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# SYNTHESIS OF BIOACTIVE MOLECULES FLUORO SUBSTITUTED BENZOTHIAZOLE COMPRISING POTENT HETEROCYCLIC MOIETIES FOR BIOLOGICAL AND PHARMACOLOGICAL SCREENING

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***ABSTRACT***

*Various 6-fluoro-7-substituted 2N(5'- substituted phenyl 1',3',4' oxadiazol-2'-yl) 2N-(p-acetamido benzene sulphonamido) (1,3)-benzothiazoles have been synthesized by condensing the compound 1 with hydrazine hydrate in the presence of ethanol gave the substituted semicarbazide. Further it is refluxed with various substituted aldehydes in the presence of ethyl alcohol and p-acetamidobenzenesulphonylchloride in presence of pyridine. The identities of compounds were confirmed on the basis of their spectral UV-Visible, IR, [1]HNMR and Mass spectral data. Further, they have been screened for their anthalimintic, anti-inflamatory ( invivo and invitro ) and anticonvulsant activities.*

***KEYWORDS:*** *Fluorine, Benzothiazole, Aromatic aldehydes, Oxadiazole etc.*

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## INTRODUCTION

The rapid progress of organic Fluorine chemistry[1-2] since 1950 has been translated as a pathfinder to invent useful biodynamic agents in Medicinal and Biochemistry.The new generation antibiotics like Norfloxacin, Ciproflaxacin, Flufloxacin, which were incorporated with fluorobenzene moiety proved their efficacy as potent bio active molecules. Now a days vast number of compounds with Fluorobenzene[3-5] moiety features in diverse areas like antibacterial, antifungal, anti-inflammatory, psychoactive agents, pesticides, herbicides etc.

The oxadiazole[6-15] drugs were the first effective chemotherapeutic agents to be employed systematically for the prevention and cure of bacterial infection in human beings. Benzothiazole with oxadiazole group etc. were reported to possess various pharmacological activity of clinical importance. Oxadiazole derivatives are well known to have antimicrobial activities, this also having anti-inflammatory, anthelmintic and anticonvulsant activities.

Based on the above observations we have synthesized some Fluoro-Benzothiazolo-oxadiazole

derivatives starting with fluoro-chloro-aniline, in hope of getting pharmacological agents with broad spectrum of clinical activity.

**MATERIALS AND METHODS**

Melting point was determined by open capillary tube method and are uncorrected. T.L.C was run on silica gel G plates using butanol, ethyl acetate and chloroform (1:2:1) as developing solvent for the purity of the compounds. I.R. Spectra were recorded on Shimadzu FTIR Spectrophotometer by using NUJOL MULL technique.

Synthesis of 6-fluoro-7-chloro-2(5'-furyl or dimethylaminophenyl 1',3',4' oxadiazol-2'-yl amino) (1,3) benzothiazoles

The schiff bases of (1,3) benzothiazoles 6-fluoro-7-chloro-2-semi carbazides was dissolved in glacial acetic acid and $FeCl_3$ solution was added with constant stirring, then reaction mixture was shaken for 1 hr. and diluted with water then kept at room temperature for 48 hrs. The solid separated was filtered washed, dried then recrystalised from alcohol.

Synthesis of 6-fluoro-7-chloro-2N- (5'-furyl or dimethylaminophenyl 1',3',4' oxadiazol-2'-yl) 2N-(*p*-acetamide benzene sulphonamido)-(1,3)-benzothiazole

6-fluoro-7-chloro-2(5'-furyl or dimethylaminophenyl 1',3',4' oxadiazol-2'-yl amino) (1,3) benzothiazoles was refluxed in oil bath with *p*-acetamido benzene sulphonyl chloride in presence of pyridine and acetic anhydride to get 6-fluoro-7-chloro-2N- (5'-furyl or dimethylaminophenyl 1',3',4' oxadiazol-2'-yl) 2N-(*p*-acetamide benzene sulphonamido)-(1,3)-benzothiazole.

