

# Suppositories in anal disorders: a review

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**Abstract. – Introduction:** Drug treatment for various ano-rectal conditions has been known since ancient times. Suppositories are one of the very feasible modes of administration for medication.

**Materials and Methods:** Medline (1950-2006) was searched for all published reports about suppositories. This study sum up various suppositories used in proctological practice, which either are in vogue and have been used with a proven degree of success, or suppositories which are described in the literature but are no more in use. This study attempts to highlight the advantages and drawbacks of each of them.

**Results:** Over 30 different types of ingredients have been found which are used singly or in conjugation in suppositories formulation. While there are only few reports of adverse reaction following use of suppositories like rectal ulcer, rectal stricture and stenosis, the overall acceptance of this mode of medication is good.

**Conclusion:** Suppositories offer to the patients an option that is less invasive and less discomforting. Suppositories could well be looked as a convenient drug delivery system in patients having ano-rectal symptoms.

*Key Words:*

Suppositories, Anal, Rectum, Proctology, Ano-rectal disorder.

## Introduction

Drugs or medications are administered through a variety of routes, the most common being the oral and parenteral route. While rectal route is less commonly used in routine practice, in proctological disorders it is being used effectively since long<sup>1</sup>. Drugs mixed with various adjuvant and administered through the rectal route do provide satisfactory pharmacokinetics with acceptable local tolerance. Suppositories and

creams are the two main modes of administration of drugs through the rectum<sup>2</sup>.

Suppositories are a medicated solid dosage form intended for insertion into the body orifices. The term suppositories have its origin in Latin and means, "to place under". It is thought that suppositories were first used in nursing facilities to be administered to elderly patients who were not capable of receiving medications through more traditional delivery systems<sup>3</sup>.

In humans the rectum comprises the last 12-19 cm of the colon and the rectal epithelium is formed by a single layer of columnar or cuboidal cells and goblets cells; its surface area is about 200-400 cm<sup>2</sup>. The absorbing surface area of the rectum is considerably smaller than that of the small intestine, as the former lack villi and microvilli. However, the epithelium in the rectum and the upper intestinal tract are histologically similar, giving them comparable abilities to absorb drugs. The veins of the rectum comprise the superior hemorrhoidal vein, which drains into the inferior mesenteric and portal system, and the middle and inferior hemorrhoidal veins, which enter the systemic venous circulation via the internal iliac veins. However, it is a little known fact that the inferior and middle hemorrhoidal veins bypass the liver and do not undergo first-pass metabolism. Therefore, the drugs delivered through suppositories to the lower and middle hemorrhoidal veins are absorbed rapidly and effectively. The rectum is an interesting area for drug absorption because it is not buffered and has a neutral pH. It also has a very little enzymatic activity, thus enzymatic degradation does not occur. The rectal mucus is more capable of tolerating various drug related irritations than the gastric mucosa<sup>2</sup>.

The ano-rectal physiology provides a sufficiently adequate surface area for drug absorption. The surface area is also permeable to non-ionized drugs. Suppositories formulations are rather efficient in variety of different bases to increase absorption and reduce complications<sup>4</sup>. The osmo-

sis process allows the drug to transfer from the vehicle in the suppositories across the membrane of the rectum, and into the hemorrhoidal veins. The higher the concentration and the greater the solubility, the more efficient is the transfer of medication<sup>5</sup>.

Several local host factors may influence absorption in the rectum: the mucus layer, the variable volume of rectal fluid, the basal cell membrane, the tight junctions and the intracellular compartments may each constitute local barriers to drug absorption; depending on histological factors and on the molecular structure of the administered drug.

Suppositories come in various sizes and shapes, which facilitates their insertion and retention in the cavity. Adult rectal suppositories weighed about 2 g while those for children are about half that weight.

## Materials and Methods

Medline (1950-2006) was searched for all published reports using the key words "Suppositories, anal, hemorrhoids, rectum and proctology". This study sum up various suppositories used in proctological practice, which either are in vogue and have been used with a proven degree of success, or suppositories which are described in the literature but are no more in use. The study attempts to highlight the advantages and drawbacks of each of them. The suppositories used for inflammatory and irritable bowel disease, malignancy and systemic infection have been excluded.

