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ESTABLISH STANDARD PARAMETERS AND CLINICAL EVALUATION OF AYURVEDIC FORMULATION *BRAHMYADI GHRITA* IN DEPRESSION

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ABSTRACT

In present era, there is increase in number of people suffering from mental disorders like schizophrenia, anxiety, psychosis, mania and depression. Depression is a state of low mood and aversion to activity that can affect a person's thoughts, behaviour, feeling and sense of well-being. It can affect a person's ability to work, form relationship, and destroy their quality of life. *Brahmi* is a proven plant used in grouping with other herbs to increase its potency on CNS. Apart from repeatedly used formulation of *Brahmi Ghrita*, a special one titled *Brahmyadi Ghrita (BG)* comprising of *Brahmi, Siddharthak, Vacha, Sariva, Kushtha, Pippali* and *Saindhav lavan*; processed in Cow Ghee is mentioned in *Ashtang hridaya* especially for various CNS conditions. Thus, the present study was undertaken to prepare & standardized the drug *(BG)* and investigates the antidepressant effects using Hamilton Depression Rating Scale test in patient of mild to moderate depression of age group of 25-50 years. Patients were selected non-randomly in two groups. BG of study group was administered after *Koshthashudhi* of 5 days in dose of 10 gms twice a day with Luke warm water on empty stomach to the patient of depression. Scores were recorded on 0, 30th and 61th day and analyzed statistically by using Friedman test within group and Mann Whitney test between two groups for result. In this study it showed that Antidepressant effect significantly ($p < 0.005$) i.e. p is 0.0043 increased in patients after 60 days of BG with conventional treatment of study group compared to standard control group who taking only conventional therapy.

Keywords: *Brahmyadi Ghrita*, Antidepressant activity, Hamilton Depression Rating Scale.

INTRODUCTION

Depression is commonest disorder in mental disorders. Depression is a state of low mood and aversion to activity that can affect a person's thoughts, behaviour, feeling and sense of well-being [1]. Global depression statistics mentioned that depression affects 121 million people worldwide [2]. It can affect a person's ability to work, form relationship, and destroy their quality of life. According to WHO, depression is expected to become the second leading cause of disease related disability by the year 2020, following heart disease [3].

Ayurveda states that the mental state of a patient must be balanced and in equilibrium. The reason behind the depressive disorders in *Ayurveda* is *pragyaapradha* (the unhealthy adaptation of physical and mental type leading into the mental imbalance). The improper diet and life style that leads the disturbed state of

mind causes the negative feelings that overwhelm the mind. In *Ayurveda Vishada* and *Avasada* are the two conditions predictable as depression. Premonitory sign and symptoms of depression are mentioned under *Unmada Vyadhi* so we can correlate depression with *Unmada*. *Charaka* quotes *Vishada* is the foremost factor to worsen the disease condition.[4] To treat *Manovikara* disease, 112 formulations are mentioned in different *Ayurvedic* classics as *Yuktivyapashray Chikitsa* viz. *Sneha kalpana-Ghrita, Taila, Choorna, Guti, Rasayoga* [mineral-herbomineral formulations].[5] Apart from these; *Sneha kalpana* plays an important role in treatment both internally and externally. If taken internally, it enters the systemic circulation and thereby stimulates the central nervous system.[6] Among them *Ghrita* preparation are centrally focused as these are the form of lipids and lipids have the ability to cross the blood brain barrier [7],[8]. Digestion of ghee in body is 96%, which is highest among all fats and oils. *Ghrita* possesses a unique property- *Sanskarsyaanuvartanam* i.e. it enhances the therapeutic efficacy of the drugs which are used along with it in the formulation without losing its own properties. *Ghrita* is *Rasayana*, good for health and enhance memory.

Brahmyadi Ghrita [9] is an herbal formulation mentioned in *Ashtanga Hridaya Uttarasthana*. *Brahmyadi Ghrita* contains *Brahmi* (Bacopa monnieri Linn), *Siddharthka* (Brassica campestris Linn.), *Vacha* (Acorus calamus Linn.), *Sariva* (Hemidesmus indicus R.Br.), *Kushtha* (Saussurea lappa C.B. Clarke), *Pippali* (Piper longum) and *Saindhva* (Rock salt). These ingredients are processed in Cow's ghee. Each ingredient of the formulation shows activity towards CNS, so the cumulative properties of *BG* may help to treat disease like depression.

