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Synthesis, anti-tuberculosis and anti-bacterial activities of sulfonamide bearing 4-((2-(5-bromo-1*H*-pyrazolo[3,4-*b*]pyridin-1-yl)-2-oxoethyl)amino)-*N*-(various substitutions)benzenesulfonamide

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In this study all the new synthesized compounds of sulfonamide bearing 4-((2-(5-bromo-1*H*-pyrazolo[3,4-*b*]pyridin-1-yl)-2-oxoethyl)amino)-*N*-(various-substitutions)benzenesul-fonamide have been synthesized by using 1-(5-bromo-1*H*-pyarazolo[3,4-*b*]pyridin-1yl)-2-chloroethanone which has been fused with various sulfa drugs in presence of potassium carbonate and DMF. All the derivatives have been recognized by physical properties like melting point and characterization by elemental analysis (CHNS) and various spectral techniques such as FT-IR, ^{1}H and ^{13}C NMR, and ESI-MS. The series of these pyrazolo[3,4-*b*]pyridin bearing sulfonamide have been synthesized and the 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* anti tubercular activity against *Mycobacterium tuberculosis* H_{37}RV. The results for the synthesized compounds have been compared against standard drugs.

Keywords: 1*H*-Pyarazolo[3,4-*b*]pyridin, sulfonamide, *in vitro* anti-tuberculosis, anti-bacterial activity, spectral studies

Sulfonamide compounds having an important class of synthetic therapeutic agents for various disease and bacteriostatic antibiotics. The key of some compounds containing sulfonamides group such as Sulfamethoxazole, Sulfapyridine, Sulfathiazole, Sulfamethazine (Figure 1) possessing interesting of bioactivity.

Sulfonamides possess different of pharmacological activity such as antibacterial[1,2] antifungal[3] antiviral HIV protease inhibitor[4] anticancer[5] carbonic anhydrase inhibitory[6,7] anti-inflammatory[8].

Other side the key intermediate of the substituted of pyarazolo scaffold such as pyrazolo[3,4-b]pyridine have been most interesting scaffold due to possessing considerable attention for medicinal discovery and wide range of significant biological therapeutic activity such as antimicrobial[9] anti malarial[10] anti-leishmanial[11] inhibitors of glycogen synthase kinase-3 (GSK-3)[12] antiviral[13] anti-HIV[14] treatment of Alzheimer's disease, infertility and anorexia nervosa[15, 16]. analgesic[17] anxiolytic[18]. hypnotic[19] corticotropic-Releasing factor (CRF) antagonist[20, 21] anti-arrhythmic[22] anti-diabetic[23] the pyrazolo[3,4-b]pyridine also inhibitors of erectile dysfunctions[24] For development and found biologically evolutions, in this ongoing work we synthesized potent and new way to fused pyrazolo[3,4-b]pyridine with various sulfonamide (sulfa drugs) and 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* anti tubercular activity against *Mycobacterium tuberculosis* H_{37}RV.

Experimental Section

Material and methods

For the synthesis of 4-((2-(5-bromo-1*H*-pyrazolo [3,4-*b*]pyridin-1-yl)-2-oxoethyl)amino)-*N*-(various-substitutions)benzenesulfonamide a novel series (Scheme I, Table I) the following chemical and reagents were used all sulfa drugs and 5-bromo-1*H*-pyrazolo[3,4-b]pyridine were acquired from commercial sources (Sigma-Aldrich). and Potassium Carbonate (K_2CO_3), dimethyl formamide, (DMF), chloro-acetyl chloride (CAC) and triethyl amine (TEA) from Merck (Germany). Pre coated aluminum 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.)

