Topic: Suppository
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Mapping of TLO with Course outcomes (Cos)

Sr. No	TLO	CO
1	Describe bases used in suppository	1
2	Evaluate the dosage form	1
3	Explain advantages and disadvantages	1
7	Evaluate suppository	2

SUPPOSITORY

- It is solid dosage form meant to be inserted into Body cavity like rectum , urethra, vagina, where they melt or soften to release the drugs and produce their local or systemic effect.

- It is comes under semi solid preparation because it is prepared by melting all ingredients (bases and other additives along with active ingredient).

- All types of suppositories are melt at normal body temperature after introducing in body cavity and produce their effect.

ADVANTANGE OF SUPPOSITORY

- It is the alternated dosage form for drugs which have less bioavailability when it is taken orally.
- Drugs having bad odour and taste can be used in suppository form.
- It is suitable for unconscious patients which can not taken drugs orally.
- It is suitable for drugs which produce irritating effect in GIT.
- It is suitable for infants and old people who find difficulty in swallowing of drugs.
- It is suitable for the drugs which are destroyed by portal circulation.

DISADVANTAGE OF SUPPOSITORY

- The manufacturing process is more difficult as compare other formulation.
- The drugs which cause irritation to mucous membrane can not be administrated by this form.
- The most important problem is storage condition because it stored at low temp. (10-20 0c). Other than the bases get liquefied.
- Leakage problem is also most critical problem along with suppository after introducing in body cavity at elevated temperature.

TYPESOF SUPPOSITORY

(A)RECTAL SUPPOSITORY-

- It is inserted in the rectal .
- The weight of suppository used in children is about 1g and in adult about 2g.
- The shape of suppository used in rectal is torpedo shape. The length is about 3 cm.

(B) URETHRAL SUPPOSITORY

- The weight of this type suppository is about 2g and 60-75 mm long in Females.
- Those intended for males weigh 4 gm each and are 100-150 mm long.
- It is available in pencil shape.

(C) VAGINAL SUPPOSITORY

- It is in oviform shape.
- It is about 3-5g in weight.
- It is contains the drugs which are used in treatment of the infections of female genitourinary tract and meant for contraception.
- It is contains the combination of polyethylene glycol of different molecular weights as suppository bases.

