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Synthesis of New Benzothiazole Derivatives as Potential Antimicrobial Agents

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Abstract: **During the initial efforts to develop novel antibiotics, a new class of benzothiazoles (3a–n) were designed and synthesized as potential antibacterial and antimycobacterial agents. Most of the synthesized compounds showed good antibacterial activity against the Gram-positive bacteria tested. The compounds 3i exhibited excellent *in vitro* activity, with a MIC value of 1 µg/mL against *Mycobacterium tuberculosis H37Rv*. These compounds were also found to have activity against *Candida albicans*, with a MIC value of 4 µg/mL.**

Index Terms: **Benzothiazole, fused heterocycles, hydrazones, antibacterial, antimycobacterial**

I. Introduction

One of the world's most important public health challenges is antimicrobial resistance [1]. There were an approximate 4.95 million (3.62–6.57) deaths related to bacterial antimicrobial resistance in the year 2019 [2]. *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Streptococcus pneumoniae*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa* were major contributors for deaths associated with resistance. The fight against bacterial infection represents one of the high points of modern medicine.

Discovery of antibiotics in the 1940s offered physicians a powerful tool against bacterial infections that has saved the lives of millions of people. Though, because of the widespread and sometimes inappropriate use of antibiotics, strains of bacteria have begun to occur that are antibiotic-resistance [3]. The advent and spread of bacterial resistance pose a major threat to human health across the globe. The number of cases of multi-drug resistant bacterial infections is increasing at an alarming rate. Moreover, the clinicians have become dependent on strong antibiotics such as Vancomycin for serious infections. Therefore, there is an urgent need for the development of novel chemical entities with high safety profiles that are particularly effective against gram-positive pathogens including the resistant strains.

Benzothiazoles are fused heterocycles, which contain a 1, 3-thiazole ring that fused to a benzene ring. Since the 1990s, various pharmacological investigations of newly synthesized benzothiazole derivatives demonstrated interesting pharmacological activities and led to the development of new medications for treating human diseases [4,5].

Benzothiazoles comprise a novel class of therapeutic compounds shown to exert a wide range of biological activities such as antimicrobial, anticancer, anthelminthic, antidiabetic, antitubercular, anti-inflammatory, antifungal, antiviral, anti-infective, anti-hypertensive and antipsychotic etc [4-7].

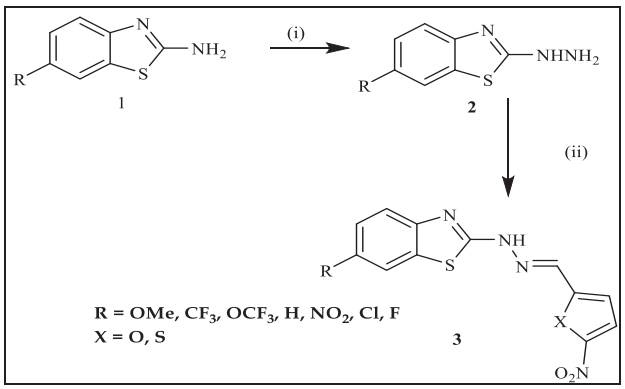
II. Chemistry

As part of antimicrobial research in our laboratory [8-10], a new class of benzothiazoles have been synthesized and evaluated for their biological activity.

Synthesis of Aryl/heterocyclic aldehyde-2-(1,3-benzothiazol-2-yl)hydrazones

The synthesis of benzothiazole hydrazones (**3a-n**) were synthesized by procedure described in Scheme 1. The key intermediates 2-hydazinobenzothiazoles have been produced by amination of 2-aminobenzothiazole by using hydrazine hydrate. The benzothiazole hydrazines were treated with appropriate aldehydes in presence of acetic acid to afford target benzothiazole hydrazones [11,12]. The details of the structures of **3a-n** were provided in Table 1.

SCHEME I.



