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Effect of a Composite Indian Herbal Preparation, CIHP (III) on Avoidance Learning during Endurance Performance of Rats

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SUMMARY

A nine week cross over study (5 weeks drug administration and 4 weeks withdrawal) was performed to see the effect of a composite Indian herbal preparation (CIHP III), viz. Mentat, on avoidance learning during endurance performance of albino rats. Runimex, a circular runaway was used for this purpose. The number of stimuli viz. electrical shock of 10 mv, in drug treated rats at an oral dose of 47.86 mg/100 g b. wt./ single dose/day for 5 days were significantly reduced as compared to rats not taking any drug. The number of stimuli decreased significantly when the drug was started in the control group. No change in avoidance learning was observed over the period of 9 weeks in another group of rats. Results indicate significant improvement in avoidance learning during endurance performance due to the intake of CIHP(III).

Table 1: Composition of CIHP (III) powder (Concentration w/w%)

Sl. No.	Name of the plant	Part of the plant used	Compo-sition
1.	*Bacopa monnieri* Pennell. (Brahmi)	Whole plant	22.3
2.	*Centella asiatica* Linn. (Mandookparni)	Whole plant	7.3
3.	*Withania somnifera* Dunel. (Ashwagandha)	Whole plant	5.5
4.	*Evolvulus alsinoides* Linn. (Shankapushpi)	Whole plant	5.5
5.	*Nardostachys jatamansi* DC. (Jatamansi)	Root	5.5
6.	*Valeriana wallichii* DC. (Tagar)	Root	5.2
7.	*Embelia ribes* Burn. (Vaividang)	Fruit	5.2
8.	*Prunus amygadalus* Batsch. Vor. dulcis (DC) Kochme	Fruit	5.2
9.	*Acorus calamus* Linn. (Vach)	Root	4.4
10.	*Tinospora cordifolia* Miers. (Guduchi)	Bark & leaves	3.7
11.	*Terminalia chebula* Retz. (Haritaki)	Fruit	3.7
12.	*Emblica officinalis* Gertn. (Amla)	Fruit	3.7
13.	*Celastrus paniculatus* Wild. (Malkangani)	Seed	3.4
14.	*Oroxylum indicum* Vent. (Sonpata)	Root	3.4
15.	*Orchis mascula* Linn. (Slep)	Root	1.8
16.	*Mucuna pruriens* Baker. (Kavach)	Root & seed	1.8
17.	*Elettaria cardamum* Maton. (Chhoti Elaichi)	Seed	1.8
18.	*Terminalia arjuna* W&A. (Arjuna)	Bark	1.8
19.	*Foeniculum vulgare* Gaertn. (Bari Saunf)	Seed	1.8
20.	*Ipomoea digitata* R. Br. (Vidhari Kand)	Root	1.8
21.	*Zingiber officinal* Roxb. (Sonth)	Root	1.4
22.	*Terminalia belerica* Roxb. (Beheda)	Fruit	1.4
23.	*Myristica fragrans* Houtt. (Jaiphal)	Seed	1.4
24.	*Syzygium aromaticum* Merr. et. Perr. (Lavang)	Clove Stalk	1.0

A large number of research activities are concerned with improving physical and mental performance in man. A complex herbal preparation CIHP (III), viz. Mentat prepared through a standardised reproducible procedure contains ingredients like Ashwagandha (*Withania somnifera* Dunel.), Malkangani (*Celastrus paniculatus* Wild), Mandokparni (*Centella*

