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SYNTHESIS AND BIOLOGICAL EVALUATION 1, 5-BENZOTHIAZEPINES AS POTENTIAL ANTI INFLAMMATORY AND ANTICONVULSANT ACTIVITY

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Abstract:
1,5-Dihydrobenzothiazepines Are Synthesized . The Compounds Have Been Screened Foranti Inflammatory And Anticonvulsant Activity. 1, 5-Dihydrobenzothiazepines Are Prepared By The Reaction Of 1,3-Diarylprop-2-Enones With O-Aminothiophenol. All The Products Were Tested For Purity By TLC And Characterized By Elemental Analysis ,IR, 1H-NMR, 13C-NMR And Mass Spectral Studies.

Keywords: ***2,****4-Difluoroacetophenone, 1,5-Dihydrobenzothiazepine, 2-Aminothiophenol, Piperidine.*

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INTRODUCTION

The 1,5-benzothiazepines[1] are important nitrogen- and sulfur-containing seven-membered heterocyclic compounds in drug research since they possess diverse bioactivities [2-9]. 1,5-benzothiazepines are the most well-known representatives of benzologs of 1,4-thiazepine **[3]** and one of the three possible benzo-condensed derivatives,viz. 1,4-**[4]**, 4,1- **[5]** and 1,5-benzothiazepines10-13.the 1, 5-benzothiazepine derivatives are of particular interest for lead discovery because they have been found active against different families of argets14-24. The first molecule of 1,5-benzothiazepine used clinically was diltiazem **[6]**, followed by clentiazem **[7]**, for their cardiovascular action. Some of the 1,5-benzothiazepine derivatives were also used clinically for cns disorders which includes thiazesim **[8]**, clothiapine **[9]** and quetiapine **[10]**. Therefore, the 1,5-ihydrobenzothiazepines are useful compounds in the drug research which has stimulated the invention of a wide range of synthetic methods for their preparation and chemical transformations25.

MATERIALS AND METHODS

Procedure for Synthesis of 1, 5-Benzothiazepines

chalcones of p-fluoroacetophenone (1 mill mole) and o-amino thiophenol (1 mill mole) was dissolved in 10 ml of boiling methanol the heat was removed and piperidine (2 drops) was added. after the mixture had cooled to room temperature the additional 10 ml of methanol was added and heated until the slurry was dissolved. Then add 1 ml of

glacial acetic acid and allow the mixture at 250c for overnight. The yellow color crystals benzothiazepine was separated out. This was recrystallised with methanol and filtered. The general structure and physical characterization data will be given below

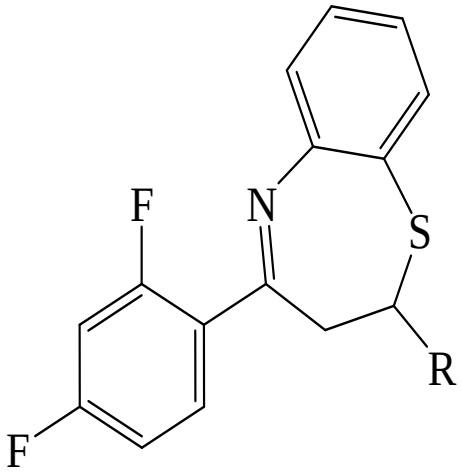


Table 1: Physical Characterization Data of Benzothiazepines (BP_1-BP_{15})

