

ORIGINAL RESEARCH ARTICLE

# Formulation and Evaluation of Suppository Prepared from *Phalavarti* and its Clinical Evaluation in *Malavrodha* (Functional Constipation)

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## ABSTRACT

**INTRODUCTION** - The *Varti Kalpana* is a unique dosage form described in Ayurveda indicated for different purposes. *Phalavarti* is specifically mentioned for *Malapravatana* (*Sharngdhara Samhhita Ut. Kh. 7/15*) and in *Udavarta* (*Chakradatta, Udavarta Chikitsa 28/13*). Though the formulation is therapeutically much potent, there is a lesser acceptance for its practical applicability in today's era due to its more hardness and less stability. Thus, to bring it to consumers' compliance with better quality, bioavailability and shelf life, it needs to be modified and convert the ancient *Phalavarti* into conventional Suppository form. **AIM AND OBJECTIVES** - Current manuscript aimed to evaluate to screen different bases in order to overcome drawbacks of traditional base and to develop suppository having better quality and stability and to assess effect of suppository prepared from *Phalavarti* (PS) in patients of *Malavarodha* (functional constipation). **MATERIALS & METHODS** - Suppositories were prepared using hot melt and trituration methods. Different bases such as Cocoa butter, Bees wax, Polyethylene glycol (1500 & 4000) and Glycero-gelatin were used as single and in combinations to develop formulation. For this clinical study, patients fulfilling the diagnostic criteria of *Malavrodha* (functional constipation) were selected. **RESULT** - From the results, it is evident to prefer combination of cocoa butter and bees wax (48:02) as a base for desirable quality and stability of formulation. Patients of *Malavrodha* (functional constipation) showed significant results in all selected parameters.

**Key Words** *Varti Kalpana, Phalavarti, Suppository base, rectal drug delivery*

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## INTRODUCTION

*Phalavarti* are meant to be inserted in the rectum, it helps *Apaana Vaata Anulomana* due to which *Mala* can be excreted easily. *Phalavarti* is used in case of constipation, retention of enemas,

disorders of GIT causing obstruction to the movement of *Apaana Vaata* and excretes *Mala* accumulated in the rectum<sup>1</sup>.

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मदनं पिप्पली कुष्ठ वचा गौराश्च सर्षपाः ।

गुड क्षार समायुक्ताः फलवर्ति प्रशस्यते ॥

(Chakradatta, *Udavartaroga Chikitsa*, 28/ 13)

Suppositories contain one or more active ingredients dispersed or dissolved in a suitable base that may be soluble or dispersible in water or melt at body temperature, suppositories are very similar to *Varti*. These are prepared by melting suppository base and incorporation of medicaments in molten mass. On rectal administration, suppository base melts at body temperature and medicaments are released. The bases are of two types: oleaginous/fatty bases (such as theobroma oil/cocoa butter and hydrogenated vegetable oils). And water miscible or soluble (such as glycerinated gelatin and polyethylene glycol polymers)<sup>2</sup>.

*Malavarodha* (functional constipation) is not separately mentioned in Ayurvedic texts as a specific disease but has been mentioned as a *Nidaana* (causative factor), *Lakshana* (symptoms) and *Upadrava* (complications) of several diseases. It can be considered as a *Lakshana* in *Udaavarta* (Retention of faeces, flatus and urine) like *Anaaha* (Obstruction), *Adhmana* (Distension), *Malaavastamba* (Hardness of faeces) due to the *Pratiloma Gati* (reverse flow) of *Apaana Vaata*<sup>3</sup>.

The Rome IV criteria categorizes disorder of chronic constipation into four subtypes: (a) Functional constipation, (b) Irritable bowel syndrome with constipation, (c) Opioid-induced constipation (d) Functional defecation disorders,

including inadequate defecatory propulsion and dyssynergic defecation.

The patients do fulfil the criteria for Functional Constipation (FC) must include two or more of the following:

- Straining more than 25% of defecations.
- Lumpy or hard stools (BSFS type 1 or 2) more than 25% of defecations.
- Sensation of incomplete evacuation more than one-fourth (25%) of defecations.
- Sensation of ano-rectal obstruction/blockage more than one-fourth (25%) of defecations.
- Manual maneuvers to facilitate more than one-fourth (25%) of defecations.
- Fewer than three spontaneous bowel movements per week<sup>4</sup>.

