Suppositories: Exploring Their Role in Modern Medicine

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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

INTRODUCTION

Suppositories are medicated, solid bodies of various sizes and shapes suitable for introduction into body cavities. The medicament is incorporated into a base such as cocoa butter which melts at body temperature, or into one such as glycerinated gelatine or PEG which slowly dissolves in the mucous secretions. Suppositories are suited particularly for producing local action, but may also be used to produce a systemic effect or to exert a mechanical effect to facilitate emptying the lower bowel. [1] The ideal suppository base should be nontoxic, no irritating, inert, compatible with medicaments, and easily formed by compression or moulding. It should also dissolve or disintegrate in the presence of mucous secretions or melt at body temperature to allow for the release of the medication. As with the ointment bases, suppository base composition plays an important role in both the rate and extent of release of medications.[2]

DEFINITION

A suppository is a dosage form used to deliver medications by insertion into a body orifice where it dissolves or melts to exert local or systemic effects. There are three types of suppositories, each to insert into a different section: rectal suppositories into the rectum, vaginal suppositories into the vagina, and urethral suppositories into the urethra of a male. [3]

Ideal Properties of Suppository bases:

- It should be non-irritant and non-reactive.
- It should shrink sufficiently to remove mold.
- It should not interfere in the release or absorption of the drug.It should melt at body temperature.
- It must maintain the proper shape and size.
- It should be stable in storage conditions. [4]

Advantages of Suppository:

- It provides rapid action.
- Best for vaginal and rectum fungal infection.
- It's easy to use for those patients, who are unable to take oral medication.
- Increase the bioavailability of drugs.
- Very useful to get local effects.

- It avoids the first-pass metabolism.

Dis-advantages of Suppository:

- Preparation is complicated compared to liquid and tablets.
- Need low temperature to store.
- It can cause irritation in some patients.
- Some patients feel embarrassed.
- Very few drugs can be delivered by this type of dosage form. [5]

Size and shape of suppositories:

The finished suppositories are created in various shapes and sizes in order to deliver the optimum therapy as per necessity, such as, type of active component, route of administration, age and condition of the patient, desired release pattern etc. They are also accessible in a variety of physical forms; they can be compressed or moulded, covered in foil or plastic, or enclosed in gelatine.

The most popular suppositories come in the following sizes: 1 g: it can be either bullet-shaped or cone-shaped and has a rounded apex. 2 g: the 2 g size is torpedo-shaped but has the same shape as the 1 g size. Their bottom or later half is progressively widening for around three quarters of their length while maintaining a blunt or pointed peak. As a result of its broadest portion, there is a benefit: after insertion, the anal sphincter muscles push the suppository into the rectum. The most typical commercial product size is 2 g. The size of a glycerol suppository for an adult is 4 g. It can also be cone-shaped with a rounded tip and weighs 4 g or 8 g. [6]

CLASSIFICATION:

There are 5 types of suppositories according to the route of administration

- Urethral suppositories
- Rectal suppositories
- Vaginal suppositories
- Ear Cones

Urethral Suppositories: Urethral suppositories called bougies are pencil shape. Those intended for males weigh 4gm each and are 100-150 mm long. Those for females are 2gm each and 60-75 mm in length.

Rectal Suppositories: Rectal suppositories come in different shapes and sizes but are usually narrowed at one end. Rectal suppositories can deliver many types of medication. For instance, they may contain glycerine to treat constipation or acetaminophen to treat a fever. Medication from a rectal suppository tends to work quickly. This is because the suppository melts inside the body and is absorbed directly into the bloodstream.

Vaginal Suppositories: Vaginal suppositories are solid medications that are inserted into the vagina with a special applicator. The body absorbs drugs from vaginal suppositories quickly. They work faster than medications you take by mouth. This is because suppositories melt inside the body and absorb directly into the bloodstream.

Nasal Suppositories: Nasal suppositories called nasal bougies or buginaria meant for introduction into nasal cavity. They are prepared with glycerogelatin base. They weigh about 1gm and length 9-10cm.

