



## Original Research Article (Clinical)

# A randomised controlled trial to evaluate the effect of *Gandhaka Rasayana* rectal suppository in post operative pain management in ano-rectal disorders



Ranjani Deshpande <sup>a,\*</sup>, Shilpa Prakash N <sup>b</sup>, Manjunath Swaroop <sup>c</sup>, Mahalakshmi Muralimohan <sup>d</sup>, Ashwin Shetty <sup>d</sup>

<sup>a</sup> Consultant Ayurveda Surgeon, Sritulasi Ayurvedalaya, Bengaluru, India

<sup>b</sup> Associate Professor, Government Ayurveda Medical College Bengaluru, India

<sup>c</sup> Director, Consultant Anaesthesiologist and Pain Specialist, JINKA Hospital (Unit of KMC), Bengaluru, India

<sup>d</sup> Consultant Physician, Aprameya Ayurveda, Bengaluru, India

## ARTICLE INFO

## Article history:

Received 11 October 2019

Received in revised form

25 June 2021

Accepted 4 July 2021

Available online 1 February 2022

## Keywords:

Ayurveda

Rectal suppository

*Guda varti*

*Gandhaka rasayana*

Post-operative pain

Diclofenac sodium

## ABSTRACT

**Background:** Poorly managed post-operative pain can lead to complications and prolonged rehabilitation. Pain Management after ano-rectal surgery becomes important as it could hamper day to day activities, disturb sleep, alter appetite and bowel evacuations and decrease the quality of life. According to *Acharya Sushruta*, pain (*Shoola*) cannot be produced without *Vata dosha* and *Shoola* (pain) is inevitable after *Shastra* (surgical) *Karma* (procedure) for which *Basti* (enema) is usually the management of choice. Rectal suppositories are one such dosage form that are extensively used in post-operative pain management especially after ano-rectal surgery.

**Materials and method:** In the study, a total of 40 patients who fulfilled the inclusion criteria were randomly divided to two groups comprising of 20 patients each. Patients of Group A were treated with *Gandhaka Rasayana* rectal suppository and Group B were treated with Diclofenac Sodium rectal suppository for post-operative 5 days.

**Results:** The overall comparative results revealed a statistically significant improvement of 85% in Group A and 80.39% in Group B. *Gandhaka Rasayana* which is *Tridoshashamaka*, *Vatamaya Nivaraka* (ameliorates diseases caused by *Vata dosha*), *Agnivardhaka* (improves appetite and metabolism) and *Shoolahara* (reduces pain) attains micro particle size with 88 *Bhavana* (trituration) that can be readily absorbed by the rectal mucosa to exhibit the required therapeutic action.

**Conclusion:** The *Bhavana Dravya* (medium of trituration) used in the preparation of *Gandhaka Rasayana* have proven analgesic, anti-inflammatory, anti-bacterial action and is also said to promote wound healing. The present study reveals that there is significant effect of *Gandhaka Rasayana* rectal suppositories in managing post-operative pain of ano-rectal disorders.

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## 1. Introduction

Pain is experienced as a result of acute or chronic tissue damage and its mere association is an unpleasant sensory and emotional experience [1]. The International Association for the Study of Pain recognizes pain relief as a human right. Surgery suppresses the immune system [2] and inevitably all patients who undergo surgical procedure experience an acute post-operative pain. Poorly

managed postoperative pain can lead to complications and prolonged rehabilitation [3] Pain management after ano-rectal surgery becomes important as it could hamper day to day activities, disturb sleep, alter appetite and bowel evacuations adversely affecting quality of life of the patient. *Shoola* (pain) is the *pradhana lakshana* (major symptom) that is seen in patients after *shastra karma* (operative procedure). Ayurveda opines that pain cannot be produced without *vata dosha* and *bastikarma* is the best procedure for treatment of vitiated *vata dosha*. Though *basti karma* is the treatment of choice, it involves a lot of practical issues like difficulty in

\* Corresponding author.

