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OVERVIEW ON SUPPOSITORY

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ABSTRACT

Suppositories are vital pharmaceutical dosage forms that play an important role in drug delivery. These dosage forms are placed into body cavities, primarily the rectum and vagina, to transmit medication into systemic circulation. Patients who cannot take medications orally due to conditions such as nausea, vomiting, or neurological disorders can utilize suppositories. Suppositories are preferred over other dosage forms because they are available in various shapes and sizes. They represent a highly practical method of administering medication.

It can be made using different bases such as cocoa butter, PEG, and fat as primary components. The preparation can be done through methods like hand rolling, compression molding, fusion molding, and automatic molding techniques. Evaluation tests include checks for weight uniformity, content uniformity, melting point determination, general appearance assessment, active ingredient assay, liquefaction time measurement, breaking strength test, disintegration test, and dissolution test[1].

KEYWORDS: *suppository, Avoid first pass metabolism, Evaluation tests , Rectal drug delivery system.*

AIM AND OBJECTIVE

Aim: To avoid first pass metabolism and to increase bioavailability by using suppository.

Objective

1. Provide Local Treatment: Suppositories can target localized conditions, such as hemorrhoids or infections.
2. Facilitate Systemic Absorption: They allow for the quick absorption of medications into the bloodstream, useful for patients who cannot take oral medications due to nausea, vomiting, or difficulty swallowing.
3. Bypass First-Pass Metabolism: Suppositories can reduce the breakdown of drugs by the liver, enhancing bioavailability and effectiveness.
4. Enhance Patient Comfort: They offer an alternative for individuals who may have trouble with oral medications or prefer not to take them.
5. Ensure Controlled Release: Suppositories can provide a sustained release of medication, improving therapeutic outcomes.
6. Pain Relief: They can administer analgesics for localized pain or systemic relief[2].

INTRODUCTION

Suppositories are solid, medicated forms of various shapes and sizes designed for placement into body cavities. The medication is mixed with a base such as cocoa butter, which melts at body temperature, or with substances like glycerinated gelatin or PEG, which gradually dissolves in the mucous secretions. Suppositories are particularly effective for delivering local effects, but they can also be utilized for systemic effects or to provide mechanical assistance in emptying the lower bowel. The optimal base for suppositories should be non-toxic, non-irritating, inert, compatible with drugs, and easily shaped through compression or molding. Additionally, it needs to dissolve or break down in the presence of mucus secretions or melt at body temperature to facilitate the release of the medication. Similar to ointment bases, the formulation of the suppository base significantly influences both the rate and extent of medication releases[3]. Suppositories are solid formulations that each hold one or more active compounds and are designed for rectal use. Typically, they are meant to be administered as a single dose for either local effect or the systemic uptake of the active compounds.

Suppositories can be Categorized into Different Types

- Rectal suppositories
- Vaginal suppositories.
- Urethral suppositories.

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- Nasal suppositories.
- Ear cones.

METHODS FOR MAKING SUPPOSITORIES

SUPPOSITORY MOULD

- The moulds utilized for making suppositories are made from various metals and come in different shapes.
- They typically consist of two or more sections that are connected with a screw mechanism.
- Within the moulds, the cavities are crafted from materials such as aluminum, brass, stainless steel, and plastics.
- Moulds come in different sizes, including capacities of 1, 2, 4, and 8 grams.

CALIBRATION OF THE MOULD

- The initial step involves creating moulded suppositories using only the base material.
- The suppositories are then combined, and the average weight is documented.
- To find the volume of the mould, the suppositories are melted in a calibrated beaker, and the volume of the liquid is measured.

LUBRICANTS UTILIZED IN MOULDS

- Cocoa butter and glycerogelatin bases are necessary for the lubrication of moulds.
- This helps to avoid the sticking of bases to the mould cavity walls.
- It also facilitates the easy extraction of suppositories from the moulds. The lubricants create a barrier between the mould cavity walls and the suppository base.
- This prevents the bases from adhering to the moulds.
- The characteristics of the lubricants should differ from those of the bases.

METHOD AND EVALUATION

Methods

1.Molding
2.Compression
3.Heat molding/fusion
4.Hand rolling & shaping
5.Automatic machine molding

1. **Molding**: Molds are typically constructed from stainless aluminum, brass, or plastic. Individual molds made of plastic are utilized to create a single suppository. Temporary molds can be made by pressing aluminum foil around an object shaped like the desired suppository, then removing the object and pouring in the melted base.