### **Suppositories Containing Local Anesthetics agents**

The local anesthetics act by numbing the nerve endings and provide temporary relief from pain and itching. These act by causing a reversible block to conduction in the sensory nerves. These are well absorbed from the mucus membrane and used as surface anesthetics<sup>6</sup>. These provide good relief from discomfort encountered in cases of strangulated hemorrhoids, fissures and perianal hematomas<sup>7</sup>.

Some commonly used local anesthetics are: Benzocaine 5 to 20%, Lidocaine 2 to 5%, Cinchocaine, Dibucaine 0.25% to 1%, Dyclonine 0.5% to 1%, Pramoxine 1% and Tetracain 0.5 to 5%.

### **Suppositories Containing Steroids**

Several glucocorticosteroids are used in rectal suppositories. They include hydrocortisone and its derivatives, diflucortolone valerate and prednisolone<sup>8</sup>. The steroids act as decongestant, anti-inflammatory and anti pruritic agents and in doing so they eliminate inflammation and mucus discharge. It has been postulated that the analgesic effect of the local anesthetics is apparently prolonged by an increase in the threshold for pain by the anti-inflammatory effect of steroids<sup>9</sup>.

### **Suppositories Containing Astringents**

The astringent causes the cells of the anal skin to clump thereby drying the skin, which gives relief from burning and itching.

Some common astringents that are used include *Hamamelis water*, which is a mild astringent prepared from twigs of *Hamamelis virginiana*. It helps in relief from the hemorrhoidal itch.

Zinc oxide 5 to 25% prevents the irritation at the perianal area by forming a physical barrier on the skin that prevents the contact of the irritated skin with aggravating liquid or stool from the rectum.

### **Vasoconstrictors in Suppositories**

Hemorrhoidal cushions contain swollen blood vessels. The vasoconstricting agents can help in relieving symptoms of hemorrhoids. On application, these drugs cause the blood vessels to shrink, thereby reducing hemorrhoidal congestion. These products additionally contain mild form of anesthetic, which helps in relieving pain and itching<sup>10</sup>.

The commonly used vasoconstrictors are: Ephedrine sulfate 0.1 to 1.25%, Epinephrine 0.005 to 0.01% and Phenylephrine 0.25%.

### **Protectants in Suppositories**

Passing hard and dry stool is the most traumatic experience in patients having anal pathology as it results in tearing of the skin around the anus, as also in tearing and cracking which ends in bleeding. Again, when this tender skin comes in contact with liquid or stool, it causes the skin to further itch and burn.

Protectants, when applied in the form of suppositories, form a physical barrier on the skin and results in reducing the pain quotient and the pruritus. These also protect the broken skin from coming in contact with offending particles in the stool.

While a variety of protectants are used in suppositories, a few commonly used are: Aluminium hydroxide gel<sup>11</sup>, Glycerin, Lanolin, *Aloe vera*, White petrolatum, Zinc oxide and Calamine.

#### ***Use of Antiseptics in Suppositories***

Being a highly contaminated area, the anal and perianal skin are susceptible to variety of organisms, which can lodge there either from the adjoining area or from the contaminated stool. The chances of contamination further increase when the skin gets bruised during defecation.

Antiseptics are used to keep the area clean and to prevent infection. The commonly incorporated antiseptics include: Benzalkonium chloride, Boric acid and Framycetine sulphate.

#### ***Use of Keratolytics in Suppositories***

Certain chemicals cause the outer layers of skin and other tissues to disintegrate when applied. They eventually help in better penetration in the tissues of other medications contained in the suppositories to bring quicker relief. The two commonly used keratolytics are: Aluminium chlorhydroxy allantoinate 0.2 to 2% and Resorcinol 1 to 3%.

#### ***Use of Calcium Dobesilate in Suppositories***

Calcium dobesilate is a veno-tonic drug, which is widely prescribed for three main indications: chronic venous disease, diabetic retinopathy and the symptoms of hemorrhoidal attack<sup>12</sup>. The drug acts on the endothelial layer and basement membrane of the blood capillaries. It reduces capillary hyperpermeability by increasing the activity of endothelial nitric oxide synthase in vascular endothelial cells, leading to an increase in nitric oxide synthesis. Along with Calcium dobesilate, the suppositories usually contain local anesthetic, steroid and astringent in addition [Smuth suppositories from Aristo Pharmaceuticals, Mumbai, India].