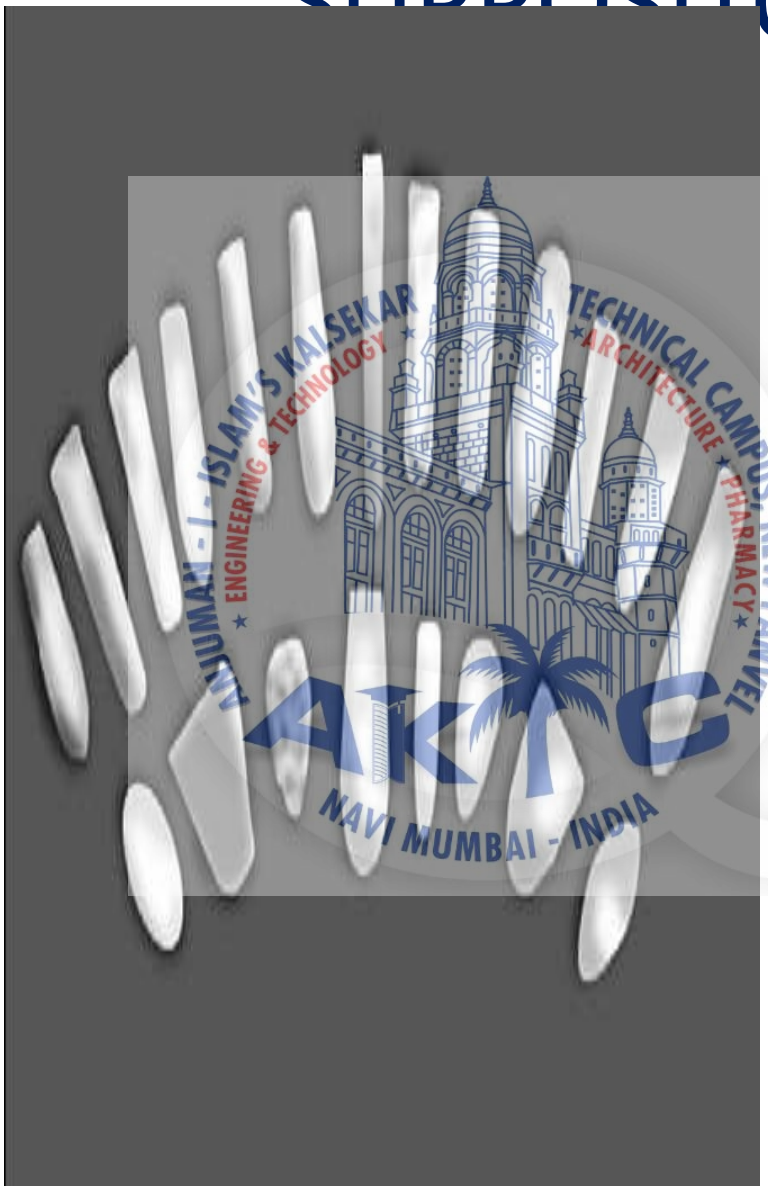
(D) NASAL SUPPOSITORY

- These suppository are meant for introduction into nasal cavity.
- It is about 1g in weight.
- The glycero- gelatin is used as suppository bases.

(E) EAR CONE

- It is also known as AURINARIES.
- These are meant for introduction into the ear.
- It is cylindrical in shape.
- It is about 1g in weight.

VARIOUS SHAPES OF SUPPOSITORY



FORMULATION OF SUPPOSITORIES

(A) SUPPOSITORIES BASES-

IDEAL PROPERTIES OF SUPPOSITRIES BASES-

The following properties should be required for bases--

- Bases should be exist in solid form at room temperature.
- It should not irritate and produced inflamed sensation in body cavity.
- It should be stable during storage condition , No change in colour, shape , odour.
- It should retain hardness

IDEAL PROPERTIES OF SUPPOSITRY BASES

- It should not reacts with drugs and additives.
- It should have good emulsifying and wetting property.
- It should have acid value less than 0.2 or zero.
- It should have iodine value less than 7.
- It should have sponification no. range between200-245.

(1) HYDROPHILIC BASES

(A) WATER DISPERSIBLEBASES-

- These are the mixture of non ionic surfactants which are chemically related to polyethylene glycol.
- These are used alone or in combination with other type of bases.
- Cellulose derivatives like methylcellulose, sod.carboxymethyl cellulose are also comes under this class.

Advantages

- They are suitable for both water soluble and oil soluble drugs.
- They do not support the growth of microbes in the preparation.
- They can be stored at elevated temperature.

Disadvantages-

- This types of bases are interact with few drugs and alter the bioavailability of these drugs.

EXAMPLES

- Polyoxyethylene sorbitan fatty acid ester(TWEENS)
- Polyoxyethelene stearates(MYRIS)
- Sorbitan fatty acid esters(SPANS)
- Combination of Tween 61(60%) and Tween 60(40%)
- Combination of Tween 61 (85%) and glyceryl monostearate (15%)

(B) WATER SOLUBLE BASES

(1) GLYCERO-GELATIN-

- This occurs as a gels
- It is a mixture of gelatin, glycerol, and water.
- According to BP the composition of the bases –

