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A REVIEW On Suppositories: Concepts, Types, Bases, Manufacturing and Therapeutic Applications

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Abstract

Suppositories are solid unit dosage forms designed for insertion into body cavities, most commonly the rectum or vagina, where they soften, melt, or dissolve and release an active pharmaceutical ingredient. They can provide local treatment or systemic drug delivery and are particularly useful when oral administration is difficult or unsuitable. The dosage form is strongly influenced by the choice of base, drug solubility, melting or dissolution characteristics, particle size, manufacturing method, storage conditions, and physiological environment. Conventional bases include lipophilic materials such as cocoa butter, hard fats and hydrogenated vegetable oils, and hydrophilic materials such as polyethylene glycol and glycerinated gelatin. This review discusses the principles of suppository formulation, types and properties of bases, methods of preparation, mechanisms of drug release, quality-control tests, packaging and stability, therapeutic applications, advantages and limitations, and recent approaches to improve drug delivery. Modern development increasingly emphasizes rational selection of excipients, controlled release, mucoadhesion, improved patient acceptability, and suitability for challenging climates. Although suppositories occupy a smaller market niche than many oral dosage forms, they remain valuable pharmaceutical systems for local and systemic therapy.

Keywords: suppositories; rectal drug delivery; vaginal dosage forms; suppository bases; polyethylene glycol; cocoa butter; formulation; evaluation

1. INTRODUCTION;

A suppository is a solid dosage form intended for insertion into the rectum and formulated to melt, soften, or dissolve at body temperature. The United States Pharmacopoeia describes suppositories as solid bodies of varying sizes and shapes adapted for rectal introduction; the drug may act locally or be absorbed systemically [1]. In pharmaceutical practice, related solid preparations may also be designed for vaginal or urethral administration, although terminology varies among pharmacopoeias and regulatory systems.

Suppositories have a long history in medicine and remain useful because they provide an alternative route when swallowing is difficult, when vomiting prevents adequate oral dosing, or when local treatment of the

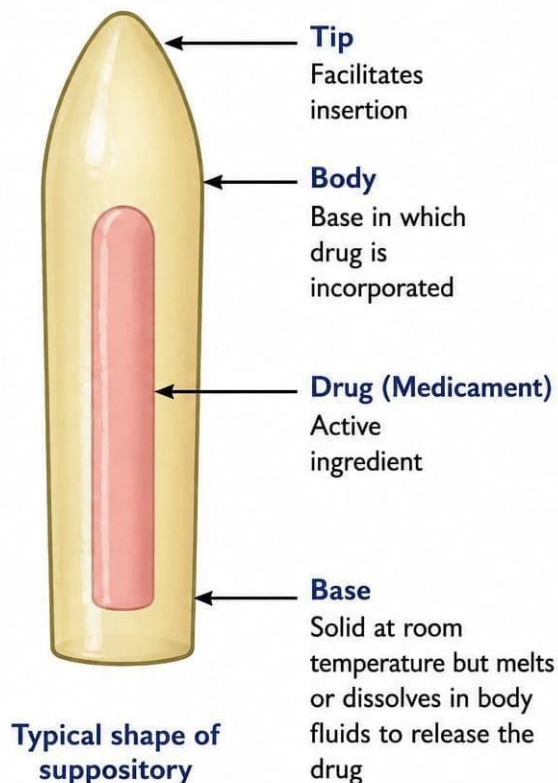
anorectal or vaginal region is desired. Rectal delivery can also partially avoid hepatic first-pass metabolism for drug absorbed from the lower rectum, although the extent of this effect is variable and depends on the site of administration and drug properties [2].

The formulation consists broadly of an active pharmaceutical ingredient incorporated into a suitable base, together with any necessary excipients. The base must be capable of maintaining the physical integrity of the product during handling and storage while permitting adequate drug release after administration. Lipophilic bases generally melt at or near body temperature, whereas hydrophilic bases such as polyethylene glycol release drug as the matrix dissolves in physiological fluid [2,3].

