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Synthesis, Characterization and Biological Activity of Some Thiophene Substituted Biheterocycles Containing Oxadiazoles

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5-(2-Amino-4,5,6,7- tetrahydro-1-benzothien-3-yl) N-substituted 1,3,4-oxadiazole-2-amines (**IVa-e**) were synthesized by treating (**IIIa-e**) with NaOH. Compounds (**IIIa-e**) were synthesized by treating 2-amino-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carbohydrazide (**II**) with isothiocyanate. Compound **II** was synthesized by treating ethyl 2-amino-4,5,6,7-tetra hydrobenzeno[b]thiophene-3-carboxylate (**I**) with hydrazine hydrate. Compound **I** was prepared by treating cyclohexanone, sulphur, ethylcyanoacetate with diethyl amine. All the synthesized compounds were charecterized by IR, NMR and mass spectrometry and then evaluated for antiinflammatory and antibacterial activity againt *Staphylococcus aureus, Escherichia coli, Bacillus pumilis, Bacillus subtilis* and *Pseudomonas aerugenosa*.

Key Words: Synthesis, Thiophene substituted biheterocycles, Oxadiazoles, Biological activity.

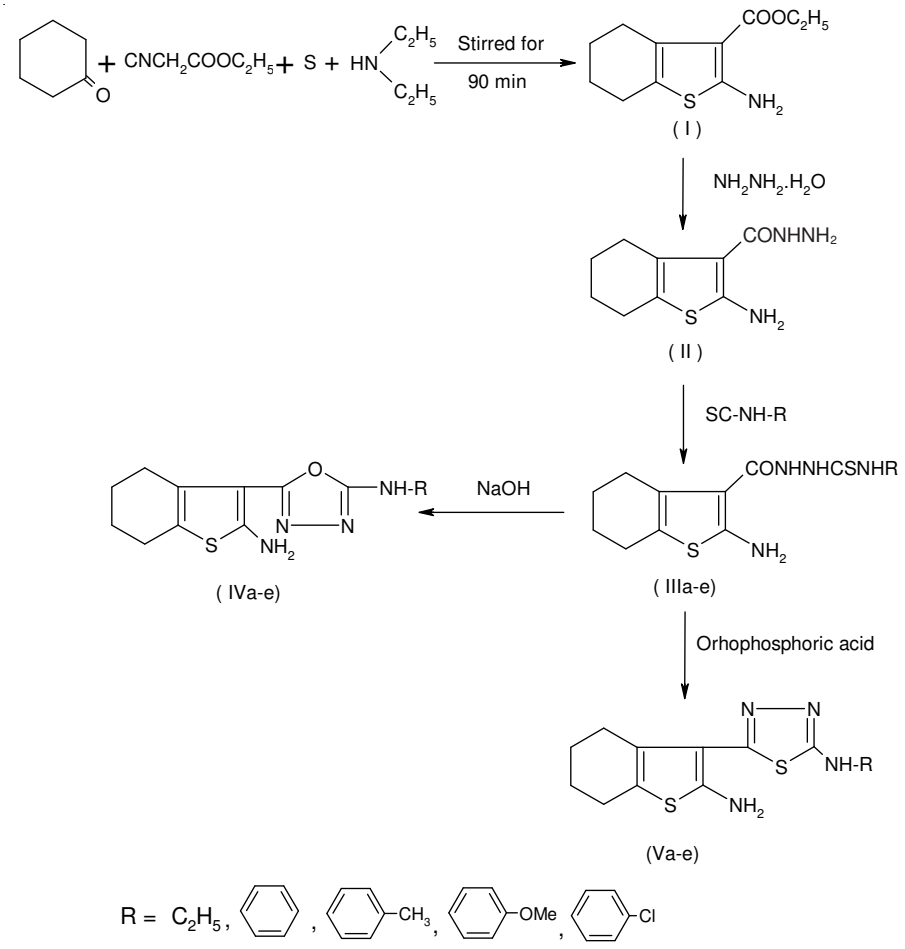
INTRODUCTION

Substituted thiophene and their biheterocycles have received considerable attention during last two decades as they have endowed with variety of biological activities and have wide range of therapeutic properties[1-3]. A literature survey indicates that oxadiazole derivatives possess different pharmacological and biological activities, having potent antibacterial activity[4-7]. It is worth to synthesize oxadiazole system incorporating thiophene substituted biheterocycles. Oxadiazole system may be viewed as cyclic analogues of important compound, which is thiosemicarbazide that often display diverse biological activities.

