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Research Article

Synthesis and antimicrobial activity of some 2-[(2- substituted-phenyl-5-methyl-1, 3-thiazolidin-4-one)-5-(2'-methylamino-4-phenyl-1', 3'- thiazolyl]-1, 3, 4-thiadiazoles

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ABSTRACT

A new 2-[(2-substituted phenyl-5-methyl-1,3-thiazolidin-4-one)-5-(2'-methylamino-4-phenyl-1',3'-thiazolyl]-1,3,4-thiadiazoles, **5(a-n)** were synthesized from 2-substituted-benzylideneamino-5-[2'-methyl-amino 4'-phenyl-1',3'-thiazolyl]-1,3,4-thiadiazole, **4(a-n)** using 2-amino-4-phenyl-1,3-thiazole as a starting material. The synthesised compounds have been screened *in vitro* for their antimicrobial activity against *Bacillus subtilis, Escherichia coli. Klebsiella pneumoniae* and *Streptococcus aureus* bacteria and *Aspergillus niger, Aspergillus flavus, Fusarium oxisporium* and *Trichoderma viride* fungi respectively. Some of the compounds displayed pronounced biological activity.

Keywords: 2-Amino-4-phenyl-1,3-thiazole; Thiadiazole; Arylidene; 4-Thiazolidinone; Antimicrobial activity.

INTRODUCTION

Thiazole template is a privileged structure fragments in modern medicinal chemistry considering its broad pharmacological spectrum and affinity for various biotargets of these class heterocyclic compounds. It is among the usually occurred heterocyclic nuclei in many marine as well as natural plant products possessing the wide range of biological applications (Hossein, 2006). Thiazole derivatives display a wide range of biological activities such as cardiotonic fungicidal, sedative, anesthetic, bactericidal and anti-inflammatory. (Theophil, 2003; Dawane, 2009) Some of thiazole derivatives, especially 2-aminothiazoles, possessed antiviral (Ghaemmaghami, 2010), antimicrobial (Siddiqui, 2007), anticancer (Bang, 2010), antiulcer (Ibrahim, 2010), anti-inflammatory (Pei, 2009) effects. Aminothiazoles and related heterocycles represents a novel class of potent and selective antitumor agents which exhibit nanomolar inhibitory activity against a range of human breast, leukemia, lung, colon, CNS, melanoma, ovarian, renal and prostate cell lines *in vitro.* (Gorczynski, 2004; Misra, 2004 ; El-Subbagh, 1999; Kayagil, 2009). Talipexol (Kitamura, 1998) and Pramipexole (Dodd, 2005) with a 2-aminothiazole moiety are used as antiparkinsonian drugs and dopamine agonists; Tigemonam (Fuchs, 1988) is an antibacterial drug and Amthamine (Eriks, 1992) is known as an antiasthmatic one. Aminothiazoles are known to be ligands of estrogen receptors (Brian,1999) as well as a novel class of adenosine receptor antagonists (Cole, 2009)whereas other analogues are used as fungicides, inhibiting in vivo growth of *Xanthomonas* and as an ingredient of herbicides or as schistosomicidal and anthelmintic drugs. (Metzger, 1984). 4-Oxo-thiazolidines and their 5- arylidene derivatives also possess a variety of therapeutic activities such as antimicrobial, (Dua, 2010; Esra, 2008) antiinflammatory, (Kohli, 2007) and anti tubercular (Verma, 2008) etc. The incorporation of 4-oxo-thiazolidines in aminothiazoles framework has been found to enhance the activity.

Thus considering all these biologically important properties of such types of compounds, different types of 2-aminothiazole derivatives were prepared. By considering the above arguments, we have synthesised several new 2-[(2- substituted phenyl-5-methyl- 1,3-thiazolidin -4-one)-5-(2'-methylamino-4-phenyl-1',3'-thiazolyl]-1, 3,4-thiadiazoles, **5(a-n)** were synthesized from 2-substituted-benzylideneamino-5-[2'-methyl-amino 4'-phenyl-1',3'-thiazolyl]-1,3,4-thiadiazole, **4(a-n)** using 2-amino-4-phenyl-1, 3-thiazole as a starting material by appropriate methods. All the synthesized compounds have been screened for their antibacterial activity against *B. substilis, E. coli, S. aureus* and *K. pneumoniae* bacteria and antifungal activity against *A. niger, A. flavus, F. oxisporium* and *T. viride* fungi respectively.

