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Synthesis, Characterization and Biological studies of Thiazolidinone analogues

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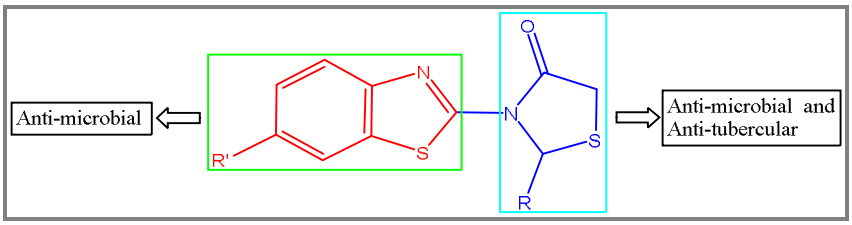
ABSTRACT

A new series of 2-(4-substituted phenyl)-3-(6-substituted benzo [d]thiazol-2-yl)thiazolidin-4-one derivatives have been prepared by hybridization of two different biologically active moieties benzothiazole and thiazolidinone. The structures of the newly synthesized compounds were established on the basis of spectral data (IR, ^{1}H and ^{13}C NMR) and elemental analysis. All the synthesized compounds were tested for antibacterial activity against Gram-positive bacteria (S. aureus, S. pyogenes) and Gram-negative bacteria (C. albicans, A. niger, A. clavatus), antifungal activity against three fungi (C. albicans, A. niger, A. clavatus) using the MIC (Minimal Inhibitory Concentration) method, anti-tubercular activity H37Rv using L. J. Slope Method. Results of biological screening reveals that compounds ***D*****$_1$**, ***D*****$_3$**, ***D*****$_6$**, ***D*****$_7$**, ***D*****$_8$** *and* ***D*****$_{10}$** *showed good antibacterial activity where as* ***D*****$_1$**, ***D*****$_5$** *and showed good antifungal activity and compound* ***D*****$_2$** *showed good antitubercular activity.*

Graphical Abstract



General structure of 2-(4-substituted phenyl)-3-(6-substituted benzo [d]thiazol-2-yl)thiazolidin-4-one(D_{1-10}):

Keywords: Benzothiazole, Thiazolidinone, Anti-microbial, Anti-tubercular, *M. tuberculosis H37Rv*.

INTRODUCTION

Benzothiazole is the combination of two rings, which contain the heterocycles thiazole and benzene. The core structure of thiazole and its pharmacologically and biologically active compounds are due to the presence of sulfur and nitrogen atoms present in the ring [**1**]. Benzothiazole is a privileged bicyclic ring system. Due to its potent and significant biological activities, it has great pharmaceutical

importance; hence, synthesis of this compound is of considerable interest. Benzothiazole moieties are part of compounds showing numerous biological activities such as antimicrobial [2-6] anticancer [7-11] anthelmintic [12], and anti-diabetic [13] activities. They have also found application in industry as antioxidants, vulcanization accelerators. Various benzothiazoles such as 2-aryl benzothiazole received much attention due to the unique structure and its uses as radioactive amyloid imagining agents [14] and anticancer agents [15].

Thiazolidinones are one of the most biologically active compounds possessing antimicrobial, anti-tubercular, anti-inflammatory and as antiviral agents, especially as anti-HIV activities [16-20]. 4-Thiazolidinones derivatives which have sulfur at first position, nitrogen at third position and a carbonyl group at fourth position. It's occurrence in nature had been recognized by penicillin, troglitazone **[**21]. Further, the thiazole nucleus also appears in the thiamine (vitamin-B), metabolic products of fungi and primitive marine animals. Thiazolidin-4-one ring system is pharmaceutically active moiety with broad spectrum of biological activities. In continuation of our interest in investing the pharmacological behaviour of thiazolidinone moieties, herein we describe a complementary approach toward the synthesis of new 2-(4-substitutedphenyl)-3-(6-substitutedbenzo[*d*]thiazol-2-yl)thiazolidin-4-one derivatives, their evaluation as inhibitors of *M. tuberculosis* strain *H37Rv* and antimicrobial activity.