Hence, in the present study, the two system such as thiophene substituted biheterocycles and oxadiazoles are attached to each other and show highly potent and less toxic antibacterial agents.

EXPERIMENTAL

All the melting points were recorded in open capillary tube and are uncorrected. IR spectra were recorded on a thermo Niolet Nexus 670 spectrometer with resolution 4 cm^{-1}. ^1H NMR spectra were recorded on Amx-400 NMR spectrometer at 400 MHz with DMSO as the solvent and TMS as internal standard. The purity was checked by thin layer chromatography using silica gel G. All the compounds were synthesized according to **Scheme-I**.



Scheme-I

Synthesis of ethyl-2-amino-4,5,6,7-tetrahydro benzo(b)thiophene-3-carboxylate (I): An equimolar mixture of cyclohexanone (0.1 mol), sulphur (0.1 mol), ethyl cyanoacetate (0.1 mol) and diethyl amine (0.1 mol) in dry ethanol (20 mL) is taken in a 500 mL round bottomed flask and stirred for 1.5 h. The mixture is then poured into ice water with constant stirring and set aside for 3 h at room temperature. The separated solid was collected by filtration, dried and recrystallized from ethanol. Yield: 82.75 % m.p. 102 ºC.

Synthesis of ethyl, 2-amino-4,5,6,7-tetrahydro benzo(b)thiophene-3-carbohydrazide (II): Compound **I** (0.1 mol) dissolved in 20 mL ethanol and stirred magnetically for 0.5 h. Then hydrazine hydrate (99 %) was added and the reaction mixture was heated under reflux on a water bath for 4 h. The mixture then poured onto ice and colourless crystalline solid separated out. The product was recrystallized from ethanol. Yield: 75.83 %, m.p. 105 ºC.

Synthesis of 2-[(2-amino-4,5,6,7-tetrahydro-1-benzothiene-3yl)carbonyl]-N-substituted hydrazine carbothioamide (IIIa-e): A suspension of compound **II** (0.1 mol) in dry benzene was reacted with an appropriate isothiocyanate (0.1 mol). The mixture was heated under reflux for 3 h on steam bath then poured onto ice. The thiosemicarbazide separated was collected, dried and recrystallized from ethanol.

2-[(2-Amino-4,5,6,7-tetrahydro-1-benzothien-3-yl)carbonyl]-N-(4-ethyl)-hydrazine carbothioamide (IIIa): IR (KBr, ν_{max}, cm^{-1}): 3384 (NH *str.*), 3299 (NH_2), 2938 (CH *str.*), 3405 (NH), 2840 (C-H) aliphatic, 1366 (C=N), 1274 (N-N), 781 (C-S-C). ^{1}H NMR (DMSO-d_6) δ: 3.8 (s, 3H of 3.NH), 7.7 (s, 2H of NH_2), 5.9-6.2 (m, 4H of Ar-H), 4.2 (s, 3H of CH_3), 1.4-2.7 (m, 8H of CH_2 aliphatic). MS m/z (%): M+1 = 376.

2-[(2-Amino-4, 5,6,7-tetrahydro-1-benzothien-3-yl)carbonyl]-N-(4- phenyl)-hydrazine carbothioamide (IIIb): IR (KBr, ν_{max}, cm^{-1}): 3384 (NH *str.*), 3299 (NH_2), 2938 (CH *str.*), 3405 (NH), 2840 (C-H) aliphatic, 1366 (C=N), 1274 (N-N), 781 (C-S-C). ^{1}H NMR (DMSO-d_6) δ: 3.8 (s, 3H of 3.NH), 7.7 (s, 2H of NH_2), 5.9-6.2 (m, 4H of Ar-H), 4.2 (s, 3H of CH_3), 1.4-2.7 (m, 8H of CH_2 aliphatic). MS m/z (%): M+1 = 376.