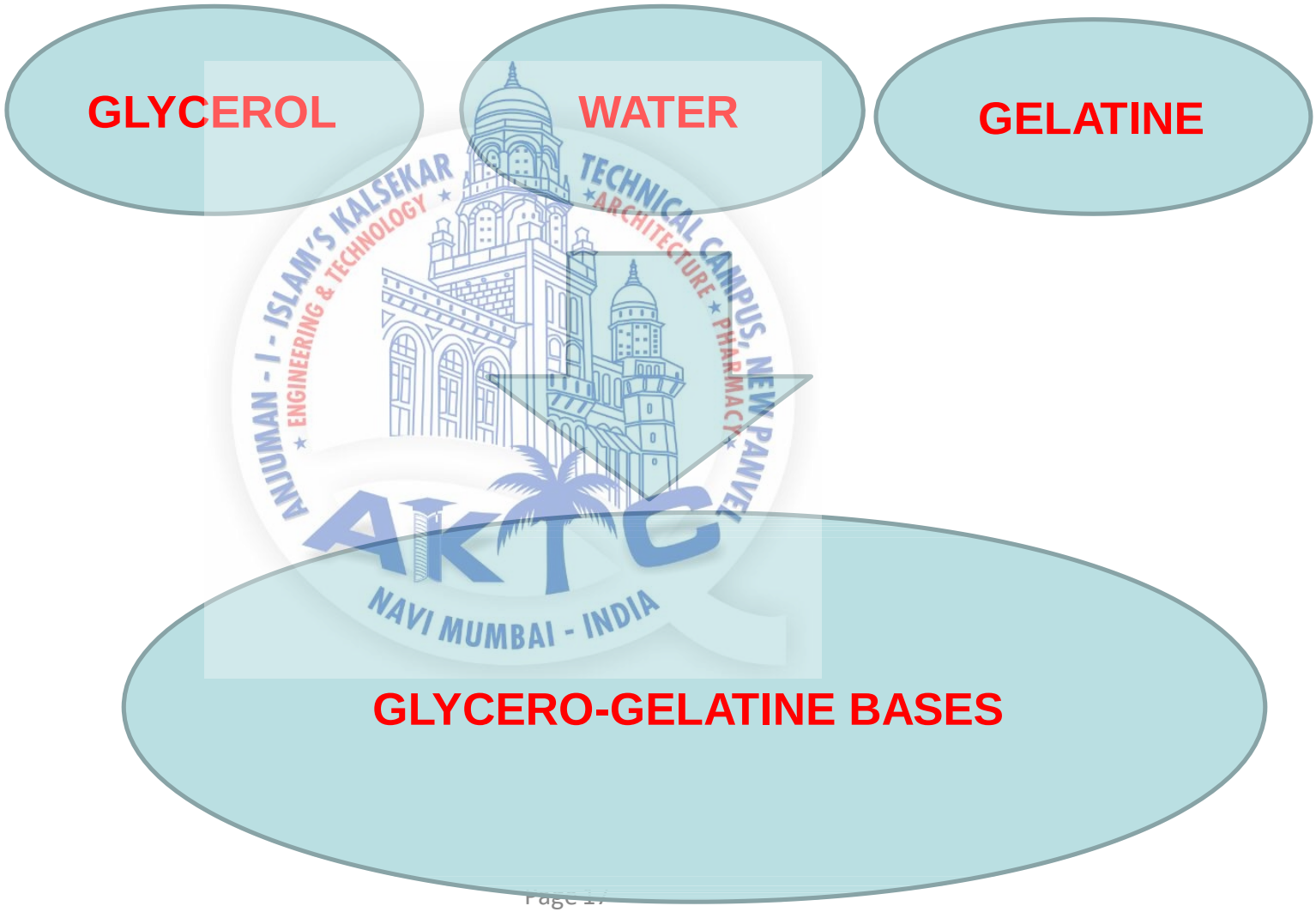
GELATIN- 14% w/w

GLYCEROL– 70% w/w

WATER– QS

- For gets a stiff mass , the quantity of gelatin should be increased to 32.5% and reduced the glycerol to 40%.

PREPARATION OF GLYCERO-GELATINE BASES



ADVANTAGES

- Suppository prepared by glycero-gelatin bases are strong and translucent unlike cocoa butter suppositories.
- This base is disperse slowly in the body cavity fluids and provides prolonged release and action of drugs.

DISADVANTAGES-

- It absorbs moisture and promotes microbial growth , so this reason preservatives are used .

DISADVANTAGES

- The bases are show incompatibility with protiens prescipitants due to the gelatin
- It causes dehydration and irritation of rectal mucosa
- It exerts undesirable laxative action.
- It requires special storage condition at about 10-15 0c.
- Handling and manufacturing of these type of suppository are difficult.

(2)POLY ETHYLENE GLYCOL(POLYGLYCOL)

- It is also called as PASTONALS (GERMANY).
- CARBOWAXES(U.S)
- They are long chain polymers of ethylene oxide.
- They occur in liquid and solids.
- Liquids have mol.weight about 200-600.
- Solid have mol.weight about more than 1000.
- They are also called as macrogols.
- They are the mixture of two or more grades of macrogols used as suppository bases.

