IJPSR (2012), Vol. 3, Issue 06 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 24 February, 2012; received in revised form 29 March, 2012; accepted 24 May, 2012

SYNTHESIS, SPECTRAL ANALYSIS AND BIOLOGICAL EVALUATION OF SOME NOVEL FLUROBENZOTHIAZOLE INCORPORATED 1, 3, 4 - THIADIAZOLE

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Keywords:
Flurobenzothiazole,
1,3,4-Thiadiazole,
Antibacterial,
Antifungal,
Anti-Inflammatory

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ABSTRACT

A new series of flurobenzothiazole incorporated 1, 3, 4 - thiadiazole compounds have been synthesized. The structure of the synthesized compounds was confirmed by UV, IR, ^{1}H NMR, Mass spectral analysis and evaluated for their antimicrobial activity against *Proteus vulgaris* NCTC 4635, *Micrococcus leutus* NL98, *Aspergillus flavus* ATCC 46646 by disc diffusion method. The compounds SH_8 and SH_{11} were also evaluated for the anti-inflammatory activity by carrageenan-induced paw oedema method. The synthesized compounds (SH_6 to SH_{11}) showed good antimicrobial activity. However the antimicrobial activity of the synthesized compounds against the tested organisms was found to be less than that of respective standard drugs used at tested dose level. The anti-inflammatory activity confirmed that the test compound SH_{11} showed superior activity in the inhibition of oedema than SH_8. However, both the test compounds were found to be less active than the standard drug used.

INTRODUCTION: Research for the development of new therapeutic agents is becoming the major interest in many academic and industrial research laboratories all over the world with the aim to discover newer, more potent molecules, with higher specificity and reduced toxicity than the existing ones. In addition, the various types of resistant microorganisms that are discovered now-a-days are becoming a great challenge for the scientists. The existing drugs that are available are either very expensive or are prone to microbial resistance. Most of the drugs that are marketed today are modified derivatives of existing pharmacophores. No new pharmacophore having a novel mechanism of action has been identified in the recent past. To overcome these problems, it becomes necessary for further investigating newer molecules to treat infections at affordable costs.

Fluorine incorporated benzothiazole and 1,3,4 - thiadiazole derivatives individually known to possess a variety of biological properties like anti-microbial [1], anti-inflammatory [2], anti-tumor [3], anti-viral [4], anti-tubercular [5], anti-convulsant [6], anthelmintic [7], antioxidants [8], anti-diabetic [9], diuretic [10], analgesic [11] anti-depressants [12], etc., It was felt interesting to bring these two biologically active moieties within a molecular frame work with a view to study their additive effect on biological properties.

With the dual aim of developing potential therapeutic agents and studying their chemistry, we undertook the synthesis and biological evaluation of flurobenzothiazole incorporated with 1, 3, 4 - thiadiazole compounds for antimicrobial and anti-inflammatory activity.

MATERIALS AND METHODS: Melting point was determined in open capillary tubes on melting point apparatus (Sunbim, Guna enterprises) and are uncorrected. The ^{1}H NMR spectra were recorded on Bruker-NMR 400 mHZ using DMSO – d_6 as solvent. The Mass spectra were recorded on JEOL GC mate mass spectrometer. The IR spectra recorded on Perkin-Elmer FT-IR spectrophotometer using KBr pellets. The UV spectra were recorded by using Double beam SHIMADZU 1700 UV spectrometer. The purity of the compounds was checked by TLC on pre-coated silica gel G plates by using ethyl acetate and chloroform (2:1) as a mobile phase and visualized in iodine vapour. Analytical grade solvents and reagents were used for throughout the experiment. Carrageenan was obtained from Sigma Chemical Co., USA. Plethysmometer (Inco Co., Ambala, India) was used for anti-inflammatory activity.

