



Formulation and Evaluation of Alum Suppositories

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ABSTRACT:

Although suppositories have been used for many years to administer drugs through the rectum and vaginal area, the current global suppository market is relatively small, mainly due to poor user acceptance but it is found to be most useful in the conditions when the patient has difficulty in swallowing, such as children and elderly people. The most essential property of any kind of suppository is that it provides a greater bioavailability of drug as it bypasses the first pass effect. Therefore, it is the most preferred dosage form for effective treatment of haemorrhoids. So here, Alum is the mainstay of the formulated suppositories for the treatment of haemorrhoids which were evaluated by various parameters such as Authentication of drug, pH, colour, odour, taste, solubility, dissolution, disintegration, drug-base interaction, content uniformity, and uniformity of weight.

KEY WORDS: Alum, Suppositories, Haemorrhoids, Anti-haemorrhoid.

Introduction

Haemorrhoids, sometimes referred to as piles, are enlarged veins in the lower rectum and anus. They resemble varicose veins in appearance. Internal haemorrhoids can form inside the rectum, while external haemorrhoid's can form under the skin around the anus. The disorder, which is relatively prevalent, is brought on by an inflammatory process of the hemorrhoidal plexus. Vein swelling in the anus and lower rectum is a frequent symptom of haemorrhoids. haemorrhoid's that don't cause any symptoms may go unnoticed by their owners. However, when symptoms do show up, they can 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. [1,2]

Depending on where they are, hemorrhoidal diseases can be classed as internal, external, or Interno-external hemorrhoids. The external hemorrhoids are found in the distal portion of the anal canal, below the dentate line, and are covered by anoderm (skin), whereas the internal hemorrhoids start above the dentate line and are covered by a mucus membrane. The characteristics of both types of hemorrhoids are present in Interno-external hemorrhoids. [3,4,5]

Hemorrhoids are thought to be caused by venous dilatation and prolapse, which are brought on by growing older, heavy lifting, straining while urinating, and extended periods of sitting. Internal hemorrhoids are characterized by painless bleeding during bowel movements and occasional protrusion. The degree, seriousness, and length of symptoms including bleeding and prolapse, problems with perineal cleanliness, and the presence or absence of pain should be the main points of attention. Constipation exposes people to hemorrhoidal disease, so it is important to carefully assess fiber intake and bowel habits, including regularity, consistency, and ease of evacuation. [6,7,8,9]

SUPPOSITORIES:

Suppositories are solid medications that are designed to be inserted into the rectum. They contain one or more active ingredients and are intended for use as a single dose for local action or systemic absorption of the active ingredients [10]. They are solid medications that contain one or more active ingredients. These active ingredients are typically mixed with excipients during manufacturing to form a homogenous system. Suppositories are generally composed of either a lipophilic base (e.g., cocoa butter, coconut oil, hydrogenated vegetable oils, and hard fats) or hydrophilic base (e.g., glycerinated gelatin and polyethylene glycols). The choice of base material depends on the type of suppository, the type of drug, and the storage conditions. [11]

ADVANTAGES OF SUPPOSITORIES: [13]

1. When drugs are taken orally, many enzymes in the gastrointestinal tract can break them down, making it difficult for the body to absorb them effectively. However, rectal administration of drugs can bypass this problem.

2. The rectum is supplied with blood from various rectal arteries and drained by at least three veins. This allows drug absorption through the venous network, bypassing the portal system and the associated first-pass metabolism in the liver.

3. Suppositories can also allow for higher drug loads to be administered, depending on the amounts of other excipients necessary in their formulation. Some researchers have suggested that drugs administered rectally enter the lymphatic system, bypassing the first-pass effect.
4. Compared to oral administration, rectal administration provides a more constant environment for drug absorption.
5. Rectal administration can be useful for patients who have difficulty swallowing, such as children and elderly people.