**BIOLOGICAL ACTIVITIES**

Anthelmintic activity [16-18]

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 compound's solutions at room temperature. Normal saline used as control. The standard drug and test compounds were dissolved in minimum quantity of dimethyl formamide (DMF) and adjusted the volume up to 10 ml with normal saline solution to get the concentration of 0.1 % w/v, 0.2 % w/v and 0.5% w/v. Albendazole 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 were frequently applied with external stimuli, which stimulates and induces movement in the worms, if alive.

**Anti-inflammatory activity (*in-vitro* models*)* [19-22]**

The synthesized compounds are screened for anti-inflammatory activity by using inhibition of albumin denaturation technique which was studied according to Muzushima and Kabayashi with slight modification.

**Anti-inflammatory activity by carrageenin induced rat hind paw edema method: (*in-vivo* model)[23-26]**

Animals were divided into control, standard, different test groups comprising of five animals in each group. They were fasted overnight with free access to water before experiment. In all groups, acute inflammation was produced by subplanter injection of 0.1 ml of freshly prepared 1% suspension of carrageenin in the right hind paw of the rats and paw of the rats and paw volume was measured plethysmometrically at 0 hr and 3 hrs after carrageenin injection. The test compounds (50 mg/kg) was administered orally, standard group was treated with diclofenac (50 mg/kg) orally 1 hr. before by injection and control group received only vehicle. Mean difference in paw volume was measured and percentage inhibition was calculated by following formula.

$$\% \text{ inhibition of edema} = \left[\frac{Vc-Vt}{Vc}\right] x\ 100$$

Where, Vt = mean paw volume of test group.

Vc = mean paw volume of control group.

**Anticonvulsant activity [27-29]**

In the present study the mice of either sex, weighing between 20-25 g were selected and

divided into control, test and standard. Before experiment the animal were fasted for 24 hrs with only water *ad-libitum*. Control group received only 0.5 ml DMF as vehicle. Standard group animals were received diazepam (4 mg/kg b.w.) oral test group animals were received the synthesized derivatives at 4 mg/kg b.w. oral in DMF.

Now for the animals of control group pentylene tetrazole (PTZ) 1ml/100 g b.w. was administered and actions like stratubs tail, jerky movements of whole body and convulsions were observed. For animals of standard test group PTZ was injected (1 ml/100 g body weight). After 30 min animals of standard and test received diazepam and synthesized derivatives respectively

**RESULTS AND DISCUSSION**

**1) Anthelmintic activity :**

The synthesized compounds were tested for anthelmintic activity.

The compounds, $F_1$, to $F_{12}$ $D_7$, $D_9$, $D_{10}$ and $D_{11}$ showed significant paralytic time of earthworms compared to standard **Albendazole** of 0.1, 0.2, 0.5% concentrations of compounds, showed comparatively better death time of earthworms with that of standard drug. After all, the synthesized compounds in overall estimation confirms the better activity against (perituma posthuma).

**2) Anti-inflammatory activity (*in-vitro*):**

The compounds, $F_3$, $F_5$, $F_6$, $F_8$, $F_9$, $F_{10}$, $F_{11}$, $F_{12}$, $D_4$, $D_6$, and $D_8$ showed significant antiinflammatory activity compare to standard **Ibuprofen** (93.87%).

**3) Anti-inflammatory activity (*In-vivo* models) :**

The above synthesized compounds were tested for anti-inflammatory activity by invivo method compared to standard Diclofenac Sodium.

The compounds $F_2$, $F_6$, $F_{11}$, $D_2$, $D_3$, $D_7$, $D_8$ and $D_{11}$ showed significant anti-inflammatory activity compare to standard drug **Diclofenac Sodium** (79.60%).

**4) Anticonvulsant activity :**

synthesized compounds were tested for anticonvulsant activity by PTZ (pentylene tetrazole) induced method **Diazepam** used as standard drug.

From the anticonvulsant activity observation the compounds $F_1$, $F_3$, $F_6$, $F_7$, $F_{10}$, $F_{12}$, $D_1$, $D_5$, $D_8$ and $D_{11}$, have shown significant anti- anticonvulsant activity.

