Pharmaceutics II

2nd Prof Pharm D

Misbah Hameed

Pharmaceutical suppositories

Suppositories are solid dosage forms intended for insertion into body orifices where they melt, soften, or dissolve and exert localized or systemic effects.

or

Suppositories are solid bodies of various weights and shapes, adapted for introduc-tion into the rectal, vaginal, or urethral orifice of the human body. They usually melt, soften, ordissolve at body temperature. A suppository may act as a protectant or palliative to the local tis-sues at the point of introduction or as a carrier of therapeutic agents for systemic or local action.

1. SUPPOSITORIES ADVANTAGES: _ Can exert local effect on rectal mucosa. _ Used to promote evacuation of bowel. _ Avoid any gastrointestinal irritation. _ Can be used in unconscious patients (e.g. during fitting). _ Can be used for systemic absorption of drugs and avoid first- pass metabolism. − Babies or old people who cannot swallow oral medication. − Post operative people who cannot be administered oral medication. − People suffering from severe nausea or vomiting.
2. SUPPOSITORIES DISADVANTAGES OF SUPPOSITORIES: − The problem of patient acceptability. − Suppositories are not suitable for patients suffering from diarrhea. − In some cases the total amount of the drug must be given will be either too irritating or in greater amount than reasonably can be placed into suppository. − Incomplete absorption may be obtained because suppository usually promotes evacuation of the bowel.

DESIRABLE PROPERTIES OF SUPPOSITORY BASES

A.Chemically and physically stable under normal conditions of use and storage

B.Nonreactive and compatible with a wide variety of drugs and auxiliary agents

C.Free from objectionable odor.

D.An aesthetically appealing appearance

E.Nontoxic, nonsensitizing, and nonirritating to sensitive tissues

F.Expansion–contraction characteristics such that it shrinks just enough on cooling so that itreleases easily from suppository molds

G.Melts or dissolves in the intended body orifice to release the drug

H.Nonbinding of drugs

I.Mixes with or absorbs some water

J.Viscosity low enough when melted to pour easily but high enough to suspend particles of soliddrug

K.Some wetting and/or emulsifying properties so that it will spread, disperse in, and release theactive ingredient(s) at the administration site

Types of suppositories:

a. Rectal suppositories for adults weigh 2 gm and are torpedo shape.Children's suppositories weigh about 1 gm.
b. Vaginal suppositories or Pessaries weigh about 3-5gm and are molded in globular or oviform shape or compressed on a tablet press into conical shapes.
c. Urethral suppositories called bougies are pencil shape. Those intended for males weigh 4 gm each and are 100-150 mm long. Those for females are 2 gm each and 60-75 mm in length.
d. Nasal suppositories: called nasal bougies or buginaria meant for introduction in to nasal cavity.They are prepared with glycerogelatin base.They weigh about 1 gm and length 9-10 cm.
e. Ear cones: Aurinaria and meant for introduction into ear. Rarely used .Theobroma oil is used as base. Prepared in urethral bougies mould and cut according to size.

Pessaries: are a type of suppository intended for vaginal use. The larger size moulds are usually used in the preparation of pessaries such as 4 g and 8 g moulds. Pessaries are used almost exclusively for local medication, the exception being prostaglandin pessaries that do exert a systemic effect.Common ingredients for inclusion in pessaries for local action include: antiseptics, contraceptive agents , local anaesthetics ,various therapeutic agents to treat trichomonal, bacterial and monilial infections.

Classifications of suppository bases

According to Allen (2), four classifications of suppository bases are usually described, based ontheir melting or dissolution properties:

1.The first is the fat- or oil-type base, which must melt at body temperature to release its medication.

2.The second is the glycerin-gelatin base suppository, which absorbs water and dissolves torelease its medication.

3.The third is the water-soluble or water-miscible polymers and surface-active agents.

