

# PHARMACEUTICS

## UNIT 4 NOTES

- **SUPPOSITORIES**
- **PHARMACEUTICAL INCOMPATIBILITY**

# SUPPOSITORIES

- Suppositories are semi solid dosage forms of various shapes & sizes meant for insertion into body cavities like rectum, vagina nose, ear etc except mouth.
- Suppositories comes under semi-solid preparations because it is prepared by melting all the ingredients.
- All types of suppositories are melt at normal body temperature.

## Types of Suppositories

There are mainly 5 types of suppositories :

- ① Rectal Suppositories
- ② Vaginal Suppositories
- ③ Urethral Suppositories
- ④ Nasal Suppositories
- ⑤ Ear Cone

## Rectal Suppositories

- Rectal suppositories are meant for insertion into rectum.
- They are generally made from theobroma oil (cocoa butter)
- They are generally available in weight of about 1-2 gram.
- They are mainly cone or torpedo shape.

### Vaginal Suppositories

- Vaginal suppositories are meant for insertion into vagina.
- They are also known as Pessaries.
- They are larger than rectal suppositories.
- They are generally available in weight of about 3-5 grams.
- Vaginal suppositories are mainly rod or conical shaped.
- They are generally used to treat vaginal infection.

### Urethral Suppositories

- Urethral suppositories are meant for insertion into urethra.
- They are also known as Bougies.
- They are generally available in weight of 2-4 grams.
- They are available in pencil shape.

### Nasal Suppositories

- Nasal suppositories are meant for insertion into nasal cavities.
- They are also known as Nasal bougies.
- They are about 9-10 cm long and weight about 1 gram.
- Nasal suppositories are thin and cylindrical in shape.

### Ear Cones

- Ear cones are meant for insertion into ears.
- They are also known as Aurinaries.
- They weigh about 1 gm
- They are cylindrical in shape

## Advantages of Suppositories

- Suppositories can be used for unconscious patients
- Suppositories are compact dosage form.
- They have less chances of side effect.
- It can be used for patients having severe nausea and vomiting.
- Suppositories are suitable for children and old aged patients who cannot swallow tablets.
- They can be used to avoid rectal and vaginal infection.

## Disadvantages of Suppositories

- Suppositories have problem of patient acceptability.
- It is not suitable for patients suffering from diarrhoea.
- Irritating drugs cannot be prepared in suppository form.
- Incomplete absorption may be obtained.
- They must be stored at low temperature otherwise they will get melt.

## Suppository Bases

- Suppository bases are the excipients that are used in the manufacturing of suppositories.
- They play an important role in the release of medication.
- Suppository bases must dissolve in the body cavity to release medication.

### Properties of Ideal Suppository Bases

- It should melt at body temperature.
- It should be inert and non-irritating.
- It should be physically and chemically stable.
- It should be good in appearance.
- It should be compatible with any medication.
- It should be stable if heated above its melting point.
- It should release medication readily.

### Types of Suppository Bases

There are mainly 3 types of suppository bases:

- ① Oily / Fatty bases
- ② Water soluble bases
- ③ Emulsifying bases

## Oily / Fatty Bases

Fatty bases are most frequently used suppository bases

- Theobroma Oil (Cocoa Butter)
- Emulsified theobroma oil
- Hydrogenated oil

### Theobroma Oil

- It is the most commonly used suppository base.
- It is also known as cocoa butter.
- It is obtained from the roasted seed of theobroma cocoa.
- It is yellowish white in colour having chocolaty odour and butter like consistency.
- It is a mixture of glyceryl esters of different fatty acids.
- Its melting point is between 30-35°C
- It is most suitable base for rectal suppositories but not suitable for pessaries, nasal and urethral suppositories.

### Emulsified theobroma Oil

- Emulsified theobroma oil are used as a base when large quantity of aqueous solution has to be used.
- They are less sticky in nature compared to theobroma oil.
- It mainly consist of :
  - 5% glyceryl monostearate
  - 10% lanette wax
  - 2-3% cetyl alcohol
  - 4% bees wax
  - 12% spermaceti

## Hydrogenated Oils

- They are sometimes used as substitute of theobroma oil
- They are also known as synthetic bases.
- They are unaffected by overheating.
- They are less viscous compared to theobroma oil
- example : Coconut oil , palm oil , cotton seed oil mixture.

