

PHARMACEUTICAL ANALYTICAL STUDY OF YASHTIMADHU GHRITA SUPPOSITORY

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ABSTRACT

Sushruta has specifically mentioned *Yashtimadhu ghrita* as *vedana sthapana* after any surgical intervention¹. Though the formulation is therapeutically much potent, there are fewer acceptances for practical applicability in today's era due to dosage form. Thus to bring them to consumers' compliance with better bio availability and shelf life, they need to be modified and developed into newer dosage form. Hence an attempt was made to convert the *Yashtimadhu Ghrita* into Suppository form. *Yashtimadhu ghrita* Suppository was prepared by using Cocoa butter and bees wax as a base. The Physical parameter of *Yashtimadhu ghrita* Suppository was within IP normal limits. Stability test of *Yashtimadhu ghrita* Suppository showed that, the Suppositories kept in room temperature were retained their shape, colour and uniformity only for 2 days; the Suppository kept in refrigerator did not undergo any physical changes up to 5 months.

Keyword: *Yashtimadhu ghrita*, *Yashtimadhu ghrita* Suppository, Stability test, Cocoa butter, Beeswax

INTRODUCTION

Pain is a natural sequel of every surgical procedure. The ability to alleviate post operative pain is one of the most noteworthy goals of surgery. Management of such pain has not yet received the concerned attention of research work. Ancient scholars considered that Ghee is able to do thousands of functions if processed accordingly. On the base of this, many *samskaras* are employed for ghee and they could obtain many pharmacological actions from it.

Sushruta has specifically mentioned *Yashtimadhu ghrita* as *vedana sthapana* after any surgical intervention¹. Previous works on *Yashtimadhu ghrita* in the

form of *Poorana* and *Pichu* have shown marked analgesic effect. Though the formulation is therapeutically much potent, there are fewer acceptances for practical applicability in today's era due to dosage form. Thus to bring them to consumers compliance with better bio availability and shelf life, they need to be modified and developed into newer dosage form with the help of modern pharmaceutical techniques.

Suppository is a solid dosage form of medicament for insertion into the body cavity other than oral root. They are in an acceptable form, safe and easier for administration with higher rate of bio availability,

faster onset in shorter peak and less wastage. The administration of suppository helps to avoid first pass metabolism, can target delivery system with lower dose and reduce systemic toxicity.

AIM AND OBJECTIVES

- ❖ To prepare and analyze suppository prepared from *Yashtimadhu Ghrita*.

MATERIAL AND METHODS

Ingredients for different ratio suppository²

In this study the active medicament is incorporated in a percentage w/w basis, finding displacement value has no relevance. So keeping this as reference by trial and error method suppositories of required hardness was prepared.

Table 1: Showing Ingredients for different ratio suppository

Sl no	Group	Ingredients	Quantity
1	A	<i>Yashtimadhu ghrita</i> Cocoa butter Beeswax Liquid paraffin	10ml 9ml 1ml 3 to 4 drops
2	B	<i>Yashtimadhu ghrita</i> Cocoa butter Beeswax Liquid paraffin	10ml 8.5ml 1.5ml 3 to 4 drops
3	C	<i>Yashtimadhu ghrita</i> Cocoa butter Beeswax Liquid paraffin	10ml 8ml 2ml 3 to 4 drops
4	D	<i>Yashtimadhu ghrita</i> Cocoa butter Beeswax Liquid paraffin	10ml 7ml 3ml 3 to 4 drops

Preparation of *Yashtimadhu ghrita* Suppository

- Initially, Mould was cleaned and dried. Mould was lubricated with Liquid paraffin and kept in the inverted position to drain.
- Cocoa butter and bees wax were grated separately and the china dish was heated over the water bath, to this measured quantity of *ghrita* was added
- The china dish was removed from the water bath, when the ghee liquefied completely
- The required quantity of Cocoa butter was also heated over the water bath and removed when 2/3rd of the Cocoa-Butter melted. The grated beeswax was also heated over the water bath and removed when liquefied completely
- All the three ingredients were mixed thoroughly to attain a uniform mixture and poured into the suppository mould until it over flows the mould
- The mould was kept in the refrigerator for 10-15 minutes. Later the excess material was scraped from the top of the mould and opened the mould and removed the suppositories
- Removed Suppositories were wrapped individually by butter paper and then with aluminum foil. Stored in airtight plastic container at 2⁰-3⁰C in refrigerator

