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A review on suppositories

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Abstract

Suppositories are pharmaceutical dosage forms that hold a crucial place in the realm of drug delivery. This review provides a comprehensive introduction to suppositories. This article explores the various aspects of suppository formulations and therapeutic applications. This review emphasizes the significance of suppositories as a valuable drug delivery option and the role they play in addressing specific patient needs. It also discusses the fundamental components of suppositories, including bases and active pharmaceutical ingredients, along with the methods of suppository preparation. The development and formulation of suppositories require a deep understanding of various factors, including base selection, drug compatibility, and patient preferences. The choice of base impacts the release and absorption characteristics of the drug, making it a pivotal consideration in suppository design. Their significance lies not only in their unique mode of administration but also in their ability to offer solutions for specific patient needs, including cases of nausea, vomiting, or difficulties with oral medication.

Keywords: Suppositories; Types of Bases; Methods of Preparation; Evaluation tests

1. Introduction

Suppositories are a medicated solid dosage forms intended for insertion into the body cavities. The term suppository has its origin in Latin and it means, to place under. Suppositories and ointments are the two main modes of administration of drugs through the rectum. They are used to deliver both systemically acting and locally-acting medications. The general principle is that the suppositories is inserted as a solid and dissolve or melt inside the body to deliver the medicine received by the many blood vessels present locally. The suppository was first used in nursing facilities to be administered to older patients who were not capable of swallowing medications. Suppositories are available in various sizes and shapes which facilitate their insertion and retention in the cavity. Adult rectal suppositories weighed about 2 g while those for children are about half that weight. The suppository may be useful as a controlled release formulation for the long-term treatment of chronic diseases like hypertension, asthma, diabetes and anaemia [1].

Definition: Suppositories are solid dosage forms intended for insertion into body orifice, where they melt, soften or dissolve and exert local or systemic effects. Suppositories are designed to be inserted into body cavities or orifices, where they dissolve and melt at body temperature, acting locally on the body. Suppositories' effects are influenced by the drug's composition, concentration, and rate of absorption in the body [2]. A substantial role is played by the systematic action of analgesics, antispasmodics, sedatives, tranquillizers, and antibacterial agents.

2. Characteristics of suppositories

- Easy to melt at room temperatures
- Can be easily inserted into body cavities, including the rectum, vagina, urethra, nose, and ear

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- They are known to melt drugs for their administration
- They have a systematic effect

2.1. Suppositories are classified as

- Rectal suppositories.
- Vaginal Suppositories.
- Urethral Suppositories.
- Nasal Suppositories.
- Ear cones.

2.2. Ideal properties of suppository base

- Bases must have a solid form at room temperature.
- It should possess a less irritating property.
- They should not produce an inflamed sensation in body cavities.
- It should be stable during storage conditions.
- They should be soft so that they can be handled easily.
- It must be nonreactive with drugs and additives.
- It should have good emulsification properties
- The acid value must lie between less than 0.2 and zero.
- It should have an iodine value of less than 7

2.3. Types of suppository bases [3]

- Fatty suppository bases
    - Theobroma oil / cocoa butter
    - Emulsified Theobroma oil
    - Hydrogenated oil
- Hydrophilic suppository bases
- Hydrophilic (Water-loving) suppository base includes two categories.
    - Water soluble Bases
    - Emulsifying Bases

2.4. Advantages of suppositories

- The drug is rapidly absorbed through the mucous membranes.
- It is a convenient route of administration for drugs that cause vomiting, irritate the GIT, and drugs that are destroyed at the acidic pH of the stomach.
- The suppositories dosage form is useful when oral therapy is restricted or oral administration is not possible.
- It is suitable for unconscious patients, uncooperative patients, and patients suffering from severe vomiting.
- It provides rapid onset of action as compared to the oral route because the absorption of the drug through rectal mucosa directly reaches blood (avoids the first-pass metabolism).
- Prolonged drug action can be achieved using suppositories dosage form.
- It does not have systemic side effects compared to other dosage forms.
- Increase in bioavailability can be achieved compared to oral dosage forms.
- The rectal route of administration offers a much more constant atmosphere for the drug to be absorbed than the oral route.
- No issue of drugs with unpleasant taste and odour, since they do not need to be swallowing.

