

PHB



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SUPPOSITORIES

Suppositories are solid dosage form containing medicament intended for insertion into the body cavities other than mouth. They may be inserted into rectum, vagina, ear and nose. After insertion the suppositories may melt at body temperature or dissolve in the cavity fluids and release the medicament.

Suppositories are used to produce:

1. Local action: **Ex-** Antiseptic astringent and local anaesthetic effect.
2. Systemic action: **Ex-** Analgesic, anti-spasmodic, sedative effect.
3. To evacuate the bowels

Advantages:

1. The drugs which cannot be taken orally (which irritates GIT or which produces vomiting) such drugs can be administered in the form of suppositories.
2. Suppositories can be administered to a person who is un-able to swallow the drug. (When he is un-conscious).
3. The drug which is decomposed or inactivated by gastric HCL or by the enzymes present in the stomach, such drugs can be administered in the form of suppositories.
4. These can be easily administered to children and the old person.
5. Drugs sensitive to acidic PH can be administered safely.
6. When-ever local effect is required. It can be placed directly at the site of action.
7. Drugs are more rapidly absorbed in rectal mucosa without ionization.
8. Non-sealing and bitter drugs can be given in this form without difficulties.

Disadvantages:

1. Irritant drugs cannot be administered in the form of suppositories.
2. Large quantities cannot be administered in the form of suppositories.

Different types of suppositories:

The suppositories are marketed in different sizes and shapes for use in the different body cavities. The common types are:

1. **Rectal suppositories:** They are meant for introduction into the rectum. Weight – 1 to 2 grams, Shape – cone.
2. **Vaginal suppositories or pessaries:** They are meant for introduction into the vagina. Weight – 4-8grams, Shape- either cone, rod and wedge in shape.

3. Urethral suppositories: They are meant for introduction into the urethra. Weight – 1grams, Length – 8 cm, Shape – pencil shaped pointed at one end then cylindrical.

4. Nasal suppositories: They are meant for introduction in the nasal cavity. Weight – 1gram, Length – 9 10cms, Shape – thin cylindrical in shape.

5. Ear cones: They are meant for introduction onto the ear, Weight – 1 gram, Shape – Thin and cylindrical shape they are very merely used.

Containers for suppositories:

Suppositories are usually dispensed in shallow, partitioned boxes which hold the suppositories in an upright position and do not allow them to come in contact with each other. Suppositories containing volatile substances must be dispensed in tightly closed glass containers.

Storage:

All suppositories are required to retain the shape at room temperature. It is therefore necessary that suppositories be stored at 10-25°C temperature.

Suppository base:

Suppository bases are used to prepare suppositories, so that they can retain its shape and firmness during storage and administration.

Ideal properties suppositories bases:

1. Melt at body temperature and dissolve or disperse at body fluids.
2. Non-toxic, non-irritant and non-sensitive.
3. Compatible with large variety of drugs.
4. Stable on storage.
5. It should be easily moulded.
6. It should release medicament.
7. It should not adhere to the mould by pouring or by cool compression.
8. It should be stable if it is heated above its melting point.
9. It should keep its shape while handling.
10. These have wetting and emulsifying properties.
11. It is vegetable or animal fat, following standard must comply.

Acid values less than – 3

Iodine value less than – 7

Saponification value – 200-275

12. It has a wetting and emulsifying property.
13. Melting and solidification points should be closed.

Classification of suppositories base with examples:

These are classified into three types they are

1. Oily bases:

Ex–cocoa butter: It is also known as theobroma oil. It is obtained from crushed and roasted seeds of theobroma cocoa.

Properties:

1. Melting point lies between 30-35°C.
2. It is composed of mixture of glyceryl esters of stearic, palmitic, oleic and other fatty acids.
3. It has smell and taste like chocolate.
4. It is a yellowish white solid.
5. Cocoa butter melts at body temperature and releases them.
6. It shows the phenomena of polymorphism, when melted and cooled,

It solidifies into different crystalline form:

1. **α form:** It melts at 24°C, obtained by sudden cooling of cocoa butter at 9°C.
2. **β¹ form:** It crystallizes out from liquefied cocoa butter by stirring at 18-23°C. Its melting point lies between 28-31°C.
3. **β - form:** It changes slowly in form which melts between 34–35°C.
4. **γ - form:** Its melting point is 18°C is obtained by pouring a cooled cocoa butter 2°C into a container, cooled at deep freeze temperature.

