# Use Of Suppositories In The Treatment Of Hemorrhoids

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**Abstract**
The aim behind of this study was to revise the importance of the presence of rectal drug delivery system amongst the medications used to treat hemorrhoids and other anorectal complications. In order to do so, the proctologic database systems like Medline were employed along with the prior scribing of the literature heavily based on the ancient Ayurveda and Persian medicine scriptures. In addition to that, various modern suppository bases were also analyzed on the basis of their physicochemical properties, pros and cons along with the physiological and pharmaceutical considerations influencing rectal drug delivery. As a result, this review became successful to conclude that there is abundant amount of literature and data regarding rectal suppositories, various bases to be incorporated, various forms of Varti and their herbal and chemical active ingredients available in proctologic accounts as well as in both Persian and Ayurvedic medicinal scriptures.

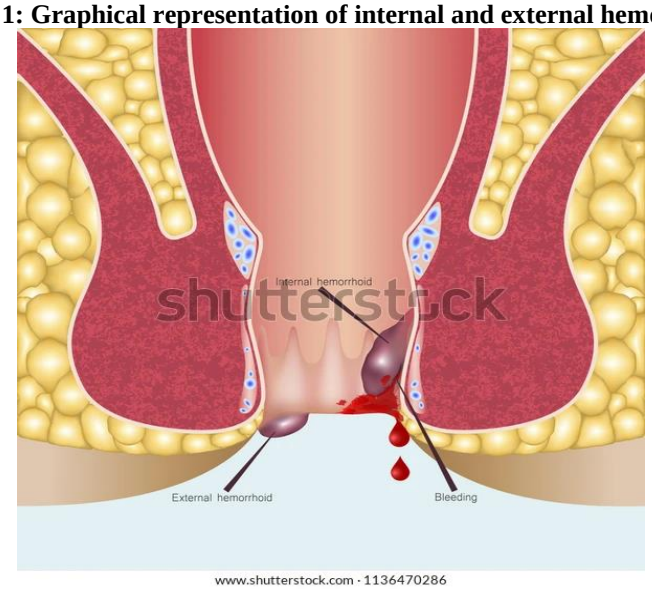
**Keywords:** Hemorrhoids, Rectum, Suppository, Suppository bases, Traditional medicine, Proctology.

## Introduction

Enlarged veins in the lower rectum and anus that resemble varicose veins are known as hemorrhoids or piles [1]. Internal hemorrhoids can form inside the rectum and external hemorrhoids can form under the skin around the anal sphincter. When symptoms do manifest, they include mucus discharge from the anus, a mass around or inside the anus, bleeding and/or pain when passing stool and a feeling of incomplete bowel emptying [2]. Regardless of gender, approximately 4.4% of the global population suffers from hemorrhoids. However, women between the ages of 45 and 65 are more likely to experience it than men. Higher socioeconomic status is linked to an increased prevalence and Caucasians are impacted more commonly than African Americans [3]. Hemorrhoids can occur as a result of long-term constipation, diarrhoea, prolonged sitting, physically demanding lifting tasks, ageing, obesity, overusing laxatives pregnancy, among other risk factors [4-6]. The treatment of symptomatic hemorrhoids includes surgical procedures like hemorrhoidectomy, stapled hemorrhoidopexy and Doppler-guided hemorrhoid artery ligation; non-operative medical interventions like medication, dietary modification and lifestyle modification; office-based procedures like rubber band ligation, sclerotherapy and infrared coagulation [7]. The goal of pharmacological hemorrhoid treatment is to lessen bleeding, pain inflammation. Topical dosage forms, such as creams, ointments suppositories that contain steroids (corticosteroid) or NSAIDs (ibuprofen, aspirin diclofenac) alone or in combination with antibiotics or anaesthetics (such as lidocaine and dibucaine), have been proven to be effective. The high frequency of negative effects, however, limits their sustained usage [8–10]. External hemorrhoids are frequently treated with creams and ointments for short-term relief.

