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Research Article

Spectral, Chemical and Pharmaceutical Analysis of Synthesized New 4*H*-1,4-Benzothiazines, and their Sulfone Derivatives

Ankita Garg[*1] Naveen Gautam[2] and Dinesh chand Gautam[1]

[1]Department of Chemistry, University of Rajasthan, Jaipur 302004, India
[2] Lal Bahadur Shastri Government P.G. College, Kotputli, Jaipur 303108, India

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ABSTRACT

The present article describes the synthesis of new 4*H*-1,4-benzothiazines via condensation and oxidative cyclization of substituted 2-aminobenzenethiols with compounds containing active methylene groups. It is believed that the reaction proceeds via intermediary of the enaminoketone system. The sulfone derivatives were synthesized by oxidation of 4*H*-1,4-benzothiazines using 30% hydrogen peroxide in glacial acetic acid. Pharmacological importance of the synthesized compounds was evaluated by their antioxidant and antimicrobial properties. The structures of the compounds have been confirmed by spectral and chemical analysis.

Keywords: 4*H*-1,4-benzothiazines, sulfone derivatives, pharmacological importance, antioxidant and antimicrobial properties.

1. INTRODUCTION

The synthesis of novel 4*H*-1,4-benzothiazines derivatives and investigation of their chemical and biological behaviour have gained more importance in recent decades for medicinal and pharmacological reasons[1-2]. Substituted benzothiazines have been found to have important activities such as analgesic[3], antimicrobial[4], antitumor[5], antimalarial[6], and anti-hepatities[7]. In some cases, 4*H*-1,4-benzothiazines are also known for their utility as dyes, photographic developers[8], ultraviolet light absorbers , antioxidants[9-10]and other industrial use. Basically, 4*H*-1,4-Benzothiazine is an analog of phenothiazine replacing an *o*-phenylene group by an ethylene linkage in phenothiazine[11-12].In addition, it is also well documented that the benzothiazine template is generally recognized as a privileged structure in medicinal chemistry to investigate both potentially antibacterial[13-14]and anticancer[15] molecules. Therefore, 4*H*-1, 4-benzothiazines and their derivatives possess excellent pharmacological / medicinal and therapeutic uses such as antihistaminic[16], antibiotic[17], antirheumatic, anti-aldose reductase, immunostimulating, antiallergic, cytotoxic activity, tranquilizer, sedative, bactericidal[18], etc. A slight change in the substitution pattern in benzothiazine nucleus cause distinguishable difference in their biological activities[19-20]. Therefore, these observations stimulated our interest to extend synthetic, structural and antimicrobial studies of 4*H*-1,4-benzothiazines, and their sulfones. On refluxing with 30% hydrogen peroxide in glacial acetic acid, 4*H*-1,4-benzothiazines yielded 4*H*-1,4-benzothiazine-1,1-dioxides. All the synthesized compounds were screened for their antioxidant and antimicrobial activities.

***Corresponding Author**
Ankita Garg
Department of Chemistry, University of Rajasthan,
Jaipur 302004, India.
Email: garg_ankita01@yahoo.com

2. MATERIALS AND METHODS

All the melting points were determined in open capillary tubes and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra (by broad band proton decoupling technique) were recorded on JEOL AL-300 spectrometer at frequencies of (300.40 and 75.45 MHz) respectively, in DMSO-d_6 using TMS as an internal standard. IR

spectra were recorded in KBr on SHIMADZU 8400S FT-IR spectrophotometer. The FAB (fast atom Bombardment) mass spectra were recorded on a JEOL SX 102/DA-600 mass spectrometer using Ar/Xe as FAB gas at an accelerating voltage of 10 KV. The purity of compounds was checked by TLC using silica gel 'G' as adsorbent, visualizing these by UV light or in an iodine chamber.