The performance of a suppository is therefore not determined by drug content alone. Important variables include the physicochemical properties of the drug, base composition, drug-base interactions, polymorphism of fatty materials, viscosity of the molten mass, particle size, mold design, cooling rate, and environmental temperature. These factors can influence hardness, disintegration, melting behavior, dissolution and ultimately bio availability [3–5].

For pharmacy students and formulation scientists, suppositories provide an instructive example of how dosage-form design links physical pharmacy, pharmaceuticals, bio pharmaceuticals, manufacturing science and patient-centered considerations. Modern research has also examined suppositories for advanced local delivery, including antiviral and other mucosal applications [6].

Aim of the review: This article summarizes the pharmaceutical principles, formulation approaches, preparation methods, evaluation parameters, therapeutic uses, advantages, limitations and recent development strategies associated with suppository dosage forms.



2. TYPES AND CLASSIFICATION OF SUPPOSITORIES;

Suppositories may be classified according to the route of administration, physical state of the base, intended therapeutic effect, or drug-release behavior.

2.1 Classification according to site of administration;

- **Rectal suppositories:** Intended for insertion into the rectum. They may produce local effects, such as laxation or treatment of anorectal inflammation, or systemic effects after absorption.
- **Vaginal suppositories** (often called pessaries or vaginal inserts): Designed for local treatment of infections, inflammation or hormonal therapy. Their formulation must account for vaginal fluid, pH, microbiota and patient acceptability.
- **Urethral suppositories:** Historically described as bougies and designed for urethral administration. Their use is comparatively limited in modern routine practice.

2.2 Classification according to base

- **Fatty or lipophilic bases:** Examples include cocoa butter, hard fats and hydrogenated vegetable oils. They generally release drug after melting at body temperature.
- **Water-soluble or water-miscible bases:** Polyethylene glycol mixtures and glycerinated gelatin are important examples. These bases dissolve or disperse in physiological fluid rather than simply melting.
- **Emulsifying or modified bases:** These contain surfactant or combinations of fatty and hydrophilic materials to modify wetting, release, hardness and stability.

2.3 Classification according to therapeutic purpose;

- **Local-action suppositories:** Intended to act at the site of administration, for example laxative, anti-inflammatory or anti-infective products.
- **Systemic-action suppositories:** Designed for absorption through mucosa to provide a systemic pharmacological effect.
- **Modified-release suppositories:** Formulated with polymers, special matrices or other technologies to prolong or regulate drug release.

Suppository geometry also affects handling and administration. Traditional shapes include torpedo, bullet, conical, oval and cylindrical forms. Shape should provide sufficient mechanical strength while minimizing discomfort and facilitating insertion. Contemporary development increasingly considers dimensions, surface properties and dissolution behavior together rather than relying only on traditional shapes [6,7].

3 SUPPOSITORY BASES AND THEIR IDEAL PROPERTIES;

The base is the major structural component of a suppository and plays a central role in drug release. A suitable base should be compatible with the drug, non-irritating, stable during storage, readily moldable, sufficiently strong for handling, and capable of releasing the drug at the intended rate. The base should also avoid excessive adhesion to the mold and should maintain acceptable physical characteristics under expected storage conditions [3].

3.1 Fatty bases

Cocoa butter (Theobroma oil) is a traditional fatty base. It has a melting range close to body temperature and therefore can provide rapid softening or melting after insertion. However, cocoa butter is polymorphic; changes in crystal form can alter melting behavior and product performance. It is also sensitive to overheating during manufacture. Modern hard fats and hydrogenated vegetable oils can provide more reproducible characteristics than natural cocoa butter [3].

3.2 Polyethylene glycol bases

Polyethylene glycol (PEGs) are water-miscible materials available in different molecular weights. By combining grades with different molecular weights, formulators can adjust hardness, dissolution rate and melting behavior. PEG bases have practical advantages in warm climates because they do not necessarily depend on melting at body temperature; they can dissolve gradually in aqueous physiological fluid [3].