2.5. Disadvantages of suppositories

- Mucosal irritation
- Patient compliance
- Erratic and undesired absorption
- Placement too high into rectum may lead to first pass metabolism
- Installation may trigger defecation reaction
- Diarrhoea& disease states affect absorption [4]

2.6. Manufacturing of suppositories

2.6.1. Methods of preparations of suppositories

- Moulding
- Compression
- Heat moulding / fusion
- Hand rolling & shaping
- Automatic machine moulding

Preparation by moulding

It is done initially by calibration and lubrication of moulds. Commercially available moulds can produce individual or large number of suppositories. Moulds are made commonly from stainless aluminium, brass or plastic. Individual plastic moulds are used to make single suppository. Temporary moulds are formed by pressing aluminium foil by putting an object having shape of desired suppository and then remove the object and pour the melted base. Various moulds for distinguished routes of administration [5].

- Urethral suppository mould
- Rectal suppository mould
- Vaginal suppository mould
- Depending on the formulation, moulds may require lubrication before the melt is poured, to facilitate clean and easy removal of the moulded suppositories.

Lubrication is seldom necessary when the base is:

- Cocoa butter
- Polyethylene glycol
- Glycerinated gelatine

A thin coating of mineral oil applied with finger on the surface of mould. Any Material which cause irritation to mucous membranes should not employed as lubricant. Lubricant should be applied with fairly stiff brush. The pharmacist should calibrate each suppository mould for the usual base so as to prepare medication suppositories, each having the proper quantity of medicaments. Each individual mould is capable of holding a specific volume of material in each of its openings.

Compression

Compression machine consists of cylinder, piston, moulds and a metallic stop plate at the bottom. Place the mass in cylinder and apply pressure. Prepared mass is filled into the mould and then is kept in cool place. After cooling these suppositories are removed from compression machine are packed.

Heat moulding/fusion

In this process, bases are melted then Drugs and additives are mixed into it. Following steps are involved

- Melting the base
- Incorporation of drug & additives into it
- Filling into cooled moulds
- Collection of suppositories

Hand rolling & shaping

The simplest and the oldest method of preparing a suppository are by hand. By rolling the well-blended suppository base containing the active ingredient into cylindrical rod of desired length and diameter, or into vaginal balls of intended weight. Starch or talc powder is spread on the rolling surface and hands to prevent the mass from adhering. Rod shaped suppositories are cut into portions to get one end pointed. This method is practical and economical for smaller number of suppositories.

Automatic moulding machine

Using this machine up to 10,000 suppositories per hour can be produced. The rate of production by automatic moulding machine is higher than hand moulding. In this, there is no chance of air entrapment or any contamination in suppositories. There are two types of machines used to run this process:

- Rotary machine
- Linear machine

Process of formation of suppositories is almost same in both types of machines but linear machine is more efficient (i.e. rate of production) in working than the former one.

2.6.2. Displacement value

The volume of a suppository from a particular mould is uniform but its weight will differ with the density of the base. It is the quantity of the drug that displaces one part of the base.

2.7. Specific problems in formulating suppositories

2.7.1. Viscosity

Viscosity of melted base is low in cocoa butter and high in PEG and glycerinated gelatin. Low viscosity base when melted the suspended particles may sediment very quickly producing non uniform distribution of drugs.

2.7.2. Remedies:

- The base should be melted at the minimum temperature required to maintain the fluidity of the base.
- The base is constantly stirred in such a way that the particles cannot settle and no air is entrapped in the suppository.
- A base with a narrow melting range closer to rectal temperature is used.
- Inclusion of approximately 2% aluminum monostearate increases the viscosity of the fatty base and also helps in homogeneous suspension of particles.
- Cetyl, stearyl, myristyl alcohol or stearic acid are added to improve the consistency of suppositories.