2-[(2-Amino-4,5,6,7-tetrahydro-1-benzothien-3-yl)carbonyl]-N-(4-methoxy phenyl)hydrazine carbothioamide (IIIc): IR (KBr, ν_{max}, cm^{-1}): 3384 (NH *str.*), 3299 (NH_2), 2938 (CH *str.*), 3405 (NH), 2840 (C-H) aliphatic, 1366 (C=N), 1274 (N-N), 781 (C-S-C). ^{1}H NMR (DMSO-d_6) δ: 3.8 (s, 3H of 3.NH), 7.7 (s, 2H of NH_2), 5.9-6.2 (m, 4H of Ar-H), 4.2 (s, 3H of CH_3), 1.4-2.7 (m, 8H of CH_2 Aliphatic). MS m/z (%): M+1 = 376.

2-[(2-Amino-4,5,6,7-tetrahydro-1-benzothien-3-yl)carbonyl]-N-(4-methyl phenyl)hydrazine carbothioamide (IIId): IR (KBr, ν_{max}, cm^{-1}): 3384 (NH *str.*), 3299 (NH_2), 2938 (CH *str.*), 3405 (NH), 2840 (C-H) aliphatic, 1366 (C=N), 1274 (N-N), 781 (C-S-C). ^{1}H NMR (DMSO-d_6) δ: 3.8 (s, 3H of 3.NH), 7.7 (s, 2H of NH_2), 5.9-6.2 (m, 4H of Ar-H), 4.6 (s, 3H of CH_3), 1.4-2.7 (m, 8H of CH_2 Aliphatic). MS m/z (%): M+1 = 376.

2-[(2-Amino-4,5,6,7-tetrahydro-1-benzothien-3-yl)carbonyl]-N-(4-chloro phenyl)hydrazine carbothioamide (IIIe): IR (KBr, ν_{max}, cm^{-1}): 3384 (NH *str.*), 3299 (NH_2), 2938 (CH *str.*) 3405 (NH) 2840 (C-H) aliphatic, 1366 (C=N), 1274 (N-N), 781 (C-S-C). ^{1}H NMR (DMSO-d_6) δ: 3.8 (s, 3H of 3.NH), 7.7 (s, 2H of NH_2), 5.9-6.2 (m, 5H of Ar-H), 1.4-2.7 (m, 8H of CH_2 aliphatic). MS m/z (%): M+1 = 376.

Synthesis of 5-(2-amino-4,5,6,7-tetrahydro-1-thiene-3-yl)-N-substituted-1,3,4-oxadiazole-2-amines (IVa-e): An equimolar mixture of compound **IIIa-e** (0.1 mol) in ethanol was slightly heated to form a solution in which aqueous sodium hydroxide (4 %) was added. To this a solution of iodine in potassium iodide (aqueous, 5 %) was added in portions with vigorous shaking until the colour of iodine persisted at room temperature. The reaction mixture was heated under reflux for 1 h and concentrated under reduced pressure; transferred to crushed ice and recrystallized from petroleum ether. The physical characteristics are presented in Table-1.

5-[(2-Amino-4,5,6,7-tetrahydro-1-benzothien-3-yl)-N-ethyl-1,3,4-oxadiazole-2-amine (IVa): IR (KBr, ν_{max}, cm^{-1}): 3384 (NH *str.*), 3299 (NH_2), 2938 (CH *str.*), 3405 (NH), 2840 (C-H) aliphatic, 1366 (C=N), 1274 (N-N), 781 (C-S-C). ^{1}H NMR (DMSO-d_6) δ: 4.2 (s, 3H of 3.NH), 7.7 (s, 2H of NH_2), 4.2 (s, 3H of CH_3), 1.4-2.7 (m, 8H of CH_2 aliphatic), 4.2-4.3 (t, 3H of CH_3), 1.2-1.3 (q, 2H of CH_2). MS m/z (%): M+1 = 265.