Same procedure was adapted for group B, C, and D

OBSERVATION**Table 2:** Showing the Physical observation of each Suppository

Group	Nature	Colour	Melting time of <i>Ghrita</i>	Melting time of Cocoa butter	Melting time of Beeswax	Changes in room temperature
A	Smooth in touch and hard in consistency	Light yellow	37 ⁰ C	35 ⁰ C	61 ⁰ C	After 4hours the Suppository started to stick to the petridish due to leakage of <i>Ghrita</i> from the Suppository
B	Smooth in touch and harder than group A suppository	Light yellow	37 ⁰ C	35.3 ⁰ C	62 ⁰ C	No changes
C	Smooth in touch and harder than group B suppository	Light yellow	37 ⁰ C	35.9 ⁰ C	64 ⁰ C	No changes
D	Smooth in touch and harder than group C suppository	Light yellow	37 ⁰ C	36 ⁰ C	67 ⁰ C	No changes

Note: Formulation B was considered as ideal for the preparation of *Yashtimadhu ghrita* suppository

PRECAUTIONS TAKEN:

- Initially, Mould was cleaned and dried. Excessive lubricant was drained by keeping the mould in the inverted position
- The temperature of water bath was maintained to 36⁰C while melting of Cocoa butter to avoid the formation of an unstable polymorph
- Continuous stirring was done to form homogeneous mixture which leads to unavoidable entry of air bubbles. Mixture was poured carefully to avoid air bubbles into the mould
- Mixture was poured into the suppository mould until it over flows the mould, to prevent hole formation on the top of the Suppository

- Suppositories were wrapped individually by butter paper and then with aluminum foil and stored at 2⁰-3⁰C in refrigerator

ANALITICAL STUDY

The analytical study reveals out purity, chemical composition of formulation as well as their strength. Physico-chemical analyses of the drugs were carried out by using current analytical methodologies. In the present study analysis is carried out for *Yashtimadhu ghrita* suppository.

- Analytical parameter of *Yashtimadhu ghrita* suppository was carried out at Government college of pharmacy, Subedha circle, Bengaluru

ORAGNOLEPTIC CHARACTERS:**Table 3:** Showing Organoleptic characters of *Yashtimadhu ghrita* Suppository

Parameter	Observation
Colour	Light yellow
Appearance	Solid form and tapered at one end
Texture	Smooth

PHYSICAL EVALUTION**1. Weight variation test³****Procedure:-**

Weighed individually 20 suppositories taken at random and determined the average weight.

2. Disintegration Time⁴**Procedure:-**

The apparatus used for measuring the melting time of the entire suppository. The suppository was completely immersed in the constant temperature water bath

(37°C) and the time taken for the suppositories to melt or disperse in the water was measured.

3. Softening and Liquefaction temperature⁵

The softening and liquefaction temperature of the suppositories was determined by Setnikar and Fantelli method.

Procedure- The suppository was introduced into the upper part of the tube. A glass rod was placed on the suppository. The outer jacket was filled with distilled water and heated on a water bath with raising the temperature. When the suppository collapsed, the glass rod sunk by a distance of 5mm, the temperature at which this occurs is the softening temperature (ST). As the temperature of the water jacket rises, the suppository liquefied, it flowed through the 3-mm constriction of the glass tube of the apparatus. The temperature at which this occurs is the liquefaction temperature (LT).

1. Liquefaction Time⁶

Setnikar and Fantali apparatus was used to determine the liquefaction time.

Procedure- The outer jacket of the apparatus was filled with distilled water and heated on a water bath to a temperature of 37°C ±0.1. The sample suppository was introduced into the top of the tube and carefully pushed down until it rests on top of the stricture (constriction). A glass rod was placed into the tube so that it rests on the top of the suppository. The time taken by the glass rod which was resting on the suppository to reach the stricture (constriction) was measured.

2. Softening Time⁶

Procedure-

The outer jacket of the apparatus was filled with distilled water and heated on a water bath to a temperature of 37°C ±0.1. The sample suppository was intro-

duced into the top of the tube and carefully pushed down its length until it rests on top of the stricture (constriction). A glass rod was placed into the tube so that it rests on the top of the suppository. When the suppository collapses, the glass rod sinks by a distance of 5mm, the time at which this occurs is the softening time.