## AIMS AND OBJECTIVES

**AIM:** To develop standard manufacturing process, preliminary analytical profile, stability and evaluate suppository prepared from *Phalavarti* (PS) to relieve *Malavrodha* (functional constipation).

**OBJECTIVE:** To formulate multiple batches and finalize the material and proportion for base of suppository, analyse various parameters, stability of suppository prepared from *Phalavarti* (PS) and assess effect of suppository prepared from *Phalavarti* in patients of *Malavarodha* (functional constipation).

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**MATERIALS & METHODS**

**Table 1** Ingredients used for PS

Sr. No.	Ingredients	Botanical Name	Part used
1	<i>Madanaphala Churna</i>	<i>Randia dumetorum</i> Lam	Fruit
2	<i>Pippali Churna</i>	<i>Piper longum</i> Linn	Fruit
3	<i>Kustha Churna</i>	<i>Sauseria luppa</i> C.B.Clark	Root
4	<i>Vachaa Churna</i>	<i>Acorus calamus</i> Linn	Rhizome
5	<i>Sweta Sarshapa Churna</i>	<i>Brassica campestris</i> Linn	Seed
6	<i>Yava Kshara Churna</i>	<i>Hordeum vulgare</i> L	Whole plant

All the ingredients enlisted in Table No. 1 were procured in fine powdered form from Sundar Ayurved Pharmacy PG Department of Rasashastra evam Bhaishajya Kalpana, J. S. Ayurveda Mahavidyalaya, Nadiad and other additives viz; Gelatin, Glycerin, PEG 1500, PEG 4000, Theobroma oil and Bees wax used for Suppository preparation were purchased from local market of Nadiad. Equipment's and

instruments with specifications were mentioned in Table No. 2.

The raw material was authenticated in the Pharmacognosy Laboratory of the institute. Suppository prepared from *Phalavarti* (PS) was prepared in pharmaceutical laboratory of PG Department of Rasashastra Evam Bhaishajya Kalpana, J.S. Ayurved Mahavidyalaya, Nadiad

**Table 2** Equipment's and instruments with specification

Sr. No.	Name of Equipment/Instrument	Equipment/Instrument specifications
1	Suppository mould	Material – Stainless Steel, Universal shape, 2 gm, 12 Hole
2	Heating device	Rectangular water bath: company – LabRon, Model no - AN ISO 9001:2015

PS has been prepared with the principle Mixing-Melting-Moulding. The multiple batches with different proportions of ingredients were

formulated to minimize the errors during procedure and to finalize the material and proportion for base of suppository.

**Table 3** Different batches-Formulations of PS

Ingredients (%w/w)	Formulation Codes								
	PS-G1	PS-G2	PS-P1	PS-P2	PS-T1	PS-T2	PS-TB1	PS-TB2	PS-TB3
<i>Phalavarti Churna</i>	50%	50%	50%	50%	50%	50%	50%	50%	50%
<b>Gelatin</b>	15%	18%	-	-	-	-	-	-	-
<b>Glycerin</b>	20%	17%	-	-	-	-	-	-	-
<b>Water</b>	15%	15%	-	-	-	-	-	-	-
<b>PEG 1500</b>	-	-	45%	47.5%	-	-	-	-	-
<b>PEG 4000</b>	-	-	05%	2.5 %	-	-	-	-	-
<b>Theobroma oil</b>	-	-	-	-	60%	40%	48%	47%	45%
<b>Bees Wax</b>	-	-	-	-	-	-	2%	3%	5%

\*G: Gycero-gelatin, P: Polyethylene glycol (PEG), T: Theobroma oil, TH: Theobroma oil & Bees wax  
In the present study, 50% of the base was added by replacing *Guda* (Jaggery) in *Phalavarti Churna*. All the different batches of suppositories were prepared by molding method. The base was

dissolved at suitable temperature in water bath and then *Phalavarti Churna* was added and mixed homogeneously. The semi-liquid mixture

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obtained was poured into a pre-lubricated (liquid paraffin) mold of 2 g and allowed to be set.