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MATERIALS AND METHODS

All the chemicals were of analytical grade and directly used without further purification. Melting points of the synthesized compounds were determined by an open capillary method and were uncorrected. The completion of the reaction was checked by TLC (Thin layer Chromatography) using Merck silica gel 60 F254 and visualized with UV irradiation (254 nm) or iodine. IR spectra were recorded on a Perkin Elmer spectrophotometer (KBr pellets) instrument (γ_{max} in cm^{-1}). ^{1}H and ^{13}C NMR spectra were recorded on Bruker Avance II 500MHz NMR Spectrometer using TMS as an internal reference and DMSO- d_6 as solvent (δ in ppm). Mass spectra of selected samples were recorded using Waters Q-T of micromass using ESI as ion source (TOF MS ES+) and LCMS 2010 shmiadzu ESI probe quadrapole detector.Compounds were routinely purified by crystallization from ethanol and checked by TLC using ethyl acetate: hexane (2:3) as a mobile phase.

General method for the synthesis of 2-(4-substituted phenyl)-3-(6-substituted benzo [d]thiazol-2-yl) thiazolidin-4-one derivatives(D_{1-10}): Substituted benzothiazole**(A)** (5 mmol) and substituted aldehyde (**B)** (5 mmol) was heated in dry dioxane (15mL) under reflux for 10 min, followed by addition of a solution of thioglycolic acid **(C)** (3 mmol) in dry dioxane (10 mL) and 1.5 g freshly fused zinc chloride. The reaction mixture was heated under reflux for an additional 8-10 h. The progress of the reaction was monitored by TLC (using Hexane: Ethyl acetate 3:2).The mixture was cooled, neutralized with aqueous $NaHCO_3$ (10 %, 30 mL). The formed solid was filtered off, washed with water three times and crystallized from ethanol to give the crystals of **D_{1-10}**.

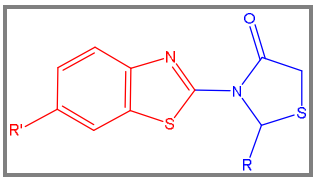
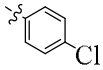
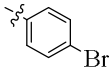
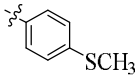
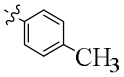
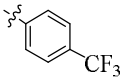
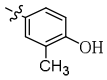


Figure 1. General structure of 2-(4-substituted phenyl)-3-(6-substituted benzo [d]thiazol-2-yl)thiazolidin-4-one(D_{1-10}):

2-(4-Chlorophenyl)-3-(6-nitrobenzo [d]thiazol-2-yl)thiazolidin-4-one(D_1): IR (KBr) ν cm^{-1}: 3054 (aromatic C-H), 1676 (C=O), 1588-1436 (C-H bend, C=C), 1366 (C-N), 860(C-Cl), 763(C-S);^{1}H NMR (DMSO-d_6) δ (ppm):7.22-8.65 (m, 7H, aromatic), 6.45(s, 1H, -CH), 3.84 (s, 2H, $-CH_2$); ^{13}C

NMR(500MHz, DMSO-d_6) δ (ppm):170.50(C=O),163.26 (N-C-N), 160.46, 144.11,132.41, 131.30, 130.86, 128.67, 128.54, 128.15, 128.00, 126.69,115.64, 113.34, 101.90 (aromatic ring), 72.35 (C-S), 33.21 (CH_2); ESI-MS: m/z: calculated 391.84(M^+), found 391.20 [M+H].

Table 1. Characterization data of compounds

Comp. No.	R'	R	Molecular Formula	M.P. ^0C	Yield %
D_1	$-NO_2$		$C_{16}H_{10}ClN_3O_2S_2$	85-87	77
D_2	$-NO_2$		$C_{16}H_{10}BrN_3O_2S_2$	92-95	76
D_3	$-OCH_3$		$C_{17}H_{13}FN_2O_2S_2$	76-79	80
D_4	$-OCH_3$		$C_{15}H_{12}N_2O_2S_3$	120-123	61
D_5	$-OCH_3$		$C_{15}H_{12}N_2O_3S_2$	105-108	59
D_6	$-NO_2$		$C_{17}H_{13}N_3O_3S_3$	145-148	84
D_7	$-NO_2$		$C_{17}H_{13}N_3O_3S_2$	140-143	82
D_8	$-OCH_3$		$C_{18}H_{13}F_3N_2O_2S_2$	149-152	70
D_9	$-OCH_3$		$C_{16}H_{13}N_3O_2S_2$	171-174	68
D_{10}	$-NO_2$		$C_{17}H_{13}N_3O_5S_2$	163-168	59

