IJPSR (2011), Vol. 2, Issue 6 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 01 March, 2011; received in revised form 05 May, 2011; accepted 28 May, 2011

SYNTHESIS, CHARACTERISATION AND ANTIMICROBIAL EVALUATIONS OF SOME NOVEL 1, 3, 4-THIADIAZOLE DERIVATIVES

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Keywords:

1, 3, 4-thiadiazole,
Synthesis,
Antibacterial and antifungal

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ABSTRACT

A series of 1, 3, 4-thiadiazole derivatives were synthesized. The structures of these compounds were established by means of IR, ^{1}H-NMR and mass spectrum analysis. All the compounds were evaluated for antibacterial and antifungal activities. Most of the compounds have shown significant antibacterial and antifungal activity when compared with the standard drugs.

INTRODUCTION: There are number of five membered heterocyclic ring containing nitrogen and sulphur atom, have turned out to be potential chemotherapeutic and pharmacotherapeutic agents. The biological profiles of thiadiazole derivatives were very extensive [1-3]. 1, 3, 4-Thiadiazole derivatives are associated with diverse biocidal activities. A large number of 1, 4-thiazolidinones have been reported to be antibacterial, anticancer and antitubercular agents [4-6]. These observations promoted us to synthesis the titled compound with presumption that incorporation of aromatic amines and thiazolidinones nuclei would produce new compounds with significant antibacterial and antifungal properties.

MATERIALS AND METHODS:

Antimicrobial activity [7]: The antimicrobial activity of the synthesized compounds was determined by cup-plate method. The organisms selected for antibacterial activity were *Staphylococcus aureus* and *Escherichia coli*. Similarly the antifungal activity was carried out by using *Aspergillus niger* and *Candida albicans*. The concentration of sample compounds was 100mcg/mL. Norfloxacin and Griseofulvin were used as standard drugs for antibacterial and antifungal activity respectively. Control test with solvents were performed for every assay but showed no inhibition of the microbial growth.

Experimental: Melting point was determined by Veego VMP-1 melting point apparatus and Labinda digital melting point apparatus in ^{o}C and are uncorrected. The purity was checked by TLC using silica gel G as stationary phase. The structure of the synthesized compound was elucidated by using Perkin Elmer Infrared- 283 spectrophotometer in KBr disc method. ^{1}H – NMR spectra was taken on their AMX – 400 MHX spectrophotometer using dimethylsulphoxide as solvent and tetramethlysilane as internal standard. Mass spectra were recorded on shimadzu 2010A LC–MS system.

Synthesis of thiosemicarbazones (I) [8]**:** Aldehydes (0.2 mol) in warm alcohol (300 mL) and a solution of thiosemicarbazide (0.2 mol) in 300 ml hot water were

mixed slowly with continuous stirring. The product, which separated, was filtered off after cooling. The melting points are reported. Suitable solvents effected the final crystallization.

Synthesis of 2-amino-5-aryl -1,3,4-thiadoazole (II) [9]**:** Thiosemicarbazone (I, 0.05 mol) was suspended in 300 mL distilled water in a one-litre beaker. Ferric chloride (0.15 mol) in 300 ml distilled water was added to it. This was heated to 80-90^{0}C and maintained for 45 min. Then using a hot water funnel, the solution was filtered. A mixture of citric acid (0.11 mol) and sodium citrate (0.05 mol) was added to the solution and stirred. After cooling the whole solution was affected by neutralization with aqueous ammonia (10%). The precipitate so obtained was filtered and washed with distilled water and allowed to dry. Suitable solvents effected the final crystallization. The results are reported in **Table 1**.

The I*R* spectrum (KBr, in cm^{-1}) of the test compound B showed absorption band at: 3177 (N-H), 3010 (aryl C-H Str), 1618 (C=N), 1509 (C=C) and 737 (C-S-C).