E-mail: [ranjani.rsdeshpande@gmail.com](mailto:ranjani.rsdeshpande@gmail.com).

Peer review under responsibility of Transdisciplinary University, Bangalore.

following strict regimens related to diet and activities of daily routine during the entire course of treatment. The preparation and administration of *basti dravya* (medicament) uses a lot of resources and is time consuming. The medicament must always be warmed before instillation and care should be taken while administering the medicament to avoid re injury of the operated wound for which the patient will always need assistance. All of these practical difficulties can be avoided by using an appropriate *vata-pittahara* and *shoola-hara dravya* converted to a suppository (*varti*) form by being molded with a *snigdha* (unctuous) *dravya* (substance) which still satisfies the definition of *basti* (*vasunivase*-staying within) by staying in the rectum for a stipulated period of time and also facilitating a quick absorption of the drug released.

Rectal suppositories are one such dosage form that are widely used in managing post-operative pain especially after ano-rectal surgeries. Sodium diclofenac suppository belongs to NSAID category which has both systemic and local analgesic effects. When used locally as a suppository it reduces the impact of pain mediators and has a rapid onset of action and slower rate of absorption [4]. Though diclofenac rectal suppository is widely used, it is associated with side effects such as headache, dizziness, light headedness, drowsiness, loss of appetite, local rectal irritation, ringing in the ears and rectal bleeding [5].

*Gandhaka Rasayana* is a *Rasayana* (rejuvenator) and possesses varied therapeutic action. It is described to have *tridosha shamana*, *vata amaya nivarana* (ameliorates diseases caused by *vata dosha*), *agni vardhana* (improves appetite and metabolism) and *shoola harana* (pain reducing) properties (*Rasa Tarangini*, *Yoga Ratnakara* [6]). Its possible usage as an analgesic was hypothesized in the current study owing to the potent analgesic, anti-nociceptive and anti-inflammatory properties of all the 11 *bhavana dravya* (medium of trituration) used in the preparation of *Gandhaka Rasayana* (see Table 1). Further, it was decided to try *Gandhaka Rasayana* as a rectal suppository to manage pain in post-operative cases of ano-rectal disorders in comparison with the standard drug Sodium Diclofenac rectal suppository.

In the current study, *Gandhaka Rasayana* was classically prepared with 88 *bhavana* (trituration) as per the text *Rasa Tarangini* [7] and was converted to a rectal suppository form using the Fusion Moulding Technique along with the binding agent Cocoa Butter in the ratio 0.3 gms:1.7 gms (*Gandhaka Rasayana*:Cocoa Butter).

Cocoa Butter (1.7 gms) was liquefied on a hot water bath and *Gandhaka Rasayana* (0.3 gms) was added to the melted cocoa butter and stirred well to form a homogenous mixture. The molds were sterilized using surgical spirit. The mixture was drawn into a 10 ml syringe and carefully instilled into the calibrated molds without letting air bubble formation. This procedure was carried out in a

single stretch for every mold. The molds were refrigerated for 30–60 min. After refrigeration, and ensuring the appropriate hardness, molds were carefully opened, suppositories collected and packed in sterile air lock covers.

## 2. Methodology

### 2.1. Trial design

The current study is a randomized parallel group study with allocation ratio 1:1. Study was approved by Government Ayurveda Medical College Institutional Ethical Committee (Ref. No/GAMC/MED15/2017–2018). Informed consent was obtained from each participant prior to recruitment. The trial was registered with the Central Trial Registry of India (CTRI/2018/09/015,826).

### 2.2. Eligibility criteria for participants

#### 2.2.1. Inclusion criteria

Post-operative patients between the age group of 20-60 years who underwent Fissurectomy/Haemorrhoidectomy/Fistulotomy.

#### 2.2.2. Exclusion criteria

Patients who were: pregnant or lactating, operated for fissure-in-ano/haemorrhoids/fistula-in-ano associated with IBS or diagnosed with Crohn's disease, in immune compromised state, suffering from systemic diseases like diabetes mellitus, tuberculosis, rheumatoid arthritis or positive for human immunodeficiency virus (HIV), venereal disease and hepatitis-B.

