

RANDOMIZED CONTROL, DOUBLE BLIND CROSS-OVER STUDY TO CLINICALLY ASSESS THE RASAYANA EFFECT OF A STANDARDIZED EXTRACT OF BRAHMI (*BACOPA MONNIERA*) IN ADULT HUMAN VOLUNTEERS

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ABSTRACT

Bacopa monniera, a medhya-rasayna (memory augmenting and rejuvenating) plant of Ayurveda is well known for its neuro-pharmacological effects. The present study was a randomized control double blind, cross over design, in which participants were randomly allocated one of the two treatment conditions: bacosides enriched standardized extract of *Bacopa monniera* (BESEB-CDRI-08) ($n=41$) or an identical capsule placebo ($n=13$). After six month the volunteer were switched to alternate treatment (cross over). The effect on hemoglobin was determined by Sahli's method, glucose estimation was done by semi auto analyzer, oxygen carrying capacity and pulse by pulse oxy-meter, hand grip by muscle strength tester and anxiety, well being, improvement in sleep abnormality and walking effect were evaluated by visual analog scale. BESEB -CDRI-08 significantly improved the treatment and period effect in hemoglobin, oxygen carrying capacity, well being, walking, and hand grip. Treatment effect was significantly improved in anxiety, sleep abnormality and decrees in glucose level and period effect was significant in pulse. The findings suggest that BESEB-CDRI-08 significantly improves the rejuvenating effect by improving the above rejuvenating factor and thus confirms the rasayana effect.

Keywords: *Bacopa monniera*, Double blind, Cross over, Rejuvenating effect, BESEBCDRI-08

INTRODUCTION

World Health Organization has stated that stress has become a "world wide epidemic." Stress, anxiety, worry, aggression have all increased significantly in recent years. Individuals throughout the world are exposed physically and mentally to constant stress, tension, and anxiety. Job-related stress is fast becoming the most prevalent reason for worker disability.

Natural products including plants, animals and minerals have been the basis of treatment of human disease. According to World Health Organization, more than 70% of the world population must use traditional medicine to satisfy their primary health needs ¹.

The emphasis on maintaining good health or *Swasthya* is crucial to Ayurveda. Ayurveda, the ancient Indian system of medicines, which dates back to about 2500 BC, has presented a total holistic approach for up-liftment of body, mind as well as spirit. Whatever is possible through the control of mind and *prana*, can be acquired through *Rasayana*. The *Rasayana* therapy (Rejuvenating therapy) aims specially at the promotion of strength and vitality. The other benefits of *Rasayana* therapy are promotion of memory and intelligence, immunity against diseases and decay, preservation of youthfulness, luster, complexion and voice, which means to improve the rejuvenating effect².

There are a number of *Rasayana* drugs among which important ones are Amalaki, Bhallataka, Nagabala, Pippali, Aswagandha, Shilajita and Svarnabhasma. Brahmi, Shankhapushpi, Guduchi and Yastimadhu are particularly intellect promoting (Medhya) *Rasayana* though they also promote physical strength. A series of clinical and experimental studies have already been conducted to assess the *Rasayana* effect of many single drugs and compound preparations.

Brahmi (*Bacopa monniera*) (Scrophulariaceae) is a perennial creeping annual plant found throughout the Indian subcontinent in wet, damp and marshy areas ^{3, 4}. Triterpenoid saponins and bacosides present in Brahmi are considered to be responsible for enhancing cognitive function ⁵. Brahmi have also potent adaptogenic activity in stress model in rats ⁶. A bacoside enriched standardized extract of *Bacopa monniera* has now been made available for clinical use by the Central Drug Institute Lucknow, India ⁷.

Bacopa has the property to improve the mental health, Antioxidant, ⁸ Antistress, ⁹ antidepressant, ¹⁰ anti-anxiety effects ¹¹. Therefore the present study has been taken to investigate the effect of Brahmi in healthy human volunteers for assessing the rejuvenating effect.

MATERIAL AND METHOD

A randomized, control, double blind, and cross-over study was designed and carried out in the pharmacology laboratory of College of Pharmacy, IFTM, Moradabad, in 2008-09. The study follows the ICMR guidelines. The clearance from Institutional Ethics Committee was taken from the college of pharmacy. 54 volunteers of different age groups were selected for study and were divided into two groups. Volunteers were of 20 to 75 years of age group from both genders, who were healthy and were not suffering from any critical illness/disease.

Subjects who were suffering from Cancer, AIDS, kidney related disorder and liver dysfunction, and undergoing treatment for any other serious chronic illness, and undergone major hospitalization or any surgery during past 3 years were not included in the study.

