

PHARMACOLOGICAL ASSESSMENT OF AYURVEDIC FORMULATION HINGWADI GHRITAIN MILD TO MODERATE DEPRESSION

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ABSTRACT

Ayurveda describes two mental disorders *Unmada* and *Apasmar*. Depression correlates with premonitory symptoms of *Unmada* and *Vishada*. Study was aim to evaluate *Hingwadi Ghrita* in Mild to Moderate Depression. For assessment and to diagnose the severity of depression Hamilton Scale Test was used. The types of severity are mild, moderate, severe and very severe depression. *Hingwadi Ghrita* was prepared following SOP and analytical values of *HG* were complied with the standard values. There is rise in number of people suffering from psychosis, schizophrenia, anxiety, mania and depression. Worldwide it is estimated that around 18% of men and 29% of women experience a depressive episode in their lifetime with suicide being the most common outcome. HAM-D test was taken before (day 0-Pre), mid (day 30- mid) & after (day 61- post) completion of *Ghrita* consumption. Patients of mild to moderate depression were non- randomly divided into two groups 6 patients in each group A- study group- *Hingwadi Ghrita* + standard antidepressant drug and group B- Standard Antidepressant Drug. As suggested by modern psychiatrists antidepressant drugs were continued to all (both groups) patients. In group A patients *Hingwadi Ghrita* was administered 10 gm bid with lukewarm water for 60 days and for *Koshthashuddhi* purpose 1gm of *Gandharva Haritaki Choorna* with lukewarm water was given for five days at bed time before administration of *HG*. Patients were advised to take *ghrita* at six day after *Koshthashuddhi* in early morning and evening on empty stomach. It was calculated as first day of *HG* administration. Primary outcome of the study is 'decrease in score' of HAM-D. Pre, mid and post scores of every patient was assessed by using Friedman Test and two groups i.e. A & B was compared using Mann Whitney test. In present study *Hingwadi Ghrita* at dose 10 gm bid for 60 days with standard antidepressant drug has shown significant (P=0.0001) antidepressant activity in patients of mild to moderate depression. Secondary outcome of the study was 'changes in certain secondary parameters', which were assessed on the basis of 'Samyak *Snigdha Lakshana*'. Easy evacuation of bowel, normal appetite was seen in patients of mild to moderate depression.

Key words: Hamilton Depression Rating Scale Test, *Hingwadi Ghrita*

INTRODUCTION

Mental Health is an essential component of health according to Ayurveda as well as modern science. Depression is a sustained mood disorder perceived by sadness, guilt,

physical and mental slowing, psychomotor retardation, loss of interest, pleasure and self-destructive ideation.

Worldwide about 350 million people suffer from depression it is estimated that by the year 2020 if current trends for demographic and epidemiological transition continue, the burden of depression will increase to 5.7% of the total burden of disease and it would be the second leading cause of disability-adjusted life years (DALYs), Depression may become a serious health condition^[1].

Ayurveda describes two mental disorders, *Unmad* and *Apasmar*^[2]. Systematic comparison of signs and symptoms of premonitory state of *Unmad*^[3] and description of the terms *Vishaad* reveal that they be fit the description of Depression^[4]. The treatment offered in Ayurveda comprises of counselling and medications. Various dosage forms are also available out of which *Ghrita* is mainly mentioned in classical text.

Hingwadi Ghrita (HG) is the first drug of choice as per *Ashtang Hridaya* (Ref: *Ash-tang Hridaya, Uttarsthana*, ch 6/22). But a systematically collected clinical data for the same is not available.

Each of the ingredients of *Hingwadi Ghrita* consisting of *Hingu* (*Ferula narthex* boiss), *Shunthi* (*Zingiber officianale*), *Marich* (*Piper nigrum*), *Pippali* (*Piper longum*), *Goghrita* (Cow ghee) *Gomutra* (Cow urine); and *Sauvarchal lavan* (Black salt) has been reported to demonstrate anti-stress, anti-anxiety, intellect promoting, neuro-stimulant and anti-convulsant activities^[5]. Taking a clue from the effects of individual drugs, experimental studies were conducted on *Hingwadi Ghrita* in dept. of RSBKV^[6]. It shows promising result as an antipsychotic, antiepileptic, antidepressant formulation in vivo. Hence it is worth of taken this formulation further and assess its antidepressant potential in clinical setting.