2.1 General procedure for the synthesis of substituted 4*H*-1,4-benzothiazines 5a-d

β-Diketone**/**β-ketoester **3a-c** (0.01 mol) was treated with a solution of 2-aminobenzenethiol **1a-c** (0.01 mol) in 5 mL of DMSO and the resulting mixture was heated under Reflux (190°C) for 20 min., then cooled and concentrated on a rotary evaporator. The residue was washed with petroleum ether and crystallized from methanol.

2.2 General procedure for synthesis of 4*H*-1,4-benzothiazine-1,1-dioxides (sulfones) 6a-d

A solution of 4*H*-1,4-benzothiazine **5a-d** (0.01 mol) in 20 mL glacial acetic acid was added to 30% hydrogen peroxide (5 mL) and then the mixture was heated under reflux for 15 min. Keeping the temperature between 50°C and 55°C. Another lot of 30% hydrogen peroxide (5 mL) was added after 15 min. without heating. Then the mixture was heated under reflux (120°C) for an additional 4-5 h, concentrated under reduced pressure and the residue was treated with crushed ice. The resultant solid product **6a-d** was filtered and crystallized from ethanol.

2.3 Biological Activity

2.3.1 Antioxidant Activity

The synthesized compounds were screened for antioxidant activity by 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging assay and 2,2-azinobis(3-ethylbenzothiazoline-6-sulfonic acid) ($ABTS^{\bullet+}$) radical cation decolorization assay.

DPPH Radical Scavenging Assay

Radical scavenging activity of all synthesized compounds was determined spectrophotometrically against stable 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical by Cuendet et al.

ABTS Radical Cation Decolorization Assay

The ($ABTS^{\bullet+}$) assay was carried out using the improved assay of RE et al., which is based on the oxidation of ABTS with potassium persulfate leading to ($ABTS^{\bullet+}$).

2.3.2 Antimicrobial assessment

Antibacterial Activity

In this method, paper disc impregnated with compounds dissolved in solvent DMF at concentrations 25, 50 and 100μg mL^{-1}. Then the disc impregnated with the solution was placed on the surface of the media inoculated with the bacterial strain. The plates were incubated at 35°C for 24 hours for bacterial cultures. After incubation, the zones inhibition around the disc were observed. Each testing is done in triplicate. Ciprofloxacin at conc. 50μg mL^{-1} was used as standard drug for antibacterial activity. Results were interpreted in terms of diameter (mm) of zone of inhibition. The % Activity Index for the complex was calculated by the formula as under:

$$\%\ \text{Activity Index} = \frac{\text{Zone of inhibition by test compound (diameter)}}{\text{Zone of inhibition by standard (diameter)}} \times 100$$

Antifungal activity

Antifungal activity of synthesized compounds was tested on fungal strains: *A. niger*, *C. albicans* using disc diffusion method. In the disc-diffusion method, disc impregnated with compounds dissolved in solvent DMF at concentrations 25, 50 and 100 μg mL^{-1} were spread over microorganism culture in nutrient agar medium. The plates were incubated at 25°C for 48 hours for fungal strains. After incubation the growth inhibiting zones around the disc was observed. Growth inhibiting zone indicates that the compounds inhibit growth of microorganism. Each experiment is done in triplicate. Griseofulvin at concentration 50 μgmL^{-1} was used as standard drug for antifungal activity. Results were interpreted in terms of diameter (mm) of zone of inhibition. The percentage inhibition was calculated by the following equation.