5-[(2-Amino-4,5,6,7-tetrahydro-1-benzothien-3-yl)-N-phenyl-1,3,4-oxadiazole-2-amine (IVb): IR (KBr, ν_{max}, cm^{-1}): 3384 (NH *str.*), 3299 (NH_2), 2938 (CH *str.*), 3405 (NH), 2840 (C-H) aliphatic, 1366 (C=N), 1274 (N-N), 781 (C-S-C). ^{1}H NMR (DMSO-d_6) δ: 7.7 (s, 1H of NH_2), 3.8 (s, 3H of 3.NH), 5.9-6.2 (m, 5H of Ar-H), 1.4-2.7 (m, 8H of CH_2 aliphatic). MS m/z (%): M+1 = 312.

5-[(2-Amino-4,5,6,7-tetrahydro-1-benzothien-3-yl)-N-(4-methoxy phenyl)-1,3,4-oxadiazole-2-amine (IVc): IR (KBr, ν_{max}, cm^{-1}): 3384 (NH *str.*), 3299 (NH_2), 2938 (CH *str.*), 3405 (NH), 2840 (C-H) aliphatic, 1366 (C=N), 1274 (N-N), 781 (C-S-C). ^{1}H NMR (DMSO-d_6) δ: 7.7 (s, 1H of NH_2), 3.8 (s, 3H of 3.NH), 5.9-6.2 (m, 4H of Ar-H), 4.2 (s, 3H of CH_3), 1.4-2.7 (m, 8H of CH_2 Aliphatic). MS m/z (%): M+1 = 343.

5-[(2-Amino-4,5,6,7-tetrahydro-1-benzothien-3-yl)-N-(4-methyl phenyl)-1,3,4-oxadiazole-2-amine (IVd): IR (KBr, ν_{max}, cm^{-1}): 3384 (NH *str.*), 3299 (NH_2), 2938 (CH *str.*), 3405 (NH), 2840 (C-H) aliphatic, 1366 (C=N), 1274 (N-N), 781 (C-S-C). ^{1}H NMR (DMSO-d_6) δ: 7.7 (s, 1H of NH_2), 3.8 (s, 3H of 3.NH), 5.9-6.2 (m, 4H of Ar-H), 4.4 (s, 3H of CH_3), 1.4-2.7 (m, 8H of CH_2 Aliphatic). MS m/z (%): M+1 = 327.

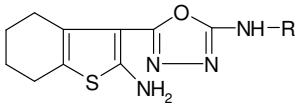
5-[(2-Amino-4,5,6,7-tetrahydro-1-benzothien-3-yl)-N-(4-chloro phenyl)-1,3,4-oxadiazole-2-amine (IVe): IR (KBr, ν_{max}, cm^{-1}): 3384 (NH *str.*), 3299 (NH_2), 2938 (CH *str.*), 3405 (NH), 2840 (C-H) aliphatic, 1366 (C=N), 1274 (N-N), 781 (C-S-C). ^{1}H NMR (DMSO-d_6) δ: 7.7 (s, 1H of NH_2), 3.8 (s, 3H of 3.NH), 6.2-7.1 (m, 4H of Ar-H), 1.4-2.7 (m, 8H of CH_2 Aliphatic). MS m/z (%): M+1 = 347.

5-[(2-Amino-4,5,6,7-tetrahydro-1-benzothien-3-yl)-N-substituted-1,3,4-thiadiazole-2-amine (Va-e): Orthophosphoric acid (10 mL, 0.1 mol) was added slowly to the compound **IIIa-e** (0.1 mol). Then the mixture was heated at 110-130 ºC for 0.5 h and then poured on to crushed ice with continuous stirring. The product was obtained, dried and recrystallized from petroleum ether. The physical characteristics are presented in Table-1.

