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Review About Herbal Based Suppositories.

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ABSTRACT

This study focuses on the formulation and evaluation of herbal-based suppositories using Herbal extract, known for its antimicrobial, anti-inflammatory, and laxative properties. Suppositories, as semi-solid dosage forms, offer a targeted drug delivery system via rectal, vaginal, or other body cavities, particularly beneficial for paediatric, geriatric, or unconscious patients. The project explores different types of suppositories, their advantages over oral dosage forms, and the significance of bypassing first-pass metabolism for enhanced drug bioavailability. Emphasis is placed on ideal suppository characteristics, base materials, manufacturing methods (moulding, compression, fusion), evaluation techniques, and stability parameters. Common challenges in formulation—such as brittleness, viscosity variations, and volume contraction—are addressed through optimized excipient selection and processing conditions. The study highlights of herbal extract in herbal pharmaceutics and supports the use of suppositories as a practical and effective dosage form for localized and systemic therapy

SEMI-SOLID DOSAGE FORM

AIM

To study about the herbal based suppositories.

OBJECTIVE

To formulate and evaluate herbal suppositories using Cassia fistula extract, aiming to harness its potential antimicrobial, anti-inflammatory, or laxative properties for rectal or vaginal drug delivery, while ensuring optimal physical characteristics, stability, and therapeutic effectiveness.

INTRODUCTION

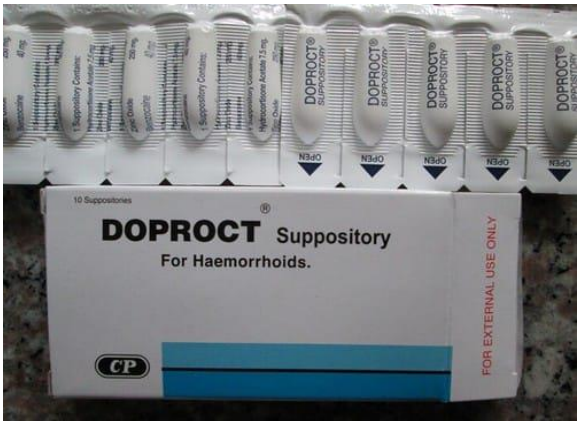
Medicated solid dosage forms known as suppositories are designed to be inserted into body cavities. The word suppository comes from the Latin term meaning "to place under."

The primary methods for administering drugs rectally are suppositories and ointments. These forms are utilized to provide both systemically acting and locally acting medications. The basic concept is that the suppository is inserted in a solid state, then dissolves or melts inside the body to release the medication into the numerous local blood vessels. Initially, suppositories were employed in nursing homes for older patients who could not swallow pills. They come in various shapes and sizes to aid in insertion and retention within the cavity.

Surfactant (e.g., polysorbate 80, tween 20) may be included into the formulation to enhance the wetting characteristic of the suppository with the rectal fluid, thus boosting the dissolving rate.[1]

DEFINITION

Solid dose forms called suppositories are meant to be inserted into bodily orifice, where they will dissolve, melt, or soften and have either local or systemic effects. Suppositories are made to be placed into bodily cavities or openings, where they work locally on the body by dissolving and melting at body temperature. The drug's content, concentration, and rate of absorption in the body all affects how suppositories work. The systematic action of analgesics, antispasmodics, sedative, tranquillizers, and antibacterial drugs all play a significant part.



An insert is a solid dosage form that is inserted into a naturally occurring body cavity other than the mouth or rectum, including the vagina and urethra.[1]

SUPPOSITORIES AND PESSARIES

Suppositories allow for the insertion of herbal preparations into a body orifice. They are commonly used for vaginal and rectal complaints. The word suppository is derived from the Latin suppositorum, which means, "something placed beneath." Pessary is an interchangeable term, referring specifically to a vaginal suppository. Suppositories, like many of the other preparations discussed in this section, are made from herbs that are anti-inflammatory to the mucous membranes, astringent to excessive discharges and damaged tissue, and antimicrobial.[3]

SUPPOSITORIES AS HERBAL FORMULATION

Herbal suppositories are a form of drug delivery system where plant-derived extracts or powders are incorporated into a suitable suppository base for local or systemic therapeutic effects. These are particularly beneficial for patients who cannot take medications orally or where a localized treatment **(e.g.,** in the rectum or vagina**)** is desired.