Two batches were prepared with Glycero-Gelatin (PS-G1 and PS-G2), using it as a base. In batch PS-G2 increased quantity of Gelatin was incorporated in the than in PS-G1. Ingredients of *Phalavarti* were taken in glass mortar in *Churna* form and mixed well to get homogenous mixture. Gelatin powder was added to prepared mixture with continuous stirring. Entire mixture was melted on hot water bath and glycerine was added to molten mixture. The temperature of hot water bath should be maintained to 34 °C while melting Gelatin.

Two batches were prepared with Polyethylene glycol (PS-P1 and PS-P2), where it was used as a base. They are available in different physical forms depending on their molecular weight. Polyethylene glycol polymers with molecular weights between 200 to 1000 are liquid and those with molecular weights above 1000 are waxy solids<sup>5</sup>. Suppositories with different melting points and solubility can be prepared by using a mixture of polyethylene glycols with different molecular weights. In this study, two different molecular weights, namely PEG 1500 and PEG 4000, were incorporated as the base. In batch PS-P2 decreased quantity of PEG 4000 was incorporated than PS-P1. The temperature of hot water bath should be maintained to 43 °C while melting PEG 1500 and 50 °C while melting PEG 4000.

Two batches were prepared with Theobroma oil (PS-T1 and PS-T2), where different proportions

of base and *Phalavarti Churna* were incorporated. The temperature of the water bath should be maintained at 36 °C while melting theobroma oil to avoid the formation of unstable polymorph. In the batch PS -T1, 60% of the base was incorporated, while in the batch PS-T2, 50% of the base was incorporated.

Three batches were prepared with Theobroma oil and bees wax (PS-TB1, PS-TB2 and PS-TB3), where they were used as a base. By using a mixture of theobroma oil and beeswax, suppositories with different melting points and solubility can be prepared. By using a blend of theobroma oil suppository, the mechanical strength increased with increasing proportion of beeswax up to 5% w/w, and beyond this concentration, brittle suppositories were formed. The specified quantity of theobroma oil was melted over the water bath and removed when 2/3<sup>rd</sup> of theobroma oil melted. The grated beeswax also melted separately over the water bath and removed when liquefied completely. The molten theobroma oil added to the liquefied beeswax and stirred steadily. The temperature of hot water bath should be maintained to 62 °C while melting Bees wax.

A total of nine formulation were prepared to determine appropriate bases in a specific ratio to avoid batch-to-batch variation.

In the standardisation process, each and every step of the standard pharmaceutical parameters mentioned in the API was followed. All different formulated suppository i.e. PS-G1, PS-G2, PS-P1, PS-P2, PS-T1, PS-T2, PS-TB1, PS-TB2, PS-

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TB3 were analysed for their organoleptic characteristic. All were brown, torpedo shaped, smooth to the touch and had a characteristic odour. The formulated suppositories were cut longitudinally and the surface was examined with the naked eye. All suppositories were free of pits, cracks and fissures. The longitudinal section of the suppositories was plain and clear.

All different formulated suppository were analysed for Melting Temperature @ 37 °C and Hardness (kg/cm<sup>2</sup>). The hardness of prepared

suppositories were tested using Monsanto hardness tester. Hardness test was carried to determine mechanical strength. The suppositories should have adequate mechanical strength for handling and transportation.

The suppositories were analyzed for its preliminary parameters as per the Ayurvedic Pharmacopeia of India in quality control laboratory, J.S. Ayurveda Mahavidyalaya, Nadiad and accelerated stability study has been done at Vasu Research center, Vadodara, Gujrat.

**Table 4** Analysis of different batches-Formulations of PS

Sr. No.	Pilot batches	Parameters	
		Melting Temperature @ 37 °C	Hardness(Kg/cm <sup>2</sup> )
1.	PS-G1	24 min. 40 Sec.	0.5
2.	PS-G2	26 min 30 sec	1.0
3.	PS-P1	30 min 05 sec(* Start only to stick with test tube )	3.0
4.	PS-P2	28 min 24 sec(*Start only to stick with test tube)	2.5
5.	PS-T1	06 min 35 sec	1.5
6.	PS-T2	10 min 28 sec	1.5
7.	PS-TB1	14 min 16 sec	2.0
8.	PS-TB2	18 min 35 sec	3.0
9.	PS-TB3	20 min 32 sec	3.5

\* G: Glycero-gelatin base, P: Polyethylene glycol (PEG), T: Theobroma oil, TB: Theobroma oil with Bees wax

Among all the above formulations showed in Table No.3, PS-TB1 prepared from proportion of the base – theobroma oil (48%) and beeswax (2%), was selected for further analytical, stability and clinical study, prepared suppository has a

hardness of 2.0 kg/cm<sup>2</sup> and a melting time @ 37 °C is 14.16 min. showed in Table No.4. This is helpful in convenient handling, storage and release of drug after administration in rectum.