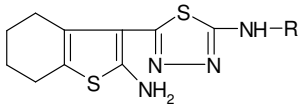
5-[(2-Amino-4,5,6,7-tetrahydro-1-benzothien-3-yl)-N-ethyl-1,3,4- thiadiazole-2-amine (Va): IR (KBr, ν_{max}, cm^{-1}): 3384 (NH *str.*), 3299 (NH_2), 2938 (CH *str.*), 3405 (NH), 2840 (C-H) aliphatic, 1366 (C=N), 1274 (N-N), 781 (C-S-C). ^{1}H NMR (DMSO-d_6) δ: 7.7 (s, 2H of NH_2), 4.2 (s, 3H of 3.NH), 4.2 (s, 3H of CH_3), 1.4-2.7 (m, 8H of CH_2 aliphatic), 4.2-4.3 (t, 3H of CH_3), 1.2-1.3 (q, 2H of CH_2). MS m/z (%): M+1 = 281.

5-[(2-Amino-4,5,6,7-tetrahydro-1-benzothien-3-yl)-N-phenyl-1,3,4- thiadiazole-2-amine (Vb): IR (KBr, ν_{max}, cm^{-1}): 3384 (NH *str.*), 3299 (NH_2), 2938 (CH *str.*), 3405 (NH), 2840 (C-H) aliphatic, 1366 (C=N), 1274 (N-N), 781 (C-S-C). ^{1}H NMR

TABLE-1
CHARACTERIZATION DATA OF COMPOUNDS **IVa-e** AND **Va-e**



IVa-e



Va-e

Compd.	R	m.f.	m.p. (ºC)	Yield (%)
IVa	Ethyl	$C_{12}H_{16}N_4OS$	108	39
IVb	Phenyl	$C_{16}H_{16}N_4OS$	105	37
IVc	4-Methoxy phenyl	$C_{17}H_{18}N_4O_2S$	107	36
IVd	4-Methyl phenyl	$C_{17}H_{18}N_4OS$	106	34
IVe	4-Chloro phenyl	$C_{16}H_{15}N_4OSCl$	109	35
Va	Ethyl	$C_{12}H_{16}N_4S_2$	98	34
Vb	Phenyl	$C_{16}H_{16}N_4S_2$	106	29
Vc	4-Methoxy phenyl	$C_{17}H_{18}N_4OS_2$	105	26
Vd	4-Methyl phenyl	$C_{17}H_{18}N_4S_2$	102	24
Ve	4-Chloro phenyl	$C_{16}H_{15}N_4S_2Cl$	101	32

(DMSO-d_6) δ: 7.7 (s, 1H of NH_2), 3.8 (s, 3H of 3.NH), 5.9-6.2 (m, 5H of Ar-H), 1.4-2.7 (m, 8H of CH_2 Aliphatic). MS m/z (%): M+1 = 329.

5-[(2-Amino-4,5,6,7-tetrahydro-1-benzothien-3-yl)-N-(4-methoxy phenyl)-1,3,4-thiadiazole-2-amine (Vc): IR (KBr, ν_{max}, cm^{-1}): 3384 (NH *str.*), 3299 (NH_2), 2938 (CH *str.*), 3405 (NH), 2840 (C-H) aliphatic, 1366 (C=N), 1274 (N-N), 781 (C-S-C). ^{1}H NMR (DMSO-d_6) δ: 7.7 (s, 1H of NH_2), 3.8 (s, 3H of 3.NH), 5.9-6.2 (m, 4H of Ar-H), 4.2 (s, 3H of CH_3), 1.4-2.7 (m, 8H of CH_2 aliphatic). MS m/z (%): M+1 = 359.

5-[(2-Amino-4,5,6,7-tetrahydro-1-benzothien-3-yl)-N-(4-methyl phenyl)-1,3,4-thiadiazole-2-amine (Vd): IR (KBr, ν_{max}, cm^{-1}): 3384 (NH *str.*), 3299 (NH_2), 2938 (CH *str.*), 3405 (NH), 2840 (C-H) aliphatic, 1366 (C=N), 1274 (N-N), 781 (C-S-C). ^{1}H NMR (DMSO-d_6) δ: 7.7 (s, 1H of NH_2), 3.8 (s, 3H of 3.NH), 5.9-6.2 (m, 4H of Ar-H), 4.4 (s, 3H of CH_3), 1.4-2.7 (m, 8H of CH_2 aliphatic). MS m/z (%): M+1 = 343.