3. Determination of incubator liquefaction temperature⁷

In this procedure, air is used as the heating medium to provide gradually increasing temperature to liquefy the Suppository.

Procedure: This test was carried out in Hot air oven. The Suppository was kept inside the oven and temperature was set to 25°C. Later temperature was gradually increased to liquefy the Suppository. The time at which this occurs is the incubator liquefaction temperature.

4. Determination of collapsing weight⁸(CW)

This test is helpful for assessment of physical stability in respect to the shape of the suppository.

Procedure: Collapsing load tests were carried out by using Sergio Fantelli apparatus. The sample suppository was introduced into the top of the tube and carefully pushed down until it rests on top of the stricture (constriction). A glass rod was placed into the tube so that it rests on the top of the suppository. Weights are kept over the glass rod in increasing order and the weight at which the suppository crumbles was recorded.

Weight of the Glass rod: - 126gms

Weight of the 2Rs coin: - 6gms

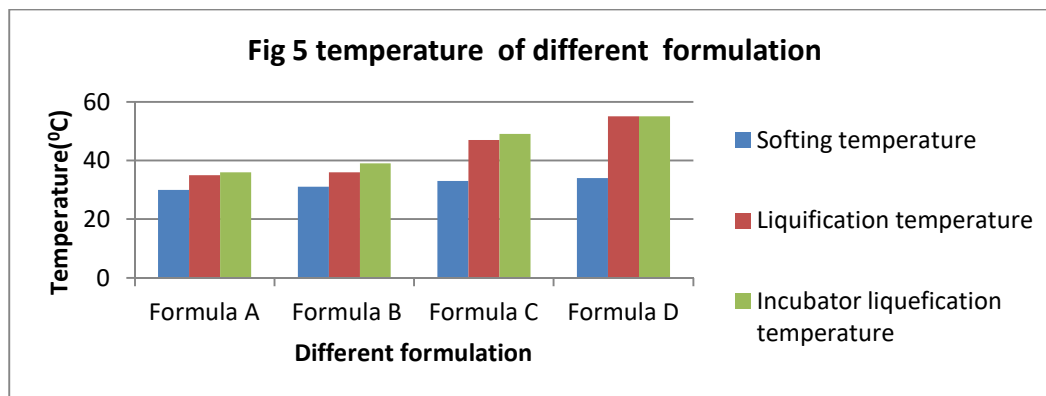
Weight of the 1Rs coin: - 4gms

Weight of the 5Rs coin: - 7gms

Table 4:- Showing Results of Physical Parameters of *Yashtimadhu ghrita* Suppository

Formula-tion code	Disintegra-tion time	Softening tempera-ture(°C)	Liquefaction tempera-ture(°C)	Softening time	Lique-faction time	Incubator lique-faction temper-ature(°C)	Collaps-ing weight
F-A	2.20mins	30°C	35°C	3mins	7mins	36°C	145gms
F-B	2.67mins	31°C	36°C	4mins	9mins	39°C	146gms
F-C	10mins	33°C	47°C	09mins	14mins	49°C	147gms
F-D	10mins	34°C	55°C	11mins	17mins	55°C	148gms

Average weight:-0.9945gms



8. Stability test⁹

Stability of a drug has been defined as the ability of a particular formulation in specified container, to retain within its physical, chemical, the therapeutic and toxicological specifications.

Drug instability of pharmaceutical formulation may be detected in some changes in the physical appearances, color, odor, taste or texture of the formulation.

PROCEDURE

Procedure:-

24 *Yashtimadhu ghrita* suppositories were individually wrapped by butter paper and later wrapped by aluminum foil without any air gap. These suppositories were kept in air tight plastic container and labeled.

Later these suppositories were divided into 2 groups for stability study in different temperature.