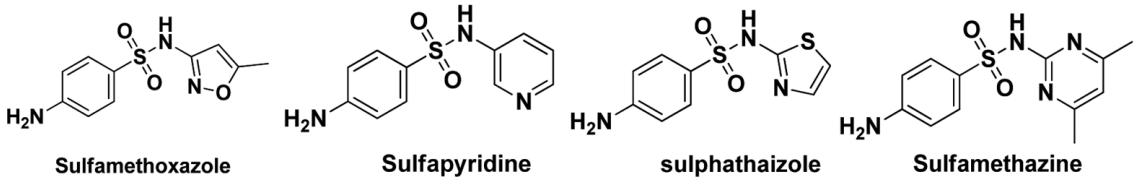
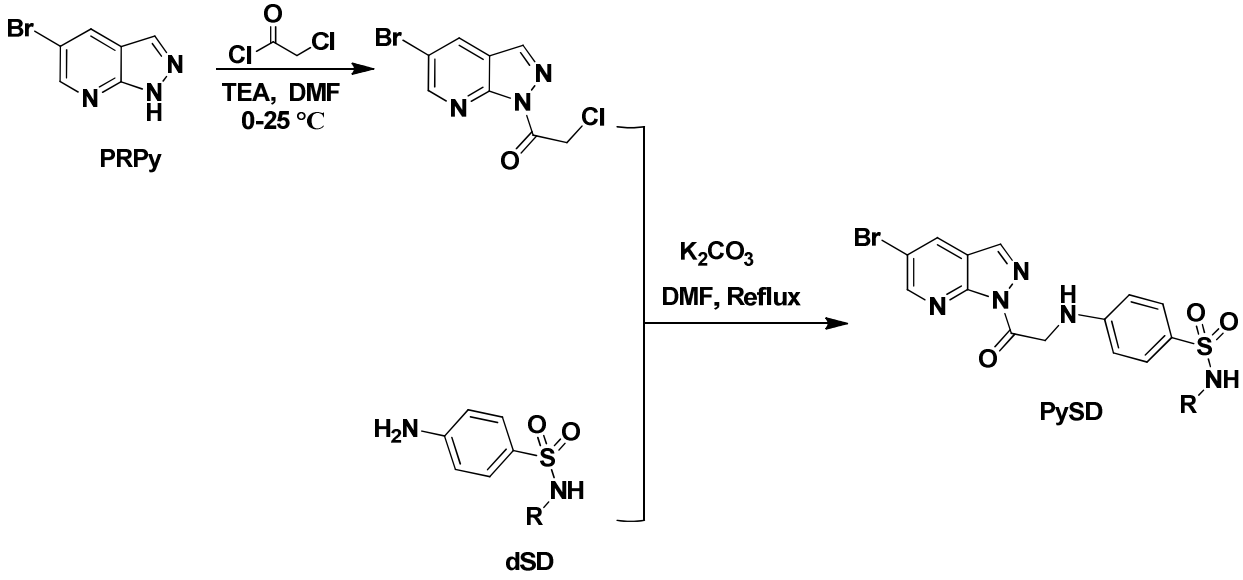


Figure 1 — Various sulfa drugs



Scheme I — Synthetic route of compounds A-J

were measured by using a Mel-temp instrument, and results are uncorrected. Infra-red spectra was recorded on Shimadzu spectrophotometer in the frequency range 4000-400 cm^{-1} using KBr pellet disc, ^{1}H 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 (δ, ppm) with TMS at the internal reference. Advion expression CMS, USA were used for recorded mass spectra. The compound were analyzed for Carbon, Hydrogen, Nitrogen oxygen and Sulphur were estimated on CHNS analyzer serial No.: 15084053

General synthesis of 1-(5-bromo-1*H*-pyrazolo[3,4-b]pyridine1-yl)-2chloroethanone

A mixture of 5-Bromo-1*H*-pyrazolo[3,4-b]pyridine (PRPy) (0.01 mol) with Chloroacetyl chloride (0.015 mol) and 4-5 drops of TEA(triethylamine) in 25 mL DMF as solvent in RBF at 0-5ºC. The reaction mixture was stirred for 12 hr at RT. The Completion of the reaction was Checked by TLC using toluene: Acetone (30%). The solution poured in to ice water. Obtained solid was filtered by vacuum pump and crystalline it in Ethanol. (83% yield).