Reagents and conditions: (i) Hydrazine hydrate, glycol, 140 °C, 4h; (ii) Aromatic aldehydes, ethanol, cat AcOH, reflux, 2h.

TABLE I.
Representative Compounds 3a-m

S.No	Compound	R	X
1	**3a**	-H	-O
2	**3b**	-H	-S
3	**3c**	-OCH_3	-O
4	**3d**	-OCH_3	-S
5	**3e**	-CF_3	-O
6	**3f**	-CF_3	-S
7	**3g**	-OCF_3	-O
8	**3h**	-OCF_3	-S
9	**3i**	-NO_2	-O
10	**3j**	-NO_2	-S
11	**3k**	-F	-O
12	**3l**	-F	-S
13	**3m**	-Cl	-O
14	**3n**	-Cl	-S

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III. Biological Activity

A. Antibacterial and antifungal activity

Antibacterial activity of compounds **3a-n** were screened for their antibacterial activity against *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Bacillus subtillis*, *Escherichia coli*, *Klebsiella pneumoniae,* and *Pseudomonas aeruginosa* (Table 2) and the antifungal activity was evaluated against yeast *Candida albicans* (MTCC 227). The antimicrobial activities were measured in the inhibitory zones (in mm) and were determined by using agar well method (cup plate method) [13,14]. Antibiotics Streptomycin, Ciprofloxacin and Amphotericin B were used as positive controls against bacteria and fungi respectively. In all determinations, tests were performed in duplicate, and results were reported as the mean of at least three determinations. In Table 2, all compounds exhibited moderate to good antibacterial activity. Compounds **3a-n** showed significant inhibition against all the bacteria tested. Compounds are more active against gram positive bacteria than gram negative bacteria. Compounds **3b**, **3i**, and **3m** showed good antibacterial activity. In compounds **3a-n**, introduction of thiophen group instead of nitro furan group leads to decrease in the antibacterial activity against gram positive bacteria, this trend reverses in gram negative species. The significant inhibition shown by the compounds **3b**, **3i**, and **3m** might be due to the presence of nitrofuran ring on the benzothiazole system.

The more active compounds **3i**, and **3m** were further screened for antimicrobial activity in variable concentrations. The antimicrobial activity shown in the zone of inhibition, compound **3m** was found to be the most active compound among the series detailed in Table 3. Compound **3m** exhibited remarkable antibacterial and antifungal activity.

TABLE II.
Antibacterial and Antifungal Activity of Benzothiazole Analogs (**3a-n**) Expressed in Zone of Inhibition in mm

Compounds/Concentrations	*Staphylococcus aureus*		*Staphylococcus epidermis*		*Bacillus subtillis*		*Escherichia coli*		*Klebsiella pneumoiae*		*Pseudomonas aeruginosa*		*Candida albicans*	
	50 µg/ml	100 µg/ml	50 µg/ml	100 µg/ml	50 µg/ml	100 µg/ml	50 µg/ml	100 µg/ml	50 µg/ml	100 µg/ml	50 µg/ml	100 µg/ml	50 µg/ml	100 µg/ml
3a	--	13	10	14	--	17	--	12	--	--	--	--	--	23
3b	--	15	15	10	--	14	--	18	--	--	--	--	--	25
3c	--	--	--	12	--	11	--	21	--	15	--	--	--	24
3d	--	--	--	--	--	10	--	25	14	12	14	15	--	20
3e	12	14	17	--	10	15	10	15	--	10	--	17	--	31
3f	--	--	--	--	--	--	09	19	--	10	10	--	--	16
3g	--	14	10	12	10	17	--	21	--	11	--	13	--	28
3h	--	12	--	--	--	13	--	15	--	14	--	12	--	18
3i	1	17	13	23	--	21	--	14	--	10	--	--	--	40
3j	--	--	--	13	--	17	--	16	--	11	--	11	--	--
3k	10	12	10	14	--	17	--	21	--	11	--	12	--	27
3l	--	11	--	--	--	--	--	--	--	--	--	--	11	21
3m	19	26	19	--	17	30	--	34	--	20	--	30	--	30
3n	--	10	--	--	--	15	--	16	--	--	--	--	--	20
STR	22		18		17		21		22		29		--	
CIP	32		35		32		>40		20		30		--	
AT-B	--		--		--		--		--		--		16	