4.The fourth is a group of bases containing disintegrating agents, natural gums, effervescentagents, collagen, fibrin, hydrogels, etc

According to the USP, there are six general classes of suppository bases:

1.Cocoa butter 2.Cocoa butter substitutes 3.Glycerinated gelatin 4.Polyethylene glycol base 5.Surfactant base 6.Tableted suppositories or insert

A. Cocoa Butter NF

1.Descriptiona.Cocoa butter is the fat from the seeds of Theobroma cacao(chocolate beans). It may beobtained either by expressing the oil from the seeds or by solvent extraction. Chemically, itis a mixture of triglycerides of saturated and unsaturated fatty acids, primarily stearic,palmitic, oleic, lauric, and linoleic.b.It is a mellow, yellowish solid with a mild odor and bland taste. It is a solid at room tem-perature but melts at body temperature with a melting point of 31° to 34°C. The specificgravity of the melt is 0.858 to 0.864. It is available as bars or grated.c.Cocoa butter does not contain emulsifiers, so it does not absorb significant amounts ofwater.Tween 61, a tan, waxy, solid, nonionic surfactant, can be added (5% to 10%) to increasethe water absorption properties of cocoa butter (7), although addition of nonionic surfac-tants reportedly gives suppositories with poor stability on storage 2.Solubility: It is insoluble in water, slightly soluble in alcohol, and soluble in boiling absolute alcohol.

Cocoa butter is bland and nonirritating to sensitive membrane tissues. It is also an excellentemollient and is used alone or in topical skin products for this property

B. Cocoa butter substitutes

1.Descriptiona.The USPhas the following description of cocoa butter substitutes:Fat-type suppository bases can be produced from a variety of vegetable oils, such as coconut orpalm kernel, which are modified by esterification, hydrogenation, and fractionation to obtainproducts of varying composition and melting temperatures (e.g., Hydrogenated Vegetable Oil andHard Fat). These products can be so designed as to reduce rancidity. At the same time, desiredcharacteristics such as narrow intervals between melting and solidification temperatures, andmelting ranges to accommodate various formulation and climatic conditions, can be built in (1).b.Chemically, this type of base is composed primarily of mixtures of triglyceride esters of sat-urated fatty acids in the C-12 to C-18 range, with lesser amounts of mono- and diglyc-erides. Other additives include beeswax, lecithin, polysorbates, ethoxylated fatty alcohols,and ethoxylated partial fatty glycerides

C. Glycerinated gelatin bases

1.Description:This base consists of 70 parts of glycerin, 20 parts of gelatin, and 10 parts of water(1).The method of preparation is like that for glycerinated gummy gel base.These bases are used infrequently because they are more difficult to make and offer few advan-tages.3.The base material has a soft, rubbery consistency (rather like the candy, gummy worms), whichmakes them suitable for vaginal administration but not firm enough for rectal use 4.They do not melt but dissolve slowly in the mucous secretions of the vagina; they have beenrecommended for sustained release of local antimicrobial agents (7). Glycerinated gelatin sup-positories should be moistened before insertion.5.Glycerinated gelatin suppositories are hygroscopic, so they must be dispensed in tight containers.6.They are reported to support mold or bacterial growth, so they should be stored in the refrig-erator and should contain a preservative (e.g., methylparaben 0.18%, propylparaben 0.02%)

D. Polyethylene glycol bases

1.Description: Polyethylene glycol (PEG) suppository bases are composed of blends of polyeth-ylene glycol polymers of various molecular weights. Polyethylene Glycol is described in Chap-ter 23, Ointment Bases, and properties of some PEG polymers that are used often for phar-maceutical applications are given in Table 24.1. Formulas for some PEG suppository bases aregiven in Table 24.2.2.Some commercial polyethylene glycol suppository bases also contain additional components,such as surfactants.Two widely used bases are Polybase (Paddock Labs) and PEGblend (GallipotInc.): Both contain a mixture of polyethylene glycols plus the emulsifier polysorbate 80. Poly-base is a white solid with an average molecular weight of 3,440 and a specific gravity of 1.177at 24° C (13,17).3.PEG suppository bases are formulated so they do not melt at body temperature but rather dis-solve in body fluids. Suppositories made from these bases should be moistened with waterbefore insertion

E. Surfactant or water-dispersible bases

1.Several nonionic surfactants, such as polyoxyethylene sorbitan fatty-acid esters and the poly-oxyethylene stearates, are used alone or in combination with other suppository vehicle mate-rials to make suppository bases

One blend that could be easily made in the pharmacy contains 60% Tween 61 and 40% Tween60 (7). Both of these compounds are solids at room temperature. They are available throughvendors of compounding drugs and chemicals.