On basis of observation and result obtained from different formulation, three batches were prepared to develop the SMP of product (PS) showed in Table No.5.

**Table 5** Ingredients used for PS

Sr. No.	Name of ingredient	PS <sub>1</sub>	PS <sub>2</sub>	PS <sub>3</sub>
1	Madanphala Churna	5 g	5 g	5 g
2	Pippali Churna	5 g	5 g	5 g
3	Kustha Churna	5 g	5 g	5 g
4	Vachaa Churna	5 g	5 g	5 g
5	Shweta sarshapa Churna	5 g	5 g	5 g
6	Yava kshara Churna	5 g	5 g	5 g
7	Theobroma oil	28.8 g	28.8 g	28.8 g
8	Bees wax	1.2 g	1.2 g	1.2 g

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**Table 6** Result of three batches PS

Sr. No.	Parameters	PS <sub>1</sub>	PS <sub>2</sub>	PS <sub>3</sub>	Avg.
1	Wt. of Ingredients 1 to 8 (g)	60	60	60	60
2	Total wt. of Suppository (g) (12 No.)	46.12	46.31	46.34	46.25
3	Average wt. of one suppository (g)	3.84	3.85	3.86	3.85
4	Wt. loss (g)	13.88	13.69	13.66	13.74
5	Wt. loss (%)	23.13	22.81	22.76	22.9

The obtained suppositories have an average weight of 3.85 g. A total weight loss of 22.9% was observed, which is mentioned in Table No.6. This could be due to fact that material during preparation of PS to avoid cavity formation in the suppository, and also because

the material stick on vessel. An overall yield of 77.08% was obtained. The total time duration required for preparation of PS was 40 minutes. It is advised to pack PS in single unit rapped with aluminium foil and stored in suitable food grade plastic container at 2<sup>0</sup>C to 8<sup>0</sup>C in refrigerator.

**Table 7** Physico-chemical analysis of PS

Sr. No.	Parameters	Phalavarti Suppository			
		PS <sub>1</sub>	PS <sub>2</sub>	PS <sub>3</sub>	Avg.
1.	<b>Loss on Drying</b>	2.20 %	2.24 %	2.19 %	<b>2.21 %</b>
2.	<b>Acid value</b>	2.46	2.38	2.28	<b>2.37 %</b>
3.	<b>Peroxide value</b>	0.00	0.00	0.00	<b>0.00</b>
4.	<b>Melting Time @ 37<sup>0</sup> C</b>	14 min. 38 sec.	15 min 12 sec.	13 min 40 sec.	<b>14 min. 30 sec.</b>
5.	<b>Hardness (Kg/cm<sup>2</sup>)</b>	2.0	2.5	2.0	<b>2.1</b>
6.	<b>Softening Temperature</b>	40 <sup>0</sup> C	39 <sup>0</sup> C	41 <sup>0</sup> C	<b>40<sup>0</sup> C</b>
7.	<b>pH</b>	5.65	5.48	5.57	<b>5.56</b>
8.	<b>Specific gravity</b>	0.98	0.97	0.96	<b>0.97</b>