The test were conducted in duplicate and repeated thrice; STP, Streptomycin; CIP, Ciprofloxacin (50 µg/mL); AT-B, Amphotericin (100 units); (--), bacteria are resistant to the compound at the concentrations.

TABLE III.
ANTIBACTERIAL AND ANTI-FUNGAL ACTIVITY OF **3m**, AND **3i** ANALOGS IN DIFFERENT CONCENTRATIONS EXPRESSED IN ZONE OF INHIBITION IN mm

Compounds	**3m**					**3i**					**CIP**	**AT-B**	**Nys**
Concentration in µg/mL	10	25	50	75	100	10	25	50	75	100	50	20	20
Staphylococcus aureus	17	21	24	25	27	9	11	15	17	19	26	NT	NT
Staphylococcus epidermis	17	22	27	28	29	9	10	12	13	23	34	NT	NT
Bacillus Subbtilis	19	22	26	28	28	--	10	14	17	21	32	NT	NT
Escherichia coli	17	21	24	25	27	9	11	15	17	19	38	NT	NT
Pseudomonas aeruginosa	17	22	27	28	29	9	10	12	13		40	NT	NT
Klebsiella pneumoniae	19	22	26	28	28	--	10	14	17	21	21	NT	NT
Candida albicans	NT	18	23	25	28	NT	--	--	--	--	NT	14	--
Aspergillus niger	NT	--	10	24	27	NT	--	--	--	--	NT	23	26
Aspergillus sp	NT	10	10	15	19	NT	--	--	--	--	NT	14	16

The test were performed in duplicate and repeated thrice; CIP, Ciprofloxacin (50 µg/mL); AT-B, Amphotericin (100 units) Nys, Nystatin-1 (20 µg/mL); (--), bacteria are resistant to the compound at the concentrations.

TABLE IV.
ANTIMYCOBACTERIAL ACTIVITY OF COMPOUNDS **3a-m** AGAINST *M. TUBERCULOSIS H37RV* (MIC IN µg/mL)

S. No.	**Compound**	**Molecular Formula**	**Molecular Weight**	**CMR** (Molar refractivity)	**MIC (µg/mL)**	**C log P** (Hydrophobicity)
1	**3a**	$C_{12}H_8N_4O_3S$	288.28	7.63	>16	3.24
2	**3b**	$C_{12}H_8N_4O_2S_2$	304.01	8.23	>16	3.78
3	**3c**	$C_{13}H_{10}N_4O_4S$	318.31	8.25	>16	3.54
4	**3d**	$C_{13}H_{10}N_4O_3S_2$	334.37	8.85	>16	4.07
5	**3e**	$C_{13}H_7F_3N_4O_3S$	356.28	8.14	>16	4.19
6	**3f**	$C_{13}H_7F_3N4O_2S_2$	372.35	8.74	>16	4.72
7	**3g**	$C_{13}H_7F_3N_4O_4S$	372.28	8.30	>16	4.65
8	**3h**	$C_{13}H_7F_3N_4O_3S_2$	388.34	8.89	>16	5.18
9	**3i**	$C_{12}H_7N_5O_5S$	333.28	8.26	**1**	3.09
10	**3j**	$C_{12}H_7N_5O_4S_2$	349.35	8.84	>16	3.62
11	**3k**	$C_{12}H_7FN_4O_3S$	306.27	7.65	>16	3.38
12	**3l**	$C_{12}H_7FN_4O_2S_2$	322.34	8.24	>16	3.91
13	**3m**	$C_{12}H_7ClN_4O_3S$	322.73	8.13	>16	3.95
14	**3n**	$C_{12}H_7ClN_4O_2S_2$	338.79	8.72	>16	4.48
RMP					0.25	0.5
INH					0.5	-0.7

RMP, Rifampicin; INH, Isoniazid; the Chem Draw Ultra, version 9.0 was used to calculate the values of Molar refractivity and Hydrophobicity of the above compounds.

