Synthesis, Anti-tuberculosis and Anti-bacterial activities of sulfadimethoxine bearing N-(2,6-dimethoxypyrimidin-4-yl)-4-(4-oxo-2-(substituted) phenylthiazolidin-3yl) benzenesulfonamide

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Abstract

All the new compounds of sulfadimethoxine bearing N-(2,6-dimethoxypyrimidin-4-yl)-4-(4-oxo-2-(substituted)phenylthiazolidin-3yl)benzenesulfonamide **7a-7h** were synthesized by condensations of sulfadimethoxine **4** with different aromatic aldehydes **5a-5h** in presence of a catalytic quantity of glacial ACOH formed intermediate **6a-6h** Schiff bases with good yield in the first step of reactions. Intermediate **6a-6h** Schiff bases followed by cyclization with mercaptoacetic acid produced 5-member ring containing targeted compounds **7a-7h.** All the derivatives were recognized by physical properties like melting point (M.P) and characterized done by elemental analysis (CHNS) also different recognized spectral techniques such as FT-IR, ^{1}H NMR, ^{13}C NMR and ESI-MS (Mass spectroscopic).

The novel series of sulfonamide bearing thiazolidinone were synthesized and final derivatives have been evaluated for bioactivity such as anti-bacterial activity against gram +ve and gram -ve And also screened for their *in vitro* antitubercular activity against Mycobacterium tuberculosis H_{37}RV. All results for scaffolds compare against the standard drug.

Keywords: Sulfadimethoxine, Thiazolidinone, *in vitro* anti-tuberculosis, Anti-bacterial activity, Schiff base

Introduction

The sudden improvement and extensive investigations of heterocyclic compounds in areas of research and synthesis in the field of medicinal chemistry nowadays because of possessing a wide range of effective therapeutic properties.[1] Ongoing our study we mainly focus numbers of strategies that applying for finding new moieties having efficient inhibitory control against organism and move violently to improvement for resistant strain.[2]

The structure of Sulfonamide containing RSO_2NH_2 functionality having an important class of synthetic therapeutic agents. The key of some compounds containing sulfonamides group such as Amprenavir**,** Celecoxib, Sildenafil, (Figure-1) having interesting of bioactivity.

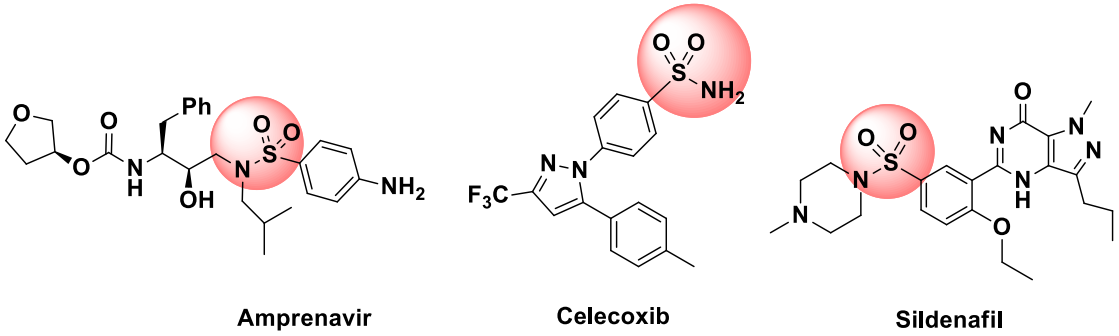


Figure-1 Famous sulfonamide derivatives

This most versatile moiety shown to demonstrate a broad range of activities such as antibacterial[3], [4], antifungal[5], antiviral HIV protease inhibitor[6], anticancer[7], carbonic anhydrase inhibitory[8][9], anti-inflammatory[10].