Suppositories are solid objects of varying weights and forms that are designed to be inserted into the urethral, vaginal, or rectal orifice; where they melt, soften, or dissolve at body temperature to release the medicine that is contained inside. The active components are often used in a single dose for local action or systemic absorption [11, 12]. Bases are used the vehicles for preparing suppositories. There are two different kinds of bases: oleagineous/fatty bases (theobroma oil, cocoa butter hydrogenated vegetable oils) and water miscible or soluble bases (glycerinated gelatin, polyethylene glycol polymers, often known as macrogols), according to research conducted [13]. Internal hemorrhoids respond well to rectal suppositories. Suppositories are typically administered following a bowel movement, which allows the medication to be released over a longer period of time and have a longer-lasting impact. The medication can relieve all pain and discomfort brought on by hemorrhoids because it is absorbed by the rectal tissue [14].

**Figure 1: Graphical representation of internal and external hemorrhoid.**




**Source**: https://www.shutterstock.com/image-vector/internal-hemorrhoids-external-1136470286

**References from ancient texts about rectal dosage forms**

When we explore the historical sources, we find that suppositories were characterized as a significant dosage form, not only as a medication delivery system but also as a technique for preserving pharmaceutical components. In contrast to modern medicine, which classifies suppositories as rectal, suppositories in the described manuscripts included nasal, vaginal, urethral, rectal (as drug delivery dosage forms) and ocular (as a storage mechanism) suppositories [15,16]. Rectal suppositories were initially used in Egyptian society (3150 B.C.) [17, 18]. Other records [19-21] demonstrated its use as a dose form in traditional Chinese, Persian and Ayurvedic remedies. Rectal suppositories were described as solid dosage forms with different diameters, shaped like a little chestnut or a date kernel. They were applied to both local and systemic disorders. Some of the main local diseases addressed by this type of dose form were hemorrhoids, anorectic inflammation and lesions, anal fissures and inadvertent bowel leaks [22, 23].

Varti Kalpana has been a popular notion in Ayurveda since prehistoric times. This ancient composition has been somewhat modified in modern suppositories. Medicines were powdered, triturated formed into the Varti shape, resembling a lamp wick, hence the name Varti Kalpana [24]. Different varieties of Varti have been explained in Ayurvedic literature from the perspectives of size, indication at a specific site, composition actions [25]. Phala Varti is one of these varieties, which is manufactured from several medications and is used in excretory channels such as the rectum, vagina urinary tracts. Guda Varti, which falls under Phala Varti, is used to treat constipation, enema retention, GIT diseases that hinder the passage of Vata and vitiate the Dosha to excrete Mala stored in the rectum [26, 27]. Varti has a diameter equivalent to the size of the thumb. When used, the Varti is first soaked in Ghrita and then slowly inserted into the rectum. Faecal matter excretion occurs within 3–4 minutes after using Guda Varti [28, 29].

**Methodology**

Medline (1950-2021) was deployed to search all published papers that included the terms "suppositories, anal, hemorrhoids, and rectum proctology." The study aims to highlight the advantages and disadvantages of each. Suppositories used to treat inflammatory and irritable bowel problems, cancer, and systemic infections were excluded from the study. Confirmed evidence of the most commonly used herbs, which were frequently used in rectal suppository formulations, was derived from the mentioned ancient manuscripts as well as electronic databases including Science Direct, PubMed, Scopus, and Google Scholar to accord with traditional indications and pharmacological effects of the herbs. Numerous current suppository bases were analyzed using structural, logical, and systematic literary source analysis methods.

**Advantages of suppositories**

- **Increased enzymatic drug stability:** Drug degradation is caused by several proteolytic and other enzymes in the GIT (Gastrointestinal Tract), which hinders adequate absorption after oral administration.
- **Partial evasion of the hepatic first pass:** The rectum receives substantial blood supply from the different rectal arteries. It is emptied by at least three veins drug absorption takes place via this venous network. It is commonly assumed that the inferior and inferior venacava are related to the middle rectal veins. This allows the portal system and the accompanying first-pass metabolism in the liver to be bypassed.
- **Increased drug load:** Suppositories allow for two to three times the drug load to be delivered, depending on the other excipients required in their formulation.

