Ind. J. Physiol. Pharmac., Volume 33, Number 1, 1989

A NEUROPYCHOPHARMACOLOGICAL PROFILE OF "CINKARA", A POLYHERBAL PREPARATION

M.R. SAKINA, E.A. KHAN, M.E. HAMDARD AND P.C. DANDIYA*

Institute of History of Medicine & Medical Research, Hamdard Nagar, New Delhi - 110 062

(Received on November 30, 1988)

Summary : "Cinkara", a polyherbal preparation reduced pentobarbitone induced hypnosis in mice, decreased apomorphine induced fiighting, aggression and stereotypy and increased amphetamine induced aggregated toxicity in mice. It also increased immobility of rats in forced swimming test, an action which was not blocked by chlor-promazine, and increased ambulation in open arena test. It did not modify electrically induced convulsions or haloperidol catalepsy. It is suggested that the preparation possesses a central nervous system stimulant activity but unlike other CNS stimulants, it lowers aggressive activity in rats.

Key words : Cinkara MES stereotype behavioural despair.

INTRODUCTION

Cinkara (Hamdard), a non-alcoholic polypharmaceutical herbal tonic, consists of vitamins (A, B_1, B_2, C, D_3 and niacinamide) and glycerophosphates alongwith aqueous extract from thirteen plants in a flavoured syrupy base.

Cinkara has been reported to increase psychomotor and mental functions as tested in healthy normal volunteers by digital cancellation test, arithmetic tests and critical fusion frequency test (1). Cinkara is said to have a positive influence on the mental activity, growth and intellectual functioning of children. It has also been claimed to play some role in the treatment of mental subnormality (2).

We are reporting here on the behavioural effects of this preparation in animals and on its possible mechanism of action.

MATERIAL AND METHODS

Male or female albino rats (125-200 g, Haffkine strain) and mice (18-30 g) were employed. Cinkara was given orally, twice daily (0.5 ml in rats and 0.15 ml in mice) for 5 days, since preliminary experiments had shown that the maximum behavioural changes occurred in between 3 to 6 days. Controls received syrup base in the same volume. Animals were used on 6th day for tests.

Behavioural despair in rats (forced swimming) (3) : The rats were individually forced to swim in glass cylinders (40 cm : 18 cm D.) containing water upto 15 cm mark for 15 min. Next day they were subjected to the test for 5 min to measure 'immobility' (floating passively in the water in a slightly hunched but upright position, with head just above the surface).

The effect of d-amphetamine (3 mg/kg, ip) or chlorpromazine (3 mg/kg ip) was also tested in control and treated animals.

Pentobarbitone sleeping time (4) : Pentobarbitone sodium (40 mg/kg, ip) was given to control and Cinkara treated mice. Time intervals between the loss and regaining of righting reflex was taken as the sleeping time.

* Corresponding Author

Apomorphine (2.5 mg/kg, ip) induced stereotypy and fighting behaviour (5) : Fighting was graded by trained observers blind to the 'treatment' rats under a bell jar at 5, 10, 15, 30, 45 and 60 min (n=10). Similarly, stereotype scores (See Table II) were noted in individual rats with the help of hand counters, total possible scores being 200.

Amphetamine (1.5 or 3 mg/kg, ip) induced stereotypy in mice (6) : Observations were made in the same way as described above (n=20).

Amphetamine toxicity in aggregated mice (7) : Treated or control mice were put together at room temperature (32°C) in a single cage after giving amphetamine (10 mg/kg or 20 mg/kg, ip). The mortality was recorded after 3, 12, 24 hr.

Maximal electroshok induced convulsions (MES test) in rats (8) : Electro-convulsio-meter was used to deliver 150mA current for 0.2 sec through ear-electrodes. Duration of various phases of convulsions was recorded in secs.

Haloperidol (3 mg/kg, ip) induced catatonia in rats (9) : Catalepsy was a scored (0 to 3.5) as described by Dandiya et al. (9).

Open arena test (10) : A mouse was placed for two min in a circular wooden arena (84 cm D) with sunmica wall. The base was marked with 3 concentric circles divided into segments by lines radiating from the floor centre. The markings provided 25 floor units of approximatly equal size and these were used to score the ambulation of the animal. Hand operated counters were used to record ambulation ("Walking around" score, the number of radial segments of the arena crossed by the subject), rearing (the number of times the rat stood on its hind legs), preening and defecation responses. Data were analysed employing the students 't' test and Wilcoxon's sum rank test.