Synthesis of 4-((2-(5-bromo-1*H*-pyrazolo[3,4-b]pyridin-1-yl)-2-oxoethyl)amino)-N-(various-substitutions)benzenesulfonamide

Above synthesized derivative of 1-(5-bromo-1*H*-pyarazolo[3,4-*b*]pyridin-1yl)-2-chloroethanone (0.01 mol) was reacted with various sulfa drugs (0.01 mol) in presence of potassium carbonate (0.02 mol) and DMF. The reaction was stirred at RT for 8 hr. The Completion of the reaction was checked by TLC using toluene: Acetone (20%). The product was poured into water and stirred for 1 hr. The obtained solid was collected and dried. Crystallize into ethanol.

Antibacterial activity

Antibacterial activities of all synthesized compounds **A-J** were evaluated by reported *in vitro* agar well diffusion method[25]. The inhibitions zone was measured were the microorganism inhibited after the incubation was done and were compare with

standard streptomycin (1000µg/mL). shown in Table II.

The minimum concentration or maximum dilution which was required for kill bacterial growth regard as minimum Inhibitory concentration (MIC). MIC values shown in Table III.

In vitro anti-mycobacterial activity

According to Lowenstein Jensen (L-J) medium the all synthesized compounds **A-J** were assayed for Anti-mycobacterial activity, following reported method[25]. The colony forming units (c.f.u) was determination by taken 10 fold dilution of standard drug 1mg/mL

Table I — Physical characterization data and substitutions of present synthetic compounds

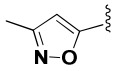
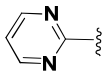
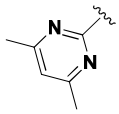
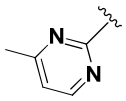
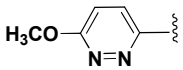
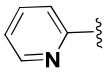
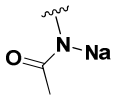
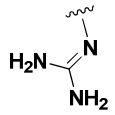
Entry	PySD Compd	m.p. (°C)	Mol. Wt.	Mol. Formula	Yield (%)
A		~255	493.36	$C_{17}H_{13}BrN_6O_3S_2$	74.1
B		~210	408.98	$C_{14}H_{12}BrN_5O_3S$	72.3
C		248-250	491.32	$C_{18}H_{15}BrN_6O_4S$	70.5
D		~238	488.32	$C_{18}H_{14}BrN_7O_3S$	70.8
E		271-273	516.37	$C_{20}H_{18}BrN_7O_3S$	69.7
F		>262	502.34	$C_{19}H_{16}BrN_7O_3S$	71.7
G		~265	518.34	$C_{19}H_{16}BrN_7O_4S$	68.1
H		231-233	487.33	$C_{19}H_{15}BrN_6O_3S$	69.4
I		~229	474.26	$C_{16}H_{13}BrN_5NaO_4S$	68.3
J		~215	452.29	$C_{15}H_{14}BrN_7O_3S$	67.2

Table II — Antibacterial activity of compounds **A-J**

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.)
A	28	1.166	23	0.958	29	1.208	29	1.208
B	19	0.791	20	0.833	22	0.917	19	0.791
C	32	1.333	30	1.250	29	1.208	30	1.250
D	29	1.208	28	1.166	30	1.250	26	1.083
E	19	0.791	22	0.917	18	0.750	21	0.875
F	21	0.875	19	0.791	21	0.875	18	0.750
G	18	0.750	27	1.125	17	0.708	20	0.833
H	18	0.750	25	1.041	15	0.625	19	0.791
I	30	1.250	31	1.291	30	1.250	24	1.000
J	20	0.833	17	0.708	26	1.083	18	0.750
Std	24	-	24	-	24	-	24	-

Table III — *MIC* results of compounds **A-J**

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)
A	12.5	25	12.5	50
B	200	200	100	200
C	25	12.5	25	12.5
D	50	100	50	100
E	100	200	200	200
F	200	100	100	50
G	200	200	200	200
H	100	50	100	50
I	100	25	50	25
J	100	200	50	100
Std	6.25	6.25	3.125	6.25

Mycobacterium tuberculosis suspension with marked on L-J medium. H_2KO_4P (potassium di hydrogen phosphate), $MgSO_4$ (magnesium sulfate anhydrous), magnesium citrate, (Loba chemie), L-asparagines, malachite green and glycerol these all reagents was 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 were allow to stay for incubated at 37ºC for 42 days with using standard bacterial suspension. standard drug rifamacine and isoniazide was used as medium for comparison of colony forming units (c.f.u) on drug free control, reading was taken weekly. percentage inhibition was calculated by below equation.

$$\% \, Inhibition = \frac{Cc - Ct}{Cc}$$

where

c = Control

t = Test

Characterization

The synthesized compounds of 4-((2-(5-bromo-1*H*-pyrazolo[3,4-*b*]pyridin-1-yl)-2-oxoethyl)amino)-*N*-(various-substitutions)benzenesulfonamide were characterized by IR, ^{1}H and ^{13}C NMR, ESI-MS and CHNS elemental analysis.

