IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS)
e-ISSN:2278-3008, p-ISSN:2319-7676. Volume 13, Issue 5 Ver. IV (Sep – Oct 2018), PP 24-29
www.iosrjournals.org

Conventional Synthesis and Characterization of novel Benzothiazole derivatives containing Indole moieties with Anti inflammatory and anti Convulsant Activities.

Srinivasa Murthy.M[1], Aleti Rajareddy[2]
[1]*Vignan Institute of Pharmaceutical Sciences, Department of pharmaceutical, Chemistry, Near Ramoji film city, Deshmukhi-508284*
[2]*Mall Reddy Pharmacy College, Department of pharmaceutical Chemistry Dhulapally, maisammaguda, Sec-bad-500043*
**Corresponding author: A.Rajareddy*

Abstract: *The"(E)-5-chloro-1-((E)-1-((7-chloro-6-fluorobenzo[d]thiazol-2-yl)imino)ethyl)-3-(p-tolylimino) indolin-2-one" was to synthesize, purify, characterize and evaluate the biological activity of newly synthesized structural analogs of Benzothiazole derivatives Indole moieties. All these molecules (**5a-5o**) were characterized by FTIR, H[1]NMR and mass spectral analysis along with physical data. The biological potentials of the newly synthesized compounds are evaluated for their anticonvulsant and anti-inflammatory activities. From anti-inflammatory evaluations, dose level of 200mg/kg of test compounds reported significantly higher activity when compared to dose level of 20 mg/kg. Moreover, compound 5f, 5h, 5k and 5o (200 mg/kg) resulted in similar anti-inflammatory activity when compared with Diclofenac (20 mg/kg). All the compounds were evaluated for their anticonvulsant activity. Three compounds 5e, 5j and 5o showed promising anticonvulsant activities in Maximal Electroshock Seizure test (MES) and phenytoin (dose: 25mg/kg) used as a standard.*

Key Words: *Substituted benzaldehyde, 2-amino benzothioazole, Isatine and - Anti inflammatory and anti Convulsant Activities.*

Date of Submission: 10-10-2018 Date of acceptance: 26-10-2018

I. Introduction:

Heterocyclic compounds containing a ring made up, in addition to carbon atoms, other elements (heteroatoms), most often nitrogen, oxygen, and sulfur, and less frequently phosphorus, boron, and silicon

Although the parent compound, benzothiazole is not widely used, many of its derivatives are found in commercial products or in nature. [1-3].

Thiazole rings are planar and aromatic. Thiazoles are characterized by larger pi-electron delocalization than the corresponding oxazoles and have therefore greater aromaticity. This aromaticity is evidenced by the chemical shift of the ring protons in proton NMR spectroscopy (between 7.27 and 8.77 ppm), clearly indicating a strong diamagnetic ring current. The calculated pi-electron density marks C5 as the primary site for electrophilic substitution, and C2 as the site for nucleophilic substitution. Since most of the benzothiazole derivatives were reported for their diversified activity such as antitumor, antitubercular, antimalarial, anticonvulsant, anthelmintic, analgesic, anti inflammatory and antifungal.

Isatin or 1H-indole-2, 3-dione is an indole derivative. The compound was first obtained by Erdman and Laurent in 1841 as a product from the oxidation of indigo dye by nitric acid and chromic acids. The compound is found in many plants. In recent years, indole derivatives have acquired conspicuous significance due to their wide spectrum of biological activities.

II. Materials And Methods: [4-7]

The synthesized compounds were screened for anthelmentic activities. Fourier Transform IR spectrometer (model Shimadzu 8700) in the range of 400-4000 cm^{-1} Using KBr pellets and values are reported in cm^{-1} and the spectra were interpreted. ^{1}H-NMR spectra were recorded on DPX-200 MHz NMR spectrometer using DMSO-d_6 and chemical shifts (δ) are reported in parts per million down field from internal reference Tetramethylsilane (TMS) and the Spectra were interpreted. Mass spectra were recorded on Mass spectrophotometer (model Shimadzu) by LC- MS and the spectra were interpreted. Precoated Silica gel G plates were used to monitor the progress of reaction as well as to check the purity of the compounds**:** n-Hexane: Ethyl acetate (8:2).

