

A psycho-pharmacological study of BRHAT VATACINTAMANI RASA classical ayurvedic drug

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SUMMARY

The psycho-pharmacological effect of BRHAT VATACHINTAMANI RASA (BVC) an Ayurvedic preparation was investigated, both in animal and clinical models. It was observed that BVC possess a sedative or quitening effect in that it significantly decreased the spontaneous motor activity, and also lowered the exploratory behavior of the amphetamine treated animals. This was further evident by increase in climbing out time and taming effect on animal in isolation induced aggression test. Apart from very high dose it seems have little effect on pentobarbital sleeping time and narcotic analgesic test. The drug BVC increases performance of the animal in forced locomotor test. The effect of VATACHINTAMANI RASA on clinical study was not significant.

Key words: Psychopharmacological; Ayurveda; Brhat Vatacintmani Rasa

INTRODUCTION

The System of Ayurveda, has had a much wider recognition and prevalence in the past, dating back as early as to the dawn of human civilization and the Vedic period. This system has undergone many vicissitudes in the course of its long and chequered history. However, it still remains the mainstay of medical relief to the majority of the people in this country. During the medieval period the system of Unani medicine was introduced and it was only in the sixteenth century A.D. that the western (allopathic) system came to be introduced in this country. However, Ayurveda continues to be the largest system of medical relief for the masses. The system of Ayurveda embraces, within its inventory, drugs of plant, animal and mineral origin, both single drugs and compound formulations. Although Ayurveda does not rule out any substance from being used as a potential source of medicine, presently about 1000 single drugs and 8000 compound formulations of recognized merit are in vogue.

All the main classical works on Ayurveda, such as Caraka Samhita, Susruta Samhita, Astanga Sangraha and Astanga Hrdaya deal with drugs, their composition and action in addition to the other aspects of the medical system. Some of the Ayurvedic books known as Nighantugranthas like Dhanvantarinighantu, Kaiyadevanighantu, Bhavaprakasanighantu, Rajanighantu, etc. deal mainly with single drugs, describing their habitat, characteristics and therapeutic action. Ayurvedic compound formulations are divided into two groups, viz. (i) Kasthausadhi (predominantly plant drugs) and (ii) Rasansadhi (predominantly metals and minerals).

There are many authentic books on both the groups of compound formulations. While Sarngadhara samhita, Cakradatta, Bhaisajya ratnavali, Sahasrayogam, Bharat Bhaisajya Ratnakara, etc., deal with both the groups of formulations, others like Rasendra Sarasangraha, Rasaratna Samuccaya, Rasaprakasa Sudhakara, Ayurveda prakasa, Rasatarangini, Rasayogasagara etc., deal only with Rasansadhi group of formulations. There are several categories of Kasthansadhi formulations, such as Asavarista, Avaleha, Ohrta, Curna, Taila, etc. and of Rasansadhis, such as Bhasma, Pisti, Lauha, Mandura, Kupipakva Rasayana etc.

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Centrally acting drugs, by definition, influence the function of the nervous system and therefore, inevitably affect behaviour, and indeed the desired effect of such drugs is, in general, alteration of behaviour. Investigation of the action of these agents, therefore, includes the need to measure behavioral change. This measuring must be done both qualitatively, so that the type of behaviour influenced, can be recognized, and quantitatively, so that the magnitude of the effect can be estimated. The success of any procedure that is to evaluate the behavioral effects of a drug, therefore, depends on the ability of the procedure to discriminate among different types of behaviour and on its susceptibility to accurate measurement. Looking at the situation in the simplest terms, there are two methods that are used to approach these problems. The first, and by far the more common, is the development of a simple "test". This development involves the selection of some variable that can be assessed precisely and that gives repeatable results. The second depends on the direct observation of a wide range of activities and is derived largely from the methods developed in assessing behavioral pharmacology.

The drug under study is known as BRHAT VATACINTAMANI RASA (BVC). The presence of the word "Vata', in the name of the formulation attracted the attention of the author. According to Ayurvedic sciences, the human physiology is divided in three principal segments. They are Vata; Pitta and Kapha.

The physiological concept of Vata includes, *intercilia*, all activating and/or dynamic functions of the body; exhibition of enthusiasm, concentration, increased circulation and respiration, voluntary actions of every kind. In comparison, Vata resembles the central and autonomic nervous systems of the modern physiology (Anonymous, 1948).