DISADVANTAGES OF SUPPOSITORIES:^[13]

- a) In many cultures, rectal administration of drugs is not widely accepted, which has led to pharmaceutical companies avoiding rectal dosage forms, except for the most obvious indications and situations.
- b) There is a potential for non-specific drug loss when drugs are administered rectally. This can occur due to ineffective absorption caused by premature loss from the rectum and interaction of fecal matter with the drug or excipient. This can reduce absorption and diminish effectiveness.
- c) The limited fluid in the rectum (3 ml) may limit the dissolution of drugs, particularly those with low aqueous solubility.
- d) Formulation difficulties can arise due to factors such as melting, liquefaction, solubility, particle size, etc.
- e) Rectal administration of drugs is generally more expensive than tablets.

TYPES OF SUPPOSITORIES:^[12]

1] Rectal suppository:

Rectal suppositories are a type of medication that is inserted into the rectum. They come in different shapes and sizes, with adult suppositories weighing around 2 grams and tapered to resemble a torpedo shape. Children's suppositories, on the other hand, weigh about 1 gram and are smaller in size. The suppository base is usually made of materials that melt or soften at body temperature, which allows the medication to be absorbed into the bloodstream. Unlike tablets, suppositories are not compressed because the amount of liquid in the rectal cavity is insufficient for tablet disintegration.

2] Vaginal suppository:

Vaginal suppositories, also known as pessaries, are solid medications that are inserted into the vagina. They come in different shapes and sizes, with an average weight of 3-5gms. They are usually molded in the globular or oviform shape or compressed on a tablet pressed into modified conical shapes. Compressed tablets weighing about 3gms are used as vaginal suppositories. The moisture level in the vagina is sufficient to allow ready dissolution of a tablet if it is formulated to require minimum water for disintegration. The compressed tablet for vaginal use is usually almond-shaped to ease insertion and provide maximum surface area, which facilitates tablet disintegration and hastens dispersion of the drug on the vaginal wall.

3]Urethral Suppository:

Urethral suppositories, also known as bougies, are solid medications that are inserted into the urethra. They are pencil-shaped and pointed at one end. For males, urethral suppositories weigh about 4g each and are 100-150 mm long. For females, they weigh about 2g each and are usually 60-75 mm in length.

METHODS FOR PREPARATION OF SUPPOSITORIES:^[14]

1.The Hand Rolling method:

It is the simplest and oldest way of preparing suppositories when only a small number of suppositories need to be manufactured in a cocoa butter foundation. It has the benefit of not requiring the cocoa butter to be heated. The active components and grated cocoa butter are triturated in a mortar to create a substance that resembles plastic. The bulk is first rolled into a smooth cylinder using a big spatula or a small flat board on a pill tile after being shaped into a ball in the palm of the hands.

2. The Compression Moulding method:

It is a process used to prepare suppositories. In this method, grated suppository ingredients and medicine are mixed and pressed into a special mold to make a suppository. The process involves first squeezing a small amount of base into the mold and determining the capacity of the mold by weighing the finished suppository. When adding an active ingredient, part of the suppository base should be omitted based on the density factor of the active ingredient.

3. Melt moulding method:

In this method, the suppository base is melted first, and then the drug is dispersed or dissolved in the melted base. The mixture is then poured into suppository molds and allowed to cool and set. Once the mixture has set, the suppository is removed from the mold. This method can be used with all types of suppositories and is recommended for most of them. The components are measured by weight but assembled by volumetric density calculations and geometry calibrations to provide accurate dosages.

Alum: A new treatment for hemorrhoids called ALTA (Aluminium Potassium Sulphate and Tannic Acid): Zione, developed by Mitsubishi Pharma Corporation in Osaka, Japan, is effective for both hemorrhaging and prolapse of internal hemorrhoids. It is expected to replace surgical treatments. [15-17] Alum is a type of chemical compound that contains aluminum and is usually a hydrated double sulfate salt. It is naturally obtained from minerals such as kalinite, alunite, leucite, and bauxite. Alum has several advantages, including cost-effectiveness, availability, nontoxicity, reusability, and eco-friendliness. [18,19]