General procedures

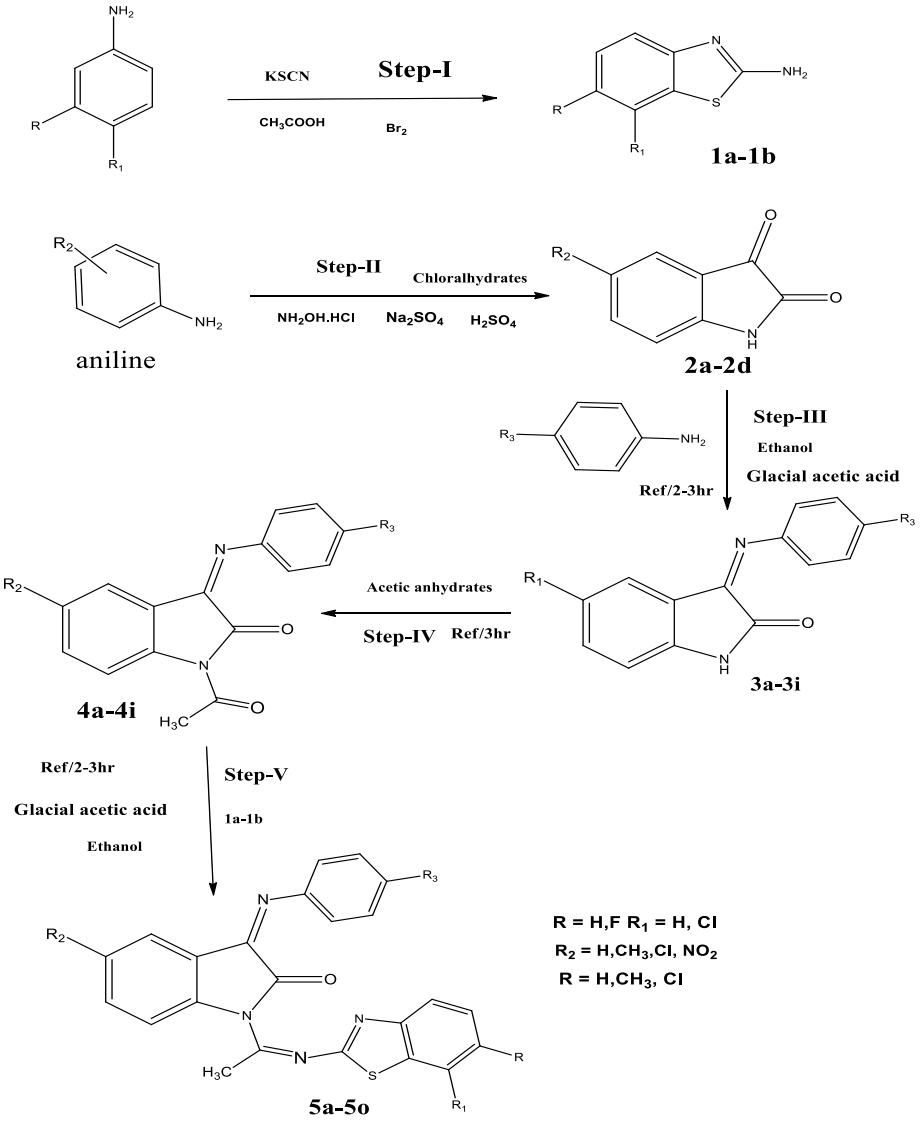
***Step: 1: Preparation of 2-aminobenzothiazole*:**

Aniline (4.6g, 0.05mol) and potassium thiocyanat (3.8g, 0.05mol) were dissolved in absolute ethanol containing 4 ml of con. HCl .To this mixture bromine in glacial acetic acid (6.75ml, 0.125 mol) was added and the reaction mixture was refluxed for 1 hr. Then it was cooled in ice bath. The precipitate obtained was filtered, washed with cold water and dried. The crude product was recrystallized from ethanol.