The probable site of action of the drug, under study, is the central nervous system. As a consequence of this, the different experiments carried out during the progress of this project work, involved probing into the different probable actions of the drug in the central and autonomic nervous system.

MATERIALS AND METHODS

Composition of the drug

BRHAT VATACINTAMANI RASA

1.	Svarna bhasma	3 parts
2.	Raupya bhasma	2 parts.
3.	Abhraka bhasma	2 aprts
4.	Lauha bhasma	5 parts
5.	Pravala bhasma	3 parts
6.	Mauktika bhasma	3 parts
7.	Suta bhasma (rasa sindura)	7 parts

8. Kanya (kumari) rasa q.s.(mardana) for one day

Dosage

125 mg

Important therapeutic use

Vata pittaja roga, bhrama, pralapa (Dasa)

Experimental animal

The experimental animal used to explore various pharmacological aspects of BRHAT VATACINTAMANI RASA, was mice. Mice, both male and female [cr1: CFW (Swiss Webster) BR] weighing between 20-30 gram, were purchased from the animal resource branch of International Center for Diarrhoeal Diseases and Research, Bangladesh. In a metallic cage, having a dimension of 30×20×13 cm, the animals, in groups of six, were housed. The room, where these cages were kept, had natural right cycle. As bedding in the cages, softwood shavings were employed.

The animals were fed with mouse chow (prepared according to the formula developed in the BCSIR, Dhaka) and were provided with tap water ad libitum, except during the short time when they were removed from their respective cages for the purpose of performing various tests on them. The newly received animals in the laboratory were allowed 4 days to adjust to the food and water restrictions, incurred during transit and to adapt themselves with this new environment, before being employed in the experiments. In order to record drug doses administered and the corresponding responses to be observed, during the entire course of the work, the animals were carefully marked on different parts of their body. This enabled the author to identify and to distinguish a single animal in a group.

Preparation and injection of the test drug

Accurately weighed, powdered BRHAT VATAC-INTAMANI RASA was administered as a suspension with 0.9% normal saline being the continuous phase. A concentration that permits optimal accuracy of dosage, without the injected volume contributing excessively to the total body fluid, was given to the test animals in the treated group. Thus, the volume administered to the test animals (mice) was 0.01 ml/gm body weight. The route of administration of the drug was intraperitoneal (i.p).

Controls

A control group of 5 mice were simultaneously injected intraperitoneally, instead of the drug, with 0.9% normal saline, in a volume of 0.01 ml/gm body weight.

EXPERIMENTAL METHODS

a. Effect on the spontaneous motor activity

To study the effect of the drug on spontaneous motor activity, brick chip displacement method was employed. Previously washed and dried brick chips were spread evenly on a wire netting having a mesh size of 28. Over it, an observation tank was placed. Mice in groups of two were introduced in the observation tanks. Graded doses of drugs were given. Brick chips, displaced through the wire netting, due to spontaneous motor activity, were recorded with five minute interval for a total period of one hour. Similar recordings were made for the control group (Siegmund *et al.*, 1952).

b. Effect on amphetamine induced hyperactivity

As with the previous experiment, in this experiment too, brick chip displacement method was used - the detail of this method is discussed in the previous experimental model. Test animals were pre-treated with graded doses of the drug (BVC), one hour prior to the administration of d-amphetamine, in a dose of 4 mg/kg, (Vane, 1961) intraperitoneally, so as to obtain responses ranging between 0-100%. In 0.9% normal saline treated control, as well as, in the treated groups, recordings of the displaced brick chips were made with five minutes interval for a period of one hour.

c. Effect on rectal temperature

The rectal temperature of the animals, in groups of 5, was measured by a thermometer, 60, 120, 240 minutes after intraperitoneal acute administration of graded doses of the drug under study. Temperature readings for control animals, in group of 5, injected with 0.9% normal saline i.p., were also recorded (Kobayashi and Tobe, 1976).

d. Climbing test in mice

The probable potential of BRHAT VATACINTAMANI RASA as a CNS depressant, was explored by this particular experiment. A group of mice, when put in a cage (60×50×35) with glass walls, their sides darkened and supplied with a ladder made of net, all the animals normally climb up the ladder within 10 minutes. After the administration of a CNS depressant drug, a certain percentage of the mice - depending on the dose administered - do not climb up the ladder (Sandberg, 1957) Mice, in group of 5, were put simultaneously, into the cage and were observed during 10 minute period. The graded doses of drug, under study, were injected intraperitoneally and the number of animals which did not climb out the ladder and/or the total time taken by mice, in groups of 5, to climb out the ladder was recorded 60, 120 and 240 minutes after drug administration. Such readings for control animals, injected 0.9% saline i.p., were also recorded.