AIM: To evaluate *Hingwadi Ghrita* in Mild to Moderate Depression.

OBJECTIVES:

- To prepare standardised *Hingwadi Ghrita*.
- To analyze *HG* in laboratory and compare with pre-established Standard values.
- To assess the antidepressant effect of *HG* clinically on a small sample of patients of depression, using Hamilton scale.

MATERIAL AND METHODS:

Study design: Open label nonrandomized standard controlled clinical trial

Study site - Dept. of Rasashastra and Bhaishajya Kalpana & Bharati Ayurved Hospital, Pune.

Permission from Ethics Committee: Permission from BVDU/COA-EC was obtained

Approval Date: 7/04/2015

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

Subject: Pre-diagnosed (as per ICD-10 criteria) patients of mild (range=8-13) to moderate (range=14-18) depression as per Hamilton's rating scale

Sample size: 12 (This study is pilot study type therefore 12 sample size decided)

Phase of trial: Phase II

Inclusion criteria:

- Patients willing to participate in the study
- Pre-diagnosed patients of Mild to Moderate Depression
- Patients of age group 25-50 years of either sex.

Exclusion criteria:

- Patient suffering from bipolar depression, depression with dementia and depressive disorder with other concomitant disease like Hypertension, Diabetes Mellitus.
- Patients undergoing any accidental shock, trauma and pregnant woman are also excluded.

Study Groups:

Study Group- Formulation under evaluation (study drug *Hingwadi Ghrita*) with standard antidepressant, 6 patients.

Standard Control Group– Standard antidepressants (sertraline, citalopram, fluoxetine) only already prescribe to the patient. 6patients.

Study drug: *Hingwadi Ghrita* (Ref: *Ashtang Hridaya, Uttarsthana*, ch 6/22)

Drug Dose: 10 gm twice a day

Treatment Duration: 60 days.

Criteria for Assessment: HAM-D^[7].

Hingwadi Ghrita Preparation steps

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 BVDUCOA 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. 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 1: Organoleptic tests

Organoleptic parameters	<i>Hingu</i>	<i>Shunthi</i>	<i>Marich</i>	<i>Pippali</i>	<i>Sauvarchal lavan</i>
<i>Shabda</i>	-	<i>Kat</i>	-	<i>Kat</i>	-
<i>Sparsha</i>	<i>Khar</i>	<i>Khar</i>	<i>Khar</i>	<i>Khar</i>	<i>Snigdha</i>
<i>Rupa</i>	<i>Pita varna</i>	Brownish outer layer and inner creamy white	<i>Krishna varna</i>	<i>Krishna varna</i>	<i>Raktavarna</i>
<i>Rasa</i>	<i>Katu, Tikta</i>	<i>Katu</i>	<i>Katu, Tikta</i>	<i>Katu, Tikta</i>	<i>Katu, Tikta</i>
<i>Gandha</i>	<i>Ugra</i>	<i>Ugra</i>	<i>Saumya</i>	<i>Saumya</i>	<i>Ugra</i>

Procurement of Animal source drugs:

Fresh sample of cow ghee, cow urine was procured from the authenticated source Dvarkadhish Krishi Govidnyan Anusandhan Sanstha, Purandar, Pune.

Authentication of Cow urine and Cow ghee:

was done by referring API parameters in departmental laboratory and Bhide lab Pune.

Table 2: Organoleptic tests of *Gomutra* and *Goghrita*

Tests	<i>Gomutra</i>	<i>Goghrita</i>
<i>Shabda</i>	NA	NA
<i>Sparsha</i>	<i>Jalawat</i> (liquid)	<i>Snigdha</i> (oily)
<i>Rupa</i>	<i>Pitabh</i> (dark yellow)	<i>Pitabh</i> (yellowish)
<i>Rasa</i>	<i>Kashaya</i>	<i>Madhur</i>
<i>Gandha</i>	<i>Gomutra gandha</i>	<i>Sugandh</i>

Table 3: Analytical values of Cow ghee and Cow urine:

Cow ghee	Parameters	Reading	Cow urine	Parameters	Reading
	Acid value	0.86		pH	7.84
	Moisture	0.19%		Specific Gravity	1.283
	pH	5.16		Viscosity	8.96
	Specific Gravity	0.9184		Turbidity	187.7
	Saponification value	227.09			
	Iodine value	33.59			
	Peroxide value	1.4613			