2-(4-Bromophenyl)-3-(6-nitrobenzo [d]thiazol-2-yl)thiazolidin-4-one (D_2): IR (KBr) ν cm^{-1}: 3062 (aromatic C-H), 1677 (C=O), 1588-1436 (C-H bend, C=C), 1366 (C-N), 760(C-S), 567 (C-Br);^{1}H NMR (DMSO-d_6) δ (ppm):7.14-8.70 (m, 7H, aromatic), 6.49(s, 1H, -CH), 3.85 (s, 2H, $-CH_2$);^{13}C NMR(500MHz, DMSO-d_6) δ (ppm):166.09(C=O), 163.69(N-C-N), 162.46, 140.11, 139.41, 134.30, 133.86, 131.67, 129.74, 129.65, 128.90, 126.69, 126.63, 124.98 (aromatic ring), 73.55 (C-S), 38.98 (CH_2);ESI-MS: m/z: calculated 436.30 (M^+), found 432.95[M+H].

2-(4-Fluorophenyl)-3-(6-methoxybenzo [d]thiazol-2-yl)thiazolidin-4-one(D_3): IR (KBr) ν cm^{-1}: 3056 (aromatic C-H), 1675 (C=O), 1555-1420(C-H bend, C=C), 1366 (C-N), 1222(C-F),758(C-S);^{1}H NMR (DMSO-d_6) δ (ppm):7.00-7.60 (m, 7H, aromatic), 6.40 (s, 1H, -CH), 3.82 (s, 2H, $-CH_2$), 3.75 (s, 3H, OCH_3); ^{13}C NMR(500MHz, DMSO-d_6) δ (ppm):170.12(C=O), 163.64(N-C-N),162.41, 156.18, 145.42, 134.39, 130.87, 130.47, 129.34, 118.90, 115.65, 114.69, 114.13,104.93 (aromatic ring), 72.57 (C-S), 55.80(CH_3), 33.94 (CH_2);ESI-MS: m/z: calculated 360.42 (M^+), found 360.20 [M+H].

3-(6-methoxybenzo [d]thiazol-2-yl)-2-(thiophene-2-yl)thiazolidin-4-one(D_4): IR (KBr) ν cm^{-1}: 3030 (aromatic C-H), 1676 (C=O), 1577-1406 (C-H bend, C=C), 1359 (C-N),779(C-S);^{1}H NMR (DMSO-d_6) δ (ppm):6.80-7.60 (m, 6H, aromatic), 6.00(s, 1H, -CH), 3.87 (s, 2H, $-CH_2$), 3.75 (s, 3H, $-OCH_3$); ^{13}C NMR(500MHz, DMSO-d_6) δ (ppm):171.9 (C=O), 164.20(N-C-N), 154.85, 146.20,

140.50, 131.30, 128.90, 127.90, 126.40, 119.00,116.80, 106.00(aromatic ring), 65.00 (C-S), 56.11(-OCH_3), 34.50 (CH_2); ESI-MS: m/z: calculated 348.45 (M^+), found 342.80 [M+H].

2-(furan-2-yl)- 3-(6-methoxybenzo [d]thiazol-2-yl)-thiazolidin-4-one(D_5): IR (KBr) ν cm^{-1}: 3032 (aromatic C-H), 1675 (C=O), 1579-1409 (C-H bend, C=C), 1366 (C-N),756(C-S);^{1}H NMR (DMSO-d_6) δ (ppm):6.20-7.60 (m, 6H, aromatic),6.05 (s, 1H, -CH), 4.02 (s, 2H, -CH_2), 3.82 (s, 3H, CH_3); ^{13}C NMR(500MHz, DMSO-d_6) δ (ppm):172.23 (C=O), 163.51(N-C-N), 156.67, 151.50, 145.33, 142.01,130.23,114.31, 113.34, 112.90, 112.31, 103.45 (aromatic ring), 77.34 (C-S), 34.82(CH_2); ESI-MS: m/z: calculated 332.39 (M^+), found 332.30 [M+H].

2-(4-(Methylthio)-phenyl)- 3-(6-methoxybenzo [d]thiazol-2-yl)-thiazolidin-4-one(D_6): IR (KBr) ν cm^{-1}: 3033 (aromatic C-H), 1678 (C=O), 1591-1434 (C-H bend, C=C), 1362 (C-N), 709(C-S);^{1}H NMR (DMSO-d_6) δ (ppm):7.15-8.71 (m, 7H, aromatic),6.33 (s, 1H, -CH), 3.92 (s, 1H, -CH_2), 2.32 (s, 3H, CH_3); ^{13}C NMR(500MHz, DMSO-d_6) δ (ppm):171.56(C=O), 163.89(N-C-N), 159.43, 144.08,129.56, 128.92, 128.61, 128.14, 126.21, 121.32, 114.36, 113.23, 113.07 (aromatic ring), 77.33 (C-S),35.63 (CH_2); ESI-MS: m/z: calculated 403.49 (M^+), found 403.20 [M+H].