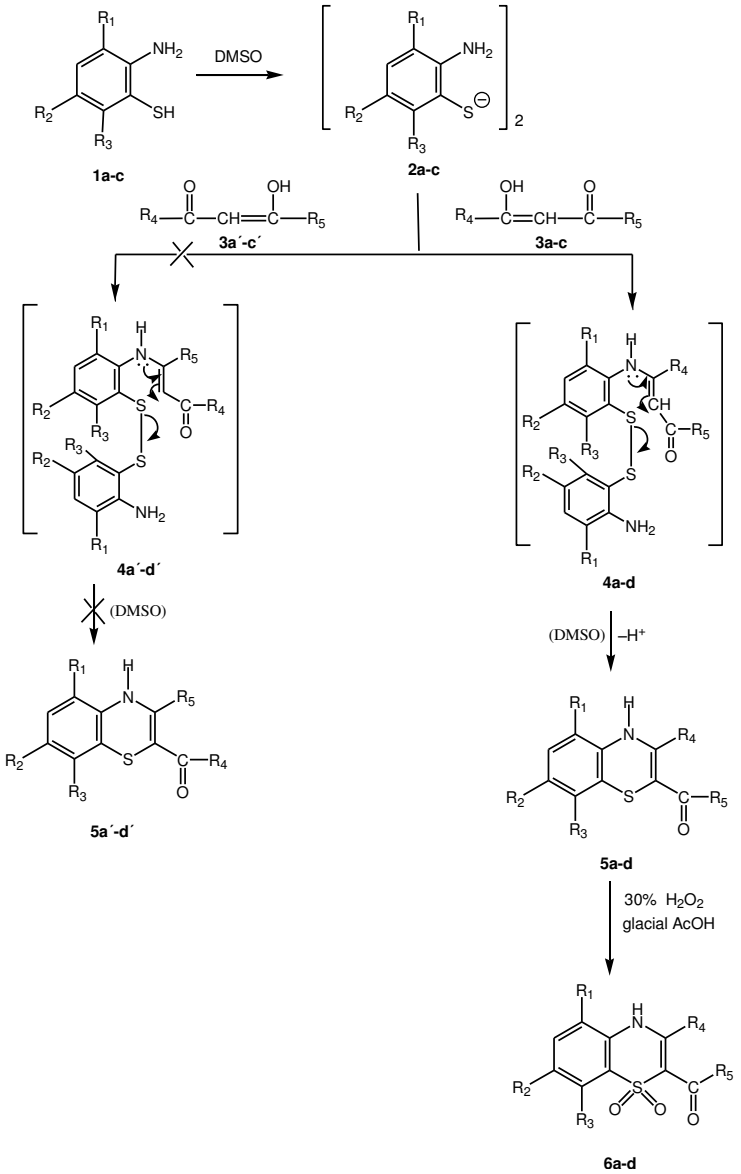
$$\%\ \text{Inhibition} = (C–T)\ 100/C$$

Where, C and T are the diameters of the fungal colony in the control and the test plates, respectively.

Minimum Inhibitory Concentrations

Minimum inhibitory concentrations (MICs) are defined as the lowest concentration of antimicrobials that inhibit the visible

growth of a microorganism after overnight incubation at 37°C. Determination of the MIC is a semi quantitative test[21-22], which gives an approximate idea of the least concentration of an antimicrobial (test) solution needed to parent microbial growth. The MIC was determined by the liquid dilution method. Two gram positive bacteria (*Staphylococcus aureus* and *Bacillus subtilis*) and two gram negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*) were used as quality control strains. For the antifungal activities of the compounds *Candida albicans* and *Aspergillus niger* were tested. Ciprofloxacin and Griseofulvin were used as standard antibacterial and antifungal agents. The stock solutions of test compounds with 1 to 20 µg/mL concentrations were prepared with aqueous methanol. Inoculums of the overnight culture were prepared. In a series of tubes, 1 mL each of stock solutions of test compound with different concentrations was taken and 0.4 mL of the inoculums was added to each tube. Further 4.0 mL of sterile water was added to each of the test tubes. These test tubes were incubated for 22-24 hours and observed for the presence of turbidity. The absorbance of the suspension of the inoculums was observed with spectrophotometer at 555 nm. The end result of the test was the minimum concentration of antimicrobial (test) solutions, which gave clear solution, i.e. no visual growth.