RESULTS

Behavioural despair in rats : The immobility time of Cinkara pretreated animals was higher than the controls. Chlorpromazine produced little change in this test. Amphetamine reduced the immobility per se and in Cinkara treated animals. (Table I).

Pentobarbitone sleeping time : Pretreatment with Cinkara reduced the pentobarbitone induced sleeping time in mice (mean time, min ± S. E. M., control 33.08 ± 5.44 ; treated 13.48 ± 1.48 ; $P<0.001$).

TABLE I : Effects of Cinkara alone and with other rugs on the total duration of immobility in forced swimming test.

S. No.	Drugs & Dose (mg/kg	No. of rats used	Duration of immobility (sec) Mean±S.E.M	P. value
1	Control	42	239.38±1.47	—
2	Cinkara	34	265.38±1.63	<0.001 vs 1
3	d-Amphetamine (3 mg/kg, ip)	22	85.4 ±1.87	<0.001 vs 1
4	Cinkara+d Amphetamine (3 mg kg, ip)	15	106.6 ±2.29	<0.001 vs2 NS. vs3
5	Chlorpromazine	5	240 ±2.2	NS vs 1
6	Chlorpromazine (3 mg/kg, ip)+ Cinkara	5	266.8 ±1.46	NS vs2

Apomorphine induced stereotypy and fighting behaviour in rats : Cinkara decreased the apomorphine induced fighting and stereotype movements like scratching,

ambulation and vocalisation but increased the rearing and salivation (Table II).

TABLE II : The effect of Cinkara on apomorphine induced fighting (10 pairs of rats) and storeotype behaviour (20 rats)

S.No.	Parameters	Total Scores	
		Control	Cinkara
1	Fighting	71	14*
2	Stereotype		
	Scratching	94	21*
	Vocalisation	66	8*
	Rearing	18	133*
	Sniffing	102	94
	Wall licking	61	64
	Self grooming	20	23
	Ambulation	129	18*
	Salivation	10	118*

*P value <0.05
(Wilcoxon's sum rank test)

Amphetamine induced stereotypy : Cinkara-treated group exhibited increased circling self grooming, wall licking, ambulation, sniffing, salivation, awakening, scratching and decreased congregation (Table III).

TABLE III : Influence of Cinkara-pretreatment on amphetamine-induced stereotypy.

S.No.	Parameters	Amphetamine treatment			
		1.5 mg/kg		3 mg/kg	
		Control	Pretreatment	Control	Pretreatment
1	Searching Movement of head	96	92*	100	92
2	Circling	14	100*	28	104*
3	Licking Lips	70	70	21	83*
4	Rearing	18	138*	14	141*
5	Self Grooming	12	108*	14	101*
6	Wall Licking	18	95*	17	93*
7	Ambulation	42	122*	39	118*
8	Sniffing	35	120*	37	124*
9	Congregation	49	51	59	51
10	Salivation	10	100*	14	119*
11	Awakening	30	119*	25	118*
12	Scratching	26	115*	29	117*

* P value <0.01

Amphetamine toxicity in aggregated mice : Cinkara increased the number of deaths due to amphetamine toxicity in aggregated mice (Fig. 1).

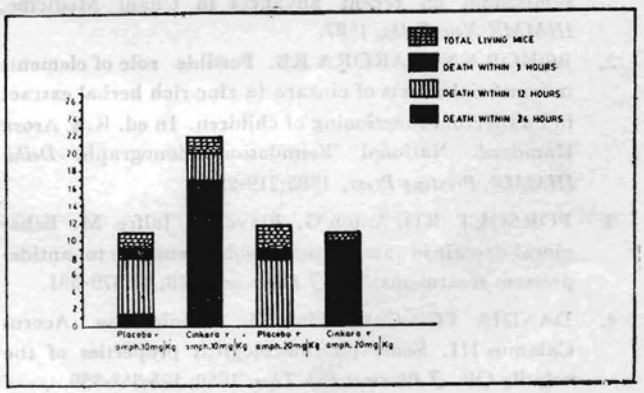

Fig 1 : The effect of Cinkara on Amphetamine induced toxicity in aggregated mice. The 'Y' axis gives the number of mice taken for each study.