2.8. Lubricants

Cocoa butter adheres to suppository molds because of very low volume of contraction. Aqueous lubricant may be used to remove the suppositories easily from the molds. They are applied by wiping, brushing or spraying. The mold surfaces may be coated with Teflon to reduce the adhesion of base to mould wall.

2.9. Volume contraction

When the bases are cooled in the mould volume of some bases may contract. Volume contraction produces

- Good mold release facilitating the ejection from mould.
- Contraction void formation at the top: This imperfection can be solved by adding slight excess base over the suppositories and after cooled the excess is scrapped off.

2.9.1. Brittleness

Cocoa butter base is not brittle but synthetic fat bases with high degree of hydrogenation and high stearate containing bases are brittle. Brittle suppositories produce trouble during manufacture, handling and packaging and during use [6].

Causes: Rapid chilling (shock cooling) of the melted bases in an extremely cold mould.

2.9.2. Remedies

- The temperature difference between the melted base and mold should be as small as possible.
- Addition of small amount of Tween 80, castor oil, glycerin or propylene glycol imparts plasticity to a fat and makes it less brittle.

3. Quality control tests for prepared suppositories

Quality control procedures for manufactured suppositories include identification, assay, and, in some cases, water content, residual solvent, dissolution, and content uniformity. Suppository quality control includes physical and chemical aspects of the product. Physical analysis includes visual examination (physical appearance), uniformity of weight, uniformity of texture, melting point, liquefaction time, melting and solidification time, and mechanical strength. Chemical testing includes analysis of the activity and dissolution testing. The uniformity of texture can be assessed by sectioning a suppository longitudinally and laterally, and ensuring that each section presents a smooth, uniform surface [7].

3.1. Visual examination

Colour and the surface characteristics of the suppository are relatively easy to assess. It is important to check for the absence of fissuring, pitting, fat blooming, exudation, sedimentation and the migration of the active ingredients. Suppositories can be observed as an intact unit and also by splitting them longitudinally.

- **Shape:** It is advisable to check the shape of the suppository to see if it is consistent, irrespective of whether the suppository is in desired shape.
- **Surface condition:** The following can be checked: brilliance, dullness, mottling, cracks, dark regions, axial cavities, bursts, air bubbles, holes, etc.
- **Color:** The intensity, nature and homogeneity of the color should be verified.
- **Odour:** Verification of odour can prevent confusion when similar suppositories are being processed. A change in the odour may also be an indication of a degradation process.
- **Weight**: Suppositories can be weighed on an automatic balance, obtaining the weight of 10 suppositories. If the weight is found to be too small, it is advisable to check whether the mould is being well filled and whether there are axial cavities or air bubbles caused by badly adjusted mechanical stirring or the presence of an undesirable surfactant.
- **Melting range:**In general, the melting point should be equal to or less than 37 °C. A non-destructive method must be used because if the suppository is melted before a measurement is made, the suppository constituents may be transformed into a metastable state. The melting test consists of placing a suppository on the surface of water thermostatically controlled at 37 °C and verifying the complete melting of the suppository in a few minutes.

3.2. Melting point determination

The use of a U-shaped capillary tube to determine melting point provides precise information for excipients control and consistency in production for those suppositories containing soluble active principles. The melting point can also be determined by placing a small-diameter wire into the mould containing the suppository melt before the form solidifies. The form is then immersed in water, held by the wire and the temperature of the liquid is raised slowly (about 1 °C every 2-3 minutes) until the suppository slips off the wire; this is the melting point of the suppository.