Experimental Animals: The animals (Wistar albino rats of either gender) were obtained from the Kings Institute of Preventive Medicine, Guindy, Chennai. Animals were housed in animal house in Adhiparasakthi College of Pharmacy in standard environmental conditions of temperature (25±20º C), humidity (55±10%) and light (12:12 hour light: dark cycle). The animals were fasted prior to dosing but water was given *ad-libitum*. The anti-inflammatory activity was carried out as per CPCSEA (Committee for the Purpose of Control and Supervision of Experiments on Animals) guidelines after obtaining the approval from the Institutional Animal Ethical Committee.

Synthesis of 2-Amino-6-Fluoro-7-Chloro-(1,3)-Benzothiazole [13]: To the glacial acetic acid (20 ml) which was cooled below room temperature, added 8 gm (0.08 mole) of potassium thiocyanate and 1.44 gm (0.01 mole) of 4-flouro-3-chloro aniline. The mixture was placed in cold mixture of ice and salt and mechanically stirred. 1.6 ml of bromine in 6 ml of glacial acetic acid was added from a dropping funnel at such a rate that temperature never rose beyond 0º C. After all the bromine was added (105 minutes) the solution was stirred for 2 hours in ice cold condition and at room temperature for 10 hours. It was then allowed to stand overnight, during the period orange precipitate settled at the bottom, water (6 ml) was added quickly in it and slurry was heated to 85º C on a steam bath and filtered while hot. The orange residue was placed in a reaction flask and treated with 10 ml of glacial acetic acid heated again to 85º C on a steam bath and filtered hot. The combined filtrate was cooled and neutralized with concentrated ammonia solution up to pH-6. The precipitate was collected and recrystallized from benzene and ethanol (1:1) after treatment with charcoal gave yellow crystal of 2-amino-6-fluoro-7-chloro benzothiazole.

Synthesis of 6-Fluoro-7-Chloro-(1,3)-Benzothiazole-2-Thiosemicarbazide [14]: 20.1 gm (0.1 mole) of 2-amino-6-fluoro-7-chloro benzothiazole was dissolved in 50 ml of ethanol (95%) and 8 ml of ammonia solution was added to it. The reaction mixture was cooled below 30º C and 8 ml of carbon disulphide was added slowly within 15 minutes with continuous shaking. After complete addition of disulphide the solution was cooled to stand for 1 hour. Then 9.4 gm of sodium chloro acetate (0.1 mole) was added to it. The reaction was exothermic. To it 20 ml of 50% hydrazine hydrate was added. The mixture was warmed gently, filtered and boiled to half of its volume and kept overnight. Next day, the product thiosemicarbazide was filtered and recrystalised from ethanol.

Synthesis of 7-Chloro-6-Fluoro-N- (5-Aryl -1, 3, 4-Thiadizol-2-yl) 1-3-Benzothiazol-2-Amine [15]: A mixture of 6- fluro- 7- chloro-(1, 3)- benzothiazole- 2- thiosemi carbazide (0.01 mole), an aromatic acid (0.1 mole) and phosphrous oxychloride (25 ml) was refluxed for 18 – 24 hours. After cooling to the room temperature the reaction mixture was slowly poured to crushed ice and kept overnight. The solid separates out was filtered, dried and recrystallized from methanol.

Synthesis of 7-Aryl-6–Fluoro-N- (5- Aryl -1, 3, 4 - Thiadizol-2-yl) 1-3-Benzothiazol-2-Amine [16]: 0.0025 mole of 7-chloro-6-fluoro-N-(5-aryl-1, 3, 4-thiadizol-2-yl)1-3-benzothiazol-2amine was treated with equimolar quantity (0.0025 mole) of various substituted aromatic amines and refluxed for 2 hours in the presence of DMF. The mixture was then cooled and poured in the crushed ice. The solid separated was filtered, dried and recrystallized from benzene and absolute alcohol (1:1).