2. **Compression**: The compression apparatus includes a cylinder, a piston, molds, and a metallic stop plate at the base. The mass is placed inside the cylinder, and pressure is applied. Once the prepared mass is put into the mold, it is stored in a cool area. After it has cooled, the suppositories are taken out from the compression machine and packed.

3. **Heat molding/fusion:** This technique involves melting the base and mixing in the drugs and additives. The following steps are carried out:
   - Melting the base,
   - Mixing in the drug and additives,
   - Pouring into cooled molds,
   - Gathering the suppositories.

4. **Hand rolling & shaping:** This is the most basic and traditional method for making a suppository, done manually. It involves rolling a well-mixed suppository base that contains the active ingredient into a cylindrical rod of the desired length and diameter, or into vaginal balls of specific weight. To stop the mixture from sticking, starch or talc powder is sprinkled on the rolling surface and on the hands. The rod-shaped suppositories are then cut into sections to create a pointed end.

5. **Automatic machine molding:** This machine can produce as many as 10,000 suppositories each hour. The production rate of an automatic molding machine surpasses that of hand molding. In this process, there is no risk of air entrapment or contamination in the suppositories. There are two primary types of machines utilized for this process[4].
   - Rotary machine
   - Linear machine

Evaluation Test

1. Weight uniformity
2. Content uniformity assessment
3. Melting point determination
4. General appearance assessment
5. Active content assay
6. Liquefaction duration
7. Breaking assessment
8. Disintegration assessment
9. Dissolution test[5].

Quality Control Tests for prepared suppositories

Quality control procedures for produced suppositories encompass identification, assay, and occasionally, water content, residual solvents, dissolution, and content uniformity. The quality control of suppositories addresses both their physical and chemical properties. Physical evaluations involve visual inspections (appearance), weight uniformity, texture uniformity, melting point, liquefaction duration, melting and solidification times, and mechanical strength assessments. Chemical analyses involve measuring the potency and conducting dissolution tests. The texture uniformity can be evaluated by cutting a suppository both longitudinally and laterally, ensuring that each segment has a smooth, consistent surface.

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1.Visual assessment

The color and texture of the suppository are relatively straightforward to evaluate. It is crucial to confirm that there are no signs of fissures, pitting, fat blooming, exudation, sedimentation, or movement of the active ingredients. Suppositories can be examined as whole units and also by dividing them lengthwise.

- **Surface quality:** The following conditions can be assessed: shine, dullness, discoloration, cracks, dark spots, axial cavities, ruptures, air pockets, holes, etc.
- **Color:** It is important to check the color's intensity, quality, and uniformity.
- **Odour**: Assessing the odour helps avoid mix-ups when similar suppositories are being handled. A change in odour may also indicate that degradation is occurring.
- **Weight:** Suppositories can be weighed using an automatic scale to obtain the combined weight of ten suppositories. If the weight is found to be insufficient, it is advisable to confirm that the mould is adequately filled and check for any cavities or air bubbles due to improper mechanical agitation or an unwanted surfactant.
- **Melting range**: Typically, the melting point should be at or below 37◦C. A non-destructive method is necessary because melting the suppository prior to measurement could cause its components to enter a metastable state. The melting test involves placing a suppository on a water surface maintained at 37◦C and observing its complete melting within a few minutes.

2. Determining Melting Point

Utilizing a U-shaped capillary tube for melting point determination offers accurate data for monitoring excipients and ensuring consistency during the production of suppositories that include soluble active ingredients. Alternatively, melting point can be established by inserting a thin wire into the mold containing the melted suppository prior to its solidification. The suppository is then suspended in water using the wire, and the temperature of the water is gradually increased (approximately 1°C every 2-3 minutes) until the suppository detaches from the wire; this indicates the melting point of the suppository.

3. Time for Liquefaction

Liquefaction testing gives insight into how a suppository behaves when exposed to a maximum temperature of 37°C. The common method utilized is Krowczynski's method, which assesses the duration needed for a suppository to melt under pressures akin to those experienced in the rectum (approximately 30 g) while in the presence of water at 37°C. Typically, the liquefaction process should not exceed around 30 minutes. For Krowczynski's method, the required apparatus comprises a glass tube with a diameter of 16 mm and a length of 235 mm, featuring a reduction of approximately 6 mm at the base. One end is sealed with a small rubber stopper to make cleaning easier after use. A thermometer that is graduated in tenths of a degree Celsius is employed. The tube and thermometer are secured in position by a large rubber stopper fitted with two openings in a 225 mm long, 50 mm diameter tube, which is equipped with side tubes to allow water at 37°C from a constant-temperature water bath to flow.

