Int. J. Chem. Sci.: 8(1), 2010, 470-474

CNS ACTIVITY OF NEW INDOLE DERIVATIVES

K. S. NATARAJ[*], J. VENKATESHWARA RAO[a] and K. N. JAYAVEERA[b]

SRR College of Pharmaceutical Sciences, Valbhapur, Elkathurthy,
KARIMANGAR - 505 476 (A.P.) INDIA
[a]Talla Padmavathi College of Pharmacy, WARANGAL (A.P.) INDIA
[b]OTRI- Jawaharlal Nehru Technological University, ANANTAPUR (A.P.) INDIA

ABSTRACT

Twenty one new 2-{(benzalamino-4-hydroxybenzyl) (1, 3, 4)-oxadiazino[6, 5-b]} indole derivatives have been synthesized by condensing 2-amino-4-[(1, 3, 4)oxadiazino[6,5-b]indole-3-yl]-phenol with various aromatic aldehydes. The intermediates, on the other hand, have been synthesized by the cyclization of 3-amino-4-hydroxy-benzoic acid (2-oxo-1, 2-dihydro-indol-3-ylidene)-hydrazide in presence of concentrated H_2SO_4. The title compounds have been purified and characterized by their analytical and spectral data. They have screened for their gross behavioral studies, effects on locomotor activity and on pentobarbitone sodium induced sleeping time. All the test compounds exhibited reduction in locomotor activity, compound **(9)** exhibited more effect among all the test compounds and potentiation of pentobarbitone sodium induced sleeping time ranges from 166.66 per cent to 276.66 per cent. The compound **(15)** showed more activity with a potentiation of 276.60 per cent in experimental animals.

Key words: (1, 3, 4) Oxadiazino-[5, 6-b] Indole, Isatin derivatives, Locomotor activity, Pentobarbitone sodium

INTRODUCTION

It is known from the literature that indole derivatives exhibit varied biological and pharmacological properties[1-7] viz. antimicrobial, antiviral, anti-neoplastic, analgesic, CNS activities. In view of these observations, the synthesis of new (1, 3, 4)oxadiazino-[5, 6-b]-indole derivatives has been carried out. For this purpose, the required indole-2,3-diones were prepared and condensed with 3-amino-4-hydroxybenzoic acidhydrazide in ethanol to get the respective 3-amino-4-hydroxy-benzoic acid (2-oxo-1,2-dihydro-indol-3-ylidene)-hydrazide. These compounds were cyclized using concentrated sulfuric acid to get respective 2-amino-4-[(1, 3, 4)oxadiazino[6, 5-b]indole-3-yl]-phenol. These compounds were refluxed with aromatic aldehyde, ethanol and few drops of acetic acid to get the title compounds as shown

[*]Author for correspondence; Ph.: +91 9866250050; E-mail: kalakondan@yahoo.com

in Fig. 1. The compounds were characterized by their physical, analytical and spectral data (IR and PMR, Mass). The data on locomotor activity and effect on pentobarbitone sodium induced sleeping time activities are presented in Table 1.

Table 1: CNS activity of new (1, 3, 4)-oxadiazino-[5, 6-b]indole(V) derivatives

Compound	Substituents				Locomotor activity on mice		Pentobarbitone induced sleeping time	
					Before admin. of drug (for 1 min)	After half an hour of admin. of drug (for 1 min)	Duration of action (min)	Percent effect (%)
	R^1	R^2	R^3	R^4				
(1)	F	H	H	H	39.12	9.96	72.22	240.73
(2)	F	H	Cl	H	41.76	8.96	58.55	195.16
(3)	F	OH	H	H	38.89	10.21	73.26	242.20
(4)	F	H	OCH_3	H	35.28	11.85	69.85	232.83
(5)	F	H	OCH_3	OCH_3	38.45	12.45	51.06	170.20
(6)	F	H	$N(CH_3)_2$	H	42.00	14.36	70.45	234.83
(7)	F	H	OH	OCH_3	43.92	18.12	58.29	194.30
(8)	Cl	H	H	H	40.57	8.27	78.11	260.36
(9)	Cl	H	Cl	H	42.58	6.76	50.00	166.66
(10)	Cl	OH	H	H	39.72	10.00	75.26	250.86
(11)	Cl	H	OCH_3	H	36.92	9.24	68.38	227.93
(12)	Cl	H	OCH_3	OCH_3	37.89	10.11	63.11	210.36
(13)	Cl	H	$N(CH_3)_2$	H	30.12	11.56	79.10	263.66
(14)	Cl	H	OH	OCH_3	34.00	15.66	56.12	187.06

Cont…

Compound	Substituents				Locomotor activity on mice		Pentobarbitone induced sleeping time	
					Before admin. of drug (for 1 min)	After half an hour of admin. of drug (for 1 min)	Duration of action (min)	Percent effect (%)
	R^1	R^2	R^3	R^4				
(15)	CH_3	H	H	H	30.76	15.26	83.00	276.66
(16)	CH_3	H	Cl	H	32.65	10.28	82.39	274.63
(17)	CH_3	OH	H	H	33.45	12.45	50.11	167.03
(18)	CH_3	H	OCH_3	H	30.58	16.74	81.89	272.96
(19)	CH_3	H	OCH_3	OCH_3	31.11	12.00	79.26	264.20
(20)	CH_3	H	$N(CH_3)_2$	H	36.00	12.11	54.10	180.33
(21)	CH_3	H	OH	OCH_3	32.65	10.89	68.44	228.13
Control							30	100