### 2.3. Settings and locations where the data was collected

Operated cases of Fissurectomy/Haemorrhoidectomy/Fistulotomy from Sri Jayachamarajendra Institute of Indian Medicine (SJIIM) fulfilling the eligibility criteria were recruited in the present study.

## 3. Intervention

Two, 0.3 gms of *Gandhaka Rasayana* rectal suppositories and one, 100 mg of Voltaren Sodium Diclofenac rectal suppository was inserted into the rectum of patients from Group A and B respectively after the operative procedure. Anal pack was placed and pressure bandage was applied. After 12 hours another similar administration was repeated. The treatment was repeated for 5 days.

Post-operative regimen for patients from both groups included removal of anal pack 6th hour post operatively and daily dressing with betadine. They were also prescribed 6 g of *Sonamukhi* (*Cassia*

**Table 1**  
*Bhavana dravya* used in preparation of *Gandhaka Rasayana* and its pharmacological activities [8–16].

Sl no	Content	Pharmacological Activity
1	<i>Gandhaka</i> (Sulphur)	<i>Kaphavatahara</i> , <i>uttama rasayana</i> (rejuvenator), <i>agnivardhaka</i> (improves appetite and metabolism), <i>twak rogahara</i> (cures diseases of skin)
2	<i>Godugdha</i> (Cow's milk)	<i>Godugdha</i> being <i>madhura</i> in <i>rasa</i> and <i>vipaka</i> , <i>sheeta</i> in <i>veerya</i> helps in reducing <i>teekshnata</i> of <i>gandhaka</i> (helps in reducing the pungentness and toxins)
3	<i>Twak</i> ( <i>Cinnamomum zeylanicum</i> )	Anti-nociceptive, anti-inflammatory, anti-microbial, enhances wound healing
4	<i>Ela</i> ( <i>Elettaria cardamomum</i> )	Anti-inflammatory, analgesic, anti-bacterial
5	<i>Patra</i> ( <i>Cinnamomum tamala</i> )	Anti-inflammatory and analgesic effect.
6	<i>Nagakeshara</i> ( <i>Mesua ferrea</i> )	Analgesic, anti-inflammatory and anti-microbial activity.
7	<i>Guduchi</i> ( <i>Tinospora cardifolia</i> )	Possess both central and peripheral analgesic activity involving opioid receptor mechanism and inhibition of prostaglandin synthesis mechanism.
8	<i>Triphala</i> ( <i>Phyllanthus emblica</i> , <i>Terminalia Chebula</i> and <i>Terminalia bellirica</i> )	Potent analgesic activity
9	<i>Bhringaraja</i> ( <i>Eclipta alba</i> )	Anti-nociceptive, analgesic and anti-bacterial activities
10	<i>Ardra</i> ( <i>Zingiber officinale</i> )	Anti-inflammatory, analgesic and antipyretic activity

*angustifolia*) choorna with hot water at bedtime and hot water sitz bath –20 mins twice a day for 5 days.

The first suppository was inserted during post-operative wound dressing by the surgical team member and the next dose was inserted at, 12th hour post surgery by the patient. Participants were instructed with all necessary information needed for self insertion of rectal suppositories. A general follow up was done on the 15th post operative day to assess pain and the status of post-operative wound.

#### 4. Outcomes

##### 4.1. Primary Outcome

Patients were assessed daily in the post-operative period for 5 days for pain subjectively, using Visual Analogue Scale [17], objectively for Tenderness using Soft Tissue Tenderness Grading System [18] and for sphincter tone using Digital Rectal Examination Scoring System for Resting Pressure and Squeeze Pressure [19]. A general follow up was done on the 15th day post operatively to assess pain and the status of post-operative wound. However, this was not considered as a statistical outcome measure for the present study.