WHY USE HERBAL SUPPOSITOSITORIES?

- Bypass First-Pass Metabolism – Direct absorption into systemic circulation.
- Localized Effect – Effective for infections, inflammations, and hemorrhoids.
- Alternative to Oral Dosage – Ideal for nausea, vomiting, or unconscious patients.
- Sustained Release – Depending on base and formulation.

SUPPOSITORIES AND INSERT SHAPES

Suppositories come in a variety of form and weights; the shape and size of a suppository must allow.It to be easily entered into the intended orifice without causing undue distensions.Once entered, it must be held for the right duration of time.

IDEAL PROPERTIES OF SUPPOSITORIES

- It must retain the shape and size.
- It shoulld melt at body temperature.
- It should be non-irritant.
- It should shrink sufficiently to remove from mould.
- It should not interfere in release or absortion of drug.
- It should permit incorporation of drug.
- It should be compatiple with variety of drug.
- It should be physically stable on storage.[3]

ADVANTAGES

- It avoid first pass effect.
- Melt at body temperature.
- It gives localized and systemic action.
- It can be given to unconscious patient.
- It is easy to use for pediatric and geriatic patients.
- Useful to promote evacuation of bowel.
- Convenient for those drug causes GIT irritation, vomiting etc.

DISADVANTAGES

- Irritant drug cant administered.
- Need to store at low temperature.
- Cant easily prepared.
- Cost-expensive.
- Some drug may be degraded by the microbialflora present in the rectum.

What are the side effects of suppositories?

Suppositories are safe to use, but like all medications, there can be risks or side effects. Some of those are:

- It falls out or leaks out before it absorbs
- It doesn’t work and you need to take a different medication
- You have irritation in the area where you put it in

THE FOLLOWING TIPS MAY HELP PEOPLE WHO NEED TO USE SUPPOSITORIES:

- Avoid exercise or vigorous movement for 60 minutes after inserting the medication.
- Do not use petroleum jelly, such as vaseline to lubricate the suppository. This stops it from melting. Only use water, or a water-based lubricant.
- Store suppositories in the refrigerator or another cool place, so they do not melt. Always follow the storage directions on the label.

TYPES OF SUPPOSITORY

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

NEWER CONCEPT OF SUPPOSITORY

- Tablet suppositories.
- Layered suppositories.
- Coated suppositories.
- Capsule suppositories.

RECTAL SUPPOSITORIES

Rectal route is the efficient and economical method for the patients who have difficulty in swallowing especially in children and some adults. This route is beneficial in certain conditions like nausea, vomiting, inflammatory bowel diseases and hemorrhoids where parenteral and oral administration of drug is not possible. This route offers the advantage of being relatively painless. [4]

- ✓ Rectal suppositories are inserted using the fingers, although specific vaginal inserts can be inserted high in the tract using an instrument.

- ✓ Rectal suppositories are typically about 32 mm (1.5 inch) long, are cylindose of a drug administered dose may be greater than or less than dose of the same drug given orally, depending on such factors as

1. The constitution of the patient (physiological factors) .
2. The physiochemical nature of the drug and its ability totraverse the physiologic barriers to absorption, and
3. The nature of the suppository vehicle and its capacity tolerase the drug and make it available for absorption. Some that are absorbed better orally as compared to rectally, and some cases where the oral and rectal doses are comparable.

- ✓ The weight of the suppository may vary depending on the density of the base and the medications include within.
- ✓ In somecases, the doses are different, for example lincomycin, chloralhydrate requires four times the dose rectally, as compared to orally and empirically, phenytoin requires about three times the dose

  rectally as compared to orally and have one or both ends tapered.
- ✓ Some rectal suppositories are shaped like a bullet, a torpedo, or the little finger. Depending on the density of the base, rectal suppositories for use by infants and children.

SOME FACTORS OF DRUG ABSORPTION FROM RECTAL SUPPOSITORIES

The dose of a drug administered rectally may be greater than or less than the dose of the same drug given orally, depending on such factors as the constitution of the patient, the physicochemical nature of the drug and its ability to traverse the physiologic barriers to absorption, and the nature of the suppository vehicle and its capacity to release the drug and make it available for absorption.

WHAT ARE RECTAL SUPPOSITORIES FOR ?

