As discussed in the study of $H[Fe(H_2P_2O_7)_2(H_2O)_2].4H_2O$, here too, iron is in Fe (III) state with octahedral surrounding and the ligand groups are bonded through covalent bonding forming $Na_5[Fe(P_2O_7)_2(H_2O)_2].3H_2O$.

Comparison of the Spectra.—Mossbauer spectra give the same values of Isomer shift in the two cases, *i.e.*, 0·433 mm/sec. in the case of pyrophosphoric acid complex and 0·44 mm/sec. in the sodium pyrophosphate complex. This goes to show that the electron density in both the phosphate complexes is roughly the same but the difference in quadrupole splitting in these two types of complexes shows that the symmetry around ferric ion in pyrophosphoric acid complex is more distorted than in the complex of sodium pyrophosphate.

1. Rogers, L. B. and Reynolds, C. A., *J. Am. Chem. Soc.*, 1949, 71, 2081.
2. Subrahmanya, R. S., *J. Indian Inst. Sci.*, 1956, 38 A, 87.
3. Banerjee, S and Mitra, S. K., *Sci. and Cult.*, 1951, 16, 530.
4. Friksson, E. and Hogskol, K. L., *Ann.*, 1949, 16, 39.
5. Watters, J. I. and Kolthoff, I. M., *J. Am. Chem. Soc.*, 1948, 70 (23), 2455.
6. Vaid, J. and Ramachar, T. L., *Curr. Sci.* 1954, 23, 396.
7. Haldar, B. C., *Nature*, 1950, 166, 744.
8. Mustaev, A. K. and Yakdovenko, T. L. *Issled. Khim. Redkikh Soputstuuyushchikh Elem. Akad. Nauk. King. SSR, Inst. Neurg. Fig. Khim.*, 1966, 66, 69339 X, (Russ.), 82.
9. Growther. J. P. and Westman, A. E. R., *Cand. J. Chem.*, 1954, 32, 42.
10. Vanwazer, J. R., Griffith, E. J. and McCullough, J. F., *J. Am. Chem. Soc.*, 1955, 77, 287.

CENTRAL STIMULANT ACTIVITY OF A BENZOCYCLOHEPTENE DERIVATIVE IN MICE: COMPARISON WITH (+) AMPHETAMINE

K. RAMABADRAN*

Psychopharmacology Research Laboratory, Sandoz Ltd., CH-4002, Basle, Switzerland

ABSTRACT

7-Dimethylamino-5, 6, 8, 9-tetrahydro-7-phenyl-7H-benzocycloheptene hydrochloride has been tested for its central stimulant activity by using two models in mice. This compound increases spontaneous locomotor activity and antagonises reserpine-induced catalepsy and hypothermia. The results reveal that it could possibly stimulate the central nervous system like (+) amphetamine.

INTRODUCTION

PRELIMINARY studies with the compound, 7-Dimethylamino-5, 6, 8, 9-tetrahydro-7-phenyl-7H-benzocycloheptene hydrochloride** showed that it could stimulate the central nervous system in mice and hence it was decided to test this property at three dose levels in two models, (1) on spontaneous locomotor activity, (2) against reserpine-induced catalepsy and hypothermia. Results obtained in such a study provide the basis for this report.

MATERIALS AND METHODS

(a) Stimulation of Spontaneous Locomotor Activity in mice

Spontaneous locomotor activity was taken as a parameter of behavioural excitation[1]. It was recorded by means of a conventional light beam cage[2,3]. The light and sound-proof cabinet contained 4 identical cages, each 22 cm × 37 cm × 8 cm, crossed by 6 light beams. Five mice (18–25 g) were placed in each cage 15 min. after subcutaneous administration of the compound/vehicle and the number of light beam interruptions taking place was recorded at 30 min. intervals for 7 hours, through an automatic counter. Experiments were repeated 6 times, giving a total of 30 mice per treatment. The mean total 'motility count for 5 mice over the recording period, and the mean, and Standard error of mean were calculated. Statistical comparisons were carried out by means of Student's *t* test.

The experiments were performed on male albino mice (NMRI Strain). The animals were kept under standard laboratory conditions (constant temperature 22 ± 1° C, humidity 60% and light on between 8 a.m. and 8 p.m.) and had no prior experience in the activity cages.

The substance was dissolved in one or two drops of glacial acetic acid and the pH was adjusted to 5–6. Control animals received the vehicle at the same pH. Three doses of the substance, 2·5, 5 and 10 mg Kg^{-1} were studied.