SYNTHETIC SCHEME

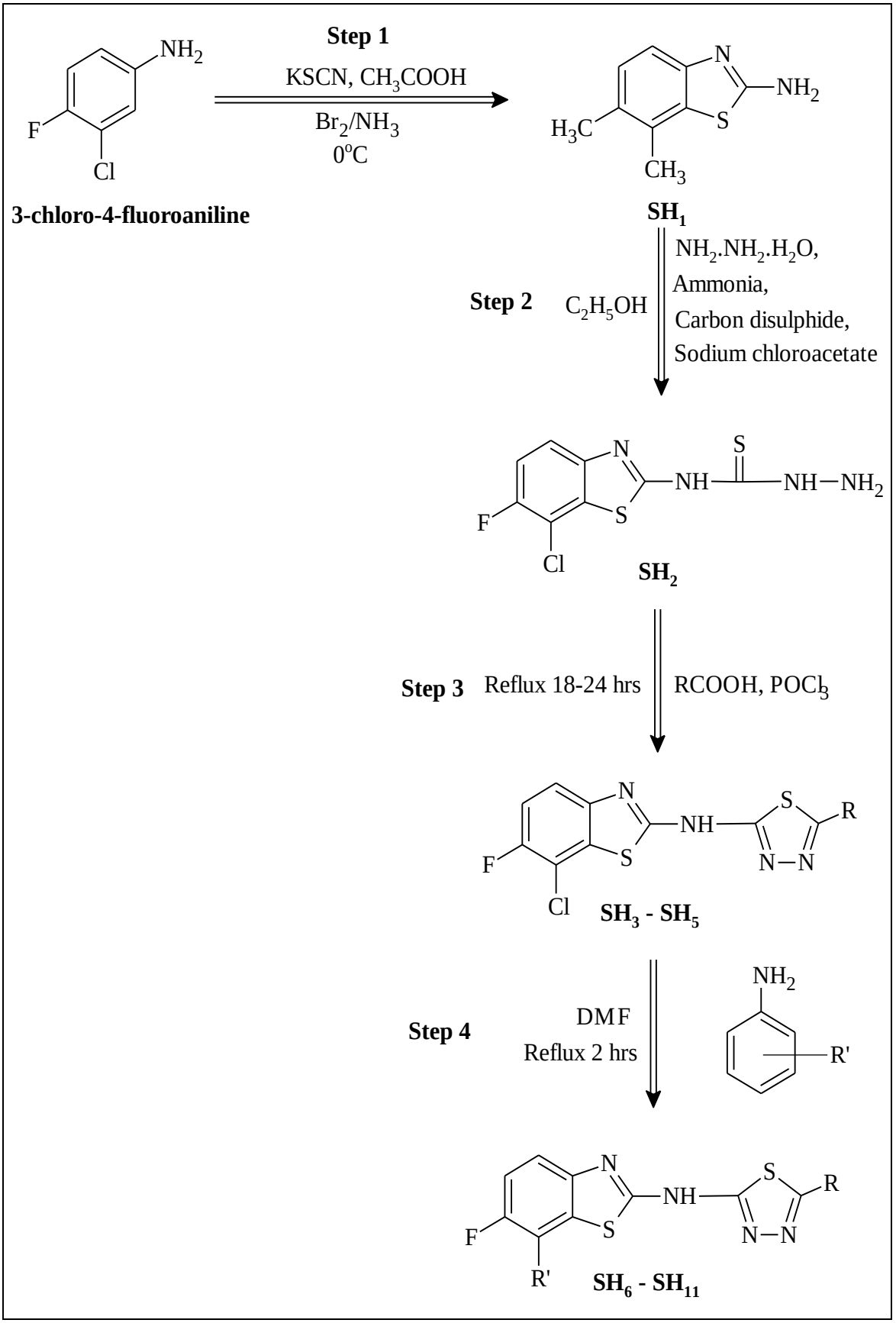
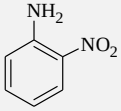
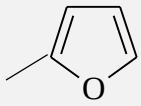
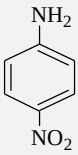
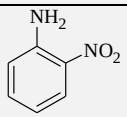
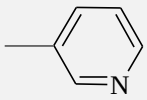
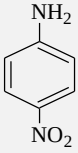
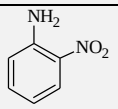
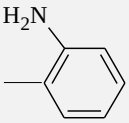
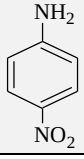


