Chapter- 16

Suppositories-II

Mr. Ashutosh Jain
Assistant Professor,
Rajiv Gandhi Institute of Pharmacy,
Faculty of Pharmaceutical Science & Technology,
AKS University Satna, (M.P.)

ABSTRACT

Suppositories are prepared using various methods, each tailored to ensure the appropriate incorporation and release of the active ingredient. The three primary methods of preparation are the molding method, the compression method, and the hand-rolling method.

Molding method involves melting the suppository base, incorporating the drug, and pouring the mixture into molds to solidify. This method is widely used for its simplicity and precision in dosage. **Compression method** involves mixing the drug with a suppository base under high pressure, forming a solid mass that is then compressed into the desired shape. This method is suitable for heat-sensitive drugs. **Hand-rolling method** is the oldest and least commonly used, involving manual shaping of the suppository mass by rolling it into cylindrical forms. This method is labor-intensive and less precise.

Displacement value is crucial in suppository formulation, representing the amount of base displaced by a specific amount of drug. It is calculated to ensure accurate dosing. The formula for displacement value (DV) is: DV=Weight of drug Weight of base displaced\ text{DV} = \frac{\text{Weight of drug}}{\text{Weight of base displaced} }DV=Weight of base displacedWeight of drug For instance, if 1 gram of drug displaces 0.5 grams of base, the displacement value is 2. Accurate DV calculation is vital to maintain the consistency and efficacy of suppositories.

Evaluation of suppositories involves various tests to ensure their quality, safety, and efficacy. **Uniformity of weight** ensures each suppository contains the intended amount of drug. **Melting range test** verifies that the suppository melts at body temperature for proper drug release. **Disintegration test** checks how quickly the suppository breaks down in the body, crucial for timely drug release. **Dissolution test** assesses the rate at which the drug is released from the suppository, ensuring it meets therapeutic needs. **Content uniformity test** ensures each suppository contains a consistent amount of the active ingredient.

These evaluation parameters are essential to ensure that suppositories provide consistent, effective, and safe drug delivery. Understanding the methods of preparation, displacement value calculations, and evaluation criteria helps pharmacists formulate high-quality suppository medications tailored to patient needs.

16.1 Methods of Preparations of Suppositories

The preparation of suppositories involves several steps and can be done using various methods depending on the type of base, the active ingredient, and the desired properties of the final product. Here's a detailed overview of the common methods used for preparing suppositories:

1. Fusion Method

Overview: This method involves melting the base, mixing it with the active ingredient, and then allowing it to cool and solidify in molds.

a. Steps:

i. **Melting the Base**: Heat the suppository base (e.g., cocoa butter or PEG) until it becomes a clear, liquid state.

ii. **Incorporating the Active Ingredient**: Add the active drug to the melted base, ensuring thorough mixing to achieve uniform distribution.

iii. **Pouring into Molds**: Pour the mixture into suppository molds while it is still in liquid form.

iv. **Cooling and Solidifying**: Allow the filled molds to cool and solidify. The suppositories can then be removed from the molds.

b. Advantages:

i. Simple and straightforward.

ii. Suitable for bases that melt and re-solidify easily.

c. Disadvantages:

i. Requires careful temperature control to prevent degradation of heat-sensitive drugs.

2. Compression Method

Overview: This method involves compressing a powder mixture of the base and active ingredient into a suppository shape using a mechanical press.

a. Steps:

i. **Preparing the Powder**: Blend the active ingredient with a suitable suppository base in powdered form.

ii. **Filling the Mold**: Compress the powder mixture into suppository molds using a tablet press or similar equipment.

iii. **Ejecting the Suppositories**: Remove the compressed suppositories from the molds.

b. Advantages:

i. Useful for bases that do not melt or dissolve easily.

ii. Can produce suppositories with consistent shape and size.

c. Disadvantages:

i. Requires specialized equipment and may not be suitable for all types of bases.

3. Hand Rolling Method

Overview: This manual method involves mixing the base and active ingredient, then forming the mixture into suppositories by hand.

a. **Steps**:
   i. **Mixing**: Blend the active ingredient with the suppository base until a homogeneous mixture is achieved.
   ii. **Shaping**: Manually roll the mixture into cylindrical or torpedo-shaped forms.
   iii. **Cooling**: Place the shaped suppositories in a cooling environment to solidify.

b. **Advantages**:
   i. Suitable for small-scale or experimental preparations.
   ii. Simple and does not require complex equipment.

c. **Disadvantages**:
   i. Labor-intensive and less consistent in shape and size.
   ii. Not practical for large-scale production.