##### 4.2. Secondary outcome

As this was an exploratory study, we also tried to explore if the drug had any effect on wound healing and this was recorded clinically everyday assessing the progress of healing based on stage wise clinical signs. The wound was observed for appearance and filling up of healthy granulation and maximum approximation of operated wound within 5 days. The need for oral analgesics, pain score comparison between individual operative procedures, average duration taken for relief from pain after insertion of suppository and adverse drug reaction were also assessed.

#### 5. Sample size and randomisation

A convenient sample of 40 patients, 20 in each group was randomized with simple random technique based on footfalls in our clinical department. Alternation of patients to each group was done by the guide. The estimated duration of the trial was for one year. Trial ended 4 months prior to estimated date with efficient procurement of required resources. The template of consort flow diagram is shown in Fig. 1.

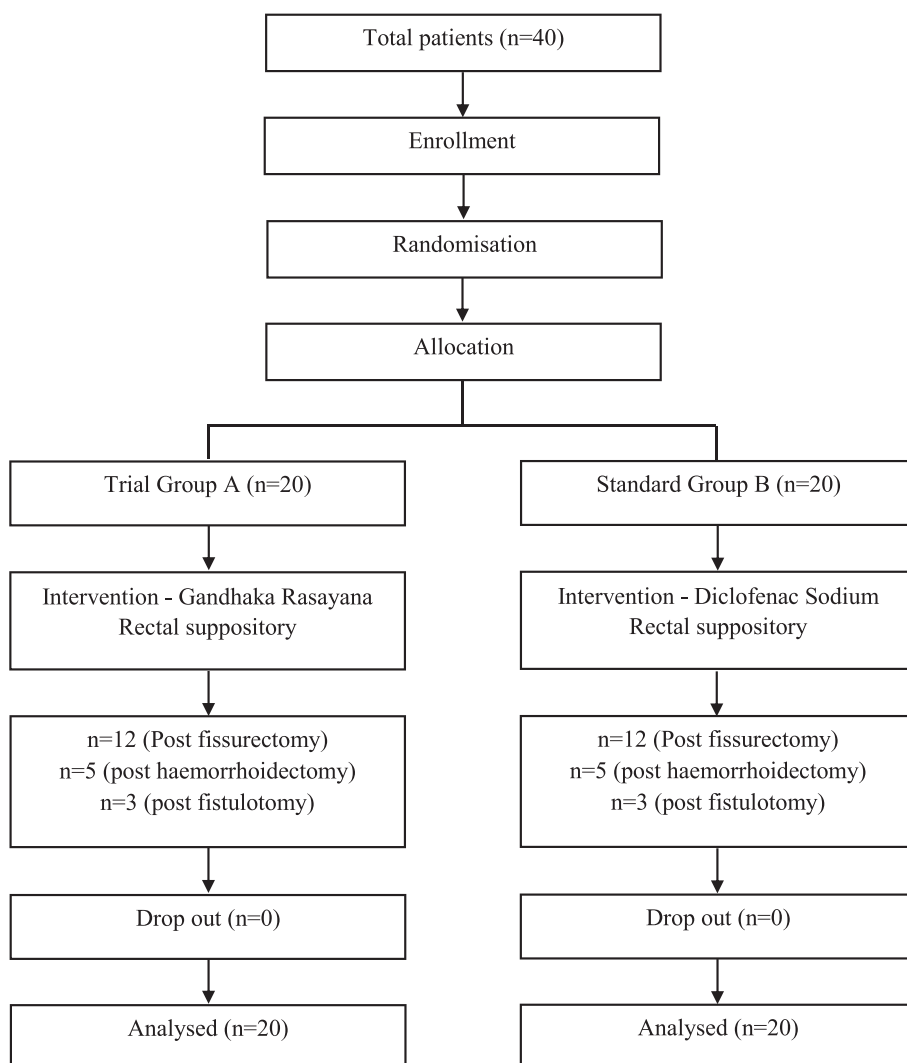


Fig. 1. Consort Flow Chart

**Table 2**  
Details of mean score of subjective, objective parameters and pain score of individual procedures between groups.

