µl	Lyses	No Lyses	No Lyses
	20 µl	Lyses	No Lyses	No Lyses
	30 µl	Lyses	50% Lyses	50% Lyses
6t	10 µl	Lyses	No Lyses	No Lyses
	20 µl	Lyses	No Lyses	No Lyses
	30 µl	Lyses	No Lyses	No Lyses

No Lyses: No cytotoxic Activity

Lyses: Cytotoxic Activity

**Table 4: Optical density of test compounds**

Compounds	Conc.	Observed O. D. (at 570 nm)		
		HeLa	K – 562	HEK – 293
6k	10 µl	1.32 (55.0%)	2.18(83.84%)	1.68(62.22%)
	20 µl	1.45(60.41%)	2.15 (82.69%)	1.64(60.74%)
	30 µl	1.52(63.33%)	2.0(76.92%)	1.53(56.66%)
6r	10 µl	1.38(57.5%)	2.17(83.46%)	2.51(92.96%)
	20 µl	1.35(56.25%)	1.96(75.38%)	2.48(91.85%)
	30 µl	1.36(56.66%)	1.78(68.46%)	1.82(67.40%)
6t	10 µl	1.41(58.75%)	2.54(97.69%)	2.42(89.62%)
	20 µl	1.40(58.33%)	2.51(97.53%)	2.10(77.77%)
	30 µl	1.38(57.50%)	2.46(94.61%)	1.96(72.59%)
DMSO	---	2.4	2.6	2.7



**Table 5: MTT assay of test compounds**

Compounds	Conc.	MTT assay (In %)		
		HeLa	K – 562	HEK – 293
6k	10 µl	55.00%	83.84%	62.22%
	20 µl	60.41%	82.69%	60.74%
	30 µl	63.33%	76.92%	56.66%
6r	10 µl	57.50%	83.46%	92.96%
	20 µl	56.25%	75.38%	91.85%
	30 µl	56.66%	68.46%	67.40%
6t	10 µl	58.75%	97.69%	89.62%
	20 µl	58.33%	97.53%	77.77%
	30 µl	57.50%	94.61%	72.59%

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