Synthesis of 2-nitrophenyl-5-aryl- 1, 3, 4-thiadoazol-2-yl-methanediamine (III) [10]**:** A mixture of 2-amino- 5-aryl-1, 3, 4-thiadoazole (2.22g, 0.01 mol) and 2-nitro aniline (1.38g, 0.01 mol) and formaldehyde (2mL) were taken in a beaker. The mixture was refluxed in water for 4hrs. After the completion of reaction, ice-cold water was added to the reaction mixture and solid thus separated was filtered and dried to get 2-nitrophenyl-5-aryl-1, 3,4-thiadoazol-2-yl-methanediamine. Finally it was recrystallized from ethanol. The compounds 1-8 were s**y**nthesized by similar procedure. The yield and m.p. are listed in **Table 1**. A series of 1, 3, 4-thiadiazole derivatives were synthesized in good yield using the synthetic route outlined in scheme **(Fig. 1).**

TABLE 1: PHYSICAL DATA OF THE SYNTHESIS OF 2-NITROPHENYL-5-ARYL-1, 3,4-THIADOAZOL-2YL-METHANEDIAMINE

Compd. No.	Substituent R	Substituent Ar	Mol. Formula	Mol. Wt.	M.P. ^{0}C	Yield %
A	C_6H_5NH	C_6H_5	$C_{15}H_{14}N_4S$	282	278	65
B		C_6H_4OH	$C_{15}H_{14}N_4SO$	298	231	52
C		$C_6H_4N(CH_3)_2$	$C_{17}H_{19}N_5S$	325	182	57
D		C_6H_4OH	$C_{15}H_{14}N_4SO$	298	218	72
E		C_6H_4Cl	$C_{14}H_{13}N_4SCl$	316	237	75
F		$C_6H_4NO_2$	$C_{15}H_{13}N_5SO_2$	327	198	68
G		C_4H_3S	$C_{13}H_{12}N_4S_2$	288	180	75
H	C_6H_5NCl	C_6H_5	$C_{15}H_{13}N_4SCl$	316	268	52
I		C_6H_4OH	$C_{15}H_{13}N_4SOCl$	332	218	45
J		$C_6H_4N(CH_3)_2$	$C_{17}H_{18}N_5SCl$	359	192	79
K		C_6H_4OH	$C_{15}H_{13}N_4SOCl$	332	213	62
L		C_6H_4Cl	$C_{15}H_{12}N_4SCl_2$	351	232	59
M		$C_6H_4NO_2$	$C_{15}H_{12}N_5SO_2Cl$	361	212	61
N		C_4H_3S	$C_{13}H_{11}N_4S_2Cl$	322	184	57

The IR spectrum (KBr, in cm^{-1}) of the test compound B showed absorption band at: 3477 (N-H str.), 2223 (aryl C-H Str.), 1568 (Ar C-C str.) 1429 (C=N str.) and 737 (C-S- str.). The ^{1}H-NMR (δ, ppm) of the test compound B exhibited characteristic proton peaks at: 6.84 - 8.06 (10H, Ar-CH), 6.68 (1H, NH), 4.72 (1H, NH), 4.38 (2H, CH_2).

The ^{1}H-NMR (δ, ppm) of the test compound I exhibited characteristic proton peaks at: 6.84 - 8.06 (9H, Ar-CH), 6.68 (1H, NH), 4.72 (1H, NH), 4.38 (2H, CH_2).