3-(6-nitrobenzo [d]thiazol-2-yl)-2-(p-tolyl)-thiazolidin-4-one(D_7): IR (KBr) ν cm^{-1}: 3030 (aromatic C-H), 1677 (C=O), 1554-1422 (C-H bend, C=C), 1362 (C-N), 735(C-S); ^{1}H NMR (DMSO-d_6) δ (ppm):7.00-8.70 (m, 7H, aromatic),6.37 (s, 1H, -CH), 3.80 (s, 1H, -CH_2), 2.22 (s, 3H, CH_3); ^{13}C NMR(500MHz, DMSO-d_6) δ (ppm):173.19(C=O), 163.54 (N-C-N), 159.23, 144.01, 136.92, 130.92, 130.31, 130.11, 128.53, 128.36, 124.23, 121.15, 119.30, 113.32, 112.78, (aromatic ring), 77.30 (C-S), 38.82 (CH_2); ESI-MS: m/z: calculated 371.43 (M^+), found 370.60 [M+H].

3-(6-methoxybenzo [d]thiazol-2-yl)-2-(4-trifluoromethyl) phenyl)thiazolidin-4-one (D_8): IR (KBr) ν cm^{-1}: 3062 (aromatic C-H), 1676 (C=O), 1578-1409 (C-H bend, C=C), 1363 (C-N), 1228 (C-F), 749(C-S); ^{1}H NMR (DMSO-d_6) δ (ppm):6.96-7.58 (m, 7H, aromatic),6.00 (s, 1H, -CH), 3.88 (s, 2H, -CH_2), 3.79(s, 3H, CH_3);^{13}C NMR(500MHz, DMSO-d_6) δ (ppm):172.89 (C=O), 163.45 (N-C-N), 149.38, 149.02, 136.92, 130.91, 130.61, 130.40, 128.81, 124.93, 121.61, 114.34, 113.23,112.52, 103.72 (aromatic ring), 72.32 (C-S),35.80 (CH_2);ESI-MS: m/z: calculated 410.43 (M^+), found 409.74 [M+H].

3-(6-methoxybenzo [d]thiazol-2-yl)-2-(pyridin-4-yl)thiazolidin-4-one (D_9): IR (KBr) ν cm^{-1}: 3062 (aromatic C-H), 1675 (C=O), 1573-1412 (C-H bend, C=C), 1374 (C-N), 738(C-S);^{1}H NMR (DMSO-d_6) δ (ppm):6.93-8.56 (m, 7H, aromatic), 6.47(s, 1H, -CH), 3.86(s, 3H, -OCH_3),3.80 (s, 2H, CH_2);^{13}C NMR(500MHz, DMSO-d_6) δ (ppm):165.89(C=O),163.43 (N-C-N),149.35, 136.99, 130.98, 130.69, 130.41, 130.25, 128.83, 124.94, 121.62, 114.04, 112.89, 112.61, 103.79 (aromatic ring), 77.36 (C-S), 38.84 (CH_2);ESI-MS: m/z: calculated 343.42 (M^+), found 343.10 [M+H].

2-(4-hydroxy-3-methoxyphenyl)-3-(6-nitrobenzo [d]thiazol-2-thiazolidin-4-one (D_{10}): IR (KBr) ν cm^{-1}: 3360 (O-H), 3054 (aromatic C-H), 1675 (C=O), 1571-1432 (C-H bend, C=C), 1371 (C-N), 756(C-S);^{1}H NMR (DMSO-d_6) δ (ppm):9.95(s, 1H,-OH), 6.95-8.70 (m, 6H, aromatic), 6.45 (s, 1H, -CH), 3.87 (s, 2H, -CH_2), 3.85 (s, 3H, CH_3);^{13}C NMR(500MHz, DMSO-d_6) δ (ppm):165.99, 165.49(C=O), 163.81,163.41(N-C-N),149.31, 149.18, 136.09, 130.12, 130.61,130.12,130.25, 128.81, 124.97, 121.61, 114.01, 113.87, 112.89 (aromatic ring), 77.46 (C-S), 40.12-38.83 (CH_2);ESI-MS: m/z: calculated 403.43 (M^+), found 402.89[M+H].