- **Lymphatic delivery:** Many researchers have researched and proposed that some medications enter the lymphatic system after rectal administration, skipping the first-pass impact.
- **Stable and continuous environment:** When compared to the oral route, the rectal route provides a far more stable environment for the medicine as it is absorbed.
- **Patients with swallowing difficulties:** Children and the elderly who have difficulty swallowing can greatly benefit from rectal administration.
- **Avoiding accidental or purposeful overdosing:** Certain medicines, such as orally administered sedatives, may raise concerns about the likelihood of severe accidental or intentional overdosing. Rectal administration, in particular, eliminates this risk [30, 31].

**Disadvantages of suppositories**

- **Patient acceptance and compliance:** Because many cultures are hesitant to consider rectal administration as a dose form, pharmaceutical companies tend to avoid rectal dosage forms, save for the most clear purposes and conditions.
- **Non-specific drug loss:** Ineffective absorption due to premature rectum loss and faecal matter interaction with the medicine or excipient may limit absorption and diminish effectiveness.
- **Limited fluid in the rectum:** A small volume (3 ml) may hinder drug dissolution, especially if the drug has poor water solubility.
- **Formulation:** Melting, liquefaction, solubility, particle size other factors can all cause formulation issues.
- **Expensive:** They are more expensive than tablets [32, 33].

**Physiological considerations influencing rectal drug delivery**

The superior hemorrhoidal vein empties into the inferior mesenteric and portal systems, while the middle and inferior hemorrhoidal veins join the systemic venous circulation via the internal iliac veins. The inferior and middle hemorrhoidal veins, on the other hand, bypass the liver and do not undergo first-pass metabolism [34, 35]. Because it is not buffered and has a neutral pH, the rectum is an attractive location for drug absorption. It also has extremely little enzyme activity; therefore, no enzymatic breakdown takes place [36]. The rectal mucus can tolerate greater drug-related irritations than the gastric mucosa. Rectal gut-wall metabolism and microorganism metabolism in the rectal lumen may reduce bioavailability [37, 38].

**Choice of a suppository base**

To formulate an anti-hemorrhoidal suppository, the base that will be used must have the following characteristics:

- Chemical and physical resistance during storage and usage;
- Compatibility with a broad range of active medicinal ingredients and excipients;
- Lack of odor;
- Aesthetically pleasing appearance;
- Non-toxicity, absence of sensitivity and irritation to sensitive body tissues;
- Expansion-compression properties, such that when cooled, suppositories must be compressed sufficiently to be easily released from the molds;
- To melt and dissolve a medical material in the targeted cavity of the body;
- Mixing and accommodating a small amount of water;
- The melt's viscosity should be low enough to allow for simple casting of the suppository mass into molds, yet high enough to suspend the API solid particles.
- Wetting and/or emulsifying properties for maximum API release [39].

The physicochemical features of the medication (e.g., solubility and particle size) and the composition of the suppository base (including the use of surfactants or other additives) might confer distinct drug release profiles [40, 41]. When medications that are dissolved (soluble) in the suppository base dissolve or melt onto the mucosal surface, the drug molecules diffuse out. The opposing solubility qualities of medications that are distributed (insoluble) in the suppository base urge the drug to leave the dose form and subsequently begin solubilizing in the physiological fluid [42, 43]. As a result, hydrophilic medications tend to release better in lipophilic bases, while lipophilic drugs release better in hydrophilic bases.

**Various suppository bases**

There are currently around 40 bases available for the preparation of various types of suppositories. However, an ideal base should be melting at a rectal temperature of 36 ºC, non-toxic, non-irritating, compatible with a wide range of medications, have wetting and emulsifying capabilities, be stable in storage be conveniently made by moulding. Fatty bases should have an acid value of less than 0.2, a saponification range of 200–245 a brief interval between melting and solidification points. A few widely accepted bases are theobroma oil (cocoa butter), hydrophilic bases such as glycerinated gelatin, different polyethylene glycols, water dispersible bases so on [44].