Another side the key intermediate of the substituted of thiazoldinones, which belong to an important group of heterocyclic compound, have been widely explored for their application in the field of medicine. Thiazolidinones with a carbonyl group at position 2(I), 4(II) on 5(III) have been subjects of extensive study in the field of 4-thiozolidinones. Lots of research work on 4-thiozolidinones has been done in the past. Moreover, 4-thiozolidinones have been studied comprehensively because of their ready accessibility. Thiazolidinones and their derivatives display a large variety of activities such as Antituberculosis[11], Antimicrobial[12][13], AntiHIV[14], Anti Leukemia[15],

Antioxident[16]. In view of these findings, it appeared of interest to synthesize newer thiazolidinones derivatives with better potency.

We expansion our ongoing work and bring into being synthesized biologically active N-(2,6-dimethoxypyrimidin-4-yl)-4-(4-oxo-2-(substituted)phenylthiazolidin-3yl)benzenesulfonamide **7a-7h** and evaluate well-recognized pharmacophore with different range of activity such as antibacterial activity against gram +ve and gram -ve strains with minimum inhibition concentration (MIC) and also *in vitro* antitubercular activity against Mycobacterium tuberculosis $H_{37}RV$.

Experimental section

Material and methods

The synthesis of the novel a series N-(2,6-dimethoxypyrimidin-4-yl)-4-(4-oxo-2-(substituted) phenylthiazolidin-3yl)benzenesulfonamide **7a-7h** the following chemical and reagents were used acquired from commercial sources (Sigma-Aldrich). and Potassium Carbonate (K_2CO_3), dimethylformamide, (DMF), Mercaptoacetic acid from Merck (Germany). Pre-coated aluminium sheets (silica gel 60 $F_{254,}$ Merck) were used for thin-layer chromatography (TLC) and spots were visualized under ultraviolet light. Melting point (M.P) was measured by using a Mel-temp instrument, and results are uncorrected. Infra-red spectra were recorded on Shimadzu spectrophotometer in the frequency range 4000-400 cm^{-1} using KBr pallet disc, ^{1}H NMR and, ^{13}C NMR spectra were recorded on Bruker at 400 MHz and 100 MHz in DMSO solution and chemical shifts were recorded in parts per million (ppm) with TMS at the internal reference. Advion expression CMS, USA were used for recorded mass spectra. The compound was analyzed for Carbon, Hydrogen, Nitrogen oxygen and Sulpher was estimated on CHNS analyzer serial NO. : 15084053

General synthesis of derivatives of 4-((Substituted)benzylideneamino)-N-(2,6-dimethoxypyrimidine-4-yl)benzensulfonamide (Schiff base) 6a-6h

A mixture of sulfadimethoxine **4** (0.1 mol) and appropriate different aromatic aldehydes **5a-5h** (0.1 mol) in ethanol (50 ml) in the presence of the catalytic amount of glacial acetic acid (4 to 5 drops) was refluxed for 5 h. The solvent was removed under reduced pressure and the product cooled it. The solid product filtrated and washed with some hot ether and then allow to dried with air and product recrystallized from chloroform to get 4-

((Substituted)benzylideneamino)-N-(2,6-dimethoxypyrimidine-4-yl)benzensulfonamide **6a-6h** with light yellow coloured the reaction was continuously observed by thin layered chromatography (TLC) with using ethyl acetate: hexane (4:7). This following reaction steps of the Schiff bases shown in **scheme-1.**

General synthesis of derivatives of N-(2,6-dimethoxypyrimidin-4-yl)-4-(4-oxo-2-(substituted)phenylthiazolidin-3yl)benzenesulfonamide 7a-7h

A mixture of Schiff base **6a-6h** (0.01 mol) and mercapto acetic acid (0.012 mol) in DMF (25 ml) containing a pinch of anhydrous zinc chloride was refluxed for 9-10 h. the reaction was continuously observed by thin layered chromatography (TLC) with using ethyl acetate: hexane (4:7). The reaction mixture was then cooled and poured into ice-cold water. The resulting solid was filtered, washed several times with water and then recrystallized from ethanol

