

### 13. SUPPOSITORY

They are solid single-dose preparations whose shapes, volumes and consistencies are suitable for rectal administration. There are also such vaginal preparations in the treatment of local infections.

Reasons for suppository administration by rectal route are preferred:

- 1- Conditions in which the patient can not be given medication by mouth
  - after surgery
  - gastrointestinal disorders
  - infant / elderly patients
  - the patient that has mental disorders
- 2- Oral application is not appropriate for the active substance
  - the active substance is not stable in the pH of the gastrointestinal tract
  - enzymatic degradation of the active substance in the gastro-intestinal tract
  - the first pass of the active substance from the liver

Suppositories can be prepared in different shapes (conical or torpedo) and sizes (usually 1-4 g). Their active ingredient content may be in a wide range of 0.1-40%.

Suppositories are used to create both local and systemic effects. They can be applied, for example, to relieve pain and irritation in the hemorrhoids for local effect. It is also possible to obtain local effects with suppositories of astringent, antiseptic, local anesthetic, vasodilator and antiinflammatory active substances. Systemic effect can be achieved with suppositories containing antiasthmatic, antirheumatic and analgesic active substances.

#### 13.1. Suppository Bases

The active substance is prepared in a suitable bases.

An ideal suppository bases should carry:

- Must be dissolved / dispersed in body fluids
- Mucous membrane penetration / contact ability should be higher
- It should not be irritant / toxic
- Must be compatible with active substances
- The difference between the melting point and the freezing point should not be excessive.
- It should not be spoiled quickly, it should be stable for a long time.
- It can be easily poured into the mold at room temperature, but it must not stick to the mold.
- It must be suitable for production using the melting method or the pressure shaping method.
- The shape should not deteriorate during storage / use of the preparation.

Suppository bases are examined in 4 groups;

1. Ointment bases
2. Synthetic or semi-synthetic bases
3. Non-ionizing surface active agent
4. Water soluble and water dispersible bases

## 1. Fatty Bases

### Cocoa Butter:

This is a natural material. It can change its physical properties because of temperature. When working with cocoa butter, when the temperature rises above 35 ° C, unstable polymorphs such as  $\alpha$ ,  $\beta^1$  and  $\gamma$  form. The  $\beta$ -polymorph is the most stable and the one with the highest melting point. The solidification of the suppository containing this polymorph is only about 15 ° C.

Working with cocoa butter;

Continuous control of the temperature and not exceeding 35 ° C,

When working at higher temperatures, firstly about 1/3 base is put aside and then the suppository is prepared by adding part of the separated solid (~ 1/3) and dissolving the other part. This process is called "seeding".

Another thing to keep in mind when working with cocoa butter is that some substances lower or increase the degree of melting of the base. When working with substances that can effect lower the degree of melting, spermaceti can be added to the base up to 20% of the base, or wax can be added up to 4% of the base to prevent the formulations from melting. On the other hand, when working with substances that can increase the degree of melting, liquid oils such as sesame oil, bread oil etc. (usually 0.1-0.5%) should be added in the appropriate amount to formulation.

Chloral hydrate, phenol, camphor, essences, balsams have a tendency of to lower the melting point of cocoa butter.

Silver nitrate and lead acetate have a tendency of to increase the melting point of cocoa butter.

### Hydrogenated oils:

For the preparation of hydrogenated oils, vegetable oils are hydrogenated and obtained in solid form with special reactions and with the aid of a catalyst. Hydrogenated peanut oil, soybean oil, sunflower oil and hazelnut oil are the most commonly used. Some commercial examples are Suppolanol, Suppositol, Suppocire.

## 2. Synthetic or semi-synthetic bases

### Witepsol:

It is a saturated semi-synthetic triglyceride. The monoglycerides in the structure play an emulsifying role. Thus, the bases acquires the ability to hold water. Witepsol is described according to its chemical structure and physical properties. It is named as Witepsol H, Witepsol S, Witepsol W, Witepsol E according to the -OH groups it contains.

### Massa Estarinum:

It is a mixture of mono-, di- and triglycerides of fatty acids with a carbon number of C11-C17.

### Mglyol:

It is a mixture of triglycerides of fatty acids with a carbon number of C8-12.

Other than these, Adeps solidus, Massuprol, Lasuprol, Suppository Base G, Rectonal ve Hexenol take place in this group.

## 3. Non-ionizing surface active agent

Polyoxyethylene fatty acid esters and polyoxyethylene stearate are used. They can be used alone or as an emulsifier in other bases.

Tween 61 is often used as a suppository bases. A mixture of Industrial Tween 60-Tween 61 and Tween 61-glyceryl laurate is also widely used.

#### 4. Water soluble and water dispersible bases

##### Polyethylene Glycol Derivatives (Carbowax, Suppogen, Postonal, Polywachs):

They are long lasting, do not hydrolyze and are not degraded by oxidation. The construct is not suitable for microorganism reproduction. They are suitable bases for antiseptic substances. They easily dissolve the active substance in the rectum due to their solubility in water.

##### Glycerin-Gelatin-Water Bases:

The suppositories prepared with this bases do not dissolve in body temperature but it dissolves in the mucous juice and releases the active substance. It is a good bases for antiseptic substances. Because it contains 40-60% glycerin, it is susceptible to microorganism and fungus reproduction. For this reason, it is necessary to add preservative. Without active substance, they are used as a faeces softener in treatment.

##### Glycerin-Soap Bases:

It consists of glycerin and sodium stearate soap. Glycerin should be stored in tightly closed cups wrapped in cellophane paper or tin leaves as it is moisture-attracting.

