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Synthesis and antibacterial activity of some substituted 2-phenyl benzothiazole

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Abstract

Discovery and development of effective as well as safe drugs has brought a progressive era in human healthcare that is accompanied by drug resistant bacterial strains. So, there is constant need of new antibacterial agent having novel mechanism to act against the harmful pathogens. The present study deals with antimicrobial evaluation of some substituted 2-phenyl-benzothiazole were synthesized by condensing substituted benzoic acid with 2-amino thiophenol in the presence of phosphoric acid. Structures of all the compounds were characterized by spectral and elemental analysis. All the novel synthesized compounds were screened for antibacterial activity against strains of three gram negative and gram positive microorganism. It was also found that compounds 1, 4, 6 and 7 showed very good antibacterial activity whereas the other entire compound showed mild to moderate antibacterial activity as compared to standard drug.

Keywords: Antimicrobial evaluation, Drug resistant bacterial strains, Gram negative microorganism

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Introduction

The raising prevalence of multidrug resistant bacteria needs the constant invention of innovative antibacterial agent to counter balance them.[1-4] On the basis of exhaustive literature review it has been found that benzothiazole nucleolus posses good potential to act as antibacterial agent. [5-7] Compounds containing 2-substituted benzothiazole moiety have shown a variety of useful pharmacological actions and many of these have gained very wide importance in research.[8-11] So in present study, some substituted 2-phenyl-benzothiazole were synthesized and subjected to antimicrobial evaluation.

Materials and Methods

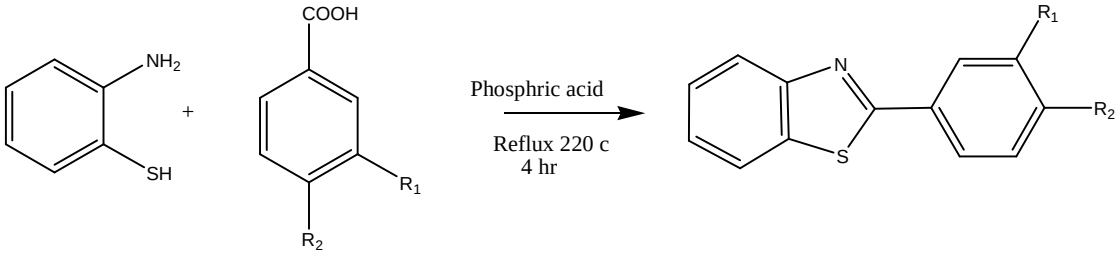
Experimental

Chemicals and solvents were of reagent grade and used without further purification. Melting points was determined by open capillary method and are uncorrected. All the reactions were monitored using Thin Layer Chromatography (TLC) in which the glass plates coated with Silica Gel G as stationary phase were used. The TLC plates were developed in Iodine Chamber unless otherwise mentioned. The infrared spectra were recorded using KBr as the medium, using JASCO FT-IR-6100 model. The proton NMR spectra were measured at CSMCRI, Bhavanagar. The mass spectra were recorded at Panjab University, Chandigarh.

Experimental Methods

General procedure for preparation of Substituted 2-Phenyl Benzothiazole

Equimolar amount of substituted benzoic acid and *o*-aminothiophenol were added to 15 g of polyphosphoric acid and refluxed for 4hr at 220 ^{0} C. The reaction mixture was cooled and poured in ice cold 10%sodium carbonate solution. The precipitate was filtered and recrystallised from methanol (90%). [12-32] Physical characterization of the data is described in table 1 and spectral data is described in table 2.



Compounds	R_1	R_2
Comp-1	NH_2	H
Comp-2	Cl	H
Comp-3	Br	H
Comp-4	NO_2	H
Comp-5	H	Cl
Comp-6	H	Br
Comp-7	H	NO_2

Table 1:- Physical data of synthesized compounds

Compounds	Melting Point	R_f value	Molecular weight	Molecular Formula	Percentage yield
Comp-1	121-123^{0}c	0.86	228	$C_{13}H_{12}N_2S$	70.3
Comp-2	107-109^{0}c	0.87	263	$C_{13}H_7NCl_2F$	63.1
Comp-3	113-115^{0}c	0.92	352	$C_{17}H_{16}N_2SCl_2$	58.2
Comp-4	113-115^{0}c	0.89	430	$C_{17}H_{16}N_2SCl_2Br$	69
Comp-5	105-107^{0}c	0.62	318	$C_{14}H_8N_2S_2O_3$	72.2
Comp-6	179-182^{0}c	0.50	286	$C_{14}H_{10}N_2S_2O$	38.1
Comp-7	137-140^{0}c	0.52	433	$C_{21}H_{16}N_3SCl_2F$	39