4. Test for Suppository Penetration

A test for suppository penetration can be utilized to find the temperature at which the suppository becomes sufficiently malleable for a penetrating rod to pass through its entirety. The temperature is set to the level required for testing, typically around 37°C. The suppository is positioned within the apparatus, and the penetration rod is carefully aligned. The apparatus containing both the suppository and the penetration rod is immersed in a temperature-controlled bath, and a stopwatch is initiated. The time is noted once the penetration rod descends through the softened suppository.

5. Mechanical strength/crushing test

Suppositories can be categorized as either brittle or elastic by assessing the mechanical force necessary to break them. Trials have been conducted to gauge the mass (in kilograms) that a suppository can withstand without fracturing. An acceptable outcome is a pressure of at least 1.8–2 kg. The suppository is set in an upright position, and increasingly heavier weights are placed on it until it deforms and fails. The objective of this test is to ensure that the suppository can be safely transported under typical conditions and effectively administered to the patient [6].

Advantages

a) Enhanced drug stability against enzymes: Various proteolytic and other enzymes present in the gastrointestinal tract (GIT) cause degradation of drugs, which hinders effective absorption when taken orally.
b) Some reduction of hepatic first pass: The rectum has a rich blood supply from multiple rectal arteries and is drained by at least three veins, allowing for drug absorption via this venous system. It is commonly noted that the inferior vena cava is linked to the middle rectal veins, facilitating a bypass of the portal system and the first pass metabolism in the liver.
c) Increased drug capacity: Suppositories can accommodate two to three times higher doses of drugs, depending on the quantity of other excipients needed in their formulation.
d) Lymphatic absorption: Numerous studies have indicated that some drugs, following rectal administration, may enter the lymphatic system, bypassing first pass metabolism.
e) Stable and consistent environment: In contrast to oral administration, the rectal route offers a much more stable environment for drug absorption.
f) Suitable for individuals with swallowing difficulties: Rectal administration can be particularly beneficial for children and elderly individuals who have trouble swallowing.

Disadvantages

a) Patient acceptance and adherence: In various cultures, there is a hesitation to accept rectal administration as a form of medication, leading pharmaceutical companies to generally avoid producing rectal dosage forms unless absolutely necessary.
b) Risk of non-specific drug loss: Absorption may be ineffective due to early expulsion from the rectum and the potential interaction between the drug or excipient and fecal matter, which could hinder absorption and reduce efficacy.

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c) Limited rectal liquid volume: The small volume (3 ml) may restrict the dissolution of drugs, particularly those with low solubility in water.
d) Formulation challenges: Factors like melting, liquefaction, solubility, and particle size can create difficulties in the formulation process.
e) Higher costs: Rectal dosage forms tend to be more expensive when compared to tablets.

Applications of Suppository

Suppositories are primarily utilized for patients who are unconscious, children, and elderly individuals. They serve both systemic and local purposes when other routes of administration are not feasible. A variety of medications have been formulated into suppository form, as illustrated below.

Different types of medications included in suppositories are categorized as follows:

1. Antibiotics: such as Ceftizoxime and Amoxicillin, using Thiobroma and Cefmetazole.
2. Analgesics: including Indomethacin and Paracetamol, utilizing PEG and glycerol-gelatin, as well as Etodolac and Ketoprofen, also with PEG.
3. Bronchodilators/anti-asthmatics: like Theophylline and Terbutaline[7].

DISCUSSION

The use of drug treatments for various ano-rectal issues dates back to ancient civilizations. Today, both modern and traditional medications are increasingly utilized in proctology. The rectal route, which can provide local or systemic effects, presents an intriguing option for treatment. Two significant benefits of these therapeutic methods are their ease of use and quick absorption. Suppositories represent a highly practical form of medication delivery. The drug is mixed into a base that either melts at body temperature or dissolves in mucus secretions, resulting in localized or systemic effects. Amid efforts to contain costs and the potential dangers of AIDS and other communicable diseases, administering drugs via suppositories is emerging as an effective and practical solution. It is widely acknowledged that the market for over-the-counter suppository therapies is substantial. In proctology, suppositories are primarily employed to achieve local effects, such as providing anti-inflammatory and anesthetic relief for hemorrhoidal issues. Treatments for hemorrhoids typically include astringents, local anesthetics, veno-tonic agents, and components aimed at reducing inflammation.

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