5-[(2-Amino-4,5,6,7-tetrahydro-1-benzothien-3-yl)-N-(4-chloro phenyl)-1,3,4- thiadiazole-2-amine (5e): IR (KBr, ν_{max}, cm^{-1}): 3384 (NH *str.*), 3299 (NH_2), 2938 (CH *str.*), 3405 (NH), 2840 (C-H) aliphatic, 1366 (C=N), 1274 (N-N), 781 (C-S-C). ^{1}H NMR (DMSO-d_6) δ: 7.7 (s, 1H of NH_2), 3.8 (s, 3H of 3.NH), 6.2-7.1 (m, 4H of Ar-H), 1.4-2.7 (m, 8H of CH_2 aliphatic). MS m/z (%): M+1 = 364.

Antibacterial activity: All the synthesized compounds **IVa-e** were evaluated *in vitro* for antibacterial activity against *S. aureus, B. subtilis, B. pumilus, E. coli* and *P. aeruginosa* at concentrated 100 µg/mL by paper disc method with DMF as solvent control and nutrient agar was employed as culture media. After 24 h hot incubation at 37 ºC the zone of inhibition were measured in mm.

RESULTS AND DISCUSSION

Antiinflammatory activity: All the compounds (**IVa-e, Va-e**) at dose each of 1000 mg/kg exhibited significant antiinflammatory activity in acute inflammatory models in rats. Results are given in Table-2, compounds **IVd**, **IVe**, **Vc**, **Vd** and **Ve** exhibited maximum inhibition of 40.66, 56.42, 42.54, 47.56 and 48.51 %, respectively and compounds **IVa, IVb, IVc, Va, Vb** exhibited a good reduction in the paw oedema volume 35.00, 32.14, 39.02, 35.00 and 35.71 % as compared to standard diclofenac sodium showed reduction in oedema volume by 74.88 % in caragenan induced reduction in paw oedema volume of the rats (Table-2). Thus, it is found that the compounds **IVd**, **IVe**, **Vc**, **Vd** and **Ve** have shown significant antiinflammatory activity and compounds **IVa**, **IVb**, **IVc**, **Va**, **Vb** shown good antiinflammatory activity. The significant activity mainly due to the presence of oxadiazole or thiadiazole ring system and substituents at 2nd position of the same. Tetrahydrobenzothiophene moiety at 5th position of oxazole or thiadiazole ring may also be responsible for marked anti-inflammatory activity.

TABLE-2
ANTIINFLAMMATORY ACTIVITY OF COMPOUNDS **IVa-e** AND **Va-e** IN CARRAGEENAN INDUCED ACUTE RAT PAW OEDEMA MODEL

Group	Treatment	Dose (mg/kg)	Paw oedema volume							
			After 0.5 h		After 1.0 h		After 2.0 h		After 3.0 h	
			Mean	% ROV	Mean	% ROV	Mean	% ROV	Mean	% ROV
1	Control	0.5 mL	0.180	–	0.51	–	0.58	–	0.55	–
2	Standard	50	0.119	32.14	0.40	38.00	0.38	46.62	0.21	74.88
3	**IVa**	1000	0.430	10.40	0.46	26.98	0.65	27.70	0.91	35.00
4	**IVb**	1000	0.260	7.00	0.53	17.50	0.56	20.44	0.56	32.14
5	**IVc**	1000	0.270	3.57	0.48	25.00	0.47	33.80	0.50	39.02
6	**IVd**	1000	0.220	17.86	0.51	20.41	0.49	30.93	0.49	40.66
7	**IVe**	1000	0.400	16.63	0.42	33.33	0.45	50.00	0.61	56.42
8	**Va**	1000	0.430	10.40	0.46	26.98	0.65	27.70	0.91	35.00
9	**Vb**	1000	0.400	16.63	0.43	31.70	0.51	43.30	0.90	35.71
10	**Vc**	1000	0.230	12.14	0.51	20.76	0.45	36.62	0.47	42.54
11	**Vd**	1000	0.240	14.29	0.45	29.69	0.48	32.39	0.43	47.56
12	**Ve**	1000	0.450	6.25	0.47	25.30	0.50	44.44	0.72	48.51

ROV = Reduction in paw oedema volume.