***Steps 2: Synthesis of substituted Isatin from Aniline*:**

9 gm of Chloral hydrate was taken into the round bottom flask and dissolved in 120 ml water. To that 13 gm of sodium sulphate, a solution of 5.4 gm of Aniline in 30 ml of water containing 5.12 gm of concentrated hydrochloric acid (4.34 ml) to dissolve the amine and solution of 11 gm of hydroxylamine hydrochloride in 50 ml of water were added. Flask was then heated vigorously until the reaction was completed. After it, the solution containing beaker was cooled in running water followed by the filtration of reminder crystallized product with suction pump and air dried.

18.4 gm of concentrated sulphuric acid (10.0 ml) was warmed to 50^0C and 2.5 gm of dry isonitrosoacetanilide was added in such a rate so as to keep the temperature between 60-70^0C but not higher. External cooling was applied at this stage so that the reaction could be carried out more rapidly after the addition of isonitroso compound was finished. The solution was heated to 80^0C and kept at this temperature for about 10 min to complete the reaction. Then the reaction mixture was cooled to room temperature and poured it into ten times its volume of cracked ice. After standing for 90 mints, the final product was filtered with suction pump followed by washing with cold water to remove sulphuric acid and dried in air.



Scheme-I

Step 3: Synthesis of Isatin Schiff's bases (3a-3i)

A mixture of equimolar quantity of substituted aromatic aniline (0.01mol) and Compound 2a-2d was dissolved in 20ml of ethanol, refluxed for 2-3hrs in the presence of few drops of (2ml) glacial acetic acid. The progress of the reaction was monitored by TLC (n-Hexane: EtoAc 7:3). The reaction mixture was cooled to room temperature and keep in refrigerator for overnight to get precipitate. A solid was obtained, which was filtered off and recrystallized from methanol or ethanol to give crystalline solid.

Step-IV: Synthesis of 1-acetyl-3-(phenylimino) indolin-2-one derivatives:

To take 0.005mol of compound (3a-3i, Iastin schiff's base) was taken into the round bottom flask and to it add 5.1ml of acetic anhydride was added. Then whole of the content was of refluxed for about 4hrs and then the solution was poured into beaker contains crushed ice fallowed by the filtration and drying of the product.

Step-V: General procedure: Synthesis of novel 1-((E)-1-(benzo[d]thiazol-2-yl) imino) ethyl)-3-(phenylimino) indolin-2-one (5a-5o)

A mixture of equimolar quantity of substituted N-acetyl Isatin derivatives (0.01mol) and Compound 1a-1b was dissolved in 20ml of ethanol, refluxed for 2-3hrs in the presence of few drops of (2ml) glacial acetic acid. The progress of the reaction was monitored by TLC (n-Hexane: EtoAc 8:2). The reaction mixture was cooled to room temperature and keep in refrigerator for overnight to get precipitate. A solid was obtained, which was filtered off and recrystallized from methanol or ethanol to give crystalline solid.

5a: (E)-1-((E)-1-(benzo[d]thiazol-2-yl) imino) ethyl)-3-(phenylimino) indolin-2-one. M.P. 219–221°C; Mol. formula: $C_{23}H_{16}N_4OS$, yield 78%, IR (ν cm−1): 3143, 3054(C-H *Str*, Ar), 2930, 2891, 2793(C–H *Str*, Aliphatic), 2311 (C-S-C *Str*), 1684(C=O *Str*, Indole), 1588 (C=N *Str*), 1515 (C=CH *Str*), 1431 (C=C *Str*, Ar). ^{1}H-NMR (DMSO) $\delta\delta$ ppm: 8.38-8.27(d, 2H, Ar-H), 8.11-7.88(d, 2H, Ar-H), 7.84-7.77(t, 3H, Ar-H), 7.69-7.67 (d, 2H, Ar-H), 7.55-7.54 (d, 2H, Ar-H), 7.51-7.41 (t, 3H, Ar-H). 3.33(S, 3H, -CH_3); Mass (ESI-MS): m/z 396(M), 397(M + 1, 100%).

