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Impact of *Brahmi Ghrita* on Cognition in Damaged Liver

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Abstract

Brahmi Ghrita consists of a high percentage of *Ghrita* and mentioned for the treatment of *Unmada* and *Apasmara*. Hence, it is necessary to evaluate its effect on liver. *Brahmi Ghrita* was prepared by using *Bacopa monnieri, Acorus calamus, Convolvulus pluricaulis, Sassurea lappa* as per standard procedure of *Sneha kalpana.* The effect of this *Ghrita* was assessed on serum glutamic oxaloacetic transaminase, Serum Glutamic Pyruvate Transaminase and alkaline phosphate activity along with its cognitive function (assessed on elevated maze plus and passive avoidance) in the dose of 400 and 800 mg/kg body weight on animals. Cognitive functions (learning and memory) of the treated animals increased, where as serum glutamic oxaloacetic transaminase, serum glutamic pyruvate transaminase and alkaline phosphate decreased. *Brahmi Ghrita* increases cognitive function and decreases the serum glutamic oxaloacetic transaminase, serum glutamic pyruvate transaminase and alkaline phosphate level in animals.

Key-Words: *Brahmi Ghrita*, Cognitive function, Transaminase

Introduction

Self awareness along with the accompanying capacity for reflection and acquisition and processing of knowledge is called mind. It is well known that the mind can cause certain physical symptoms but the exact mechanism in which the mind can cause certain other symptoms is not clear. In general, the conviction is that psychological factors are important in the development of many diseases. Relationship between the brain and the liver has been known for many years [1] and patients with chronic liver disease frequently experience neurological problems. Patients typically present early with liver disease or later with the neurological syndrome [2] which consists of various subtle neuropsychiatric symptoms such as a change in behaviour or performance at school [3] and abnormality of movement [4,5]. There are many other conditions in which the brain and liver are damaged by the same or similar mechanisms. In *Ayurvedic* classics there are three main etiological factors for origin and progression of all disorders i.e. [overuse, disuse or misuse of faculties, factors relating to the intellect and factors related to time] among them factors relating to the intellect is most common cause of psychosomatic disorders.

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It may be defined as improper functional disturbances between body and mind may occur due to disturbance of learning and comprehension, retention of knowledge and power of recollection [6]. It increases all blemishes which are involved in the development of disorders that may be psychological, somatic and psychosomatic in nature. In another reference present in *Ayurvedic* classics, it is claimed that psychological as well as somatic disorders affect each other. Due to disturbance of power & acquisition of memory, power of retention and power of recollection of memorized things, a person is not able to avoid diseases. *Ayurveda* claims that several plants have *Medhya* (intellect promoting) properties such as *Convolvulus pluricaulis, Centella asiatica, Bacopa monnieri, Acorus calamus*, *Zingiber officinale* and *Celastrus paniculatus* [7]. Besides this, these are also indicated for treatment of various somatic disorders. These herbs are indicated for improving Intellectual power and also for treating somatic disorders. So, present study was planned to examine the classical claim for scientific validation.

Material and Methods

Pharmaceutical study

Brahmi Ghrita was prepared by using *Bacopa monnieri, Acorus calamus, Convolvulus pluricaulis, Sassurea lappa* and Old Clarified butter [8] these herbs

were collected from local market of Varanasi and authenticated by department of *Dravyaguna*, Institute of Medical Sciences, Banaras Hindu University. During processing of drug, *kalka* (paste) was prepared by *Bacopa monnieri, Acorus calamus, Convolvulus pluricaulis, Sassurea lappa* all together mixed with *Ghrita & svarasa (juice)* of *Bacopa monnieri* and heated intermittently on and off (2 hours in 1st ,6 hours in 2nd and 1½ hours in third day) for three days. Thus the *Brahmi Ghrita* was prepared for further study [9] in the dose of 400 and 800 mg/kg body weight to animals

Study design

Animals

Eighteen Charles Foster rats of either sex weighing between 160-180 gm used for experimental study. The animals were obtained from the Central Animal House, Institute of Medical Sciences, Banaras Hindu University, Varanasi. The animals were housed in polypropylene cages at an ambient temperature of 25ºC±1ºC and 45-55% relative humidity, with a 12:12 h light/dark cycle. Animals were provided with commercial food pellets and water *ad libitum* unless stated otherwise. They were acclimatized to laboratory conditions for at least one week before using them for the experiments. Principles of laboratory animal care (NIH publication number # 85-23, revised in 1985) guidelines were always followed and prior approval of Institutional Animal Ethical Committee (No. Dean/10-11/150) of Banaras Hindu University was obtained before commencing the study.