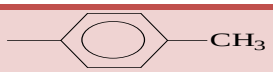
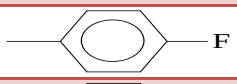
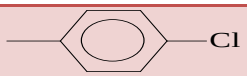
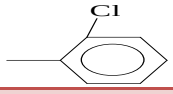
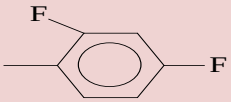
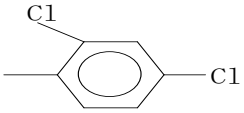
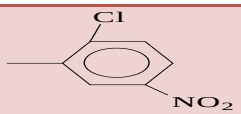
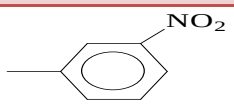
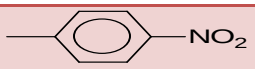
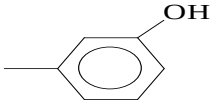
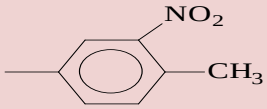
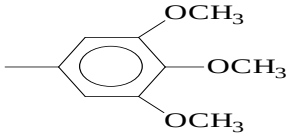
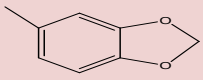
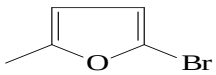
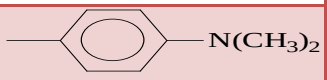
Compound	R	Molecular Formula	Relative Molecular Mass (RMM)	Melting Point (^Oc)	Yield %
BP_1		$C_{22}H_{17}F_2NS$	365	140-143	89
BP_2		$C_{21}H_{14}F_3NS$	369	153-154	89
BP_3		$C_{21}h_{14}clf_2ns$	385	143-145	93
BP_4		$C_{21}h_{14}clf_2ns$	385	120-123	71
BP_5		$C_{21}H_{13}F_4NS$	387	138-141	75
BP_6		$C_{21}H_{13}Cl_2F_2NS$	420	117-120	86
BP_7		$C_{21}h_{13}clf_2n_2o_2s$	430	164-167	77
BP_8		$C_{21}H_{14}F_2N_2O_2S$	396	142-145	82
BP_9		$C_{21}H_{14}F_2N_2O_2S$	396	130-131	89
BP_{10}		$C_{21}H_{15}F_2NOS$	367	226-229	84
BP_{11}		$C_{22}H_{16}F_2N_2O_2S$	410	176-179	94
BP_{12}		$C_{19}H_{12}BRF_2NOS$	441	156	85
BP_{13}		$C_{22}H_{15}F_2NO_2S$	395	156-157	74
BP_{14}		$C_{19}H_{12}BRF_2NOS$	420	132-135	79
BP_{15}		$C_{23}H_{20}F_2N_2S$	394	114-117	88

Table 2: IR Spectral Data (Kbr Disc) of Benzothiazepines (BP_1-BP_{15})

Compound	Position Of Absorption Band (Cm^{-1})
Bp_1	1585 (C=N), 1505 (C=C), 1395 (C-N), 923 (C-F) And 654 (C-S).
Bp_2	1625 (C=N), 1509 (C=C),1399 (C-N), 689 (C-S) And 931 (C-F)
Bp_3	1595 (C=N), 1502 (C=C), 1384 (C-N), 778 (C-Cl), 921 (C-F) And 667 (C-S)
Bp_4	1596 (C=N), 1510 (C=C), 1365 (C-N), 688 (C-S), 923 (C-F) And 805 (C-Cl)
Bp_5	1612 (C=N), 1501 (C=C),1382 (C-N), 689 (C-S), 913 (C-F) And 944 (C-F)
Bp_6	1593 (C=N), 1502 (C=C), 1382 (C-N), 687 (C-S), 925 (C-F) And 805 (C-Cl)
Bp_7	1588 (C=N), 1520 (N=O, Asymmetric), 1505 (C=C), 1382 (C-N), 1340 (N=O, Symmetric), 656 (C-S), 933 (C-F) And 781 (C-Cl)
Bp_8	1580 (C=N), 1522 (N=O, Asymmetric), 1501 (C=C), 1385 (C-N), 1345 (N=O, Symmetric), 924 (C-F) And 689 (C-S)
Bp_9	1586 (C=N), 1515 (N=O, Asymmetric), 1506 (C=C), 1380 (C-N), 1338 (N=O, Symmetric), 925 (C-F) And 713 (C-S)
Bp_{10}	1653 (C=N), 1528 (C-N), 1502 (C=C), 925 (C-F) And 694 (C-S)
Bp_{11}	1642 (C=N), 1548 (N=O, Asymmetric), 1510 (C=C), 1380 (C-N), 1338 (N=O, Symmetric), 927 (C-F) And 668 (C-S)
Bp_{12}	1648 (C=N), 1505 (C=C), 1365 (C-N), 1225 (-O-Ch_3), 923 (C-F) And 678 (C-S)
BP_{13}	1592 (C=N), 1502 (C=C), 1370 (C-N), 1232 (-O-CH_2-O-), 921 (C-F) And 689 (C-S)
BP_{14}	1602 (C=N), 1505 (C=C), 1340 (C-N), 664 (C-S), 933 (C-F) And 790 (C-Br)
BP_{15}	1608 (C=N), 1509 (C=C), 1390 (C-N), 1175 (-N-$(CH_3)_2$), 933 (C-F) And 679 (C-S)