5b: (E)-5-chloro-1-((E)-1-(benzo[d]thiazol-2-yl) imino) ethyl)-3-(phenylimino) indolin-2-on. M.P. 213-215°C; Mol. formula: $C_{23}H_{15}N_4OSCl$, yield 82%, IR (ν cm−1): 3037, 2932(C-H *Str*, Ar), 2872(C–H *Str*, Aliphatic), 2346 (C-S-C *Str*), 1721(C=O *Str*, Indole), 1555(C=N *Str*), 1520(C=CH *Str*), 1432 (C=C *Str*, Ar), 771(C-Cl *Str*, Ar). ^{1}H-NMR (DMSO) $\delta\delta$ ppm: 8.37-8.28(t, 3H, Ar-H), 7.88-7.84(t, 3H, Ar-H), 8.10(s, 1H, Ar-H), 7.83-7.68(d, 4H, Ar-H), 7.58-7.57(d, 2H, Ar-H), 7.55-7.51 (d, 2H, Ar-H), 3.39(s, 3H, -CH_3); Mass (ESI-MS): m/z 430(M), 431(M + 1, 100%),432(M + 2, 30%).

5c: (E)-1-((E)-1-(benzo[d]thiazol-2-yl) imino) ethyl)-3-(p-tolylimino) indolin-2-one. M.P. 203–205°C; Mol. formula: $C_{24}H_{18}N_4OS$, yield 77%. IR (ν cm−1): IR (ν cm−1): 3100 (C-H *Str*, Ar), 2987,2882(C–H *Str*, Aliphatic), 2336(C-S-C *Str*), 1705(C=O *Str*, Indole), 1663, 1546(C=N *Str*), 1506(C=CH *Str*), 1459(C=C *Str*, Ar), 797(C-Cl *Str*, Ar), 588(C-F *Str*, Ar). ^{1}H-NMR (DMSO) $\delta\delta$ ppm: 8.57-8.35(d, 4H, Ar-H), 8.06-8.04(d, 4H, Ar-H), 7.94-7.92(t, 2H, Ar-H), 7.82-7.75(t, 2H, Ar-H), 3.31(s, 3H, -CH_3), 1.97-1.94(s, 3H, -CH_3); Mass (ESI-MS): m/z 410(M), 411(M + 1, 100%).

5d: (E)-5-chloro-1-((E)-1-(benzo[d]thiazol-2-yl) imino)ethyl)-3-(p-tolylimino)indolin-2-one.M.P. 231-233°C; Mol. formula: $C_{24}H_{17}N_4OSCl$, yield 66%. IR (ν cm−1): 3093(C-H *Str*, Ar), 2976, 2884(C–H *Str*, Aliphatic), 2383(C-S-C *Str*), 1699(C=O *Str*, Indole), 1578(C=N *Str*), 1565(C=CH *Str*), 1476(C=C *Str*, Ar), 803(C-Cl *Str*, Ar). ^{1}H-NMR (DMSO) $\delta\delta$ ppm: 8.47-8.37(d, 2H, Ar-H), 7.95-7.88(d, 4H, Ar-H), 7.40-7.39(t, 2H, Ar-H), 7.35(s, 1H, Ar-H), 7.35-7.34(d, 2H, Ar-H), 3.34-3.30(s, 3H, -CH_3), 1.986-1.982(s, 3H, -CH_3); Mass (ESI-MS): m/z 444(M), 445(M + 1, 100%), 446(M + 2, 30%).