B. Antimycobacterial activity

All the synthesized compounds were evaluated for the antitubercular activity, and the results are concise in Table 4. The compounds **3a-n** were initially tested against *Mycobacterium tuberculosis H37Rv* at 16 µg/mL as the single concentration. From this screening, the active compounds were selected further to conduct broth microdilution assay to find out Minimum Inhibitory Concentration (MIC) [15,16]. The compounds showing at least 90% inhibition in the initial screen were retested to determine the actual MIC. This has been achieved by serial dilution at lower concentrations against *Mycobacterium tuberculosis H37Rv* using the Nitrate Reductase Assay (NRA). In addition to the NRA reagent to microtiter plate, a change in color to pink indicates the growth of bacteria. The possible lowest concentration of the compound that shows no change in the color relative to controls is defined as MIC. Isoniazid and Rifampicin were used as reference drugs. The compound **3i** has shown good antimycobacterial activity 1 µg/mL (Table 4). Further investigation of other areas of biological properties of these synthesized compounds (**3a-n**) are going on and the results will be communicated soon.

VI. EXPERIMENTAL DATA

*General procedure for the synthesis of heterocyclic aldehyde-2-(1,3-benzothiazol-2-yl)hydrazones (**3a-n**)*

2-hydrazeno-benzothiazoles (1 eq) and heterocyclic aldehydes (1 eq) were dissolved in a small amount of ethanol (10 mL). To the above mixture, a catalytic amount of acetic acid was added, and it was stirred for 1 hour. After that period, the reaction has stopped. On filtration, the precipitate was collected washed with cold methanol (3 X 30 mL) followed by cold chloroform (2 X 20 mL). Recrystallization has been done to afford pure respective hydrazones by using hot methanol.

5-Nitrofuran aldehyde-2-(1,3-benzothiazol-2-yl)hydrazone ***(3a)***

The compound **3a** was prepared according to the above-defined method by using 2-hydrazeno-benzothiazole (165 mg, 1 eq) and 5-nitro-2-furancarboxaldehde (140 mg, 1 eq). Yield: 260 mg (85%).

^{1}H NMR (DMSO-d_6, 200 MHz): δ 6.90 (d, 1H, J = 3.7 Hz), 7.22 (d, 1H, J = 8.7 Hz), 7.43 (m, 1H, J = 2.9, 8.0 Hz), 7.60 (d, 1H), 7.7 (d, 1H, J = 3.7 Hz), 7.8 (s, 1H), 7.84 (m, 1H), 12.3 (bs, 1H); ESIMS: *m/z* 289 $(M+H)^+$.

5-Nitrothiophen aldehyde-2-(1,3-benzothiazol-2-yl)hydrazone ***(3b)***

The compound **3b** was synthesized as per the above procedure using and 2-hydrazino-benzothiazole (165 mg, 1 eq) and 5-nitro-2-thiophencarboxaldehde (156 mg, 1 eq) Yield: 256 mg (84 %).

^{1}H NMR (DMSO-d_6, 200 MHz): δ 7.00 (dd, 1H, J = 8.0, 2.9 Hz), 7.19-7.15 (m, 3H, J = 4.3, 7.1 Hz), 7.35 (d, 1H, J = 8.0 Hz), 7.79 (s, 1H), 7.83 (d, 1H, J = 4.3 Hz), 12.0 (bs, 1H); ESIMS: *m/z* 305 $(M+H)^+$.

