UNIT-IV

Suppositories :-

#Defination :- Solid dosage forms intended for insertion into the body orifices or Cavity where it; melt, soften dissolve and exert Localized or Systemic effects.

→ Suppositories are Commonly used rectally and vaginally and occasionally Urethrally.

Type of Suppositories :-

① Rectal Suppositories :-

→ These are ment for insertion into the rectum for producing systemic effect.

→ The rectal Suppositories meant for adults usually weigh 2 gm and are torpedo shape. (Child Suppositories 1 gm).

→ The rectal Suppositories which are used for Systemic effect may Contain analgesics, antispasmodic and Sedative effect.

② Vaginal Suppositories :-

→ The vaginal Suppositories are also known as pessaries.

→ They are ment for insertion into the vaginal Cavities.

→ They weigh about 3-5 gm and are molded in globular or oviform Shape or Compressed on a tablet press into Conical.

③ Urethral Suppositories :-

- These are also Called as bougies and are of pencil

shape.

→ The urethral Suppositories are ment for insertion into the urethra.

→ The urethral Suppositories intended for males weigh 4 gm each and are 100-150 mm long and those for females are 2 gm each & and 60-75 mm in Lenth.

(4) Nasal Suppositories :-

→ The nasal Suppositories are called as nasal bougies or bugination.

→ The nasal Suppositories are ~~ment~~ meant for introduction into nasal cavity.

→ They weigh about 1 gm and have length of 9-10 cm.

Advantage :-

- It is a Simple method
- It gives Suppositories that are more elegant than hand moulded Suppositories.
- In this method Sedimentation of solid in the base is prevented.
- Suitable for heat labile medicament.

Disadvantage :-

- Air entrapment may take place.
- This air may cause weight variation.
- The drug and/or the base may be oxidized by this air.

Type of bases use in Suppositories:-

① Fatty Bases
② Hydrophilic Suppository Bases
③ Water dispersible Base.

① Fatty Bases:-

(a) Cocoa Butter (Theobroma oil):-

It is the most widely used Suppository base. it Satisfy many requirement for ideal Suppository base:

① Bland ② Non reactive ③ Melt at body temperature.

-Cacao butter is thought to exist in 4 crystalline States;

(1) α - crystal - Melt at 22°C - Unstable.
(2) γ - crystal - Melt at 18°C - Unstable
(3) β - crystal - Melt at 27°C - Unstable
(4) β - Stable crystal - Melt at 34-36°C - Stable

② Hydrophilic Suppository Bases:-

- Glycerin base is basically use in Hydrophilic Suppository because glycerin is hygroscopic, there Suppositories are packed in material that protect them from environmental moisture

→ This base do not Melt at body temp. but dissolve in the secretions of the body Cavity in which they are inserted.

③ Water-Dispersible base :-

- Several non-ionic Surface active material, closely related Chemically to PEG as Suppository bases.
- The bases Can be used for formulation both water-Soluble and oil-Soluble drug (e.g. tween & span).
- Another type of water dispersible Suppository vehicle is based on the use of water Soluble Cellulose derivatives. e.g. Methylcellulose & Sodium Carboxymethyl Cellulose.

Advantages :-

1. Stable on Storage at elevated temperature.
2. Compatible with many drug.
3. No Support of microbial growth, non toxic and non Senstive.

Method of preparation of Suppositories :-

① Hand Rolling :-

→ It is the oldest and Simplest method.

→ This method is employed for small Scale production.

The drug is made into fine powder ⇒ Incorporated into Suppository base ⇒ By trituration or kneading ↓ Mass is rolled into rod shape by fingers ⇐ Rods are cut in pieces ⇐ Desired shape is given by hand

② Compression Molding :-

- This method follows the same procedure are that of hand molding except the base containing the drug is compressed into suppositories using a hand operated machine.

Advantage :-

→ It is a simple method skipping the task of hand rolling.
→ Suppository formed is more elegant than hand molded one.

Disadvantage :-

Entrapping of air may occurs causing.
- weigh variation
- oxidation of drug or base used.

③ Fusion Molding :-

- This is the approach exercised on both small and large scale industry due to its efficacy.
- The melted mass of the base containing the drugs is poured into suppository molds.
- Fusion moulding process involves the following steps.
- Firstly melting the suppository base.
- Then the drug is either dispersed or dissoved in the melted base
- The mixture is then removed from the heat and poured into a suppository mould.
- The melt is allowed to congeal.
- Now the suppositories are removed from the mold.