**Stability study of PS**

**Table 8** Result of stability study of PS

Sr. No.	Parameters	0 month	3 month	6 month
<b>Organoleptic Analysis</b>				
1	Description	Brown colour	Brown colour	Brown colour
2	Odour	Characteristic	Characteristic	Characteristic
<b>Physico-Chemical Analysis</b>				
1	Loss on Drying	2.17 %	2.20 %	2.23 %
2	Acid Value	2.24	2.34	2.85
3	Peroxide Value	0.00	0.00	0.00
4	Melting Time @37 <sup>0</sup> C	14 min. 40 sec.	12 min. 30 sec.	12 min. 10 sec.
5	Softening temperature	43 <sup>0</sup> C	44 <sup>0</sup> C	46 <sup>0</sup> C
6	pH	5.52	5.54	5.57
7	Specific Gravity@55 <sup>0</sup> C	0.96	0.96	0.96
<b>Heavy Metal Analysis</b>				
1	Lead	0.260 ppm	Not Applicable	
2	Cadmium	0.036 ppm		
3	Mercury	0.976 ppm		
4	Arsenic	0.556 ppm		
<b>Microbiological Analysis</b>				
1	Total Microbial Plate Count	1713 cfu/g	Not Applicable	1101 cfu/g
2	Total Yeast & Mould Count	582 cfu/g		167 cfu/g
3	Staphylococcus aureus	Absent		Absent
4	Salmonella Sp.	Absent		Absent

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5	Pseudomonas aeruginosa	Absent	Absent
6	Escherichia coli	Absent	Absent

**HPTLC Fingerprinting**

HPTLC study of PS was carried out in comparison. All tracks were scanned under 254 nm, 366 nm and 540 nm.

**Track 1:** *Phalavarti* Suppository (0 month)

**Track 2:** *Phalavarti* Suppository (6 month)

**Table 9** The result of the PS HPTLC Fingerprinting

Spot No.	R <sub>f</sub> @ 254 nm		R <sub>f</sub> @ 366 nm		R <sub>f</sub> @ 540nm	
	Track 1	Track 2	Track 1	Track 2	Track 1	Track 2
1.	0.29	0.29	0.40	0.40	0.11	0.11
2.	0.58	0.58	0.56	0.56	0.40	0.40
3.	0.60	0.60	0.58	0.58	0.45	0.45
4.	0.66	0.66	0.74	0.74	0.58	0.58
5.	0.77	0.77	-	-	0.63	0.63
6.	-	-	-	-	0.69	0.69
7.	-	-	-	-	0.74	0.74
8.	-	-	-	-	0.77	0.77
9.	-	-	-	-	0.81	0.81
10.	-	-	-	-	0.88	0.88

**Clinical study**

For this clinical study, patients fulfilling the diagnostic criteria of *Malavrodha* (functional constipation) were selected from O.P.D. of Kayachikitsa Department, P.D. Patel Ayurveda Hospital, Nadiad affiliated under Gujrat Ayurveda University, Jamnagar.

**Ethical committee clearance:** As this was clinical research, Institutional Ethics Committee (IEC) approval was taken prior to initiation of research vide its letter no. JSAM/IECHR/134/09-2021

**CTRI registration:** The study was registered in the Clinical Trial Registry of India with no. CTRI/2022/04/042002 on 21/04/2022

The total number of cases selected for the study was thirty, excluding dropout. These 30 patients were assigned for the clinical study of *Phalavarti*

Suppository (PS). The group was analyzed and result was estimated.

Criteria for inclusion was age between 20-70 years, Gender: male and female, Patient having symptoms of constipation as when bowel defecation occur three or fewer times a week with or without hard stool and are difficult to pass and Patient who not take any oral laxative medication

Criteria for exclusion was patients diagnosed with secondary constipation like underlying general neurological disease such as Parkinson’s disease, multiple sclerosis, disease associated with peripheral neuropathy, patients having conditions like intestinal obstruction, piles, fissure, fistula, pregnant women, lactating mother

**Study type:** Interventional

**Study design:** Single group pilot study

**Sample size:** 30 patients

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**Table 10** Treatment schedule for administration of PS

Sr. No.	Contain	PS
1	Kalpanaa	Phalavarti suppository
2	Maatra	1 suppository
3	Aushadhakaala	Any day time
4	Prayoga vidhi	Rectal route
5	Kaala	3 days
6	Follow up	Every day

All the patients will be assessed before and after treatment for clinical sign and symptoms of

constipation, as per No. of frequency mentioned in Table No. 13, Satisfactory or unsatisfactory described in Table No.14, duration of evacuation bowel showed in Table No.12 The Bristol stool from scale showed in Table No. 11. Treatment schedule for administration of PS was mentioned in Table No. 10.

