Research Article

Analgesic and Anti Inflammatory Activity of 1,3,4-Oxadiazoles Derivaties

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ABSTRACT
The work is mainly focused on the nitrogen containing oxadiazoles compounds and their analgesic, anti-inflammatory potantials. The oxadiazoles compounds were screened for analgesic activity by tail flick method and the anti inflammatory activity by carrageenan induced paw oedema method. The standard drugs used were pentazocine and diclofenac sodium for analgesic and anti inflammatory activity respectively. In both the methods the compound *o*-thiophene 1, 3, 4 oxadiazole showed highly significant analgesic and anti inflammatory activity. In the analgesic activity the substituents like 3, 4, 5- $(OCH_3)_3$, p- $(CH_3)_2N$, 3, 4 – $(OCH_3)_2$ showed significant activity similarly in the anti inflammatory activity, the substituents like *p*-OCH_3, *p*-F showed significant activity.

Keywords: oxadiazole derivatives, analgesic, anti inflammatory activity.

INTRODUCTION

Oxadiazoles are five membered heterocyclic compounds with two nitrogen atoms and one oxygen atom. Depending on the position of hetero atoms they are named as 1, 2, 3; 1, 2, 4; 1, 2, 5; and 1, 3, 4 oxadiazoles. All of these were reported to possess one or the other biological activities. In general nitrogen and oxygen heterocyclic were reported to possess wide variety of biological activities.

The incorporation of heterocyclic moieties with Oxadiazoles was proved to show enhanced activities. 1, 3, 4 - Oxadiazoles are well known compounds that are found to possess varied biological and pharmacological activities. They are associated with antibacterial, antifungal, analgesic, anti-inflammatory[1], antituberuclar, anticancer activities[2]. Some of the recent studies have shown that Oxadiazoles are reported to possess antileprotic, paralytic, hypnotic & sedative, hypoglycemic and antimalarial actions.

MATERIAL AND METHOD

Oxadiazoles are five membered heterocyclic compounds with two nitrogen atoms and one oxygen atom. Depending on the position of hetero atoms they are named as 1, 2, 3; 1, 2, 4; 1, 2, 5; and 1, 3, 4 - Oxadiazoles. LD_{50} of oxadiazoles were carried out as per OECD 425 guidelines. Three doses were selected and they were screened for both activities.

Screening of analgesic drugs by Tail Flick method[3,4]

The tail flick test was performed according to the method described by Jansen et al(1963). The basal reaction time of each rat was determined using tail withdrawal response when the tip of the tail was exposed to radiant heat. Rats with basal reaction time between 3 and 5 s were selected for the test. The animals were treated with test a compounds and 30, 60, 90 and 120 min later the reaction time was evaluated. The cut off time of 10-12 s was observed to prevent damage to the tail. All experimental groups were composed of 6 animals. Data obtained from animal experiment were expressed as mean ± standard error (S.E.M.). The statistical significance of difference between groups was assessed by means of analysis of variance (ANOVA) followed by Dunnett's test.

Screening of anti inflammatory drugs by carrageenan induced paw oedema method[4,5] Edema was induced in the left hind paw of Wistar rat (200-250 g) by the sub plantar injection of 0.1 ml of 1% carrageenan in distilled water. Both sexes were used. Female pregnant rats were excluded. Each group composed of 6 animals. The animals which were bred in our laboratory were housed under standard condition and received a diet of commercial food pellets and water ad libitum. During the maintenance but they were

entirely fasted during the experimental period. Our studies were in accordance with recognized guidelines on animal experimentation.

The test compounds were given intraperitoneally 30 minutes before carrageenan injection. The difference in the paw volume of the injected and the control were compared for each animal and expressed as ratio of final paw volume in initial paw volume.

All experimental groups were composed of 6 animals. Data obtained from animal experiment were expressed as mean ± standard error (S.E.M.). The statistical significance of difference between groups was assessed by means of analysis of variance (ANOVA) followed by Dunnett's test.