MATERIALS AND METHODS

Melting points were taken in open capillaries and are uncorrected. Purity of compounds was monitored on

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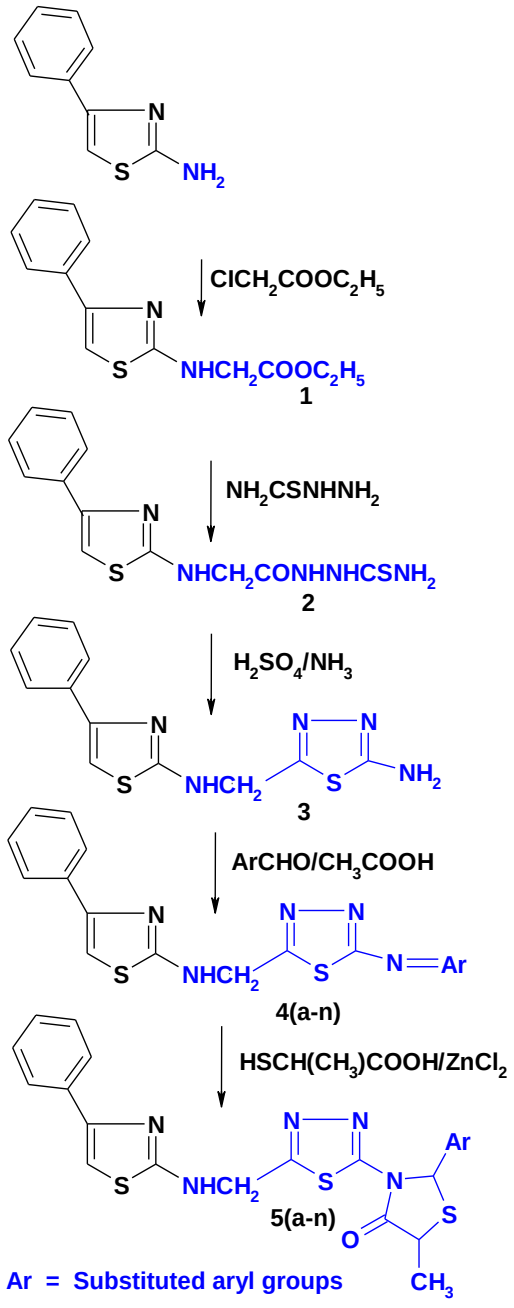
silica gel "G" coated TLC plates. All instrumental analysis was performed in the Central Drugs Research Institute Lucknow (India). IR spectra were recorded in KBr disc on a Schimadzu 8201 PC, FTIR spectrophotometer (ν_{max} in cm^{-1}) and ^{1}HNMR spectra were measured on a Brucker DRX-300 spectrometer in $CDCl_3$ at 300 MHz using TMS as an internal standard. All chemical shifts were reported as δ (ppm) values. The FAB mass spectra were recorded on a Jeol SX–102 mass spectrometer. Elemental analyses were performed on a Carlo Erba–1108 analyzer. The analytical data of all the compounds were highly satisfactory. For chromatographic purification Merck silica Gel 60 (230-400 Mesh) was used. The reagent grade chemicals were purchased from the commercial sources and purified by either distillation or recrystallization before use.

Scheme 1



General procedure for the synthesis of the new compounds

Preparation of 2-(Ethylaminoacetate)-4-phenyl-1,3-thiazole (1)

A mixture of 2-amino-4-phenyl-1,3-thiazole (0.35 mole, 61.68 g) and ethyl-chloroacetate (0.35 mole, 42.87 g) with K_2CO_3 (6.168 g) in methanol (300 ml) was kept overnight at room temperature. The reaction mixture was refluxed on a steam bath for about 1 hr. It was cooled, filtered and solvent was distilled off under reduced pressure. The solid obtained, dried over $CaCl_2$, recrystallised with ethanol to furnish colourless needles of compound **1**.