EXAMPLES

- **PEG 4000- 33 parts**
  PEG 6000- 47 parts
  PURIFIED WATER- 20 parts

- **FOR HARD SUPPOSITORY**
  PEG 1000- 75 parts
  PEG 4000- 25 parts

- **FOR SOFT SUPPOSITORY**
  PEG 1000- 96 parts
  PEG 4000- 4 parts

ADVANTAGES

- This base is thermostable.
- It does not get degraded or hydrolysed.
- It does not support microbial growth.
- It dose not move out from body cavity after introducing.
- It has good water absorbing capacity.
- It is chemically stable.

DISADVANTAGES

- It is susceptible to rancidification,so it should be stored in dry place away from light.
- It melt easily in warm weather,so it should stored in cool place in warm season.
- Large quantities of water can not be incorporated into the bases.So emulsifier such as tween 61 (6-10%) are useful to increase the absorption of water.
- The physical characteristics of the bases are change from batch to batch.
- Some times leakage may be occur after introducing in body cavity.

(2) LIPOPHILIC BASES

(a) COCOA BUTTER

- It is natural triglyceride.
- Among all fatty acid about 40% are unsaturated fatty acid .
- It can exist in more than one crystalline form or exhibits polymorphism.
- At room temperature ,it is yellowish-white with a paints,chocolate like odour.
- It consists of a mixture of ester of oleic acid,palmatic acid,stearic acid and other fatty acid with glycerol.

ADVANTAGES

- It is liquified readily on warming and sets rapidly on cooling.
- It has emollient effect which is useful to relieve inflammation.
- It shows good release of water soluble drugs.
- It does not cause irritation in mucous membrane.

DISADVANTAGES

- It is susceptible to rancidification ,so it should be stored in dry place away from light.
- It gives soft suppository when formulated along with chloral hydrate , phenol, volatile oil, which have lower melting point.
- The physical property of the base is vary from batch to batch.
- It required extra lubricant during poring in holder.
- Some times leakage may be occur.

(B) ANTI OXIDANTS

- It is protect the drugs and bases from getting degraded due to oxidation.
- These are commonly used in all types of suppositories.

EXAMPLES-

- Ethyl or propyl gallate
- Ascorbic acid
- Butylated hydroxy anisole (BHA)
- Butylated hydroxy toluene (BHT)
- Hydroquinone
- Tocopherol

(C) EMULSIFYING AGENTS

- These are increase the water absorbing capacity of fatty bases.
- **EXAMPLES**
- Poly sorbates (TWEEN 61)
- Wool alcohol
- Wool fats

(D)HARDENING AGENTS

- These are involved in those formulation where the melting point of the bases is decrease by the drugs.
- These are the agents which are used to bring the melting point to normal.
- EXAMPLES
- Beeswax
- Macrogols at high molecular weight.

(E) PRESERVATIVES

- ϖ These are the agents which are used in prevent the growth of microbial in suppository which contains water soluble bases.

ϖ **EXAMPLES**

ϖ **Chorocresol**

ϖ **Methyl paraben**

ϖ **Propyl paraben**

(F) THICKENING AGENTS

- These are the agents which are used to increases the viscosity of molten bases and prevent sedimentation of suspended in solid bases.

- **EXAMPLES**

- Aluminium monostearate
- Colloidal silica
- Magnisium stearate
- Steary alcohol

(G) PLASTICIZERS

- These are the agent which are used to improved flexibility of suppositories.
- It is also used to make the less brittles to suppositories.

- **EXAMPLES**
- Castor oils
- Glycerine
- Glycol
- Tween 80
- Tween 85

METHODS OF PREPARATION OF SUPPOSITORIES

MOLDS USED IN PREPARATION OF SUPPOSITORIES-

- **Molds used in preparation of suppositories are the metals devised with different shape.**
- **It is consists of two or more parts which are joined with a screw.**
- **In side the molds the cavities are made up of aluminium , brass, stainless steel , plastics.**
- **Molds have different capacities like 1,2,4,8gm.**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ENGINEERING & TECHNOLOGY
ARCHITECTURE
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AKTC
NAVI MUMBAI - INDIA

PLASTICS MOLDS

CALIBRATION OF THE MOLDS

- The first step is to prepare molded suppositories from base material alone.
- The suppository's combined and average weight is recorded.
- To determine the volume of the mold, the suppositories are melted in a calibrated beaker, and the volume of the melt is determined.