Analytical data

4-((2-(5-Bromo-1*H*-pyrazolo[3,4-b]pyridin-1-yl)-2-oxoethyl)amino)-N-(thiazol-2-yl)benzenesulfonamide, A: Yellow solid, m.p ~255ºC. Anal. Calcd for $C_{17}H_{13}BrN_6O_3S_2$: C, 41.39; H, 2.66; N, 17.03; O, 9..73; S, 13.00. Found C, 41.40; H, 2.62; N, 17.10; O, 9.77, S, 12.97%. IR (KBr): 3390 (sulfa-NH), 3220 (pyrazolo-NH) 3022 (C-H_{str} saturated hydrocarbon), 1705 (C=O) 1615 (C=N_{str}) 1345 (C-N_{str}), 1520 (aromatic ring), 1396 Asy., 1142 Syn., (O=S=O), 1520 cm^{-1} (thiazole ring); ^{1}H NMR (400 MHz, DMSO); δ 3.52, 3.77 (s 2H -CH_2), 7.19-7.46 (d, aromatic Protons), 7.54-7.57 (d, aromatic Protons), 6.62, 7.79 (d 1H and d 1$H_{thiazole}$), 7.78 (s 1H Ar-H Pyridine), 8.30 (s, 1H pyrazolo) 7.46 (s 1H Ar-H Pyridine), 11.82 (s, 1H -NH); ^{13}C NMR (100 MHz, DMSO-d_6); ESI-MS: *m/z* Calcd 491.97. Found $[M + H]^+$ 492.9.

4-((2-(5-Bromo-1*H*-pyrazolo[3,4-b]pyridin-1-yl)-2-oxoethyl)amino)-N-(thiazol-2-yl)benzenesulfonamide, B: Yellow solid, m.p ~210ºC. Anal. Calcd for $C_{14}H_{12}BrN_5O_3S$: C, 40.99; H, 2.95; N, 17.07; O, 11..70; S, 7.82. Found C, 41.01; H, 2.91; N, 17.10; O, 11.77, S, 7.77%. IR (KBr): 3470 (Asy-NH), 3422 (Sym-NH), 3220 (pyrazolo-NH) 3011 (C-H_{str} saturated hydrocarbon), 1710 (C=O) 1617 (C=N_{str}) 1352 (C-N_{str}), 1580 (aromatic ring), 1357 Asy., 1162 cm^{-1} Syn., (O=S=O); ^{1}H NMR (400 MHz, DMSO): δ 4.18, 4.39 (s 2H -CH_2), 7.18-7.20 (d, aromatic Protons), 7.84-7.86 (d, aromatic Protons), 6.82 (s, SO_2NH), 8.31 (s 1H Ar-H Pyridine), 8.52 (s, 1H pyrazolo) 8.69 (s 1H Ar-H Pyridine), 11.98 (s, 1H -NH); ^{13}C NMR (100 MHz, DMSO-d_6); ESI-MS: *m/z* Calcd 408.98. Found $[M + H]^+$ 409.9.