e. Effect on isolation induced aggression

Mice were kept isolated in a metallic cage (30×20×13 cm) for a period of 120 hours. This period of isolation induced aggressive tendencies towards violation of isolation. Most of the mice then attacked another mouse placed in the cage (Yen *et al.*, 1958; Janssen *et al.*, 1960). Intraperitoneal administration of graded doses of the drug was made and time taken for first signs of aggressive intent, on part of the mice towards a newly introduced mouse to that cage, was recorded 60, 120 and 240 minutes after drug administration. Similar recordings for control animals, after being administered with 0.9% saline were also made.

f. Effect on pentobarbital sleeping time

Pentobarbital, in a sub-hypnotic dose of 50 mg/kg, was administered, intraperitoneally, 60 minutes after administering graded doses of the drug

(BVC) through the same route. In order to measure the onset and end point of sleeping time, loss and regain of righting reflex was noted (Tedeschi *et al.*, 1968). Similar recordings were also made for control animals.

g. Effect on forced locomotor activity

Mice were so trained, that they walk on a rotating rod, having a diameter of 3 cm, for a period of 120 seconds. Graded doses of the drug, BRHAT VATACINTAMANI RASA, were administered intraperitoneally, in groups of 5 animals each and the number of animals falling from the rotating rod and/or their performance in negotiating the rotating rod is noted for 120 seconds (Dunham *et al.*, 1957). Similar recordings for 0.9% saline treated controls were made concurrently.

h. Test for narcotic analgesic activity

The method developed by Woolfe and MacDonald was employed in this experiment (Woolfe and MacDonald, 1944). The main instrument is a hot plate, which was maintained at constant temperature of 55+0.5°C. Over the hot plate, is a hollow glass cylinder, 15 cm in diameter, into which the mouse is dropped, so that it is forced to stand or walk on the heated metal plate. The first signs of discomfort shown by a mouse on the hot plate are, that it sits on its hind legs and licks or blows its front paws to cool them. With the passage of a few seconds, the pain is too great to be borne. Similar recordings for control animals alter being administered with 0.9% saline i.p were also made.

Clinical study Subjects

Twenty-two subjects, eighteen male and four female, were selected for a single blind clinical study with the drug BRHAT VATACINTAMANI RASA. The essential criteria of selecting the subjects were

- a. They were healthy and free from both physical and neurological diseases
- b. They were not taking any other medicines concurrently.

In this single blind study, the subjects themselves

randomly picked up a number, which was assigned as his/her serial number. Subjects bearing odd serial numbers comprised the treated group and the subjects having the even serial number made up the control group. Special serial numbers were provided to the females, so as to make sure that they are equally represented in the treated as well in the control group.

Four different experiments were carried out with the subjects. The effects of BVC on body temperature, on concentration, on normal blood pressures and on blood pressure after exercise, were explored in this particular clinical study.

a. Effect on the body temperature

Oral temperature, of the subjects, was recorded with an ordinary clinical thermometer, one hour before and one hour after administration of the drug, BVC, to the treated and placebo to the control group.

b. Effect on concentration

Every subject was provided with a list of 7500 digits, presented in random order. The subjects were asked to cancel all the "59" s from the provided list within 30 minutes. One hour after the administration of the drug, to the treated group and placebo, to the control group, the subjects were again asked to cancel all the "67" s, from the provided list, within a period of 30 minutes. Recordings were made for the total number of the digits cancelled, the percentage of the cancelled digits - calculated on the basis of the digits cancelled and the total number of the cancelable digits - and the errors committed (Ghosh *et al.*, 1966). Similar recordings were also made for the control group.

c. Effect on the normal blood pressure

Normal (resting) blood pressure, of the subjects, was recorded with an ordinary sphygmomanometer and a stethoscope, one hour before and one hour after the administration of drug, to the treated group and placebo, to the control group.

d. Effect on the blood pressure after exercise

The subjects were made to run up and down three stairs, three times each. Afterwards, blood pressure,

of the subjects, was recorded. Such recordings were made one hour prior to and one hour after the administration of the drug, to the treated group, and placebo, to the control group.