Antibacterial activity

The antimicrobial activities for all synthesized compounds7**a-7h** were evaluated by reported in vitro agar well diffusion method[18]. The inhibitions zone was measured were the microorganism inhibited after the incubation was done and were compared with standard streptomycin (1000µg/ml). Shown in table-**2**

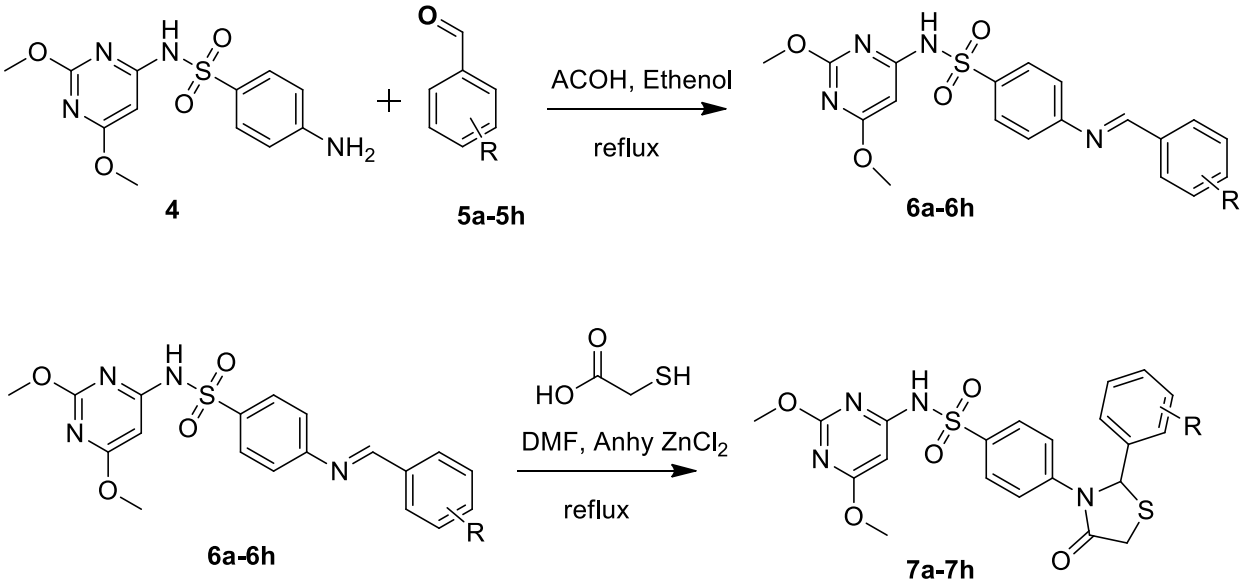
The minimum concentration or maximum dilution which was required to kill bacterial growth regard as minimum Inhibitory concentration (MIC). MIC values are shown in table-**3**

In vitro anti-mycobacterial activity

According to Lowenstein Jensen (L-J) medium, the all synthesized compounds **7a-7h** were assayed for Antimycobacterial activity, following reported method[17] The colony forming units (c.f.u) was a determination by taken 10 fold dilution of standard drug 1mg/ml *Myco.tuberculosis* suspension with marked on L-J medium. H_2KO_4P (potassium dihydrogen phosphate), $MgSO_4$ (magnesium sulfate anhydrous), magnesium citrate, (Loba Chemie), L-asparagines, malachite green, and glycerol these all reagents were included in L-J medium. The concentration of 2% v/v and 4% v/v were dissolved into 100 ml culture medium for inspections. The medium was allowed to stay for incubated at 37 ºC for 42 days with using standard bacterial suspension. Standard drug rifamacine and isoniazid was

used as a medium for comparison of colony-forming units (c.f.u) on drug-free control, reading was taken weekly. Percentage inhibition was calculated by the below equation.