4-((2-(5-Bromo-1*H*-pyrazolo[3,4-b]pyridin-1-yl)-2-oxoethyl)amino)-N-(5-methylisoxazol-3-yl) benzenesulfonamide, C: Yellow light solid, m.p 248-

250ºC. Anal. Calcd for $C_{18}H_{15}BrN_6O_4S$: C, 44.00; H, 3.08; N, 17.11; O, 13..03; S, 6.53. Found C, 44.05; H, 3.02; N, 17.10; O, 13.07, S, 6.47%. IR (KBr): 3395 (sulfa-NH), 3240 (pyrazolo-NH) 3034 (C-H_{str} saturated hydrocarbon), 1718 (C=O) 1617 (C=N_{str}) 1312 (C-N_{str}), 1542 (aromatic ring), 1348 Asy., 1182 cm^{-1} Syn., (O=S=O); ^{1}H NMR (400 MHz, DMSO): δ 2.05 (s, -CH_3), 4.22, 4.42 (s 2H -CH_2), 7.15-7.17 (d, aromatic Protons), 7.77-7.79 (d, aromatic Protons), 7.41, (s $1H_{methoxazole}$), 8.30 (s 1H Ar-H Pyridine), 8.22 (s, 1H pyrazolo) 8.58 (s 1H Ar-H Pyridine), 12.05 (s, 1H -NH); ^{13}C NMR (100 MHz, DMSO-d_6); ESI-MS: *m/z* Calcd 491.32. Found $[M + H]^+$ 492.4.

4-((2-(5-Bromo-1*H*-pyrazolo[3,4-b]pyridin-1-yl)-2-oxoethyl)amino)-N-(pyrimidin-2-yl) benzenesulfonamide, D: Yellow light solid, m.p ~238ºC. Anal. Calcd for $C_{18}H_{14}BrN_7O_3S$: C, 44.27; H, 2.89; N, 20.08; O, 9.83; S, 6.57. Found C, 44.25; H, 2.92; N, 20.02; O, 9.87, S, 6.47%. IR (KBr): 3340 (sulfa-NH), 3277 (pyrazolo-NH) 3058 (C-H_{str} saturated hydrocarbon), 1725 (C=O) 1620 (C=N_{str}) 1315 (C-N_{str}), 1551 (aromatic ring), 1351 Asy., 1149 cm^{-1} Syn., (O=S=O); ^{1}H NMR (400 MHz, DMSO): δ 3.79,4.01 (s 2H -CH_2), 7.18-7.21 (d, aromatic Protons), 7.54-7.56 (d, aromatic Protons), 6.55, (m, $1H_{pyrimidin}$), 6.61,7.42 (d, $2H_{pyrimidin}$), 8.22 (s 1H Ar-H Pyridine), 7.58 (s, 1H pyrazolo) 7.78 (s 1H Ar-H Pyridine), 11.83 (s, 1H -NH), 12.46 (s, 1H -NH); ^{13}C NMR (100 MHz, DMSO-d_6); ESI-MS: *m/z* Calcd 487.01. Found $[M + H]^+$ 488.1.

4-((2-(5-Bromo-1*H*-pyrazolo[3,4-b]pyridin-1-yl)-2-oxoethyl)amino)-N-(4,6-dimethylpyrimidin-2-yl)benzenesulfonamide, E: White solid, m.p 271-273ºC. Anal. Calcd for $C_{20}H_{18}BrN_7O_3S$: C, 46.52; H, 3.51; N, 18.99; O, 9.30; S, 6.21. Found C, 46.55; H, 3.52; N, 18.92; O, 9.27, S, 6.23%. IR (KBr): 3355 (sulfa-NH), 3245 (pyrazolo-NH) 3057 (C-H_{str} saturated hydrocarbon), 1710 (C=O) 1622 (C=N_{str}) 1322 (C-N_{str}), 1559 (aromatic ring), 1355 Asy., 1152 cm^{-1} Syn., (O=S=O); ^{1}H NMR (400 MHz, DMSO): δ 2.19 (s, 3H CH_3) 2.25 (s, 3H CH_3), 4.22,4.45 (s 2H -CH_2), 7.17-7.19 (d, aromatic Protons), 7.79-7.81 (d, aromatic Protons), 6.92, (s, $1H_{pyrimidin}$), 8.32 (s 1H Ar-H Pyridine), 8.17 (s, 1H pyrazolo) 8.66 (s 1H Ar-H Pyridine), 12.22 (s, 1H -NH); ^{13}C NMR (100 MHz, DMSO-d_6); ESI-MS: *m/z* Calcd 515.37. Found $[M + H]^+$ 516.4.