For minimizing error of the large data, the volunteers were distributed in randomized, double blind, cross over design, in which participants were randomly allocated one of the two treatment conditions: BESEB-CDRI-08 group ($n=41$) or placebo group ($n=13$). After six month the volunteer were switched to alternate treatment (cross over). The volunteers received 1 capsule each, either of BESEB-CDRI-08 (300mg) or placebo containing lactose for 180 days. The BESEB-CDRI-08 capsule were obtained from the Lumen Research Foundation, Chennai, the sole license of CDRI patented process of bacopa extract. Both kind of capsule were identical in shape, size and color. Fixed numbers of capsules were given to the volunteers into a dark colored coded container. In addition to the trial regime (one bottle for 4 weeks), additional capsules ranging in number from 1-10 (randomly allocated) were also placed in the bottles so that compliance could be accurately examined. After the completion of 4 weeks, participants were asked to bring their bottles and the remaining capsules were counted. Participants were excluded if greater than 10% of the total number of capsules required were not consumed by the end of the 4 weeks. At each study visit including the initial visit all volunteers went for same determination. A clinical assessment of each eligible volunteer was

carried out at a base line (0 month) and scheduled monthly clinical visits up to 12 months.

The effect on hemoglobin was determined by Sahli's method, glucose estimation was done by semi auto analyzer, oxygen carrying capacity and pulse by pulse oxy-meter, hand grip by muscle strength

tester and anxiety, well being, improvement in sleep abnormality and walking effect were evaluated by visual analog scale.¹²

Statistical analysis: Statistical analysis was done by using cross-over analysis of variance on area under the curve of data obtained. The significance level was observed at (p<0.05) and (p<0.001)

RESULTS

Table 1: Effect of BESEB-CDRI-08 on Hemoglobin in healthy human Volunteers

	Degree of Freedom	SS	MS	F	p
Treatment Effect	1	12.02	12.02	16.94	0.001*
Period Effect	1	20.22	20.22	28.5	0.001*
Individual Effect	53	1311.08	24.74		
Error	52	36.89	0.71		
Total	107	1369.96			

SS=sum of squares, MS= mean sum of squares, F= variance ratio, p= significance.*=significant

Table 2: Effect of BESEB-CDRI-08 on oxygen carrying capacity in healthy human volunteers

	Degree of Freedom	SS	MS	F	p
Treatment Effect	1	16.81	16.81	7.35	0.009*
Period Effect	1	119.28	119.28	52.16	0.001*
Individual Effect	53	1144.68	21.6	9.44	
Error	52	118.91	2.29		
Total	107	1386.21			

SS=sum of squares, MS= mean sum of squares, F= variance ratio, p= significance.*=significant

Table 3: Effect of BESEB-CDRI-08 on Pulse in healthy human volunteers

	Degree of Freedom	SS	MS	F	p
Treatment Effect	1	133.15	133.15	1.8	0.186
Period Effect	1	2027.2	2027.2	27.36	0.001*
Individual Effect	53	175780.2	3316.61		
Error	52	3853	74.1		
Total	107	181851.1			

SS=sum of squares, MS= mean sum of squares, F= variance ratio, p= significance.*=significant

Table 4: Effect of BESEB-CDRI-08 on well being in healthy human volunteers

	Degree of freedom	SS	MS	F	p
Treatment Effect	1	411.08	411.08	21.8	0.001*
Period Effect	1	660.15	660.15	35.01	0.001*
Individual Effect	53	3635.87	68.6		
Error	52	980.61	18.86		
Total	107	5342.75			

SS=sum of squares, MS= mean sum of squares, F= variance ratio, p= significance.*=significant

Table 5: Effect of BESEB-CDRI-08 on Effect on Walking in healthy human volunteers

	Degree of Freedom	SS	MS	F	p
Treatment Effect	1	2965.75	2965.75	129.72	0.003*
Period Effect	1	2977.56	2977.56	130.24	0.006*
Individual Effect	53	13207.69	249.2		
Error	52	1188.85	22.86		
Total	107	18310.44			

SS=sum of squares, MS= mean sum of squares, F= variance ratio, p= significance.*=significant

Table 6: Effect of BESEB-CDRI-08 on Anxiety in healthy human volunteer

	Degree of Freedom	SS	MS	F	p
Treatment Effect	1	0.01	0.01	0	0.01*
Period Effect	1	19.5	19.5	0.87	0.356
Individual Effect	53	12239.79	230.94		
Error	52	1167.62	22.45		
Total	107	13433.91			