5j:1-((E)-1-((7-chloro-6-fluorobenzo[d]thiazol-2-yl) imino) ethyl)-3-(phenyl imino) indolin-2-one. m.p. 231-233°C; Mol. formula: $C_{23}H_{14}N_4OSClF$, yield 80%, IR (ν cm−1): IR (ν cm−1): 3035(C-H *Str*, Ar), 2987, 2878(C–H *Str*, Aliphatic), 2302(C-S-C *Str*), 1728(C=O *Str*, Indole), 1583(C=N *Str*), 1532(C=CH *Str*), 1454(C=C *Str*, Ar), 787(C-Cl *Str*, Ar), 590(C-F *Str*, Ar). ^{1}H-NMR (DMSO) $\delta\delta$ ppm: 8.43-8.33(d, 2H, Ar-H), 8.06-8.04(d, 2H, Ar-H), 7.94-7.92(t, 3H, Ar-H), 7.82-7.75(d, 2H, Ar-H), 7.17-7.14(t, 2H, Ar-H), 3.83(s, 3H, -CH_3); Mass (ESI-MS): m/z 448(M), 449(M + 1, 100%), 450(M + 2, 30%).

Anti-inflammatory activity [8-9]

Anti-inflammatory activity of the newly synthesized novel Benzothiazole derivatives containing Indole moieties was determined by carrageenan induced rat paw edema assay in albino rats. Synthesized test compounds with dose level 200 mg/kg were administered and compared with that of standard drug Diclofenac (20mg/kg). The paw volumes were measured using the mercury displacement technique with the help of plethysmograph immediately before and 1h after carrageenan injection.

.

Anticonvulsants activity [10]

Maximum Electroshock induced convulsions (MES) were carried out for testing anticonvulsant activities using groups of albino mice in the 20-25 g weight range, 6 mice each. Each compound suspended in 0.5%

carboxymethylcellulose (CMC) was administered intraperitoneally at three dose levels (25, and 30mglkg). Maximal electroshock seizures (MES) were induced 30 rnin after administration of the compound by application of a 60-Hz current of 50 mA for 0.2 s via corneal electrode into the eyes. The protection was defined as the abolition of hind-leg tonic maximal extension component of the seizure. The subcutaneous phenytoin seizure threshold test (sc-PTZ) was carried out by an intraperitoneal administration of phenytoin (25 mg/kg). Animals were observed over 2 h. Failure to observe the generalized clonic seizure is defined as protection.

III. Results And Discussion:

Synthesis:

The characterization data of all compounds **5a-5o** are given the experimental section. All the synthesized compounds gave satisfactory analysis for the proposed structures, which were confirmed on the basis of their elemental analysis by FT-IR, LC-MASS and ^{1}H NMR data. The present work which involve the reaction between Aniline and ammonium thiocyanat to give 2-aminobenzothiazole. The substituted Isatin can be prepared by the reaction between substituted aniline with Chloral hydrate and hydroxylamine and Sulphuric acid. Then it can be reaction with substituted Aromatic amine to give Isatin Schiff's bases derivatives, which on undergo acetylation and reacting with 2-aminobenzothiazole to give novel Benzothiazole derivatives containing Indole moieties. The synthesized compounds were screened for Anti-inflammatory and Anticonvulsant activity activities.

Spectroscopy:

The structures of all the newly synthesized compounds were characterized as **5a-5o**on the basis of satisfactory analytical and spectral data including IR, LC-MASS and ^{1}H NMR data.

***Biological activity*:** The biological potentials of the newly synthesized compounds are evaluated for their anticonvulsant and anti-inflammatory activities. From anti-inflammatory evaluations, dose level of 200mg/kg of test compounds reported significantly higher activity when compared to dose level of 20 mg/kg. Moreover, compound 5f, 5h, 5k and 5o (200 mg/kg) resulted in similar anti-inflammatory activity when compared with Diclofenac (20 mg/kg). All the compounds were evaluated for their anticonvulsant activity. Three compounds 5e, 5j and 5o showed promising anticonvulsant activities in Maximal Electroshock Seizure test (MES) and phenytoin (dose: 25mg/kg) used as a standard.