Yield 74%, m.p. 159-61°C Anal. Calcd for $C_{13}H_{14}N_2O_2S$: C, 59.54, H, 5.34, N, 10.68%; found C, 59.51, H, 3.32, N, 10.63%; IR (υ,cm^{-1}): 3358 (-NH), 1720 (C=O), 3022, 2846, 1593, 1418, 740 (thiazole with aromatic ring); ^{1}HNMR(δ,ppm):1.90 (t, 3H, J=7Hz, -$COOCH_2\underline{CH_3}$), 4.42 (q, *J=3.5Hz*, 2H, -CH_2), 7.82 (t, *J=2.8Hz,* 1H, -NH), 6.66 (s, 1H, -CH, C-5 of thiazole), 6.86-7.72 (m, 5H, Ar-H); Mass(FAB) : 262 (M^+), 217, 189, 175, 134, 133, 77, 56, 45.

Preparation of 2-Acetylamino-thiosemicarbazide-4-phenyl-1,3-thiazole (2)

The compound **1** (0.17 mole, 44.54 g) and thiosemicarbazide (0.17 mole, 15.49g) in methanol (250 ml) was refluxed on a steam bath for about 10 hr. It was filtered, cooled and purified over the column of silica gel using acetone: methanol (6:4v/v) mixture as an eluent. The eluate was concentrated and the product was recrystallised with ethanol to give compound **2**.

Yield 87%, m.p. 131-33°C. Anal. Calcd for $C_{12}H_{13}N_5OS_2$: C, 46.90, H, 4.23, N, 22.80% ; found C, 46.83, H, 4.16, N, 22.71%; IR(υ,cm^{-1}): 3400, 3275 (-NH_2), 3352 (-NH),; ^{1}HNMR : (δ,ppm): 8.12 - 8.35 (m, 4H, -$NHNHCSNH_2$), 7.80 (t, *J=5.0 Hz*, 1H, -NH), 4.44 (d, *J=5.0Hz,* 2H, -CH_2), 6.62 (s, 1H, -CH,C-5 of thiazole), 6.89-7.76 (m, 5H, Ar-H); Mass(FAB) :307(M^+), 291, 232, 217, 189, 175, 134, 133, 77, 59, 56.

Preparation of 2-Amino-[5-(2'-methylamino - 4'-phenyl-1',3'-thiazolyl)]-1,3,4-thiadiazole (3)

The equimolar mixture of compound **2** (0.125 mole, 38.37 g) and con. H_2SO_4 (0.125 mole, 12.25 g, AR grade) in methanol (150 ml) was kept overnight at room temperature. It was refluxed on a steam bath for about 8 hr. After cooling the reaction mixture, it was neutralized with concentrated liq.ammonia and filtered. The solvent was removed *in vacvo*, solid thus obtained was dried and purified over the column of silica gel using chloroform: methanol (5:5 v/v) mixture as eluent. The eluate was concentrated and the product was recrystallised from ethanol to give compound **3**.

Yield, 90%, m.p. 162-64°C. Anal. Calcd. for $C_{12}H_{11}N_5S_2$: C, 49.82, H, 3.80, N, 24.22%, found : C, 49.76, H, 3.72,

Table 1: Characterization data of the compounds 4(b-n) and 5(b-n)