**Table 11** The Bristol stool from scale<sup>6</sup>

Score	Type	Description
3	Type 1(constipation)	Separate hard lumps, like nuts (hard to pass)
2	Type 2(constipation)	Sausage-shaped but lumpy
1	Type 3(Ideal stool, Easy to defecate)	Like a sausage but with cracks on its surface
0	Type 4(Ideal stool, Easy to defecate)	Like sausage or snack, smooth and soft
-	Type 5(Lack of dietary fiber)	Soft blobs with clear-cut edges(passes easily)
-	Type 6(Diarrhoea)	Fluffy pieces with ragged edges, a mushy stool
-	Type 7(Diarrhoea)	Watery, no solid pieces entirely liquid

B.T.	A.T.DAY 1	A.T.DAY 2	A.T.DAY 3

**Table 12** Time duration of evacuation of bowel

Score	Time	Observation		
		Before	A.T.Day1	A.T.Day2
0	0-15min			
1	16-30min			
2	31-45min			
3	46-60min			
4	Not passed			

**Table 13** No. of frequency

Sr. No.	No. of frequency	Observation		
		Day 1	Day 2	Day 3
1	Once			
2	Twice			
3	More than two time			

Assessment of patient’s satisfaction on bowel evacuation – Bowel evacuation will be considered satisfactory when investigator get ‘no’ answer from the patient for all of the following

questions. Bowel evacuation will be considered satisfactory when investigator get ‘no’ answer from the patients for all of the following questions:

**Table 14** Questions for bowel evacuation satisfactory or unsatisfactory

Sr. No.	Question	Observation		
		Day 1	Day 2	Day 3
1	On evacuation straining? – Yes / No			
2	On evacuation lumpy or hard stool? – Yes / No			
3	Sensation of incomplete evacuation? – Yes / No			

Satisfactory / Unsatisfactory

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**Statistical analysis:** This is a single group, pre-post designed clinical study. Hence, obtained data were analyzed with descriptive statistics. Number of patients who had relief in various signs of functional constipation were calculated and tabulated with the help of descriptive statistics, and quantitative data i.e. Bristol stool

form scale and evacuation time period were evaluated with paired t test for hypothesis testing. Test was performed by using a level of P value < 0.01 were considered as significant. Average of the percentage improvement was calculated.

**Total Effect of *Phalavarti* suppository**

**Table 15** No. of frequency of 30 patients of *Malavrodha* (functional constipation)

Sr. No	No. of frequency	Before treatment		After treatment					
		N	%	Day 1- N	%	Day 2- N	%	Day 3- N	%
1	Not passed	15	50	-	-	-	-	-	-
2	Once	15	50	23	76.66	23	76.66	21	70
3	Twice	-	-	7	23.33	7	23.33	9	30
4	More than two time	-	-	0	0	0	0	0	0

The data of Table No. 15 shows that before treatment 50% patients were not passed the stool while 50 % had one time bowel evacuation. After treatment is was found that at day one 76.66% patients have one time bowel evacuation and

23.33% patients have twice bowel evacuation. At day two it was found the same. At third day 70% patients have one time bowel evacuation and 30% patients have twice bowel evacuation.

**Table 16** Assessment of patient's satisfaction on Bowel evacuation

Question No.	B. T.		After treatment			
	Yes	Percentage	Yes	Percentage	No	Percentage
1	30	100	1	96.66	29	96.66
2	30	100	3	76.66	27	90
3	30	100	5	16.66	25	83.33

The data mentioned in Table No.16 shows before treatment all patients had evacuation straining, lumpy and hard stool and sensation of incomplete evacuation. After treatment 96.66% patients have no evacuation straining, 90% patients have no lumpy or hard stool and 83.33% patients have no

sensation of incomplete evacuation. Which show the better effect of PS. As per the assessment criteria 83.33% bowel evacuation will be considered satisfactory.

**Table 17** Effect of *Phalavarti* suppository observed in 30 patients of *Malavrodha* (functional constipation)

Assessment criteria	N	Mean score		Difference of mean	Improvement (in %)	SD	Paired t value	P value
		BT	AT					
Bristol stool from scale	30	2.30	0.23	2.07	89.85	0.52	21.73	0.0017
Evacuation time	30	2.83	0.13	2.70	95.29	1.26	11.70	0.0021

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The data mentioned in Table No.17 shows that *Phalavarti* suppository (PS) installation in dose one PS for once a day for 3 days in affected patients of *Malavrodha* (functional constipation) showed significant results in all parameters. The significant result at  $< 0.01$  was found in Bristol stool from scale and evacuation time of stool. Calculation specifies that mean relief of therapy in type of stool was 89.85%, in Evacuation time 95.29% was found.