Table: 1 Physical data of Compounds 4a-4i

Compound	Molecular Formula	R	R_1	Molecular Weight (gms)	M.P (^{0}C)	%Yield	R_f value
4a	$C_{16}H_{12}N_2O_2$	H	H	264.09	137-139	69	0.73
4b	$C_{16}H_{14}N_2O_2$	Cl	H	298	181-183	72	0.82
4c	$C_{17}H_{14}N_2O_2$	H	CH_3	278	193-195	68	0.63
4d	$C_{17}H_{13}N_2O_2Cl$	Cl	H	312	153-155	75	0.59
4e	$C_{17}H_{14}N_2O_2$	CH_3	H	278	186-188	82	0.73
4f	$C_{18}H_{16}N_2O_2$	CH_3	CH_3	292	187-189	80	0.72
4g	$C_{16}H_{11}N_3O_4$	4-NO_2	H	309	225-227	76	0.57
4h	$C_{17}H_{13}N_3O_4$	3-NO_2	CH_3	323	183-185	74	0.63
4i	$C_{16}H_{11}N_2O_2Cl$	H	Cl	298	167-169	69	0.57

Table 2: Physical data of (5a-5o)

Compound	Molecular Formula	R	R_1	R_2	R_3	Molecular Weight (gms)	M.P (^{0}C)	%Yield	R_f value
5a	$C_{23}H_{16}N_4OS$	H	H	H	H	396	219–221	78	0.63
5b	$C_{23}H_{15}N_4OSCl$	H	H	Cl	H	430	213-215	82	0.76
5c	$C_{24}H_{18}N_4OS$	H	H	H	CH_3	410	203–205	77	0.57
5d	$C_{24}H_{17}N_4OSCl$	H	H	Cl	CH_3	444	231-233	66	0.61
5e	$C_{24}H_{18}N_4OS$	H	H	CH_3	H	410	191-193	67	0.53
5f	$C_{25}H_{20}N_4OS$	H	H	CH_3	CH_3	424	217-219	74	0.81
5g	$C_{23}H_{15}N_5O_3S$,	H	H	H	NO_2	441	251-253	76	0.67
5h	$C_{24}H_{17}N_5O_3S$,	H	H	NO_2	CH_3	455	231-233	81	0.51
5i	$C_{23}H_{15}N_4OSCl$	H	H	H	Cl	430	187–189	78	0.83
5j	$C_{23}H_{14}N_4OSClF$	Cl	F	H	H	448	231-233	80	0.59

5k	$C_{24}H_{16}N_4OSClF$	Cl	F	CH_3	H	462	193-195	78	0.75
5l	$C_{25}H_{18}N_4OS$	Cl	F	CH_3	CH_3	476	215-217	78	0.84
5m	$C_{23}H_{13}N_4OSFCl_2$	Cl	F	H	Cl	482	263-265	81	0.66
5n	$C_{23}H_{13}N_5SClF$	Cl	F	NO_2	H	493	243–245	68	0.71
5o	$C_{23}H_{13}N_4OSCl_2F$	Cl	F	Cl	H	482	225-227	76	0.77

Table-: Anti-inflammatory activity of novel benzothiazole derivatives containing indene moieties against (carrageenan induced acute rat paw oedema model)