Group 1:- 12 *Yashtimadhu ghrita* suppositories were taken in air tight plastic container and kept in room temperature. Daily each suppositories were unwrapped and observed for any physical changes

Group 2:- 12 *Yashtimadhu ghrita* suppositories were taken in air tight plastic container and kept in refrigerator for 5 months. The refrigerator temperature was maintained to 2-3°C throughout the procedure and every 15 days each suppositories were unwrapped and observed for any physical changes

Observation

Group 1

Table 5: Physical characteristics of *Yashtimadhu Ghrita* Suppository (Group 1) in room temperature

Storage time in days	Storing temperature	Physical Characteristics				
		Colour	Homogeneity	Odor	Disintegration time	Weight
Initial (23-11-2018)	24°C	Light yellow	Uniform	-	2.6 minutes	1.002gms
24-11-2018	25°C	Light yellow	Become too sticky and lost its consistency	-	-	-

Group 2

Table 6: Physical characteristics of *Yashtimadhu Ghrita* Suppository (Group 2) in refrigerator temperature (2-4°C)

Storage time in days	Physical Characteristics				
	Colour	Homogeneity	Odor	Disintegration time	Weight
Initial (27-11-2018)	Light yellow	Uniform	-	2.67 minutes	1.0210gms
15 days	Light yellow	Uniform	-	2.66 minutes	1.0210gms
30 days	Light yellow	Uniform	-	2.66 minutes	1.0210gms

45days	Light yellow	Uniform	-	2.60mins	1.0210gms
60days	Light yellow	Uniform	-	2.60mins	1.0210gms
75days	Light yellow	Uniform	-	2.60mins	1.0210gms
90days	Light yellow	Uniform	-	2.60mins	1.0210gms
105days	Light yellow	Uniform	-	2.59mins	1.0210gms
120days	Light yellow	Uniform	-	2.60mins	1.0210gms
135days	Light yellow	Uniform	-	2.57mins	1.0210gms
150days	Light yellow	Uniform	-	2.56mins	1.0210gms

DISCUSSION

Discussion on *Yashtimadhu ghrita* Suppository preparation

In this study the active medicament is incorporated in a percentage w/w basis, finding displacement value has no relevance. So keeping this as reference by trial and error method suppositories of required hardness was prepared.

While preparing Suppositories beeswax was added to the formula as a base in different ratio to attain a good hardness and to increase the melting point of the formulation

Initially, Mould was cleaned and dried. Liquid paraffin was used as a lubricant as it is ideal for oily base and it facilitates the de-molding and smooth surface of the Suppository.

Whenever cocoa butter or glycerol-gelatin is used as a base for the preparation of Suppositories it is necessary to lubricate the mould otherwise Suppositories with smooth surface will not be obtained because of the sticky nature of the bases which will stick to the sides of the moulds. The lubricant applied must be of different nature than the base, otherwise it will be absorbed and fail to provide a buffer film between the Suppository and the metal of the mould

Excessive lubricant was drained by keeping the mould in the inverted position; otherwise it may give excess softness and oily layer to the outer surface the Suppositories

The temperature of water bath was maintained to 36⁰C while melting of Cocoa butter to avoid the formation of an unstable polymorph of Cocoa butter. Beta form is the most stable and suitable form for the preparation of suppositories. which melt between 30⁰C- 36⁰C, if more temperature was given to this ,it will convert into another form of polymorph(alpha form of Cocoa

butter) which melt in between 20-25⁰C temperature, and not suitable for the preparation.

Continuous stirring was done to form homogeneous mixture or else it may leads to unavoidable entry of air bubbles. A cold or frozen mould should not be used as fractures or fissures may occur throughout the suppository.

Mixture was poured into the suppository mould until it over flows the mould to prevent the formation of hollows on the tops of the finished suppositories because cocoa butter contracts on cooling and hollows are formed at the top of the suppositories.

The mould should be kept at room temperature for 5 minutes, so that the melt does not prematurely solidify as it is poured down the sides of the mould cavity. Premature solidification could result in unfilled mould tips and deformed suppositories.

The prepared Suppositories were rolled in butter paper to avoid moisture absorption. And then it is sealed in double wrap aluminum foil to avoid contamination.

As per the quantity mentioned, every Suppository should weigh about 1gm, but after preparation, each Suppository weighed in between 0.98 - 1.03gms as the air bubbles displaced the base in the moulds

Formula A(10ml:9ml:1ml) became Sticky when kept in room temperature for 4 hours, the *ghrita* started oozing out, It may be due to insufficient quantity of beeswax for the preparation. As it helps to increase the melting temperature of the formulation, other formulas are not shown any physical changes in room temperature. As the quantity of beeswax increases in the formula the melting temperature of the beeswax also increased

Discussion on Analytical study

Uniformity of Weight/ Weight variation –

The weight variation study for all the suppositories should be within the acceptable range, which indicates that calibration of mould was perfect.