These animals were divided in to three groups, six animals in each group namely control and two groups of *Brahmi Ghrita* treated in dose of 400 and 800 mg/kg body weight of animals. Only food and water was given to control group animals, no drug was given.

Cognitive Function

Transfer latency on elevated plus maze: This test was used to assess the retention of learning and memory [10]. It consisted of two opposite open arms crossing each other, of the same dimensions with walls. The arms were connected with a central square to give the apparatus a plus sign appearance. The maze was kept in a dimly lit room elevated 50 cm above floor level. On day 1, a rat was placed on the far end of one of the open arms, facing away from the centre, and the time taken by the animal to enter one of the closed arms (transfer latency on day 1) was recorded with the help of a stop watch and rat was placed in home case. On day 2 and Day 9 same procedure was repeated, in this way transfer latency was again recorded.

Passive avoidance test: This test uses normal behaviour of rats [11].The step through passive avoidance behaviour was evaluated by using the light-dark apparatus, which had two walls of wood and the remaining two walls of transparent plexiglass. It is divided into two equal compartments (30x25x30 cm) by a Plexiglas with a 10x10 cm. opening in the centre. A guillotine door between the two compartments controlled the opening. The light compartment was painted white and a 15 W lamp illuminated it. The interior of the dark chamber was painted black and had a ceiling. Each compartment had a copper grid floor. To ensure electrical separation, there was a 1.5-cm gap between the two floors in the light-dark box at the opening between the two chambers, and behaviour was evaluated by using the light-dark apparatus, which had two walls of wood and the remaining two walls of transparent plexiglass.

On day 1, a rat was placed in the white box and time taken by it to enter into the dark box was noted. As soon as the rat entered the dark box, the guillotine door was closed and an electric shock (0.5 mA, 3 sec) was delivered to it. The rat was then placed to its home cage. On the following day (24 h retention interval) each rat was again placed in the white box and was given a 5-min inhibition period. Latency to step through to the dark chamber was recorded. Electric shock was not delivered on day 2. If the animal remained in the white box for a 5-min test period, the maximum score of 300 sec. was assigned. On day 9 (after a gap of one week), latency to step through was again recorded to test the retention of the passive avoidance learning.

Biochemical study

Blood of rats was collected through retro-orbital technique for haematological and biochemical investigations. Haematological analysis was performed by Sysmex XE-2100 haematology auto analyser (Sysmex-Corporation, Kobe, Japan) using fluorescent dye and hydrodynamic focusing method. For serum biochemical analysis ERBA CHEM-7 auto analyser (ERBA diagnostics, Manheim, GmbH, Germany) was used. AST, ALT, alkaline phosphatase and creatinine were analysed using kinetic method whereas glucose, cholesterol, albumin, total protein and blood urea nitrogen were analysed by end point method. [12].

Results and Discussion

In cognitive study, it was observed that rats treated with both dose (400 and 800 mg/kg body weight) of *Brahmi Ghrita* showed increased cognitive function in comparison to control group rats as well as Day 1 in all experimental protocol. (Details are summarized in table 1 & 2).

Biochemical study revealed that SGOT, SGPT and Alkaline phosphate were significantly decreased in drug treated animals in dose dependent manner which was higher in control groups animals (Details are summarized in table 3).