✱ Displacement Value & its Calculation:-

→ The displacement value is a measure of the amount of active substance (in grams) that displaces 1g of base.

→ This value is dependent on the density of the active ingredient.

→ Density describes the relationship blw the mass of a substance and the space which the mass takes up.

→ The displacement values of some of the medicament used in suppositories with reference to cocoa butter are given below.

Drug	Displacement value
1. Aminophyllin	1.5
2. Boric acid	1.5
3. Castor oil	1.0
4. Tannic acid	1.0

— The displacement value of a given medicament may be determined as follows:

1. prepare and weigh 6 suppositories containing theobroma oil (or other base) = a gram.
2. prepare and weigh 6 suppositories containing say 40% medicament = b gram.
3. Calculate the amount of theobroma oil present in medicated suppositories.

$$\frac{60}{100} \times b = c \text{ gram}$$

④ Calculate the amount of medicament present in the medicated Suppositories. 65

$$\frac{40}{100} \times b = d \text{ gram}$$

⑤ Calculate the amount of theobroma oil displaced by d gram of medicament = (a - c) gram.

⑥ Displacement value of medicament = $\frac{d}{a-c}$

✱ Evaluation test for Suppositories :-

① Test of Appearance :-

→ All the Suppositories should be uniform in size and shape.
→ They should have elegant appearance.
→ Individual Suppositories should be examined for cracks and pits due to entrapment of air in the molten mass.

② Breakage test (test of physical strength) :-

- The tensile strength of suppositories is measured in this test to assess their ability to withstand the rigors of normal handling
→ The apparatus used is called as breaking test apparatus.

③ Test of dissolution Rate :-

- It is the amount of dosage form that gets dissolve in body fluid in unit time. It is a measure of the rate of drug release from the suppository.

④ Test of melting Range :-

Both macromelting range and micromelting range are determined as follows.

(a) Macromelting range :-

It is a measure of the thermal Stability of the Suppository. It is the time taken by the entire Suppository to melt in a constant temp. water bath. This test is Conducted using the tablet disintegration apparatus. The Suppository is immersed in a Constant water bath. finally, the melting range is recorded.

(b) Micromelting range :-

The melting range of the fatty base is measured in Capillary tubes.