TABLE 1: DIFFERENT SUBSTITUTIONS IN COMPOUNDS SH_6 – SH_{11}

Compound Code	R'	R
SH_6		
SH_7		
SH_8		
SH_9		
SH_{10}		
SH_{11}		

Evaluation of Antimicrobial Activity [17]: The antimicrobial screening of the synthesized compounds (SH_6 - SH_{11}) was carried out by determining the zone of inhibition using disc diffusion method. The synthesized compounds was dissolved in DMSO and sterilized by filtering through 0.45 µm millipore filter. Final inoculums of 100 µl suspension containing 10^8 CFU/ ml of each bacterium and fungus used. Nutrient agar (anti-bacterial activity) and sabouraud's dextrose agar medium (anti-fungal activity) was prepared and sterilized by an autoclave (121°C and 15 lbs for 20 min) and transferred to previously sterilized petridishes (9 cm in diameter).

After solidification, petriplates was inoculated with bacterial organisms in sterile nutrient agar medium at 45°C, and fungal organism in sterile Sabouraud's dextrose agar medium at 45°C in aseptic condition. Sterile Whatmann filter paper discs (previously sterilized in U.V. lamp) were impregnated with synthesized compounds at a concentration of 25 and 100 mg/disc was in the organism-impregnated petri plates under sterile condition.

The plates were left for 30 minutes to allow the diffusion of compounds at room temperature. Antibiotic discs of ciprofloxacin (100 µg/disc) and ketaconazole (100 µg/disc) was used as positive control, while DMSO used as negative control. Then the plates were incubated for 24 hours at 37±1°C for antibacterial activity and 48 hours at 37±1°C for anti-fungal activity.

The zone of inhibition was calculated by measuring the minimum dimension of the zone of no microbial growth around the disc.

Evaluation of Anti-inflammatory activity [18]: The anti-inflammatory activity of the synthesized derivative SH_8 and SH_{11} was evaluated by carrageenan-induced paw oedema method. Wistar albino rats of either sex (150-200 g) were randomly selected and the animals were divided into control, standard and test groups, each consisting of three animals.

The first group was treated with 1% polyethylene glycol (1%) suspension which served as control, second group was administered with a dose of 20 mg/kg suspension of diclofenac sodium intra-peritoneally which served as standard and other groups was treated with 50 mg/kg of suspension of test compounds in polyethylene glycol. After 30 minutes, the rats were injected with 0.1 ml of carrageenan (1% w/v) to the sub plantar region of left paw of the rats.

The volume of paw was measured using mercury displacement technique with the help of plethysmograph in control and animals treated with standard and test compounds at 0, 1, 2 and 3 hours after injection of carrageenan.

The percentage inhibition of oedema was calculated by using formula,

$$\text{Percentage Reduction} = \frac{V_o - V_t}{V_o} X\ 100$$

Where, V_t = mean paw volume of the test drug, Vo = mean paw volume of the control.

TABLE 2: *IN-VITRO* ANTI-MICROBIAL ACTIVITY OF SYNTHESIZED COMPOUNDS BY DISC DIFFUSION METHOD

Microorganisms	Diameter of Zone of inhibition in mm													
	SH_6		SH_7		SH_8		SH_9		SH_{10}		SH_{11}		Ketaconazole (µg/disc)	Ciprofloxacin (µg/disc)
	25 (mg)	100 (mg)	25 (mg)	100 (mg)	25 (mg)	100 (mg)	25 (mg)	100 (mg)	25 (mg)	100 (mg)	25 (mg)	100 (mg)	100	100
Micrococcus luteus	17	28	17	27	14	18	14	17	11	14	15	17.6	-----	32
Proteus vulgaris	14	17	12	16	22	26	17.6	19	12	14.6	12	16.1	-----	29
Aspergillus flavus	11	16	14	18.6	17	21.6	21	23	21	25	23	27	30	-----