RESULTS

a. Effect on spontaneous motor activity

The results obtained in this experiment show a dose-dependant quietening or sedating effect. The data is presented in Table 1.

b. Effect on amphetamine induced hyper activity

The experimental results indicate a dose dependant antagoinism of the amphetanime induced hyperactivity in animals. The data is presented in the Table 1.

c. Effect in rectal temperature

In high dose, 1000 mg/kg, BRHAT VATACINTAMANI RASA showed a state of hypothermia and this was also evident, in a lesser extent, in smaller doses. The data is presented in Table 2.

d. Climbing out test in mice

Mice, receiving 250 mg/kg of BRHAT VATACINTAMANI RASA, showed marked increase in climbing out time. This was also evident in mice, which received 500 mg/kg of BVC, in a lesser extent. The data is presented in Table 3.

e. Effect on isolation induced aggression

The drug showed substantial taming effect and the data is presented in 3.

f. Effect on pentobarbital sleeping time

BRHAT VATACINTAMANI RASA, in high doses, potentiated the actions of pentobarbital but, in smaller doses, similar effects were not substantiated. The data is presented in Table 4.

g. Effect on forced locomotor activity

It was observed that the drug, BRHAT VATACINTMANI RASA, increased efficiency in mice, to negotiate the rotating rod. The data is presented in Table 5.

h. Test for narcotic analgesic activity

Apart from the high doses, the drug BVC did not seem to have any narcotic analgesic activity. The

data is presented in Table 6.

RESULTS OF CLINICAL STUDY

a. Effect on the body temperature

This experiment yielded no significant indication of the effect of the drug, BRHAT VATACINTAMANI RASA, on the body temperature. The experimental data is presented in the Table 7.

b. Effect on the concentration

No significant effect of the drug BRHAT VATACINTAMANI RASA was observed on the concentration of the subjects. In Table 8, experimental data is presented.

c. Effect on the normal blood pressure

In this experiment, no significant effect of the drug, Bye, on the normal (resting) blood pressure, was obtained. The experimental data is presented in the Table 9.

d. Effects on the blood pressure after exercise

It was (Table 9) seen that the drug, BRHAT VATACINTAMANI RASA, did not have a significant effect on the blood pressure, of the subjects, after exercise.

DISCUSSION

The drug under study, BRHAT VATACINTAMANI RASA, has a probable site of action in the Central Nervous System (CNS) -deducted from the presence of the word VATA in the very name of the drug. It is also probable that the drug can alter the activating and/or dynamic functions of the body. In order to explore the presence of such activity of the drug, its effects on the spontaneous motor activity of the animals, was tested.

The results obtained presented in Table 1 most emphatically indicate that the drug does alter the activating and/or dynamic functions of the animals. Another striking feature of this experiment was that, a dose dependant sedating or quietening effect of the drug was evident. Animals receiving higher doses of the drug (500 mg/kg i.p.) did become more sedate and did displace a lot fewer brick chips.

Amphetamine, one of the main members of the phenyl ethylamine sympathomimetics, by virtue of its ability to release catecholamine from their intraneuronal storage sites, can induce a state of hyperactivity, marked by greatly increased locomotion (Bowman and Rand, 1980a) As the drug under study, BRHAT VATACINTAMANI RASA, had already proven to possess sedating effects, the next test performed was aimed at exploring its ability to counter the stimulating effects of a stimulant (amphetamine). The results obtained (Table 1) show that, the animals belonging to the treated groups were much more sedate than those of the control groups. In fact, the animals of the control group were so much stimulated that two of them started fighting - which ended in the death of one animal. Here too, like the previous experiment, a dose-dependant quietening action was evident.

The classic CNS depressants and/or tranquillizers have got the ability to produce a state of hypothermia. The viability of the drug BRHAT VATACINTAMANI RASA, in producing a state of hypothermia, was experimented in the rectal temperature test. The results presented in Table 2, does indicate that the drug, BRHAT VATACINTAMANI RASA, in small dose, does not produce discernible hypothermia. However in large doses (1000 mg/kg i.p.), did produce a fall in body temperatures of the animals.