It is a chemical compound that has been used in large amounts for water purification for human consumption without any noticeable side effects. Therefore, its use for hemorrhoid treatment is unlikely to cause undesirable side effects associated with corticosteroids and NSAIDs. Moreover, alum can be used for a prolonged period due to the low amount required for treatment [20]. Potash alum, also known as potassium alum or potassium aluminium sulfate, is a chemical compound that has been reported to have antibacterial activity when added to water. It has been found to be effective against various epidemic-causing enteric pathogens such as *Vibrio cholerae*. [21] According to a study published in the Journal of the Anus, Rectum and Colon, ALTA: Zione, a new treatment for hemorrhoids, works by cutting off the blood flow to the hemorrhoids. This leads to a decrease in the size of hemorrhoids and fibrosis of the collagen fiber, which prevents prolapsing symptoms. [22] It has also been used topically and internally in traditional systems of medicine such as Ayurveda and traditional Chinese medicine [23] along with the antihemorrhoidal property, it also has other pharmacological properties like Antiseptic [24,25], Antimicrobial [26], Antihemorrhagic [27], Antibacterial [28], etc



Figure 1. Alum

PREPARATION OF HERBAL SUPPOSITORIES: [20]

By Melt Moulding Method:

1. A 2 gm of suppository mould was taken apart, cleaned up, and dried. With the help of cotton wool and soap spirit, the mould was lubricated.
2. Using Analytical balance, the alum was weighed.
3. Beeswax was first heated to a temperature of around 64 °C in a water bath until it melted fully, then used to create base formulations with shea butter and beeswax. Beeswax was melted and then added, followed by the shea butter, which was then gradually blended in.
4. To avoid heating up the shea butter too much, care was taken.
5. The process was repeated for the formulations made with theobroma oil and beeswax plus shea butter, but the formulations made with theobroma oil and theobroma oil plus shea butter required shredding, weighing, and heating to a uniform mixture in a stainless-steel container over a water bath at 37°C.
6. On a warm tile, alum was mixed into a small amount of the base before being combined with the remaining base and whipped until homogenous.
7. After cooling, the molten mass was poured into the mould until it was fully filled. After that, the mould was placed in the refrigerator for around 30 minutes to solidify. With a warm spatula, the extra base was scraped off the mould's top. The suppositories were taken out of the mould, packaged, and kept in storage until they were needed again.

IDENTIFICATION AND AUTHENTICATION OF ALUM SAMPLE:

1. The physical characteristics of the alum have been identified in appearance, colour, odour, taste, pH and solubility. The presence of essential elements Al^{3+} , K^{+} , and SO_4^{2-} was investigated by qualitative chemical tests.

a) Identification test of Aluminium ion: [29]

To test for presence of aluminium, 1g powdered alum was added to 10ml distilled water in a test tube, then 0.1 M NaOH solution was added dropwise to 1ml of above solution and 1ml aqueous Ammonia was added, occurrence of white precipitate indicated the presence of Aluminium.

b) Test of Potassium Ion:^[29]

A cotton swab was moistened with distilled water was then dipped into a container containing the powdered alum and then introduced to a nonluminous flame from a Bunsen burner. A violet colour change of the flame indicated the presence of potassium ions present in the alum.

c) Identification Test of Sulphate Ion:^[29]

To identify the presence of Sulphate ion, about 1 ml of dilute hydrochloric acid was added to 2 ml of the aqueous solution of the alum, then 0.2 M barium chloride (BaCl₂) solution was added to the resulting solution dropwise. The formation of a white precipitate indicated the presence of sulphate ion.

2) Determination of pH of Solution:^[29]

One gram of grounded alum powder was weighed and dissolved in 10 ml of distilled water. The mixture was then filtered, and the pH of the filtrate was determined using a previously calibrated pH meter under room temperature.