**Formulated and marketed drugs**

As per the findings of the search carried out on Medline, the drugs of the following categories were found to be incorporated inside an anti-hemorrhoidal suppository.

**Local Anesthetics agents**

Local anaesthetics numb nerve endings, providing brief relief from pain and irritation. These work by inducing a reversible block in sensory nerve conduction. These are easily absorbed through the mucus barrier and are employed as topical anaesthetics [45]. These provide effective pain relief in situations involving strangulated hemorrhoids, fissures perianal hematomas [46]. Lidocaine 2 to 5%, Benzocaine 5 to 20%, Dibucaine 0.25% to 1%, Dyclonine 0.5% to 1%, Pramoxine 1%, Cincocaine 1% and Tetracain 0.5 to 5% are some of the most often used local anaesthetics.

**Steroids**

Rectal suppositories include a variety of glucocorticosteroids. Hydrocortisone and its derivatives, diflucortolone valerate and prednisolone are among them [47]. Steroids serve as decongestants, anti-inflammatory anti-pruritic substances, reducing inflammation and mucus secretion. It has been proposed that the analgesic effect of local anaesthetics is seemingly sustained by an elevation in pain threshold caused by steroids' anti-inflammatory impact [48].

**Astringents**

The astringent causes the cells of the anal skin to clump, drying the area and relieving heat and irritation. Hamamelis water, a moderate astringent made from the twigs of Hamamelis virginiana, is one of the most commonly used astringents. It aids in the treatment of hemorrhoidal irritation. Zinc oxide (5–25%) reduces perianal irritation by generating a physical barrier on the skin that prevents inflamed skin from coming into contact with irritating fluids or stool from the rectum [49].

**Vasoconstrictors**

Swollen blood vessels are found in hemorrhoidal cushions. Vasoconstricting medications can help relieve hemorrhoid symptoms. These medications stimulate blood vessels to constrict, minimizing hemorrhoidal congestion. These products also contain a moderate anesthetic, which aids in the relief of discomfort and itching [50]. Ephedrine sulphate (0.1 to 1.25%), epinephrine (0.005 to 0.01%) and phenylephrine (0.25%) are the most commonly used vasoconstrictors.

**Calcium Dobesilate**

Calcium dobesilate is a venotonic medication that is commonly used to treat three conditions: chronic venous illness, diabetic retinopathy hemorrhoidal attack symptoms [51]. The medication affects the endothelial layer and basement membrane of blood vessels. It decreases capillary hyperpermeability by boosting the activity of endothelial nitric oxide synthase in vascular endothelial cells, which results in increased nitric oxide generation [52, 53]. In addition to calcium dobesilate, the suppositories typically contain a local anaesthetic, steroid astringent.

Apart from above medicines, evidences of various medicinal plants were found in the literature of Persian medicine which were found effective in the treatment of hemorrhoids, whose details is mentioned in the following table.

**Table 1: Commonly used medicinal plants in anti-hemorrhoidal suppository formulations with their Persian and scientific names and mechanisms of action.**

| No. | Persian name | Scientific name | Mechanism of action |
|---|---|---|---|
| **1** | Barzad (Barijeh) | *Ferula gummosa* Boiss | Anti-inflammatory effect [54] |
| **2** | So'd (Oyar salam) | *Cyperus longus* L. | N.A. |
| **3** | Katan (Bazrak) | *Linum usitatissimum* L. | Anti-inflammatory and analgesic effects and anti-constipation [55] |
| **4** | Irsa | *Iris pseudoacorus* L. | N.A. |
| **5** | Afsantin | *Artemisia absinthium* L. | Anti-inflammatory effect [56] |
| **6** | Shooniz | *Nigella sativa* L. | Anti-inflammatory and Analgesic [57] |
| **7** | Kondor | *Boswellia sacra* Flueck. | Analgesic effect [58] |
| **8** | Gall (Mazoo) | *Quercus* spp. | Anti-inflammation [59] |
| **9** | Halileh | *Terminalia chebula* L. | Anti-diarrheal and anti-inflammatory activities [60- 62] |
| **10** | Amoleh | *Phylantus emblica* L. | Anti-inflammation [63] |
| **11** | Heltit (Anghouzeh) | *Ferula asafoetida* L. | Antispasmodic, anti-ulcerogenic, and anti-inflammatory activities [64] |
| **12** | Hanzal | *Citrullus colocynthis* (L.) Schrad. | Purgative activity and anti-ulcer [65] |
| **13** | Moord | *Myrtus communis* L. | Anti-inflammatory and Analgesic [66] |
| **14** | Barhangh | *Plantago major* L. | Anti-ulcerogenic, Anti-inflammatory and analgesic activities [67] |
| **15** | Samgh-e arabi | *Acacia nilotica* (L.) Delile | N.A. |