Parameter	Group A			Group B		
	POD 1	POD 5	%	POD 1	POD 5	%
VAS	1.40	0.00	100%	2.75	0.65	76.36%
STTGS	0.90	0.00	100%	1.55	0.15	90.32%
ST-SP and RP	1.00	0.00	100%	1.65	0.25	84.85%
Average Pain Score Of Individual Procedures Between Groups						
Fissurectomy	0.48			1.71		
Haemorrhoidectomy	0.48			1.88		
Fistulotomy	0.12			1.32		

- POD- Post Operative Day
- VAS-Visual Analogue Score
- STTGS-Soft Tissue Tenderness Grading System
- ST-Sphincter Tone
- SP-Squeeze Pressure
- RP-Rest Pressure

5.1. Statistical methods

Unpaired Student t test was used to compare groups for primary outcome.

The mean of recorded pain score was evaluated of patients undergoing either fissurectomy/haemorrhoidectomy/fistulotomy from Group A and was compared with the mean pain score recorded by patients from Group B.

Study flow chart.

6. Demographic detail and baseline data

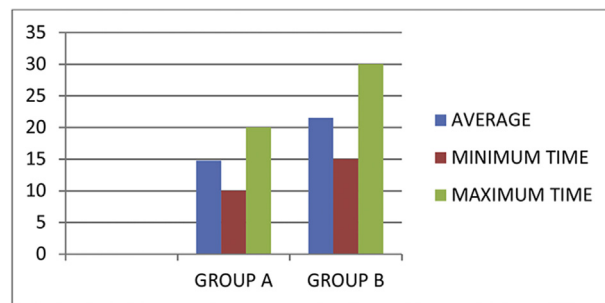
Out of 40 patients enrolled in the study, 21 were males and 19 females, with maximum patients between the age group of 28–37 years in both the groups. It was also seen that maximum of 29 patients were accustomed to mixed diet (Veg+Non-veg diet).

7. Outcome and estimation

The results evaluated using subjective and objective variables were classified under four groups as poor response, moderate response, good response and excellent response. Poor response was with < 24% reduction, moderate response was with 25–49% reduction, good response was with 50–74% reduction and excellent response was with 75–100% reduction in subjective and objective parameters.

8. Results

Statistical analysis for pain using Visual Analogue Scale in Group A showed mean score of 1.40 on post operative day 1 which was reduced to 0.00 on post operative day 5 with 100% improvement and the mean score in group B was 2.75 on post operative day 1



**Fig. 3.** Details showing the minimum, maximum and average duration taken for onset of analgesia between groups.

reduced to 0.65 on post operative day 5 with 76.36% improvement in (Table 2).

Assessment of Soft Tissue Tenderness Grading System in Group A showed mean score of 0.90 on post operative day 1 reduced to 0.00 on post operative day 5 with 100% improvement and the mean score which was 1.55 on post operative day 1 reduced to 0.15 on post operative day 5 with 90.32% improvement in Group B (Table 2).

Assessment of Sphincter Tone for Squeeze and Rest Pressure in Group A showed that the mean score which was 1.00 on post operative day 1 was reduced to 0.00 on post operative day 5 with 100% improvement and the mean score which was 1.65 in Group B on post operative day 1 was reduced to 0.25 on post operative day 5 with 84.85% improvement (Table 2).

Assessment for the need of oral analgesics was done by advising the use of oral analgesics only on perception of severe pain and the need for such consumption was recorded (Fig. 2). In Group A the mean score of use of analgesics reduced from 0.35 on POD1 to 0.00 on POD5 whereas from 1.10 on POD1 to 0.45 on POD5 in Group B. The observation indicates considerable reduction in need for the use of analgesics on subsequent post-operative days in Group A as compared to Group B.

Assessment on wound healing revealed a total of 9 patients from Group A in whom almost a complete closure of the operated wound was observed within the study period (pictures attached).

Pain Score was also recorded against individual operative procedure as the threshold of pain perceived with each of the procedures varies and it was seen that the trial drug showed better results with individual operative procedures too in comparison to the standard drug (Table 2).