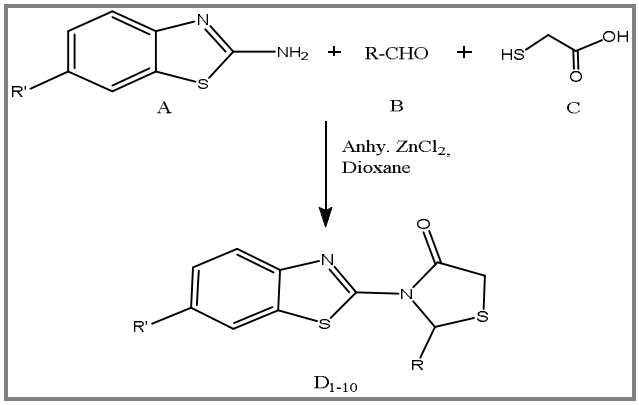
In vitro antimicrobial assay: The Minimum inhibitory concentrations (MICs) of synthesized compounds were carried out by broth micro dilution method as described by Rattan [22]. Minimum inhibitory concentrations (MICs) of the tested compounds are shown in table 2. The different compounds **D_{1-10}** were tested for *in vitro* against two Gram positive (*S. aureus* MTCC 96, *S.pyogenes* MTCC 442) and two Gram negative (*E. coli* MTCC 443, *Pseudomonas aeruginosa* MTCC 1688) bacteria for antibacterial and three fungal species (*C. albicans* MTCC 227, *A. niger* MTCC 228 and *A.*

clavatus MTCC 1323) for antifungal activity. Gentamycin, ampicillin, chloramphenicol, ciprofloxacin and norfloxacin were used as a standard antibacterial agent whereas Griseofulvin and nystatin were used as a standard antifungal agent.

In vitro antitubercular assay: Tubercle bacilli are aerobes which grow in specially enriched media containing egg, asparagines, potatoes, serum and meat extracts. Their colonies appear in 2-6 weeks. The drug susceptibility test to determine MIC by L. J. Slope method has been employed [17]. *M. tuberculosis H$_{37}$Rv* [Acid Fast Bacilli] (MTCC-200) was used for screening of anti-tubercular activity. DMSO was used as diluents/ vehicle to get desired concentration of drugs to test upon standard bacterial strains. Each synthesized compound was diluted obtaining 2000 µg mL^{-1} concentration, as a stock solution and then many dilutions were made as shown in antimicrobial activities.

RESULTS AND DISCUSSION

Chemistry: The general procedure for the synthesis of final compounds (**D$_{1-10}$**) is depicted in the scheme. According to the scheme, 2-(4-substitutedphenyl)-3-(6-substitutedbenzo[d]thiazol-2-yl)thiazolidin-4-one derivatives (**D$_{1-10}$**) has been synthesized by condensation reaction between substituted benzothiazole, substituted aldehydes and thioglycolic acid in dioxane in the presence of catalytic amount of anhydrous Zinc chloride. The reaction protocol is illustrated in the following scheme.



Scheme. 2-(4-substitutedphenyl)-3-(6-substitutedbenzo[d] thiazol-2-yl)thiazolidin-4-one derivatives.

Biology

Antimicrobial activity: The minimum inhibitory concentrations (MIC) for the antimicrobial potency of **B$_{1-10}$** were screened against four different bacterial strains and three different fungal strains. The susceptibility of the organisms was determined by the broth micro-dilution method and compared with standard drugs; gentamycin, ampicillin, chloramphenicol, ciprofloxacin, norfloxacin, nystatin and griseofulvin. The results of this activity are described in table 2. Compound **D$_1$** with a–Chloro group at position 4 on benzaldehyde demonstrated remarkable activity (MIC= 100 µg/mL) against *E. coli*, comparable to ampicillin. While other compounds with -F group at 4th position showed good activity against *P. aeruginosa*. Compounds **D$_6$**, **D$_7$** and **D$_8$** derivatives were more potent than other compounds against *S. aureus* while compounds **D$_7$** and **D$_9$** exhibited significant activity against *S. pyogenes*. Compounds **D$_1$**, **D$_3$**, **D$_5$**, **D$_7$**, **D$_8$**and **D$_{10}$** showed encouraging potency against *C. albicans* compared with griseofulvin. Moreover, **D$_5$** was found to be more potent against *A. niger* and *A. clavatus*. Other compounds showed very high MIC values and seem to be poor to moderately active.