4-((2-(5-Bromo-1*H*-pyrazolo[3,4-b]pyridin-1-yl)-2-oxoethyl)amino)-N-(4-methylpyrimidin-2-yl)benzenesulfonamide, F: Yellow solid, m.p >262ºC. Anal. Calcd for $C_{19}H_{16}BrN_7O_3S$: C, 45.43; H, 3.21; N, 19.52; O, 9.55; S, 6.38. Found C, 45.42; H, 3.22; N, 19.52; O, 9.57, S, 6.37%. IR (KBr): 3350 (sulfa-NH), 3241 (pyrazolo-NH) 3052 (C-H_{str} saturated hydrocarbon), 1715 (C=O) 1621 (C=N_{str}) 1321 (C-N_{str}), 1550 (aromatic ring), 1365 Asy., 1153 cm^{-1} Syn., (O=S=O); ^{1}H NMR (400 MHz, DMSO): δ 2.19 (s, 3H CH_3), 4.18,4.39 (s 2H -CH_2), 7.18-7.20 (d, aromatic Protons), 7.75-7.77 (d, aromatic Protons), 6.82, (s, $1H_{pyrimidin}$), 8.22 (d, $1H_{pyrimidin}$), 8.31 (s 1H Ar-H Pyridine), 8.10 (s, 1H pyrazolo) 8.56 (s 1H Ar-H Pyridine), 12.10 (s, 1H -NH); ^{13}C NMR (100 MHz, DMSO-d_6); ESI-MS: *m/z* Calcd 501.34. Found $[M + H]^+$ 502.4.

4-((2-(5-Bromo-1*H*-pyrazolo[3,4-b]pyridin-1-yl)-2-oxoethyl)amino)-N-(6-methoxypyridazin-3-yl)benzenesulfonamide, G: Yellow solid, m.p ~265ºC. Anal. Calcd for $C_{19}H_{16}BrN_7O_4S$: C, 44.03; H, 3.11; N, 18.92; O, 12.35; S, 6.19. Found C, 44.05; H, 3.15; N, 18.82; O, 12.47, S, 6.17%. IR (KBr): 3352 (sulfa-NH), 3245 (pyrazolo-NH) 3077 (C-H_{str} saturated hydrocarbon), 1722 (C=O) 1631 (C=N_{str}) 1322 (C-N_{str}), 1557 (aromatic ring), 1364 Asy., 1150 cm^{-1} Syn., (O=S=O); ^{1}H NMR (400 MHz, DMSO): δ 3.55 (s, 3H CH_3), 4.24,4.49 (s 2H -CH_2), 7.22-7.24 (d, aromatic Protons), 7.82-7.84 (d, aromatic Protons), 7.05, (d, $1H_{pyrimidin}$), 7.11 (d, $1H_{pyrimidin}$), 8.24 (d, $1H_{pyrimidin}$), 8.35 (s 1H Ar-H Pyridine), 8.10 (s, 1H pyrazolo) 8.56 (s 1H Ar-H Pyridine), 12.10 (s, 1H -NH); ^{13}C NMR (100 MHz, DMSO-d_6); ESI-MS: *m/z* Calcd 517.02. Found $[M + H]^+$ 517.1.

4-((2-(5-Bromo-1*H*-pyrazolo[3,4-b]pyridin-1-yl)-2-oxoethyl)amino)-N-(pyridin-2-yl)benzenesulfonamide, H: Light yellow solid, m.p 231-233ºC. Anal. Calcd for $C_{19}H_{15}BrN_6O_3S$: C, 46.83; H, 3.10; N, 17.25; O, 9.85; S, 6.58. Found C, 46.85; H, 3.15; N, 17.22; O, 9.87, S, 6.57%. IR (KBr): 3350 (sulfa-NH), 3252 (pyrazolo-NH) 3072 (C-H_{str} saturated hydrocarbon), 1717 (C=O) 1652 (C=N_{str}) 1323 (C-N_{str}), 1575 (aromatic ring), 1355 Asy., 1154 cm^{-1}; Syn., (O=S=O); ^{1}H NMR (400 MHz, DMSO): δ 4.23,4.44 (s 2H -CH_2), 7.21-7.23 (d, aromatic Protons), 7.80-7.82 (d, aromatic Protons), 6.82-8.37 (m, $6H_{pyridine}$), 11.89 (s, 1H -NH); ^{13}C NMR (100 MHz, DMSO-d_6); ESI-MS: *m/z* Calcd 486.01. Found $[M + H]^+$ 487.02.