3.3 Glycerinated gelatin

Glycerinated gelatin is a hydrophilic base traditionally used particularly for vaginal preparations. It can provide a firm product but generally dissolves more slowly than some other bases. Its properties depend on the proportions of gelatin, glycerin and water and on the drug and excipients incorporated.

3.4 Important selection criteria

- Compatibility with the active ingredient and other excipients.
- Appropriate melting, softening or dissolution characteristics.
- Adequate mechanical strength and resistance to deformation.
- Minimal irritation to mucosal tissue.
- Chemical and physical stability during processing and storage.
- Efficient drug release and, when required, predictable systemic absorption.
- Suitability for the intended manufacturing method and packaging.

Drug release from fatty bases can involve melting of the vehicle, movement of drug particles toward the base-fluid interface, dissolution in surrounding fluid and diffusion away from the interface. Thus, drug aqueous solubility and lipid solubility can strongly affect release [5].

4 FORMULATION DESIGN;

Successful suppository formulation requires integration of drug physicochemical properties with base characteristics and the intended therapeutic objective. The formulation scientist should first define the target product profile, including route, dose, release characteristics, stability requirements, storage conditions and patient-use considerations.

4.1 Drug-related factors

- Dose and potency: High-dose drugs may require a base with sufficient capacity and acceptable dimensions.

- Particle size: Smaller particles may improve uniformity and dissolution, although excessive surface area can affect aggregation and processing.
- Solubility: The relative solubility of the drug in the base and physiological fluid can influence release.
- Partition coefficient: Lipophilic drugs may remain associated with fatty bases, potentially slowing release.
- Stability: The drug must remain chemically stable during heating, cooling and storage.

4.2 Excipients used in suppositories

Besides the base, formulations may contain surfactant, suspending agents, antioxidants, preservatives, buffers, plasticizers, polymers or other functional excipients. Surfactant can improve wetting and may modify release, but their concentration must be optimized because increasing surfactant concentration does not necessarily produce a proportional increase in drug release [4].

4.3 Dose replacement and displacement value

Because the active drug occupies volume within a mold, it displaces a portion of the base. The amount of base required therefore depends on the drug's displacement characteristics. In extemporaneous or small-scale formulation, displacement value is important for achieving the intended dose and consistent fill weight. Mold calibration and pilot batches help reduce variability.

4.4 Controlled-release design

Modified-release suppositories can use polymeric matrices, coated particles, mucoadhesion systems, multi layer designs or other strategies to regulate drug diffusion and residence time. The objective is to achieve reproducible release while maintaining physical integrity and patient acceptability. Research on advanced rectal systems has highlighted the need to connect in vitro release results with pharmacokinetic and clinical outcomes [2,7].

A rational formulation approach therefore considers the complete chain: drug properties → base selection → manufacturing conditions → physical quality → drug release → mucosal interaction → pharmacokinetics and clinical performance.

5 METHODS OF PREPARATION;

Suppositories can be prepared by several methods, depending on the base, formulation scale and desired product characteristics.

5.1 Fusion and molding method

Fusion or molding is the most widely used manufacturing approach. The base is melted carefully, the drug is dissolved or uniformly dispersed, and the molten mixture is poured into suitable molds. The product is then cooled until sufficiently solid. For heat-sensitive drugs, temperature and residence time must be minimized. PEG-based systems are commonly prepared by melting and mixing followed by controlled cooling and molding [3].

General steps

- Clean and inspect the mold; determine mold capacity when necessary.
- Weigh the base and active ingredients accurately.
- Melt the base using controlled heating and avoid unnecessary overheating.
- Incorporate the drug by dissolution or uniform dispersion according to its solubility.
- Mix continuously or sufficiently to minimize sedimentation and ensure homogeneity.
- Pour the mass into the mold with minimal air entrapment.
- Allow controlled cooling and solidification.
- Remove the suppositories carefully and inspect them.
- Pack immediately in suitable protective material.