Table 3: ^{1} H NMR Spectral Data of Benzothiazepines (BP_1 – BP_{15})

Compound	Chemical Shift (Δ) In Ppm
BP_1	4.94 (Dd, $J_{2,3a}$ = 5.1 Hz, $J_{2,3b}$ = 12 Hz, 1H, C_2-H), 3.25 (Dd, $J_{3a,3b}$ = 14.4 Hz, $J_{3a,2}$ = 9.9 Hz, 1H, C_3-H-3a), 3.04 (T, $J_{3b,3a}$ = $J_{3b,2}$ = 12.9 Hz, 1H, C_3-H-3b), 2.40 (3H, S, Ar-CH_3), 7.22 (1H, S, Ar-H), 7.61 (3H, M, Ar-H), 7.20-8.10 (7H, Ar-H).
BP_2	5.27 (Dd, $J_{2,3a}$ = 5.1 Hz, $J_{2,3b}$ = 12 Hz, 1H, C_2-H), 3.50 (Dd, $J_{3a,3b}$ = 14.4 Hz, $J_{3a,2}$ = 9.6 Hz, 1H, C_3-H-3a), 2.97 (T, $J_{3b,3a}$ = $J_{3b,2}$ = 12.9 Hz, 1H, C_3-H-3b), 7.05 (1H, S, Ar-H), 7.19 (3H, M, Ar-H), 7.20-8.09 (7H, Ar-H).
BP_3	5.0 (Dd, $J_{2,3a}$ = 5.1 Hz, $J_{2,3b}$ = 12 Hz, 1H, C_2-H), 3.53 (Dd, $J_{3a,3b}$ = 14.4 Hz, $J_{3a,2}$ = 9.9 Hz, 1H, C_3-H-3a), 3.39 (T, $J_{3b,3a}$ = $J_{3b,2}$ = 12.9 Hz, 1H, C_3-H-3b), 7.25 (1H, S, Ar-H), 7.65 (3H, M, Ar-H), 7.22-8.08 (7H, Ar-H).
BP_4	4.89 (Dd, $J_{2,3a}$ = 5.1 Hz, $J_{2,3b}$ = 12 Hz, 1H, C_2-H), 3.43 (Dd, $J_{3a,3b}$ = 14.4 Hz, $J_{3a,2}$ = 9.6 Hz, 1H, C_3-H-3a), 3.36 (T, $J_{3b,3a}$ = $J_{3b,2}$ = 12.9 Hz, 1H, C_3-H-3b), 7.12 (1H, S, Ar-H), 7.72 (3H, M, Ar-H), 6.95-7.60 (7H, Ar-H).
BP_5	5.31 (Dd, $J_{2,3a}$ = 5.1 Hz, $J_{2,3b}$ = 12 Hz, 1H, C_2-H), 3.36 (Dd, $J_{3a,3b}$ = 14.4 Hz, $J_{3a,2}$ = 9.9 Hz, 1H, C_3-H-3a), 2.87 (T, $J_{3b,3a}$ = $J_{3b,2}$ = 12.9 Hz, 1H, C_3-H-3b), 7.08 (1H, S, Ar-H), 7.30 (3H, M, Ar-H), 6.98-8.12 (6H, Ar-H).
BP_6	5.10 (Dd, $J_{2,3a}$ = 5.1 Hz, $J_{2,3b}$ = 12 Hz, 1H, C_2-H), 3.27 (Dd, $J_{3a,3b}$ = 14.4 Hz, $J_{3a,2}$ = 9.6 Hz, 1H, C_3-H-3a), 2.66 (T, $J_{3b,3a}$ = $J_{3b,2}$ = 12.9 Hz, 1H, C_3-H-3b), 7.15 (1H, S, Ar-H), 7.20 (3H, M, Ar-H), 7.05-7.95 (6H, Ar-H).
BP_7	4.32 (Dd, $J_{2,3a}$ = 5.1 Hz, $J_{2,3b}$ = 12 Hz, 1H, C_2-H), 3.74 (Dd, $J_{3a,3b}$ = 14.4 Hz, $J_{3a,2}$ = 9.9 Hz, 1H, C_3-H-3a), 3.51 (T, $J_{3b,3a}$ = $J_{3b,2}$ = 12.9 Hz, 1H, C_3-H-3b), 7.09 (1H, S, Ar-H), 7.12 (3H, M, Ar-H), 6.98-8.10 (6H, Ar-H).
BP_8	5.42 (Dd, $J_{2,3a}$ = 5.1 Hz, $J_{2,3b}$ = 12 Hz, 1H, C_2-H), 3.38 (Dd, $J_{3a,3b}$ = 14.4 Hz, $J_{3a,2}$ = 9.6 Hz, 1H, C_3-H-3a), 2.86 (T, $J_{3b,3a}$ = $J_{3b,2}$ = 12.9 Hz, 1H, C_3-H-3b), 7.30 (1H, S, Ar-H), 7.80 (3H, M, Ar-H), 7.48-8.60 (7H, Ar-H).