3) Determination of Solubility of Alum in Water:^[30]

To determine solubility of the powdered alum in water, 65 g of powder was weighed accurately and added into 100 ml of distilled water at 25 C ± 2°C. Then mixture was shaken well at time intervals for the first 30 minutes and then left uninterrupted for 2 hours at room temperature. The mixture was filtered, and 7.3 ml of the filtrate was diluted to 300 ml. The diluted solution was then analysed by complexometric back titration with ethylenediaminetetraacetic acid (EDTA). In this method, 10 ml of the diluted filtrate was pipetted into a conical flask. 50 ml of 0.01 M EDTA was added and boiled for about 5 minutes and after cooling to room temperature, 5 drops of solo chrome black were added to the mixture, and a blue colour change was observed. About 1 ml of 10% ammonia solution was added to the mixture. The resultant solution was then titrated with 0.01 M zinc sulphate solution until a pink colour was observed as an endpoint, and the titre value was recorded. The difference between the EDTA volume added and the titre value was then calculated (EDTA volume (ml) – titre value of zinc sulphate (ml)). The amount of alum was calculated using formula

Mass of alum = 23.73 mg × (EDTA vol(ml) – titre value of zinc sulphate) × dilution factor (DF).

EVALUATION TESTS OF FORMULATED SUPPOSITORIES:

Physical Characteristics of Formulated Suppositories:

1.Sensory Evaluation:^[31]

The formulated suppositories were evaluated for colour, texture, appearance, feel, and shape to ensure consistency between products. The odour of the prepared suppositories was verified by smelling each of the various formulations and recorded.

2.Surface Condition:^[31]

The surfaces of the suppositories were inspected for various parameters such as brilliance, dullness, mottling, cracks, dark regions, axial cavities, bursts, air bubbles, and holes. Observations were recorded.

3.Uniformity of Weight of Suppositories:^[31]

20 suppositories from each formulation were randomly selected and collectively weighed. They were also weighed individually. The mean weight of the suppositories was determined as A and B as the individual weight of each suppository. The individual suppository weight was deducted from the mean weight of the suppositories (A-B). The percentage deviation of each suppository from the mean was also calculated using the following formula: $\frac{|A - B|}{A} \times 100\%$, where A is the mean weight of the suppositories and B is the individual weight. For all weights of suppositories, not more than two suppositories must deviate from the mean weight by more than 5% and none of the suppositories must deviate by more than 10%.

4.Disintegration Test of Suppositories:

The USP tablet disintegration apparatus was used to test 6 suppositories from each batch. A plastic disc was placed on each suppository, and the basket rack of the disintegration apparatus was used to hold them. The time it took for all 6 suppositories to melt or soften at 37°C ± 2°C in 1000 ml of distilled water was recorded and the mean of six determinations and the standard deviation were calculated.

5.Content Uniformity of Suppositories:^[32]

10 individual suppositories were randomly selected from the formulations and assayed individually for their drug contents. Each suppository was weighed and placed in a 100 ml beaker which was filled with 50ml of deionized water. The mixture was heated on a water bath at 50°C and made up to 100 ml mark with more deionized water. The solution was filtered into a 200ml conical flask using Whatman filter paper and funnel. The filtrate was analyzed using the complexometric back titration method as described under the solubility test. This was repeated for the ten randomly selected suppositories and the average content and standard deviation were determined.

6.Dissolution test on Suppositories:

The USP apparatus II was used to conduct dissolution test on suppositories. The experiment was carried out at a temperature of $37^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$, using 900 ml deionized water with a pH 6.8 and a paddle speed of 50 rpm. At a specified time interval, 10 ml of the dissolution medium was pipetted from the vessel and filtered immediately into a test tube. To replace the withdrawn medium, 10 ml of fresh dissolution medium was withdrawn from the reservoir. The filtrate was then diluted with distilled water to the 100 ml mark of the volumetric flask and analysed by complexometric titration as described above under the solubility/content test. The concentration of the alum released was calculated and the percentage release and cumulative percentage release were determined. The procedure was repeated at specific time intervals of 15, 30, 45, 60, 90, 120, 150, and 180 minutes. A plot of cumulative percentage drug release against time was established.

CONCLUSION:

The formulated Herbal Suppositories containing Alum along with the bases was formulated successfully developed where the formulation was subjected to various evaluations including Authentication of drug, pH, colour, odour, taste, solubility, dissolution, disintegration, drug-base interaction, content uniformity, and uniformity of weight.

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