Advantages:

1. Solid at even high room temperature but melt quickly at body temperature.
2. It is very stable.
3. It is chemically inert.
4. It is non-reactive.
5. Miscible with many ingredients.

Disadvantages:

1. Over heating changes its physical characters because of polymorphism. Each has different melting points

α form -24°C

β¹form -28°C–31°C

β form -34°C–35°C

γ form -18°C

β 1 changes slowly into stable β form.

2. Melt in warm weather.
3. Adherence to mould.
4. It causes rancidity.
5. Deterioration during storage due to oxidation.
6. Poor water absorbing base.
7. It is costly.
8. Leakage of melted base.
9. Its melting is lowered by overheating and by incorporation of substances like camphor, phenol.

Hydrogenated oil: It is used as a substitute for theobroma oil. It is obtained by hydrogenation of various vegetable oils, such as Arachis oil, cotton seed oil, coconut oil, palm oil etc. It is used as a substitute for theobroma oil.

These have certain advantages over theobroma oil.

1. Resistant to oxidation.
2. Good emulsifying and water absorbing capacities.
3. Lubrication of mould is not necessary.

2. Water soluble or water miscible base:

1) Glycerol-gelatin base:

It is also known as glycerine suppositories. It is a mixture of glycerine and water which is made stiff by the addition of gelatine. Suppositories prepared from this base are translucent gelatinous solids. This base is hydrophilic in nature slowly dissolves in the aqueous secretions and release the medicaments slowly and continuously. This base may be used to prepare all types of suppositories but it is particularly used as a base in vaginal suppositories. These suppositories if required to be stored, must have preservatives like methyl paraben and propyl paraben.

To avoid incompatibility reactions suitable type of gelatin is used two grades of gelatin are available.

1. Pharmagel A (Type A): It is acidic in nature and used for acidic drugs. Its iso-electric point lies between 7 to 9.

2. Pharmagel B (Type B): It is alkaline in nature and used for alkaline drugs. Its iso-electric point lies between 4 to 7.5

Disadvantages:

1. They are more difficult to prepare and handle.
2. They are hygroscopic therefore they must be stored in well closed containers.
3. Gelatin is incompatible with many drugs. Ex-Tannic acid, FeCl_3 .

4. They support bacterial and mould growth.

II) Poly- ethylene glycol:

These are known as macrogols or carbo- waxes. They are widely used for preparing suppositories.

They are chemically stable and physiologically inert. They do not support bacteria and mold growth.

Poly ethylene glycols are available in different physical forms.

1. Molecular weight 200-1000 is liquids.
2. Molecular weight higher than 1000 are was like solids.

Advantages:

1. These are non-irritant and chemically stable.
2. These absorb water and have excellent solvent property.
3. Physical properties can be varied by addition of high and low molecular weight polymer.

Disadvantage:

1. High solubility of PEG leads to super saturations which in turn makes crystals and fracture the product on storage.
2. They are hygroscopic and hence require special storage conditions to store them.
3. They are incompatible with certain drugs like tannins and phenol etc.

III) Soap glycerine base: It is mixture of gelatin and sodium stearate. It contains 95% of glycerine.

The soap is generally produced by interaction of stearic acid and Na_2CO_3 . Glycerin-90 g, Na_2CO_3 - 4.5 g, Stearic acid - 7.5 g

Disadvantages: It is very hygroscopic

3. Emulsifying bases:

It contains mono-glycerides as emulsifying agent. It forms w/o type emulsion. It can absorb very easily.

I) Massa esterinum: It is mixture of mono, di, triglycerides of saturated fatty acids. It is a white brittle solid. It melt at 33-35°C.

II) Witepsol: It consists of glyceryl esters, mainly of lauric acid, to which a very small amount of glyceryl mono-stearate is added to improve its water absorbing capacity.

Advantages:

1. Lubrication of mould is not required. Non-irritant and resistant to oxidation.
2. Over-heating does not affect solidifying points.
3. These solidify rapidly
4. Their emulsifying and water absorbing capacities are good.

Disadvantages:

1. They should not be cooled in refrigerator because they become brittle.
2. They are less viscous on melting which results in sedimentation of other substances.

Displacement value:

The quantity of the drug which displaces one part of the base is known as displacement value.

The volume of suppositories prepared from a particular mould is uniform.

Their weights will vary when compare to the plain suppositories. It is due to the variation of the medicament with the density of the base.