BP_9	5.42 (Dd, $J_{2,3a}$ = 5.1 Hz, $J_{2,3b}$ = 12 Hz, 1H, C_2-H), 3.47 (Dd, $J_{3a,3b}$ = 14.4 Hz, $J_{3a,2}$ = 9.7 Hz, 1H, C_3-H-3a), 3.10 (T, $J_{3b,3a}$ = $J_{3b,2}$ = 12.9 Hz, 1H, C_3-H-3b), 7.18 (1H, S, Ar-H), 7.25 (3H, M, Ar-H), 7.25-8.20 (7H, Ar-H).
BP_{10}	3.85 (Dd, $J_{2,3a}$ = 5.1 Hz, $J_{2,3b}$ = 12 Hz, 1H, C_2-H), 3.34 (Dd, $J_{3a,3b}$ = 14.4 Hz, $J_{3a,2}$ = 9.0 Hz, 1H, C_3-H-3a), 2.41 (T, $J_{3b,3a}$ = $J_{3b,2}$ = 12.9 Hz, 1H, C_3-H-3b), 7.25 (1H, S, Ar-H), 7.30 (3H, M, Ar-H), 7.15-7.80 (7H, Ar-H), 6.85 (1H, S, Ar-OH).
BP_{11}	4.16 (Dd, $J_{2,3a}$ = 5.1 Hz, $J_{2,3b}$ = 12 Hz, 1H, C_2-H), 3.23 (Dd, $J_{3a,3b}$ = 14.4 Hz, $J_{3a,2}$ = 9.9 Hz, 1H, C_3-H-3a), 2.53 (T, $J_{3b,3a}$ = $J_{3b,2}$ = 12.9 Hz, 1H, C_3-H-3b), 2.50 (3H, S, Ar-CH_3), 7.30 (1H, S,Ar-H), 6.70 (3H, M, Ar-H), 7.45-8.78 (6, Ar-H)
BP_{12}	3.06 (Dd, $J_{2,3a}$ = 5.3 Hz, $J_{2,3b}$ = 12 Hz, 1H, C_2-H), 2.83 (Dd, $J_{3a,3b}$ = 14.4 Hz, $J_{3a,2}$ = 9.9 Hz, 1H, C_3-H-3a), 2.0 (T, $J_{3b,3a}$ = $J_{3b,2}$ = 12.9 Hz, 1H, C_3-H-3b), 7.22 (1H, S,Ar-H), 6.60 (3H, M, Ar-H), 7.30-7.50 (5H, Ar-H), 3.70 (3H, S, Ar-OCH_3), 3.88 (6H, S, 2xar-OCH_3)
BP_{13}	4.94 (Dd, $J_{2,3a}$ = 5.1 Hz, $J_{2,3b}$ = 12 Hz, 1H, C_2-H), 3.25 (Dd, $J_{3a,3b}$ = 14.4 Hz, $J_{3a,2}$ = 9.1 Hz, 1H, C_3-H-3a), 3.14 (T, $J_{3b,3a}$ = $J_{3b,2}$ = 12.9 Hz, 1H, C_3-H-3b), 7.25 (1H, S,Ar-H), 7.40 (3H, M, Ar-H), 6.10 (2H, S, O-CH_2-O), 7.21-7.85 (6H, Ar-H)
BP_{14}	5.07 (Dd, $J_{2,3a}$ = 5.3 Hz, $J_{2,3b}$ = 12 Hz, 1H, C_2-H), 4.10 (Dd, $J_{3a,3b}$ = 14.4 Hz, $J_{3a,2}$ = 9.2 Hz, 1H, C_3-H-3a), 3.39 (T, $J_{3b,3a}$ = $J_{3b,2}$ = 12.9 Hz, 1H, C_3-H-3b), 7.10 (1H, S,Ar-H), 6.80 (3H, M, Ar-H), 6.80-7.30 (5H, Ar-H)
BP_{15}	4.96 (Dd, $J_{2,3a}$ = 5.3 Hz, $J_{2,3b}$ = 12 Hz, 1H, C_2-H), 3.83 (Dd, $J_{3a,3b}$ = 14.4 Hz, $J_{3a,2}$ = 9.2 Hz, 1H, C_3-H-3a), 3.26 (T, $J_{3b,3a}$ = $J_{3b,2}$ = 12.9 Hz, 1H, C_3-H-3b), 3.20 (6H, S, N-$(CH_3)_2$, 7.20 (1H, S,Ar-H), 7.45 (3H, M, Ar-H), 6.70-8.20 (7H, Ar-H)