Anti-tubercular activity: All the synthesized compounds of series have been evaluated for their anti-tubercular activity. Determination of MIC of the sample compounds against *Mycobacterium tuberculosis H37Rv* were performed by the agar micro dilution method, where twofold dilutions of each test compound have added into 7H10 agars supplemented with OADC and organism. A culture

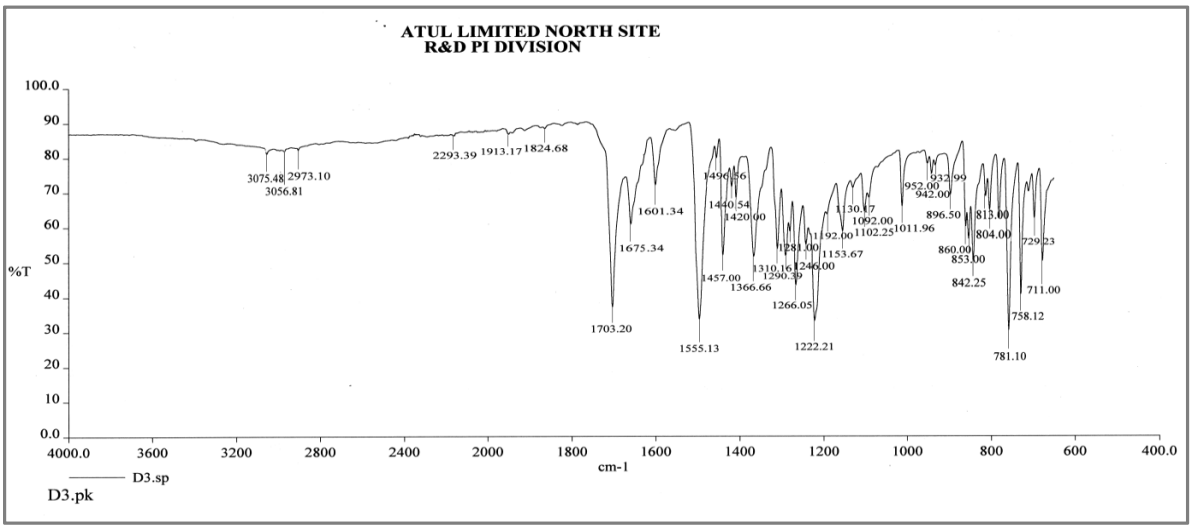


Figure 2. IR spectrum of compound D_3

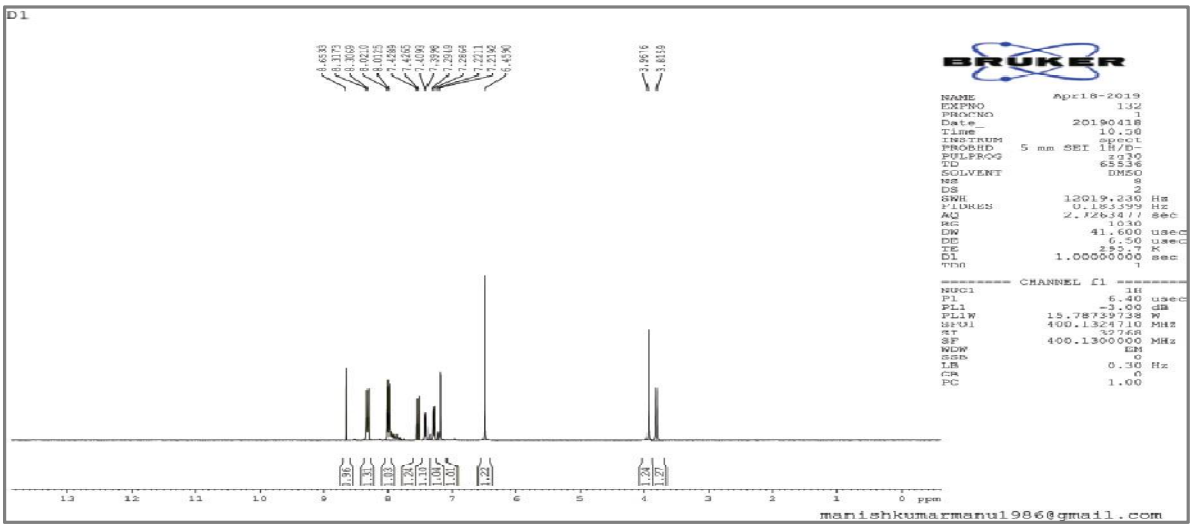


Figure 3. ^{1}H NMR spectrum of D_1

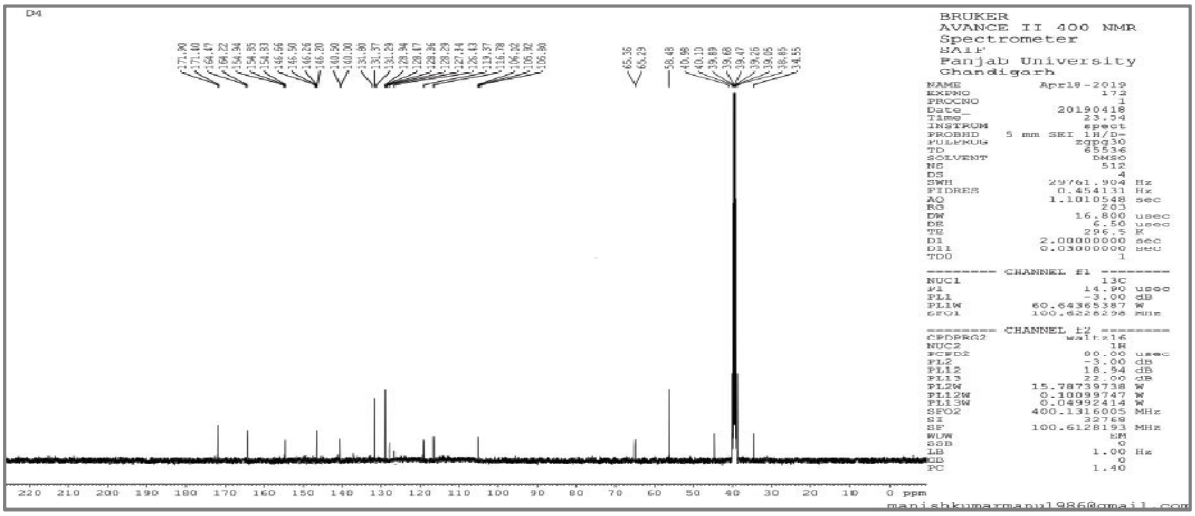


Figure 4. ^{13}C NMR spectrum of D_4

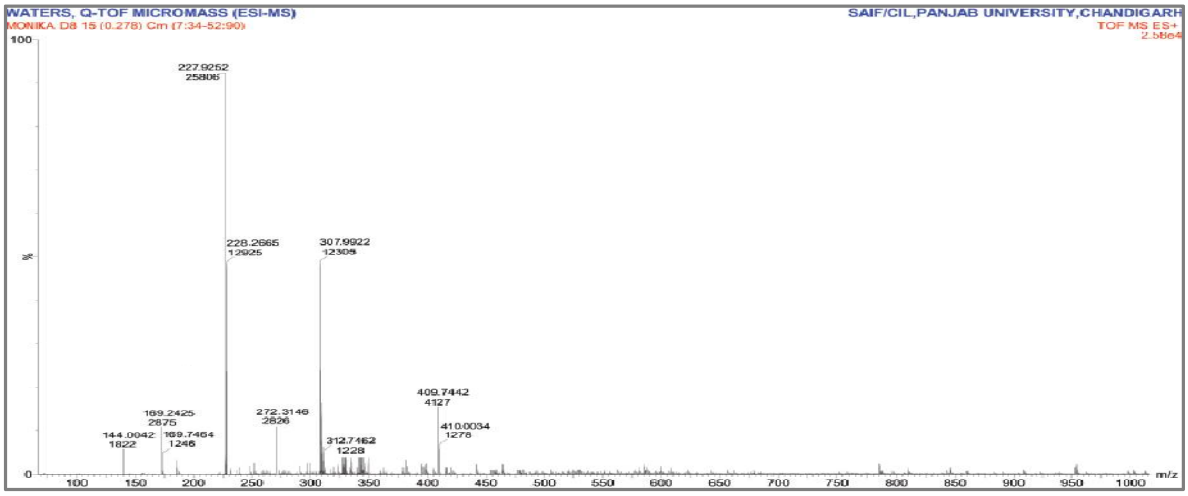


Figure 5. Mass spectrum of D_8

Table 2. Antibacterial and Antifungal data of compounds **D_{1-10}**

Compound No.	Minimal Bactericidal Concentration (µg mL^{-1})				Minimal Fungicidal Concentration (µg mL^{-1})		
	E. coli	*P. aeruginosa*	*S. aureus*	*S. Pyogenes*	*C. albicans*	*A. niger*	*A. clavatus*
	MTCC443	MTCC1688	MTCC96	MTCC442	MTCC227	MTCC28	MTCC133
D_1	**100**	250	100	250	**500**	500	500
D_2	125	250	125	62.5	250	250	500
D_3	125	**50**	250	62.5	**500**	500	1000
D_4	250	250	500	500	250	500	500
D_5	250	250	125	250	**100**	**100**	**100**
D_6	125	100	**250**	250	250	500	**100**
D_7	125	100	**50**	**100**	**500**	500	250
D_8	500	500	**250**	250	**500**	**100**	250
D_9	250	100	500	**100**	125	500	500
D_{10}	250	**50**	100	62.5	**500**	500	**100**
Drug	Micromolar (µg mL^{-1})						
Gentamycin	0.05	1	0.25	0.5	-	-	-
Ampicillin	100	-	250	100	-	-	-
Chloramphenicol	50	50	50	50			
Ciprofloxacin	25	25	50	50			