5-Nitrofuran aldehyde-2-(6-methoxy-1,3-benzothiazol-2-yl)hydrazone ***(3c)***

The compound **3c** was synthesized as per the above procedure of **3a** using and 2-hydrazino-6-methoxy-benzothiazoles (178 mg, 1 eq) and 5-nitro-2-furancarboxaldehde (140 mg, 1 eq) Yield: 267 mg (89 %).

^{1}H NMR (DMSO-d_6, 200 MHz): δ 3.76 (s, 3H), 6.84 (dd, 1H, J = 9.0, 2.25 Hz), 6.96 (d, 1H, J = 3.7 Hz), 7.27 (d, 1H, J = 2.2 Hz), 7.35 (d, 1H, J = 9.0 Hz), 7.58 (d, 1H, J = 3.7 Hz), 7.96 (s, 1H), 12.4 (bs, 1H); ESIMS: *m/z* 319 $(M+H)^+$.

5-Nitrothiophen aldehyde-2-(6-methoxy-1,3-benzothiazol-2-yl)hydrazone ***(3d)***

The compound **3d** was synthesized as per the above given procedure using 2-hydrazino-6-methoxy-benzothiazoles (165 mg, 1 eq) and 5-Nitro-2-nitrothiophen carboxaldehde (157 mg, 1 eq). Yield: 281 mg (88 %).

^{1}H NMR (DMSO-d_6, 200 MHz): δ 3.76 (s, 3H), 6.84 (dd, 1H, J = 9.0, 2.25 Hz), 7.19 (d, 1H, J = 4.7 Hz), 7.27 (d, 1H, J = 2.2 Hz), 7.30 (d, 1H, J = 9.0 Hz), 7.8 (d, 1H, J = 4.7 Hz), 7.96 (s, 1H), 12.4 (bs, 1H); ESIMS: *m/z* 335 $(M+H)^+$.

5-Nitrofuranaldehyde-2-(6-trifluoromethyl-1,3-benzothiazol-2yl)hydrazone ***(3e)***

The compound **3e** was synthesized as per the above given procedure of **3a** using 2-hydrazino-6-trifluoromethyl-benzothiazole (233 mg, 1 eq) and 5-nitrofuran aldehyde (141 mg, 1 eq). Yield: 300 mg (84 %).

^{1}H NMR (DMSO-d_6, 200 MHz): δ 6.9 (d, 1H, J = 3.7 Hz), 7.22 (d, 1H, J = 8.7 Hz), 7.43 (m, 1H, J = 2.9, 8.0 Hz), 7.58 (d, 1H, J = 3.7 Hz), 7.60 (d, 1H), 7.84 (m, 1H, J = 4.3 hz), 12.3 (bs, 1H); ESIMS: *m/z* 357 $(M+H)^+$.

5-Nitrothiophen aldehyde-2-(6-trifluoromethyl-1,3-benzothiazol-2yl)hydrazone ***(3f)***

The compound **3f** was synthesized as per the above given procedure of **3a** using 2-hydrazino-6-trifluoromethyl-benzothiazole (233 mg, 1 eq) and 5-nitrothiophen aldehyde (157 mg, 1 eq) Yield: 315 mg (85 %).

^{1}H NMR (DMSO-d_6, 200 MHz): δ 7.19 (d, 1H, J = 4.38 Hz), 7.22 (d, 1H, J = 8.7 Hz), 7.43 (m, 1H, J = 2.9, 8.0 Hz), 7.60 (d, 1H), 7.84-7.82 (m, 2H, J = 4.3 Hz), 12.3 (bs, 1H); ESIMS: *m/z* 373 $(M+H)^+$.

5-Nitrofuran aldehyde-2-(6-trifluoromethoxy-1,3-benzothiazol-2yl)hydrazone ***(3g)***

The compound **3g** was synthesized according to the procedure described for **3a** by using 5-nitrofuran aldehyde (141 mg, 1 eq) and 2-hydrazino-6-trifluoromethoxy-benzothiazole (249 mg, 1 eq) (yield 316 mg, 85 %).