Rectal suppositories are used for administering medications when you cannot do so orally such methods may be especially helpful for young childern and older adults who cannnot take medications by mouth. [5]

POSSIBLE SIDE EFFECTS

Leakage of the medication, as well as personal pain and discomfort, are all possible side effects associated with rectal suppositories. Proper insertion and following post-administration instructions may help reduce these effects.[5]

ADVANTAGES OF RECTAL SUPPOSITORIES

- **Bypasses the digestive system:** Useful for patients who are vomiting, unconscious, or unable to swallow pills.
- **Avoids first-pass metabolism:** Some drugs absorbed rectally skip liver metabolism, increasing bioavailability.
- **Localized treatment:** Ideal for conditions like hemorrhoids or constipation, delivering medication directly to the affected area.
- **Reduced gastric irritation:** Less likely to cause nausea or stomach upset compared to oral medications.
- **Rapid absorption:** Certain drugs can be absorbed quickly into the bloodstream for fast relief.
- **Useful in pediatric and geriatric care:** Easier to administer to infants or elderly patients who struggle with oral medications.

DISADVANTAGES OF RECTAL SUPPOSITORIES

- **Patient discomfort or embarrassment:** Some people find rectal administration awkward or unpleasant.
- **Erratic absorption:** Drug absorption can vary depending on placement, rectal contents, or circulation.
- **Risk of defecation:** Inserting a suppository may trigger a bowel movement, reducing effectiveness.
- **Limited surface area:** The rectum has a smaller absorption area compared to the intestines.
- **Storage challenges:** Suppositories often require refrigeration and careful handling to maintain shape.

RECTAL SUPPOSITORIES AS MEDICATION:

Rectal administration of medication may be performed with any of the following:

- A suppository, a solid drug delivery system inserted into the rectum, where it dissolves or melts to exert local or systemic effects.
- A micro-enema, a small amount (usually less than 10 millilitres) of a liquid-drug solution injected into the rectum.
- A large volume enema to inject liquid into the colon either to cleanse feces from as much of the colon as possible or to deliver a drug solution.
- A specialized catheter designed for rectal administration of medications and liquids, that can be placed safely and remain comfortably in the rectum for repeated use.

MECHANISMS AND EFFECTS:

- Drug that is administered rectally will in general (depending on the drug) have a faster onset, higher bioavailability, shorter peak, and shorter duration than oral administration.
- Another advantage of administering a drug rectally, is that it tends to produce less nausea compared to the oral route and prevents any amount of the drug from being lost due to emesis (vomiting).
- In addition, the rectal route bypasses around two-thirds of the first-pass metabolism as the rectum's venous drainage is two-thirds systemic (middle and inferior rectal vein) and one-third hepatic portal system (superior rectal vein). This means the drug will reach the circulatory system with significantly less alteration and in greater concentrations.[6]

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.[7]

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.[7]

NASAL SUPPOSITORIES

- ✓ These suppository are meant for introduction into nasal cavity.
- ✓ It is about 1g in weight.
- ✓ The glycero gelatin is used as the suppository base.

EAR CONES

- ✓ It is also known as **"AURINARIES".**
- ✓ These are meant for introduction into ear.
- ✓ It is cyclindrical in shape.
- ✓ It is about 1g in weight.

TABLET SUPPOSITORIES

- ✓ This sort of tablets is made by compressing tablets.
- ✓ These suppositories used for both rectal and vaginal uses.
- ✓ Pessaries tablet suppositories have an almond like form.
- ✓ Rectal pills are protected with thin layers of polyethylene glycol for protecting.[8]

LAYERED SUPPOSITORIES

- ✓ Distinct medications are contained in distinct layers in those kind of suppositories.
- ✓ To enable the separation of medications that are incompatible with one another.
- ✓ Likewise, medications with varying melting points can be added to regulate the rate of absorption.[8]

COTAED SUPPOSITORIES

- ✓ Among other things, polyethylene glycol and cetyl alcohol are present in such suppositories.
- ✓ These substances regulate their rate of disintegration, give lubricating qualities, and offers storage protection.

CAPSULE SUPPOSITORIES

- ✓ In those suppositories, soft gelatin capsules of various sizes and shapes are created.
- ✓ Suppositories of the kind are loaded with liquids, semisolids or solids.
- ✓ The use of these kinds of capsules is growing.