Table 2. Structural elucidation data of the synthesized compounds

Comps	IR spectra data $^{cm-1}$	Mass	UV
1	3133.44 (Ar C-H), 1402.1(C=C),1652.88 (C=N),1558.38 (C-C),1320.18 (C-N),3534.31(N-H),	226, 210, 149, 134, 76, 69, 57	230
2	3152.43, 1420.15, 1642.27, 1550.17, 753.15,	264, 210, 191,136, 108, 82, 76, 55	340
3	2917.13, 1507.27, 1314.42, 757.01, 1473.51	352, 282, 256, 210, 178, 123, 76	310
4	2924.85, 1561.27, 1333.68, 686.61, 1646.13, 600.78.	380, 382	305
5	3117.72, 1419.51, 1687.66, 1607.56, 1541.9	318, 280, 241, 194, 167, 151, 137, 105, 77, 65	259
6	2974.03, 1607.56 , 1705.92 , 1318.25, 1625.88	288, 209, 171, 137, 120, 108, 77, 69	290
7	2958.60, 1278.72, 1523.66, 1718.46, 1349.11	511, 509	292

Structural Elucidation

Structural elucidation of the synthesized compound was done by means of IR, NMR, and Mass spectroscopy.

Compound- 1

^{1}NMR ($CDCl_3$) δ ppm: 4 (2H, m, NH_2), 6.5-7.2 (4H, m, Aryl- H), 7.5-8.2 (4H, m, 2-benzothiazole)

Antibacterial Evaluation

Antibacterial activity of synthesized compounds was evaluated against gram positive bacteria like *Staphylococcus aureus* (MTCC 737), *Bacillus cereus* (MTCC 430) and Gram negative bacteria *Klebsiella pneumoniae* (MTCC 109), *Escherichia coli* (MTCC 1687).[33-35] Broth and slants of master cultures were prepared aseptically from concentrated culture and incubated for 24 hrs at 37ºC ± 1ºC. Stock solution of 1000 µg/ml was prepared in 20 % v/v water in DMSO. Using the stock solution, 600 µg/ml, 400 µg/ml, 200µg/ml and 150 µg/ml solutions were prepared for assay. Ciprofloxacin was used. 20 % v/v WFI in DMSO was used as a control. Cup-plate agar diffusion method was used to for Antimicrobial screening of the synthesized compound which was interpreted by mean diameter of inhibition zone in mm

Results and Discussion

The results of antimicrobial evaluation suggest that all the compounds have very good potential to act as antibacterial agents. Compound 1, 7, 6, 4 showed very good activities against the entire test microorganism. All synthesized compounds are more active against gram positive microorganism as compared to gram negative one. Compound 7 has highest antibacterial activity against all the test microorganisms. The zone inhibition is described in table 3 and 4.

Table 3. Zone of Inhibition of the Synthesized Compounds against test gram positive Microorganism