For comparison purposes, (+) amphetamine sulphate was administered subcutaneously at similar

* Present address: K. Ramabadran, Service de Pharmacotoxicologie, Institut Pasteur, 28, Rue du Docteur Roux, 75724 Paris Cedex 15, France.

** Also known by the Code SYA-33118.

doses and its stimulant activity on locomotion was studied in a similar manner. (+) Amphetamine sulphate was dissolveed in 0·9% sodium chloride solution and used.

A total of 240 mice were used for this study, 120 for each compound.

(b) Antagonism of Reserpine-induced Catalepsy in Mice

Mice (18–25 g) in groups of 10 were injected intraperitoneally with reserpine (5 mg Kg^{-1}) 17 h before intraperitoneal administration of the compound under investigation. Catalepsy was assessed at 30 min, 1 h, 2 h, 3 h, and 5 h by an observer who did not know the treatment using the method of Zetler and Moog[4]. The antagonism of catalepsy, *i.e.*, the ability to walk off a twine-covered vertical pole in a co-ordinated manner, was recorded. Control animals retain their position when placed on the side of the pole. The rectal temperature was recorded by a heat-sensitive thermistor probe. The probe was inserted to a depth of 3 cm and retained *in situ* until a constant temperature was displayed on the telethermometer.

The effects of three doses of the compound, 0·1, 1 and 10 mg Kg^{-1} were studied. 4 groups of 10 mice each were used for this study. One group served as a control.

Results

(a) Stimulation of Spontaneous Locomotor Activity in Mice

The benzocycloheptene derivative caused a dose-dependent and significant stimulation of spontaneous activity (Table I). Maximum stimulation was observed 1 to 2·5 h after its administration. The increase in activity was stastistically significant till 5·5 h in the case of 10 mg Kg^{-1}, 3 h with 5 mg Kg^{-1} and 2 h with 2, 5 mg Kg^{-1}.

(+) Amphetamine sulphate stimulated locomotion from 2·5 mg Kg^{-1} in a dose-dependent (Table II). Increase in locomotor activity lasted nearly 3 hours. The activity was significant till 3·5h in the case of 10 mg Kg^{-1}, till 3h with 5 mg Kg^{-1} and till 2h with 2·5 mg Kg^{-1}.

TABLE I

The effect of the benzocycloheptene derivative on the spontaneous locomotor activity in mice. Results are expressed as the mean number of light beam interruptions of a group of 5 mice for 7 h period, with Standard error of the mean. Six groups of 5 mice were investigated for each treatment and dose level. Experiments commenced 15 min after drug administration

Treatment in mg Kg^{-1} SC		No. of counts for 7 h ± S.E.M.	Statistical significance compared to control
Control		8017 ± 2121	-
Benzocycloheptene derivative	2·5	15647 ± 4933	$P < 0·01$
,,	5·0	24217 ± 3687	$P < 0·001$
,,	10·0	31797 ± 5474	$P < 0·001$

TABLE II

The effect of (+) amphetamine sulphate on the spontaneous locomotor activity in mice. Other details are as given in Table I

Treatmert in mg Kg^{-1} SC		No. of counts for 7 h ± S.F.M.	Statistical significance compared to control
Control		7010 ± 2475	
(+) Amphetamine sulphate	2·5	16488 ± 4758	$P < 0·01$
,,	5·0	22394 ±7677	$P < 0·001$
,,	10·0	23826 ±9198	$P < 0·01$

The percentage increase in spontaneous locomotor activity between (+) amphetamine sulphate and benzacycloheptene derivative has been compared in Table III.

TABLE III

Percentage increase in spontaneous locomotor activity: comparison between (+) amphetamine and benzocycloheptene derivative

Doses mg Kg^{-1}	Percentage increase when compared to control	
	(+) amphetamine sulphate	Benzocycloheptene derivative
2·5	135	95
5·0	219	202
10·0	240	297

(b) Antagonism of Reserpine-induced Catalepsy in Mice

The compound exhibited a dose dependent antagonism of reserpine-induced catalepsy and hypothermia. The antagonistic activity started 30 min after the drug administration and the peak effect

was observed at 60 min and started declining afterwards. The antagonism existed till 1 h at a dose of 0, 1 mg Kg^{-1}. At doses, 1 and 10 mg Kg^{-1}, the antagonism was observed till 2 h and 5 h respectively.

Discussion

The benzocycloheptene derivative and (+) amphetamine sulphate have been shown to produce dose-dependent stimulation of spontaneous locomotor activity in mice. The intensity of stimulation was almost same between (+) amphetamine sulphate and the compound under investigation over a period of 7 h. The stimulation of locomotor activity by (+) amphetamine sulphate has been attributed to be mediated by brain dopamine[5-7] and noradrenaline[8-10].