Norfloxacin	10	10	10	10	-	-	-
Griseofulvin	-	-	-	-	500	100	100
Nystatin	-	-	-	-	100	100	100

of used microorganism *M. tuberculosis H37Rv* growing on the L–J medium has been harvested in 0.85% saline with 0.05% Tween-80. A suspension of compounds was prepared in DMSO. This suspension was added to (in tubes) 7H10 middle brook's medium (containing 1.7 mL medium and 0.2 mL OADC supplement) at different concentrations of compound keeping the volume constant, that is, 0.1 mL medium was allowed to cool keeping the tubes in the slanting position. These tubes were incubated at 37°C for 24 h followed by streaking of *M. tuberculosis H37Rv*. Growth of bacilli was seen after 30 days of incubation. Compounds containing tubes were controlled with control tubes where the medium alone was incubated with *H37Rv*. The concentration at which complete inhibition of colonies occurred has taken as active concentration of the test compound. Isoniazid have used as standard drug. The MIC levels of screened compounds (**D_{1-10}**) against these organisms have given in table 3. The data predicted in table 3 revealed that the compounds, demonstrated variable inhibitory effects on the growth of the tested *M. tuberculosis H37Rv* strains. Among the screened **D_2** containing electron withdrawing group (NO_2) showed moderate activity against *M. tuberculosis H37Rv* compared to isoniazid. Other compounds did not show satisfactory results.

Table 3. Anti-tubercular data of compounds $\mathbf{D_{1\text{-}10}}$

Compound No.	MIC (µg mL^{-1})
$\mathbf{D_1}$	100
$\mathbf{D_2}$	**62.5**
$\mathbf{D_3}$	1000
$\mathbf{D_4}$	200