5a, 6a: R_1 = Cl; R_2 = Cl; R_3 = OCH_3; R_4 = R_5 = CH_2CH_3
5b, 6b: R_1 = Cl; R_2 = H; R_3 = NO_2; R_4 = R_5 = CH_2CH_3
5c, 6c: R_1 = F; R_2 = Br; R_3 = H; R_4 = CH_2CH_3; R_5 = OCH_3
5d, 6d : R_1 = F; R_2 = Br; R_3 = H; R_4 = CH_3; R_5 = $OCH(CH_3)_2$

Scheme 1 : Synthesis of 4*H*-1,4-benzothiazines **5a-d**,and their sulfone derivatives**6a-d.**

3. RESULTS AND DISCUSSION

The starting substituted 2-aminobenzenethiols **1a-c** (Scheme-1) were prepared by two different methods, first method involved the condensation of substituted arylamines (having occupied para position) with sulfur monochloride which in turn produced the Herz compound (thiazothiolium chloride) which on alkaline hydrolysis produced sodium salt of the corresponding 2-aminobenzenethiol **1a-b**, while in other method 2-aminobenzenethiols were synthesized by alkaline hydrolysis of corresponding 2-aminobenzothiazoles, the thiazole to prepare 2-aminobenzenethiol **1c** was prepared by the cyclization of substituted phenylthiourea. The phenylthiourea derivatives were obtained by the reaction of ammoniumthiocyanate with substituted anilines.

A mixture of 2-aminobenzenethiols **1a-c** and β-diketone**/**β-ketoester **3a-c** was heated under reflux conditions in DMSO, which led to condensation and oxidative cyclization. Oxidation of 2-aminobenzenethiols produced bis-(2-aminophenyl) disulfide **4a-d**, which in turn underwent cyclization to form 4*H*-1,4-benzothiazines **5a-d** by Scission of a sulfur-sulfur bond. This cleavage is due to high reactivity of the α-position of the enaminoketone system towards nucleophillic attack. Compounds **5a-d** were converted into their corresponding sulfones **6a-d** by treatment with 30% hydrogen peroxide in glacial acetic acid.

The structures proposed to the synthesized compounds are well supported by spectroscopic data and elemental analysis. In the IR spectra of compounds **5a-d**, a single peak is seen in the region of 3370-3245 cm^{-1} due to NH stretching vibration. These compounds also exhibit a band at 1650-1620 cm^{-1} due to C=O stretching vibrations. A slight shift, towards higher frequencies is observed for sulfone derivatives **6a-d** due to an increased electron-accepting ability of sulfones compared with the parent system. Compounds **6a-d** exhibit intense peaks in the regions of 1380-1249 cm^{-1}, 1178-1140 cm^{-1} and 570-530 cm^{-1}, which can be ascribed to vibrations of the sulfonyl group. The signals for C-S stretching vibrations in the region of 1085-1067 cm^{-1} are also observed in the IR spectra of compounds **6a-d.** The given structures of products **5a-d**, and **6a-d** are fully consistent with their ^{1}H NMR spectra. A multiplet in the region of δ 7.92-6.36 ppm is due to the the presence of aromatic protons in all compounds **5a-d**, and **6a-d**. A singlet in the region δ 8.93-8.46 ppm can be ascribed to the NH function. The given compounds **5a-d**, and **6a-d** are also fully consistent with their ^{13}C NMR spectra. Spectral and chemical analysis resultsare shown in **Tables 1-8.**

The synthesized compounds were also screened for antioxidant and antimicrobial activities.The synthesized compounds were screened for antioxidant activity by 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging assay and 2,2-azinobis(3-ethylbenzothiazoline-6-sulfonic acid) ($ABTS^{\bullet+}$) radical cation decolorization assay.The results are tabulated in **Tables 9 and 10.**

All the compounds tested against for their *in vitro* antibacterial activity against the four strains of bacteria (two gram negative *E. coli*, *Pseudomonas aeruginosa* and two gram positive *Bacillus subtilis*, *Staphylococcus aureus*) and antifungal activity against the two strains of fungi (*C. albicans* and *A. niger*). The activity indices of tested compounds against certain bacteria and fungi were calculated and the results are tabulated in **Tables 11 and 12.** The antibacterial and antifungal activity increases with increase in concentration of test compounds.