The probable potential of BRHAT VATACINTAMANI RASA, as a Central Nervous System depressant,

was further explored by the climbing out test. The results, as presented by Table 3 indicate that, while, in case of the group receiving 250 mg/kg of BRHAT VATACINTAMANI RASA, a sedating effect or lack of interest in climbing out was noted 30 minutes after acute administration of BRHAT VATACINTAMANI RASA in fact only 60% of them climbed out, the same effect was not clearly witnessed in the group which received 500 mg/kg of BRHAT VATACLNTAMANI RASA. Although the effects of the drug did start to diminish, with the passage of time, the group, which received 250 mg/kg of BRHAT VATACINTAMANI RASA, did take a lot more time to climb out, than the control animals and did exhibit a state of sedation.

Aggression is a term, which is safer to describe than to define. In context of the experiment on isolation- induced aggression, aggression can be defined as, invasion of one animals territory by another and the expression of territorial assertiveness by the animal, whose territory is being invaded (Kalat). This experiment was performed to investigate the possible taming effects of BRHAT VATACINTAMANI RASA. The results, as presented in the Table 3, show that the drug, BRHAT VATACINTAMANI RASA, does possess a taming effect and it can also be safely concluded that the effect is dose-dependant. The most interesting feature of their experiment is that, while animals in the control group and in the treated groups, before

Table 1. Tabular representation of locomotion test

C	Weight of displaced brick chip (in grms.)		
Groups	Spontaneous Mean±S.E.	Amphetamine induced Mean±	
Control	10.04±6.58	6.04±1.35	
BVC 250 mg/kg	4.20±2.26	1.29±0.26	
BVC 500 mg/kg	$1.04 \pm .09$	1.08±0.18	

^{***}indicates p<0.001, **indicates p<0.01, *indicates p<0.05

Table 2. Tabular representation of the effect of rrr on temperature

Name of the	Constants		Time of study	
study	Groups	+60min Mean±S.E.	+120min Mean±S.E.	+240 min Mean±S.E.
	CONTROL	99.52±0.43	100.8±0.08	101.1±0.21
Effect on Normal	250 mg/kg*	99.22±0.17	101.36±0.13	100.16±0.19
Temperature	500 mg/kg*	98.82±0.41	100.36±0.27	100.14±0.26
	1000 mg/kg*	98.76±0.54	98.48±0.49	100.46±0.27

^{***}indicates *p*<0.001, **indicates *p*<0.01, *indicates *p*<0.05

Time of study Name of the Groups +60min +120min +240 min 0 min study Mean±S.E. Mean±S.E. Mean±S.E. Mean±S.E. Control 2.20±0.63 7.0±1.63 4.10±1.25 1.30±0.16 Climbing-out test 250 mg/kg 4.00±0.77 3.13±0.45 10.0±0.99 8.20±1.07 (in min) 500 mg/kg 3.47±0.36 6.45±1.41 5.20±0.25 6.15±1.85 Aggression time (Min) Isolation Induced Control 47±18.63 100±22.01 88±21.25 46±17.31 Aggression test 197±29.37 250 mg/kg 27±11.25 127±18.38 192.20±32.07 500 mg/kg 41.8±7.63 190±11.43 201±10.38 212.4±10.40

Table 3. Tabular presentation of different neuropharmacological study

the administration of the drug, were taking lot more and lot less times to show first expressions of aggression respectively, after the administration of the drug, the aggression time for the control group remained almost identical while it increased manifold, in case of the treated group. Another striking feature of the result is that, while the treated animals were showing a lot more aggressive intent, prior to the administration of the drug, they did not seem to be interested in aggression rather in submission, after the administration of the drug.

Pentobarbital, a member of the barbiturate group of sedative - hypnotic, due to its ability to depress the limbic system and the reticular activating system, can induce sleep (Bowman and Rand, 1980b). The possible potentiating effects of BRHAT VATACINTAMANI RASA to such effects of a sedative-hypnotic was investigated in the experiment on pentobarbital sleeping time. The experimental results, presented in the Table 4, show that BRHAT VATACINTAMANI RASA, in large dose (1000 mg/kg i.p.), does have a potentiating effect on pentobarbital sleeping time. Although, the same

Table 4. Tabular presentation of pentobarbital sleeping time test

	Sleeping Time (Min)		
Groups	Onset Mean±S.E.	Duration Mean±S.E.	
Control	5.00±1.19	34.2±4.50	
250 mg/kg	4.80 ± 1.13	36.8±10.52	
500 mg/kg	5.00±1.36	33.6±12.24	
1000 mg/kg	5.6±3.39	46.2±13.44	

^{***}indicates p < 0.001, **indicates p < 0.01, *indicates p < 0.05

cannot be said about the results obtained with the smaller doses.