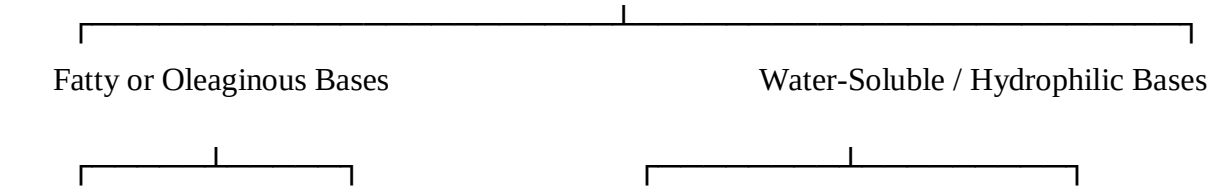
SUPPOSITORY BASES

- ❖ Suppository bases are crucial for preserving their hardness and shape as well as for their proper insertion into bodily cavities.
- ❖ Although many bases are employed, theobroma oil, polyethylene glycol, and glycerol gelatin base meet the aforementioned criteria

IDEAL PROPERTIES

- ✓ It should release the medicaments readily.
- ✓ It should be compatible with a variety of drugs.
- ✓ It should melt at body temperature or disperse in the body fluids.
- ✓ It should be nontoxic and nonirritating to mucous membranes.[3]

TYPES OF SUPPOSITORY BASES



OILY BASES OR OLEAGINOUS BASES

- Cocoa butter or Theobroma oil
- Emulsified cocoa butter.
- Hydrogenated oils.

A. **Theobroma cocoa seed (chocolate bean).**

Cocoa butter contains triglycerides of both saturated and unsaturated fatty acids. It is a yellow substance that solidifies at normal temperatures but melts at body temperature. rature. It has a distinct and powerful fragrance. Cocoa butter does not absorb water because there are no emulsifiers. Cocoa butter's ability to absorb water can be increased by adding Tween-61, a non-ionic, waxy, solid, tan surfactant. However, cocoa butter has a number of advantageous properties, including a soft foundation that does not irritate sensitive membrane tissues, being widely available, being simple to use for creating suppositories without the need for tools, and being inexpensive .

B. **Cocoa Butter Substitute**

These are the beginning ingredients derived from various vegetable oils, such as coconut or palm kernel oil, and are transformed through the processes of etherification, hydrogenation, and fractionation to produce products with varying composition and melting points. They can be designed to reduce rancidity after extended storage. This type of suppository base is usually composed of saturated fatty acid triglyceride esters.

C. **Wietepsol**

A white, waxy, brittle substance known as "Witepsol" melts into a clear or yellowish liquid with nearly any odor. Emulsifiers are incorporated, which allow it to absorb a small amount of water. Witepsol is available in around 20 different versions, divided into the H, W, S, and E series. Class H15 is the most commonly utilized in pharmaceutical practice. Its melting point ranges from 33.5 °C to 35.5°C, which is similar to its pour point range of 32 °C to 34 °C.

D. **Fatty Base.**

It's an opaque, white, waxy mass with no flavor. This combines triglycerides from coconut and palm kernel oils. They serve as suspension and emulsifying agents. Melting temperatures for this base range from 32 to 36.5 degrees Celsius. Before adding the active medicinal components, slowly and steadily heat the base to 49-54 °C, but do not exceed the needed temperature. When the liquid reaches a temperature of 43 to 49 degrees Celsius, suppositories should be poured.

WATER-SOLUBLE OR HYDROPHILLIC BASES

A. Polyethylene glycol (PEG)

These are polymer blends containing varying molecular weights of polyethylene glycol. Surfactants and other additives, like polyethylene glycol bases, are occasionally utilized in commercial suppositories. Polybase, manufactured by Paddock Labs in the United States, and Gallipot Inc.'s PEG blend are among the most popular bases. Both contain a mixture of polyethylene glycols and the emulsifier polysorbate-80.Polyethylene Glycol Polymers have received much attention as suppository bases in recent years because they possess many desirable properties. They are chemically stable, nonirritating, miscible with water and mucous secretions, and can be formulated, either by molding or compression in a wide range of hardness and melting point. Like glycerinated gelatin, they do not melt at body temperature, but dissolve to provide a more prolonged release than theobroma oil.[10]

B. Glycero-Gelatin base

This is a mixture of glycerol and water made into a stiff jelly by adding gelatin. It is used for the preparation of jellies, suppositories and pessaries. The stiffness of the mass depends upon the proportion of gelatin 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 gelatin is selected for the purpose. Two types of gelatins are used as suppository base:

Type-A or Pharmagel-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.