#### ***Suppositories Containing Policresulen***

Policresulen is a polymolecular organic acid. It coagulates necrotic or pathogenically altered tissue in anorectal disorder and promotes desquamation of such tissues. The healthy tissues surrounding the wound are not affected. As a local hemostatic, Policresulen coagulates blood proteins thereby inducing muscle fibers of small vessels to contract and thus any hemorrhage in the anal canal or in the perianal area could be controlled. It also induces hyperemia in the

wound area and thereby stimulates regeneration and re-epithelization process. It also has an antimicrobial property which guards against infection and prevents inflammation. Policresulen also has astringent property and thus it suppresses oozing<sup>13</sup>.

#### ***Other Ingredients in Suppositories***

Imiquimod containing suppositories have been successfully used to prevent recurrence of anal condylomata<sup>14</sup>. Trimebutine, an anal sphincter relaxant, has been used to relieve post hemorrhoidectomy pain<sup>15</sup>. Ketoprofen suppositories were recommended in patients after anal surgery<sup>16</sup>.

A sedative cryotherapy was being used with the intention of producing tissue hypothermia, giving cool numbing effect over the hemorrhoids<sup>17</sup>. Promethazine suppositories were proposed for hemorrhoidal complications while trichloroacetic acid was used for the treatment of anal fissures<sup>18</sup>. A compound Carragenates suppositories has been shown to be useful in the treatment of mixed hemorrhoids<sup>19</sup>.

Few old references have described use of Roinal<sup>20</sup>, Glycofuranoside derivatives<sup>21</sup>, Indacine<sup>22</sup>, Prothanon<sup>23</sup>, Rhubarb and Aloe<sup>24</sup>, Phenylandanediol<sup>25</sup>, Proctoglivinol in suppositories forms<sup>26</sup>. However, they are no more in use.

The various ingredients in suppositories form with their use; adverse effects and contraindications for their use have been elaborated in Tables I and II.

#### ***Insertion Technique of Suppositories***

It has been suggested that the suppositories should be inserted with the patient lying on the left lateral side with the right knee bent. The suppositories should be dipped in water before use, which facilitates the easy insertion of the suppositories. It should be kept in cold water or refrigerator for half an hour before use if the suppositories are too soft to be inserted, especially during warm weather. Emptying of bowel should be avoided for at least an hour after insertion of the suppositories to allow it to be fully absorbed.

Although, it is a practice to introduce the tapering end of the suppositories first and the base at last, one randomized study has found that the retention rate was higher and spontaneous expulsion rate was lower when the suppositories was introduced with "base first" technique<sup>27</sup>. It was postulated that reversed vermicular contractions

**Table I.** Ingredients in suppositories, their uses and adverse effects.

Ingredients	Indications	Contraindications	Adverse effects
Local anesthetics (Lignocain, Cinchocain, Centbucridine)	Anal pain due to strangulated hemorrhoids, anal fissure, and post anal surgery.	Known sensitivity to these agents	Local irritation and anal cryptitis or proctitis.
Steroids (Hydrocortisone, Prednisolone)	Hemorrhoids, anal fissures, pruritus ani	Infective lesions like anal , fistula abscess and cryptitis.	Systemic absorption on prolonged use
Astringents [Hamamelis water, Zinc oxide, Allantoin)	Anal cryptitis, pruritus ani, hemorrhoids	Known sensitivity	Local reaction
Vasoconstrictors [Phenylephrine]	Hemorrhoids, hemorrhoidal thrombosis.	Known sensitivity	Headache, flushing, tachycardia.
Protectants and Emollients (Aloe vera, Zinc oxide, Calamine)	Hemorrhoids, anal fissures, pruritus ani	Known sensitivity	No specific adversity
Antiseptics (Boric acid, Benzalkonium chloride, Framycetine sulphate)	Proctitis, anal cryptitis, anal fissures	Known sensitivity	Pruritus, local irritation and burning
Keratolytic (Aluminium Chloride, Resorcinol)	Anal fissures, Anal rhagades	Known sensitivity, inflammatory bowel disease, pregnancy	Skin excoriations, mucosal ulcerations.
Calcium dobesilate	Bleeding hemorrhoids, hemorrhoidal attack	Known sensitivity, pregnancy	Agranulocytosis
Policresulen	Hemorrhoids, anal fissures, infective anal lesions.	Inflammatory bowel disease	Local allergic reactions