4. Extrusion Method

Overview: This method involves extruding a homogeneous mixture of the base and active ingredient through a mold to form suppositories.

a. **Steps**:
   i. **Preparing the Mixture**: Blend the active ingredient with the suppository base to form a homogeneous paste.
   ii. **Extruding**: Push the paste through a cylindrical extruder that shapes the suppositories.
   iii. **Cutting and Cooling**: Cut the extruded material into individual suppositories and allow them to cool and solidify.

b. **Advantages**:
   i. Produces suppositories with consistent size and shape.
   ii. Suitable for continuous production.

c. **Disadvantages**:
   i. Requires specialized equipment.
   ii. Not suitable for all base types.

5. Cold Process Method

Overview: This method involves mixing the active ingredient with a cold, solid base and then molding it without heat.

a. **Steps**:
   i. **Blending**: Mix the active ingredient with a solid base (like PEG) at room temperature.
   ii. **Molding**: Shape the mixture into suppositories using molds.
   iii. **Setting**: Allow the suppositories to set and harden at room temperature or in a refrigerator.

b. **Advantages**:
   i. Useful for heat-sensitive drugs.
   ii. No need for melting or heating, which preserves the integrity of sensitive compounds.

c. **Disadvantages**:
   i. Limited to bases that are solid at room temperature and can be easily mixed without heating.

16.2 Displacement Value & its Calculations of Suppositories

Displacement value (also known as **displacement factor**) is a crucial concept in the preparation of suppositories, particularly when using a base that needs to account for the volume occupied by the active ingredient. It helps in determining the correct amount of base to use so that the final suppository has the desired weight and shape.

1. Definition of Displacement Value

- **a.** **Displacement Value**: The volume (or weight) of base displaced by a given amount of active ingredient. It represents the volume occupied by the active ingredient in the suppository base. This value helps in adjusting the amount of base to ensure that the total volume of the suppository is correct after adding the active ingredient.

2. Importance

- **a.** **Accurate Dosage**: Ensures that each suppository contains the correct amount of active ingredient.
- **b.** **Consistent Size and Weight**: Helps in maintaining uniformity in the size and weight of suppositories.

3. Calculation of Displacement Value: To calculate the displacement value, follow these steps:

- **a.** **Determine the Displacement Value of the Active Ingredient**
  - **i.** **Weigh a Known Amount**: Weigh a known amount of the active ingredient (e.g., in grams).
  - **ii.** **Prepare a Suppository**: Mix this amount with the suppository base and mold it into suppositories.
  - **iii.** **Measure the Volume Displaced**: Measure the volume of base that is displaced by the active ingredient. This can be done by the difference in volume before and after adding the active ingredient.
- **b.** **Calculate the Displacement Value**
  The displacement value can be calculated using the formula:

$$\text{Displacement Value} = \frac{\text{Volume of Base Displaced}}{\text{Weight of Active Ingredient}}$$

  - **i.** **Volume of Base Displaced**: The volume of base displaced by the active ingredient (usually measured in milliliters).
  - **ii.** **Weight of Active Ingredient**: The weight of the active ingredient added (measured in grams).
- **c.** **Use the Displacement Value in Formulation**
  When preparing suppositories:
  - **i.** **Calculate the Amount of Base Needed**: Subtract the volume of base displaced by the active ingredient from the total volume needed for the suppository.
  - **ii.** **Adjust the Base Amount**: Adjust the amount of base accordingly to ensure the final suppository has the desired weight and size.

d. For example, if the total volume needed for a suppository is 2 grams and the displacement value of the active ingredient is 1.5 ml/gram, and you are using 0.5 grams of the active ingredient:

i. **Volume Displaced** = 0.5 grams × 1.5 ml/gram = 0.75 ml

ii. **Amount of Base Required** = Total Volume - Volume Displaced

iii. **Amount of Base Required** = 2 grams - 0.75 grams = 1.25 grams

4. Practical Considerations

a. **Consistency**: Ensure that the displacement value is consistent across batches of active ingredients and bases.

b. **Measurement Accuracy**: Accurate measurement of both the active ingredient and the volume displaced is crucial for the correct formulation.

c. **Base Properties**: The properties of the suppository base (e.g., melting point, solubility) can affect the displacement value.