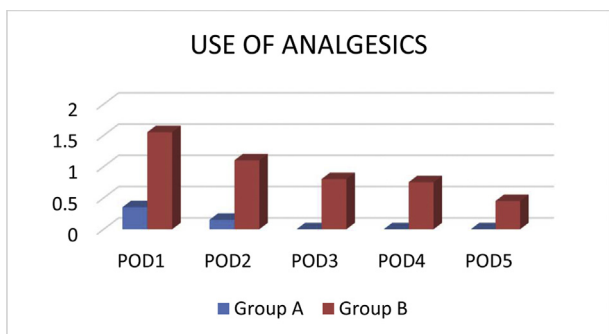
Assessment on average duration taken for relief from pain after insertion of suppository was seen to be 14.75mins in Group A and 21.5mins in Group B showing quicker onset of action in Group A (Fig. 3).

Patients were asked to report any sort of discomfort experienced during the study and up to 15th day of follow up. Two patients from Group B reported prolonged bleeding up to POD10 and POD12 respectively.

Comparative analysis of the overall effect of the treatments in both the groups was done statistically with Unpaired T Test. The

**Table 3**  
Table showing details of assessment of total effect of therapy.

Effect of treatment	No of patients in group A	No of patients in group B
Class	Grading	
0–25%	Poor improvement	0
26–50%	Moderate improvement	0
51–75%	Good improvement	3
76–100%	Excellent improvement	17



**Fig. 2.** Details showing the need for oral analgesics between groups.

**Table 4**  
Table showing details of comparative results of Group-A and Group-B.

Signs and Symptoms	Group A (Mean Score)	Group B (Mean Score)	T Value	P Value
Pain-visual analogue scale	0.44	1.71	9.12	<0.05
Soft tissue tenderness grading system	0.27	0.81	6.22	<0.05
Sphincter tone assessment scale (s.p)	0.29	0.83	5.90	<0.05
Sphincter tone assessment scale (r.p)	0.29	0.83	5.90	<0.05
Use of analgesics	0.10	0.93	5.29	<0.05

test shows that the treatment efficacy is statistically significant in both the groups. In Group A, overall result was 85% and Group B overall result was 80.39%. Thus Group A shows better overall result in comparison to Group B (Tables 3 and 4).

## 9. Discussion

Post-operative pain is a specific type of acute pain that inevitably causes tissue trauma and release of potent mediators of inflammation and pain [20]. Poorly managed post-operative pain could potentially hamper the daily routine of the patient. Failure to manage the same precisely could lead to its chronicity.

The current study was undertaken in post-operative cases of fissurectomy, haemorrhoidectomy and fistulotomy and for the first time an Ayurvedic rectal suppository was explored to study its potential benefits in reducing pain compared to Diclofenac Sodium rectal suppository. During the study we found that patients treated with *Gandhaka Rasayana* rectal suppository had improved therapeutic outcomes compared to the patients treated with Sodium Diclofenac rectal suppository. While the patients demonstrated good compliance to the treatment, many conveyed they would prefer oral pain medication. Preparation of suppositories demanded high precision and skillfulness. Care was taken at every step to achieve good finish of the end product. Excessive heating of cocoa butter was noticed to have an effect on solid configuration of suppository at room temperature leading to early liquefaction on storage. Accumulation of air bubbles within the mould cavity during its filling rendered suppositories brittle leading to breakage.

*Vata prakopa* (aggravation of *vata dosha*) inevitably follows the process of *abhighata* (injury), here in the context *shastra karma janita abhighata* (post operative tissue injury). Thus the management of *shastra karma janita vrana* (post operative wound) should focus on *prakupita vata dosha shamana* (pacification of aggravated *vata*), *shoolaharana* (reduction in pain) and *vrana-ropana* (wound healing). Thus in the current study *Gandhaka Rasayana* which possesses all the above mentioned properties was selected and converted to a *varti* i.e. rectal suppository form and was inserted into the rectum.