Table 1: Physical and analytical data of 4*H*-1,4-benzothiazines and their sufone derivatives **5a-d** and **6a-d.**

Compounds	Molecular formula	m.p. (°C)	Yield (%)	% Found (Calcd.)		
				C	H	N
5a	$C_{14}H_{15}NO_2SCl_2$	82	48	50.64 (50.60)	4.57 (4.52)	4.27 (4.22)
5b	$C_{13}H_{13}N_2O_3SCl$	105	72	49.96 (49.92)	4.19 (4.16)	8.92 (8.96)
5c	$C_{12}H_{11}NO_2SBrF$	88	64	43.29 (43.24)	3.35 (3.30)	4.26 (4.20)
5d	$C_{13}H_{13}NO_2SBrF$	68	66	44.91 (44.96)	3.71 (3.75)	4.09 (4.03)
6a	$C_{14}H_{15}NO_4SCl_2$	215	50	46.19 (46.15)	4.16 (4.12)	3.89 (3.85)
6b	$C_{13}H_{13}N_2O_5SCl$	295	48	45.23 (45.28)	3.79 (3.77)	8.18 (8.13)
6c	$C_{12}H_{11}NO_4SBrF$	240	66	39.49 (39.45)	3.05 (3.01)	3.87 (3.84)
6d	$C_{13}H_{13}NO_4SBrF$	160	52	41.19 (41.16)	3.47 (3.43)	3.63 (3.69)

Table 2: Infrared spectral data of substituted 4*H*-1,4-benzothiazines **5a-d** (in cm^{-1}).

Compounds	A	B	C	D	E	F	G	H
5a	3370	1620	1250 1040	760	1455 1330	2915	-	-
5b	3335	1650	-	780	1410 1325	2900	-	-
5c	3330	1635	1260 1045	-	1420 1340	2890	1260	650
5d	3245	1645	1245 1040	-	1450 1330	2920	1255	645

A = N–H stretching vibrations.
B = C=O stretching vibrations.
C = C–O–C Asymmetric and symmetric vibrations.
D = C-Cl stretching vibrations.
E = C-H deformation vibrations of CH_3 group.
F = C–H stretching vibrations in CH_3
G = C–F stretching vibrations.
H= C–Br stretching vibrations.

Table 3: ^{1}H NMR spectral data of substituted 4*H*-1,4-benzothiazines **5a-d.**

Compounds	δ (in ppm)	No. of Hydrogen	Multiplicity	Assignment
5a	8.82	1	Singlet	NH proton
	7.89-6.88	1	Singlet	Aromatic proton
	3.79	3	Singlet	OCH_3 protons at C_8
	2.06	2	Quartet	CH_2 of C_2H_5 at C_3
	1.04	3	Triplet	CH_3 of C_2H_5 at C_3
	2.95	2	Quartet	CH_2 of COC_2H_5 at C_2
	1.11	3	Triplet	CH_3 of COC_2H_5 at C_2
5b	8.93	1	Singlet	NH proton
	7.39-6.58	2	Multiplet	Aromatic protons
	2.02	2	Quartet	CH_2 of C_2H_5 at C_3
	1.01	3	Triplet	CH_3 of C_2H_5 at C_3
	2.94	2	Quartet	CH_2 of COC_2H_5 at C_2
	1.16	3	Triplet	CH_3 of COC_2H_5 at C_2
5c	8.84	1	Singlet	NH proton
	7.76-6.71	2	Multiplet	Aromatic protons
	2.05	2	Quartet	CH_2 of C_2H_5 at C_3
	1.09	3	Triplet	CH_3 of C_2H_5 at C_3
	3.78	3	Singlet	CH_3 of $COOCH_3$ at C_2
5d	8.46	1	Singlet	NH proton
	7.48-6.89	2	Multiplet	Aromatic protons
	1.74	3	Singlet	CH_3 protons at C_3
	4.36	1	Heptet	CH proton of $COOCH(CH_3)_2$ at C_2
	1.39	6	Doublet	CH_3 proton of $COOCH(CH_3)_2$ at C_2

