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Synthesis, Characterisation and *invitro* Anti inflammatory and Anthelmintic activities of 1, 3, 4-Oxadiazole derivatives

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Abstract: The synthesis of 1,3,4-oxadiazole derivatives was carried out by refluxing the mixture of aldehyde with semicarbazide hydrochloride in ethanol using sodium acetate as a catalyst.Finally it was treated with sodium carbonate,iodine,potassium iodide to produce title compounds.The newly synthesized compounds were tested for its anti inflammatory and anthelmintic activity.Compound 1A,1B,1E exhibited significant anti inflammatory activity when compared with standard Diclofenac sodium. The structures of newly synthesized compounds were established on the basis of elemental analysis, IR, ^{1}HNMR and MASS spectral data.
Key words: Anti inflammatory,Anthelmintic activities.

Introduction

During past decades,compounds bearing heterocyclic nuclei have received much attention due to their chemotherapeutic value in the development of novel anti inflammatory ,anthelmintic,anti tubercular,anti fungal, anti microbial activities.The oxadiazole chemistry has been developed extensively and is still developing. Presently there are a number of drugs used clinically which comprise oxadiazole moiety in association with various heterocyclic rings.In view of these,a project was under taken to synthesize a new series of 1,3,4-oxadiazoles containing aldehyde moiety by condensation reaction and evaluated the new compounds for their pharmacological activity .The title compounds were screened for anti inflammatory activity by HRBC membrane stabilization method and anthelmintic activity studies were carried out by Garg method (Vagdevi et al;).Synthesis of the title compounds was shown in scheme I.

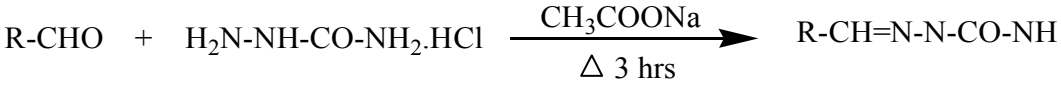
Experimental

Melting points were determined in open capillary tubes and were found uncorrected.IR spectra were recorded on FT-IR spectrometer (Perkin Elmer) using KBR disc method.1HNMR spectra were recorded on 1H FT-NMR (Brucker AMX 400 MHz) spectrometer in DMSO.The compounds were analyzed for elemental analysis and the percentage of elements were found to be near that of the calculated values.Physical data of the compounds are recorded in Table-1 and the spectral data are recorded in Table-2.

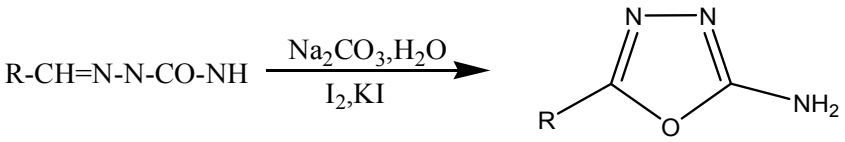
Procedure for preparation of 1,3,4-oxadiazole derivatives

A mixture of aldehyde (0.03mole) and semicarbazide HCl (0.05mole) in ethanol (20ml) was refluxed for 3 hours at 100^{0}C. Solvent was distilled off and the solid mass thus obtained was used for further reaction The mixture of above solid mass (0.01mole) and sodium carbonate (0.01mole) was dissolved in water (25ml). Iodine (0.01mole) and potassium iodide (0.01mole) was refluxed for 2 hours at 100^{0}C. The reaction mixture was then concentrated,
allowed to cool, the solid product obtained was filtered, washed with water and re-crystallized using methanol.

SCHEME-I



Aldehyde Semicarbazide Hydrochloride Intermediate



Derivatives of 1,3,4-oxadiazole

R=$C_8H_8O_3$, $C_9H_{10}O_3$, C_7H_6O, $C_7H_6O_2$, $C_7H_5NO_3$, C_9H

Results and Discussion

Pharmacological Evaluation

Anti inflammatory and anthelmintic activities

The synthesized compounds were screened for their *invitro* anti-inflammatory activity by membrane stabilization method. All the synthesized compounds showed good anti-inflammatory activity. Out of all the synthesized compounds 1A, 1B, 1E showed significant anti-inflammatory activity when compared with that of standard where as the compound 1C, 1D, 1F, 1G showed less when compared with that of standard diclofenac. The literature shows that the compounds having methoxy,nitro,hydroxyl groups possess significant anti inflammatory activity .when compared to other groups .The synthesized compound 1A,1B,1E possess OCH_3,OH,nitro group in its structure. So the anti inflammatory activity may be due to the presence of the respective functional groups as evidence in literature. The anthelmintic activity was carried out using two species of earth worms. The synthesized compounds showed good anthelmintic property the activity may

be due to presence of methyl and nitro group in the compound which has been proved in the earlier report**.** The paralyzing and death times were noted and their means are calculated which were tabulated in Table4.