TABLE 3: ANTI-INFLAMMATORY ACTIVITY OF COMPOUNDS SH_8 and SH_{11} BY CARRAGEENAN INDUCED PAW OEDEMA METHOD

Compound Code	Dose (mg/kg)	Paw Oedema Volume (in ml) at			
		0 hour mean±SEM	1 hour mean±SEM	2 hours mean±SEM	3 hours mean±SEM
Control	-	0.33±0.066	0.9±0.088	1.1±0.088	1.47±0.057
Diclofenac Sodium	20	0.23±0.033	0.46±0.066** (48.88)	0.53±0.088** (51.51)	0.53±0.088*** (62.14)
SH_8	50	0.53±0.057	0.59±0.058* (34.44)	0.69±0.057* (37.27)	0.80±0.065*** (45.51)
SH_{11}	50	0.46±0.066	0.53±0.066* (41.11)	0.61±0.066** (44.54)	0.72±0.066*** (51.20)

SEM = Standard Error Mean, n = 3 in each group.*p< 0.05, **p < 0.01 and ***p<0.001 when compared to control (One-way ANOVA followed by Bonferroni test); Figures in the parenthesis indicate % inhibition of paw oedema

RESULTS AND DISCUSSION: The structure of the synthesized compounds was established by spectral (UV, IR, ^{1}H NMR and Mass) analysis data and were as follows:

Compound SH_1: Yield = 47.5%, mp = 212º C, R_f = 0.57, λ_{max} (MeOH) 232.50, IR (KBr) cm^{-1} 3228 (N-H stretching), 3288 (Ar C-H stretching), 1637(C=N stretching), 1543 (Ar C=C ring stretching), 1346 (Ar C=N stretching), 1193 (C-F stretching), 617 (C-S stretching). ^{1}H NMR (DMSO – d_6) δ: 8.09 (1H, d, Ar-H of benzothiazole), 7.20 (1H, d, Ar-H of benzothiazole), 4.0 (2H, s, NH_2). EI-MS *m/z* 202.63 (Calculated for $C_7H_4ClFN_2S$: 202.63).

Compound SH_2: Yield = 51.63%, mp = 241º C, R_f = 0.69, λ_{max} (MeOH) 247.28, IR (KBr) cm^{-1} 3473 (N-H stretching), 3077 (Ar C-H stretching), 1645 (C=N stretching), 1452 (Ar C=C ring stretching), 1337 (Ar C-N stretching), 1216 (Ali C-F stretching), 715 (C-Cl stretching), 686 (C-S stretching). ^{1}H NMR (DMSO – d_6) δ: 8.09 (1H, d, Ar-H of benzothiazole), 7.20 (1H, d, Ar-H of benzothiazole), 4.0 (1H, s, NH), 2.0 (3H, s, NH & NH_2). EI-MS *m/z* 352.79 (Calculated for $C_8H_6ClFN_4S_2$: 276.74).

Compound SH_3: Yield = 36.5%, mp = 224º C, Rf = 0.62, λ_{max} (MeOH) 280.50, IR (KBr) cm^{-1} 3392 (N-H stretching), 3032 (Ar C-H stretching), 1653 (C=N stretching), 1477 (Ar C=C ring stretching), 1337 (Ar C=N stretching), 1029 (C-F stretching), 844 (C-Cl stretching), 714 (Ar C-H stretching), 642 (C-S stretching). ^{1}H NMR (DMSO – d_6) δ: 8.09 (1H, d, Ar-H of benzothiazole), 7.4 (1H, d, CH of furan), 7.20 (1H, d, Ar-H of benzothiazole), 6.3 (2H, d, CH of furan), 4.0 (1H, s, NH). EI-MS *m/z* 352.79 (Calculated for $C_{13}H_6ClFN_4OS_2$: 352.79).