Brahmyadi Ghrita had been evaluated for its Nootropic and Antipsychotic activity in department of RSBK [10]. However till date this particular formulation has not been assessed as Antidepressant clinically. Therefore, for present study *BG* is selected to assess its effect in patients from mild to moderate range in depression.

AIM AND OBJECTIVES-

AIM:

Clinical Evaluation of *Brahmyadi Ghrita* in Mild to Moderate Depression.

OBJECTIVES:

- To manufacture *B.G.* following pre-established Standard Operating Procedure (SOP).
- To established standard parameters of *Brahmyadi Ghrita*.
- To assess the antidepressant effect of *B.G.* in patients of depression of age group 25-50 years using Hamilton Depression Rating scale test.

MATERIALS AND METHODOLOGY-

To complete aim of the study following methodology was followed:

A. **Pharmaceutics of *Brahmyadi Ghrita*-**

In present Study *Brahmyadi Ghrita* was manufactured according to the reference of *Ashtanga Hridaya, Uttarsthan,* chapter no.1 *Balopacharaniya Adhyaya*, verse no. 42 in pharmacy of Rasa Shastra & Bhaishajya Kalpana, BVDUCOA, Pune and standardized in Bhide laboratory, Pune.

Pre step-

Raw drug selection: The Identification and selection of best sample was done by Consensus method. Identification of all raw ingredients was done by 12 experts from Dravya Guna Vigyan and Rasa Shastra & Bhaishajya Kalpana department of BSDT's Ayurveda College, Wagholi and Sumatibhai Shah Ayurved Mahavidyalaya, Hadapsar. The responses were counted on 3 point scale and

final score was noted. For selection of best samples, 12 record sheets of standard identification parameters given in Ayurvedic Pharmacopeia of India were prepared which is given below in table. According to it each sample was selected.

Authentication of raw drugs: All raw drugs were authenticated as per the standards given API in analytical laboratory of our Department.

Table No 1: Organoleptic parameters of raw drugs with observation

Organoleptic parameters	***Brahmi***	***Siddharthak***	***Vacha***	***Sariva***	***Kushtha***	***Pippali***	***Saindhav lavan***
Shabda	-	-	*Kat*	-	*Kat*	*Kat*	-
Sparsha	*Khara*	*Slakshana*	*Khara*	*Khara*	*Khara*	*Khara*	*Slakshana*
Roopa	Green	Yellow	Creamish	Dark Brown	Brown	Greenish Black	Pinkish White
Rasa	Bitter	Bitter	Pungent Bitter	Sweetish slightly acrid	Slightly bitter	Pungent	Salty
Gandha	Specific odor	Specific odor	Aromatic	Characteristic aromatic	Strong aromatic	Aromatic	-

Table No. 2: Analytical values of raw drugs (Brahmi, Siddharthak, Vacha) as per API

Name of the parameter	**Brahmi**		**Siddharthak**		**Vacha**	
	Standard values	**Obtained values %**	**Standard values**	**Obtained values %**	**Standard values**	**Obtained values %**
pH	NA	5	NA	6	NA	6.2
Moisture content	NMT 10%	3%	NMT 10%	5%	NMT 10%	4%
Foreign matter	NMT 2%	1%	NMT 2%	0.5%	NMT 1%	0%
Total ash	NMT 18%	3%	NMT 5%	4%	NMT 7%	7%
Alcohol soluble extractive	NLT 6%	25.6%	NLT 8%	16%	NLT 9%	22.4%
Water soluble extractive	NLT 15%	22.4%	NLT 16%	24%	NLT 16%	32%
Fixed oil	-	-	NLT 35%	37.5%	-	-
Volatile oil	-	-	-	-	NLT 2%	2%

Table No. 3: Analytical values of raw drugs (Sariva, Kushtha, Pippali) as per API

Name of the parameter	**Sariva**		**Kushtha**		**Pippali**	
	Standard values	**Obtained values %**	**Standard values**	**Obtained values %**	**Standard values**	**Obtained values %**
pH	NA	7.2	NA	6	NA	6
Moisture content	NMT 10%	4%	NMT 10%	3%	NMT 10%	4%
Foreign matter	NMT 2%	0%	NMT 2%	0%	NMT 2%	1%

Total ash	NMT 4%	3%	NMT 4%	4%	NMT 7%	6%
Alcohol soluble extractive	NLT 15%	19.2%	NLT 12%	20.8%	NLT 5%	19.2%
Water soluble extractive	NLT 13%	16%	NLT 20%	30.4%	NLT 7%	12.8%