Anticonvulsant Activity:

Experimental Animals:

Healthy Swiss albino mice weighing about 25-30 g were used in experiments. Animals were housed in Polypropylene cages maintained under standard conditions (12 hours light / dark cycle; 25 ± 30 c, 45-65 % humidity) and had free access to standard feed and water.

Maximal Electroshock Seizure Test (MES)

Maximal seizures were elicited by a 60Hz alternating current of 50Ma intensity delivered for 0.2 seconds via corneal electrodes. A drop of 0.9% w/v sodium chloride instilled in each eye prior to application of electrodes assured adequate electrical contact. Test solutions of all the compounds were prepared in 1% sodium CMC and animals were dosed intraperitoneally 30 min prior to testing. Abolition of the hind limb tonic extension component of the seizure was defined as protection in the MES test. Animals were divided into varies groups of six each. Group I served as control (vehicle treated, i.p.); Group II served as standard (received Phenytoin sodium 25mg/kg body weight, i.p.), Group III was treated with test compound at 200mg/kg body weight, i.p. respectively. The current was delivered after 30 min. of intraperitonial administration of control and standard. The incidence and duration of HLTE was noted.

Statistical Analysis

The data are expressed as mean + S.E.M. The data were statistically analyzed using one-way analysis of variance (ANOVA), followed by Duncan's multiple range post test and Chi square test. Values of $p < 0.05$ were considered significant.