SUPPOSITORY BASES

Classification of suppository bases

1. Fatty bases – they melt at body temperature.

2. Water-soluble or water miscible base – they dissolve or disperse in rectal secretions.

3. Emulsifying bases – they emulsify small amount of aqueous solution of drug.

FATTY BASES

Example: Theobroma oil (Cocoa butter), Synthetic fats.

Theobroma oil (Cocoa butter)

It is a yellowish-white solid having chocolate flavour.

It is a mixture of glyceryl esters of stearic, palmitic, oleic and other fatty acids.

Synthetic Fats As a substitute of Theobroma oil a number of hydrogenated oils, e.g. hydrogenated edible oil, arachis oil, coconut oil, palm kernel oil, stearic and a mixture of oleic and stearic acids are recommended.[8]

WATER SOLUBLE AND WATER MISCIBLE BASES

Glycero-Gelatin base
This is a mixture of glycerol and water made into a stiff jelly by adding gelatine.
It is used for the preparation of jellies, suppositories and pessaries. The stiffness of the mass depends upon the proportion of gelatine used which is adjusted according to its use.
The base being hydrophilic in nature, slowly dissolves in the aqueous secretions and provide a slow continuous release of medicament. Glycerogelatin base is well suited for suppositories containing belladonna extract, boric acid, chloral hydrate, bromides, iodides, iodoform, opium, etc.
Depending upon the compatibility of the drugs used a suitable type of gelatine is selected for the purpose. Two types of gelatines are used as suppository base

a. Type-A or Pharma gel

A which is made by acid hydrolysis (has isoelectric point between 7 to 9 and on the acid side of the range behaves as a cationic agent, being most effective at pH 7 to 8) is used for acidic drugs.

b. Type-B or Pharma gel

It is prepared by alkaline hydrolysis (having an isoelectric point between 4.7 to 5 and on the alkaline side of the range behaves as an anionic agent, being most effective at pH 7 to 8) is used for alkaline drugs

Soap-Glycerine Suppositories

- The soap glycerine suppositories have the disadvantage that they are very hygroscopic, therefore they must be protected from atmosphere and wrapped in waxed paper or tin foil.[9]
- In this case gelatine and curd soap or sodium stearate which makes the glycerine sufficiently hard for suppositories and a large quantity of glycerine up to 95% of the mass can be incorporated.
- Further the soap helps in the evacuation of glycerine.

Methods of preparations of suppositories:

Following methods are used for manufacturing of suppositories

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

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.

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.

Fusion moulding:

It involves first melting the suppository base, and then dispersing or dissolving the drug in the melted base. The mixture is removed from the heat and poured into a suppository mold.

When the mixture has congealed, the suppositories are removed from the mold. The fusion method can be used with all types of suppositories and must be used with most of them. [11]

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.

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.

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.

EVALUATION TESTS

1. Uniformity of weight
2. Content Uniformity test
3. Melting point determination test
4. General appearance test
5. Assay of active contents
6. Liquefaction time
7. Breaking test
8. Disintegration test
9. Dissolution test

Uniformity of weight:

- Weigh 20 suppositories individually
- Determine their average weight.
- Not more than two of individual weights should deviate from the average weight more than 5% and none deviates by more than 10%. [12]

Content Uniformity Test

- Take 10suppositories; determine the active ingredients of each of the 10 suppositories by using a suitable analytical method.

- If not more than one of the individual values thus obtained is outside the limit i.e. % of the average value and none of them is outside the limit i.e. 25% of the average value.