Table No. 4: Physico chemical values of Saindhav lavan

Name of the parameter	**Obtained values %**
pH	6
Moisture content	0%
Foreign matter	0%

Table No 5: Organoleptic of cow ghee

Organoleptic test	**Cow ghee**
Shabda	---
Sparsha	*Snigdha*
Roopa	*Snigdha, Pita Varna*
Rasa	*Madhur*
Gandha	*Sugandhi*

Table No. 6: Analytical test of cow ghee

Analytical Parameter	**Reading of cow ghee**
pH	5.19
Specific Gravity	0.9346 gm/ml
Wt/ml	0.9gm
Free Fatty acid	0.68%
Moisture content	0.09%
Saponification value	227.81
Acid value	3.08
Iodine value	33.97
Refractive index	1.4549
Viscosity	19.62 CPS

Note: All tests were performed in **triplicate and average value was considered**.

Obtained values of all the drugs sample **complies with the API** standard.

Main procedure- *Brahmyadi Ghrita* was prepared as per standard guideline stated in *Shrangdhar samhita* to manufacture medicated ghee was followed [1:4:16][11]. All herbal fine powdered drugs were mixed with each other and then paste of this mixture was made by adding little water. Cow ghee was heated initially and cooled to room temperature. Paste and water was added to it. The whole mixture was then heated on low flame to achieve *Ayurvedic* testing parameters.[12]

Analysis of *Brahmyadi Ghrita*-

Table no.7: Organoleptic parameters of Brahmyadi Ghrita

Organoleptic parameter	Observation
Touch	Unctuousness
Color	Light greenish
Taste	Bitter++
Odor	Ghee odor

Table no. 8: Analytical values of *Brahmyadi Ghrita*

Parameter	Reading
pH	7
Specific gravity	0.945
Saponification value	293.12
Acid value	2.468
Peroxide value	1.71
Free Fatty Acid	0.78%
Total Fats	94.65

B. Clinical Study

MATERIALS:

Prior to clinical study proposal was sent to BVDUCOA Human Ethics Committee and permission was obtained.

Proposal No.- BVDU/COA/29/2014-15

Approval date: 07/04/2015

CTRI Registration date: 30/06/2016

CTRI Registration No. - **REF/2016/06/011642**

- **Study design**- Open Labeled Non-Randomized Standard Control clinical trial
- **Study site**-Department of Rasa Shastra & Bhaishajya Kalpana, Bharati Vidyapeeth Deemed University, College Of Ayurveda, Pune
- **Subjects**-Pre-diagnosed Patients of depression from mild to moderate range as per ICD 10 criteria.
- **Sample size:**12 (This is pilot study to evaluate antidepressant effect of *Brahmyadi Ghrita*)

Inclusion criteria-

- Patients of mild to moderate range of depression (range 8-13 =Mild Depression, 14-18= Moderate Depression
- Age group= 25-50 years
- patients of either gender
- Patients willing to sign informed consent form

Exclusion criteria:

- Patients with other psychiatric disorders like psychosis, schizophrenia, anxiety, mania.
- Pregnant women.
- Patients with chronic illness like DM, HTN, Cancer, Hyper/Hypo thyroidism.
- Patients suffered from any shock and trauma.
- Patients with suicidal tendency/ thoughts

Other instructions:

There was no intervention in exercise and their routine work and their routine prescribed conventional medicines. Patient was asked to restrict food enriched with oil butter cheese.

Drugs:

Group A- Study Group: *Brahmyadi Ghrita* with prescribed conventional therapy to 6 patients

Group B- Standard Control Group– Standard antidepressants (citalopram, sertraline, fluoxetine) only to 6 patients.

Drug Dose: 10 gm twice a day with Luke warm water on empty stomach.

METHDOLOGY:

A written informed consent was obtained from patient before screening for the eligibility criteria. Only those subjects who was fulfil the eligibility criteria were recruited.

Selected patients were non-randomly allocated into 2 groups Group A and Group B.

After grouping each patient was asked to take the Hamilton Depression Rating scale test. The scores were recorded.

1 gm. of *Gandharva Haritaki Choorna* with lukewarm water at bed time for 5 days was given to the patient of study group for *Koshthashuddhi*. After 5 days *Brahmyadi Ghrita* was given to the patient. 6^{th} day of study period was calculated as 1^{st} day of *Brahmyadi Ghrita* administration.

Drug administration was done as per group from Day 1 to Day 60.