5.2 Compression molding

Compression molding forms suppositories by forcing a prepared mass into molds without requiring extensive melting. This method may be useful when heat could damage the drug or base. The formulation must possess appropriate plasticity and flow under pressure.

5.3 Hand rolling

Hand rolling is an older extemporaneous method in which a plastic mass is rolled and divided into individual doses. It can be useful in limited settings but generally provides less dimensional uniformity than industrial molding and is unsuitable for many modern formulations.

5.4 Industrial manufacturing considerations

At manufacturing scale, mixing, temperature control, filling accuracy, cooling rate, demolding, inspection, packaging and process validation must be controlled. Fatty bases require particular attention to crystal structure and thermal history because polymorphic changes can alter melting behavior and performance [3].

6. EVALUATION AND QUALITY CONTROL;

Quality control ensures that each suppository meets predefined specifications for identity, strength, physical integrity, uniformity and drug release. Common evaluation tests are selected according to pharmacopoeial requirements and product characteristics.

6.1 Appearance

Suppositories should have an acceptable shape, surface and color and should be free from cracks, pits, excessive bloom, air pockets and visible particulate irregularities. Longitudinal cutting can help identify internal defects and non-uniform distribution.

6.2 Weight variation / mass uniformity

Individual units are weighed and compared with the average mass. Excessive variation can indicate problems in filling, mixing, sedimentation or mold operation. Published formulation studies commonly use multiple individual units to assess weight uniformity [8].

6.3 Drug content and content uniformity

Assay confirms the amount of active ingredient present, while content-uniformity procedures assess dose consistency between individual units. Analytical methods such as UV-visible spectrophotometry or chromatography may be used depending on the drug and formulation.

6.4 Melting or softening behavior

For fatty suppositories, melting characteristics provide information about whether the product will soften appropriately at body temperature while remaining stable during storage. Thermal behavior is influenced by base composition, polymorphism and processing history.

6.5 Disintegration and dissolution

Disintegration measures the time required for the dosage form to break down under specified conditions. Dissolution or in vitro release testing provides information about the rate and extent of drug liberation. Studies with indomethacin have shown that the choice of water-soluble versus oil-soluble base can substantially influence release [4].

6.6 Mechanical strength and breaking test

The product should be sufficiently strong to withstand handling and insertion but should not be excessively hard if rapid drug release is required. Mechanical testing can help identify the effect of base composition and processing.

6.7 Stability

Stability studies examine changes in appearance, assay, degradation products, melting behavior, hardness and release performance over time. Packaging must protect against heat, moisture, oxygen and physical deformation as appropriate.

7. DRUG RELEASE, ABSORPTION AND THERAPEUTIC APPLICATIONS;

7.1 Mechanism of drug release

After insertion, the dosage form interacts with the physiological environment. A fatty base may melt and spread, whereas a hydrophilic base may dissolve or swell. The drug then partitions into surrounding fluid and

can diffuse toward the mucosal surface. The rate-limiting step depends on drug solubility, particle size, base properties, inter facial behavior and physiological conditions [2,5].

7.2 Rectal absorption

The rectum offers a relatively small surface area and variable fluid volume compared with the gastrointestinal tract. Absorption can therefore be influenced by the position of the formulation, fecal matter, motility, mucosal condition and the physicochemical properties of the drug. Drug absorbed from the lower rectum may partially bypass first-pass hepatic metabolism, but this is not complete or predictable for all products [2].

7.3 Local therapeutic applications

- Laxative therapy, including glycerin and bisacodyl-type preparations.
- Local anti-inflammatory therapy for anorectal disorders.
- Local treatment of selected infections and inflammatory conditions.
- Vaginal therapy for selected fungal or bacterial infections and other local conditions.