MES test and haloperidol catatonia : Cinkara did not protect rats in MES test nor did it cause any significant change in haloperidol induced catatonia in rats upto 120 min.

Open field arena : Cinkara treated group showed increased rearing response when compared to the controls. (Mean scores; control 10.8, treated 18.5; $P<0.5$) while no significant effect was seen on ambulatory, preening and defecation responses.

DISCUSSION

That Cinkara-pretreatment reduced pentobarbitone induced sleeping time in mice is indicative of its stimulant effect. A CNS stimulant could also increase aggressive activity and lower electroshock threshold for convulsions Interestingly, however, apomorphine given to rats pretreated with cinkara, brought about a less intensive fighting, scratching and ambulation while it caused increased rearing and salivation response as compared to controls. The alteration in the rearing response is indicative of an elevated exploratory activity. Thus, while aggressive activity is lowered, exploratory activity is enhanced by cinkara. On the other hand, cinkara acted much like amphetamine as it enhanced the amphetamine induced circling, rearing, self grooming, wall licking, ambulation, sniffing, salivation and scratching in mice. However, an antidepressent, amphetamine, is known to decrease the immobility in rats under despair (3) while cinkara brought about an opposite effect in these experiments. When cinkara was given with amphetamine it, however, did not reverse the amphetamine induced increase in the immobility in mice. The fact that Cinkara was able to increase the immobility in rats indicates that it is unlike the usual antidepressants or CNS stimulants. Its effect is more like low doses of caffeine than that of amphetamine (3). Thus cinkara has little similarlty with apomorphine, and to a large degree resembles amphetamine and to a smaller extent caffeine.

In view of the effect of cinkara on various behavioural parameters, its failure to protect the rats from electroshock was not unexpected. Since its actions are not blocked by chlorpromazine in the swimming test, it does not seem to act on the D_2-dopamine-receptors, which is supported by the observation that it did not alter haloperidol-induced catalepsy.

REFERENCES

1. RAINA RK, KAPOOR S, KHAJURIA V. Effects of a herbal polypharmaceutical on psycho motor and mental functions in healthy volunteers, paper presented in symposium on recent advances in Unani Medicine, *IHMMR New Delhi*, 1987.
2. BOHORA NK, ARORA RB. Possible role of elements in beneficial effects of cinkara (a zinc rich herbal extract in intallectual functioning of children. In ed. R.B. Arora Hamdard National Foundation Monograph, *Delhi, IHMMR, Printing Press*, 1985:219-226.
3. PORSOLT RD, Anton G, Blavel N, Jalfre M. Behavioral despair in rats : A new model sensitive to antidepressant treatments. *Eur J Pharmac.* 1978; 47:379-391.
4. DANDIA PC, Cullumbine H. Studies on Acorus Calamus III. Some pharmacological properties of the volatile Oil. *J Pharmac Exp Ther.* 1959; 125:353-359.
5. PATNI SK, DANDIYA PC. Apomorphine induced biting and fighting behavior in reserpinized rats and an approach to the mechanism of action. *Life Sci* 1974; 14:737-745.
6. DANDIA PC, PATNI SK, KULKARNI SK An analysis of some aspects of amphetamine induced stereotyped behaviour. *J Pharmac (Paris)* 1975; 6:385-390.
7. MENON MK, DANDIA PC. Mechanism of the protective effect of reserpine on aggregated mice treated with d-amphetamine. *J Pharm Pharmac* 1967; 19:596-602.
8. MISTRA AK, DANDIYA PC, KULKARNI SK. Anticonvulsant activity of some trimethoxybenzylidene - 2-thiohydantoin derivatives. *Ind J Pharmac* 1973; 449-450.
9. DANDIYA PC, BANERJEE P. Biphasic effects of dopamine agoinsts on haloperidol induced catalepsy. *Ind J Pharmac* 1986; 18:9-13.
10. DANDIYA PC, KULKARNI SK. Open field test : Its statut in psychopharmacology *Ind J Pharmac Edu.* 1977; 31-34.