Type-B or Pharmagel-B which 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.[10]

MANUFACTURING OF SUPPOSITORIES

1. **Methods of preparations of suppositories**
    - Moulding
    - Compression
    - Heat moulding/fusion
    - Hand rolling & shaping
    - Automatic machine moulding
    - Preparation by moulding

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

- 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 calihvate rouch suppository mould for the usual hase suas to prequire medication sopparsitories, rach 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 haml. By tolling the well-blended suppositury base containing the active ingredient into cylindrical rod of desired length and diameter, or into vaginal balls of intended weight. Starch or tale powder is spread on the rolling surface and hands to prevent the mass from adbering. Rud shaped suppositories are cut into portions to get one end pointed. This method is practical and economical for smaller number of suppositories.

AUTOMATIC MACHINE MOULDING

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 efficient (Le. rate of production) in working than the former one.

SPECIFIC PROBLEMS IN FORMULATING SUPPOSITORIES[11]

1. **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. **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.

❖ **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.

3. **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.

4. **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.

5. **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.

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

❖ **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.

EVALUATIONS[12]

1. **Surface appearance and shape.**

To evaluate: absence of fissuring absence of migration of active ingredient, absence of pitting, absence of fat blooming (dullness of surface).

2. **Weight uniformity test**

The weight uniformity test was carried out according to the British Pharmacopoeia (B.P., 2011). Twenty suppositories of each formulation were randomly selected, and their mean weight and standard deviation were determined (Hargoli et al., 2013). Hardness test.The mechanical strength of suppositories was determined using the suppository hardness tester (Model S.B.T., Erweka, Germany) at room temperature (25±0.5°C). Ten randomly selected suppositories from each formulation were subjected to different progressive weights (Akl et al., 2019). The weight required for the suppository to collapse was recorded in kg force to measure resistance to crushing. To study the effect of M.P. addition on the mechanical strength of the formulations, base suppositories (without M.P.) were also prepared, and their hardness was tested.[13]

3. **Melting point determination:**

   Melt the suppositories rapidly at a temperature not exceeding 100°C above complete melting, inserting one end of a glass-capped tube into the melt until one material column to a height of 8-12 inches.Cool the tube to 150°C and maintain the temperature at 15-170°C for at least 16 hours. Connect the tube to a thermometer in a heating vessel containing water at 150°C so that the bottom end of the column of material is 30 mm below the surface of the water. Heat the water and stir continuously until the temperature rises at a rate of 20 degrees per minute.The temperature at which the molten material starts to rise in the pipe is called the melting point. The dissolution of suppositories should not exceed the information mentioned in the monograph.

4. **Liquification or softening time tests of rectal suppositories**

   The "softening test" measures the liquefaction time of rectal suppositories are an apparatus that simulate in-vitro conditions (at 37°C).

5. **Breaking test**

   It is designed as a method for measuring the fragility or brittleness of suppositories. The apparatus consists of double-wall chamber in which the test suppository is placed. Water at 37°C is pumped through the double walls of the chamber, and the suppository, contained in the drug inner chamber, supports a

disk to which a rod is attached. The outer end of the rod consists of another disc to which weights are applied.

6. **Mechanical strength**

   It is a force necessary to break a supp. And indicate whether supp is brittle or elastic. (not less than 1.8-2 Kg) by Erweka method.[14]

7. **Melting & solidification**

Solidification can be determine by using evacuated flask into which the melt is placed, the temp of cooling is noted to determine the solidification point.

8. **Dissolution testing**

The patterned is measured by using the same melting range apparatus. If the volume of water surrounding the suppository is known, then by measuring aliquots of the water for drug content at various intervals within the melting period. A (time versus drug release) curve could be established and can plotted.