The method of the forced locomotor test, as designed by Dunham and Miya (Dunham and Miya, 1957) is aimed at testing possible neurotoxic properties of the drug under study. If the drug, BRHAT VATACINTAMANL RASA, possessed any neurotoxic properties, it will diminish reflexes, both mono and poly synaptic, produce in coordinated motor activity and/or generalized muscular weakness or numbness. (Bowman and Rand, 1980c). By analyzing the results, presented in Table 5, it can be clearly seen that, the group of animal receiving 500 mg/kg of BRHAT VATACINTAMANI RASA, performed most efficiently on the rotating rod. The efficiency in negotiating the rotating rod, by the animal, receiving 1000 mg/kg body weight of BRHAT VATACINTAMANI RASA, also increased. However, the efficiency of the group of animals, which received 250 mg/kg body weight of BRHAT VATACINTAMANI RASA, did not increase noticeably. A dose-dependant increase in efficiency was not clearly established.

A multitude of experience, differing greatly in

Table 5. Tabular presentation of locomotor activity test

	Mean fault committed in rotating rod		
Groups	0 Min	+60 Min	
Control	5.0±1.35	3.4±1.1	
250 mg/kg	4.6 ± 1.9	2.6±1.3	
500 mg/kg	5.6±2.3	$.04 \pm .09$	
1000 mg/kg	3.8±1.48	1.2±.19	

^{***}indicates p<0.001, **indicates p<0.01, *indicates p<0.05

^{***}indicates p<0.001, **indicates p<0.01, *indicates p<0.05

Table 6. Tabular presentation of narcotic analgesic test

C	Time For Pain Perception (Sec)		
Groups	0 Min	+60 Min	
Control	10.4±3.35	13±3.1	
250 mg/kg	14.0 ± 1.12	13.8±4.3	
500 mg/kg	14.4±3.38	16.8±2.11	
1000 mg/kg	10.00±1.21	15.0±.96	

intensity, quality, duration and meaning, are collectively denoted by the word 'pain' (Bowman and Rand, 1980d). Results obtained in the test for narcotic analgesic activity, presented in Table 6, indicate that, in high doses, 1000 mg/kg body weight, the drug increased the time taken for the experience of pain sensation. But narcotic analgesic activity of the drug, BRHAT VATACINTAMANI RASA was not clearly established.

The clinical trial conducted to explore the effects of BRHAT VATACINTAMANI RASA on body temperature, experimental data of which is presented in Table 7 produced no statistically significant effects of the drug on body temperature. The paired 't' test performed with the experimental results yielded a value of 0.8728 for the treated group. This was found to be insignificant at 5% level of significance.

Although concentration is a commonly used

term, it is difficult to define with precision. It can describe as a state of deep thought and/or consciousness. Consciousness, itself can be defined as, the process of experiencing external and internal environment in ways that separate immediate stimuli from immediate responses (Ruch, 1984).

The clinical trial on concentration (Table 8) yielded no significant results. For the treated and the control group, the calculated value of "t", in paired 't' test, was 1.1525 and 0.3862 respectively. This was found to be insignificant at 5% level of significance.

However, only 54.54% of the subjects in the control group, compared to 90.90% subjects in the treated group, could search more number of digits, in order to cancel '67', in the second time (after drug). This points towards a possible indication that the drug, BRHAT VATACINTAMANI RASA, can increase speed of work, if not efficiency.

The clinical trials conducted to probe the effects of the drug on the normal (resting) blood pressure and blood pressure after exercise (Table 9), also yielded insignificant results, as was deducted by calculating the value of "t" by the paired "t" test and by comparing it with the Table value of "t".

The failure of the clinical trial to substantiate any effect of the drug can be attributed to a variety of

Table 7. Tabular presentation of effect of BVC on body temperature

Body temperature (degree fahrenheit)					
Con	trol	BV	/C		
Before Drug	After Drug	Before Drug	After Drug		
99±1.56	98.44±1.35	99±2.03	98.85±1.51		

Table 8. Tabular presentation of effect of BVC on concentration

Percentage of cancelled digits					
Cor	ntrol		BVC		
Before Drug	After Drug	Before Drug	After Drug		
50.05±6.54	51.15±8.54	48.01±4.03	50.40±5.51		