That means the weight of the medicament may not displace the same volume, because of the variation in the densities. But the medicament displaces the same volume of the base.

To prepare an accurate suppository an allowance (extra weight) may be given or the alteration in the density of the mass due to the added medicaments.

It is calculate by applying displacement value.

Ex- Iodoform – 0.9g, Cocoa butter base – 2.0g. Make into suppositories send 8 Nos. one to be inserted into rectum at bed time.

Displacement value of Iodoform is 4.0

Calculation:

Calculate 2 suppositories extra. The base given is 2g so 2g weight suppository mould is used.

Weight of cocoa butter for the suppository 2g Therefore weight of cocoa butter for 10 suppositories $2 \times 10g = 20g$

Weight of iodoform for the suppository = 0.9 g Therefore of iodoform for 10 suppositories = $0.9 \text{ g} \times 10 = 9 \text{ g}$. Displacement value of cocoa butter required.

= Total amount of base - total amount of drug/Displacement value

= $20 - 9.0/4.0$

= $20 - 2.25$

= 17.75 g

Formula for 10 iodoform -9.0 g

Cocoa butter – 17.75 g

Determination of displacement value:

Displacement value of a medicament can be calculated as follows.

1. Prepare and weight 10 suppositories containing theobroma oil or any other base = a grams
2. Prepare and weight 10 suppositories containing 40% of medicament= b grams.
3. Calculate the amount of theobroma oil present in the medicated suppository= $60/100 \times b = c$ grams.
4. Calculate the amount of medicament present in the medicated suppository= $40/100 \times b = d$ grams.

5. Calculate the amount of theobroma oil displaced by d grams of medicament. Let x be (a-c) grams

Displacement value of medicament = d

(a-c)

Displacement value of some drugs:

Drug		Displacement value
Chloralhydrate	-	1.5
Hydro-cortisone	-	1.5
Aminophylline-		1.5
Tannicacid	-	1.0
Phenobarbitone	-	1.0
Bismuthsubgallate	-	2.5
ZnO	-	5.0

Different methods of Preparation of Suppositories:

It can be prepared by following method:

1. Heat process:

I) Fusion method

2. Cold process:

I) Cold compression method

II) Hand moulding (Rolling Method)

1. Heat process:

I) Fusion method:

1. The suppository mould is thoroughly washed and dried.
2. The inner surface of the mould (cavities) is lubricated with liquid paraffin or any suitable lubricant.
3. Calculate the base required as per displacement value of medicament.
4. Heat the dish over the water bath or steam bath.
5. Take calculated amount of base place on dish and is melted at 30-35°C.
6. Remove the dish when 2/3 of the base melts.
7. Place the weighed quantity of medicaments on a warmed tile. Over it pour the melted base.
8. Mix it thoroughly with a flexible spatula and transfer the mixed mass to a dish and stir to form a homogenous mass.
9. Warm the dish over water bath for few seconds so that mass becomes pourable.
10. Pour this melted mass into cavities of mould kept over ice. Fill each cavity to overflowing to prevent the formation of hollow voids on cooling.

11. Precaution must be taken while filling the cavities to stir continuously to ensure uniform distribution of medicament.
12. Mould is kept in a cool place or over ice for 10-15 minutes.
13. The excess mass is scrapped off with a knife.
14. The mould joint is then separated and the suppositories are removed and packed. This method is useful for both small and large scale method.
15. For a large scale method, pouring, cooling and removal can be performed by machine.

2. Cold process:

1) Cold compression method:

1. The suppositories are formed at mould.
2. This method does not require heat and stirring so it is best suitable for thermolabile and insoluble drugs.
3. It is un-suitable for glycerol-gelatin Suppositories.
4. In this method mass is prepared by first mixing the powdered medicament with an equal amount of cocoa butter in a motor.
5. Allowance (extra weight) is made for un-avoidable wastage.
6. It is prepared by using machine. This machine contains cylinder pistons, narrow opening, mould and stop plate.
7. Then add remaining quantity of grated cocoa butter gradually.
8. The mixture is then transferred to the cylinder of the machine and pressure is applied.
9. The pressure forced the material from cylinder to mould through narrow opening.
10. The pressure is further applied stop plate F is removed and the finished suppositories are taken out.
11. The operation is repeated for the next set of suppositories.



II) Hand moulding (Rolling Method):

It is ancient method of preparing the suppositories. The suppository base is rolled and then desired shape is given with the hand. This method I not used nowadays.