*The test compounds were administered in a dose of 100 mg/kg (body weight)

EXPERIMENTAL

Methods

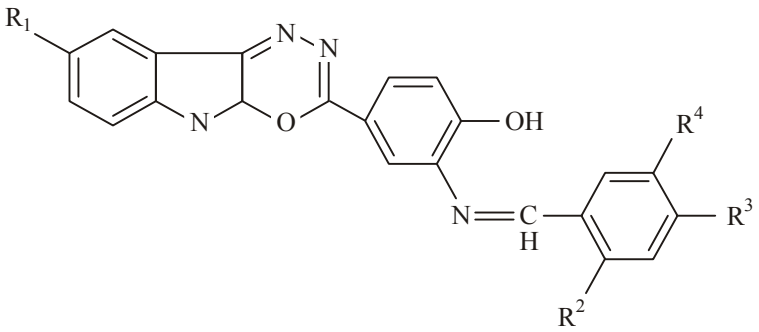

Fig. 1: Structure of synthesized compounds

Action on central nervous system gross behavioral studies[8]

Healthy albino mice weighing between 20 to 25 g were fasted for 24 hours and divided into groups of six animals each. Each of the test compounds (10 mg) was suspended in 0.3 mL of tween solution (one drop dissolved in 1 mL of distilled water) and the volume made up with saline solution to get 10 mg/mL concentration. The suspension of test compounds was administered, intraperitoneally in dose of 100 mg/kg (body weight). The control group of animals received only the vehicle. The animals were observed for gross behavioral changes, continuously, for 7 hours starting from the administration of compounds.

The locomotor activity was studied with Actophotomotor after half an hour of administration of the test compounds. The results are presented in Table 1.

Effect on pentobarabitone sodium induced sleeping time[9]

Healthy albino mice weighing between 20 and 28 g were fasted for 24 hours before the experiment and were divided into groups of six animals each. The test compounds were administered intraperitoneally at a dose of 100 mg/kg (body weight). The control group of animals was given only the vehicle. After 30 minutes, pentobarbitone sodium was administered intraperitoneally to all groups of animals at a dose of 35 mg/kg (body weight).

The time of administration of test compounds and pentobarbitone sodium, the time of loss and gain of righting reflex were recorded in all the groups of test animals and percentage effect on pentobarbitone sodium induced sleeping time by the test compounds was calculated using the formula given in eq. (1), considering righting reflex in control an 100%. The results are presented in Table 1.

$$\% \text{ Effect} = \frac{\text{Average duration of loss of righting reflex in text group}}{\text{Average duration of loss of righting reflex in control group}} \quad \ldots(1)$$

RESULTS AND DISCUSSION

The gross behavioral studies of the test compounds revealed that all the test compounds exhibited the CNS depression in the mice. The other features observed was frequent excretion of urine. The data pertaining to the results of the effect of the test compound on locomotor activity show that all the test compounds reduced locomotor activity. Compound **(9)** exhibited more effect among all the test compounds. Compound **(8)**, **(10)** and **(12)** were next to the compound **(9)** in the order of reduction in the locomotor activity.

The results of effect on pentobarbitone sodium induced narcosis showed that all the test compounds potentiated the pentobarbitone sodium induced sleeping time from 166.66 per cent to 276.66 per cent. The compound **(15)** showed more activity with a potentiation of 276.60 per cent. Compound **(16)** and **(18)**, **(19)**, **(13)** and **(8)** were found to be next in the order of potentiation of pentobarbitone sodium sleeping time with 274.63, 272.96, 264.20, 263.66, 260.36 per cent, respectively and rest of the compounds showed moderate percentage of potentiation of pentobarbitone sodium sleeping time.

ACKNOWLEDGEMENT

The authors are thankful to the Prof. Dr. B. Agaiah, Principal, SRR College of Pharmaceutical Sciences for providing necessary facilities to carry out this research work.

REFERENCES

1. M. Sarangapani, M. Jessy Jacob, B. Srinivas and Raghunandan N, Indian Drugs, **38(5)**, 264-268 (2001).
2. S. N. Pandeya, V. S. Laximi and A. Pandeya, Indian. J. Pharm. Sci., **65(3)**, 213-222 (2003).
3. M. Sarangapani, A. Narayana Reddy, Y. Jayamma and V. M. Reddy, Indian Drugs., **35(6)**, 336-343 (1998).
4. M. S. Y. Khan and M. Akhtar, Indian J. Chem., **42B**, 903-904 (2003).
5. S. P. Singh, S. K. Shukla and L. P. Awasthi, Curr. Sci., **52**, 16 (1983).
6. Anku Patel, Sanjay Bari, Gokul Talele, Jitendra Patel and Manda Sarangapani, Iran. J. Pharmac. Res., **4**, 249-254 (2006).
7. S. B. Bari, A. O. Agrawal, and U. K. Patel, J. Science, **19(3)**, 217-221 (2008).
8. Turner Robert, Screening Methods in Pharmacology, **Vol. I**, Academic Press, NY, (1965) p. 99, 26.
9. Turner Robert, Screening Methods in Pharmacology, **Vol. I**, Academic Press, NY, (1965) p. 70.

Accepted : 27.11.2009