Melting Point Determination Test

- Melt the suppositories rapidly at a temperature not more than 100C above the point of complete fusion, insert one end of glass capillary tube into the melted substance so that a column of substance become 8-12 high rise into it.
- Cool the tube to 150C and maintain the temperature at 15-170C for not less than 16 hours. Attached the tube to thermometer in the heating vessel containing water at 150C so that the lower end of the column of substance is 30 mm below the surface of water. Heat the water with constant stirring, so that the temperature rise at a rate of 20C per minute.
- The temperature at which partially melted substance begins to rise in the tube is regarded as the melting point. The melting point of suppositories should not rise more than that given in the monograph.[13]

General Appearance:

- The suppository when cut longitudinally and examined with the naked eye the internal and external surfaces of the suppository should be uniform in appearance.
- Compliance with the standard indicates satisfactory subdivision and dispersion of suspended material
- Surface appearance and colour can be verified usually to assess absence of fissuring, pitting, exudation, migration of the active ingredients.

Assay of Active contents:

- Official limits in IP and BP for the active contents in suppositories is 95- 105%
- Dissolve a number of suppositories equivalent to 8 grams of glycerol in 50ml of water and add quantity sufficient to produce 250 ml.
- Take 5ml of this solution and 150ml of water and 0.25ml of Bromocresol purple solution and add 0.1M NaOH to neutralize the blue color of indicator.
- Add 1.6 grams of sodium metaphenolate and allow to stand for 15 minutes and titrate with 0.1M NaoH to same blue colour.
- Each ml of 0.1M NaOH=0.00921 grams of glycerol.[14]

Liquefaction Time

- It is the time required to liquefy the suppositories. A modification of the method developed by krowcynski is another useful test of finished suppositories. It consists of a U-tube partially submersed in a constant temperature water bath.
- A construction on one side holds the suppository in place in the tube. A glass rod is placed on top of the suppository, and the time for the rod to pass through to the constriction is recorded as the softening time.
- This can be carried out at various temperatures from 35.5 to 370C, as a quality control check and can also be studied as a measure of physical stability over time.

Breaking Test:

- Brittleness of suppositories is a problem for which various solutions have already been described. The breaking test is designed as a method for measuring the fragility or brittleness of suppositories.
- The apparatus used for the test consists of a double-wall chamber in which the test suppository is placed. Water at 370C is pumped through the double walls of the chamber, and the suppository contained in the dry inner chamber, supports a disc to which a rod is attached.
- The other end of the rod consists of another disc to which weights are applied. The test is conducted by placing 600g on the platform. [15]
- At 1-min intervals, 200g weights are added, and the weight at which the suppository collapses is the breaking brittleness characteristics of the suppository.
- Differently shaped suppositories have different breaking points. The designed breaking point of each of these variously shaped suppositories is established as the level that withstands the break forces caused by various types of handling i.e., production, packaging etc.

Disintegration test

- Apparatus: A transparent sieve of glass or suitable plastic of height 60mm with an internal diameter of 52mm. A metal device consisting of two stainless discs each of which contain 39 holes, each 4mm in diameter. Diameter of the disc is closely similar to the internal diameter of the sleeve. Discs are separated by a distance of 30mm. Metal device is attached to outer sleeve by means of three equally spaced hooks.
- Method: Place a suppository on the lower perforated disc of metal device and then insert the device into the cylinder and attach this to the sleeve.
- Repeat the same operation with further two suppositories, metal device and sleeve. Place each piece of apparatus in a vessel containing at least five litres of water at 370C fitted with a slow stirrer and by holding the top of apparatus 90mm below the surface of water. [16]

- Disintegration is complete when molded suppositories are:

1. Completely dissolved
2. Dispersion into its components

Dissolution testing

- Testing for the rate of in vitro release of drug substances from suppositories has always posed a difficult problem, owing to melting deformation, and dispersion in the dissolution medium. Early testing was carried out by simple placement in a beaker containing a medium. [17]
- In an effort to control the variation in mass or medium interface, various means have been employed, including a wire mesh basket, or a membrane, to separate the sample chamber from the reservoir.
- Samples sealed in dialysis tubing or natural membranes have also been studied. Flow cell apparatus have been used, holding the sample in place with cotton, wire screening and most recently with glass beads. [18]

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. It is also administered in unconscious patients. Suppositories are non-invasive and less discomforting. In conclusion, suppositories represent a versatile and valuable dosage form within the field of pharmaceuticals. 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.

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