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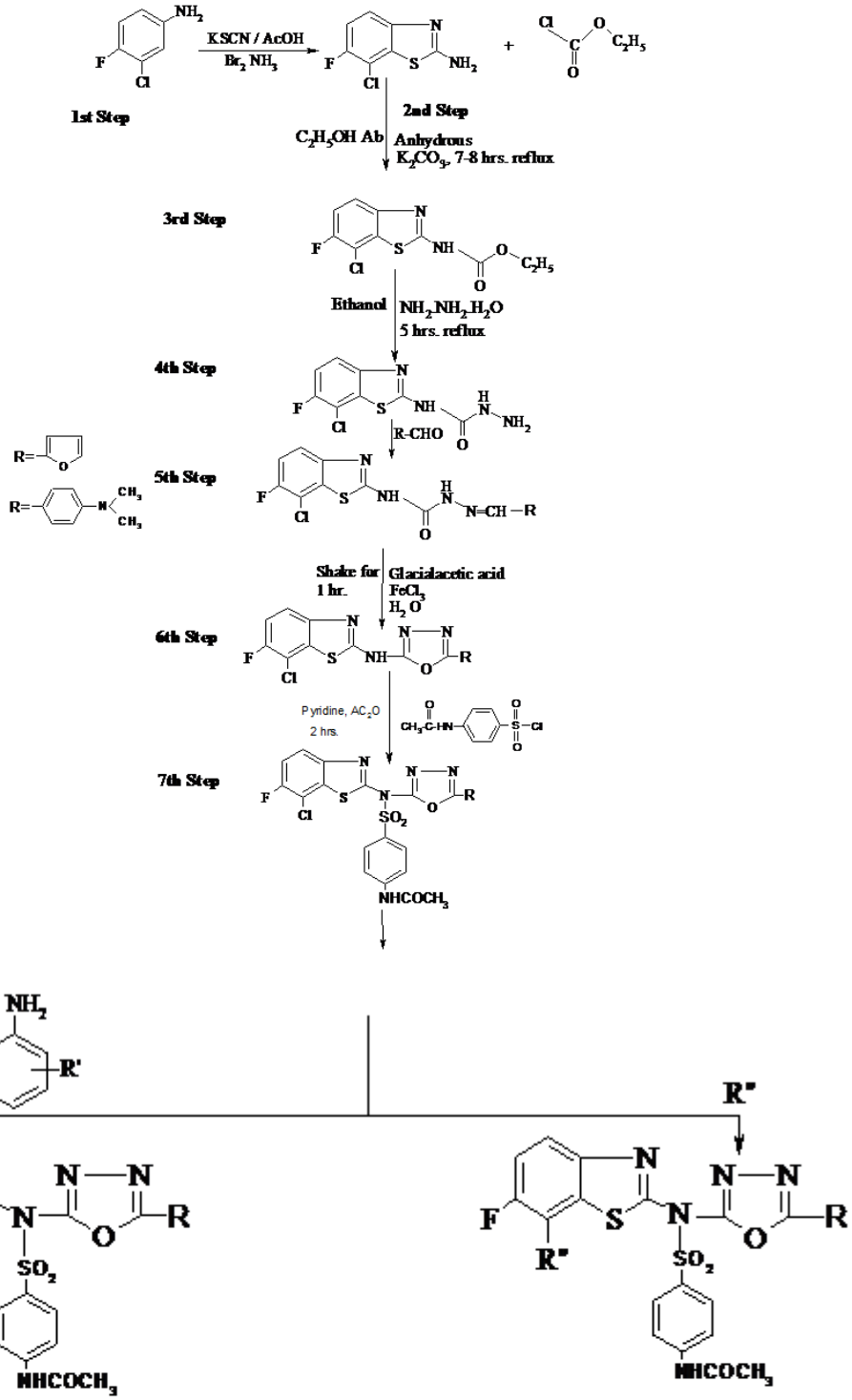


R' = o, m, p Nitro
o, m, p Chloro
= Diphenyl
=
= p-methyl
= PABA

R" = Morpholine
= Piperazine
= N-Methylpiperzine

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