$\mathbf{D_5}$	500
$\mathbf{D_6}$	250
$\mathbf{D_7}$	1000
$\mathbf{D_8}$	200
$\mathbf{D_9}$	500
$\mathbf{D_{10}}$	250
Drug	Micromolar (µg mL^{-1})
Isoniazid	0.20

CONCLUSION

A new series of 2-(4-substituted phenyl)-3-(6-substituted benzo [d]thiazol-2-yl)thiazolidin-4-one derivatives ($\mathbf{D_{1\text{-}10}}$)has been efficiently formulated via condensation reaction between substituted benzothiazole, substituted aldehydes and thioglycolic acid in dioxane in the presence of catalytic amount of anhydrous Zinc chloride. Final compounds were evaluated against anti-bacterial and antifungal species. Compound $\mathbf{D_1}$ demonstrated remarkable activity (MIC= 100 µg mL^{-1}) against *E. coli*, comparable to ampicillin. Compounds $\mathbf{D_3}$and $\mathbf{D_{10}}$ showed good activity against *P. aeruginosa*. Compounds $\mathbf{D_6}$, $\mathbf{D_7}$ and $\mathbf{D_8}$ derivatives were more potent than other compounds against *S. aureus*, while compounds $\mathbf{D_7}$ and $\mathbf{D_9}$ exhibited significant activity against *S. pyogenes*. Compounds $\mathbf{D_1}$, $\mathbf{D_3}$, $\mathbf{D_5}$, $\mathbf{D_7}$, $\mathbf{D_8}$ and $\mathbf{D_{10}}$ showed encouraging potency against *C. albicans* compared with griseofulvin. Moreover, $\mathbf{D_5}$ was found to be more potent against *A. niger* and *A. clavatus*. Other compounds showed very high MIC values and seem to be poor to moderately active. Compound $\mathbf{D_2}$ exhibited good anti-tubercular activity due to the presence of electron withdrawing group (NO_2).

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