RESULTS AND DISCUSSION

The acute oral toxicity were performed by OECD test guidelines-425, shows LD50> 2000 mg/kg. The analgesic activity was carried out by tail flick method and the anti inflammatory activity was carried out by carrageenan induced paw oedema method. The standard drugs used were pentazocine and diclofenac sodium for analgesic and anti inflammatory activity respectively.

In both the methods the compound P-OCH_3, 1, 3, 4 oxadiazole showed highly significant analgesic and anti inflammatory activity. In the analgesic activity the substituents like 4-methyl, 3,4-di methoxy, 3-hydroxy showed significant activity similarly in the anti inflammatory activity, the substituents like 4-chloro , 3.hydoroxy showed significant activity.

The compounds P-OCH_3, 1, 3, 4 oxadiazole showed highly significant analgesic and anti inflammatory activity.

Table 1: The following table shows LD_{50} values for the following 1, 3, 4- oxadiazoles

	Oxadiazole moiety	LD_{50}(mg/kg)
1.	m-nitro oxadiazole	>5000
2.	3-bromo oxadiazole	>5000
3.	4-OH oxadiazole	>5000
4.	4-Chloro oxadiazole	=2000
5.	2,5-Dimethoxy oxadiazole	>5000
6.	3-OH-4-methoxy oxadiazole	>5000
7.	3-OH oxadiazole	>5000
8.	4-methyl oxadiazole	>5000
9.	3,4-Dimethoxy oxadiazole	>5000
10.	p-$_{OCH3}$ oxadiazole	=2000

Table 2: The following tables shows the analgesic activity of 1, 3, 4 oxadiazoles by Tail Flick method

Groups	Dose (mg/kg)	Reaction time(s) (s) before	Reaction time (s)after 2 hours	Increase in reaction time
Control	Vehicle	2.56 ± 0.15	3.1 ± 0.14	0.54 ± 0.01
Pentazocine	10	2.36 ± 0.22	5.45 ± 0.18	3.09± 0.004**
m-nitro oxadiazole	250	2.56 ± 0.15	3.10 ± 0.12	0.54 ±0. 003
	500	2.00 ± 0.17	2.53 ± 0.18	0.53± 0.001
	1000	2.88 ± 0.20	3.41 ± 0.21	0.53±0.01
3-bromo oxadiazole	250	2.21 ± 0.25	2.76 ± 0.19	0.55±0.04
	500	2.53 ± 0.06	3.06 ± 0.04	0.53± 0.02
	1000	2.53 ± 0.07	3.06 ± 0.06	0.53± 0.01
4-OH oxadiazole	250	2.58± 0.13	3.11 ± 0.08	0.53± 0.05
	500	2.56 ± 0.22	3.11 ± 0.21	0.55± 0.02
	1000	2.78 ± 0.25	3.38 ± 0.25	0.60± 0.01**
4-Chloro oxadiazole	100	2.88 ± 0.25	3.48 ± 0.25	0.60± 0.01**
	200	2.665 ± 0.19	3.20± 0.18	0.55± 0.01
	400	2.65 ± 0.20	3.20 ± 0.21	0.55± 0.01
2,5-Dimethoxy oxadiazole	250	2.65 ± 0.19	3.26± 0.14	0.61± 0.05 **
	500	2.71 ±0.19	3.35 ± 0.16	0.64± 0.03 **
	1000	2.93 ± 0.19	3.80 ± 0.15	0.87 ± 0.04 **
3-OH-4-methoxy oxadiazole	250	2.16 ± 0.19	2.68 ± 0.21	0.52± 0.02
	500	3.15± 0.23	3.95 ± 0.15	0.80± 0.07 **
	1000	2.65 ± 0.23	3.70 ± 0.25	1.05± 0.02 **
3-OH oxadiazole	250	2.60 ± 0.24	3.43 ± 0.22	0.83± 0.02**
	500	2.63 ±0.26	3.40± 0.23	0.77±0.03**
	1000	2.76± 0.27	3.56 ± 0.22	0.88± 0.05 **
4-methyl oxadiazole	250	3.06 ± 0.27	3.88 ± 0.19	0.82± 0.08 **
	500	2.78 ± 0.23	3.55 ± 0.20	0.77± 0.03**
	1000	2.68 ± 0.21	3.58 ± 0.20	0.90± 0.01 **
3,4-Dimethoxy oxadiazole	250	2.48± 0.21	3.35 ± 0.17	0.87± 0.04**
	500	2.68 ± 0.21	3.58 ± 0.20	0.90± 0.01**
	1000	2.48 ± 0.21	3.35 ± 0.17	0.87± 0.04**
p-OCH_3 oxadiazole	100	2.21 ± 0.25	3.13 ± 0.27	0.92± 0.02**
	200	2.53 ± 0.06	3.53 ± 0.08	0.10 ± 0.02**
	400	2.36 ± 0.22	5.10 ± 0.16	2.74± 0.06**