^{1}H NMR (DMSO-d_6, 200 MHz): δ 8.42 (bs, 1H), 7.44-7.41 (m, 2H), 7.36 (d, 1H), 7.27 (d, 1H, J = 2.4 Hz), 7.30 (d, 1H, J = 3.9 Hz), 7.14 (d, 1H, J = 8.6 Hz), 6.48 (d, 1H, J = 3.9 Hz); ESIMS: *m/z* 373 $(M+H)^+$.

5-Nitrothiophen aldehyde-2-(6-trifluoromethoxy-1,3-benzothiazol-2yl)hydrazone ***(3h)***

The compound **3h** was synthesized according to the procedure described for **3a** by using 5-nitrothiophen aldehyde (157 mg, 1 eq) and 2-hydrazino-6-trifluoromethoxy-benzothiazole (249 mg, 1 eq) (yield 329 mg, 85 %).

^{1}H NMR (DMSO-d_6, 200 MHz): δ 12.7 (bs, 1H), 8.14-8.10 (m, 2H, J = 7.7, 4.3 Hz), 7.83 (m, 1H), 7.51 (d, 1H, J = 4.5 Hz), 7.35-7.30 (m, 2H), 6.93 (dd, 1H, J = 2.4, 8.7 Hz), 3.77 (s, 3H); ESIMS: *m/z* 389 $(M+H)^+$.

5-Nitrofuran aldehyde-2-(6-nitro-1,3-benzothiazol-2yl)hydrazone ***(3i)***

The compound **3i** was synthesized as per the method described for the synthesis of **3a** using 2-hydrazino-6-nitro-benzothiazole (210 mg, 1 eq) and 5-nitrofuran aldehyde (141 mg, 1 eq). Yield: 280 mg (84 %).

^{1}H NMR (DMSO-d_6, 200 MHz): δ 7.15-7.12 (m, 2H, J = 2.4, 6.8 Hz), 7.30 (m, 1H, J = 7.8 Hz), 7.43 (m, 1H), 7.71 (d, 1H, J = 3.9 Hz), 8.10 (s, 1H), 12.7 (bs, 1H); ESIMS: *m/z* 334 $(M+H)^+$.

5-Nitrothiophen aldehyde-2-(6-nitro-1,3-benzothiazol-2yl)hydrazone ***(3j)***

The compound **3j** was synthesized as per the method described for the synthesis of **3a** using 5-nitrothiophen aldehyde (157 mg, 1 eq) and 2-hydrazino-6-nitro-benzothiazole (210 mg, 1 eq). Yield: 300 mg (86 %).

^{1}H NMR (DMSO-d_6, 200 MHz): δ 7.15-7.12 (m, 2H, J = 2.4, 6.8 Hz) 7.30 (m, 1H, J = 7.8 Hz), 7.43 (m, 1H), 8.15-8.09 (m, 2H, J = 4.7 Hz), 12.0 (bs, 1H); ESIMS: *m/z* 350 $(M)^+$.

5-Nitrofuran aldehyde-2-(6-fluoro-1,3-benzothiazol-2yl)hydrazone ***(3k)***

The compound **3k** was synthesized synthesized as per the method described for the synthesis of **3a** using 2-hydrazino-6-fluoro-benzothiazole (183 mg, 1 eq) and 5-nitrofuran aldehyde (140 mg, 1 eq). Yield: 260 mg (86 %).

^{1}H NMR (DMSO-d_6, 200 MHz): δ 6.84 (dd, 1H, J = 9.0, 2.2 Hz), 6.96 (d, 1H, J = 3.7 Hz),7.27 (d, 1H, J = 2.2 Hz), 7.35 (d, 1H, J = 9.0 Hz), 7.58 (d, 1H, J = 3.7 Hz), 7.96 (s, 1H), 12.4 (bs, 1H); ESIMS: *m/z* 307 $(M)^+$.