$$\% \, Inhibition = \frac{Cc - Ct}{Cc}$$ Where c = Control t = Test



Scheme-1 Synthetic route of compounds 7a-7h

Table 1 Physical data and substitutions of present synthetic compounds 7a-7h

Entry	Compounds	M.P(°C)	Molecular Weight	Molecular Formula	Yield%
7a	C_6H_5	~245	472.54	$C_{21}H_{20}N_4O_5S_2$	71.8
7b	4-Cl, C_6H_5	~226	506.98	$C_{21}H_{19}ClN_4O_5S_2$	73.6
7c	2,4-Cl, C_6H_5	245-250	541.43	$C_{21}H_{18}Cl_2N_4O_5S_2$	71.5
7d	2-OH, C_6H_5	~236	488.54	$C_{21}H_{20}N_4O_6S_2$	69.8
7e	4-OH, C_6H_5	259-263	488.54	$C_{21}H_{20}N_4O_6S_2$	72.3
7f	4- CH_3, C_6H_5	>255	488.56	$C_{22}H_{22}N_4O_5S_2$	80.5
7g	3-NO_2, C_6H_5	~249	517.53	$C_{21}H_{19}N_5O_7S_2$	75.9
7h	2-O CH_3, C_6H_5	226-230	502.56	$C_{22}H_{22}N_4O_6S_2$	78.8

Characterization

The synthesized compounds of N-(2,6-dimethoxypyrimidin-4-yl)-4-(4-oxo-2-(substituted) phenylthiazolidin-3yl)benzenesulfonamide **7a-7h** were characterized by IR, ^{1}H NMR, ^{13}C NMR, ESI-MS and CHNS elemental analysis.

Analytical data

N-(2,6-dimethoxypyrimidin-4-yl)-4-(4-oxo-2-phenylthiazolidin-3-yl)benzenesulfonamide (7a) Yellow solid, Anal. Calcd for $C_{21}H_{20}N_4O_5S_2$: C, 53.38; H, 4.27; N, 11.86; O, 16.93; S, 13.57%; found C, 53.40; H, 4.28; N, 11.80; O, 16.92, S, 13.57%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3345 (NH), 3052 (C-H_{str} saturated hydrocarbon) 1747(CO,Cyclic), 1620 (C=N_{str}) 1382 Asy., 1123 Syn., (O=S=O), 676(C-S-C); ^{1}H NMR (400 MHz, DMSO) δ 3.68(d, CH2-thiozole), 7.11-8.99 (m, aromatic Protons), 6.52 (s, 1Hpyrimidine), 11.89 (s, 1H -NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.01, 162.97, 161.50, 145.55, 139.25, 135.05, 132.15, 129.91, 129.04, 123.11, 121.06, 82.11, 74.24, 54.12, 54.09, 33.36. ESI-MS: *m/z* calculated 472.09, found $[M + H]^+$ 473.01.

4-(2-(4-chlorophenyl)-4-oxothiazolidin-3-yl)-N-(2,6-dimethoxypyrimidin-4-yl)benzene sulfonamide (7b) Yellow solid, Anal. Calcd for $C_{21}H_{19}ClN_4O_5S_2$: C, 49.75; H, 3.78; Cl, 6.99; N, 11.05; O, 15.78; S, 12.65%; found C, 49.80; H, 3.77; Cl 7.01, N, 11.12; O, 16.02, S, 12.57%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3350 (NH), 3058 (C-H_{str} saturated hydrocarbon) 1752 (CO,Cyclic), 1625 (C=N_{str}) 1378 Asy., 1121 Syn., (O=S=O), 670 (C-S-C); ^{1}H NMR (400 MHz, DMSO) δ 3.65 (d, CH2-thiozole), 7.20-8.79 (m, aromatic Protons), 6.54 (s, 1Hpyrimidine), 11.78 (s, 1H -NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.01, 164.00, 160.50, 147.35, 140.11, 136.02, 131.17, 125.25, 128.94, 121.98, 121.06, 83.01, 75.15, 55.10, 54.09, 33.44. ESI-MS: *m/z* calculated 506.05, found $[M + H]^+$ 507.01.