Table 4 ^{13}C NMR spectral data of substituted 4*H*-1,4-benzothiazines **5a-d.**

Compounds	13C NMR δ (in ppm)
5a	113.7 (C-2), 140.0 (C-3), 117.4 (C-5), 131.4 (C-6), 122.4 (C-7), 127.6 (C-8), 24.8 (CH2 of C2H5 at C-3), 9.1 (CH3 of C2H5 at C-3), 195.9 (C=O at C-2), 29.7 (CH2 of COC2H5 at C-2), 7.8 (CH3 of COC2H5 at C-2), 56.5 (OCH3 at C-8)
5b	104.3 (C-2), 134.7 (C-3), 112.4 (C-5), 139.1 (C-6), 115.9 (C-7), 124.4 (C-8), 27.1 (CH2 of C2H5 at C-3), 9.1 (CH3 of C2H5 at C-3), 165.9 (C=O at C-2), 30.1 (CH2 of COC2H5 at C-2), 7.3 (CH3 of COC2H5 at C-2)
5c	108.6 (C-2), 141.4 (C-3), 122.3 (C-5), 125.4 (C-6), 121.4 (C-7), 130.7 (C-8), 25.1 (CH2 of C2H5 at C-3), 8.3 (CH3 of C2H5 at C-3), 194.7 (C=O at C-2), 56.7 (CH3 of COOCH3 at C-2)
5d	109.3 (C-2), 137.3 (C-3), 111.2 (C-5), 128.7 (C-6), 119.2 (C-7), 144.6 (C-8), 16.7 (CH3 at C-3), 168.9 (C=O at C-2), 68.3 (CH of COOCH(CH3)2 at C-2), 22.0 (CH3 of COOCH(CH3)2 at C-2)

Table 5: Characteristic vibrations of the sulfonyl group in the 4*H*-1,4-benzothiazine sulfones **6a-d** (in cm^{-1}).

Compounds	ν_{sym} (SO_2)	$\nu_{bending}$ (SO_2)	ν_{asym} (SO_2)
	KBr	KBr	KBr
6a	1166 1157	560 530	1338 1285 1249
6b	1165 1155	565 545	1380 1278 1260
6c	1178 1150	560 535	1345 1280 1250
6d	1155 1140	570 542	1375 1285 1260

Table 6: Infrared spectral data of substituted 4*H*-1,4-benzothiazines and 4*H*-1,4-benzothiazine sulfones **6a-d** (in KBr*) (in cm^{-1})

Compounds	A	B	C
6a	3370 (3388)	1620 (1638)	1065 (1085)
6b	3335 (3355)	1650 (1665)	1055 (1068)
6c	3330 (3350)	1635 (1650)	1040 (1067)
6d	3245 (3260)	1645 (1665)	1068 (1080)

* The bands given in brackets refer to sulfones

A = N–H stretching vibrations,

B = (C=O) stretching vibrations.

C = ν (C=S) stretching vibrations.

Table 7: ^{1}H NMR spectral data of substituted 4*H*-1,4-benzothiazine sulfones **(6a-d)**