Main procedure:

In present study *Hingwadi Ghrita*^[8] was prepared in BVDUCOA following SOP. *Hingu* shodhan was done (Ras.Ta.24/576). Cow ghee was heated on a low flame in a thick bottom vessel. Heating was discontinued as fumes appeared. Then fine paste (*kalka*) was made by

tritulating powdered ingredients (all ingredients) with water using stone mortar and pestle. This triturated bolus was added to the cow ghee. Then cow urine was added to the mixture and a homogenous mixture was prepared. It was then subjected to heat on low flame until the testing criteria occurred.

Table 4: Organoleptic tests of HG

Parameter	Observation
Shabda	-
Sparsha	Snigdha
Rupa	Blackish Brown++
Rasa	Tikta++
Gandha	Ugra, Gomutragandhi++

Table 5: Analytical values of HG:

Parameter	Readings
Moisture	0.09%
Refractive Index	1.4549
pH	4.68
Specific Gravity	0.9104gm/ml
Saponification value	180.81
Iodine value	39.14
Acid value	2.78
Viscosity	19.52

METHODOLOGY:

Consent was taken from patients/patients relative. Pre-assessment Test (HAM-D) was administered to all the patients

included in the study. As suggested by modern psychiatrists antidepressant drugs were continued to all (both groups) patients. For study group A, 1gm of *Gandharva Haritaki*

Choorna with lukewarm water was given for five days at bedtime for *Koshthashuddhi*. On same day 300 gm *Hingwadi Ghrita* bottle was provided to patients and showed them how to take measured dose of ghee followed by lukewarm water. Patients were advised to take *Ghrita* at six day after *Koshthashuddhi* in early morning and evening on empty stomach. It was calculated as first day of *HG* administration. On every 15th day finished bottles were collected and another bottle with 300 gm of *Hingwadi Ghrita* was given to patient. In all 1200 gm of *Hingwadi Ghrita* was given in 60 days per patient. HAM-D was administered at day 0-Pre, day 30- mid and day 61- post.

Diary was given to each patient for maintained the record of *HG* consumption. Calendar was given for marking the days when *ghrita* was taken. Patients were also instructed to tick mark other parameters (*Samyak Snigdha Lakshana*) given in diary after consumption of *ghrita* from Day 1 to Day60.

No change prescribed in patients' exercise, routine work and other ongoing conventional medicines during study period and patient asked to control oil and ghee and avoid extra oily and fatty food items.

Every 15 day follow up of patient was taken.

Bar Diagram given below.

A patient who missed medicine for 3 consecutive days i.e. 6 doses, dropped out from the study and new patient recruited.

After completion of study whole data was collected, organised and analysed. Analysed data was then subjected to suitable statistical tests and results were obtained.

RESULTS AND OBSERVATIONS:

Primary Outcome of Study

1. 'Decrease in Hamilton Scale Test Score' is assessed pre, mid and post treatment every patient of each group using Friedman test.

1.1. Study Group: *Hingwadi 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 0.0001 which 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 Mid Score -Day 30, HAM-D Mid Score -Day 30 vs HAM-D Post Score -Day 61 showed not significant result. HAM-D Pre Score -Day 0 vs HAM-D Post Score -Day 61 result is significant.