## Water Soluble or Water Miscible Bases

They mainly contain :

- Glycero - gelatin
- Polyethylene glycol

## Glycero - Gelatin

- It is a mixture of glycerin and water.
- It is most widely used for the preparation of vaginal suppositories.
- It is colourless and transparent in nature.
- It is soft in nature
- It melts at 30-35°C
- It is hygroscopic in nature

## Polyethylene Glycols

- They are commonly known as polyglycols.
- Almost all the drugs are compatible with these bases, however they are incompatible with phenols.
- They are available in very different - different forms.

## Emulsifying Bases

They mainly contain :

- Witepsol
- Massa estarinum
- Massupol

### Witepsol

- They consist of triglycerides of fatty acids
- It should not be cooled rapidly as they are brittle in nature.
- They are non-irritant.

### Massa Estarinum

- It is a mixture of mono, di and tri-glycerides of fatty acids.
- It is a white, odourless, tasteless solid.
- Its melting point is between 33-35°C.



## **METHOD OF PREPARATION**

Suppositories can be prepared by following three methods :

- ① Hand Rolling Method
- ② Compression Moulding / Cold compression method
- ③ Hot Process / Fusion Method

### ① Hand Rolling Method

- It is the simplest and oldest method of suppository preparation.
- Hand rolling method is useful when we prepare a small number of suppositories.
- In this method first we mix the drug with the suppository bases and after that by rolling with our hand, we provide this mixture a suppository shape.
- Although this method is simple and economical but it is very time consuming and rarely used now-a-days.

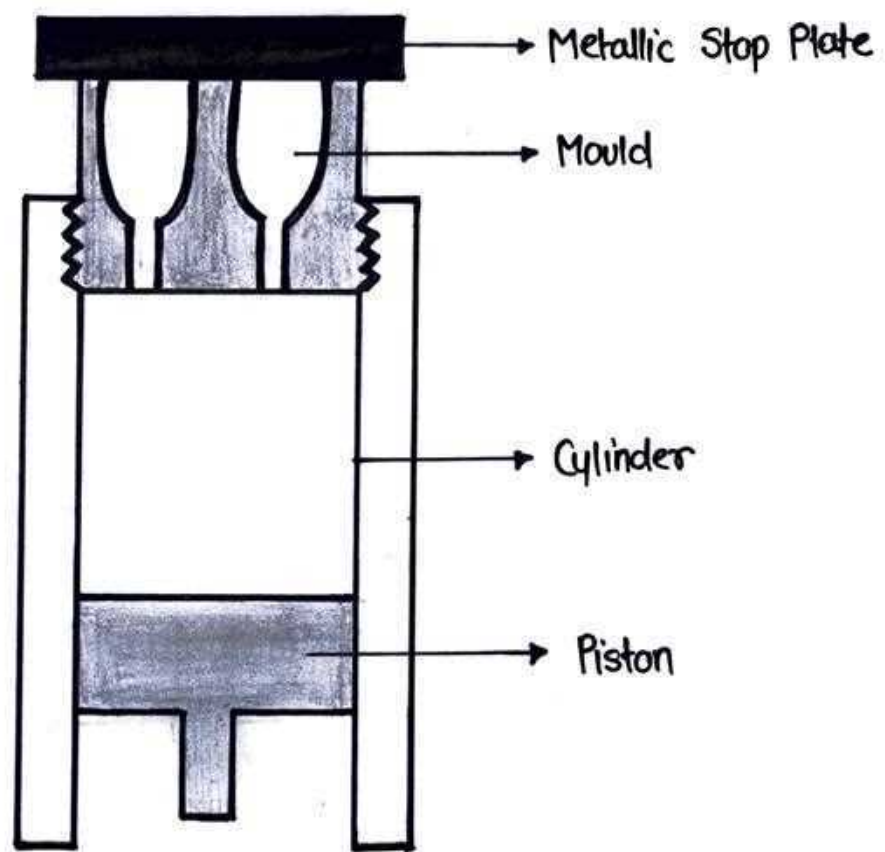
### ② Compression Moulding Method

- It is also known as cold compression method.
- Heating is not required in this method.
- On small scale it is prepared in mortar and pestle but in large scale it is prepared in compression machine

**Compression Machine** : The compression machine consist of a cylinder piston, molds and a metallic stop plate.

## Procedure of compression moulding

- First mix the drug with base and prepare a proper suppository mass.
- Now place the suppository mass in the cylinder.
- Now cylinder is closed and pressure is applied by piston.
- When suppository mass is filled in the mould stop plate is removed.
- Collect the prepared suppositories and leave them for dry.