Table:1 Physical and Analytical Data of 1,3,4 oxadiazole Derivatives

S.No	Compound	Mol. Formula	m.p^{0}C	Yield in Percentage	Elemental Analysis of Compounds (%) Found			
					C	H	N	O
1	**1A**	$C_9H_9N_3O_3$	119	76	52.17	4.38	20.28	23.17
2	**1B**	$C_{10}H_{11}N_3O_3$	132	83	54.29	5.01	19.00	21.70
3	**1C**	$C_9H_9N_3O$	140	70	61.70	5.18	23.99	9.13
4	**1D**	$C_8H_7N_3O_2$	147	75	54.24	3.98	23.72	18.06
5	**1E**	$C_8H_6N_4O_3$	136	80	46.61	2.93	27.18	23.28
6	**1F**	$C_9H_9N_3O$	145	82	61.70	5.18	23.99	9.13
7	**1G**	C8H7N30	150	76	59.62	4.38	26.07	9.93

Table:2 Spectral characterization of 1,3,4-oxadiazole derivatives

S. No.	COMPOUNDS	IR	NMR	MASS
1	**1A**	2771,1536,1434,1680, 1140, 3864, 1230	3.73-6.87	209.53
2	**1B**	3250,1502,1486,1692,1114	3.83-6.93	221.12
3	**1C**	2794,1370,1299,1658,1154	2.35-7.36	175.19
4	**1D**	2696,1400,1269,1621,1158	4.0-7.31	177.49
5	**1E**	2869,1452,1405,1673,1211	4.0-8.25	206.16
6	**1F**	3185,1299,1269,1692,1164	3.81-7.14	177.49
7	**1G**	3644,1277,1230,1683,1121	4.0-7.48	162.47

Table3 : Data on anti inflammatory activity of 1,3,4 –oxadiazole derivatives

S.No	Compounds	Concentration µg/ml Absorbance at 540nm			% Prevention of Lysis
		25	50	100	
1	**1A**	0.15±0.001**	0.19±0.002*	0.20±0.001*	69.6
2	**1B**	0.20±0.04*	0.22±0.07*	0.16±0.04**	58.1
3	**1C**	0.35 ±0.03*	0.36±0.01*	0.38±0.005*	28.6
4	**1D**	0.32±0.03*	0.33±0.04*	0.35±0.05*	31.0
5	**1E**	0.22±0.001*	0.28±0.007*	0.27±0.08**	60.5
6	***1F***	*0.30±0.04**	*0.35±0.04**	*0.32±0.04**	*30.2*
7	**1G**	0.20±0.04*	0.27±0.04*	0.25±0.06*	43.3
8	**Control**	-	-	-	-
9	**Diclofenac**		0.14±0.002*		74.8

Table4: Anthelmintic activity of 1,3,4-oxadiazole derivatives

Compound	Earthworm Species			
	P.excavatus		*P.sansibaricus*	
	Mean Paralysis Time (min)	Mean Death Time (min)	Mean Paralysis Time (min)	Mean Death Time (min)
1A	09.35±0.67	11.23±0.53	11.91±0.99	13.97±0.64
1B	09.52±0.54	11.52±0.57	11.03±0.20	13.73±0.07
1C	09.95±0.51	11.99±0.98	15.00±0.62	17.45±0.60
1D	07.56±0.56	09.76±0.94	09.23±0.45	11.89±0.57
1E	09.88±0.90	11.92±0.99	14.95±0.63	16.21±0.96
1F	08.23±0.56	10.35±0.47	12.00±0.98	14.95±0.74
1G	08.65±0.23	10.98±0.34	10.34±0.47	12.00±0.95
Control	-	-	-	-
Piperazine Citrate	13.40±0.47	14.63±0.50	20.07±0.68	33.34±0.89

Conclusion

In conclusion the 1,3,4 Oxadiazole containing methyl, nitro possess significant anti inflammatory activity and the compound Containing methoxy hydroxyl and nitro possess significant anthelmintic activity.

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