Table 4: Using One-Way Analysis Of Variance (ANOVA)

S. No	Treatment Group b	Mean± SE (sec)			Recovery	Mortality
		Flexion	THLE	Clonus		
1	Control (0.9% saline)	3.6	6.2	8.4	Dead	100%
2	BP-1	1.3	3.2	8.5	88	50%
3	BP-2	2	4.8	14.2	76	83.33%
4	BP-3	2.5	2.75	12.5	119.2	**0%**
5	BP-4	1.6	3.2	10.3	94	16.66%
6	BP-5	1.25	2.5	17.5	80.7	**0%**
7	BP-6	1.8	2.8	14	86	16.66%
8	BP-7	1.6	7.3	8	62	33.33%
9	BP-8	1.8	7.6	9	65	33.33%
10	BP-9	2	4.3	15	120	33.33%
11	BP-10	1.8	4.8	16	112	33.33%
12	BP-11	1.5	3	7.7	92.3	16.66%
13	BP-12	2	5	9.5	67	83.33%
14	BP-13	2.6	5.8	10	65	83.33%
15	BP-14	0.85	2.7	6.2	57	**0%**
16	BP-15	2	5	9.5	67	83.33%
Standard	Phenytoin Sodiuma	1.2	00	6.75	48.5	0%

a 25 mg/kg b.wt, b 200 mg/kg b.wt, THLE: Tonic Hind Limb Extension and SE: Standard Error

DISCUSSION ON THE RESULTS:

All the newly synthesized compounds Bp-(1-15) were studied for their anticonvulsant The pharmacological data of all the compounds of this series are reported in table 3. The compounds evaluated for their anticonvulsant activity against maximal electric shock induced seizers at a dose 200mg/kg body wt; ip; and found to exhibit substantive anticonvulsant activity. the compounds Bp(1-15) substituted with different moieties at second and fourth positions

of 1,5-benzothiazepine ring. Among the series of compounds tested it was observed that compounds Bp-3(having 4- chloro phenyl group at second position of Benzothiazepines ring), Bp-5(having 2, 4-difluoro phenyl group), Bp- 14(having 32Bromo furfuryl group) and Bp-15(having 4-dimethylamino phenyl group) exhibit maximum degree of anti convulsant activity with 0% mortality. The remaining results were shown in table 2

Anti-Inflammatory Activity:

Carrageenan-Induced Rat Paw Edema Method Was Used To Determine The Anti-Inflammatory Activity Of The Prepared Compounds.

Materials:

Carrageenan Required For Inducing The Inflammation Was Obtained From Hi-Media (Mumbai) Whereas Sodium CMC Was Of Merck Grade And The Required Saline (Core Health Care) Was Purchased From A Local Supplier. Aceclofenac Used As Standard Was Supplied As A Gift Sample By Jagsonpal, New Delhi.

Preparation of Sodium CMC Suspension:

1 G Of Sodium CMC Was Triturated In 100 Ml Of Distilled Water To Give The Required Stock Suspension Of Sodium CMC. This Stock Suspension Was Used For Suspending All The Test Compounds As Well As The Standard Drug.

Preparation of Carrageenan Suspension:

100 Mg Of Carrageenan Powder Was Sprinkled In 10 Ml Of Saline And Set Aside For 1 Hr. Then It Was Mixed With The Help Of A Magnetic Stirrer To Get A Homogenous 1 % Suspension Of Carrageenan.

Experimental Procedure:

Albino Rats Of Either Sex, Weighing Between 150-200 Mg, Supplied By M/S Ghosh Enterprises, Kolkata Were Divided Into Twenty Seven Groups Of Six Animals Each. All These Groups Were Kept For Fasting Overnight And Only Allowed Water *Ad Libitum*.

