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Synthesis and Evaluation of Antibacterial and Antiinflammatory Activity of 7-Alkyl/Aryl amino-6-fluoro-2-phenyl Carboxamido-1,3-benzothiazoles

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Substituted-1,3-benzothiazole is synthesized by 2-amino-7-chloro-6-fluorobenzothiazoles with aroyl chloride and later on obtained compound were refluxed in equimolecular with various substituted amines. These were characterized by spectral data and were screened for biological and pharmacological activity.

Key Words: Phenyl carboxamido benzothiazoles, Antibacterial and Antifungal activity.

INTRODUCTION

A number of the fluro benzothiazoles[1] were reported to possess different biological and pharmacological activities[2-7]. These observations stimulated us with a presumption that phenyl carboxamido benzothiazoles would produce new compounds of better activities.

EXPERIMENTAL

All melting points were taken in open capillary tube and are uncorrected. The IR spectra were recorded with KBR pellets on Shimadzu FT-IR-8400S Spectrophotometer. ^{1}H NMR were recorded on Avance 300 MHz spectrophotometer.

Synthesis of 7-chloro-6-fluoro-2-(substituted phenyl carboxamido) benzothiazole: A solution of triethylamine (0.101 g, 0.001 mol) and 2-amino-7-chloro-6-fluoro benzothiazole (**II**) (0.203 g, 0.001 mol) in 10 mL of 1,4-dioxane was stirred on a magnetic stirrer at 50-60 ºC for 1 h. To this added dropwise, a solution of different aroyl chloride (0.001 mol) in the 10 mL

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dry 1,4-dioxane at the same temperature. After the addition, reaction mass was stirred for 3 h. It was then poured in crushed ice. The solid separate out was filtered and washed with 1 % potassium bicarbonate solution and water. Recrystallized with suitable solvent. The characteristic data of the synthesized compounds is given in Table-1.

TABLE-1
CHARACTERISTIC DATA OF 7-ALKYL/ARYL-AMINO-6-FLUORO-2-(SUBSTITUTED PHENYL CARBOXAMIDO)BENZOTHIAZOLE

Compd. no.	R	R^1 and R^2	m.p. (ºC)
IVA	H	Dimethyl amino	181
IVB	H	Diethyl amino	218
IVC	H	N-methyl piperzino	210
IVD	H	Piperazino	220
IVE	H	Morpholino	185
IVF	H	*p*-Toludino	215
IVU	NO_2	Dimethyl amino	178
IVV	NO_2	Diethyl amino	176
IVW	NO_2	Piperazino	180
IVX	NO_2	N-methyl piperzino	178
IVY	NO_2	Morpholino	181
IVZ	NO_2	*p*-Toludino	295

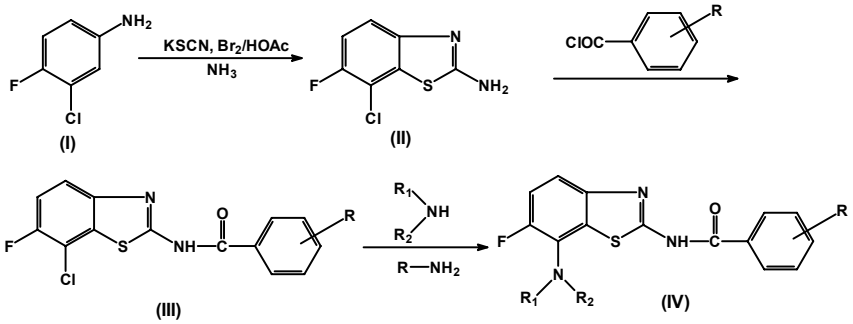
All the compounds gave satisfactory C, H, N analyses.

III: (R=H): m.p. 230 °C, IR: (KBr, ν_{max}, cm^{-1}); 3090 (-NH), 1680 (C=O); 1610 (C=N), 1150 (C-F), 685(C-CL). ^1H NMR ($CDCl_3$ δ ppm): 6.9-8.0 (m, 7H, Ar-H), 11.25 (S, CONH). M/s: m/2 306 (M^+) peak. This happens to be agreement with mass number of assigned structure.

General procedure for synthesis of new 7-alkyl/aryl-amino-6-fluoro-2(substituted phenyl carboxamido)benzothiazole: A mixture of 7-chloro -6-fluoro-2-(substituted phenyl carboxamido)benzothiazole (0.01 mol) and different amine (0.002 mol) in equimolar quantities in DMF (20 mL) refluxed for 2-4 h in oil bath. The reaction mixture was cooled and poured over crushed ice. The solid separated out was filtered and recrystallized with suitable solvent.

IVA: IR (KBr, ν_{max}, cm^{-1}): 3095 (NH); 1690 (C=O); 1610 (C=N), 1175 (C-F); ^1H NMR: (δ, ppm) 1.6 (S, 6H, $N(CH_3)_2$), 7.0-8.1(m, 7H, Ar-H) 11.0 (S, 1H, CONH).