Compounds	δ (in ppm)	No. of Hydrogen	Multiplicity	Assignment
6a	8.76	1	Singlet	NH proton
	7.92-6.53	1	Singlet	Aromatic proton
	3.75	3	Singlet	OCH_3 protons at C_8
	2.02	2	Quartet	CH_2 of C_2H_5 at C_3
	1.01	3	Triplet	CH_3 of C_2H_5 at C_3
	2.88	2	Quartet	CH_2 of COC_2H_5 at C_2
	1.13	3	Triplet	CH_3 of COC_2H_5 at C_2
6b	8.77	1	Singlet	NH proton
	7.48-6.36	2	Multiplet	Aromatic protons
	2.06	2	Quartet	CH_2 of C_2H_5 at C_3
	1.10	3	Triplet	CH_3 of C_2H_5 at C_3
	2.88	2	Quartet	CH_2 of COC_2H_5 at C_2
	1.12	3	Triplet	CH_3 of COC_2H_5 at C_2
6c	8.75	1	Singlet	NH proton
	7.68-6.58	2	Multiplet	Aromatic protons
	2.03	2	Quartet	CH_2 of C_2H_5 at C_3
	1.05	3	Triplet	CH_3 of C_2H_5 at C_3
	3.73	3	Singlet	CH_3 of $COOCH_3$ at C_2
6d	8.53	1	Singlet	NH proton
	7.54-6.48	2	Multiplet	Aromatic protons
	1.88	3	Singlet	CH_3 protons at C_3
	4.39	1	Heptet	CH proton of $COOCH(CH_3)_2$ at C_2
	1.28	6	Doublet	CH_3 proton of $COOCH(CH_3)_2$ at C_2

Table 8: ^{13}C NMR spectral data of substituted 4*H*-1,4-benzothiazine sulfones **6a-d.**

Compounds	^{13}C NMR δ (in ppm)
6a	113.9 (C-2), 141.1 (C-3), 116.8 (C-5), 130.2 (C-6), 122.7 (C-7), 126.9 (C-8), 25.1 (CH_2 of C_2H_5 at C-3), 9.3 (CH_3 of C_2H_5 at C-3), 196.3 (C=O at C-2), 28.8 (CH_2 of COC_2H_5 at C-2), 7.5 (CH_3 of COC_2H_5 at C-2), 55.6 (OCH_3 at C-8)
6b	105.1 (C-2), 133.9 (C-3), 113.0 (C-5), 139.7 (C-6), 116.1 (C-7), 123.9 (C-8), 27.6 (CH_2 of C_2H_5 at C-3), 9.1 (CH_3 of C_2H_5 at C-3), 166.2 (C=O at C-2), 30.7 (CH_2 of COC_2H_5 at C-2), 7.8 (CH_3 of COC_2H_5 at C-2)
6c	107.9 (C-2), 142.1 (C-3), 122.8 (C-5), 124.8 (C-6), 121.8 (C-7), 131.0 (C-8), 25.6 (CH_2 of C_2H_5 at C-3), 8.7 (CH_3 of C_2H_5 at C-3), 195.4 (C=O at C-2), 56.1 (CH_3 of $COOCH_3$ at C-2)
6d	110.0 (C-2), 136.7 (C-3), 111.9 (C-5), 127.9 (C-6), 120.1 (C-7), 144.0 (C-8), 16.9 (CH_3 at C-3), 167.7 (C=O at C-2), 69.2 (CH of $COOCH(CH_3)_2$ at C-2), 22.6 (CH_3 of $COOCH(CH_3)_2$ at C-2)

Table 9: Antioxidant activity of synthesized benzothiazines **5a-d.**

Compounds	DPPH% Inhibitory (1 mg/mL)	$ABTS^{\cdot+}$ activity at different time intervals				
		0 min.	1 min.	2 min.	4 min.	6 min.
5a	64.82±1.07	0.698	0.059	0.047	0.039	0.031
5b	25.24±0.06	0.689	0.642	0.610	0.413	0.400
5c	59.14±1.16	0.685	0.172	0.101	0.100	0.093
5d	44.57±1.09	0.699	0.092	0.070	0.062	0.009
Ascorbic acid	-	0.694	0.040	0.003	0.003	0.003

Table 10: Antioxidant activity of synthesized sulfones derivatives **6a-d.**

Compounds	DPPH% Inhibitory (1 mg/mL)	$ABTS^{\cdot+}$ activity at different time intervals				
		0 min.	1 min.	2 min.	4 min.	6 min.
6a	62.44±0.08	0.684	0.312	0.269	0.134	0.213
6b	49.14±0.05	0.695	0.170	0.150	0.099	0.070
6c	53.45±1.24	0.692	0.111	0.089	0.056	0.034
6d	29.24±1.07	0.699	0.549	0.499	0.412	0.329
Ascorbic acid	-	0.694	0.040	0.003	0.003	0.003

Table 11 Antimicrobial assessment of 4*H*-1,4-benzothiazines **5a-d**.