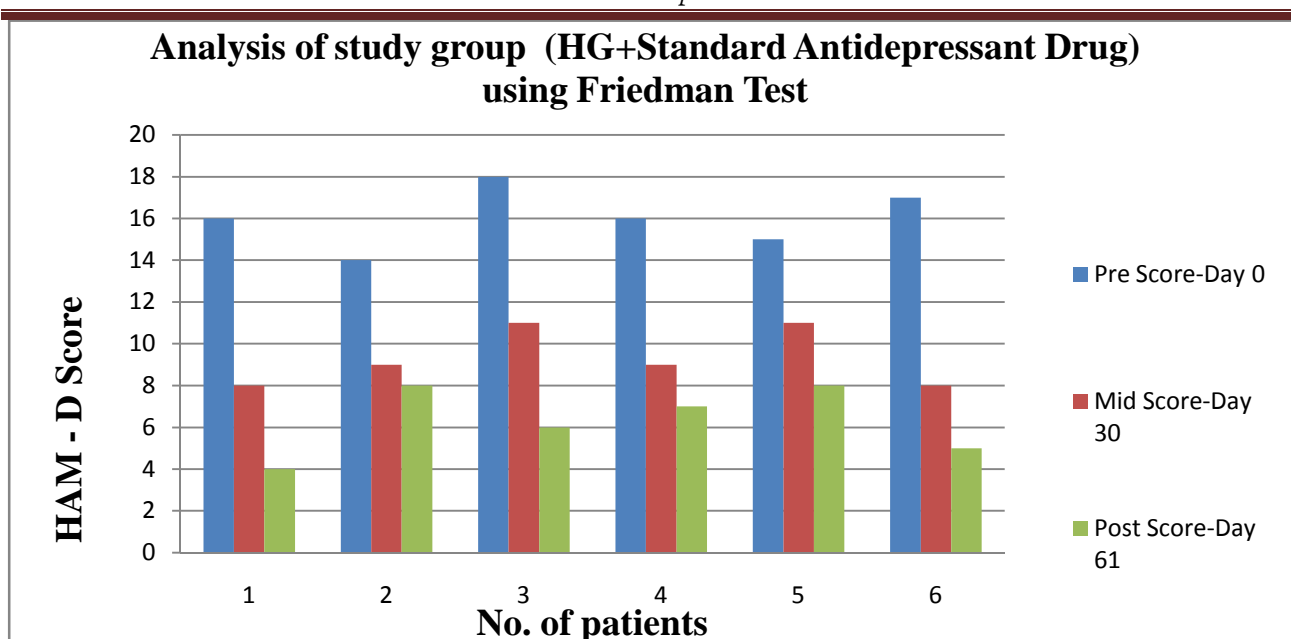


Figure 1

1.2. Standard Control Group: Standard Antidepressant Drug (no study drug) was given to the patients and HAM-D pre (day0), HAM-D mid (day 30) and HAM-D post (day61) score are compared using “Friedman test”.

Interpretation: ‘P’ value of standard control group is 0.0001 which is less than 0.05 showed significant results. Here standard control group

treatment shows antidepressant effect in mild to moderate depression patients during 60 days. HAM-D Pre Score-Day 0 vs HAM-D Mid Score–Day 30, HAM-D Mid Score –Day 30 vs HAM-D Post Score –Day 61 showed not significant result. HAM-D Pre Score–Day 0 vs HAM-D Post Score–Day 61 result is significant.

Bar Diagram given below.