16.3 Evaluation of Suppositories

Evaluating suppositories ensures that they meet quality and effectiveness standards. Proper evaluation involves several tests to assess the physical, chemical, and microbiological properties of the suppositories. Here's a detailed overview of the evaluation process:

1. Physical Evaluation

a. **Appearance**:

i. **Color and Shape**: Suppositories should have a uniform color and shape. Any irregularities might indicate poor manufacturing processes.

ii. **Surface Texture**: Should be smooth and free from cracks, bubbles, or defects.

b. **Size and Weight**:

i. **Uniformity**: Each suppository should have a consistent size and weight. Variations can affect dosing and efficacy.

ii. **Measurement**: Use a balance to weigh individual suppositories and calipers or other measurement tools to check dimensions.

c. **Consistency**:

i. **Firmness**: Suppositories should have the appropriate firmness; neither too soft nor too hard. This can be assessed by gently pressing the suppository or using a texture analyzer.

2. Chemical Evaluation

a. **Drug Content Uniformity**:

i. **Content Analysis**: Determine the amount of active ingredient in each suppository to ensure uniform distribution. This can be done using techniques such as High-Performance Liquid Chromatography (HPLC) or Spectrophotometry.

ii. **Assay Testing**: Measure the concentration of the active ingredient to ensure it meets the labeled amount.

b. **Release Profile**:

i. **In Vitro Release Testing**: Evaluate how well and how quickly the active ingredient is released from the suppository. This typically involves placing the suppository in a dissolution apparatus and sampling the release over time.

ii. **Dissolution Testing**: Follow official pharmacopoeial methods or guidelines to assess the rate and extent of drug release.

c. **Stability Testing**:
   i. **Storage Conditions**: Test suppositories under different conditions (e.g., temperature, humidity) to assess their stability over time.
   ii. **Shelf Life**: Determine how long the suppositories remain effective and safe to use.

3. Microbiological Evaluation

a. **Sterility Testing** (for sterile suppositories):
   i. **Microbial Contamination**: Ensure that the suppositories are free from microbial contamination, especially important for suppositories used for internal conditions.
   ii. **Tests**: Conduct sterility tests using methods such as membrane filtration or direct inoculation.

b. **Preservative Efficacy Testing**:
   i. **Preservative Levels**: Verify the effectiveness of preservatives in preventing microbial growth. This is particularly important for suppositories containing preservatives.

4. Mechanical Properties

a. **Melting Point**:
   i. **Determination**: Measure the melting point of the suppository base to ensure it melts at the desired body temperature. This is important for the proper release of the drug.
   ii. **Testing Methods**: Use a melting point apparatus or similar equipment to determine the melting point.

b. **Disintegration Testing**:
   i. **Disintegration Time**: Assess how quickly the suppository disintegrates at body temperature. This ensures that the suppository will release the active ingredient as intended.
   ii. **Methods**: Use a disintegration tester designed for suppositories.

5. Packaging and Storage

a. **Packaging Evaluation**:
   i. **Integrity**: Ensure that the packaging protects the suppositories from environmental factors and contamination.
   ii. **Labeling**: Verify that labels are accurate and include necessary information such as dosage, storage conditions, and expiration date.

b. **Storage Conditions**:
   i. **Suitability**: Ensure that suppositories are stored under conditions that maintain their stability and efficacy. This includes appropriate temperature and humidity control.

16.4 Classification

Suppositories can be classified based on various criteria, including their use, route of administration, and composition. Here's a detailed classification:

1. Based on Route of Administration

a. **Rectal Suppositories**:
   i. **Purpose**: Administered through the rectum, primarily for local or systemic effects.
   ii. **Uses**: Treat conditions such as hemorrhoids, constipation, or nausea; or deliver systemic medications for conditions like fever or pain.

b. **Vaginal Suppositories**:
   i. **Purpose**: Inserted into the vaginal cavity for local treatment.
   ii. **Uses**: Used for conditions like vaginal infections, hormone replacement therapy, or contraception.

c. **Urethral Suppositories**:
   i. **Purpose**: Administered into the urethra.
   ii. **Uses**: Treat urinary tract infections or erectile dysfunction.