(N.A.: Mechanism of action unknown or yet to be discovered.)
In Persian language, the suppositories used to treat hemorrhoids are called as *Shyaf -e bavasir* the active ingredient in it (in all dosage forms of Persian medicine) is called as *Amood*, contains the extracts of *Aloe vera* L., *Peganum harmala* L., *Commiphora myrrha* (Nees) Engl. and *Hedera helix* L [68].

**Discussions**

Hemorrhoids have a significant influence on quality of life, despite their low morbidity. So, in order to treat hemorrhoids, rectal administration has been thoroughly investigated as a viable drug delivery strategy, particularly for treatments that are either too irritating to the gut or more effective when not metabolised by the liver. Suppositories provide patients with a less intrusive and less uncomfortable choice. It is also a convenient medicine administration strategy for patients, particularly those with rectal symptoms [69]. Local anaesthetics, corticosteroids, vasoconstrictors, antiseptics, keratolytics, protectants (such as mineral oils and cocoa butter), astringents (substances that produce coagulation, such as witch hazel) other ingredients may be present in these formulations [70, 71]. According to a review of the literature, the acceptable technological performance of suppositories contributes to increased API bioavailability [72]. As shown in Table 1, the herbs claimed to be used as ingredients of anti-hemorrhoidal rectal suppositories in Persian medicine manuscripts include Ferula gummosa Boiss., Cyperus longus L., Linum usitatissimum L., Iris pseudoacorus L., Nigella sativa L., Boswellia sacra Flueck., Quercus spp., Terminalia chebula L., Phylantus emblica L., Ferula asafoetida L., Papaver somniferum L., Myrtus communis L., Plantago major L., Citrullus colocynthis L., Schrad, Acacia nilotica L. Delile, etc.. Some of these have been researched for their anti-inflammatory, analgesic anti-ulcer properties, although their efficacy in hemorrhoidal diseases has yet to be determined. Varti is also depicted in ancient Ayurvedic literature as a wick, although current literature depicts torpedo-shaped intentions that serve the same goal of simple insertion as that of Varti [73]. Varti's varieties referenced in our classics, according to the administration site as Guda Varti (suppositories), Shishna Varti (urethral bougies) and Yoni Varti (pessaries) are similar to contemporary suppositories [74]. The process of releasing medicinal material from a suppository foundation is complex and unpredictable. The time required for API breakdown and diffusion into the rectal or vaginal lumen is also a stage restricting a drug's release rate [75]. In practice, because bioavailability tests are typically difficult to execute, it is critical to monitor the efficiency of the drug delivery system by closely monitoring therapy results. As a result, the most significant task at the stage of medication creation is the selection of a rational and adequate suppository base [76].

**Conclusion**

This article helped to demonstrate the utility of suppositories in the treatment of hemorrhoidal conditions along with the advantages and disadvantages of their usage. For that purpose, this article also assorted the various evidences of suppositories and the constituent APIs in the proctologic databases like Medline as well as in the ancient texts like Ayurveda and Persian medicine and the comparison of their descriptions with the attributes of conventional and modern form of suppositories. This article also conducted an analytical review of a variety of modern suppository bases, including a description of their physical and chemical properties, benefits and drawbacks, so that in the future it will be possible to select a suitable excipient when formulating anti-hemorrhoidal active ingredients in the form of suppositories.

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