Chronic liver disease and acute liver failure may result in cognitive impairment including memory, attention and psychomotor function [13]. Cognitive dysfunction in liver disease can range from subtle changes in attention and concentration, inability to perform day to day task [14] as well as disruption to sleep-wake cycle [15] and poorer quality of life [16] gross impairment leading to death. AST (previously known as SGOT, serum glutamic oxaloacetic transaminase) and ALT (also known as SGPT, serum glutamic pyruvic transaminase) are hepatocellular enzymes involved in amino acid metabolism. These enzymes are sensitive indicators of liver cell injury [17]. ALT is found in cytosol whereas AST activity is highest in the mitochondria. The AST and ALT levels are increased to some extent in almost all liver disease but moderately elevated in acute hepatitis, neonatal hepatitis, chronic hepatitis, autoimmune hepatitis, drug induced hepatitis. It was observed that *Brahmi Ghrita* (400 and 800 mg/kg body weight) treated rats showed significantly decreased values of AST, ALT and alkaline phosphate as compared to control group. In *Brahmi Ghrita* formulation *Brahmi* have maximum percentage, so that properties of formulation are mainly dependent on pharmacological property of *Brahmi* and it is reported for its hepatoprotective action [18] beside this aquous, methanolic extract *Saussurea lappa* was reported for anti hepatotoxic activity [19], ethanolic extract of *Acorus calamus* also Anti hepatotoxic activity[20] This shows that hepato protective activity of *Brahmi Ghrita* formulation is may be synergetic action of *Bacopa monnieri, Acorus calamus and Saussurea lappa*. Transfer latency on modified elevated plus maze might be shortened if animal has previous experience of entering the open arm and shortened transfer latency could be related to memory. In our study, it was observed that BG (400,800 mg/kg body weight) treated rats showed significantly reduced transfer latency as compare to control group animals. It may be due to increase in learning and memory because shortening of transfer latency is related to increased memory. In passive avoidance test, BG (400, 800 mg/kg body weight) treated rats showed significantly increased step through latency as compare to control group rats, an increase of step through latency is defined as learning [21]. This indicates that *Brahmi Ghrita* in both doses increases learning in experimental animals. It our study, it was observed that *Brahmi Ghrita* increases cognitive function as well as decreases biochemical parameters like AST, ALT and alkaline phosphate. Thus it *Brahmi Ghrita* is might be helpful in liver disorders as well as cognition level of animals.

Conclusion

Brahmi Ghrita enhances the cognitive function in animals besides this it lowers serum level of the SGOT, SGPT and alkaline phosphate. Thus our finding suggest the use of *Brahmi Ghrita* is helpful is psychosomatic disorders without affecting liver function.

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Table 1: Effect of *Brahmi ghrita* on transfer latency in elevated plus maze test

Treatment	Dose (mg/kg)	Transfer latency (sec)		
		Day 1	Day 2	Day 9
Control		40.50 ± 6.38	37.00 ± 3.29	**36.67 ± 5.32**
BG	400	36.17±6.77	24.50 ± 3.15$^{***,\#\#}$	**26.50 ± 5.68** $^{*,\#\#}$
BG	**800**	**40.33±9.35**	**21.33 ± 3.50**$^{***,\#\#\#}$	**23.33 ± 5.43** $^{**,\#\#}$

BG- *Brahmi ghrita*, n= Six animals in each group, Values are Mean ± SD, *p< 0.05, **p<0.01, ***p<0.001 compared to control, #p<0.05, ##p<0.01, ###p<0.001 compared to day1

Table 2: Effect of *Brahmi ghrita* on step through latency in passive avoidance test

Treatment	Dose (mg/kg)	Step through latency (sec)		
		Day 1	Day 2	Day 9
Control		26.83 ± 5.53	29.67 ± 3.88	**30.67 ± 5.05**
BG	400	28.5 ± 6.53	45.17± 8.18$^{**,\#\#\#}$	**64.67± 3.56**$^{***,\#\#\#}$
BG	**800**	**32.17 ± 6.40**	**52.83± 4.54**$^{***,\#\#\#}$	**65.00± 7.32**$^{***,\#\#\#}$

BG- *Brahmi ghrita*, n= Six animals in each group, Values are Mean ± SD, *p<0.05, **p<0.01, ***p<0.001 compared to control, #p<0.05, ##p<0.01, ### p< 0.001 compared to day1

Table 3: Effect of *Brahmi ghrita* on biochemical changes regarding enzymes of liver

Group	Dose	SGOT (U/ml)	SGPT (U/ml)	A. Phosphate(U/ml)
Control	-	123.67±3.33	131.00±1.79	378.72±7.81
BG	400	87.33±3.61**	76.00±7.77***	311.52±2.52***
BG	800	44.17±2.32***,##	52.5±2.51***,##	83.27±4.03***,###

BG- *Brahmi ghrita*, n= Six animals in each group, SGOT: serum glutamic-oxaloacetic transaminase, SGPT: Serum Glutamic Pyruvate Transaminase, A. Phosphate: Alkaline phosphate, U/ml: Unit per mililiter, Values are Mean ± SD, ***p<0.001 compared to control, ##p<0.01, ###p<0.001 compared to BG 400 group.

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