Compound SH_4: Yield = 42.19%, mp = 192º C, R_f = 0.57, λ_{max} (MeOH) 282.45, IR (KBr) cm^{-1} 3292 (N-H stretching), 3090 (Ar C-H stretching), 3022 (Ar CH stretching), 1632 (C=N stretching), 1543 (C=C, C=N ring stretching), 1454 (Ar C=C stretching), 1341 (Ar C-Nsec vibrations), 1032 (C-F stretching), 844 (C-Cl stretching), 716 (Ar C-H bending), 645 (C-S stretching). ^{1}H NMR (DMSO – d_6) δ: 8.85 (1H, d, CH of pyridine), 8.81 (1H, s, CH of pyridine), 8.09 (1H, d, Ar-H of benzothiazole), 7.97 (1H, d, CH of pyridine), 7.44 (1H, d, Ar-H of benzothiazole), 7.20 (1H, d, Ar-H of benzothiazole), 4.0 (2H, s, NH). EI-MS *m/z* 377.84 (Calculated for $C_{14}H_7ClFN_5S_2$: 377.84).

Compound SH_5: Yield = 39.42%, mp = 227º C, R_f = 0.53, λ_{max} (MeOH) 284.60, IR (KBr) cm^{-1} 3388 (N-H stretching), 3078 (Ar C-H stretching), 1634 (C=N stretching), 1546 (N-H bending), 1458 (Ar C=C stretching), 1116 (C-F stretching), 809 (C-Cl stretching), 685 (C-S stretching). ^{1}H NMR (DMSO – d_6) δ: 8.09 (1H, d, Ar-H of benzothiazole), 7.23 (1H, d, CH of aromatic ring), 7.20 (1H, d, Ar-H of benzothiazole), 6.97 (1H, t, CH of aromatic ring), 6.68 (1H, t, CH of aromatic ring), 6.52 (1H, d, Ar-H), 4.0 (3H, s, NH_2). EI-MS *m/z* 377.84 (Calculated for $C_{15}H_9ClFN_5S_2$: 377.84).

Compound SH_6: Yield = 54.79%, mp = 210º C, R_f = 0.81, λ_{max} (MeOH) 297.50, IR (KBr) cm^{-1}. 3477 (N-H asymmetrical stretching), 2925(Aromatic C-H stretching), 1741 (C-H out of plane bending), 1569 (C=N stretching), 1507 (NO_2 asymmetrical stretching), 1345 (C-N stretching). ^{1}H NMR (DMSO – d_6) δ: 8.20 (1H, d, Ar – H of aniline group), 7.87 (1H, d, CH of furan), 7.68 (1H, t, Ar – H of aniline group), 7.60 (1H, t, Ar – H of aniline group), 7.54 (1H, d, Ar – H of benzothiazole), 7.31 (1H, d, Ar – H of benzothiazole), 7.17 (1H, d, Ar – H of aniline group), 6.86 (1H, d, CH of furan) 6.68 (1H, t, CH of Furan), 4.39 (2H, s, NH). EI-MS *m/z* 454.45 (Calculated for $C_{19}H_{11}FN_6O_3S_2$: 454.45).

Compound SH_7: Yield = 43.53%, mp = 212º C, R_f = 0.69, λ_{max} (MeOH) 302.50, IR (KBr) cm^{-1} 3361 (N-H stretching), 2923 (Ar C-H stretching), 1505 (C=N stretching), 1109 (C-F stretching), 753 (C-S Stretching). ^{1}H NMR (DMSO – d_6) δ: 8.03 2H, d, Ar – H of aniline group, 7.87 (1H, d, CH of furan), 7.52 (1H, d, Ar – H of benzothiazole), 7.30 (1H, d, Ar – H of benzothiazole), 7.26 (2H, m, Ar – H of aniline group), 6.86 (1H, d, CH of furan), 6.68 (1H, t, CH of furan), 4.39 (2H, s, NH). EI-MS *m/z* 454.45 (Calculated for $C_{19}H_{11}FN_6O_3S_2$: 454.45).