## DISCUSSION

The study was planned with the aim to develop a standard manufacturing process along with analytical profile and also to evaluate *Phalavarti* Suppository (PS) in *Malavrodha* (functional constipation).

**Two batches were prepared with Glycerogelatin (PS -G1 and PS -G2)**, in both batches, appearance and mechanical strength were not suitably achieved. These suppositories tend to disperse slowly in mucus secretions, so they may provide prolonged release of active ingredients. However, because glycerinated gelatin-based suppositories have a tendency to absorb moisture as a result of the hygroscopic nature of glycerin, they must be protected from atmospheric moisture, difficult to prepare as well as handle and this may cause inconvenience during storage.

**Two batches were prepared with Polyethylene glycol (PS-P1 and PS-P2)**, PEG also belongs to the class of laxatives. The suppositories of both batches become brittle when cooled too quickly

and may become brittle during storage, which may be due to the relatively high melting point of polyethylene glycols. Which may lead to slow release of the medicament and inconvenience for administration.

**Two batches were prepared with Theobroma oil (PS-T1 and PS-T2)**, the temperature of the water bath should be maintained at  $36^{\circ}\text{C}$  while melting theobroma oil to avoid the formation of unstable polymorph. Since the melting point of Theobroma oil is  $36^{\circ}\text{C}$ , it begins to liquefy during handling in warm weather. This may cause inconvenience during handling and administration.

**Three batches were prepared with Theobroma oil and bees wax (PS-TB1, PS-TB2 and PS-TB3)**, by using a mixture of theobroma oil and beeswax, suppositories with different melting points and hardness can be prepared. The proportion of beeswax was gradually increased from 2% to 5% to achieve sufficient hardness and to make the suppository easy to handle while administration. The  $\beta$ -form of Theobroma oil is most stable and suitable for the preparation of suppositories, which melts between  $30^{\circ}\text{C}$  to  $36^{\circ}\text{C}$ . If a higher temperature is applied to the theobroma oil, it transforms into another polymorphic form, i.e. the " $\alpha$ " form of theobroma oil, which melts at a temperature between  $20$ - $25^{\circ}\text{C}$  and is not stable for preparation. The temperature of the hot water bath should be maintained at  $62^{\circ}\text{C}$  while melting beeswax.

All suppositories showed good mechanical strength in the range of 1.50 to  $3.50\text{ kg/cm}^2$

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except PS-G1 and PS-G2 batches (Glycero-gelatin base). Suppositories prepared with PEG base was found harder than other combination. The melting time is the time required for the suppository to completely melt at  $37^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$  in a water bath, where  $37^{\circ}\text{C}$  is the rectal temperature. The melting time plays an important role in the release of the active ingredients

Among all the above formulations, PS -TB1, prepared from different proportion of the base – theobroma oil (48%) and beeswax (2%), was selected for further analytical, stability and clinical study, prepared suppository has a hardness of  $2.0\text{ kg/cm}^2$  and a melting time @  $37^{\circ}\text{C}$  is 14.16 min. Which is showed in table No. 4.

The average pH was 5.56, which was slightly acidic. The specific gravity of PS averaged 0.96, which was lower than that of water. The average value of loss on drying was 2.21%. The high value of LOD indicates high moisture content in the product. The average value of acid value and peroxide value for PS were 2.37 and 0.00 respectively, indicating the rate of degradation during prolonged storage, which affects the stability and shelf life. The average value of melting time at  $37^{\circ}\text{C}$  for PS was 14 minutes and 30 seconds. It provides information about the behaviour of a suppository when exposed to a maximum temperature of  $37^{\circ}\text{C}$ . The normal rectal temperature of humans averages  $37.5^{\circ}\text{C}$ . The higher the melting time is, delays drug effect. In general, the melting time should not exceed about 30 minutes. The average value of hardness for PS was  $2.7\text{ kg/cm}^2$ . This is evidence

that the suppository can be administered to patients under normal conditions. The average value of Softening temperature for PS was  $40^{\circ}\text{C}$  (Table 7). In general Softening temperature should be near about  $35^{\circ}\text{C}$  to  $40^{\circ}\text{C}$ . Heavy metal analysis of PS for Mercury, Lead, Arsenic and Cadmium were found below permissible limit, mentioned in Table No. 8.