IVF: IR (KBr, ν_{max}, cm^{-1}): 3100 (NH), 1660 (C=O), 1608 (C=N), 1160 (C-F); ^1H NMR Spectra (δ, ppm) 1.8 (S, 3H, CH_3), 6.8-8.0 (m, 11H, Ar-H), 11.25 (S, 2H, NH).



Scheme-I

Antibacterial activity: All the synthesized compounds (**IVA-IVF**) and (**IVU-IVZ**) were screened for their antibacterial activity by cup plate diffusion technique[8-11] at concentration of 50 and 100 µg/mL using gram +ve and gram -ve organism. The zone of inhibition was measured in millimeter and reported in Table-2. The activity was compared with procaine penicillin and streptomycine.

TABLE-2
ANTIBACTERIAL ACTIVITY OF 7-ALKYL/ARYL-AMINO-6-FLUORO-2-(SUBSTITUTED PHENYL CARBOXAMIDO)BENZOTHIAZOLE

Compd.	Zone of inhibition (mm)			
	Staphylococcus aureus		*Escherichia coli*	
	50 µg	100 µg	50 µg	100 µg
IVA	11	14	13	14
IVB	10	12	10	13
IVC	12	14	13	16
IVD	11	13	10	12
IVE	12	16	10	11
IVF	13	15	11	15
IVU	11	12	10	11
IVV	12	10	13	14
IVW	11	13	10	13
IVX	10	10	10	11
IVY	12	13	11	15
IVZ	10	15	12	16
Procaine penicillin	19	22	–	–
Streptomycin	–	–	18	21

Antiinflammatory activity: The antiinflammatory activity of the test compounds have been evaluated by albumin denaturation method[6,12,13]. It is revaled that none of them could inhibit albumin denaturation in comparison with standard drug, diclofinac sodium which is exhibited 85.05 % inhibition of albumin denaturation. However, five out of synthesized

compounds could inhibit albumin denaturation considerably. The rest of the compound tested were found to be devoid of any inhibition of albumin denaturation.The result so obtained are recorded in Table-3.

TABLE-3
ANTIINFLAMMATORY ACTIVITY OF 7-ALKYL/ARYL-AMINO-6-FLUORO-2-(SUBSTITUTED PHENYL CARBOXAMIDO)-BENZOTHIAZOLE

Compd.	Absorbance value (Mean ± SD)	Inhibition of denaturation (%)
IVB	0.110 ± 0.004	26.43
IVC	0.113 ± 0.040	29.88
IVE	0.109 ± 0.004	25.28
IVV	0.111 ± 0.001	27.58
IVZ	0.114 ± 0.002	31.03
Diclofenac sodium	0.161 ± 0.001	85.05

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REFERENCES

1. R. Feller, *J. Fluorine Chem.*, **33**, 366 (1995).
2. B.M. Gurupadian, E. Jayachandran, B. Shivakumar, A.N. Nagappa and L.V.G. Nargund, *Indian J. Heterocycl. Chem.*, **7**, 213 (1998).
3. P. Gopkumar, E. Jayachandran, B. Shivakumar, A.N. Nagappa, L.V.G. Nargund and B.M. Gurupadian, *Indian J. Heterocycl. Chem.*, **11**, 39 (2001).
4. D.S. Rao, E. Jayachandran and B. Shivakumar, *Indian J. Heterocycl. Chem.*, **14**, 65 (2004).
5. D.S. Rao, E. Jayachandran, G.M. Sreenivasa and B. Shivakumar, *Orient. J. Chem.*, **21**, 113 (2005).
6. E. Jayachandran, L.V.G. Nargund, B. Shivakumar and K. Bhatia, *Orient. J. Chem.*, **19**, 139 (2003).
7. V.M. Sreenivasa, E. Jayachandran, B. Shivakumar and L.V.G. Nargund, *Indian Drugs*, **36**, 139 (1999).
8. V.S. Murthy, A.N. Nagappa and L.V.G. Nargund, *Indian J. Heterocycl. Chem.*, **8**, 23 (1998).
9. D. Robbert, Clinical Analysis, Microbiology, Remington's Pharmaceutical Science, Mack Publishing Company, Pennsylvania, pp. 524-527 (1991).
10. Biological Assay, Indian Pharmacopeia, Government of India, Vol. 2, p. A-88 (1996).
11. Test for Microbial Contamination, British Pharmacopoeia, Department of Health Scottish Home and Health Department, Vol. 2, pp. 16-173 (1988).
12. S.K. Sangal and P.K. Rastogi, *Chem. Abstr.*, **104**, 34029x (1980).
13. H.P. Rang, M.M. Dale and J.M. Ritter, Antiinflammatory and Immuno-supressant Drug, Pharmacology, International Student Edition, Churchill Livingstone, Edinburg, edn. 3, pp. 246-66 (1995).

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