Sodium acetyl((4-((2(5-bromo-1*H*-pyrazolo[3,4-b pyridin-1-yl)-2-oxoethyl)amino)phenyl)sulfonyl)-amide, I: Light yellow solid, m.p ~229ºC. Anal. Calcd for $C_{16}H_{13}BrN_5NaO_4S$: C, 40.52; H, 2.76; N, 14.77; O, 13.49; S, 6.76. Found C, 40.55; H, 2.78; N, 14.75; O, 13.47, S, 6.82%. IR (KBr): 3172 (pyrazolo-NH) 3088 (C-H_{str} saturated hydrocarbon), 1720 (C=O) 1645 (C=N_{str}) 1337 (C-N_{str}), 1553 (aromatic ring), 1347 Asy., 1140 cm^{-1}; Syn., (O=S=O).); ^{1}H NMR (400 MHz, DMSO): δ 1.95 (s, 3H CH_3), 4.21,4.40 (s 2H -CH_2), 7.18-7.20 (d, aromatic Protons), 7.81-7.83 (d, aromatic Protons), 8.21 (s 1H Ar-H Pyridine), 8.64 (s 1H Ar-H Pyridine), 12.21 (s, 1H -NH); ^{13}C NMR (100 MHz, DMSO-d_6); ESI-MS: *m/z* Calcd 472.98. Found $[M + H]^+$ 473.89.

4-((2-(5-Bromo-1*H*-pyrazolo[3,4-b]pyridin-1-yl)-2-oxoethyl)amino)-N-(diaminomethylene) benzenesulfonamide, J: Light yellow solid, mp ~215ºC. Anal. Calcd for $C_{15}H_{14}BrN_7O_3S$: C, 39.83; H, 3.12; N, 21.68; O, 10.61; S, 7.09. Found C, 39.85; H, 3.15; N, 21.65; O, 10.67, S, 7.05%. IR (KBr): 3475 (Asy-NH), 3424 (Sym-NH), 3155 (pyrazolo-NH) 3052 (C-H_{str} saturated hydrocarbon), 1720 (C=O), 1645 (C=N_{str}) 1356 (C-N_{str}), 1575 (aromatic ring), 1387 Asy., 1147 cm^{-1}; Syn., (O=S=O); ^{1}H NMR (400 MHz, DMSO): δ 4.22,4.45 (s 2H -CH_2)7.14-7.18 (d, aromatic Protons), 7.94-7.96 (d, aromatic Protons), 6.81 (m, br, 1$H_{guanidine}$), 8.24 (s 1H Ar-H Pyridine), 8.67 (s 1H Ar-H Pyridine), 12.10 (s, 1H -NH); ^{13}C NMR (100 MHz, DMSO-d_6); ESI-MS: *m/z* Calcd 451.01. Found $[M + H]^+$ 452.02.

Results and Discussion

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 (Figure 2).

Determination of activity index

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

The synthesized this new series of 4-((2-(5-bromo-1*H*-pyrazolo[3,4-*b*]pyridin-1-yl)-2-oxoethyl)amino)-*N*-(various-substitutions)benzenesulfonamide **A-J** were evaluated their anti bacterial activity with streptomycin as standard drugs, the concentration was 1000 µg/mL. The considerable results showed for all new final synthesized compounds of **A-J** were good, moderate and lowest active against gram negative and Gram positive bacteria. On the bases of this results we terminate that zone inhibition of antibacterial activity of **A**, **C**, **D** and **I**, were increased than their sulfa drugs distinct while the another compounds inhibition zones were decreased compared to standard, shown in Table II.

The MIC values of these **A-J** series showed substantial results (Figure 3). For all derivatives such as **A,C,D** and **I** compounds showed very good MIC values shown in Table III and other compound shown moderate to average MIC values. Although, the compounds **A** and **C** showed very good zone inhibition activity as well as in MIC for all bacterial strains.