### ③ Fusion Moulding / Hot Process Method

- In this process, the bases are melted using heat
- This method is not suitable for heat sensitive suppository bases.

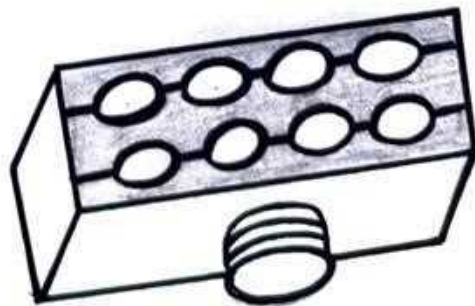
#### Procedure

- Firstly melting the suppository base.
- Now add the drugs and other additives in the melted suppository base and prepare a mass.
- Now remove the mixture from the heat and transfer into the suppository mould.
- Now mixture is left for cooling and acquiring shape.
- After that suppositories are removed from the mould.

#### Suppository Moulds

- Suppository moulds are generally made of stainless steel, copper, aluminium or plastic
- They are available in various shape & sizes
- Small scale moulds are capable of producing 6-12 suppositories in a single operation while industrial moulds produce thousands of suppositories in a single operation.
- Before placing suppositories, it is very important to lubricate the mould so that they will not get stuck on their wall.
- Different bases required different ~~moat~~ lubricants.

- \* Cocoa Butter : soft soap
- \* Glycerol-gelatin : Liquid paraffin
- \* Emulsifying base : No lubrication required



## EVALUATION TEST FOR SUPPOSITORIES

The following tests are performed for evaluation of suppositories:

- ① Test of appearance
- ② Test of Physical strength
- ③ Test of dissolution rate
- ④ Test of melting range
- ⑤ Test of softening
- ⑥ Test for uniformity of drug content

### Test of Appearance

- All the suppositories should be uniformed in size and shape.
- They must have good appearance.
- Individual suppositories should be examined for cracks and pits.
- According to B.P. when suppositories cut longitudinally, then its external and internal surfaces should be uniform in appearance.

### Test of Physical Strength

- The test is carried out to check the brittleness and elasticity of suppositories.
- In this test suppositories are positioned in upright position and weight is put on it
- The weight is increased continuously until the suppository gets break or loses its structure.
- An ideal suppository should have to bear 1.8 - 2.0 kg weight

### Test For Dissolution

- The test is performed to check the amount of drug that gets dissolved in body fluid in unit time.
  - It is measure of rate of drug release from the suppository.
  - There are two types of apparatus used for testing the dissolution rate of suppositories :
- ① Suppository dialysis cell : For lipophilic suppositories
  - ② Stationary basket : For Hydrophilic suppositories

### Test For Melting Range

- The test is performed to check the melting time of the suppositories.
- In this test suppositories left in a water bath at  $37^{\circ}\text{C}$
- It should be melted within 30 minutes.

### Test For Softening

- It is also known as liquefaction test.
- The test is performed to check the softness of suppositories.
- In this we measure the time required for suppositories to completely gets liquify.

### Test For Uniformity of Drug Content

- The test is performed to check the uniformity of drug present in suppository bases.
- All the suppositories should contain the same labelled quantity of drug.

## DISPLACEMENT VALUE

- The quantity of the drug that displaces one part of suppository base is known as displacement value.
- When a suppository mould is filled by suppository, then volume of suppositories are same but their weight can be vary due to the nature of drug.

### Determination of displacement value

- Lets suppose we have to determine the displacement value of suppositories containing theobroma oil as base.
- Follow the following procedure :
- Prepare and weight 6 suppositories containing theobroma oil as a base (No medicament added) = a gram
- Now calculate weight of 6 suppositories containing 40% medicament = b gram
- Now amount of theobroma oil present in medicated suppositories =  $\frac{60}{100} \times b \Rightarrow c \text{ gram}$
- Now amount of medicament present in medicated suppositories =  $\frac{40}{100} \times b \Rightarrow d \text{ gram}$

$$\text{Displacement value of the medicament} = \frac{d}{a-c}$$

# PHARMACEUTICAL INCOMPATABILITY

- When two or more ingredients are mixed together to prepare a medicine and an undesired change takes place which affects the physical, chemical and therapeutic properties of the medicament then the phenomenon is termed as **Incompatibility**.
- Incompatibilities are usually unintentional.