4-(2-(2,4-dichlorophenyl)-4-oxothiazolidin-3-yl)-N-(2,6-dimethoxypyrimidin-4-yl)benzene sulfonamide (7c) Light yellow solid, Anal. Calcd for $C_{21}H_{19}Cl_2N_4O_5S_2$: C, 46.59; H, 3.35; Cl, 13.10; N, 10.35; O, 14.78; S, 11.84%; found C, 46.80; H, 3.58; Cl 13.20, N, 10.22; O, 15.02, S, 11.87%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3355 (NH), 3054 (C-H_{str} saturated hydrocarbon) 1742 (CO,Cyclic), 1627 (C=N_{str}) 1368 Asy., 1122 Syn., (O=S=O), 665 (C-S-C); ^{1}H NMR (400 MHz, DMSO) δ 3.70 (d, CH2-thiozole), 7.30-8.77 (m, aromatic Protons), 6.50 (s, 1Hpyrimidine), 11.80 (s, 1H -

NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.01, 164.12, 161.53, 148.30, 140.19, 136.17, 133.00, 127.23, 124.90, 121.98, 120.86, 85.01, 77.22, 55.13, 54.15, 33.70. ESI-MS: *m/z* calculated 540.01, found $[M + H]^+$ 541.04.

N-(2,6-dimethoxypyrimidin-4-yl)-4-(2-(2-hydroxyphenyl)-4-oxothiazolidin-3-yl)benzene sulfonamide (7d)

Light yellow solid, Anal. Calcd for $C_{21}H_{20}N_4O_6S_2$: C, 51.63; H, 4.13; N, 11.47; O, 19.65; S, 13.13%; found C, 51.70; H, 4.18; N, 11.40; O, 19.62, S, 13.17%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3585 (Ar-OH), 3357 (NH), 3060 (C-H$_{str}$ saturated hydrocarbon) 1744 (CO,Cyclic), 1630 (C=N$_{str}$) 1358 Asy., 1144 Syn., (O=S=O), 662 (C-S-C); ^{1}H NMR (400 MHz, DMSO) δ 3.74 (d, CH2-thiozole), 7.40-8.98 (m, aromatic Protons), 6.67 (s, 1Hpyrimidine), 11.50 (s, 1H -NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.11, 167.23, 163.50, 149.32, 142.15, 137.10, 134.10, 128.13, 125.00, 122.52, 120.96, 87.21, 78.22, 56.03, 54.85, 33.99. ESI-MS: *m/z* calculated 488.08, found $[M + H]^+$ 489.04.

N-(2,6-dimethoxypyrimidin-4-yl)-4-(2-(4-hydroxyphenyl)-4-oxothiazolidin-3-yl)benzene sulfonamide (7e) Light yellow solid, Anal. Calcd for $C_{21}H_{20}N_4O_6S_2$: C, 51.63; H, 4.13; N, 11.47; O, 19.65; S, 13.13%; found C, 51.72; H, 4.20; N, 11.41; O, 19.63, S, 13.18%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3580 (Ar-OH), 3358 (NH), 3064 (C-H$_{str}$ saturated hydrocarbon) 1747 (CO,Cyclic), 1629 (C=N$_{str}$) 1357 Asy., 1140 Syn., (O=S=O), 667 (C-S-C); ^{1}H NMR (400 MHz, DMSO) δ 3.72 (d, CH2-thiozole), 7.42-8.90 (m, aromatic Protons), 6.65 (s, 1Hpyrimidine), 11.52 (s, 1H -NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.17, 167.20, 163.30, 149.34, 142.15, 137.10, 134.10, 128.13, 125.00, 122.50, 120.90, 87.24, 78.28, 56.12, 54.80, 33.80. ESI-MS: *m/z* calculated 488.08, found $[M + H]^+$ 489.02.