or pressure gradient of the anal canal might have been responsible for this finding. It was also suggested that a “torpedo-shaped” suppositories should be designed which would have a better acceptability and efficacy.

### **Complications Following Use of Suppositories**

Suppositories containing non-steroidal anti-inflammatory drugs are commonly used for relief

of pain in the pediatric, obstetrical and general surgical practice. However, reports are available where these suppositories have caused complications like rectal and anal ulcerations<sup>28</sup>, rectal stricture<sup>29</sup>, anal stenosis, proctitis<sup>30</sup> and peri-rectal cellulites<sup>31</sup>.

Systemic absorption of topically applied steroids can occur in children<sup>32</sup>.

Calcium dobesilate is known to cause agranulocytosis<sup>33,34</sup>.

**Table II.** Suppositories for various ano-rectal pathologies

Pathology	Ingredients in suppositories
Bleeding hemorrhoids	Astringents, vasoconstrictors, protectants, Calcium dobesilate and Policresulen
Hemorrhoidal thrombosis	Local anesthetics, vasoconstrictors and Calcium dobesilate
Anal fissure	Local anesthetics, steroids, protectants, antiseptics, keratolytics and Policresulen
Pruritus ani	Steroids, astringents and protectants
Anal cryptitis and proctitis	Local anesthetics, astringents and antiseptics
Anal rhagades	Keratolytic, antiseptics and policresulen
Post anal surgery	Local anesthetics, vasoconstrictors, antiseptics and Calcium dobesilate

## Discussion

Drug treatment for various ano-rectal conditions has been known since ancient times. Today, modern as well as traditional drugs are being increasingly used in proctology practice. Rectal route with local or general effects is an interesting possibility of a treatment modality. Easy use and rapid absorption are two major advantages of these therapeutic options<sup>4</sup>.

Suppositories are a very feasible mode of administration for medication. The medicament is incorporated into a base, which either melts at body temperature or dissolves in the mucus secretions and exerts localized or systemic action. Within the era of cost-containment and the risk of AIDS and other communicable blood borne diseases, drug delivery through suppositories is proving an effective and viable option<sup>5</sup>.

It is well recognized that over-the-counter therapy with suppositories is an enormously large market. Suppositories are mainly used in proctology practice to produce a local action, such as anti-inflammatory and anesthetic effect for hemorrhoidal conditions. Preparations for hemorrhoids usually contain astringents, local anesthetics, veno-toner drugs and anti-inflammatory components.

However, as much as suppositories are useful, there are some disadvantages of using them too. They may not be a preferred option for the patient as it is inconvenient to use them. Absorption of drugs can be erratic and unpredictable. Some suppositories either leak or are expelled after insertion resulting in a futile exercise. Nevertheless, complications of serious nature have been reported after use of medicated suppositories<sup>31</sup>.

There is, thus, a need to become more creative in deciding the optimal mode of delivery of drugs to the patients. This route of drug delivery should be made more convenient in nursing facilities and institutionalized care settings. It is important to assess if the patient can self-administer a suppositories or not.

There appears to be relatively good acceptance by patients for suppositories administration, especially if the value of this drug delivery system is explained to them, and if the ingredients of the suppositories are chosen and formulated in a manner best suited to the individual patient. The myth that suppositories are given to only those who cannot swallow is required to be eliminated from the patients mind. In addition, counseling

may be required to educate patients on proper suppositories administration.

In conclusion, rectal administration is yet to be truly explored as a potential drug delivery system, particularly for drugs that are either too irritating for the gut or are more effective when not metabolized by the liver. Suppositories offer patients an option that is less invasive and less discomforting. Suppositories could well be looked as a convenient drug delivery system in patients having ano-rectal symptoms.

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