*5-Nitrothiophen aldehyde-2-(6-fluoro-1,3-ben Zothiazole-2-yl)hydrazone (**3l**)*

The compound **3l** was synthesized according to the method given for the synthesis of **3a** using 2-hydrazino-6-fluoro-benzothiazole (183 mg, 1 eq) and 5-nitrothiophen aldehyde (157 mg, 1 eq). Yield: 260 mg (80 %).

^{1}H NMR (DMSO-d_6, 200 MHz): δ 7.18 (d, 1H, J = 4.3 Hz), 7.21 (d, 1H, J = 8.7 Hz), 7.59 (d, 1H), 7.43 (m, 1H, J = 2.9, 8.0 Hz), 7.82-7.84 (m, 2H, J = 4.3 Hz), 12.3 (bs, 1H); ESIMS: m/z 323 $(M+H)^+$.

*5-nitro-2-furaldehyde-2-(6-chloro-1,3-benzothiazole 2-yl)hydrazone (**3m**)*

The compound **3m** was synthesized according to the method given for the synthesis of **3a** using 2-hydrazino-6-chloro-benzothiazole (199 mg, 1 eq) and 5-nitrofuran aldehyde (140 mg, 1 eq). Yield: 261 mg (84 %).

^{1}H NMR (DMSO-d_6, 200 MHz): δ 6.85 (dd, 1H, J = 9.1, 2.3 Hz) 6.97 (d, 1H, J = 3.6 Hz), 7.27 (d, 1H, J = 2.3 Hz), 7.34 (d, 1H, J = 9.1 Hz), 7.60 (d, 1H, J = 3.6 Hz), 7.88-7.90 (s, 1H), 12.4 (bs, 1H); ESIMS: m/z 323 $(M)^+$.

*5-Nitrothiophen aldehyde-2-(6-chloro-1,3-benzothiazol-2yl)hydrazone (**3n**)*

The compound **3n** was synthesized according to the method given for the synthesis of **3a** using 2-hydrazino-6-chloro-benzothiazole (199 mg, 1 eq) and 5-nitrothiophen aldehyde (157 mg, 1 eq). Yield: 287 mg (85 %).

^{1}H NMR (DMSO-d_6, 200 MHz): δ 7.19 (d, 1H, J = 4.3 Hz), 7.22 (d, 1H, J = 8.7 Hz), 7.43 (m, 1H, J = 2.9, 8.0 Hz), 7.60 (d, 1H), 7.84-7.82 (m, 2H, J = 4.3 Hz), 12.3 (bs, 1H); ESIMS: m/z 339 $(M+H)^+$.

V. Conclusions

Herein, demonstrate the synthesis and antimicrobial potency of a new class of benzothiazoles against Gram-positive, Gram-negative and *Mycobacterium. tuberculosis* bacteria. Amongst the synthesized compounds, **3b** and **3m** have shown potent *in vitro* antibacterial activity. Interestingly, these compounds have also exhibited good antibacterial activity against resistant strains of Gram- positive and Gram-negative. The compound **3i** has shown potent antimycobacterial activity against *Mycobacterium tuberculosis H37Rv*. Further investigations of these new classes of compounds for their potential biological properties are under process.

References

[1] F. Prestinaci, P. Pezzotti, and A. Pantosti, “Antimicrobial resistance: a global multifaceted phenomenon”. Pathog Glob Health, vol. 109, pp. 309–318, 2015.

[2] C. J. L. Murray et al. “Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis” Lancet, vol. 399, pp. 629–655, January 2022.

[3] R. I. Aminov, “A brief history of the antibiotic era: lessons learned and challenges for the future”, Front Microbiol, vol. 1, pp. 134, December 2010.

