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Suppositories

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INTRODUCTION

- Suppositories are semisolid dosage forms of medicament for insertion into body orifices other than mouth.
- Suppositories are commonly used rectally and vaginally and occasionally urethral.
- They have various shapes and weights.

ADVANTAGES

- Avoids first pass effect.
- Melts at body temperature.
- Both localized and systemic action.
- Easy to use for pediatric and geriatric patients.
- Administered to unconcious patient.
- Convenient for drugs that causes GI irritation, vomiting etc.

DISADVANTAGES

- Irritant drug cant administered.
- Embarrassment to patients.
- Need to store at low temp.
- Cant easily prepared , Cost-expensive.
- fluid content of the rectum is much less than that of the small intestine; this may effect dissolution rate, etc.
- Some drug may be degraded by the microbial flora present in the rectum.

TYPES OF SUPPOSITERIES

1. Rectal suppositories.
2. Vaginal suppositories.
3. Urethral suppositories.
4. Nasal suppositories.
5. Ear cones.

RECTAL SUPPOSITORIES

- They are meant for the insertion into the rectum for systemic or local action
- For adults weigh 2 gm and are torpedo shape. Children's suppositories weigh about 1 g
- Cocoa butter is generally used as the base in these preparations.

VAGINAL SUPPOSITORIES (PESSARIES)

- These are inserted into the vagina.
- weigh about 3-5 gm and are molded in conical, rod shaped, and oval.
- These are generally used to combat infections occurring in the female genitourinary area, to restore the vaginal mucosa to its normal state and for contraception.

URETHRAL SUPPOSITORIES

- They are meant for insertion into the urethra.
- They are thin long and cylindrical at one end to facilitate insertion.
- They generally weigh about 2 -4 gm
- They are very rarely used.

NASAL SUPPOSITORIES

- They are meant for the insertion into the nasal cavity.
- They are thin cylindrical in shape.
- They are always prepared using the glycerogelatin base.
- They are about 9-10 cm long and weigh about 1 gm.

EAR CONES

- These are meant for introduction into the ear
- They are long, thin, and cylindrical in shape
- They weigh about 1gm
- Theobroma oil is generally used as the base

SUPPOSITORY BASES IDEAL PROPERTIES:

- It must retain the shape and size on storage.
- It should melt at body temperature after insertion.
- It should be non-irritant.
- It should shrink sufficiently to remove from mould.
- It should not interfere in release or absorption of drug.

- It should permit incorporation of drug.
- It should be compatible with variety of drugs.
- It should be physically stable on storage.
- It should not be soften or harden on storage.

TYPES OF BASES

1. Oleaginous/ Fatty bases

- Cocoa butter (Theobroma oil)
- Emulsified Theobroma oil.
- Hydrogenated oils.

2. Hydrophilic bases (Water soluble and miscible)

- Glycero-gelatin base.
- Soap-glycerin base.
- Polyethylene glycol.

3. Emulsifying/Synthetic bases

- Witepsol
- Massa estarinum
- Massuppol.

FATTY OR OLEAGINOUS BASES

- **Cocoa butter (Theobroma oil)** Cocoa butter is fat obtained from the roasted seed of Theobroma cocoa.
- **Properties**
  - At room temperature it is a yellowish, white solid having a faint, agreeable chocolate like odour.
  - Chemically, it is a triglyceride (combination of glycerin and one or different fatty acids) primarily of oleopalmitostearin and oleodistearine.
  - It melts at 30 - 350C,

- Advantages
  - Melting just below the body temperature.
  - Maintaining its solidity at usual room temperatures.
  - Readily liquefy on heating and solidify on cooling. Disadvantages
  - Exhibits marked polymorphism.
    Rancidity.
  - Sticks to mould.
  - Leakage from body cavity.
  - Costly.
  - Immiscibility with body fluid.
  - Chloral hydrate or lactic acid liquefy it.

EMULSIFIED THEOBROMA OIL

- When large quantity of aqueous solutions are to be incorporated.
- A combination of
  - Glyceryl monostearate 5 %,
  - Lenette wax 10 %,
  - Cetyl alcoho 2 – 3 %,
  - Bees wax 4 %,
  - Spermaceti wax 12 %

HYDROGENATED OILS

- Hydrogenation of various vegetable oils such as arachis oil, cotton seed oil, coconut oil, palm oil etc.
- Used as substitute for theobroma oil because it has advantages like:
  - They are resistant to oxidation.
  - Lubrication of mould is not necessary.
  - Colorless and odourles suppositories can be prepared.

WATER SOLUBLE AND WATER MISCIBLE BASES

Glycero-gelatin base:

- It is a mixture of glycerin and water which is made stiff by the addition of gelatin.
- The suppositories can dissolve or disperse in the body fluids and release the drugs.
- Type-A Gelatin and Type-B Gelatin.
- Disadvantages:
  - Hygroscopic
  - Bacterial growth.
  - Incompatibility – Tannic acid, ferric chloride and gallic acid.
  - Physiological action – Laxative.

SOAP-GLYCERIN SUPPOSITORIES:

- In glycero-gelatin suppositories the gelatin is replaced with sodium stearate or curd soap.
- Hygroscopic.

Polyethylene glycols:

- Water soluble polymers available from mwt of 200 to 8000.
- Available in different consistencies from liquids, semi solids and solids.
- Advantages:
  - Chemically stable
  - Non irritant
  - Free from bacterial growth.
  - Dissolves slowly in body fluids.
  - Free from sticking.

- Emulsifying bases:
- Witepsol:
- Triglycerides of saturated vegetable fatty acids with varying percentages of partial esters.
- A small amount of Bees wax is added as hardening agent.
- Should not be cooled rapidly because it may leads to brittle suppositories.
- Proper lubrication is necessary.