2. Based on Therapeutic Use

a. **Laxative Suppositories**:
   i. **Purpose**: Designed to relieve constipation by stimulating bowel movements.
   ii. **Ingredients**: Often contain agents like glycerin or bisacodyl.

b. **Antihemorrhoidal Suppositories**:
   i. **Purpose**: Used to alleviate symptoms of hemorrhoids, such as pain, itching, and inflammation.
   ii. **Ingredients**: May include corticosteroids, anesthetics, or astringents.

c. **Anti-inflammatory Suppositories**:
   i. **Purpose**: Reduce inflammation and pain in local areas.
   ii. **Ingredients**: Often contain nonsteroidal anti-inflammatory drugs (NSAIDs) or corticosteroids.

d. **Antifungal Suppositories**:
   i. **Purpose**: Treat fungal infections in the vaginal area.
   ii. **Ingredients**: Commonly contain antifungal agents like clotrimazole or miconazole.

e. **Hormonal Suppositories**:
   i. **Purpose**: Deliver hormones for conditions such as hormone replacement therapy or contraception.
   ii. **Ingredients**: Include hormones like estrogen or progesterone.

3. Based on Composition

a. **Fatty Bases**:
   i. **Description**: Bases that are solid at room temperature but melt at body temperature.
   ii. **Examples**: Cocoa butter, hydrogenated vegetable oils.

iii. **Characteristics**: Provide a smooth release of the active ingredient as they melt.

b. **Water-Soluble or Water-Miscible Bases**:
   i. **Description**: Bases that dissolve or disperse in bodily fluids.
   ii. **Examples**: Polyethylene glycol (PEG), glycerin.
   iii. **Characteristics**: Useful for heat-sensitive drugs and can provide a controlled release.

c. **Emulsion Bases**:
   i. **Description**: Combinations of fat and water.
   ii. **Examples**: Hydrophilic ointments.
   iii. **Characteristics**: Balances the properties of fatty and water-soluble bases.

d. **Combination Bases**:
   i. **Description**: Mixtures of different base types to achieve specific properties.
   ii. **Examples**: Mixtures of cocoa butter with PEG.
   iii. **Characteristics**: Allows for customization based on the drug and desired release profile.

4. Based on Release Mechanism

a. **Melting Type Suppositories**:
   i. **Description**: Suppositories that release their active ingredient as the base melts at body temperature.
   ii. **Examples**: Cocoa butter-based suppositories.
   iii. **Characteristics**: The drug is released as the base melts and mixes with body fluids.

b. **Dissolution Type Suppositories**:
   i. **Description**: Suppositories that dissolve in body fluids, releasing the drug as they dissolve.
   ii. **Examples**: PEG-based suppositories.
   iii. **Characteristics**: The drug is released as the base dissolves in bodily fluids.

c. **Disintegration Type Suppositories**:
   i. **Description**: Suppositories that break apart in body fluids, releasing the drug.
   ii. **Examples**: Some combination bases.
   iii. **Characteristics**: The base disintegrates, allowing the drug to be released in fragments.

Multiple-Choice Questions (Objective)

1. What is a suppository?
   a) A liquid dosage form
   b) A solid dosage form designed for insertion into body cavities
   c) A type of tablet
   d) An injectable form of medication

2. Which of the following is a common base used in suppositories?
   a) Polyethylene glycol (PEG)
   b) Ethanol
   c) Acetone
   d) Glycerol

3. What type of suppository is used to treat hemorrhoids?
   a) Urethral suppository
   b) Vaginal suppository
   c) Rectal suppository
   d) Oral suppository

4. Which of the following is an advantage of using suppositories?
   a) Variable absorption
   b) High patient acceptance
   c) Avoiding first-pass metabolism
   d) Short shelf life

5. Which method involves melting the base and mixing it with the active ingredient before cooling in molds?
   a) Compression method
   b) Fusion method
   c) Hand rolling method
   d) Cold process method

6. Which type of base melts at body temperature to release the active ingredient?
   a) Fatty base
   b) Water-soluble base
   c) Emulsion base
   d) Combination base

7. What is the purpose of an antifungal suppository?
   a) To relieve constipation
   b) To reduce inflammation
   c) To treat fungal infections
   d) To deliver hormones

8. What does the displacement value of a suppository indicate?
   a) The weight of the active ingredient
   b) The volume of base displaced by the active ingredient
   c) The melting point of the base
   d) The storage temperature

9. Which of the following is a disadvantage of suppositories?
   a) Consistent absorption
   b) Ease of administration
   c) Potential local irritation
   d) Long shelf life

10. Which method of suppository preparation is suitable for heat-sensitive drugs?
   a) Fusion method
   b) Compression method
   c) Hand rolling method
   d) Cold process method

11. What type of suppository is used for hormone replacement therapy?
   a) Rectal suppository
   b) Vaginal suppository
   c) Urethral suppository
   d) Oral suppository

12. Which of the following is NOT a type of base used in suppositories?
   a) Fatty base
   b) Water-soluble base
   c) Emulsion base
   d) Alcohol base