Every 15 days follow up was taken and on every 30^{th} day Hamilton scale was used again for assessment.

A patient who has missed medicine for 3 sequential days i.e. 6 doses, was dropped out from the project and new patient was recruited.

A dairy was given for marking dose and symptoms of depression which patient felt during treatment.

On day 61 each participant was made to take the same test (Hamilton Scale Test) again. Results were recorded.

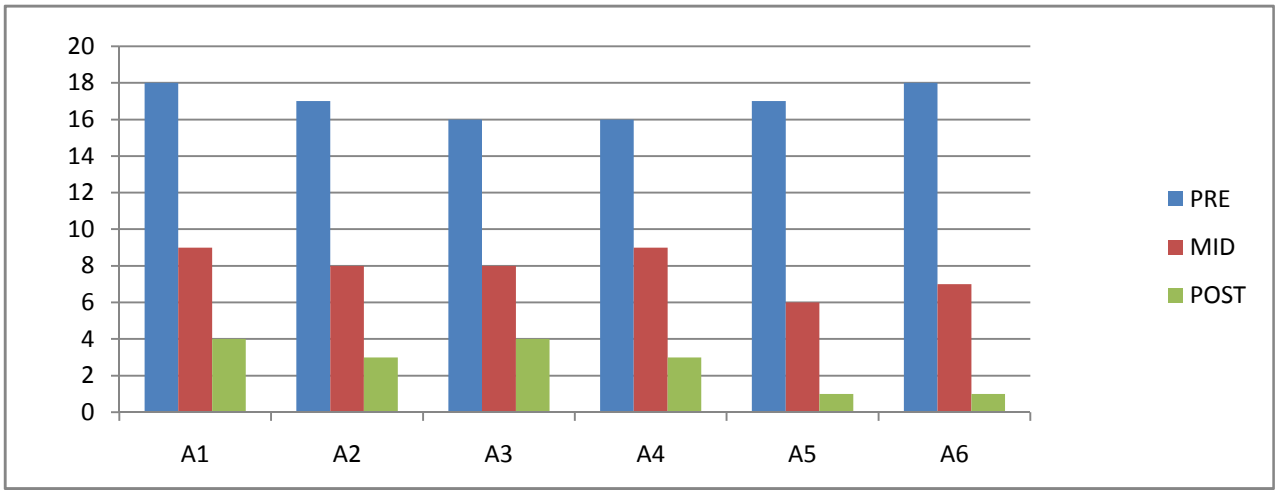
Data was organized and analyzed.

OBSERVATION AND RESULTS-

Study Group: *Brahmyadi Ghrita* + Standard Antidepressant Drug were given to the patients and HAM-D pre (day 0), HAM-D mid (day 30) and HAM-D post (day 61) score are compared using "Friedman test".

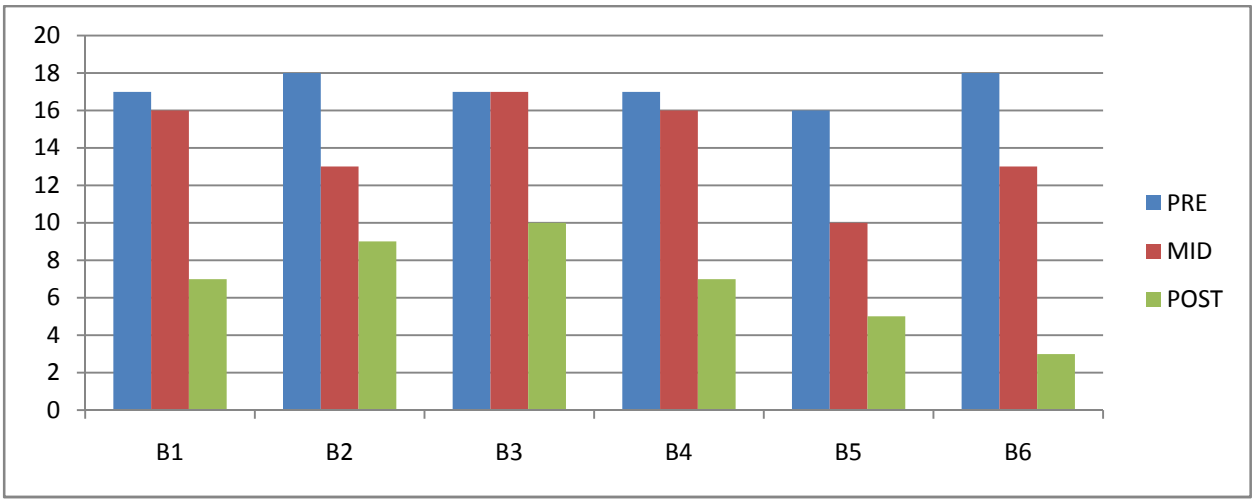
Interpretation: 'P' value of study group is 0.0001which is less than 0.05 showed significant results. Here study group treatment shows antidepressant effect in mild to moderate depression patients during 60 days. HAM-D Pre Score -Day 0 vs HAM-D Post Score -Day 61 result is significant.