LUBRICANTS USED IN MOLDS

- Cocoa butter and glycero-gelatine bases are required lubrication of molds.
- This is prevent sticking of bases to the wall of molds cavity.
- It is also useful in easy removal of suppositories from the molds.
- The lubricants are form a film between the wall of mold cavity and base of suppositories so it prevent adhering of bases to the molds.
- The nature of lubricants should be different from nature of bases.

EXAMPLES

(1) FOR COCOA BUTTER BASES

ALCOHOL (90%) - 50ml
GLYCEROL - 10ml
SOFT SOAP - 10 gm

(2) LIQUID PARAFFIN

(3) ARACHIS OILS

MANUFACTURING OF SUPPOSITORIES

- Hand molding
- Automatics Machine Molding
- Compression Molding
- Heat Molding

1) HAND MOLDING-

- Hand molding is useful when we are preparing a small number of suppositories.
- It is suitable for thermo labile drugs.
- It is more economical methods.
- It is more time consuming and not uniformity process.

STEPS INVOLVED IN HAND MOLDING

- The drugs and other additives are made into a fine powder .
- It is incorporated into the suppository base by kneading with it or by trituration in a mortar.
- Then these masses are rolled into the shape of a cylindrical rod on the rolling tile in presence of lubricants to prevent the adherence of masses.
- Then cut the rods and made one end to pointed.

DRUG+ADDITIVES → FINE POWDER

↓

MIXED IN BASES

↓

APPLY LUBRICANTS ON ROLLING TILE

↓

ABOVE MASSES ARE ROOLED IN

↓

CYLINDRICAL SHAPE

↓

CUT THE RODS

↓

PACKED

↓

STORED

(2) AUTOMATIC MACHINE MOLDING

- All the operations in pour molding are done by automatic machines.
- Using this machine, up to about 10,000 suppositories per hour can be produced.
- By this the rate of production of suppositories is more higher than hand molding.
- In this ,there are no chance of air entrapment and contamination of suppositories.
- In this ,if any mass deposited in mold is not removed during cleaning, so produce overweight suppositories with mold marks.

There are two types of machines used they are following---

(a)Rotary Machine-

- **The rate of production of suppositories are about 3500-6000/hr.**
- **This machine consists of a turn table in which metal molds are fitted.**
- **This table rotates sequentially, the mold gets filled with drug , additives, bases and cooled and ejects the suppositories.**
- **Before mass filled in mold ,the lubricant are apply in mold wall.**
- **The excess mass is removed by the scraping unit.**
- **The cooling system results the solidification of suppositories.**