0.05 Ml Of 1 % Carrageenan Suspension Was Slowly Injected Subcutaneously Into The Sub plantar Region Of The Left Hind Paw To Produce Inflammation In All The Groups. Groups III To XXVII Were Treated With **Benzothiazepines BP_1 To BP_{15}** (10 Mg/Kg). Group I Used As Carrageenan Treated Control Was Given Only 1 % Sodium CMC Gel (1 Ml/Kg) Whereas Group II Received Aceclofenac (2 Mg/Kg). All These Doses Were Administered Orally And The Induced Paw Edema In Each Group Was Measured To Assess The Anti-Inflammatory Activity.[94]

Measurement of Paw Thickness:

The Percent Increase At Each Time Interval Was Determined By Using The Formula: Yt-Yo / Yo X 100

Yt = Paw Thickness At Time T Hours (After Injection),

Yo = Paw Thickness At Time 0 Hours (Before Injection)

The Percent Inhibition Of Paw Oedema Thickness Was Calculated By Using The Formula:

$$\text{Percentage Inhibition} = \left[1 - \frac{Y_t}{Y_c}\right] \text{ X } 100$$

Where Yt= Average Increase In Paw Thickness In Groups Tested With Chalcones And The Standard.

Yc= Average Increase In Paw Thickness In Control

The Results Of Anti-Inflammatory Activity Of Aceclofenac And The Compounds Tested Are Shown In **Tables 5**

Table 5: Percentage Inhibition in Paw Thickness at Various Time Intervals

Compound Code	% Inhibition In Paw Thickness At Various Time Intervals					
	0.5 Hr	**1 Hr**	**2 Hr**	**3 Hr**	**4 Hr**	**6 Hr**
BP--1	10 ± 1*	14 ± 2	47 ± 1	56 ± 2	84 ± 2	**87 ± 1**
BP-2	11 ± 1	15 ± 1	48 ± 2	57 ± 1	85 ± 1**	**88 ± 1**
BP-3	13 ± 1	17 ± 1	50 ± 1**	59 ± 1	87 ± 1	**89 ± 1**
BP-4	12 ± 1	16 ± 2	49 ± 1	58 ± 2	86 ± 2	**89 ± 1**
BP-5	10 ± 1	14 ± 2	46 ± 1	55 ± 1*	84 ± 1**	**86 ± 2***
BP-6	08 ± 1**	13 ± 1*	44 ± 1	54 ± 1	83 ± 1	**84 ± 1**
BP-7	07 ± 1	12 ± 1	43 ± 1	53 ± 2	81 ± 1	**83 ± 2**
BP-8	09 ± 1	14 ± 1	46 ± 2	54 ± 1	84 ± 1	**85 ± 2**
BP-9	15 ± 1	18 ± 2**	51 ± 1	61 ± 2	89 ± 2	**90 ± 2***
BP-10	16 ± 1	18 ± 1	52 ± 1**	62 ± 1	89 ± 1	**90 ± 1**
BP-11	16 ± 1	18 ± 2	52 ± 2	61 ± 1	89 ± 1	**90 ± 1***
BP-12	14 ± 1	18 ± 1	51 ± 2	60 ± 2	88 ± 1	**90 ± 1**
BP-13	04 ± 1*	09 ± 1	41 ± 1	51 ± 1	77 ± 1	**78 ± 2**
BP-14	05 ± 1	10 ± 2*	41 ± 2	52 ± 2*	79 ± 1	**80 ± 1***
BP-15	**04 ± 1**	**08 ± 1**	**40 ± 1**	**50 ± 1**	**76 ± 2****	**76 ± 1**

Values Are Expressed As Mean ± (N=5)

P<0.05, P**<0.01 Compared To Control, Student T-Test*

CONCLUSION

Anti-Inflammatory Activity:

The anti-inflammatory activity of the newly synthesized benzothiazeoines **(bp-1** to **bp-15)** has been evaluated by using Carrageenan-induced rat paw edema method. The results of the evaluation have been viewed by taking aceclofenac as the standard drug.

The results of anti-inflammatory activity revealed that the compounds **bp-1** to **bp-15** exhibited moderate to considerable activity when compared with reference standard aceclofenac, but not at an identical dose level as the standard drug was tested at 2 mg/kg, whereas the benzodiazepines were tested at a dose of 10 mg/kg. Benzodiazepines tested in this present study also showed some degree of anti-inflammatory activity. Some of these compounds were substituted with electron releasing substituent's on the aromatic ring at different positions.

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