13. What is the primary advantage of using suppositories for local treatment?
   a) High systemic absorption
   b) Targeted therapy with minimal systemic side effects
   c) Long duration of action
   d) Short shelf life

14. What type of suppository is primarily used for erectile dysfunction?
   a) Rectal suppository
   b) Vaginal suppository
   c) Urethral suppository
   d) Oral suppository

15. Which evaluation method measures how quickly a suppository disintegrates at body temperature?
   a) Drug content uniformity
   b) Release profile
   c) Melting point determination
   d) Disintegration testing

16. What is the typical shape of a rectal suppository?
    a) Spherical
    b) Cylindrical or torpedo-shaped
    c) Square
    d) Flat

17. What factor can cause variable absorption of suppositories?
    a) Uniform base composition
    b) Consistent body temperature
    c) Variations in rectal or vaginal environment
    d) Standardized insertion technique

18. Which base is known for melting at body temperature and providing a smooth release of the drug?
    a) Polyethylene glycol (PEG)
    b) Cocoa butter
    c) Glycerin
    d) Hydrophilic ointment

19. How is the displacement value of a suppository base calculated?
    a) By measuring the melting point of the base
    b) By determining the volume of base displaced by a given amount of active ingredient
    c) By calculating the weight of the base
    d) By assessing the solubility of the active ingredient in the base

20. Which of the following is an emulsion base used in suppositories?
    a) Polyethylene glycol (PEG)
    b) Cocoa butter
    c) Hydrophilic ointment
    d) Glycerin

Short Answer Type Questions (Subjective)

1. Define suppositories and describe their key characteristics.
2. Explain the advantages of using suppositories as a dosage form.
3. What are the main types of suppositories based on their route of administration?
4. Describe the fusion method for preparing suppositories.
5. What is the role of the base in a suppository?
6. How do fatty bases differ from water-soluble bases in suppository formulations?
7. Explain the concept of displacement value in suppository preparation.
8. What are the disadvantages of using suppositories?
9. How is the drug content uniformity of suppositories evaluated?
10. Describe the melting point determination test for suppositories.
11. What are the common therapeutic uses of rectal suppositories?
12. How do vaginal suppositories provide localized treatment?

13. What are the advantages and disadvantages of using cocoa butter as a suppository base?
14. Explain the purpose of using urethral suppositories.
15. What factors can affect the absorption of suppositories?
16. Describe the process of disintegration testing for suppositories.
17. How can suppositories be stored to maintain their stability?
18. What are the clinical applications of antifungal suppositories?
19. Explain the importance of proper insertion technique for suppositories.
20. Describe the role of preservatives in suppository formulations.

Long Answer Type Questions (Subjective)

1. Discuss the different types of suppository bases, including their properties, advantages, and disadvantages.
2. Explain the various methods of suppository preparation, highlighting the advantages and disadvantages of each method.
3. Describe the process of evaluating suppositories, including physical, chemical, microbiological, and mechanical properties.
4. Discuss the therapeutic applications of rectal, vaginal, and urethral suppositories, providing specific examples for each.
5. Explain the importance of displacement value in suppository formulation and demonstrate how it is calculated with an example.
6. Describe the advantages and disadvantages of using suppositories as a dosage form, focusing on patient compliance and drug absorption.
7. Discuss the role of suppositories in providing localized treatment and how they compare to other dosage forms in this regard.
8. Explain the challenges associated with the storage and stability of suppositories and how they can be addressed.
9. Describe the clinical considerations for using suppositories in pediatric and geriatric patients.
10. Discuss the future trends and innovations in suppository formulations and their potential impact on drug delivery.

Answer Key for MCQ Questions

1. b) A solid dosage form designed for insertion into body cavities
2. a) Polyethylene glycol (PEG)
3. c) Rectal suppository
4. c) Avoiding first-pass metabolism
5. b) Fusion method
6. a) Fatty base
7. c) To treat fungal infections
8. b) The volume of base displaced by the active ingredient
9. c) Potential local irritation
10. d) Cold process method
11. b) Vaginal suppository

12. d) Alcohol base
13. b) Targeted therapy with minimal systemic side effects
14. c) Urethral suppository
15. d) Disintegration testing
16. b) Cylindrical or torpedo-shaped
17. c) Variations in rectal or vaginal environment
18. b) Cocoa butter
19. b) By determining the volume of base displaced by a given amount of active ingredient
20. c) Hydrophilic ointment

*****