Reserpine-induced cataleptic state is said to be due to the depletion of catecholamines and serotonin in the central nervous system. (+) Amphetamine sulphate antagonises the cataleptic state of reserpine by stimulating the adrenergic[11] and serotoninergic receptors[12]. Van Rossum *et al.*[13] has presented evidence for a direct action of (+) amphetamine on adrenergic receptors in brain.

Because of the above considerations, it may be possible that the central stimulant activity of the new compound, a derivative of benzocycloheptene, could involve the mediation of the transmitters, catecholamines and serotonin as in the case of (+) amphetamine sulphate or by a different mechanism. Further experiments are necessary to establish the suggested mechanisms.

Acknowledgements

The authors is thankful to Sandoz Ltd., Switzerland, for providing facilities to carry out the experiments in their Psychopharmacology Research Laboratory.

1. Smith, C. B., *J. Pharmacol. Exp. Ther.*, 1965, 147, 96.
2. Johnson, A. M., Loew, D. M. and Vigouret, J. M., *Br. J. Pharmac.*, 1976, 56, 59.
3. Stula, A. D. and Meier, M., *Neuropharmac.*, 1976, 15, 383.
4. Zetler, G. and Moog, E., *Naunyn Schmiedebergs. Pharmak.*, 1958, 232, 442.
5. Costa, E., Gropetti, A. and Naimzada, M. K, *Br. J. Pharmac.*, 1972, 44, 742.
6. Van Rossum, J. M. and Hurkmans, J. A. T. M., *Int. J. Neuropharmac.*, 1964, 3, 227.
7. —, *Int. J. Neurobiol.*, 1970, 12, 307.
8. Svensson, T. H. and Waldeck, B., *Psychopharmacologia, Berl.*, 1970, 18, 357.
9. Maj, T., Grabowska, M. and Gajda, C., *Eur. J. Pharmac.*, 1972, 17, 208.
10. Anden, N. E., Strombom, U. and Svensson, T. H., *Psychopharmacologia, Berl.*, 1973, 29, 289.
11. Innes, I. R. and Nickerson, M., *The Pharmacological Basis of Therapeutics*, Eds. Goodman, L. S. and Gilman, A., The Macmillan Company, London, 1971, p. 503.
12. Vane, J. R., *Adrenergic Mechanisms* (a Ciba foundation symposium), Eds. Vane, J. R., Wolstenholme, G. E. W. and O'Conor, Maeve., J. and A. Churchill Ltd., London, 1960, p. 356.
13. Van Rossum, J. M., Van der Schoot, J. B. and Hurkmans, J. A. T. M., *Experientia*, 1962, 18, 229.

SOME ADDITIONS TO THE LICHEN FLORA OF INDIA
I. Genus *Hypotrachyna* (Vain.) Hale (Parmeliaceae)

P. G. PATWARDHAN AND A. V. PRABHU

Department of Mycology and Plant Pathology, M.A.C.S. Research Institute, Poona 411 004 (India)

IN our on-going research project on the lichen flora of Western Ghats (south western India) we have so far determined sixty-nine species belonging to the genera *Bulbothrix, Hypogymnia, Hypotrachyna, Menegazzia, Parmelina, Parmotrema, Parmelia, Pseudoparmelia, Relicina* and *Xanthoparmelia* of the family Parmeliaceae. Careful search of the literature revealed that of these sixty-nine species twenty-two taxa were not previously recorded under the composite genus *Parmelia* Ach. (Awasthi, 1965[1]) from Indian subcontinent. Six species of the genus Hypotrachyna, which constitute additions to the lichen flora of India are detailed in this note. Chemical studies were carried out by thin-layer chromatography (TLC) using EMerck precoated silica gel F_{254} aluminium plates and B.D.A. and H.E.F. solvent systems (Culberson, 1972[2]). Specimens referred to in the text are deposited in the Lichen unit of the Ajrekar Mycological Herbarium (AMH).

The genus *Hypotrachyna* (Vain.) Hale is one of the recently segregated genera from the old composite genus Parmelia Ach. (Hale, 1974[3]). It is characterised by non-ciliate thallus and dichotomously branched rhizines.

1. *Hypotrachyna costaricensis* (Nyl.) Hale
   = *Parmelia costaricensis* Nyl.

Thallus corticolous, closely adnate to the substratum, 2–4 cm broad; lobes sublinear to linear, 2–3 mm broad, isidiate, isidia cylindrical, erect,