*Bhavana* (trituration) *samskara* (process) enhances the quality of the drug. *Gandhaka Rasayana* used in this study was classically prepared with 88 *bhavana* using 11 *bhavana dravya* (drugs used for trituration) which possess potent analgesic, anti-inflammatory and antinociceptive properties (Table 1). The classical method of preparation of *Gandhaka Rasayana* would have probably played a vital role in the therapeutic action exhibited in comparison to a pharmaceutical preparation of the same which typically does not follow this process.

The bio availability of drugs from suppositories is greatly influenced and is dependent on rectal vein morphology, drug's particle size and the process of diffusion. The superior rectal vein drains into the inferior mesenteric and the portal system. The middle and the inferior rectal veins enter the systemic venous circulation via the internal iliac veins and bypass hepatic first pass metabolism. The drugs delivered through suppositories to the lower and middle rectal veins are thus

absorbed rapidly and effectively. It has been accepted that at least 50–70% of drugs suitable for rectal administration is absorbed via direct pathway described above. Therefore a drug administered rectally will in general have a faster onset and higher bioavailability [21].

The Ph of rectal fluid is 7.5 with no buffering capacity. Hence, the drug inserted through the rectum remains chemically stable [21]. This means the drug will reach the circulatory system with significantly less alteration and in greater concentration. The rectal mucosa is better capable of tolerating various drug related irritations compared to the gastric mucosa. The drug absorption by the rectal route is also governed by particle size [21]. This implies that drug delivered through rectal route must have very small particle size for its absorption.

The drug release behavior is important in case of drugs having micro particle size. Colo-rectal absorption is a simple diffusion process through the lipid membrane [21]. Diffusion is a rapid drug release process where the drug is uniformly distributed or dissolved in the matrix and the release occurs by erosion of the matrix. In case of rectal suppository the binding agent melts at rectal temperature and releases the drug for rectal absorption.

According to a study, *Gandhaka Rasayana* prepared with the classical method of 88 *bhavana* renders its particle size that ranges between 0.5 and 875  $\mu\text{m}$  and that 90% of particles are below 26.92  $\mu\text{m}$  [22]. This infers that the particle size of *Gandhaka Rasayana* is very small and thus capable of getting easily absorbed through the rectal mucosa. In *Gandhaka Rasayana* rectal suppository, the active drug, the *Gandhaka Rasayana* is dissolved in cocoa butter which acts as the binding agent to form a solid suppository. The suppository thus when inserted into the rectum melts and dissolves at the rectal temperature and releases the drug, i.e. the *Gandhaka Rasayana*.

There are many sources available on management of post operative pain using other Ayurvedic interventions like *basti* and *pichu* from the grey literature however, peer reviewed data is not available for comparison for a Ayurvedic drug being used as a rectal suppository because of which standard drug from modern medicinal system was selected for comparison. Based on the clinical outcomes from the present study, it can be hypothesized that *Gandhaka Rasayana* rectal suppository follows the same pharmacokinetics as any other rectal suppository studied under modern pharmacology and future studies are recommended for confirmation.

## 10. Conclusion

Comparative analysis of the overall effect of treatment for post operative pain relief in both groups showed better results in participants treated with *Gandhaka Rasayana* rectal suppository. Added relief from pain and good post operative wound healing was observed compared to the participants treated with Sodium Diclofenac rectal suppository. Though the results of the new drug seem to be exaggeratively positive, the results obtained are a sequel of thorough analysis of procured data and warrants further study.

### Source of Funding

None.

### Conflict of interest

No conflict of interest.

### Author contributions

Dr Ranjani Deshpande: Conceptualization, Methodology, Investigation, Resources, Writing Original draft.

Dr Shilpa Prakash N: Supervision and Project Administration.

Dr Manjunath Swaroop: Supervision.  
 Dr Mahalakshmi Muralimohan: Resources.  
 Dr Ashwin Shetty: Resources.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jaim.2021.07.001>.

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