Group	Treatment	Dose mg/kg	Paw oedema volume				
			0 hr	1 hr	2 hr	3 hr	4hr
1	control	10	0.62±0.028	0.75±0.006	0.96±0.004	1.6±0.028	1.7±0.002
2	Diclofenac	20	0.28±0.024	0.24±0.064	0.18±0.006	0.15±0.006	0.16±0.034
3	5a	200	0.26±1.2	0.20±1.8	0.16±2.2	0.19±1.2	0.20±0.002
4	5b	200	0.25±3.2	0.22±4.8	0.17±2.4	0.19±1.7*	0.24±5.2
5	5c	200	0.24±0.014	0.22±0.011	0.17±0.17	0.19±0.002	0.24±0.008
6	5d	200	0.28±3.4*	0.27±6.5	0.16±2.4	0.24±1.9	0.22±2.4
7	5e	200	0.30±0.028	0.25±0.017	0.22±0.014	0.18±0.006	0.17±0.003
8	5f	200	0.23±0.072*	0.29±0.068	0.20±0.089**	0.19±0.004	0.24±0.058
9	5g	200	0.24±0.009	0.19±0.012	0.20±0.068	0.24±0.009	0.18±0.007
10	5h	200	0.22±0.012*	0.20±0.009	0.18±0.007**	0.17±0.010	0.15±0.014**
11	5i	200	0.29±0.018	0.14±0.023	0.16±0.015	0.18±0.020	0.23±0.014
12	5j	200	0.35±0.026	0.28±0.044*	0.24±0.011*	0.22±0.007	0.18±0.002
13	5k	200	0.32±0.012	0.25±0.48	0.22±0.029	0.18±0.009**	0.14±0.023
14	5l	200	0.31±0.018	0.24±0.019	0.27±0.004	0.15±0.062	0.19±0.058
15	5m	200	0.25±0.028**	0.22±0.019	0.17±0.015	0.15±0.011*	0.19±0.068
16	5n	200	0.30±1.2	0.20±4.8	0.18±7.2	0.17±0.022	0.22±0.042
17	50	200	0.25±0.018	0.28±0.21	0.23±0.012	0.20±0.009	0.18±0.010**

Data analyzed by one way ANOVA followed by Dunnett's test (n=5).*p<0.05 and **p<0.01

Table-2: Anticonvulsant activity of novel benzothiazole derivatives containing indene moieties against Maximum Electroshock induced convulsions (MES)

Group	Treatment	Flexion(s)	Extension(s)	Clonus(s)	Stupor(s)	Recovery(s)
1	Control	6.28±0.22	12.32±0.004	14.30±0.028	6.54±0.022	184.5
2	Phenytoin	4.48±0.004***	0.00±0.000***	8.15±0.014***	0.90±0.028***	16.5
3	5a	6.78±0.022*	12.80±0.016***	13.72±0.003*	6.25±0.004***	92.0
4	5b	5.81±0.027*	3.97±0.028*	11.91±0.088*	5.62±0.011*	88.7
5	5c	4.36±0.004**	3.22±0.024*	5.20±0.011*	1.90±0.002*	78.0
6	5d	2.92±0.040*	2.79±0.058*	3.48±0.022*	1.22±0.012*	85.0
7	5e	3.50±0.079***	3.0±0.014*	2.92±0.004*	1.94±0.0028*	78.0
8	5f	2.96±0.002*	2.90±0.003*	1.42±0.008*	1.58±0.025*	94.0
9	5g	2.50±0.012*	2.10±0.015*	1.28±0.011***	1.40±0.028*	65.0
10	5h	1.85±0.004*	1.72±0.005*	1.32±0.002*	1.24±0.009***	74.0
11	5i	3.92±0.009*	7.85±0.005*	8.42±0.006	1.75±0.007*	77.4
12	5j	5.27±0.011***	8.92±0.045*	9.5±0.074*	1.82±0.009*	84.9
13	5k	4.98±0.058*	10.80±0.095***	5.91±0.085*	2.42±0.007*	72.3
14	5l	6.70±0.152*	3.80±0.078*	7.64±0.013*	1.23±0.014*	92.0
15	5m	4.21±0.034*	4.0±0.098*	8.5±0.029*	2.12±0.081*	94.0
16	5n	2.69±0.005*	3.72±0.078*	12.8±0.014*	2.45±0.078*	72.0
17	5o	5.68±0.004***	4.75±0.002*	4.20±0.005*	1.98±0.089*	74.0

