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Anthelmintic Activity of Newly Synthesized Moities of Fluoro Benzothiazole Schiff's Base.

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ABSTRACT

4-Fluoro-3-chloroanilline treated with Potassium thiocyanate in presence of Glacial acetic acid and bromine was converted into 2-amino-6-fluoro-7-chlorobenzothiazole. The synthesized compound in presence of p-dimethylaminobenzaldehyde refluxed in ethanol to obtained 6-fluoro-7-chloro benzothiazole Schiff's base. The above said compound was treated with ortho, meta and para nitroanillines, ortho, meta, para chloroanillines, morpholino, Piperazine, diphenylamine in the presence of DMF to obtain different new moities. Some new moities showed promising anthelmintic activity.

KEY WORDS: Benzothiazole, Schiff's base, Anthelmintic Activity.

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INTRODUCTION

Reports on fluorine[1] incorporated bioactive moieties are playing pharmacological activity, Amongst the heterocyclic compounds containing sulphur and nitrogen have attracted maximum attention as they are full of ramifications especially in industrial and biological applications. Fluorobenzothiazoles [2] are found to posses broad spectrum of pharmacological activity of clinical importance like anti-tubercular [3], anti-cancer [4, 5], anti-inflammatory [6], anti-microbial [7, 8] properties. This enthused us to prepare new moieties of fluorobenzothiazoles schiff's [9,10] base in hope of obtaining potent clinically useful biodynamic moieties .The said new moities were screened for their anthelmintic activity according to method described in detail by Kailashraj and Kurup [11] *Perituma posthuma* (Earthworms obtained from Horticulture Department) of nearly equal size were selected for present work.

MATERIAL AND METHODS

Purity of compounds was checked by TLC. Melting points were determined by open capillaries method and uncorrect. IR spectra (NaCl) are recorded on FTIR (Schimadzu-84005) spectrophotometer using nujol mull technique.

First Step

Synthesis of 2-amino-6-fluoro-7-chloro-(1,3)benzothiazole [12]

To the glacial acetic acid (20ml) which is cooled below room temperature, 8gm (0.08mol) of potassium thiocyanate and 1.45g (0.01 mol) of fluorochloroaniline was added. The mixture was placed in freezing mixture of ice and salt, mechanically stirred while 1.6ml of bromine in 6ml of glacial acetic acid was added, from a dropping funnel at such a rate that the temperature never raised beyond room temperature. After all the bromine was added (105min), the solution was stirred for 2 hours below room temperature and at room temperature for 10 hours, it was then allowed to stand overnight, during which period an orange precipitate settle at the bottom, water (6ml) was added quickly and slurry was heated at 85^0c on a steam bath and filtered hot. The orange residue was placed in a reaction flask and treated with 10ml of glacial acetic acid heated again to 85^0c and filtered hot. The combined filtrate was cooled and neutralized with concentrated ammonia solution to p^H 6. A dark yellow precipitate was collected. Recrystalised from benzene, ethanol of (1:1) after treatment with animal charcoal gave yellow plates of 2-amino-6-fluoro-7-chloro-(1,3) benzothiazole. After drying in a oven at 80^0c, the dry material (1gm 51.02%) melted at 210-212^0c. UV 307.4, 269nm, IR 1542cm^{-1}(aromatic C=C) and 3475cm^{-1} (NH_2); 1456 cm^{-1}(thiazole), 1215 cm^{-1}(aromatic-F), 712 cm^{-1}(aromatic-Cl).

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Second Step

Synthesis of 2-[p-dimethylaminobenzylidine]-6-fluoro-7-chloro (1, 3) benzothiazole [12]

0.01 mol of 2-amino-6-fluoro-7-chloro (1, 3) benzothiazole with 0.015 mol solution of p-dimethylaminobenzaldehyde, added 20 ml ethanol and 3-4 drops of HCl and refluxed for 2-3 hrs. Solution cooled and poured into crushed ice. Recrystalised with benzene and ethanol.

Preparation of various derivatives (E_1-E_9)

Schiff's base treated with equimolar quantities of various aromatic amines, refluxed for 2 hours in presence of DMF, recrystalised from alcohol and benzene.