asiatica Linn.), Shankpushpi (*Evolvulus alsinoides* Linn.) and Brahmi (*Bacopa monnieri* Panell) (Table 1). These are used in the management of nervous disorders and are highly acclaimed in Ayurveda, the ancient Indian system of medicine. Verma and Kulkarni[1] studied the effect of this preparation (CIHP, III), on anxiety and transfer latency (TL) in mice on elevated plus-maze. They found the reduction in the per cent time spent in open arms and the percent preference of open arms for the first arm entry following acute as well as chronic drug administration. Experimental finding associated CIHP(III) administration with improved acquisition and retention of learning in mice[2]. Bhattacharya[3] further found that subchronic administration of CIHP(III) in rats can facilitate learning using step-down latency in a passive avoidance and transfer latency in elevated plus-maze. He also studied its antidepressant and antiaggression activities in rats and mice using standard behavioural paradigms. Clinical studies have indicated that the CIHP (III) was effective in anxiety-neurosis, depression, cognitive deficit, behavioural disturbances in mentally retarded children, hyper kinetic states, nocturnal enuresis and aggressive behaviour[4-6].

Brahmi (*Bacopa monnieri*) one of the ingredient of CIHP (III) is effective in facilitating mental retention capacity[7] and the consolidation of an experience by improving the intermediate memory as well as long term memory. Another ingredient of CIHP(III) *Centella asiatica* (Mandookparni) is reputated as brain tonic. Preliminary pharmacological experiments show that drug has tranquilising, sedative and spasmolytic properties. It is anabolic and showed improvement in general ability and behavioural pattern of retarded children[8].

In none of the studies enumerated above, avoidance learning during endurance performance of rats has been investigated. We have studied this in albino rats as an experimental model. The results of this study are being reported in this communication.

MATERIALS AND METHODS

Seventeen female white albino rats (body weight 50-60 g) were taken. They were provided with food (rat feed, Lipton India Ltd.) and water *ad libitum*. The rats were kept in the animal house where the room temperature was maintained at 35 ± 5°C. The rooms were lighted between 0900 and 1730 hrs. At 1730 hrs lights were switched off for night.

The Runimex, a circular runway, manufactured by Columbus Instrument, USA was used for investigating the effect of CIHP(III) on avoidance learning during endurance performance of the rats. A dedicated computer was used as a controller for automatic presentation of stimuli in the form of light, sound and electrical shock. The Runimex software disc contained programs for training the rats. The rats were forced to run in the Runimex to avoid electrical shock (10 mv). When the number of avoidance reached eight percent or 80%, the rats were considered to have been trained. It took five days for their training in our case.

The rats were divided into three groups A, B and C. CIHP (III) powder was refluxed in 75% alcohol for 6 hrs. It was filtered and vacuum dried. The alcoholic extract, equivalent on the

dry weight basis to the dose of 47.86 mg/100 g body weight, was used. Group A rats were given single dose of CIHP (III) daily for 5 days. Their avoidance learning was tested on Rumimex after one week. The group B rats were not given any drug and treated the same way as group A rats. Group C rats were treated as control through out the study to see the effect of aging, if any. Group A and B rats were tested for their avoidance learning for four weeks. The drug was withdrawn in group A rats and started in group B rats after 4 weeks. The complete experiment was repeated in the same way. The computerised records were obtained per minute through the computer in terms of time taken, average speed, distance travelled, run time, rest time and number of stimuli required to make the rat run till it got exhausted and refused to respond to stimuli inspite of repeated electrical shocks. The results were expressed as mean ±SEM. The significance of difference was calculated by Student's '*t*' test using Epistat software.

RESULTS

Results have been presented in Tables 2,3 and 4. Total time taken for the run was similar in group B (no drug treatment) rats and group A (drug administered) for 1st to 5th weeks. There was significant decrease in average speed in the 1st, 2nd, 3rd, 4th and 5th weeks in group B rats as compared to group A rats. Distance travelled was significantly lower in group B rats as compared to group A rats except for the 1st week. Total run time was significantly lower and rest time significantly higher in group B rats as compared to group A rats except for the 1st week. The number of stimuli was significantly higher in group B during 3rd, 4th and 5th week as compared to group A rats. (Table 2).