N-(2,6-dimethoxypyrimidin-4-yl)-4-(4-oxo-2-(p-tolyl)thiazolidin-3-yl)benzenesulfonamide (7f) White solid, Anal. Calcd for $C_{22}H_{22}N_4O_5S_2$: C, 54.31; H, 4.56; N, 11.51; O, 16.44; S, 13.18%; found C, 54.40; H, 4.58; N, 11.60; O, 16.62, S, 13.17%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3345 (NH), 3050 (C-H$_{str}$ saturated hydrocarbon) 1752 (CO,Cyclic), 1622 (C=N$_{str}$) 1377 Asy., 1128 Syn., (O=S=O), 672 (C-S-C); ^{1}H NMR (400 MHz, DMSO) δ 2.22 (s, 3H, CH$_3$), 3.60 (d, CH$_2$-thiozole), 7.33-8.97 (m, aromatic Protons), 6.58 (s, 1Hpyrimidine), 11.79 (s, 1H -NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.15, 162.94, 161.40, 145.45, 139.28, 135.23, 132.25, 129.98, 129.56, 123.24, 121.24, 82.11, 74.24, 54.12, 54.09, 33.36. ESI-MS: *m/z* calculated 486.10, found $[M + H]^+$ 487.02

N-(2,6-dimethoxypyrimidin-4-yl)-4-(2-(3-nitrophenyl)-4-oxothiazolidin-3-yl)benzene sulfonamide (7g) Yellow solid, Anal. Calcd for $C_{21}H_{19}N_5O_7S_2$ C, 48.74; H, 3.70; N, 13.53; O, 21.64; S, 12.39%; found C, 49.05; H, 3.77; N,

13.52; O, 21.72, S, 12.50%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3355 (NH), 3063 (C-H_{str} saturated hydrocarbon) 1747 (CO,Cyclic), 1635 (C=N_{str}) 1382 Asy., 1124 Syn., (O=S=O), 663 (C-S-C); ^{1}H NMR (400 MHz, DMSO) δ 3.64 (d, CH2-thiozole), 7.22-8.76 (m, aromatic Protons), 6.61 (s, 1Hpyrimidine), 11.05 (s, 1H -NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 171.01, 163.10, 161.11, 146.30, 141.15, 136.62, 131.44, 125.22, 128.74, 121.12, 121.06, 83.1, 75.12, 54.11, 54.01, 33.43. ESI-MS: *m/z* calculated 517.07, found $[M+H]^+$ 507.98.

N-(2,6-dimethoxypyrimidin-4-yl)-4-(2-(2-methoxyphenyl)-4-oxothiazolidin-3-yl)benzene sulfonamide (7h)

White solid, Anal. Calcd for $C_{22}H_{22}N_4O_6S_2$: C, 52.58; H, 4.41; N, 11.15; O, 19.10; S, 12.76%; found C, 52.60; H, 4.58; N, 11.20; O, 19.12, S, 12.80%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3356 (NH), 3054 (C-H_{str} saturated hydrocarbon) 1756 (CO,Cyclic), 1632 (C=N_{str}) 1367 Asy., 1132 Syn., (O=S=O), 662 (C-S-C); ^{1}H NMR (400 MHz, DMSO) δ 3.22 (s, 3H,O- CH_3), 3.61 (d, CH_2-thiozole), 7.30-8.92 (m, aromatic Protons), 6.61 (s, 1Hpyrimidine), 11.09 (s, 1H -NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.17, 161.98, 161.30, 144.42, 140.02, 136.20, 133.12, 129.90, 129.16, 123.44, 121.24, 82.11, 74.24, 54.12, 54.09, 33.36. ESI-MS: *m/z* calculated 502.10, found $[M + H]^+$ 503.03.