Table No. 1 Analytical Data of the Compounds (E_1-E_9)

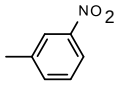
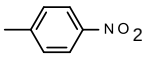
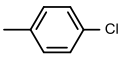
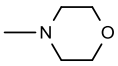
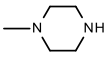
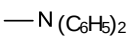
Compds	R	M.P (ºC)	Yield (%)	Molecular Formula	Molecular Wt.	Elemental Analysis Data (Calculated in %)		
						C	H	N
E_1		172	63	$C_{22}H_{18}N_5O_2SF$	435	60.68	4.13	16.09
E_2		190	69	$C_{22}H_{18}N_5O_2SF$	435	60.68	4.13	16.09
E_3		180	77	$C_{22}H_{18}N_5O_2SF$	435	60.68	4.13	16.09
E_4		172	57	$C_{22}H_{18}N_4SFCl$	425	62.11	4.23	13.17
E_5		162	76	$C_{22}H_{18}N_4SFCl$	425	62.11	4.23	13.17
E_6		168	69	$C_{22}H_{18}N_4SFCl$	425	62.11	4.23	13.17
E_7		170	52	$C_{20}H_{17}N_4OSF$	380	63.15	4.47	14.17
E_8		167	58	$C_{20}H_{18}N_5SF$	379	63.32	4.74	18.46
E_9		132	77	$C_{28}H_{23}N_4SF$	466	72.10	4.93	12.01

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Table2. IR spectral assignments of synthesized compounds (E_1-E_9)

Compounds	Characteristic absorption bonds (in cm^{-1})						
	C=N Str.	Aro.C=C Str.	C-F Str.	NO_2	C-Cl	3º-Nitrogen	C-H
E_1	1630	1688	1232	1396	---	3088	3477
E_2	1570	1677	1243	1399	---	3084	3433
E_3	1600	1667	1244	1409	---	3066	3409
E_4	1630	1610	1228	---	1197	3080	3435
E_5	1667	1600	1300	---	1198	3100	3400
E_6	1700	1656	1345	---	1127	3090	3434
E_7	1625	1693	1244	---	---	3074	3456
E_8	1630	1606	1247	---	---	3095	3479
E_9	1620	1780	1271	---	---	3074	3477

Anthelmintic Activity Screening:

The synthesized compounds are screened for anthelmintic activity by using earthworms. Six earthworms of nearly equal size were placed in standard drug solution and test compounds solutions at room temperature. Normal saline was used as control. The standard drug and test compounds were dissolved in minimum quantity of DMF and the volume was adjusted upto 15 ml. with normal saline solution to get the concentration of 0.1%, 0.2% and 0.5%.Piperazine Citrate was used as a standard drug. The compounds were evaluated by the time taken for complete paralysis and death of earthworms. The mean lethal time for each test compound was recorded and compared with standard drug. The time taken by worms to become motionless was noted as paralysis time. To ascertain the death of the motionless worms, these were frequently applied the external stimuli, which stimulates and induces movement in the worms, if alive.

The mean lethal time and paralysis time of earthworms for different test compounds and standard drug are tabulated in Table 3.

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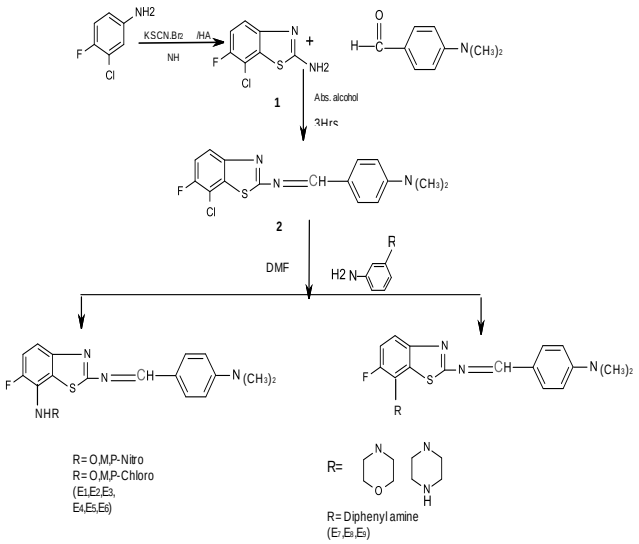
Table3. Anthelmintic Activity of synthesized compounds (E_1-E_9)

Compounds	Concentration (%)					
	Time for paralysis (min.)			Time for death (min.)		
Control	--	--	--	--	--	--
Piperazine citrate	65	53	44	75	60	55
E_1	82	77	70	148	132	128
E_2	79	74	68	142	134	126
E_3	77	71	67	144	132	120
E_4	78	73	65	141	129	119
E_5	72	69	63	139	125	112
E_6	75	65	58	146	133	122
E_7	71	66	61	140	129	117
E_8	69	60	57	128	122	114
E_9	64	59	52	139	135	127

RESULTS AND DISCUSSION

An attempt is made to synthesize the novel analogs of the fluorobenzothiazole schiff's base using p-dimethylamino benzaldehyde and screened for anthelmintic activity using *Perituma posthuma* (Earthworms obtained from Horticulture Department) of nearly equal size and some of the analogs showed significant activity.

SCHEME



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