Comp	*Ar*	Yield (%)	M.P. (^{o}C)	Molecular formula	Found% (Calcd)		
					C	H	N
4b	2-ClC_6H_4	74	145-47	$C_{19}H_{14}N_5S_2Cl$	55.33 (55.40)	3.32 (3.40)	16.91 (17.01)
4c	3-ClC_6H_4	75	148-50	$C_{19}H_{14}N_5S_2Cl$	55.34 (55.40)	3.31 (3.40)	16.93 (17.01)
4d	4-ClC_6H_4	72	143-45	$C_{19}H_{14}N_5S_2Cl$	55.32 (55.40)	3.34 (3.40)	16.87 (17.01)
4e	2-BrC_6H_4	81	218-20	$C_{19}H_{14}N_5S_2Br$	49.89 (50.60)	2.98 (3.07)	15.29 (15.35)
4f	3-BrC_6H_4	84	208-10	$C_{19}H_{14}N_5S_2Br$	49.87 (50.60)	2.94 (3.07)	15.28 (15.35)
4g	4-BrC_6H_4	79	227-29	$C_{19}H_{14}N_5S_2Br$	49.86 (50.60)	2.97 (3.07)	15.27 (15.35)
4h	2-$OCH_3C_6H_4$	67	107-09	$C_{20}H_{17}N_5OS_2$	58.86 (58.96)	4.13 (4.17)	17.11 (17.19)
4i	3-$OCH_3C_6H_4$	68	96-98	$C_{20}H_{17}N_5OS_2$	58.89 (58.96)	4.12 (4.17)	17.10 (17.19)
4j	4-$OCH_3C_6H_4$	65	176-78	$C_{20}H_{17}N_5OS_2$	58.87 (58.96)	4.11 (4.17)	17.13 (17.19)
4k	2-$NO_2C_6H_4$	79	168-70	$C_{19}H_{14}N_6O_2S_2$	53.97 (54.02)	3.26 (3.31)	19.84 (19.90)
4l	3-$NO_2C_6H_4$	76	176-78	$C_{19}H_{14}N_6O_2S_2$	53.96 (54.02)	3.24 (3.31)	19.82 (19.90)
4m	4-$NO_2C_6H_4$	78	173-75	$C_{19}H_{14}N_6O_2S_2$	53.92 (54.02)	3.29 (3.31)	19.79 (19.90)
4n	4,4-$(CH_3)_2NC_6H_4$	91	123-25	$C_{21}H_{20}N_6S_2$	59.89 (60.00)	4.69 (4.76)	19.93 (20.00)
5b	2-ClC_6H_4	69	168-70	$C_{22}H_{18}N_5OS_3Cl$	52.79 (52.85)	3.77 (3.80)	13.96 (14.01)
5c	3-ClC_6H_4	68	169-71	$C_{22}H_{18}N_5OS_3Cl$	52.76 (52.85)	3.78 (3.80)	13.97 (14.01)
5d	4-ClC_6H_4	70	173-75	$C_{22}H_{18}N_5OS_3Cl$	52.78 (52.85)	3.76 (3.80)	13.98 (14.01)
5e	2-BrC_6H_4	81	161-63	$C_{22}H_{18}N_5OS_3Br$	48.49 (48.52)	3.46 (3.49)	12.82 (12.86)
5f	3-BrC_6H_4	78	186-88	$C_{22}H_{18}N_5OS_3Br$	48.48 (48.52)	3.47 (3.49)	12.84 (12.86)
5g	4-BrC_6H_4	80	176-77	$C_{22}H_{18}N_5OS_3Br$	48.47 (48.52)	3.45 (3.49)	12.83 (12.86)
5h	2-$OCH_3C_6H_4$	70	123-25	$C_{23}H_{21}N_5O_2S_3$	55.72 (55.75)	4.19 (4.24)	14.09 (14.14)
5i	3-$OCH_3C_6H_4$	71	130-32	$C_{23}H_{21}N_5O_2S_3$	55.73 (55.75)	4.20 (4.24)	14.10 (14.14)
5j	4-$OCH_3C_6H_4$	75	118-20	$C_{23}H_{21}N_5O_2S_3$	55.71 (55.75)	4.20 (4.24)	14.11 (14.14)
5k	2-$NO_2C_6H_4$	67	141-43	$C_{22}H_{18}N_6O_3S_3$	51.72 (51.76)	3.47 (3.52)	16.43 (16.47)
5l	3-$NO_2C_6H_4$	65	145-47	$C_{22}H_{18}N_6O_3S_3$	51.74 (51.76)	3.49 (3.52)	16.45 (16.47)
5m	4-$NO_2C_6H_4$	70	144-46	$C_{22}H_{18}N_6O_3S_3$	51.73 (51.76)	3.48 (3.52)	16.44 (16.47)
5n	4, 4-$(CH_3)_2NC_6H_4$	83	158-60	$C_{24}H_{24}N_6S_3$	56.66 (56.69)	4.69 (4.72)	16.49 (16.53)

Table 2: Antibacterial activity of the compounds 4(a-n) and 5(a-n) against various bacteria at different concentrations (ppm)