Result and discussion of biological activity

Antibacterial activity

Antibacterial activity completed by in vitro agar well diffusion method. The percentage of zone inhibition was calculated in term of active zone index in which the streptomycin was used as standard drug.

Determination of activity index

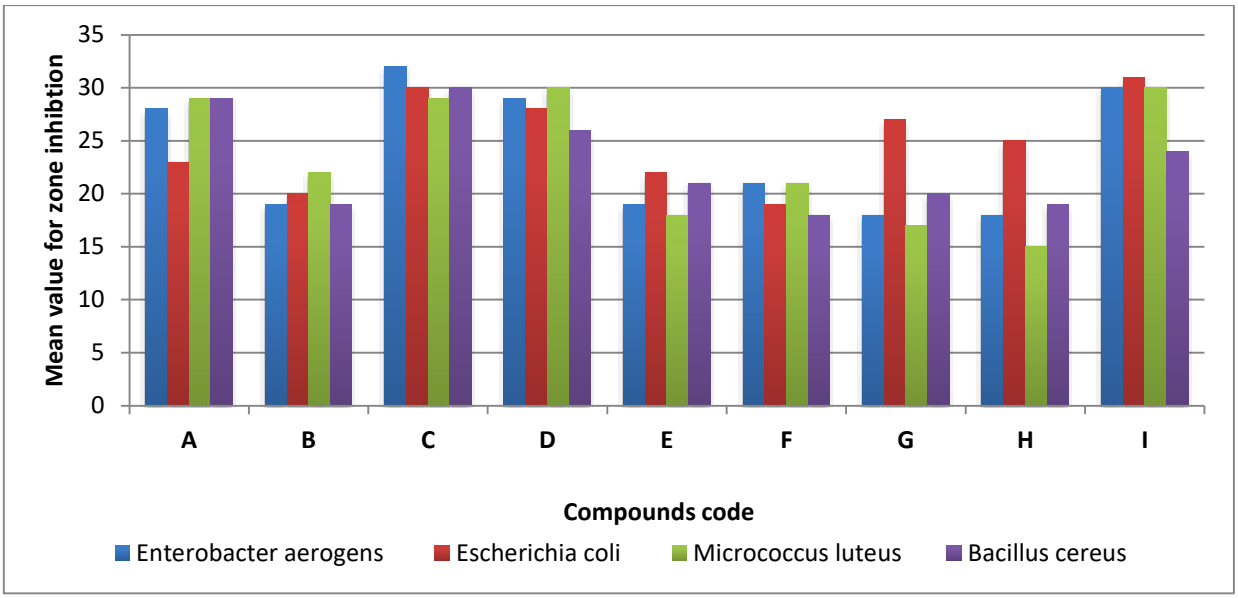
$$\boldsymbol{Activity\ index(A.I) = \frac{mean\ of\ the\ zone\ of\ inhibition\ of\ derivatives}{one\ of\ inhibition\ obtained\ for\ standard\ antibiotic\ drug}}$$

The synthesized this new series of N-(2,6-dimethoxypyrimidin-4-yl)-4-(4-oxo-2-(substituted) phenylthiazolidin-3yl)benzenesulfonamide **7a-7h** were examined for their antibacterial activity with streptomycin as standard drugs, the concentration was 1000 µg/ml. The significant results evaluated for all new ultimate synthesized compounds of **7a-7h** were found to be they're good, moderately active and lowest active against the tested microorganism gram-negative and Gram-positive bacteria. On the bases of this results, we terminate that zone inhibition of the antibacterial activity

of **7b**, **7c**, and **7g**, were showed better active to standard while another compounds inhibition zones were compared to standard moderate to low inhibition, shown in table-**2**