	S.aureus				*B.cerus*				*E .fecalis*			
	150 µg/well	200 µg/well	400 µg/well	600 µg/well	150 µg/well	200 µg/well	400 µg/well	600 µg/well	150 µg/well	200 µg/well	400 µg/well	600 µg/well
STD	23.20 ± 0.72	31.03± 0.84	35.33 ± 0.70	39.10 ± 0.95	33.10 ±1.05	36.67 ± 0.61	43.00 ± 0.92	54.87 ± 0.76	16.40 ± 0.40	18.53 ± 0.50	24.73 ± 0.70	30.67 ± 0.61
1	9.87 ± 1.21	11.70 ± 0.75	12.87± 0.70	13.70 ± 0.95	8.20 ± 0.20	12.53 ± 0.61	13.07 ± 0.31	16.13 ± 0.42	8.40 ± 0.40	10.67 ± 0.61	11.73 ± 0.61	12.67 ± 0.23
2	5.67 ± 1.50	8.17 ±1.17	9.27 ± 0.70	11.10 ± 0.95	6.40 ± 0.34	8.33 ± 0.42	8.40 ± 0.40	10.67 ± 0.61	1.93 ± 0.31	4.60 ± 0.20	8.20 ± 0.20	10.40 ± 0.35
3	4.10 ± 0.98	4.90 ± 1.08	5.33 ± 0.70	5.83 ± 0.95	4.40 ± 0.40	5.80 ± 0.20	6.33 ± 0.31	10.73 ± 0.81	2.40 ± 0.20	3.40 ± 0.20	6.20 ± 0.20	8.47 ± 0.42
4	7.33 ± 1.03	11.70 ± 0.75	13.40 ± 0.72	14.63 ± 0.95	4.46 ± 0.41	4.73 ± 0.31	6.40 ± 0.40	10.40 ± 0.40	4.33 ± 0.31	6.73 ± 0.31	9.93 ± 0.31	12.47 ± 0.42
5	6.93 ± 1.03	7.37 ± 0.78	11.47 ± 0.72	15.30 ± 0.95	4.33 ± 0.30	7.40 ± 0.20	8.33 ± 0.31	12.33 ± 0.31	2.33 ± 0.31	6.20 ± 0.20	8.33 ± 0.42	10.47 ± 0.42
6	9.93 ± 1.03	12.17±1 .17	15.27 ± 0.72	17.10 ±0.95	8.53 ± 0.11	10.33 ± 0.31	16.40 ± 0.40	20.80 ± 0.40	12.53 ± 0.61	12.80 ± 0.40	14.47 ± 0.42	16.27 ± 0.31
7	23.93 ± 1.03	28.23± 1.86	31.07 ± 0.72	32.90 ± 0.95	14.13 ± 0.41	18.33 ± 0.31	20.53 ± 0.61	24.80 ± 0.80	12.47 ± 0.42	13.60 ± 0.35	15.80 ± 0.20	21.00 ± 0.87

Table 4. Zone of Inhibition of the Synthesized Compounds against test gram negative Microorganism

	Ps. Aeruginosa				*Kl. pneumoniae*				*E. coIii*			
	150 µg/ well	200 µg/ well	150 µg/ well	600 µg/ well	150 µg/ well	600 µg/ well	400 µg/ well	600 µg/ well	150 µg/ well	200 µg/ well	400 µg/ well	600 µg/ well
STD	41.07 ± 1.01	42.00 ± 0.20	48.47 ± 0.64	54.67 ± 0.61	30.87 ± 0.76	36.53 ± 0.61	41.20 ± 1.11	42.07 ± 0.31	29.67 ± 1.53	35.60 ± 0.53	43.67 ± 1.53	52.33 ± 1.53
1	0.00	0.00	0.00	4.20 ± 0.0.20	6.07 ± 0.31	8.00 ± 0.20	10.20 ± 0.53	10.53 ± 0.61	0.00	3.23 ± 0.25	5.27 ± 0.31	6.40 ± 0.40
2	0.00	0.00	0.00	2.67 ± 0.31	4.20 ± 0.20	6.30 ± 0.30	9.33 ± 1.30	8.27 ± 0.31	1.87 ± 0.42	3.20 ± 0.20	4.03 ± 0.25	4.67 ± 0.12
3	0.00	0.00	0.00	2.20 ± 0.20	2.30 ± 0.30	2.47 ± 0.31	4.33 ± 0.31	6.33 ± 0.31	0.00	0.00	0.00	2.47 ± 0.06
4	0.00	0.00	0.00	3.00 ± 0.20	3.60 ± 0.20	4.20 ± 0.35	6.20 ± 0.20	12.07 ± 0.31	0.00	0.00	4.27 ± 0.31	5.43 ± 0.38

5	0.00	0.00	0.00	0.00	2.17 ± 0.21	3.53 ± 0.31	4.33 ± 0.31	5.53 ± 0.31	1.60 ± 0.35	0.00	0.00	0.00
6	0.00	0.00	0.00	4.07 ± 0.12	7.47 ± 0.31	8.33 ± 0.42	10.67 ± 0.61	12.27 ± 0.23	1.93 ± 0.12	2.10 ± 0.10	2.73 ± 0.31	3.20 ± 0.20
7	2.20 ± 0.20	2.47 ± 0.12	2.80 ± 0.20	3.00 ± 0.20	7.93 ± 0.31	10.60 ± 0.60	11.87 ± 0.31	16.33 ± 0.31	2.00 ± 0.40	3.33 ± 0.15	4.27 ± 0.31	6.30 ± 0.26

Conclusion

Compound containing benzothiazole ring can act as better antibacterial agent against gram positive micro organism.

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