Values are expressed as mean ± SEM for six animals; ***p<0.05, *P<0.001 compared to control group; phenytoin dose: 25mg/kg; test 30 mg/kg

IV. Conclusion

A series of novel Benzothiazole derivatives containing Indole moieties has been synthesized in good yield and screened for their anti-inflammatory activity. Most of the synthesized compounds showed significant anti-inflammatory activity. The result indicated that a compound compound 5f, 5h, 5k and 5o (200 mg/kg) resulted in similar anti-inflammatory activity when compared with standard Diclofenac (20 mg/kg). All the compounds were evaluated for their anticonvulsant activity. Three compounds 5e, 5j and 5o showed promising anticonvulsant activities in Maximal Electroshock Seizure test (MES) and phenytoin (dose: 25mg/kg) used as a standard

References:

[1]. A. Catalano, J.-F. Desaphy, G. Lentini, A. Carocci, A. Di Mola, C. Bruno,R. Carbonara, A. De Palma, R. Budriesi, C. Ghelardini, M.G. Perrone, N.A. Colabufo, D. Conte Camerino, C. Franchini, J. Med. Chem. 55 (2012)1418e1422.

[2]. A. Carocci, A. Catalano, A. Lovece, G. Lentini, A. Duranti, V. Lucini, M. Pannacci, F. Scaglione, C. Franchini, Bioorg. Med. Chem. 18 (2010) 6496e6511.

[3]. J.B. Baell, P.J. Duggan, S.A. Forsyth, R.J. Lewis, Y.P. Lok, C.I. Schroeder, Bioorg. Med. Chem. 12 (2004) 4025e4037.

[4]. Gaware Vinayak M, Dhamak Kiran B and Kotade Kiran B. reported by Synthesis and Evalution of Benzothiazole derivatives for Anthelmintic activity. *European Journal of Pharmaceutical and Medical Research. ejpmr, 2016,3(5), 454-459.*

[5]. M.M. Cavalluzzi, C. Bruno, G. Lentini, A. Lovece, A. Catalano, A. Carocci,C. Franchini, Tetrahedron: Asymmetry 20 (2009) 1984e1991.

[6]. N Siddiqui; A Rana; SA Khan; MA Bhat; SE Haque. 'Synthesis of benzothiazole semicarbazones as novel anticonvulsants-the role of hydrophobic domain', *Bioorg. Med. Chem. Lett.*, 2007, 17, 4178-4182.

[7]. Kaur H., Kumar S., Singh I., Saxena K.K. and Kumar A., "Synthesis, Characterization And Biological Activity Of Various Substituted Benzothiazole Derivatives", Digest Journal of Nanomaterials and Biostructures, 2010; 5(1):67-76.

[8]. Kulkarni, RG; Achaiah, G; Laufer, S and Chandrashekar, VM (2013), "Synthesis, p38 Kinase Inhibitory and Anti-inflammatory Activity of New Substituted Benzimidazole Derivatives", *Med Chem*, Vol. 9, 90-99.

[9]. Bele DS, Singhvi I. Synthesis, analgesic and anti-inflammatory activity of some mannich bases of 6- substituted-2-aminobenzothiazole, Int. J. Pharmacy. 2010; 10(04):0976-8157.

[10]. N Desroy; F Moreau; S Briet; GL Fralliec; S Floquet; L Durant; V Vongsouthi; V Gerusz; A Denis; S Escaich. 'Towards Gram-negative antivirulence drugs: New inhibitors of HldE kinase', Bioorg. *Med. Chem.*, 2009, 17, 1276-1289.

A.Rajareddy. " Conventional Synthesis and Characterization of novel Benzothiazole derivatives containing Indole moieties with Anti inflammatory and anti Convulsant Activities." .IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS) 13.5 (2018): 24-29