[4] A. Kamal, M. A. Syed, and S. M. Mohammed, “Therapeutic potential of benzothiazoles: a patent review (2010-2014)”, Expert Opin. Ther. Pat., vol. 25, pp. 335–349.

[5] P. C. Sharma, A. Sinhmar, A. Sharma, Harish, Rajak and D. P. Pathak, “Medicinal significance of benzothiazole scaffold: an insight view”, Journal of Enzyme Inhibition and Medicinal Chemistry, vol. 28, pp. 240–266, 2013.

[6] Y. I. Asiria, A. Alsayari, A. B. Muhsinah, Y. N. Mabkhot and M. Z. Hassan, “Benzothiazoles as potential antiviral agents”, Journal of Pharmacy and Pharmacology, vol. 72, pp. 1459–1480, 2020.

[7] R. Ali and N. Siddiqui, “Biological Aspects of Emerging Benzothiazoles: A Short Review” vol. 2013, Article ID 345198, pp. 12, June 2013.

[8] A. Kamal, P. Swapna, R. V. C. R. N. C Shetti, A. B. Shaik, M. P. N. Rao, F. Sultana, I. A. Khan, S. Sharma, N. P. Kalia, S. Kumar and B. Chandrakant, “Anti-tubercular agents. Part 7: A new class of diarylpyrrole–oxazolidinone conjugates as antimycobacterial agents”, European Journal of Medicinal Chemistry, vol. 64, pp. 239-251, 2013.

[9] A. Kamal, P. Swapna, R. V. C. R. N. C. Shetti, A. B. Shaik, M. P. N. Rao, S. Gupta; Synthesis, biological evaluation of new oxazolidino-sulfonamides as potential antimicrobial agents, European Journal of Medicinal Chemistry, vol. 62, 661 2013.

[10] A. Kamal, S. K. Ahmed, K. S. Reddy, M. N. A. Khan, R. V. C. R. N. C. Shetty, B. Siddhardha, U. S. N. Murty, A. China, and V. Nagaraja, “Synthesis and Biological Evaluation of a New Series of Benzothiazole-Benzothiadiazine Conjugates as Antibacterial Agents”, Letters in Drug Design & Discovery, 4, 550-556, 2007.

[11] A. Kamal, R. V. C. R. N. C. Shetti, P. Swapna, S. Azeeza, A. M. Reddy, I. A. Khan, S. T. Abdullah, S. Sharma, and N. T. Kalia, “Synthesis of new benzothiazole derivatives as potential anti-tubercular agents”, US2012095021 (A1), April 2012.

[12] A. Kamal, R. V. C. R. N. C. Shetti, P. Swapna, S. Azeeza, A. M. Reddy, I. A. Khan, S. T. Abdullah, S. Sharma, and N. T. Kalia, “Synthesis of new benzothiazole derivatives as potential anti-tubercular agents”, US 2016/0175303 A1, June 2016.

[13] Villanova, 1982. National Committee for Clinical Laboratory Standards (NCCLS), Standard methods for dilution antimicrobial susceptibility tests for bacteria, which grows aerobically, p. 242.

[14] National Committee for Clinical Laboratory Standards (NCCLS), Standard methods for dilution antimicrobial susceptibility tests for bacteria, which grows aerobically; approved standard-5th edition. Approved standard NCCLS document M7-A5. NCCLS: Wayne, PA, 2003.

[15] F. Dorbniewski, “Antimicrobial susceptibility testing of Mycobacterium tuberculosis”, Eucast discussion document E.DIS 8.1 DECEMBER 2001. vol. 8, ISSUE 10, P1-10, October 01, 2002.

[16] K. S. Goh, and N. Rastogi “Simple and rapid method for detection of nitrate reductase activity of Mycobacterium tuberculosis and Mycobacterium canettii grown in the Bactec MGIT960 system”, J Microbiol Methods, vol. 81, pp. 208-210, May 2010.