## Incompatibilities may occur during

- Compounding
- Formulation
- Manufacturing
- Packaging
- Dispensing
- Storage
- Administration

## Incompatibility can affect :

- Safety of medicament
- Efficacy of product
- Appearance of medicine
- Purpose of medicament

## Types of Pharmaceutical Incompatibilities

- ① Physical Incompatibility
- ② Chemical Incompatibility
- ③ Therapeutic Incompatibility

# PHYSICAL INCOMPATIBILITY

- When two or more than two substances are combined together and a physical change takes place which results in the formation of an unacceptable product, then this phenomenon is known as Physical Incompatibility.
- Physical incompatibility involves interaction between two or more substances which leads to change in colour, taste, viscosity or appearance of the product.
- The changes that occur due to physical incompatibility are usually visible and can be corrected by taking proper action.

## Correction of Physical Incompatibility

- Changing the order of mixing
- Emulsification
- Addition of suspending agents
- Change in the form of ingredient
- Addition or substitution of a therapeutically inactive substance.

## Example of Physical Incompatibility

- Immiscibility
- Insolubility
- Precipitation
- Liquefaction



## Immiscibility

Oils and water are immiscible with each other, but they can be made miscible by emulsification.

Example :

• Castor Oil	—	15 ml
• Water	—	60 ml
Make an emulsion		

Now in the above prescription castor oil is immiscible with water, to overcome this incompatibility an emulsifying agent is used to make a good emulsion.

## Insolubility

Insolubility takes place when a drug is insoluble in a particular solvent.

Example :

Ephedrine Sulphate	—	0.25 gm
Menthol	—	0.2 ml
Liquid Paraffin	—	30 ml

Now in the above prescription ephedrine sulphate is not soluble in liquid paraffin but anhydrous ephedrine is soluble in it, Hence ephedrine sulphate is substituted with anhydrous ephedrine in the above prescription to make a clear solution.

## Precipitation

A drug in a solution may be precipitated, if ~~the~~ it is insoluble in the solvent in which it is added.

example :

- Resins are insoluble in water, when it is added in the water it gets precipitated.
- It can be prevented by adding a suitable thickening agent.

## Liquefaction

When two or more solid having low melting point are mixed then get converted into liquid.

example :

- If medicament containing menthol, thymol, Camphor phenol etc mixed together, they gets converted into liquid.
- To prevent liquefaction, ingredients should be either dispensed separately or may be mixed with enough quantity of absorbent powder.

# CHEMICAL INCOMPATABILITY

- Chemical incompatibility is the result of change in chemical properties of two or more ingredients due to the chemical reaction occurs between them.
- Chemical incompatibility results in the formation of a toxic or inactive dosage form.
- If the chemical reaction between ingredients take place immediately then it is termed as immediate incompatibilities.
- If the chemical reaction takes place over a period of time then it is termed as delayed incompatibilities.

## Chemical Incompatibilities Often Occur Due to :

- Oxidation - Reduction
- Acid- base hydrolysis
- Combination Reactions
- pH change
- These reaction can be noticed by precipitation , decomposition , colour change , explosion

## Types of Chemical Incompatibilities

**Tolerated** : In tolerated incompatibilities , we change the order of mixing or diluted the substances, to overcome the chemical reaction between ingredients.

**Adjusted** : In adjusted incompatibilities , we directly add or remove a substance to overcome the chemical reaction between ingredients.

# THERAPEUTIC INCOMPATIBILITIES

Therapeutic incompatibility may be the result of prescribing certain drugs to the patient with the intention to produce a specific degree of action but the nature or intensity of the action produced is different from that intended by prescribers

## Causes of Therapeutic Incompatibilities

It may be occur due to

- Overdose / Improper dose of a single drug
- Improper dosage form
- Contraindicated Drug
- Synergistic and Antagonistic drugs

## Example of Overdose

Codeine Phosphate .....	0.5 gram
<u>Direction For Pharmacist</u>	
• Make Powders	
• Send such to powders	
• 1 dose to be taken at bed time	

In the above prescription , physician write 500 mg (0.5 gm) instead of 5 mg of codeine phosphate

## Example of Drug Interaction

Tetracycline Hydrochloride ..... 250 gms

### Direction For Pharmacist

- Make capsule, send such 10 capsules.
- Take ~~10~~ capsules every 6 hours with milk

Now in the above prescription dose is alright but the direction is wrong. tetracycline should not be given with milk because the calcium that present in milk inactivates the action of tetracycline.