Table-2 Antibacterial activity of compounds 7a-7h

Derivatives	***Enterobacter aerogens* MTCC No. 8558**		***Escherichia coli* MTCC No. 1610**		***Micrococcus luteus* MTCC No. 11948**		***Bacillus cereus* MTCC No. 8558**	
	Mean value for Zone of Inhibition (mm)	Activity Index (A.I.)	Mean value for Zone of Inhibition (mm)	Activity Index (A.I.)	Mean value for Zone of Inhibition (mm)	Activity Index (A.I.)	Mean value for Zone of Inhibition (mm)	Activity Index (A.I.)
7a	18	0.750	19	0.791	15	0.625	19	0.791
7b	21	0.875	22	0.917	26	1.083	22	0.917
7c	28	1.166	23	0.958	29	1.208	29	1.208
7d	25	1.041	23	0.958	21	0.875	22	0.917
7e	21	0.875	22	0.917	25	1.041	23	0.958
7f	15	0.625	19	0.791	15	0.625	18	0.750
7g	32	1.333	30	1.250	29	1.208	30	1.250
7h	18	0.750	15	0.625	15	0.625	19	0.791
Std	24	-	24	-	24	-	24	-



The MIC values of these **7a-7h** series showed considerable results For all derivatives such as **7b, 7c,** and **7g** derivatives showed very good MIC values compare to other compounds shown moderate to average MIC values. Although, Compound **7g** showed tremendous zone inhibition activity as well as in MIC for all bacterial strains. shown in table-**3**

Table-3 *MIC* results of Compounds 7a-7h

Derivatives	***Enterobacter aerogens*** **MTCC No. 8558** **MIC(µg/ml)**	***Escherichia coli*** **MTCC No. 1610** **MIC(µg/ml)**	***Micrococcus luteus*** **MTCC No. 11948** **MIC(µg/ml)**	***Bacillus cereus*** **MTCC No. 8558** **MIC(µg/ml)**
7a	200	200	100	200
7b	50	25	25	12.5
7c	25	12.5	50	12.5
7d	50	100	50	100
7e	100	50	50	100
7f	200	200	100	200
7g	25	12.5	25	12.5
7h	200	200	400	200
Std	6.25	6.25	3.125	6.25

In vitro anti-mycobacterial activity

In vitro anti-mycobacterial activity examined for all synthesized compounds showed excellent to average % inhibition against Myco. Tuberculosis $H_{37}Rv$. The evaluated results in (%) inhibition, values showed for **7b** (80.99%), **7d** (78.51%), **7e** (79.33) and **7g** (82.64%) had shown excellent inhibition, while others had good to average % inhibition.

From the experimental data **7b, 7d**, **7e** and **7g** have shown clearly excellent MIC values of the in vitro anti-mycobacterial activity in sequences (25, 50, 25, 6.25 µg/ml), while other derivatives showed 25 to 400 µg/ml against Myco. Tuberculosis $H_{37}Rv$. (table-**4**)

Table-4 *In vitro* Antimycobacterial activities of 7a-7h derivatives

	Lowenstein–Jensen (LJ) method (Culture: $H_{37}RV$)			
	Mean Colony forming unit (c.f.u.) on media			
Compounds	**Control**	**Treatment concentration (100µg/ml)**	**Percentage inhibition (%)**	**MIC value (µg/ml)**
7a	121	40	66.94	400
7b	121	23	80.99	25
7c	121	30	75.20	200
7d	121	26	78.51	50
7e	121	25	79.33	25
7f	121	39	67.76	400
7g	121	21	82.64	6.25
7h	121	42	65.28	400
Isoniazid	121	1	99.17	0.20

Conclusion

In abbreviation, for this present work all synthesized compounds **7a-7h** were characterized and evaluated for all targeted compounds were screened for their antibacterial activity against Gram-positive and Gram-negative bacteria, compounds as **7b, 7c,** and **7g** shown good effective inhibitions. Moreover, compounds **7b** (80.99%), **7d** (78.51%), **7e** (79.33) and **7g** (82.64%) had shown excellent inhibition for *in vitro* antitubercular activity against Mycobacterium tuberculosis H_{37}RV and all compounds confirmed by various spectral data.

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