Table 2: Effect of CIHP (III) on avoidance learning during endurance performance of rats

Gr (N)	Day	Drug starts doses	Time (Min)	Average speed (cm/sec)	Distance travelled (cm)	Run (Sec)	Rest (Sec)	Stimuli (Nos)
A (6)	7th	5	54.5 ± 3.5	11.7 ± 0.5	823.3 ± 12.0	53.2 ± 0.8	6.8 ± 0.8	15.3 ± 0.3
	14th	10	56.1 ± 3.0	12.3 ± 0.3	836.2 ± 15.2	50.7 ± 1.1	9.3 ± 1.1	14.2 ± 0.5
	21st	15	53.3 ± 3.6	11.4 ± 0.6	908.3 ± 31.5	55.1 ± 1.4	4.9 ± 1.4	11.2 ± 0.6
	28th	20	53.8 ± 3.2	12.1 ± 0.3	1000.0 ± 48.7	53.7 ± 1.1	6.3 ± 1.1	9.5 ± 0.5
	35th	25	54.7 ± 2.5	12.3 ±0.2	965.8 ± 21.2	51.4 ± 1.1	8.6 ± 1.1	9.5 ± 0.5
B (6)	7th	No drug	52.3 ± 2.8	7.9 ± 0.5*	514.3 ± 17.3	34.5 ± 1.1	25.5 ± 1.1	15.5 ± 0.4
	14th	–''–	48.6 ± 1.9	8.6 ± 0.4*	499.6 ± 12.6*	35.2 ± 0.9*	24.8 ± 0.9*	16.0 ± 0.4
	21st	–''–	48.1 ± 3.0	8.6 ± 0.4*	523.3 ± 12.6*	33.6 ± 0.9*	26.4 ± 0.9*	15.2 ± 0.4*
	28th	–''–	48.0 ± 2.7	8.5 ± 0.4*	519.1 ± 20.1*	33.0 ± 1.0*	27.0 ± 1.0*	14.5 ± 0.4*
	35th	–''–	52.2 ± 2.0	9.5 ± 1.0*	536.3 ± 20.5*	34.6 ± 0.8*	25.4 ± 0.8*	14.5 ± 0.4*

* Significantly different as compared to group A (drug starts $p>0.001$).

Table 3: Effect of CIHP (III) on avoidance learning during endurance performance of rats								
Gr (N)	Day	Drug with-drawn doses	Time (Min)	Average speed (cm/sec)	Distance travelled (cm)	Run (Sec)	Rest (Sec)	Stimuli (Nos)
A (6)	7th	–	50.0 ± 2.9	11.7 ± 0.3	894.2 ± 30.9	51.1 ± 0.9	8.9 ± 0.9	11.8 ± 0.5
	14th	–	50.6 ± 1.7	11.3 ± 0.2	828.0 ± 21.8	49.2 ± 0.7	10.8 ± 0.7	14.0 ± 0.4
	21st	–	46.6 ± 1.7	11.0 ± 0.3	781.0 ± 22.1	41.9 ± 0.6	10.1 ± 0.6	17.5 ± 0.6
	28th	–	46.6 ± 1.7	11.0 ± 0.3	781.0 ± 22.1	41.9 ± 0.6	10.1 ± 0.6	17.5 ± 0.6
B (6)	7th	Drugs starts 5	55.0 ± 2.3	13.0 ± 0.3*	833.3 ± 22.8	51.6 ± 0.6	8.4 ± 0.6	15.0 ± 0.5*
	14th	10	52.8 ± 2.4	12.3 ± 0.3*	826.0 ± 26.9	51.4 ± 0.4	8.6 ± 0.4	14.3 ± 0.6
	21st	15	56.4 ± 2.3	12.6 ± 0.7*	856.0 ± 24.8*	53.1 ± 0.9*	6.9 ± 0.9*	12.0 ± 0.6*
	28th	20	56.2 ± 1.7*	12.6 ± 0.3*	995.8 ± 36.9*	51.9 ± 0.7	8.1 ± 0.7	10.0 ± 0.3*
* Significantly different as compared to group A (drug withdrawn $p>0.001$).								