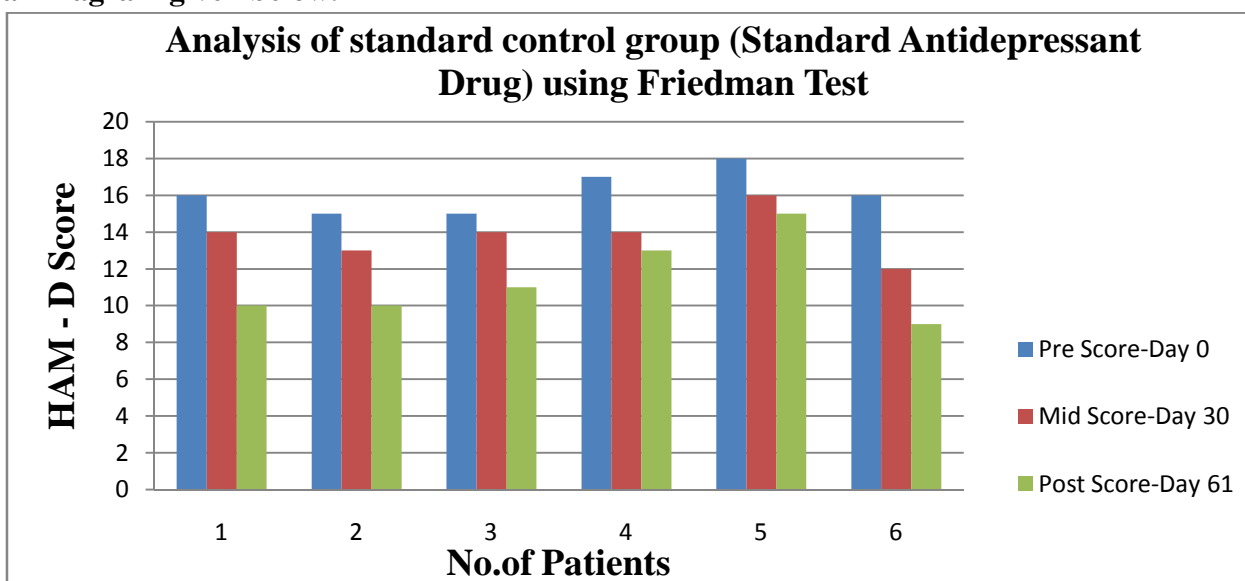


Figure 2

2. ‘Decrease in Hamilton Scale Test Score’ is assessed pre, mid and post treatment of each group using Mann Whitney test.

Comparison of study group and standard control group using Mann Whitney test showed significant result. P value is 0.005 which less Line diagram given below

than 0.05. Here HAM-D score of study group more decreased as compare to HAM-D score of standard control group. Therefore *Hingwadi Ghrita* + Standard Antidepressant Drug show more antidepressant effect than Standard Antidepressant Drug.