STABILITY STUDIES

Stability testing studies; how long a pharmaceutical product can be stored at normal and accelerated conditions without any degradation. This study helps to determine the shelf-life of that product. This testing helps to assess the physical, chemical, therapeutic stability of a product. The purpose of the stability study is to establish, based on testing a minimum of three batches of the drug substance and evaluating the stability information (including, as appropriate, results of the physical, chemical, biological, and microbiological tests), a retest period applicable to allfuture batches of the dosage form.[17]

STABILITY PROBLEMS OF SUPPOSITORIES[15]

- **BLOOMING**
  - ✓ During storage, cocoa butter suppositories sometimes show deposition of white powder on the surface.
  - ✓ This result in suppositories of disagreeable appearance.
- **HARDENING**
  - ✓ During storage, the suppositories made of fatty bases become hard.
  - ✓ It is occurs due to crystallization of bases.
  - ✓ This also affect the melting and rate of absorption of drugs.

Types of Drug stability studies: - Stability studies are mainly of following types.

- Long term stability.
- Intermediate stability.
- Accelerated stability.
- In-use stability.

The five types of stability generally recognized include

- ✓ Chemical stability.
- ✓ Physical stability.
- ✓ Microbiological stability.
- ✓ Therapeutic stability.
- ✓ Toxicological stability.

The scope and design of a stability study utilizing suppositories may vary according to the manufacturer concerned. Ordinarily the formulator of the suppository first determines the effects of temperature, light, air, pH, moisture, trace metals, and commonly used excipients orsolvents on the active ingredient(s). From this information, one or more formulations of the suppository are prepared, packaged in suitable containers, and stored under a variety of environmental conditions, both exaggerated and normal. At appropriate time intervals, samples of the suppositories are assayed for potency by use of a stability-indicating method, and observed for physical changes, including microbial growth. Such a study, in combination with clinical and toxicological results, enables the manufacturer to select the optimum formulation and container and to assign recommended storage conditions and an expiry date for each dosage form in its package.

Stability problems of suppositories include

- ❖ Cocoa butter suppositories on storage, "bloom"; i.e., they form a white powdery deposit on the surface. This can be avoided by storing the suppositories at uniform cool temperatures and by wrapping them in foils.
- ❖ Fat based suppositories harden on storage, i.e., there is an upward shift in melting range due to slow crystallization to the more stable polymorphic forms of the base.
- ❖ The suppository overwrap foil also can cause problems in time. For example, if the suppository contains an acid, the foil wrapping may be attacked and develop pinholes.
- ❖ The softening time test and differential scanning calorimetry can be used as stability indicating test methods.
- ❖ If we store the suppositories at an elevated temperature, just below its melting range, immediately after manufacture, the aging process is speeded up.

PHYSIOCHEMICAL PARAMETERS[17]

1. Penetration.
2. Solubility.
3. Texture analysis.
4. Effect of light.
5. Salt formation.
6. Partition coefficient.
7. Hygroscopicity.
8. Fine particle characteristics.

1. PENETRATION

Measured by in vivo and in vitro studies. In in vitro techniques the permeation through skin is measured directly where sampling is carried out immediately below skin surface. This is in contrast with most of the in vivo methods which measure systemic level of drug.

2. SOLUBILITY

The solubility of compounds in the vehicle need to be determined because different solubility problems can be arise like crystal formation, precipitation & coagulation. If the system is supersaturated it shows crystal growth. The methods used are shake flask method, computational screening method & miniature device.

3. TEXTURE ANALYSIS

Texture analysis used to evaluation of mechanical characteristic where a material is subjected to a controlled force from which a deformation curve of its response is generated. Primary mechanical characteristics includes hardness, springiness, adhesiveness, cohesiveness and secondary includes brittleness, gumminess, chewiness etc.

4. EFFECT OF LIGHT

The stability of compound due to presence of light affected or not need to be check. **E.g.:-** Diethanol shows a distinct instability in paraffin due to light but stable when protect from light.

5. SALT FORMATION

It improve the solubility of the drugs.A salt is a chemical combination of ionisable component, one is acidic and other is basic relative to each other. If pka of acid and base are close, stable salt may not form. When a salt formation is limited of molecule then need to synthesise prodrugs. (**e.g**.:ester and amides). Some molecules are not form salt because it does not dissociate in solvent (**e.g**.: alcohol).

6. PARTITION COEFFICIENT

Influence permeation of a drug across biological membrane.

P(o/w) = (Coil/Cwater)equilibrium Drug with extremely high partition coefficient readily penetrate the membrane.

7. HYGROSCOPICITY

When a drug molecule come in contact with moisture it retain water by capillary condensation or surface adsorption. Absorption and equilibrium moisture content depends on the atmospheric humidity, temperature & surface area.