Compounds	*E. coli*		*B. subtilis*		*P. aeruginosa*		*S. aureus*		*C. albicans*		*A. niger*	
	MIC (μg/mL) of bacterial strain	*%AI (100 μg/mL)*	MIC (μg/mL) of bacterial strain	*%AI (100 μg/mL)*	MIC (μg/mL) of bacterial strain	*%AI (100 μg/mL)*	MIC (μg/mL) of bacterial strain	*%AI (100 μg/mL)*	MIC (μg/mL) of bacterial strain	*% I (100 μg/mL)*	MIC (μg/mL) of bacterial strain	*% I (100 μg/mL)*
5a	9.11±0.18	67	14.10±0.12	61	10.36±0.13	73	11.24±0.21	69	10.67±0.42	64	9.26±0.14	50
5b	10.96±0.18	68	11.43±0.25	59	10.66±0.13	68	11.68±0.23	59	14.26±0.33	69	11.23±0.24	54
5c	11.11±0.22	69	14.62±0.18	63	9.99±0.14	67	10.87±0.18	53	11.16±0.35	72	8.67±0.13	53
5d	13.24±0.19	76	14.44±0.16	69	12.26±0.18	59	13.74±0.19	56	16.20±0.23	70	11.24±0.16	57
Ciprofloxacin	04.10±0.10	100	04.90±0.13	100	03.85±0.15	100	04.90±0.11	100	-	-	-	-
Griseofulvin	-	-	-	-	-	-	-	-	03.10±0.80	100	04.80±0.10	100

MIC:Minimum Inhibitory Concentration; AI: Activity Index; I: Inhibition

Table 12: Antimicrobial assessment of sulfone derivatives **6a-d**.

Compounds	*E. coli*		*B. subtilis*		*P. aeruginosa*		*S. aureus*		*C. albicans*		*A. niger*	
	MIC (μg/mL) of bacterial strain	*%AI (100 μg/mL)*	MIC (μg/mL) of bacterial strain	*%AI (100 μg/mL)*	MIC (μg/mL) of bacterial strain	*%AI (100 μg/mL)*	MIC (μg/mL) of bacterial strain	*%AI (100 μg/mL)*	MIC (μg/mL) of bacterial strain	*% I (100 μg/mL)*	MIC (μg/mL) of bacterial strain	*% I (100 μg/mL)*
6a	12.13±0.14	56	12.42±0.12	63	12.02±0.13	78	11.67±0.23	70	13.67±0.16	68	14.55±0.19	52
6b	14.66±0.16	63	15.71±0.13	61	13.22±0.11	68	14.36±0.19	60	16.72±0.62	70	14.67±0.14	57
6c	10.39±0.15	74	10.03±0.18	54	10.23±0.22	73	11.63±0.17	60	12.13±0.66	72	16.88±0.28	53
6d	10.93±0.18	64	11.48±0.21	53	10.62±0.13	70	15.44±0.23	63	11.73±0.28	69	16.78±0.24	54
Ciprofloxacin	04.10±0.10	100	04.90±0.13	100	03.85±0.15	100	04.90±0.11	100	-	-	-	-
Griseofulvin	-	-	-	-	-	-	-	-	03.10±0.80	100	04.80±0.10	100

MIC: Minimum Inhibitory Concentration; AI: Activity Index; I: Inhibition

4. CONCLUSIONS

In general the presence of electron withdrawing group on the aromatic ring increases the antimicrobial activities of tested compound compared to compounds having electron donating groups. All the synthesized compounds were evaluated for their antioxidant, antibacterial and antifungal activity and all these have shown moderate to higher activity against the test assay and microbes.

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