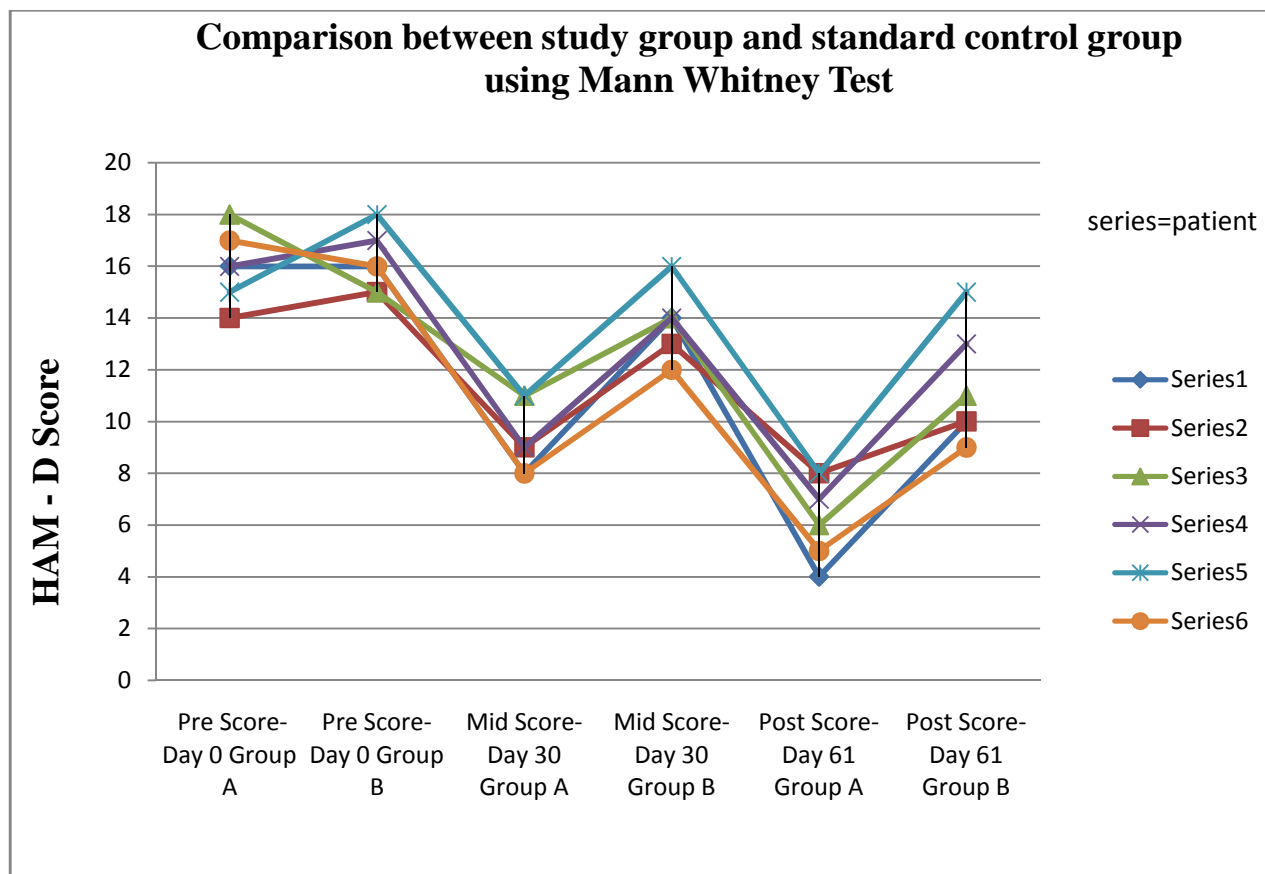


Figure 3
Secondary Outcome of Study
Evacuation of Bowel

Study Group: out of 6 patients 5 patients shown well-formed faeces and 1 patient showed hard faeces after 60 days of treatment.

Standard Control Group: out of 6 patients 4 patients shown well-formed faeces and 2 patients shown hard faeces after 60 days of treatment.

Appetite

Study Group: out of 6 patients 5 patients shown normal appetite and 1 patient shown decrease in appetite after 60 days of treatment.

Standard Control Group: out of 6 patients 3 patients shown normal appetite and 3 patients shown decrease in appetite after 60 days of treatment.

DISCUSSION

Hingwadi Ghrita was an important formulation used for treatment of mental disorders mentioned in Ayurveda. Depression correlates with premonitory symptoms of *Un-*

mada and *Vishada* [4]. The actual preparation of *HG* was done following the textual reference of *Ashtang Hridaya, Unmad*, as adapted by previous research studies on the same formulation. To obtain accurate results of the formulation for the clinical activity the procedure of manufacture and analytical parameters were complied with the standard.

The reason could be its '*snigdhatva*' which is similar to the property of *Majjadhathu* at structural level and with mind at functional level^[9]. *Ghrita* (Cow ghee) cross the blood brain barrier easily due to the lipid structure and it is *buddhivardhaka*-augmenting intelligence, *Smritivardhaka*-enhancing memory, and *Deepana*-improves appetite and is useful in the treatment of *Unmada*, *Apasmar*, *murccha* and *mada*. Again it's worth noticing that all these are the diseases affecting the nervous system in particular.

Thus, it is evident from above that *vata* dosha (*prana*, *udana* and *vyana* especially) has a key role to play in etiology of *Unmad*. Similarly, *pitta dosha* when in a normal state helps digestion, maintains normal appetite, thirst, thermal equilibrium, happiness and intelligence while normal *kapha* is unctuous, steady and is known for heaviness, virility, strength, forbearance, patience and greedlessness. *Sadhaka pitta*, *Bodhaka* and *Avalambak kapha* are relatively affected in *Unmad*. *HG*, as a formulation has *katu*, *Tiktaras* and *ushna*, *teekshnagunas*, *Unmadahar*, *Apasmarhar*, *Kaphaghna*, *Vatanulomak* and *Medhya*^[10].

Taking account of previous data its anti-depressant potential was studied through clinical trial. Group A (*HG* + Standard antidepressant drug) and Group B (Standard antidepressant drug) shows decreased in HAM-D score, both groups treatment shows antidepressant effect in mild to moderate depression patients. HAM-D score of study group more decreased as compare to HAM-D score of stan-

dard control group. Therefore *Hingwadi Ghrita* + Standard Antidepressant Drug show more antidepressant effect than Standard Antidepressant Drug. Hence *Hingwadi Ghrita* effective in mild to moderate depression patients along with Standard antidepressant drug in 60 days. *Hingwadi Ghrita* skipping standard antidepressant drug as study drug should be given for 30 days duration and study should be carried out on larger sample size.

CONCLUSIONS

Pharmaceutical Study:

Hingwadi Ghrita was prepared following the SOP, Organoleptic tests and analytical values of prepared *Hingwadi Ghrita* are complied with the standard values.

Clinical study :

In present study *Hingwadi Ghrita* at dose 10 gm bid for 60 days with standard antidepressant drug has shown significant ($P=0.0001$) antidepressant activity in patients of mild to moderate depression.

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Source of Support: Nil

Conflict Of Interest: None Declared

How to cite this URL: Takale Roshni Madhav & Wele Asmita: Pharmacoclinical Assessment Of Ayurvedic Formulation
Hingwadi Ghritain Mild To Moderate Depression International Ayurvedic medical Journal {online} 2016 {cited 2016 July}
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