SS=sum of squares, MS= mean sum of squares, F= variance ratio, p= significance.*=significant

Table 7: Effect of BESEB-CDRI-08 on Left Hand Grip in healthy human volunteers

	Degree of Freedom	SS	MS	F	p
Treatment Effect	1	2143.87	2143.87	7.22	0.01*
Period Effect	1	7012.86	7012.86	23.63	0.045*
Individual Effect	53	1407193	26550.81		
Error	52	15431.29	296.76		
Total	107	1429649			

SS=sum of squares , MS= mean sum of squares , F= variance ratio , p= significance.*=significant

Table 8: Effect of BESEB-CDRI-08 on Right Hand Grip in healthy human volunteers

	Degree of Freedom	SS	MS	F	p
Treatment Effect	1	8224.45	8224.45	15.93	0.05*
Period Effect	1	8875.66	8875.66	17.19	0.05*
Individual Effect	53	1804494	34047.06		
Error	52	26843.03	516.21		
Total	107	1842607			

SS=sum of squares , MS= mean sum of squares , F= variance ratio , p= significance.*=significant

Table 9: Effect of BESEB-CDRI-08 on Sleep Abnormality in healthy human volunteers

	Degree of Freedom	SS	MS	F	p
Treatment Effect	1	57.16	57.16	1.14	0.04*
Period Effect	1	130.14	130.14	2.61	0.112
Individual Effect	53	10768.88	203.19		
Error	52	2596.41	49.93		
Total	107	13499.13			

SS=sum of squares , MS= mean sum of squares , F= variance ratio , p= significance.*=significant

Table10: Effect of BESEB-CDRI-08 on Serum Glucose in healthy human volunteers

	Degree of Freedom	SS	MS	F	p
Treatment Effect	1	9213.3	9213.3	10.01	0.003*
Period Effect	1	0	0	0	1
Individual Effect	53	1044078	19699.58		
Error	52	47885.19	920.87		
Total	107	1104553			

SS=sum of squares , MS= mean sum of squares , F= variance ratio , p= significance.*=significant

BESEB -CDRI-08 significantly improved the treatment and period effect in hemoglobin, oxygen carrying capacity, well being, walking, and hand grip. Treatment effect was significantly improved in anxiety, sleep abnormality and decreases in glucose, and period effect was significant in pulse.

DISCUSSION

BESEB-CDRI-08 had already undergone successful evaluation during regulatory and toxicological studies. The present study is a randomized control double blind cross-over study to evaluate the rasayna effect. In Ayurveda the rasayna therapy aims at the promotion of strength and vitality. The basic principal of rasayna is an accelerated and appropriated nutrition leading to improved biological functioning of the human body. In accordance with the definition of health in Ayurveda, mental health is defined as a state of sensorial, mental, intellectual and spiritual harmony. Once this harmony is established physical health will be naturally achieved. In present study we have established these traditional claims.

BESEB-CDRI-08 showed increase in Hemoglobin concentration, better oxygen supply which resulted in improved biochemical functions. Hemoglobin is also responsible for maintenance of pH and maintenance of ionic balance in the body. It is further supported by increase in oxygen carrying capacity measured by pulse-oxymeter.

Muscles ache and sleep abnormality due to over work or stress is a common problem now days, which was reduced. Volunteers were able to sleep with more deep sleep and because of this; they awake

with freshness and sunshine face and were able to work more in day time.

Physical strength of the patient was increased which is evident from the fact that hand grip strength increased, and this finding is further substantiated by the effect on walking. The volunteers were able to walk briskly for greater distance.

Beside this the volunteers felt more energetic, due to this their work efficiency as increased. The volunteers also felt reduction in fatigue and in aggressiveness, with increase in level of concentration.

The level of glucose in human is a major factor responsible for many complications. BESEB-CDRI-08 has the potential to normalize the stress induced elevation in plasma glucose in animal¹³. Similar kind of effect was recorded in human volunteers also. This can be further be justified by decrease in elevated pulse rate and anxiety level. Thus *Brahmi* has the ability to reduce the stress born abnormalities.

All the individuals observed improvement in life style which was also observed by the researcher. These effects were observed in young, middle and older age of volunteers, thus it has the effect on this age group of volunteers. This could help them improvement in personality, in social activities and in relationship. Thus, in the present study the rasayna effect of *Brahmi* was established.

The findings suggest that *Bacopa monniera* significantly improves the rejuvenating effect by improving the above factor and thus confirms the rasayana effect.

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