

CODEN [USA]: IAJPBB

ISSN: 2349-7750

INDO AMERICAN JOURNAL OF PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.825734

Available online at: <u>http://www.iajps.com</u>

Research Article

PHARMACOLOGICAL EVALUATION OF NEWER BENZOTRIAZOLE DERIVATIVES FOR ANTIPSYCHOTIC AND ANTI INFLAMMATORY ACTIVITIES

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Abstract

The present study was undertaken to evaluate the antipsychotic potential of benzotriazole derivatives in experimental animal models. Male Wistar rats (180-220 g) and albino mice (25-30 g) were used for the study. The antipsychotic effect of the benzotriazole derivatives was evaluated on continuous avoidance response apparatus and anti-inflammatory activity by Carrageenan induced paw edema method. The benzotriazole derivative produced significant dose dependent potentiation in continuous avoidance response in rats, significantly decreased the time taken by the rat to press the lever and regulates the edema related to the time when compared with the carrageenan given alone. The results suggest that benzotriazole derivatives possess antipsychotic activity and anti-inflammatory activity. Further neurochemical investigation can explore the mechanism of action of the newer benzotriazole derivatives with respect to anti-dopaminergic functions and help to establish them as an antipsychotic agent. **Key words:** Benzotriazole derivatives, anti-psychotic activity, anti-inflammatory activity, continuous avoidance response.

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Please cite this article in press as Radhika S and Rama Rao N, Pharmacological Evaluation of Newer Benzotriazole Derivatives for Antipsychotic and Anti Inflammatory Activities, Indo Am. J. P. Sci, 2017; 4(07).

INTRODUCTION:

A large number of compounds containing benzotriazole system have been investigated through different synthetic approaches. Considerable biological applications, benzotriazoles are important intermediates, protecting groups and final products in organic synthesis. The conventional synthetic techniques have several drawbacks including strong reagents, longer reaction times, low yields of products, use of toxic solvents etc. These are inefficient and harmful to environment. Environmental scientists supposed green techniques are Microwave irradiation, Ultrasonication, Phase transfer catalysis, solvent free reactions. In the present study newer benzotriazole derivatives are compared with Conventional, Microwave irradiation under solvent free conditions and their spectral data also included [1-3].

MATERIALS AND METHODS:

Experimental Animals

Male Wistar rats (180-220 g) and albino mice (25-30 g) were used for the study. The animals were housed in colony cages and maintained under the standard environmental conditions - temperature $25 \pm 2^{\circ}$ C, 12 h light: 12 h dark cycle and $50 \pm 5\%$ relative humidity, with food and water *ad libitum*. All experiments were carried out during the light period (08.00 -16.00 h). The experimental protocol was approved by the Institutional Animal Ethics Committee (IAEC) and the care of laboratory animals was taken as per the guidelines of CPCSEA, Ministry of Forests and Environment, Government of India.

Apparatus

Continuous Avoidance Response [4-6]

Continuous avoidance response is extensively used for the screening of drugs affecting learning and

memory. The test involves training rodents to avoid punishment (normally an electric shock). At specified intervals after training; the animals are tested again for retention of such learning. So mainly the continuous avoidance response apparatus is used for learning, memory enhancement and anti-psychotic activities. Continuous avoidance response involves the acquisition of an operant response that will either terminate (escape) or prevent (avoid) an aversive event. This equipment provides a convenient test procedure in which the test animal has to anticipate time duration to press a lever to avoid shock. A compact solid state apparatus, size approx. 45x30x30cms. With wire grid, house light, avoidance key, variable intensity stimulator with variable delay timer and counters to record stimulus avoided and stimulus delivered.

Carrageenan induced hind paw edema [7-10]

Albino rats of either sex weighing 150-200 grams were divided into four groups of six animals each. The dosage of the drugs administered to the different groups was as follows. Group I - Control (normal saline), Group - II and III - Benzotriazole derivatives, Group IV - Indomethacin (10 mg/kg, p.o). All the drugs were administered orally. Indomethacin served as the reference standard antiinflammatory drug. After one hour of the administration of the drugs, 0.1 ml of 1% W/V carrageenan solution in normal saline was injected into the sub plantar tissue of the left hind paw of the rat and the right hind paw was served as the control. The paw volumes of the rats were measured in the digital plethysmograph, at the end of 0 min, 60min, 120min, 180min, 240min, 360min, and 480min. The percentage increase in paw edema of the treated groups was compared with that of the control and the inhibitory effect of the drugs was studied.

RESULTS AND DISCUSSION:

Anti-Psychotic activity

Table 1: Activity of benzotriazole derivatives on Continuous Avoidance Response apparatus

Groups	Time in Seconds				
	Delay Seconds	Delivered	Avoided		
1	15	1	1		
2	15	1	2		
3	15	1	4		
4	15	1	3		

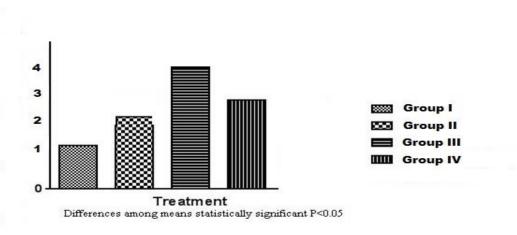


Fig 1: Graph of benzotriazole derivatives activity on Continuous Avoidance Response apparatus

<i>Anti-inflammate</i> Table 2: Effect	2 2	azole derivative	s on the percentage	e inhibition of C	arrageenan induc	ed paw edema
	Oedema volume(ml)					% Inhibition
Treatment	Doco					76 IIIIIDIUOII

	Oedelina volume(im)					% Inhibition
Treatment	Dose mg/kg	0 min	60 min	120 min	180 min	after 180 min
Control (Group-I)	Normal saline	29.56+1.93	56.55+1.63	98.56+2.54	119.56+2.53	_
Group-II (BTZ derivatives)	250 mg/kg	28.22+1.83	41.92+1.32	63.21+1.84* *	44.16+1.28**	66.50
Group-III (BTZ derivatives)	500 mg/kg	29.11+1.93	32.16+1.59	44.95+1.29	26.16+1.17**	78.11
Indomethacin (Group-IV)	10 mg/Kg	20.33+1.84	34.93+1.66	39.63+1.26* *	20.66+1.54**	82.71

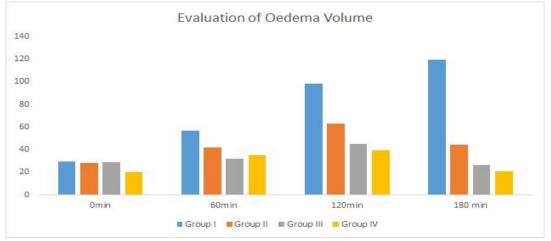


Fig 2: Graph of benzotriazole derivatives activity on paw edema response

CONCLUSION:

Animal models for anti-inflammatory and antipsychotic were standardized and evaluated using benzotriazole derivatives and found that they have shown effective anti-inflammatory and anti-psychotic activities than that of standard drugs.

ACKNOWLEDGEMENT:

The authors profoundly acknowledge UGC-New Delhi for sanctioning minor research grant for this project work. The authors are also thankful to principal and management, Chalapathi Institute of Pharmaceutical Sciences for providing necessary facilities to carry out the project work. The support rendered by Department of Pharmacology for animal activities is deeply acknowledged.

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