7.4 Systemic applications

Suppositories have been investigated or marketed for systemic delivery of analgesic, antipyretic, anti emetic, anti-inflammatory and other drugs. They may be useful when oral administration is temporarily impractical. However, systemic exposure can be variable and should be established experimentally for each formulation [2].

7.5 Examples from formulation research

Research studies have demonstrated that changes in base composition can alter release behavior. For example, indomethacin suppositories prepared with water-soluble bases showed stronger in vitro release than oil-soluble formulations under the conditions studied [4]. Other formulation investigations have evaluated tramadol and verapamil suppositories using different bases and excipients, demonstrating the importance of formulation variables in drug release and physical quality [8,9].

8. ADVANTAGES, LIMITATIONS AND RECENT DEVELOPMENTS;

8.1 Advantages

- Useful when oral administration is difficult because of vomiting, swallowing difficulty or temporary gastrointestinal limitations.
- Can provide local therapy directly at the rectal or vaginal site.
- Can provide systemic delivery for selected drugs.
- May reduce exposure to gastric degradation for some drugs.
- Can accommodate both lipophilic and hydrophilic drugs through appropriate base selection.
- Generally requires relatively simple manufacturing equipment for conventional formulations.

8.2 Limitations

- Patient acceptance may be lower than for oral dosage forms because of route and perceived messiness.
- Storage and transportation can be challenging for low-melting fatty bases, especially in hot climates.
- Drug absorption may be variable because of physiological and anatomical factors.
- Some bases can irritate mucosal tissue if poorly selected or formulated.
- Manufacturing can be affected by polymorphism, sedimentation and cooling conditions.
- Some formulations may leak after administration, reducing residence time and acceptability.

8.3 Recent formulation approaches

Recent work has moved beyond conventional suppository design toward more rational control of drug release and mucosal residence. Approaches include mucoadhesion components, polymeric matrices, modified geometries, sustained-release systems and formulations designed around user sensory preferences. Reviews of rectal drug delivery emphasize that future development should connect formulation properties with pharmacokinetics, efficacy and safety rather than relying only on traditional physical tests [6,7].

Suppositories have also been investigated as delivery vehicles for antiviral and other mucosal therapies. Such applications illustrate the flexibility of the dosage form but also highlight the importance of acceptability, distribution, retention and adherence. In advanced development, formulation design should therefore include human factors and intended-use conditions from the beginning [6].

For tropical and warm environments, water-miscible bases such as selected PEG systems may offer practical advantages because they can be less dependent on a narrow body-temperature melting point. Nevertheless, the final choice must be based on the specific drug, release target, stability data and packaging system [3].

9. CONCLUSION;

Suppositories remain an important, although specialized, pharmaceutical dosage form capable of providing both local and systemic drug delivery. Their performance depends on a combination of drug properties, base characteristics, manufacturing variables, physiological conditions and patient-related factors. Fatty bases such as cocoa butter and hard fats offer body-temperature melting, whereas hydrophilic bases such as polyethylene glycol provide water-miscible systems whose drug release occurs through dissolution and diffusion.

The development of a robust suppository requires careful selection of the base, appropriate drug incorporation, control of thermal processing, accurate filling and systematic quality evaluation. Tests such as appearance, mass uniformity, content uniformity, melting or softening behavior, disintegration, dissolution, mechanical strength and stability provide complementary information about product quality. In vitro release testing is particularly useful during formulation development, but clinical and pharmacokinetic evidence remains important when systemic delivery is intended.

Current research is increasingly directed toward controlled release, mucoadhesion, improved stability, rational drug-base selection and better patient acceptability. These approaches may expand the usefulness of suppositories in conventional and advanced drug-delivery applications. Overall, suppositories should be considered not simply as traditional dosage forms but as adaptable mucosal delivery systems whose properties can be engineered to meet defined therapeutic objectives.

Declaration of Conflicting Interests

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