Massa estarinum

- It is a mixture of mono, di and tri glycerides of saturated fatty acids having the formula $C_{11}H_{23}COOH$ to $C_{17}H_{35}COOH$.
- It is a white brittle almost odourless and taste less solid with a MP of 33.5 to 35.5 ^{0} c.

Massuppol

- It consists of glyceryl esters mainly of lauric acid to which small amount of glyceryl monostearate has been added to improve its water absorbing capacity.

PREPARATION OF SUPPOSITORIES

- Suppositories are prepared by any of the following methods:

1. Hand Rolling method
2. Hot process or Fusion method.
3. Cold compression method

Hand Rolling method

- It is an ancient method.
- The suppository base s rolled and then desired shape is given with he hand.
- Not used now a days.

HOT PROCESS OR FUSION METHOD

- It is the common method which involves
- melting of suppository base,
- incorporation of medicament,
- filling into lubricated mould and cooling the mould.

SUPPOSITORY MOULD

- Suppository moulds of varying sizes and shapes are available and are made up of SS, Nickel, Copper, Aluminium or plastic.
- Suppository moulds can be opened longitudinally by removing the screw at the time of cleaning, lubrication and removing the suppositories.
- Hot water with detergent is used for cleaning, and after cleaning lubricant is applied.

LUBRICATION OF MOULD

- Lubrication of the mould is necessary in case of theobroma oil and glycerinatd bases.
- The lubricant can be applied on to the inner surface of the mould using a brush or swab made of gauze.

Excessive lubrication of the mould is avoided by draining and keeping in inverted position on neat surface.

S. No	Base	Lubricant
1	Cocca butter	Soft soap 10 g Glycerin 10 g Alcohol 90 % 50 ml
2	Glycero-gelatin	Liquid paraffin or Arachis oil
3	Emulsifying base	No lubricant is used

CALIBRATION OF MOULD

- The calibration of the mould is necessary, because the size of the suppository from a mould remains same, but the weight varies.
- This is due to the differences in the densities of bases and medicaments.
- Calibration is done by preparing a set of suppositories using the base, weighing the suppositories and then finding the average mean.
- This will indicate the true capacity of the mould.

DISPLACEMENT VALUE

- The quantity of the drug which displaces one part of the base.
- The volume of a suppository from a particular mould is uniform but its weight will vary because of the differences in the densities of the base with the medicaments.
- The moulds are calibrated for the individual base to know the exact volume of the base required but displacement value is considered when the base is mixed with medicament.
- In order to prepare suppositories of accurate weight from an individual mould, the differences in the densities of base and medicament is taken into consideration.

METHOD OF PREPARATION

1. Clean and lubricate the mould.
2. Melt the 2/3 rd of the base in china dish using heat and stir well.
3. Add the powdered medicament to the base and mix well.
4. Warm the china dish for a few seconds with stirring.
5. Pour the melted mass into cavities of mould and keep on ice bath.
6. Remove the excess mass with sharp knife or blade.
7. Open the mould, collect the suppositories, wipe off neatly and wrap in a wax paper.

COLD COMPRESSION METHOD

- This method is useful for thermolabile and insoluble drugs as it does not involves heating and stirring of the base.
- The method is not suitable for suppositories in which glycero gelatin base or any other base which involves melting.
- Use of Hand or power operated compression machines.

- Evaluation of suppositories
- Suppositories are evaluated for the parameters like:
  - 1. Visual examination
  - 2. Weight variation test
  - 3. Melting range
  - 4. Liquefaction time
  - 5. Content uniformity test
  - 6. Dissolution test

VISUAL EXAMINATION

- Each suppository is placed vertically and examined visually for the
  - Specified shape,
  - Equal distribution of colour,
  - Dispersion of colour,
  - Migration of API to the surface.
- The surface of the prepared suppositories is observed for
  - Dullness,
  - Cracks,
  - Dark regions,
  - Air bubbles, Holes etc.,

WEIGHT VARIATION TEST

- As the suppositories are unit dosage forms, they are evaluated for the uniformity of weight.
- 10 suppositories are taken and weighed individually and noted as individual weight.
- Total weight of suppositories determined and the avge weight of suppositories is calculated.
- Then % deviation of weight of each suppository with the avge weight is determined using the formula:

- The % deviation should not be more than or less than 5 %

MELTING RANGE

- Melting range of the suppository is the temperature range where the suppository starts melting to the temperature where it melts completely.
- The release rate of the suppositories is related to the melting point.
- A number of techniques are available
  - Open capillary tube method
  - U – tube
  - Drop point method

LIQUEFACTION TIME

- Liquefaction time refers to the time taken by the suppository to become soft at the maximum temperature.
- This can be determined by suppository penetration test apparatus.
- It consists of a glass cylinder with a stage to place the suppository, and the glass rod is placed over the suppository.
- The total assembly is placed in a glass cylinder and is immersed in a water bath of 37^{0} c.
- The time taken for the glass rod to reach bottom of the cylinder is noted as liquefaction time for the suppositories.

CONTENT UNIFORMITY

- To ensure dose to dose uniformity, the content uniformity test is performed on suppositories.
- The test is based on the assay of individual content of the API in a number of suppositories.
- 10 to 20 number of suppositories are taken and analysed using suitable analytical methods to know the API content.
- The same is checked with standard limits prescribed in the official books.

DISSOLUTION TEST

- Dissolution gives the information about the % of drug release vs time periods.
- Tablet dissolution test apparatus is used.
- Two types of dissolution apparatus
  - Rotating paddle apparatus
  - Rotating basket apparatus.

Thank you