8. FINE PARTICLE CHARACTERISATIO

New drug should be tested during pre-formulation to ensure homogenous in sample and maximum surface area for interaction. Dissolution and chemical reactivity of compound is affected by size, particle size, shape and surface morphology of drug particle**.**

CRITERIA FOR EXCIPIENT SELECTION[17]

1. Suppository bases
2. Antioxidant
3. Emulsifying agent
4. Hardening agent.
5. Thickening agent.
6. Plasticizer

1. SUPPOSITORY BASE

Bases should be exist in solid form at room temperature. It should not irritate and produced inflamed sensation in body cavity. It should be stable during storage condition, No change in colour, shape, odour. It should retain hardness. It should not reacts with drugs and additives. It should have good emulsifying and wetting property. It should have acid value less than 0.2 or zero.

2. ANTI OXIDANTS

It is protect the drugs and bases from getting degraded due to oxidation. These are commonly used in all types of suppositories.

Eg: Ethyl or propyl gallate.

3. EMULSIFYING AGENTS

These are increase the water absorbing capacity of fatty bases.

Eg: Polysorbates (TWEEN 61).

4. HARDENING AGENTS

These are involved in those formulation where the melting point of the bases is decrease by the drugs. These are the agents which are used to bring the melting point to normal.

Eg: Beeswax.

5. THICKENING AGENTS

These are the agents which are used to increases the viscosity of molten bases and prevent sedimentation of suspended in solid bases.

Eg: Aluminium monostearate.

6. **PLASTICIZER**

These are the agent which are used to improved flexibility of suppositories. It is also used to make the less brittles to suppositories.

Eg: Castor oil.

PACKAGING

Aluminum metal molds have a variety of cavity diameters and several cavities per mold. Common sizes range from 1 g to 2.5 g, with cavities ranging from 6 to 100. The mold's two pieces are connected by nuts or, in certain cases, a single-centered screw.

Plastic suppository shells come in long strips that can be torn into a variety of cavities. The suppository mixture is put directly into the shell, up to the mark. These disposable molds do not require lubrication, regardless of the suppository composition.Once the mixture has solidified, the plastic mold is heat-sealed. When a patient is ready to use a suppository, they choose one shell and peel the edges off to reveal the suppository. One advantage of this sort of mold is that if the suppository melts, it will not spill out of the mold. If the material can be placed on the geals again, it will maintain its suppository shape. This sort of mold is available in 1 g to 5 g sizes and many different colours.[18]

STORAGE CONDITION

Suppository should be protected from heat, preferably stored in the refrigerator. Glycerinated gelatin suppositories should be protected from heat, moisture, and dry air by packaging in well-sealed containers and storing in a cool place. It is stored at 10-15°C, Used air tight container. The suppositories with cocoa butter stored at < 30 °C. The suppositories with glycero-gelatin stored at <35°C. The experimental data obtained in the study of the stability of the drug during storage showed that all indicators of quality, regardless of the form of suppositories PVC film in which they were stored, and the storage conditions comply with the requirements of State Pharmacopoeia of Ukraine and specifications. However, such indicators as the disintegration of suppositories and their melting temperature were slightly higher when stored at room temperature, which may be due to structural and mechanical changes during storage. A quantitative content ellagitannins contrary, at room temperature decreased slightly, which may be caused by the action of decomposition temperature and time.[17]

APPLICATION

- Suppositories are commonly utilized for unconscious, children, and elderly patients. They are employed for systemic and local acts when other avenues are unavailable. Suppositories contain a wide range of medications.
- Suppositories can be used for either local or systemic effects.
- Babies or elderly adults who are unable to swallow oral medications.
- People who are unable to move.
- Post-operative patients who are experiencing extreme nausea or vomiting.
- Helpful for patients who have severe nausea or vomiting.
- Utilized to treat intestinal obstruction.
- **There are no sources in the current document.**[18]

CONCLUSION

The formulation and evaluation of herbal-based suppositories for antibacterial activity demonstrate significant potential as an effective alternative to conventional antimicrobial therapies. The use of plant extracts with proven antibacterial properties offers a natural and biocompatible approach to managing infections, especially in localized areas such as the rectal or vaginal regions. The use of natural ingredients not only promotes patient safety and acceptance but also aligns with the growing demand for herbal and eco – friendly treatments.

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