③ Liquification time (Softening) :-

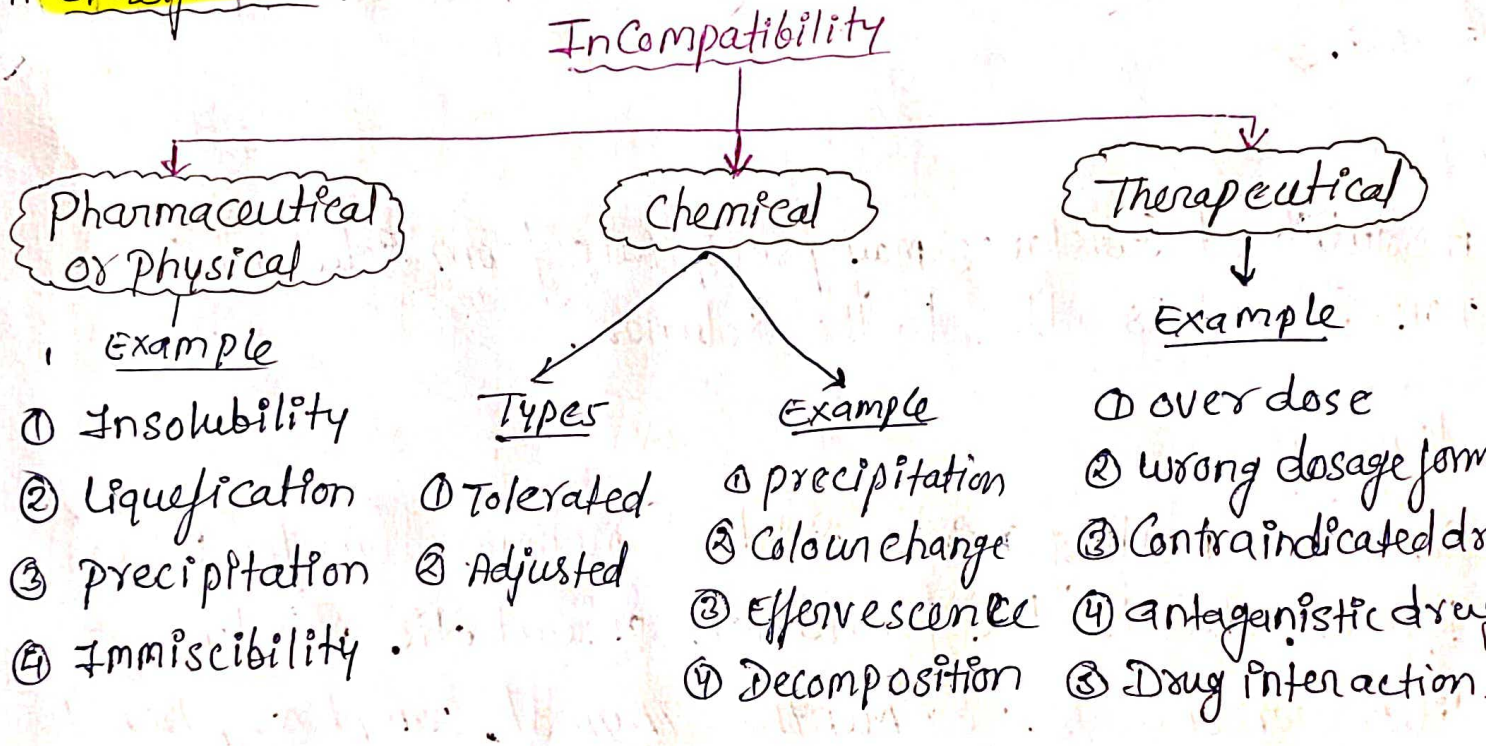
- Softening time is the time for which the Suppository melt Completely at a definite temperature.

→ This test measures the Softening time of Suppository which indicates the hardness of the base.

✱ Pharmaceutical Incompatibilites :-

Defination :- It is defined as when two or more ingredients of a prescription are mixed together, the undesired changes that may takes place in the physical, chemical or therapeutic properties of the medicament is termed as incompatibility.

Classification :-



① Physical Incompatibility :-

→ In this type of incompatibility a visible physical change takes place.
→ An unacceptable, non-uniform, unpalatable product is formed.
→ It is a result of insolubility and immiscibility, precipitation, liquefaction, adsorption and complexation of solid materials.

① Immicibility :-

→ Immiscibility is the result of the mixture of two or more immiscible liquids or an immiscible solid with a liquid.

→ Acceptable liquid product can be obtained by emulsification or solubilization.

② Insolubility :-

Liquid preparation with indiffusible solid (e.g zinc oxide, Calamine, phenacetin etc) a suspending agent is required to uniform distribution of the solids in the liquid phase for sufficiently long time so as to facilitate accurate measurment of dose.

③ precipitation :-

- A solubilised substance may precipitate from solution if a non-solvent is added to the solution.

④ Liquefaction :-

Some low melting points solids sometimes liquefy when together due to the formation of eutectic mixture or liberation of water: eg menthol, Thymol, Camphor, phenol when mixed together forms eutectic mixture.

② Chemical Incompatibilites :-

- Chemical incompatibilities is said when a chemical interaction takes place among the ingredients of a prescription.

→ Such as interactions may take place immediately upon compounding then these are termed as immediate incompatibilities.

→ It is due to oxidation-reduction, acid base hydrolysis or combination reaction.

① Adjusted Tolerated :-

This reaction is prevented by addition or substitution of one of the reacting substance with another of equal therapeutic value but not affected the medicinal value of the preparation.

Eg. Alkaloidal incompatibility.

② Tolerated :-

This reaction can be minimized by applying some suitable order of mixing or mixing the solution in dilute form but no change in the active ingredients of the preparation.

③ Therapeutic Incompatibility :-

- It 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 the intensity of the action produced is different from that intended by the prescriber.

- Therapeutic Incompatibility occurs due to the following reason: It may be due to the administration of.

- Over dose
- Improper or wrong dosage form
- Contraindicated drug.
- Synergistic and antagonistic drugs
- Drug interaction.