Comp.	*B. subtilis*		*E. coli*		*K. pneumoniae*		*S. aureus*	
	50	100	50	100	50	100	50	100
4a	-	-	-	-	-	-	-	-
4b	+	+	-	-	+	+	-	-
4c	+	+		-	+	+	-	-
4d	-	-	+	+ +	-	-	+	+ +
4e	+	+	+	+ +	-	+	-	+
4f	+	++	-	-	+	+ +	-	+
4g	+	-	+	++	-	-	-	+
4h	+	+ +	+	+ +	-	-	-	++
4i	-	+	-	+	+	+ +	+	+
4j	-	+	-	+	+	+ +	+	+
4k	+	+	-	-	+	+	-	-
4l	-	+	-	-	-	+	+	+
4m	+	+	-	+	+	+	-	+
4n	-	-	+	+	-	+	-	+
5a	-	+	-	-	-	-	-	+
5b	+ +	+ +	+	+ +	+ +	+ +	+ +	+ +
5c	+	+	+ +	+ +	+	+ +	+ +	+ +
5d	+	+	+	+ +	+ +	+ +	+ + +	+ + +
5e	+ +	+ +	+	+	+ +	+ +	+ +	+ +
5f	+ +	+ +	+ +	+ +	+ + +	+ + +	+ +	+ +
5g	+	+	+ +	+ +	+ + +	+ + +	+ +	+ +
5h	+	+	-	+	+ +	+ +	+	+
5i	+	+	+	+ +	+ +	+ +	+	+ +
5j	-	+	-	+	+	+	+	+ +
5k	+	+	+	+ +	+	+	-	-
5l	+	+	+	+	+	+	-	+
5m	+	+	-	+	+	+	-	+
5n	+	+	+	+	+ +	+ +	+	+ +
SM	+ + +	+ + + +	+ + +	+ + + +	+ + +	+ + + +	+ + +	+ + + +

SM = Streptomycin, inhibition diameter in mm (-) < 6, (+) 6-10, (++) 10-16, (+++) 16-25, (++++) 25-30.

N, 24.16%; IR(υ,cm^{-1}): 3410, 3268 (-NH_2), 3356 (-NH), 2970 (-CH_2), 1627 (-N=C-S);^{1}HNMR (δ,ppm): 4.81 (s, 1H, -NH_2), 7.94 (t, *J=5.0 Hz,* 1H, -NH), 4.41 (d, *J=5.0 Hz,* 2H, -CH_2), 6.68 (s,1H, -CH of thiazole), 6.95-7.84 (m, 5H, Ar-H).Mass(FAB):289 (M^+), 273, 215, 189, 175, 134, 133,77,58,56.

Preparation of 2-benzylidene-amino-5-[2'methylamino-4'-phenyl-1',3'-thiazolyl]-1,3,4-thiadiazole] (4a)

Equimolar mixture of compound **3** (0.0085 mole, 2.450 g) and benzaldehyde (0.0085 mole, 0.902 g) in methanol (50 ml) with 4-5 drops glacial acetic acid was refluxed on a water bath for about 2 hr. The solvent was distilled off under reduced pressure and the solid thus obtained was purified over the column of silica gel using chloroform: methanol (6:4 v/v) mixture as eluent. The eluate was concentrated and the product was recrystallised with ethanol to give crystals of compound **4a.**

Yield 75%, m.p. 176-78°C, Anal. Calcd. for $C_{19}H_{15}N_5S_2$: C, 60.47, H, 3.97, N, 18.56%, found : C, 60.36, H, 3.86, N, 18.42%; IR (υ,cm^{-1}):3357 (-NH), 2960 (-CH_2), 1546 (-N=CH); ^{1}HNMR (δ,ppm): 6.92-7.88 (m, 10 H, Ar-H), 4.91 (s, 1H, -N=CH), 4.46 *(d, J = 5Hz, 2H, -CH_2),* 7.93 (t, *J = 5.0Hz*, 1H, -NH), 6.63 (s, 1H, -CH,C-5 of thiazole). Mass (FAB); 289(M^+), 273, 215, 189, 175, 134, 133, 101, 77, 56.

Other compound **4(b-n)** was synthesized in the similar manner using compound **3** and various selected aromatic aldehydes. Characterization data are presented in **Table -1**.