*= p < 0.05 compared to control,** = p<0.01 compared to control

Table 3: The following table shows anti inflammatory activity of 1, 3, 4 oxadiazoles by carrageenan induced paw oedema method

Groups	Dose (mg/kg)	Initial paw volume (ml) (b)	Paw volume after 3hours (ml) (a)	Oedema volume (a-b)
Control	vehicle	0.22± 0.02	0.42± 0.22	0.20± 0.07
Diclofenac sodium	10	0.24± 0.09	0.33± 0.08	0.09± 0.01**
m-nitro oxadiazole	250	0.25± 0.02	0.45± 0.02	0.20± 0.07
	500	0.29± 0.01	0.50± 0.02	0.21± 0.01
	1000	0.30± 0.02	0.50± 0.07	0.20± 0.09
3-bromo oxadiazole	250	0.27± 0.06	0.46± 0.02	0.19± 0.09
	500	0.33± 0.01	0.55± 0.01	0.22± 0.01
	1000	0.34± 0.02	0.53±0.04	0.19± 0.08
4-OH oxadiazole	250	0.32± 0.06	0.51± 0.03	0.19± 0.09
	500	0.34± 0.02	0.56± 0.08	0.21± 0.05
	1000	0.34±0.08	0.54±0.02	0.20±0.05
4-Chloro oxadiazole	100	0.31± 0.07	0.42± 0.07	0.11± 0.08**
	200	0.33±0.08	0.45±0.08	0.12±0.08**
	400	0.30±0.04	0.41±0.03	0.11±0.07**
2,5-Dimethoxy oxadiazole	250	0.29±0.07	0.46±0.01	0.17±0.04
	500	0.31±0.09	0.48±0.02	0.17±0.03
	1000	0.28±0.04	0.43±0.01	0.15±0.02
3-OH-4-methoxy oxadiazole	250	0.25±0.06	0.43±0.08	0.18±0.02
	500	0.25±0.05	0.41±0.03	0.16±0.08
	1000	0.31±0.04	0.46±0.01	0.15±0.02
3-OH oxadiazole	250	0.28±0.07	0.46±0.01	0.18±0.04
	500	0.28±0.07	0.46±0.07	0.18±0.02
	1000	0.33±0.02	0.47±0.05	0.14±0.03
4-methyl oxadiazole	250	0.30±0.03	0.50±0.06	0.16±0.04
	500	0.29±0.08	0.44±0.04	0.15±0.06
	1000	0.34±0.04	0.45±0.07	0.12±0.05**
3,4-Dimethoxy oxadiazole	250	0.30±0.04	0.43±0.04	0.13±0.02
	500	0.28±0.02	0.43±0.07	0.15±0.09
	1000	0.32±0.02	0.43±0.03	0.11±0.02**
p-OCH_3 oxadiazole	100	0.23±0.02	0.33±0.07	0.10±0.01**
	200	0.25±0.03	0.37±0.07	0.12±0.02**
	400	0.28±0.03	0.40±0.07	0.12±0.02**

*= $p < 0.05$ compared to control, ** = $p<0.01$ compared to control

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