Bar Diagram given below.



X axis- Number of patients from Group A
Y axis- Hamilton Scale Test Score

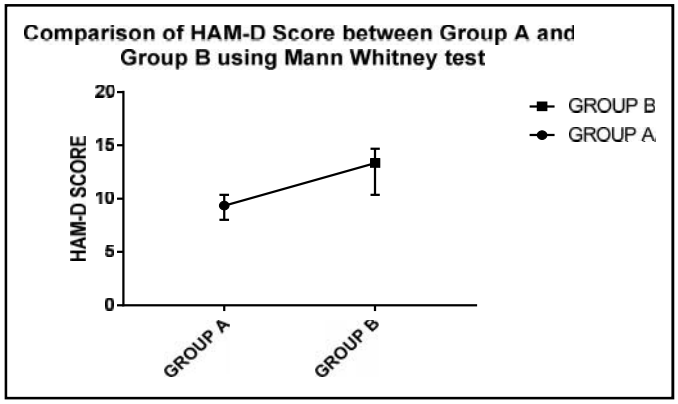
Graph 2- Scores of Group B using HAM-D Rating Scale



X axis- Number of patients from Group B
Y axis- Hamilton Scale Test Score

By using Friedman test in Group B, p value for Hamilton Depression Rating Scale is less than 0.05 i.e. 0.003<0.05therefore there is significant decrease in HAM-D score in Group B.

Graph No3 - Comparison of HAM-D Score between Group A and Group B using Mann Whitney test



By using Mann Whitney U test for comparison between treatment of Group A and Group B, it may state as treatment of Group A is more effective than Group B as p value is less than 0.05 i.e. 0.0043 <0.05.

DISCUSSION

Depression frequently occurs as a result of adverse life events, such as: losses of a lovable person, object, relationship or health, but it can also occur due to no apparent cause. As considering prevalence of depression in society and current mental health problems, patients of depression were selected for study. In *Ayurveda Vishada* and *Avasada* are the two conditions predictable as depression. Premonitory sign and symptoms of depression are mentioned under *Unmada Vyadhi* so we can correlate depression with *Unmada*.

In Ayurveda *Sidhha Ghrita* preparations are centrally focused in treatment of CNS disorders as these are the form of lipids which have ability to cross blood brain barrier.

BG[6] (*B.G.*) is an herbal formulation mentioned in *Ashtanga Hridaya Uttarasthana*. It is mentioned to possess *Medhya* and *Smrutivardhaka* activity in healthy condition. *BG* contains *Brahmi, Siddhartha, Vacha, Sariva, Kushtha, Pippali* and *Saindhva*. These ingredients are processed in Cow's ghee. Each ingredient of the formulation shows activity towards CNS, so the cumulative properties of *BG* may help to treat disease like depression

Mental health problems are more prone in younger and old age group; therefore age group of 25-50 year was selected in patient of depression.

Statistical data was analyzed by using each group was statistically analyzed using **Friedman test** for their significance set at $P<$ 0.05 is 0.0001, as it was **ordinal and non parametric paired data**.

Difference between the groups was done using **Mann Whitney U test** with the level of significance set at $P<$ 0.05 is 0.0043 as it was **ordinal and non parametric unpaired data**. The level of significance was noted and interpreted accordingly.

After statistical analysis it was found that *Brahmyadi Ghrita* when compared with only conventional therapy showed significant antidepressant effect in score of HAM-D scale test.

CONCLUSION-

Pharmaceutical study-

- SOP's for manufacturing of *BG* and standard parameters for *Brahmyadi Ghrita* were established.

Clinical study-

- The study concluded that *Brahmyadi Ghrita* has significant results with conventional therapy in Depression than only standard antidepressant conventional therapy.
- Thus we can conclude that *Brahmyadi Ghrita* can be used as antidepressant in patient of depression.

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