Compound SH_8: Yield = 54.49%, mp = 216º C, R_f = 0.84, λ_{max} (MeOH) 307.00, IR (KBr) cm^{-1} 3348 (N-H stretching), 2841 (Ar C-H stretching), 1628 (Ar C-H stretching), 1507 (C=N stretching), 1283 (Ar C-N stretching), 1101 (C-F stretching), 742 (C-S stretching). ^{1}H NMR (DMSO – d_6) δ: 9.09 (1H, s, CH of pyridine), 8.70 (1H, d, CH of pyridine), 8.20 (1H, d, Ar – H of aniline group), 8.04 (1H, d, CH of pyridine), 7.68 (1H, t, Ar – H of aniline group), 7.60 (1H, t, Ar – H of aniline group) 7.55 (1H, d, Ar – H of benzothiazole), 7.47 (1H, t, CH of pyridine), 7.32 (1H, d, Ar – H of benzothiazole), 7.16 (1H, d, Ar – H of aniline group), 6.33 (2H, s, NH). EI-MS *m/z* 465.48 (Calculated for $C_{20}H_{12}FN_7O_2S_2$: 465.48).

Compound SH_9: Yield = 47.06%, mp = 217º C, R_f = 0.81, λ_{max} (MeOH) 301.75, IR (KBr) cm^{-1} 3345 (N-H stretching), 2857 (Ar C-H stretching), 1515 (C=N stretching), 1330 (Ar C-H stretching), 1273 (Ar C-N stretching), 1108 (C-F stretching), 970 (N-N stretching), 881 (C-H stretching), 742 (C-S stretching). ^{1}H NMR (DMSO – d_6) δ: 9.09 (1H, s, Ar – CH of pyridine), 8.70 (1H, d, Ar – CH of pyridine), 8.05 (1H, d, Ar – H of pyridine), 8.04 (2H, m, Ar – H of aniline group), 7.47 (1H, t, Ar – CH of pyridine), 7.38 (1H, d, Ar – H of benzothiazole), 7.34 (2H, d, Ar – H of aniline group), 7.23 (1H, d, Ar – CH of benzothiazole), 6.62 (1H, s, NH) EI-MS *m/z* 465.48 (Calculated for $C_{20}H_{12}FN_7O_2S_2$: 465.48).

Compound SH_{10}: Yield = 49.54%, mp = 220º C, R_f = 0.58, λ_{max} (MeOH) 298.45, IR (KBr) cm^{-1} 3351(N-H stretching), 2925 (Ar C-H stretching), 1506 (C=N stretching), 1346 (Ar C-N ring stretching), 1101 (Ar C-F stretching), 1016 (N-N stretching), 743 (C-S stretching), 694 (C-H out of bending). ^{1}H NMR (DMSO – d_6) δ: 8.20 (1H, d, of aniline group), 7.68 (1H, t, Ar – H of aniline group), 7.60 (1H, t, Ar – H of aniline group) 7.46 (1H, d, Ar – H of aniline group), 7.43 (1H, d, Ar – H), 7.29 (1H, d, Ar – H of benzothiazole), 7.23 (1H, t, Ar – H), 7.12 (1H, d, Ar – H of benzothiazole), 6.96 (1H, t, Ar – H), 6.77 (1H, d, Ar – H), 6.35 (2H, s, NH_2), 4.47 (2H, s, NH). EI-MS *m/z* 479.51 (Calculated for $C_{21}H_{14}FN_7O_2S_2$: 479.51).

Compound SH_{11}: Yield = 44.04%, mp = 217º C, R_f = 0.78, λ_{max} (MeOH) 301.40, IR (KBr) cm^{-1} 3482 (N-H stretching), 2919 (Ar C-H stretching), 1504 (C=N stretching), 1285 (Ar C-N stretching), 1103 (C-F stretching), 1015 (Ar N-N stretching), 842 (C-H out of plane bending), 751 (C-S stretching). ^{1}H NMR (DMSO – d_6) δ: 8.03 (2H, d, Ar – H of aniline group), 7.51 (1H, d, Ar – H of benzothiazole), 7.41 (1H, d, Ar – H), 7.29 (1H, d, Ar – H of benzothiazole), 7.27 (2H, m, Ar – H of aniline group), 7.23 (1H, t, Ar – H), 6.96 (1H, t, Ar – H), 6.74 (1H, d, Ar – H), 4.55 (2H, s, NH_2), 4.44 (2H, s, NH). EI-MS *m/z* 479.51 (Calculated for $C_{21}H_{14}FN_7O_2S_2$: 479.51).