The stability of the product is its ability to resist deterioration. It is always expressed in terms of shelf life. Samples were used for an accelerated stability study under the  $8^{\circ}\text{C} \pm 2^{\circ}\text{C}$  and sampling times were 0, 3 and 6 months.

The stability study of PS conscripted in Table no. 8 shoes that appearance of PS was brown and torpedo shaped and the odour of PS was characteristic and remained the same throughout the study. The LOD of PS was 2.17%, 2.34%, 2.85% for 0 months, 3 months and 6 months, respectively. There was comparatively increase in loss on drying value. Acid value and peroxide values were 2.24, 2.34, 2.85 and 0.00, 0.00, 0.00 for 0 months, 3 months and 6 months, respectively. A slight increase in Acid value and no change in peroxide value were observed. Specific gravity was 0.96, 0.96, and 0.96 for 0 months, 3 months, and 6 months, respectively. No change in specific gravity was observed.

The pH of the PS was weak acidic in nature. At 0 month pH was 5.52, which increased to 5.54 at 3rd month and 5.57 at 6th month. The viscous rectal fluid distributed over the surface is evaluated to be equal to form 0.5 to 1.25 ml with a pH of approximately 7 – 7.5 and very low

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buffering capacity. The absorption of the drug when administered rectally is significant according to the pH distribution theory. The Melting time @ 37 °C was 14 min 40 seconds, 12 min 30 seconds and 12 min 10 seconds for 0 months, 3 months and 6 months, respectively. This shows that the melting time decreases at @ 37 °C. The softening temperature was 43 °C, 44 °C and 46 °C, respectively. A gradual increase in the softening temperature of PS was observed. The physico-chemical parameter were not varied beyond 25% of the initial value, therefore PS is in accordance with the stability study as per the API guideline.

HPTLC study of PS was carried out in comparison, which was mentioned in Table No. 9. All tracks were scanned under 254 nm, 366 nm and 540 nm. At 540 nm, 10 components were spotted in track of PS at 0 months. In the trace after 6 months, the same 10 components were visible. Maximum components were spotted in track of PS at 0 months and after 6 months at this wavelength. At 254 nm, 5 components were spotted in the trace of PS at 0 month. The same 5 components were visible in the trace at 6 months. At 366 nm, 4 components were spotted in track of PS at 0 months. The same 4 components were visible in the track after 6 months. All components that were present at 0 months were also visible at 6 months, again indicating that the active components were not degrading.

### Mode of action *Phalavarti* suppository:

Acharya Charaka has been mentioned the distinctive digestion of food that the food

composed six *Rasas* immediately after it digested undergoes the stage of *Paripaaka*. In last stage of *Paaka* when the food reaches to the *Pakvashaya* it is absorbed by *Vahani* and get converted into solid mass and *Katurasa* due to this *Vaata* increased. The excessive increase of *Vaata* cause excessive hardness of stool and it lead to *Malaavrodha*. PS cause *Vaata Anulomana* and due to which evacuation of bowel occur.

The quantitative data i.e. Bristol stool form scale and evacuation time period were evaluated with paired t test. The total effect of PS was mentioned as per t Value and P Value. Calculation specifies that mean relief of therapy in Type of stool was 89.85%, in Evacuation time 95.29% was found.

## CONCLUSION

Acharya Shaarangdhara is first author who has mentioned definition of *Phalavarti* along with particular size and method of administration. The adopted method for preparation of *Phalavarti* Suppository can be considered as Standard Manufacturing Procedure (SMP). The analytical parameters (Organoleptic, Physico-chemical, Microbial Limit test, Heavy metal analysis and HPTLC fingerprinting) were not varied beyond 25% of initial value in accelerated stability study which reveals that, shelf-life of *Phalavarti* suppository can be considered as of 2 years as per CCRAS and API guideline. The *Phalavarti* Suppository has significant effect on *Malaavarodha* (functional constipation) clinically.

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