F. Tableted suppositories or inserts

1.Vaginal suppositories (now usually referred to as vaginal inserts) are occasionally prepared by thecompression of powdered materials into a suitable shape.They are prepared also by encapsula-tion in soft gelatin (1).2.The compression method is suited for suppositories that contain heat-labile drugs or contain alarge proportion of insoluble ingredients

Preparation of suppositories:

1. Hand moulding: -

Hand molding is useful when we are preparing a small number of suppositories: 1. The drug is made into a fine powder. 2. It is incorporated into the suppository base by kneading with it or by trituration in a mortar. 3. The kneaded mass is rolled between fingers into rod shaped units. 4. The rods are cut into pieces and then one end is pointed.

2. Compression molding:

1. The cold mass of the base containing the drug is compressed into suppositories using a hand operated machine.

Advantages: 1.It is a simple method. 2. It gives suppositories that are more elegant than hand moulded suppositories. 3. In this method sedimentation of solids in the base is prevented. 4. Suitable for heat labile medicaments. IV Automatic Moulding machine: All the operations in pour moulding are done by automatic machines. Using this machine, up to about 10,000 suppositories per hour can be produced.

Disadvantages: 1.Air entrapment may take place. 2.This air may cause weight variation. 3.The drug and/or the base may be oxidized by this air.

1. Pour moulding: - Using a supp. mould which is made of metal or plastic. Traditional metal moulds are in two halves which are clamped together with a screw. Steps: 1. The base is melted and precautions are taken not to overheat it. 2. The drug is incorporated

in it. 3. The molten liquid mass is poured into chilled(lubricated if cocoa butter or glycrogelatin is the base)molds. 4. After solidification the cone shaped suppositories are

Lubricating the cavities of the mould is helpful in producing elegant suppositories and free from surface depression. - The lubricant must be different in nature from the suppository base, otherwise it will be become absorbed and will fail to provide a buffer film between the mass &the metal. - The water soluble lubricant is useful for fatty bases while the oily lubricant is useful for water soluble bases. - The lubricant should be applied on a pledget of gauze or with fairly stiff brush

2. Automatic Moulding machine: All the operations in pour moulding are done by automatic machines. Using this machine, up to about 10,000 suppositories per hour can be produced.

Quality control:

1. **Shape :** It is advisable to check the shape of the suppository to see if it is consistent, irrespective of whether the suppository is ogive or torpedo shaped. Surface condition The following can be checked: brilliance, dullness, mottling, cracks, dark regions, axial cavities, bursts, air bubbles, holes, etc. Color The intensity, nature and homogeneity of the color should be verified. Odor Verification of odor can prevent confusion when similar suppositories are being processed. A change in the odor may also be indicative of a degradation process.
2. Weight Suppositories can be weighed on an automatic balance, obtaining the weight of 10 suppositories. If the weight is found to be too small, it is advisable to check whether the mold is being well filled and whether there are axial cavities or air bubbles caused by badly adjusted mechanical stirring or the presence of an undesirable surfactant. It is also important to check that the batch of suppositories is homogeneous. If the weight is found to be too high, check that scraping has been carried out correctly, and also that the mixture is homogeneous. Lastly, the weight may decrease during aging when the suppositories contain volatile substances, especially if the packaging is not airtight.
3. **Melting range**: (melting point, melting zone) Melting range or melting zone is the term often preferred by some rather than melting point. Many suppository bases and medicated suppositories are mixtures, and so do not have a precise melting point. Routinely, though, we continue to call the physical phenomenon obtained under rigorous conditions the melting point.
4. Melting point determination
5. Liquefaction time: Liquefaction testing provides information on the behavior of a suppository when subjected to a maximum temperature of 37◦C.
6. Mechanical strength/crushing test: Suppositories can be classified as brittle or elastic by evaluating the mechanical force required to break them. Tests are used that measure the mass (in kilograms) that a suppository can bear without breaking. A good result is at least 1.8– 2 kg pressure.
7. Dissolution testing
8. Content uniformity testing