Preparation of 2-[(2-phenyl-5-methyl-1,3-thiazolidin-4-one)-5-(2'-methylamino-4-phenyl-1', 3'- thiazolyl-]-1, 3,4-thiadiazoles 5(a)

The compound **4a** (0.0.06 mole, 2.26g) in methanol (30 ml) with thialactic acid (0.06 mole,0.63 g) was first stirred for about 3 hr. followed by refluxing on a steam bath for about 6 hr. It was cooled, filtered and passed through a column of silica gel using chloroform: methanol (6:4 v/v) mixture as eluent. The eluate was concentrated and dried. The product was recrystallised from ethanol to give compound **5a.**

Table 3: Antifungal activity of the compounds 4(a-n) and 5(a-n) against various fungi at different concentrations (ppm)

Comp.	*A. niger*		*A. flavus*		*F. oxisporium*		*T. viride*	
	50	100	50	100	50	100	50	100
4a	-	+	-	-	+	+	-	+
4b	-	-	+	+	-	-	+	+
4c	+	+	-	-	+	+	-	+
4d	-	-	+	+	-	-	+	+
4e	+	+	+	+	+	+	+	+
4f	-	+	+	+ +	+	+	+ +	+ +
4g	+ +	+ +	+	+	+	+	-	-
4h	-	+	-	-	-	-	-	-
4i	-	+	-	-	+	+	-	+
4j	-	-	-	-	+	+	-	+
4k	+	+	-	+	-	-	-	+
4l	+	+	-	+	-	+	+	+
4m	-	+	+	+	-	-	-	-
4n	+	+	+	+	+	++	+	+
5a	+	+ +	+	+	+	+	+	+ +
5b	-	+	+	+	+	+	+ +	+ +
5c	+	+	+	+ +	+ +	+ +	-	+
5d	+	+ +	-	+	-	+	+	+
5e	++	+ +	+	+	+	++	++	++
5f	+	+ +	++	+++	+	++	++	++
5g	++	++	+	++	++	+ + +	+ +	+ +
5h	+	+	+ +	+ +	+ +	+ +	+ +	+ + +
5i	+	+ +	+ +	+ +	+	+	+	+
5j	+	+ +	+ +	+ +	-	-	-	-
5k	+	+ +	+ +	+ +	-	+	-	+
5l	+ +	+ +	+	+	-	+	+	+
5m	+ +	+ +	+	+	+	+	+	+
5n	+	+ +	+	+	-	+	+	+ +
GF	+ + +	+ + + +	+ + +	+ + + +	+ + +	+ + + +	+ + +	+ + + +

GF = Griseofulvin, inhibition diameter in mm (-) < 4, (+) 4-12, (+ +) 12-18, (+ + +) 18-27, (+ + + +) 27-30.

Yield 70%, m.p. 182-84C . Anal. calcd. for $C_{22}H_{19}N_5OS_3$: C, 56.77, H, 4.10, N 15.05% found: C, 56.56.71, H, 4.02, N 14.96%; IR(υ,cm^{-1}):3353(-NH), 2963(-CH_2), 2892(-CH_3),1712 (>C=O); ^{1}HNMR(δ,ppm): 4.49(d, *J*=5Hz, 2H,-CH_2), 7.96(t,*J*=5Hz,-NH),6.67(s,1H, C-H,C-5 of thiazole), 6.90-7.82(m,10H Ar-H), 2.23 (d *J*=5.8Hz, 3H, -CH_3), 3.86 (q *J*=5.6Hz,1H, -NCHS); Mass(FAB) : 465 (M^+) 427, 270, 212, 189, 175,152, 134, 133, 77, 56.

Other compounds **5(b-n)** were synthesized in the similar manner using compounds **4(b-n)**. Characterization data are presented in **Table -1**

ACTIVITY STUDIES

Antibacterial activity: All the compounds were evaluated *in vitro* for antibacterial activity by using filter paper disc method against different strains of bacteria *viz*. *B. substilis, E. coli, S. aureus* and *K. pneumoniae*. All the compounds along with standard antibacterial Streptomycin were used at 50 and 100 ppm concentrations. Results are present in **Table 2**.

Procedure: Solution of known concentration (50 and 100 ppm) of the test sample were made by dissolving in DMSO. Dried and sterilized filter paper discs (6mm in diameter) soaked with known amount of test agents were placed on the nutrient agar media solidified in petridishes (120 mm diameter) and inoculated with the test organisms. These plates were then kept at low temperature (4°C) for 24 hours to allow maximum growth of the organisms. The antibacterial activity was determined by measuring the diameter of zone of inhibition in mm.

