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LETTER TO THE EDITOR

ANTIDEPRESSANT ACTIVITY OF SOME PHENYLACETICACID HYDRAZONES AND 2-CHLOROPHENYL SEMICARBAZONES

Sir,

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Hydrazone derivatives play an important role as non-specific MAO inhibitors. These include drugs like phenelezine, isocarboxazid and iproniazid (1). In this study a bio-isosteric modification of phenelezine molecule was made which gave rise to a series of phenylacetic acid hydrazones ($-CH_2-$group of phenelezine has been replaced by a $-C=O$ group) and also bio-isosteric analogues semicarbazones were made with 2-chloro group on the phenyl ring to increase the lipophilicity of the molecule (2).

Fifteen compounds were synthesised and examined. Their chemical structures are shown in Fig. 1. The hydrazones and semicarbazones were prepared by condensing the appropriate carbonyl compound with few drops of glacial acetic acid, along with phenyl acetic acid hydrazide (3) and 2 chlorophenylsemicarbazide respectively. The characterisations of the compounds were done using CHN analysis, IR, UV and ^{1}HNMR spectral analysis. All test drugs in PEG 200, were administered, at a dose of 10 mg/kg, i.p., while tranylcypromine in PEG 200 was administered at a dose of 5 mg/kg, i.p.

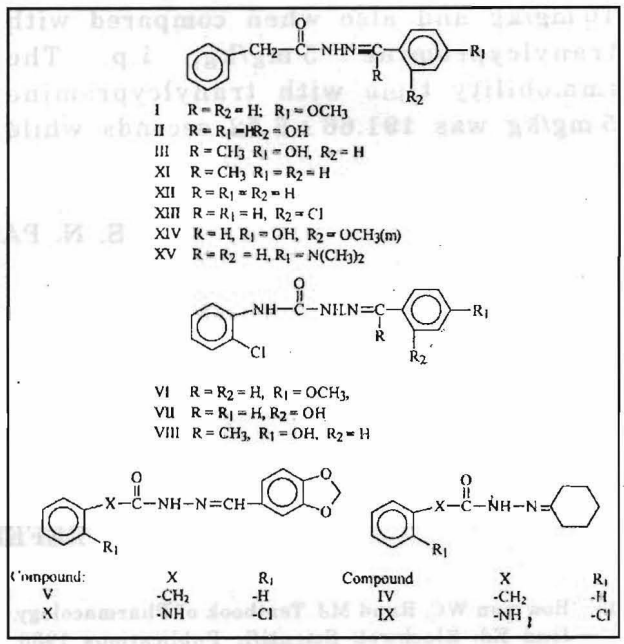

Fig. 1 : Structure of phenylaceticacid hydrazones and 2-chlorophenylsemicarbazones.

Antidepressant activity was evaluated in albino rats weighing 100 to 120 g, by Porsolt forced swimming test (4). Rats were individually placed in plexiglass cylinders (height 40 cm; diameter 18 cm), containing 15 cm of water maintained at 25°C. After 15 minutes they were removed to a 30°C drying room for 30 minutes. The next day, one hour after drug administration, the

animals were placed in cylinders again for a 6 minute test. The total duration of immobility during the last 4 minutes was noted. Six animals were used in each group and control, experiments were performed with vehicle, i.e. PEG, 2000. Data was analysed by student's 't' test.

All the compounds synthesised exhibited significant antidepressant activity at 10 mg/kg and also when compared with tranylcypromine 5 mg/kg, i.p. The immobility time with tranylcypromine 5 mg/kg was 191.66 ± 6.52 seconds while that for control animals was 225.0 ± 15.0. Among the phenylacetic acid hydrazones, compound V (116.00 ± 4.89) and XIV (111.33 ± 5.15) showed better antidepressant activity than other derivatives of phenylacetic acid hydrazones the immobility times were 116.00 ± 4.89 and 111.33 ± 5.15 respectively. Compounds VI and IX showed better antidepressant activity among 2-chlorophenylsemicarbazones (131.5 ± 9.41 and 132.16 ± 0.74 respectively). Thus, compounds of this series could serve as lead compounds for future synthesis of useful antidepressants.

S. N. PANDEYA*, H. MANJULA AND P. N. SINGH

Department of Pharmaceutics,
Institute of Technology,
Banaras Hindu University,
Varanasi – 221 005

REFERENCES

1. Bowman WC, Rand MJ. Textbook of Pharmacology. IInd Ed. Blackwell Scientific Publications 1980; 11.7–11.10.
2. Pandeya SN, Dimmock JR. An Introduction of Drug Design. 1st Ed. New Age International Publishers 1997; 207.
3. Dimmock JR, Puthucode RN, Lo MS, Quail JW, Yang J, Stables JP. Structural modification of the primary amino group of anticonvulsant arylsemicarbazones. *Pharmazie* 1996; 51(2): 83–88.
4. Borsini F, Bendotti C, Yelkov V, Rech R and Samanin R. Immobility test: Effects of 5-hydroxytryptaminergic drugs and role of catecholamines in the activity of some antidepressants. *J Pharm Pharmacol* 1981; 33(1): 33–37.

*Corresponding Author