If the weight is found to be too small, the mould may be incompletely filled or there may be air bubbles or the medicament is displaced by the base in the mould. If the weight is found to be too high, the scraping has been carried out improperly, or may be the mixture was not mixed homogeneously.

Not more than two suppositories should deviate by more than 5% and non deviate by 10% of the individual weights from average weight

➤ **Average weight:**-0.9945gms

Weight variation of the all the Suppositories were within limits of IP with % of deviation $\pm 5\%$, thus it passes the weight variation test as prescribed

Disintegration time:

The disintegration test determines whether suppositories are soften or disintegrate within a prescribed time when placed in an immersion fluid

Prepared Suppositories were subjected for Disintegration test as per IP.

It was observed that average disintegration time for Formula A and Formulation B were under the Standard normal limits (Not more than 30 minutes for fat based Suppositories).

But the average DT for Formula C and Formula D were not within the limits it may be due the variation in the quantity of beeswax used for the preparation compared to formula A and B

Liquefaction time

The time taken by the Suppositories to melt completely within $37\pm 1^\circ\text{C}$ gives the liquefaction time.

Liquefaction time of the Formula A and Formula B were within $37\pm 1^\circ\text{C}$. This indicates, both the formula will melt at body temperature but Formula C and D did not Liquefy at $37\pm 1^\circ\text{C}$. Thus Formula C and D cannot be suitable for Suppository preparation, as they did not liquefy within $37\pm 1^\circ\text{C}$. This variation may be due the higher percentage of bees wax in the formulation. Beeswax more than 15% as a base alter the melting temperature of any formula

Softening and Liquefactions temperature

The temperature at which the suppositories soften and liquefied was observed

The Softening Temperature and Liquefaction temperature of Formula A and B are comes under the normal limits (35°C to 40°C). But Formula C and D, they exceeded the normal limits, it may be due the high percentage of beeswax in the formulation, The beeswax increase the melting temperature of the formulation. Hence these two formulations are not suitable for the preparation of Suppository

Determination of incubator liquefaction temperature

These values are helpful to know the upper limit of the temperatures up to which the suppositories can be safely stored without undergoing changes in shape.

The incubator liquefaction temperature was slightly higher in relation to the LT was obtained for all formulations. The incubator liquefaction temperature of Formula B was 39°C , after this temperature it may lose its consistency and may undergo some shape variation. Thus it should be stored below 39°C .

Determination of collapsing weight (CW)

This test is helpful for assessment of physical stability in respect to the shape of the suppository

The collapsing weight of Formula B was 146gms. It can sustain this much mechanical weight while transporting to one place to another

Stability test

The Suppositories kept in room temperature are retained their shape, colour and uniformity only up to 2 days, it may be due the low liquefaction temperature of Cocoa butter ($30^\circ - 36^\circ\text{C}$), and the Softening time of the Suppository was 30°C , so after this temperature they undergo changes in shape and consistency. So Cocoa butter based Suppositories are not suitable to keep in the room temperature, and not suitable for hot climate. The Suppository kept in refrigerator, did not undergo any physical changes up to 5 month

CONCLUSION

The *Yashtimadhu ghrita* Suppository was prepared by *Yashtimadhu ghrita*, Cocoa butter and beeswax as base. Physical test showed *Yashtimadhu ghrita* Suppository was Light yellow in colour and no particular odor. Physical parameter showed that in *Yashtimadhu ghrita* Suppository, Weight variation-passed, Average weight:-0.9945gms, Disintegration time-

2.66minutes+_{-0.015}, Softening temperature-31⁰C+_{-0.1}, Liquefaction temperature-36⁰C+_{-0.12}, Softening time-4minutes+₋₀, Liquefaction time-9 minutes+_{-0.1}, Incubator liquefaction temperature-39⁰C+_{-0.02}, Collapsing weight-146gms

Stability test of *Yashtimadhu ghrita* Suppository showed, the Suppositories kept in room temperature are retained their shape, colour and uniformity only up to 2 days, the Suppository kept in refrigerator, did not undergo any physical changes up to 5 months.

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