##### Excipients that added to suppository bases:

- Emulsifier effective substances
- Materials that have water holding and liquid binding properties
- Viscosity enhancers
- Solvents
- Mechanical resistance enhancing substances
- Other excipients (stain substances, antioxidants, stabilizers, etc.)

### 13.2. Preparation of Suppository

Suppositories are prepared by 3 methods:

- 1- Hand moulding (cold preparation)
- 2- Compression moulding
- 3- Pour moulding (hot preparation)

During the preparation of the suppositories, the aim is to distribute the active substance in a very thin and homogeneous form in the bases. If the active substance is insoluble in water, it should be suspended / emulsified.

#### 13.2.1. Calculation of bases

In order to prepare the suppository, it is necessary to know how much space is occupied by active substance in the suppository bases. This depends on the intensity of each active substance. If the density of the active substance equals the density of the bases; the active substance in the suppository will cover the volume of the bases in equal weight. If the density of the active substance differs from the density of the bases, then it is necessary to calculate how much space the active substance takes for that base.

The displacement value (or replacement factor) of a drug (f) is the number of parts by weight of drug which displaces (occupies the same volume of) 1 part by weight of the base.

The displacement value is applied to insoluble materials and is listed in practice for various substances.

*Calculation of the amount of bases required by the displacement value:*

Calculation of the base required for the prescription is made with the value of the displacement value. Here is the equation:

$$M = S - [(f_1 \cdot g_1) + (f_2 \cdot g_2) + \dots + (f_n \cdot g_n)]$$

- M : Amount of bases (g)
- S : Weight of unmedicated suppository (g)
- f : displacement value (replacement factor)
- g : Amount of active substance (g)

### Example 13.1.

Rx

Procain                    0.6 g  
Cocoa butter            q.s.  
P.I. Supp. No:V

With cocoa butter, a suppository consisting of only base is prepared, frozen and removed from the mould and weighed. It is called as “Empty Mould Weight”. For example, this value is 1.8 g.

Procain f = 0.8

$$M = S - (f \cdot g)$$

$$M = 1.8 - (0.8 \times 0.6)$$

M = 1.32 g amount of cocoa butter required for a suppository

The calculation is made for 6 suppositories as 5 suppositories are required for prescription. Accordingly, the formula:

Procain                    0.6 x 6 = 3.6 g  
Cocoa butter            1.32 x 6 = 7.92 g

Preparation of the suppository: The calculated amount of cocoa butter (7.92 g) is weighed. Approximately 1/3 is divided, the remaining cocoa butter is melted by heating on a water bath so that it does not exceed 35 ° C. Then cocoa butter in solid form is added to the cocoa butter from the water bath and melting by mixing. To this mixture, procaine (3.6 g) is added and stirred until homogeneous. The resulting mass is poured into suppository moulds which have been previously pre-lubricated with liquid paraffin, while being frozen, and allowed to cool. After the freezing, the surplus left over is taken out and then the moulds are opened and the suppositories are removed. Properly packaged and labeled.

### 13.3. Controls of Suppository

1. Determination of melting period
2. Determination of the dispersion time
3. Mechanical strength/crushing test
4. In vitro active substance dissolution test
5. Active ingredient content
6. Weight deviation
7. pH control

### Practice 13.3.

#### Paracetamol-Aspirin Suppository

Paracetamol	0.2 g
Aspirin	0.1 g
Witepsol H15	q.s.

M.F. Supp.1 d.t.d. No:3

#### Preparation:

Aspirin and paracetamol are thoroughly homogenized in the mortar. It is added to Witepsol which is dissolved in a capsule on water bath and mixed well. When the mixture becomes viscous, it is poured with liquid paraffin mixed with lightly oiled mold. After the frost, the surplus on the mold is scraped with the help of a spatula. The mold is opened and the suppositories are removed. Properly packaged and labeled.

NOTE: 4 masses are studied for the suppository.

According to Witepsol H15, aspirin has a displacement value of 0.71.

#### Questions:

1. Experimentally calculate the displacement value of paracetamole and write how you did it.
2. Write the structure of the base that you used.
3. For what purpose is this suppository used?
4. Show how the value of space is calculated when the density of active material and base is given.

### Practice 13.1.

#### Chloralhydrate Suppository

Chloralhydrate	% 2
Cocoa butter	q.s.

M.ft.Supp. No: III

#### Preparation:

Firstly, weigh approximately 4 g of cocoa butter to determine (Empty Mould Weight) its weight. 2/3 of this amount is melted in a water bath at a temperature not exceeding 35°C in a capsule. Then it is taken from the water bath and the remaining cocoa butter is added and mixed with glass rod to obtain a homogenous mass. It is poured into frozen moulds, pre-coated with liquid paraffin, close to cold. After the freezing, the mould is smoothed with the help of a plastic spatula. It is removed from the mould and weighed so that the empty mould weight is found. When preparing the suppository, the losses are kept in sight and calculation is made over 1 extra. Chloral hydrate has a tendency of to lower the melting point of cocoa butter so up to 20% spermaceti must be added to the bases required to maintain the melting point, or about 4% wax must be added (4% wax is mostly preferred, as 20% spermaceti take up too much space in the bases). After you have the required amount of cocoa, dissolve the cocoa butter as described above. Wax is added to the amount required to keep the melting point from dropping. The fine powdered chlorhydrate is added and mixed. When it is close to freezing, it is poured into moulds lubricated with liquid paraffin. After the freezing, the surplus on the mold is removed with a plastic spatula and removed from the mould.