Table 4: Effect of CIHP (III) on avoidance learning during endurance performance of rats							
Gr (N)		Time (Min)	Average speed (cm/sec)	Distance travelled (cm)	Run (sec)	Rest (sec)	Stimuli (nos)
A (6) day	Initial doses						
7th B(6)	5 initial	54.5 ± 3.5	11.7 ± 0.5	823.3 ± 12.0	53.2 ± 0.8	6.8 ± 0.8	15.3 ± 0.3
7th A(6)	– Final	52.3 ± 2.8	7.9 ± 0.5	514.3 ± 17.3	34.5 ± 1.1	25.5 ± 1.1	15.5 ± 0.4
28th B(5)	– Final	46.6 ± 1.7	11.0 ± 0.3	781.0 ± 22.1	41.9 ± 0.6	10.1 ± 0.6	17.5 ± 0.6
28th C(5)	20 Initial	56.2 ± 1.7	12.6 ± 0.3	995.8 ± 36.9	51.9 ± 0.7	8.1 ± 0.7	10.0 ± 0.3
C (5)	Final	54.0 ± 2.9	9.4 ± 0.9*	497.2 ± 30.6*	35.9 ± 1.7*	24.1 ± 1.7*	15.2 ± 0.4
		52.6 ± 2.8	7.9 ± 0.6#	437.8 ± 34.15#$	35.1 ± 1.5#	24.9 ± 1.5#	15.4 ± 0.2
*Significantly different as compared to group A (initial) $p>0.001$. # Significantly different as compared to group B (final) $p>0.001$. $Significantly different as compared to group A (final) $p>0.001$.							

The average speed increased significantly in group B (drug administered) rats during 1st, 2nd, 3rd and 4th week as compared to group A (drug withdrawn) rats. Total time of the run was similar in group B and group A rats except during the 4th week where it was significantly increased. The distance travelled during 3rd and 4th week in group B rats were significantly increased as compared to group A rats. Total run time and rest times were similar in group B and A rats except during 3rd week. The number of stimuli were significantly decreased in group B rats as compared to group A rats except during 2nd week (Table 3).

There was insignificant difference in all the parameters between Group B (initial) group A (initial) and group C (initial). The distance travelled, average speed, run time, rest time in group C (initial) rats were significantly different as compared to group A (initial) rats where

as total time and number of stimuli were similar in group C (initial) rats compared with group A (initial). All the parameters in group C (final) were significantly different except total time and number of stimuli as compared to group B (final) rats. All the parameters in group C (final) were similar as compared to group A (final) except for distance travelled (Table 4).

DISCUSSION

CIHP (III) a composite herbal formulation of several CNS-active Ayurvedic drugs (Medhyarsayana-dravyas) has been shown to be effective in various clinical disorders, mental debility and poor memory[9]. It was found to improve learning acquisition and retention of learned task in normal rats with no cognitive deficit, when administered subchronically. It has been shown to be clinically effective in a variety of neuropsychiatric disorders including anxiety-neurosis, depression and aggressive behaviour[4-6].

In our study the number of stimuli in drug treated rats (group A) were significantly decreased as compared to without drug rats (group B). The number of stimuli was decreased significantly in group B rats when drug was started in that group as compared to group A in which the drug was withdrawn. Insignificant change was observed in number of stimuli in group C rats (control) suggesting that aging over the period of experiments had little effect on the avoidance learning. The average speed increased significantly in drug treated rats which would explain the increase in distance travelled. The run time increased and rest time decreased in drug treated rats. This got reversed with the cross over of drug administration. The results indicated remarkable effect of CIHP (III) on avoidance learning during endurance performance of rats. However, the mechanism of the action as to why the drug stimulated avoidance learning, remains to be investigated. In addition whether the drug stimulates incentive learning process needs study.

A systematic investigation of the effect of CIHP (III) on major neurotransmitter system can provide rational explanation for the observed behavioural effect as well as its nootropic activity[10].

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