In SH_1, the NH band at 3463-3114 cm^{-1} and NH proton signal δ 4.0 of 2-amino benzothiazole in IR and ^1H NMR spectrum respectively confirmed the formation of benzothiazole nucleus. In SH_2, three protons singlet at δ 2.0 and one proton singlet at δ 4.0 confirmed the formation of thiosemicarbazide group.

In the compounds SH_3, SH_4, SH_5 C = N band (1700 – 1430 cm^{-1}) and C – S band (800 - 600 cm^{-1}) of IR spectrum conforms the formation of 1,3,4 thiadiazole nucleus. In SH_3, two doublets at δ 6.3 and one doublet proton at δ 7.4 indicates the formation of furan ring. In SH_4, three doublet protons at δ 8.85, δ 7.97, δ 7.44 and one singlet proton at δ 8.81 confirmed the formation of an aromatic nucleus. In the case of SH_5, two triplets at δ 6.97, δ 6.68 and two doublets at δ 7.23, δ 6.52 indicates the formation of an aromatic nucleus.

The presence of nitro group in SH_6-SH_{11} was ascertained from stretching on bands at (1584 -1510 cm^{-1}) and (1365-1335 cm^{-1}) corresponding to asymmetric and symmetric O=N=O stretching respectively. The C – Cl stretching band which appeared at SH_1-SH_5 at (809 – 683cm^{-1}) was disappeared in SH_6-SH_{11}. Instead, C – N stretching band appeared at (1346.02-1255.90cm^{-1}) in SH_6-SH_{11} indicated the attachment of ortho nitro aniline (or) and para nitro aniline group.

In compounds SH_6, SH_8, SH_{10}, two doublet for 2 protons (δ 8.20, δ 7.17- δ7.46) and two triplet protons at (δ 7.68, δ 7.60) confirmed the presence of nitro group at ortho position in the aromatic ring. In compounds SH_7, SH_9 & SH_{11}, two doublet protons at (δ 7.26- δ 7.34, δ 8.03 - δ 8.04) confirmed the presence of nitro group at para position in aromatic ring.

In the mass spectrum of the synthesized compounds produced (M^+) Molecular ion peaks at 202.63, 276.74, 351.12, 362.21, 376.16, 454.45, 454.45, 463.48, 463.48, 479.51 and 479.51 values for SH_1, SH_2,SH_3, SH_4, SH_5,SH_6, SH_7, SH_8, SH_9, SH_{10}, and SH_{11} respectively corresponds to their molecular formulas.

All the compounds showed very good anti-bacterial and anti-fungal activity even at less concentration. From the data, it is evident that the compound SH_6 and SH_8 was the most potent candidate against *Micrococcus leutus and Proteus vulgaris* in the anti-bacterial studies and compound SH_{11} was the much potent candidate against *Aspergillus flavus* in the anti-fungal studies. Since only fewer species had been used in this study, it was warranted to screen these compounds with various species of resistant strains.

The anti-inflammatory activity confirmed that the test compound SH_{11} showed superior activity in the inhibition of oedema than SH_8. However, both the test compounds were found to have less activity than the standard drug diclofenac sodium.

ACKNOWLEDGEMENT

The authors wish to express their sincere gratitude to our principal Prof. Dr. T. Vetrichelvan, Adhiparasakthi College of Pharmacy, Melmaruvathur, for providing necessary facilities to carry out this research work. They also thankful to Dr. R. Murugesan, Scientific Officer, SAIF, IIT, Chennai for spectral analysis.

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