Table 9. Tabular presentation of effect of BVC on blood pressure

	Effect	on Normal Blood pre	ssure	
Blood Pressure	Cor	ntrol	BA	VC
	Before Drug	After Drug	Before Drug	After Drug
Systolic	108.27±5.23	100.54 ± 9.87	108.90±9.58	103.63±10.33
Diastolic	72.09±8.35	70.90 ± 7.43	70.27±8.97	72.27±9.63
	Effect on	Blood pressure After	Exercise	
Systolic	138.18±10.33	138.18±12.39	133.63±11.69	135±11.55
Diastolic	72.27±12.11	7.27±11.32	70.90±9.99	73.18±8.63

reasons. The most important reason is that the numbers of subjects were little another probable reason is that the scheduled programmer of the clinical trial was too exhaustive for the subjects in fact, a number of subjects were visibly exhausted after the clinical trial.

A striking and unexpected result of the clinical trial was that no less than 4 (36.36%) subjects of the treated group confessed of having a feeling of well being and that their headaches had been remedied. 2 subjects (9.09%) belonging to the treated group, complained of having fluidly defecation.

The drug had a dose-dependant quietening action. Yet like classical tranquillizers, it did not possess any potent hypothermic action (hypothermia of a measurable degree was produced only by high doses 1000 mg/kg i.p) and/or any effect on blood pressure. The observed taming effect of the drug indicated a possible increase in serotonin turnover (Kalat, 1984). The drug also did not substantially prove to be an adequate protection against stimulants, working on different sites of the CNS.

In short, BRHAT VATACINTAMANI RASA presents an intriguing and challenging case and demands further study.

REFERENCES

- Anonymous. (1948) Report of the Committee on Indigenous System of Medicine Ministry of Health; Government of India. 11, 347.
- Biological Psychology Kalat, James W, 2nd Edn. p. 311. Bowman WC, Rand MJ(1980a). *Textbook of Pharmacology*, 2nd Edn, pp. 11.38.
- Bowman WC, Rand MJ(1980b). *Textbook of Pharmacology*, 2nd Edn. pp. 8.5.
- Bowman WC, Rand MJ (1980c). *Textbook of Pharmacology*, 2nd Edn. pp. 17.33.

- Bowman WC, Rand MJ (1980d). *Textbook of Pharmacology*, 2nd Edn. pp. 16.1.
- Dasa, Govinda; Bhaisajya ratnavali; revised and edited by Kaviraj Narendranath Mitra, Jayadeva Vidyalankar Haridatta Sastri, Talchandraji Vaidya; Varanasi; Motilal Benarasi Das. Samvat 2019, pp. 502-503.
- Dunham NW, Miya TS. (1957) A Note on the Simple Apparatus for Detecting Neurological Deficit in Rats and Mice; 1. *Amer. Pharm. Assoc. Sci.* **46**, 208-209.
- Ghosh S, Kar SK. (1966) Clinical trial on brahmi Part II; Pharmacological Investigations with Normals . *J. Expt. Med. Sci.* **10**, 12-14.
- Janssen PAJ, genean AH, Niemegeers CIE. (1960) 1. pharmacol. **129**, 471.
- Kalat JW. (1984) *Biological Psychology*, 2nd Edn, pp. 313, Wadsworth Publishing Co.
- Kobayashi T, Tobe A. (1976) Pharmacological Studies on Triazine Derivatives V. *Japan J. pharmacol.* **26**, 559-570.
- Ruch JC. (1984) *Psychology: The Personal Science*, pp. 212, Wadsworth Publishing Co.
- Sandberg F. (1957) A Comparative Quantitative Study of the Central Depressant Effects of Seven Clinically Used Phenothiazine Derivatives. ArzneimiHel forschung 9, 203-206.
- Siegmund PN, Wolf M. (1952) Displacement of Sand Method for the Determination of Locomotor Activity. *Arch. Exp. Pathol. Pharmacol.* **216**, 232-235.
- Tedeschi DW, Tedeschi RE. (1968) *Importance of Fundamental Priciples in Drug Evaluation*, pp. 307–324, Raven Press, New York.
- Vane JR. (1961) Tryptamine Receptors in the Central Nervous System. *Nature* **191**, 1068-1069.
- Woolfe G, MacDonald AD. (1944) J. Phannacol. Exper. Therp. 80, 300.
- Yen HCY, Stanger R, Millman N. (1958) 1. *Pharmacol.* **122**, 85A.