Antifungal activity: All the compounds were assayed *in vitro* for antifungal activity against *A. niger, A. flavus, F. oxisporium and T. viride* fungi employing the filter paper disc method by measuring inhibition zone in mm. All the tested compounds along with standard fungicide Griseofulvin were used at 50 and 100 ppm concentrations. Results are presented in **Table 3.**

Procedure: The test samples were dissolved in DMSO to make 50 and 100 ppm concentration solutions. Sterilized symmetrical filter paper discs of 6 mm diameter

were taken in a blank petridishes sample solution 10 µl /discs were applied on the discs with the help of a micropipette in an aseptic condition. The discs were left for a few minutes in the aseptic condition for complete removal of the solvent. Isolated spore (4-6 similar) of pure fungus was inoculated in screw capped tube containing equal amount of potato dextrose agar (PDA) media and incubated at 28°C for 5-7 days for development of new pure culture that was used as inoculum. PDA medium was steamed to dissolve and dispersed 4 ml amount of it into a petridish. It was then autoclaved at 121°C for 15 minutes. It was allowed to cool to 30°C until the media became solid. Each petridish was inoculated with different types of inoculums removed from a seven days old culture fungus. Dried and sterile sample discs and standard (Fungal) disc were placed on nutrient agar plates seeded with the test organism. These were then kept at low temperature (4°C) for 24 hours to allow maximum diffusion. Finally the petridishes were inoculated at 27-28°C for 5-7 days. The activity was justified by measuring the diameter of zone of inhibition in mm.

RESULTS AND DISCUSSION

Reaction of ethylchloroacetate with 2-amino-4-phenyl-1,3-thiazole yielded 2-(ethyaminoacetate)-4-phenyl-1,3-thiazole, **(1)** followed by thiosemicarbazide resulted in the formation of 2-(acetylamino-thiosemicarbazide-4-phenyl-1,3-thiazole, **(2).** The compound **(2)** on dehydrative annulation by mineral acid afforded the thiadiazole **(3)** which on condensation with various substituted aromatic aldehydes furnished 2 substituted-benzylidene-amino-5-[2'- methyl -amino 4'-phenyl-1',3'-thiazolyl]-1,3,4-thiadiazoles, **4(a-n)**.The compounds **4(a-n)** on reaction with thiolactic acid afforded 2-[(2- substituted-phenyl-5-methyl- 1,3-thiazolidin-4-one)-5-(2'-methylamino-4-phenyl-1',3'-thiazolyl-]-1,3,4-thiadiazoles , **5(a-n**). The structures of new compounds were confirmed by elemental analysis IR, ^{1}HNMR and Mass spectral data.

All the synthesized compounds **4(a-n)** and **5(a-n)** have been screened *in vitro* for their antibacterial activity against *B. subtilis* (Bs)*, E. coli* (Ec)*, S. aureus* (Sa) and *K. pneumoniae* (Kp) at two concentrations (50 and 100 ppm) and antifungal activity against *A. niger* (An)*, A. flavus* (Af)*, F. oxisporium* (Fo) and *T. viride* (Tv) at two concentrations (50 and 100 ppm). Standard antibacterial Streptomycin and fungicide Griseofulvin were also screened under the similar conditions for comparison. The following compounds were found active against the tested bacteria :4d(Ec,Sa), 4f(Bs,Kp), 4g(Ec), 4h(Bs,Ec,Sa), 4i,4j(Kp), 5b,5c,5d,5e,5f,5g(Bs,Ec,Kp,Sa), 5i(Ec,Kp,Sa), 5h(Kp), 5k (Ec), 5n(Kp,Sa) and fungi :5f(Af,Tv), 5g(An), 4n(Fo), 5b(Tv), 5c(Af, Fo), 5d(An), 5e,5f,5g(An,Af, Fo,Tv), 5i(Af,Fo), 5j(An,Af), 5h(Fo,Tv), 5k(An,Af), 5l, 5m, 5n(An). On the basis of structural activity relationship it has been observed that among the substituents present on the phenyl ring, halo derivatives were found to be highly active against in the series. Further study reveals that bromo derivatives are highly active.

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