In vitro anti-mycobacterial activity

In vitro anti-mycobacterial activity of Tested all synthesized compounds showed excellent to average % inhibition against *Mycobacterium tuberculosis* H_{37}Rv. From the data (%) results of inhibition values showed **C** (75.20 %), **F** (80.99 %), and **G** (81.81 %) had showed excellent inhibition, while other had good to average % inhibition.

From the experiment results MIC of the *in vitro* anti-mycobacterial activity showed also excellent for **C**, **F** and **G** in sequences (25, 6.25, 6.25 µg/mL),

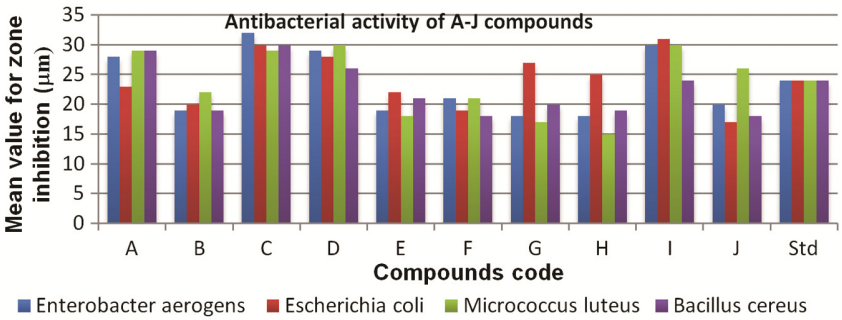


Figure 2 — Antibacterial activity of compounds **A-J**

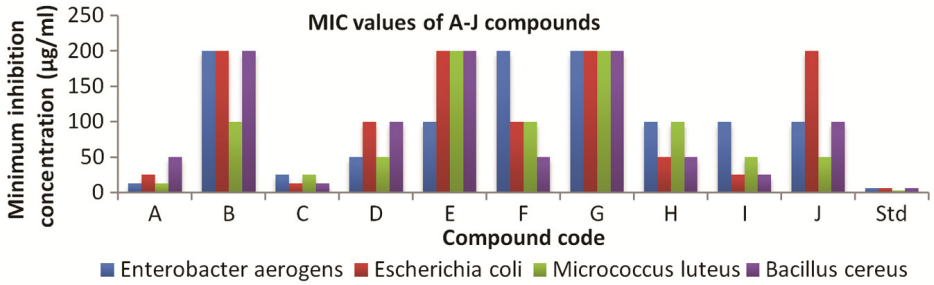


Figure 3 — MIC values of compounds A-J

Table IV — *In vitro* anti mycobacterial activities of **A-J** derivatives

Compd	Control	Treatment concentration (100µg/mL)	Percentage inhibition (%)	MIC value (µg/mL)
	Lowenstein–Jensen (LJ) method (Culture: $H_{37}RV$) Mean Colony forming unit (c.f.u.) on media			
A	121	32	73.55	25
B	121	38	68.59	50
C	121	30	75.20	25
D	121	45	62.80	200
E	121	34	71.90	50
F	121	23	80.99	6.25
G	121	22	81.81	6.25
H	121	37	69.42	50
I	121	40	66.94	100
J	121	36	70.24	50
Isoniazid	121	1	99.17	0.20

while other derivatives showed 25 to 200 µg/mL against *Mycobacterium tuberculosis* $H_{37}Rv$ (Table IV).

Conclusion

In summarized, for this present work all synthesized compounds **A-J** were derived by the different sulfonamides (sulfa-drugs) **(dSD)** clubbed with 5-Bromo-1*H*-pyrazolo[3,4-b]pyridine **(PRPy)** *via* chloro acetyl chloride (CAC). All target compounds were screened for their antibacterial activity against Gram positive and Gram negative bacteria, compounds **A, C, D** and **I** shown good potent inhibitions. Moreover, compounds **C, F** and **G** had showed excellent inhibition for *in vitro* anti tubercular activity against *Mycobacterium tuberculosis* $H_{37}RV$ and confirmed by various spectral data.

Supplementary Information

Supplementary information is available in the website ttp://nopr.niscair.res.in/handle/123456789/60.

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