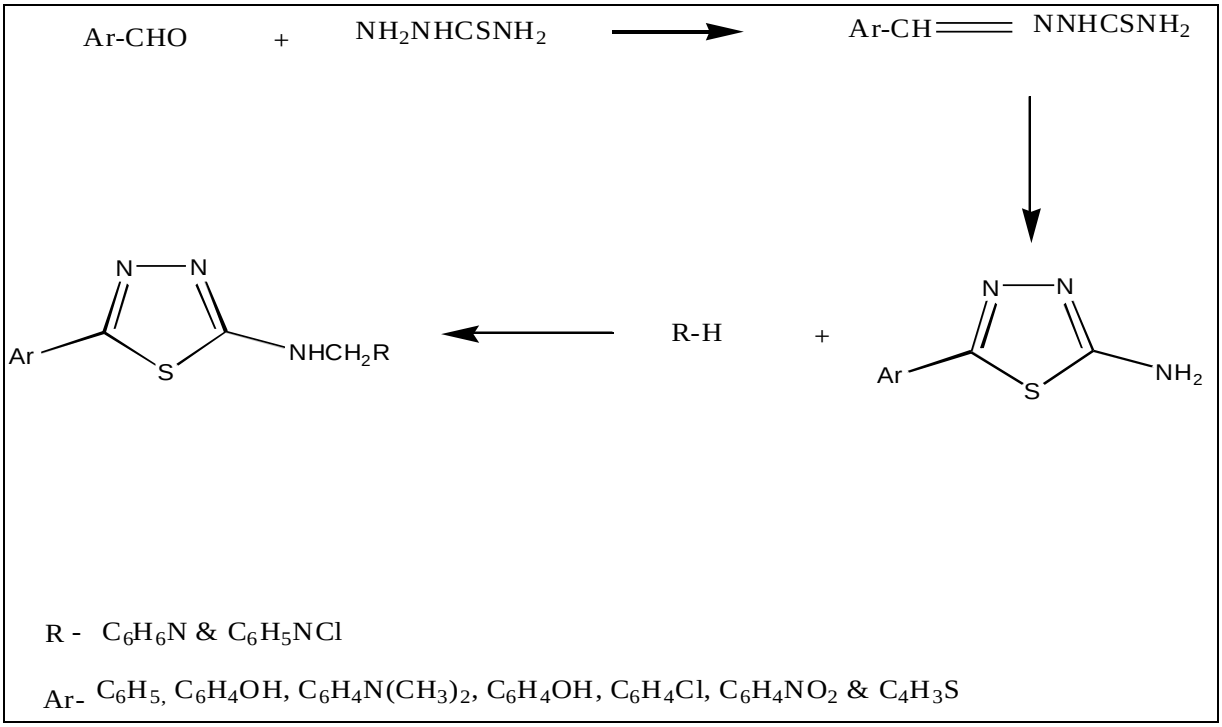

FIG. 1: SCHEME

RESULTS AND DISCUSSION: A series of 1, 3, 4-thiadiazole derivatives were synthesized and the structures of the compounds were established by means of IR, ^{1}H-NMR and mass spectrum analysis. All the compounds were evaluated for antibacterial and antifungal activity by cup plate method. Compounds **A, C, D, E, F, J** and **M** have shown significant antibacterial activity. Remaining compounds have also shown moderate or weak antibacterial activity. Compounds **A, D, E, F, J, K** and **M** have shown significant antifungal activity. Remaining compounds have also shown moderate or weak antifungal activity. The results are reported in **Table 2.** With the suitable molecular modification of these compounds can prove as potent antimicrobial agents in future.

TABLE 2: ANTIBACTERIAL AND ANTIFUNGAL ACTIVITY OF SYNTHESIZED COMPOUNDS

Compd. No.	Zone of inhibition at 100mcg/mL (in mm.)			
	E. Coli	*S. aureus*	*A. niger*	*C. albicans*
A	22	23	22	25
B	15	16	18	17
C	24	23	17	19
D	23	23	25	24
E	23	22	24	24
F	23	23	24	25
G	18	17	19	15
H	14	13	15	14
I	18	17	16	18
J	23	25	24	22
K	14	15	22	23
L	18	14	16	17
M	25	23	24	26
N	17	14	15	19
Norfloxacin	24	25	--	--
Griseofulvin	--	--	26	27

ACKNOWLEDGEMENTS: The authors are thankful to his Holiness Jagadguru Sri Shivarathri Deshikendra Mahaswamigalavaru of Suttur Mutt, Mysore and the Principal, J.S.S. College of Pharmacy, Ooty, Tamil Nadu, India, for his kind help and encouragement during our research work.

REFERENCES

1. Arun KP and Nag VL Panda CS: Indian J chem 1999; 38B:998-1001.
2. Agarwal VR, Nautiyal SR and Mukerji DD: Indian ssDrugs 1986; 23:458-465.
3. Ameya A. Chavan and Nandini R. Pai: Molecules 2007; 12:2467-2477.
4. Jitendra P. Suryavanshi and Nandini R Pai: Indian J Chem 2006; Sec B: 1227-1230.
5. Alagarswamy V, Pathak US, Rajasolomon V, Meena S, Ramseshu KV and Rajesh R: Indian J Hetero Chem 2004; 13:347-352.
6. Patel JB, Desai PS, Dessai KR and Chikhalia KH: Int J Chem 2006; 773-778.
7. Barr Al: Biol Abstr 1976; 64:25783.
8. Sanmati K. Jain and P. Mishra: Asian J Chem 2000; 12:1341-1343.
9. Sanmati K. Jain and Pradeep Mishra: Asian J Chem 2000; 12:1341-1343.
10. Pattan Shashikant R, Desai NS, Rabara PA, Bukitgar AA and Wakale VS: Indian J Pharm Educ Res 2008; 42(4):314-318.

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