Analgesic activity: The activity of all compounds and standard drug diclofenac were tested by using hot plate analgesiometer with rats at different time intervals that is 0, 0.5, 1.0, 1.5 and 2.0 h with albino mice. The mean basal reaction time of compounds **IVa-e, Va-e** and standard drug at 2 h found to be 8.08, 8.67, 9.33, 9.88, 11.83, 8.13, 8.68, 9.14, 9.89, 11.33 and 13.83, respectively (Table-3). Thus, the compounds showed significant activity and were found to be less or more equal to the standards at the given concentration levels. Hence, these compounds appear to be good analgesic agents. Perhaps the substituents at 2nd position of oxadiazole or thiadiazole ring and which contains substituted aryl, aryloxy and ethyl groups, N-C-S or N-C-O linkage present in these ring system, is contributing to the analgesic activity.

TABLE-3
ANALGESIC ACTIVITY OF COMPOUNDS
IVa-e AND **Va-e** BY EDDY HOT PLATE METHOD

Group	Treatment	Average body weight	Dose (mg/kg)	Basal reaction time (s) after				
				0	30	60	90	120
1	Control	21.5	0.2 mL	3.00	2.66	2.83	2.50	2.83
2	Standard	21.8	50	2.83	4.17	9.17	10.17	13.83
3	**IVa**	21.3	1000	4.54	4.63	5.15	6.86	8.08
4	**IVb**	22.2	1000	2.83	4.00	6.83	7.16	8.67
5	**IVc**	21.8	1000	3.50	4.67	7.67	8.17	9.33
6	**IVd**	21.7	1000	6.71	6.95	7.35	8.49	9.88
7	**IVe**	22.00	1000	3.66	4.67	8.50	9.50	11.83
8	**Va**	21.6	1000	5.72	6.08	6.59	7.31	8.13
9	**Vb**	21.9	1000	5.82	6.12	6.35	7.58	8.68
10	**Vc**	21.8	1000	3.44	4.54	6.57	7.87	9.14
11	**Vd**	21.4	1000	6.23	6.85	7.15	8.08	9.89
12	**Ve**	22.2	1000	3.16	4.17	8.33	8.83	11.33

Standard drug used: Diclofenac sodium

Antibacterial activity: The resulted **IVa-e** and **Va-e** compounds were screened for antibacterial activity study at a concentration of 1 mg/mL using DMF as a control against *Escherichia coli, Staphylococus aureus, Bacillus pumilus, Baceillus subtilis* and *Pseudomonas aureginosa* by cup-plate method on nutrient agar medium. Ampicillin 100 m/gmL used as standard. The data in the Table-4 indicates that compounds **IVe** and **Ve** were found to possess a broad spectrum activity. While compounds **IVa-d** and **Va-d** were found to exhibit moderate activities. Among these compounds **IVa**, **IVe**, **Va** and **Ve** were showed good activities. Perhaps the substituents at 2nd position of oxadiazole or thiadiazole ring and which contains substituted aryl, aryloxy and ethyl groups, N-C-S or N-C-O linkage present in these ring system, is contributing to the antibacterial activity.

TABLE-4
ANTIBACTERIAL ACTIVITY OF COMPOUNDS **IVa-e** AND **Va-e**

Sample	Zone inhibition (mm)				
	S. aureus	*B. subtilis*	*B. pumilus*	*E. coli*	*P. aeruginosa*
IVa	18	16	18	17	17
IVb	17	17	16	16	15
IVc	16	17	16	15	14
IVd	16	16	15	14	16
IVe	17	18	18	16	18
Va	16	18	18	15	16
Vb	15	16	15	14	16
Vc	15	16	14	16	15
Vd	15	16	15	14	14
Ve	18	17	18	16	18
Ampicillin	22	21	23	22	23
DMF	-	-	-	-	-

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Equilibrium Studies of Transition Metal Complexes with Tridentate Ligands Containing N, O, S as Donor Atoms

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1. Please read Shardendu Kumar Jha instead of Sherdendu Kumar Jha
2. Please read Ram Prabesh Bharti instead of Ram Pranesh Bharti