3.3. Liquefaction time

Liquefaction testing provides information on the behaviour of a suppository when subjected to a maximum temperature of 37°C. The test commonly used is Krowczynski's method which measures the time required for a suppository to liquefy under pressures similar to those found in the rectum (approximately 30 g) in the presence of water at 37°C. In general, liquefaction should take no longer than about 30 minutes. For Krowczynski's method, the apparatus consists of a 16 mm diameter glass tube, 235 mm long with an approximately 6mm diameter reduction at the base. One end is blocked with a small rubber stopper to facilitate cleaning after use. A thermostat graduated in tenths of a centigrade is used. The tube and thermometer are held in place by means of a large rubber stopper with two holes in a 225mm long tube with a 50mm diameter, fitted with lateral tubes to allow the water at 37°C from a constant-temperature water bath to circulate.

3.4. Suppository penetration test

A suppository penetration test can be used to determine the temperature at which the suppository becomes sufficiently soft for a penetrating rod to drop through its length. The temperature is adjusted to that required for the test, generally about 37 °C. The suppository is placed in the device and the penetration rod gently moved into place. The device holding the suppository and penetration rod is lowered into the constant temperature bath and a stopwatch is started. When the penetration rod drops through the softened suppository the time is recorded.

3.5. Mechanical strength/crushing test

Suppositories can be classified as brittle or elastic by evaluating the mechanical force required breaking them. Tests have used that measure the mass (in kilograms) that a suppository can bear without breaking. A good result is at least 1.8–2 kg pressure. The suppository is positioned in an upright position and increasing weights are placed on it until it loses its structure and collapses. The purpose of the test is to verify that the suppository can be transported under normal conditions, and administered to the patient [8].

3.6. Disintegration test

In disintegration test apparatus disintegration time of suppositories are measured placing suppositories in each tube and the basket rack assembly is positioned in a 1-litre beaker of water or simulated gastric fluid or simulated intestinal fluid at 37°C±2° C such that the suppository remains 2.5 cm from the bottom of the beaker. Standard motor moves the basket up and down through a distance of 5 to 6 cm at a frequency of 28 to 32 CPM (cycles per minute). USP disintegration test will be passed if all the suppositories disintegrate and the particles passed through the #10 mesh screen within the specified time.

3.7. Dissolution testing

Dissolution testing is often required for suppositories to test for hardening and polymorphic transitions of active ingredients and suppository bases. Dissolution testing methods include the paddle method, basket method, membrane diffusion method/dialysis method and the continuous flow/bead method. In vitro dissolution study is performed by using USP Type I/II Apparatus. The suppository is kept in 900 ml of dissolution fluid phosphate buffer pH 7.4 or phosphate buffer pH 6.8 or 0.1N HCl (pH 1.2) or simulated gastric fluid and stirrer rotating at specified rpm and maintaining the temperature 37±0.5° C of dissolution media. 5 ml of samples were withdrawn at different time intervals replaced with fresh medium and analyzed in UV-Visible spectrophotometer for estimation of absorbance taking a suitable blank solution. Finally, the drug release rate is calculated using suitable equation.

3.8. Content uniformity testing

In order to ensure content uniformity, individual suppositories must be analyzed to provide information on dose-to-dose uniformity. Testing is based on the assay of the individual content of drug substance(s) in a number of individual dosage units to determine whether the individual content is within the limits set [9].

4. Conclusion

The rectal route for drug delivery is underutilized despite many advantages. Although the oral route of drug administration is the most convenient route for drug administration, there are a number of circumstances where this is not possible from either a clinical or pharmaceutical perspective. Rectal administration can have a potential drug delivery system particularly for drugs that are either too irritating for the gut or more effective when not metabolized by the liver. Suppositories offer patients an option that is less invasive and less discomforting. In conclusion, suppositories represent a versatile and valuable dosage form within the field of pharmaceuticals. They offer a unique solution for drug delivery, particularly when oral administration is not feasible or effective. Suppositories can be customized to provide controlled release, site-specific targeting, and enhanced patient compliance, making them a valuable tool in addressing various medical conditions. Their versatility extends to both hydrophobic and hydrophilic drugs, further expanding their applicability. It is also administered in unconscious patients and children for the treatment of pregnancy, chemotherapy and allergy induced emesis.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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