DRUG+ADDITIVES → FINE POWDER

↓

MELT BASES + POWER

↓

HOPPER

↓

LUBRICATED THE MOLDS

↓

FILL ABOVE MIXTURE IN MOLD

↓

COOLING SYSTEM

↓

EJECTION SYSTEM

↓

PACKED → STORED

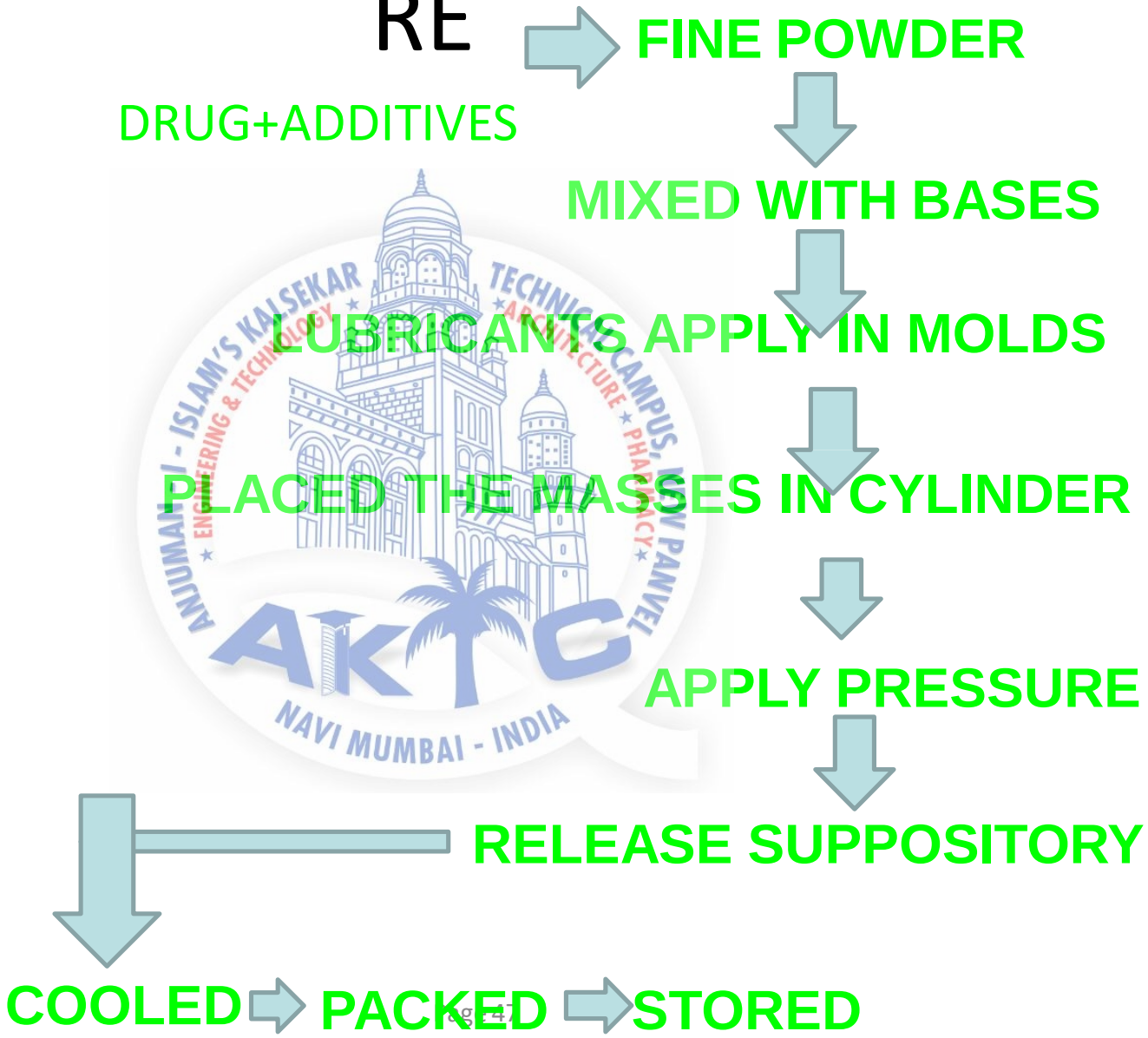
(b)LINEAR MACHINE

- It is similar to rotary machine.
- Except the rate of production is more higher than rotary machine about 10000/hr.
- All steps involved is similar to rotary machine.
- There is no chance of air entrapment and contamination of suppositories as similar to rotary machine.
- The rate of production is higher than rotary machine.

(3) COMPRESSION MOLDING

- **CONSTRUCTION- The compression machine consists of a cylinder, piston , molds, and a metallic stop plate at the bottom.**
- **WORKING- When placed the mass in cylinder and apply the pressure .**
- **Then mass fulfill in mold move and s remove the suppositories and keep them in cool placed.**
- **After cooling release them from compression machine and packed .**

PROCEDURE



- **ADVANTAGE-**

- It is suitable for thermolabile drugs because in this method no heat is required.

- Rate of production is more.

- **DISADVANTAGE-**

- The main disadvantage is air entrapment occurs during production so oxidation takes place in suppository.

(4) HEAT MOLDING

- In this process the bases are melted and the drugs , additives are mixed in bases.

- The following methods are involved in this process-

(a) Melting the bases

(b) Incorporation of the drugs and other additives

(c) Filling of mold

(d) Cooling and collection of suppositories

- **Incorporation of drug and additives-**

- the drugs and additives are in solid form , they are converted in fine powder and mixed properly on a warm tile.

- Triturate the ingredient on warm tile with the sufficient water.

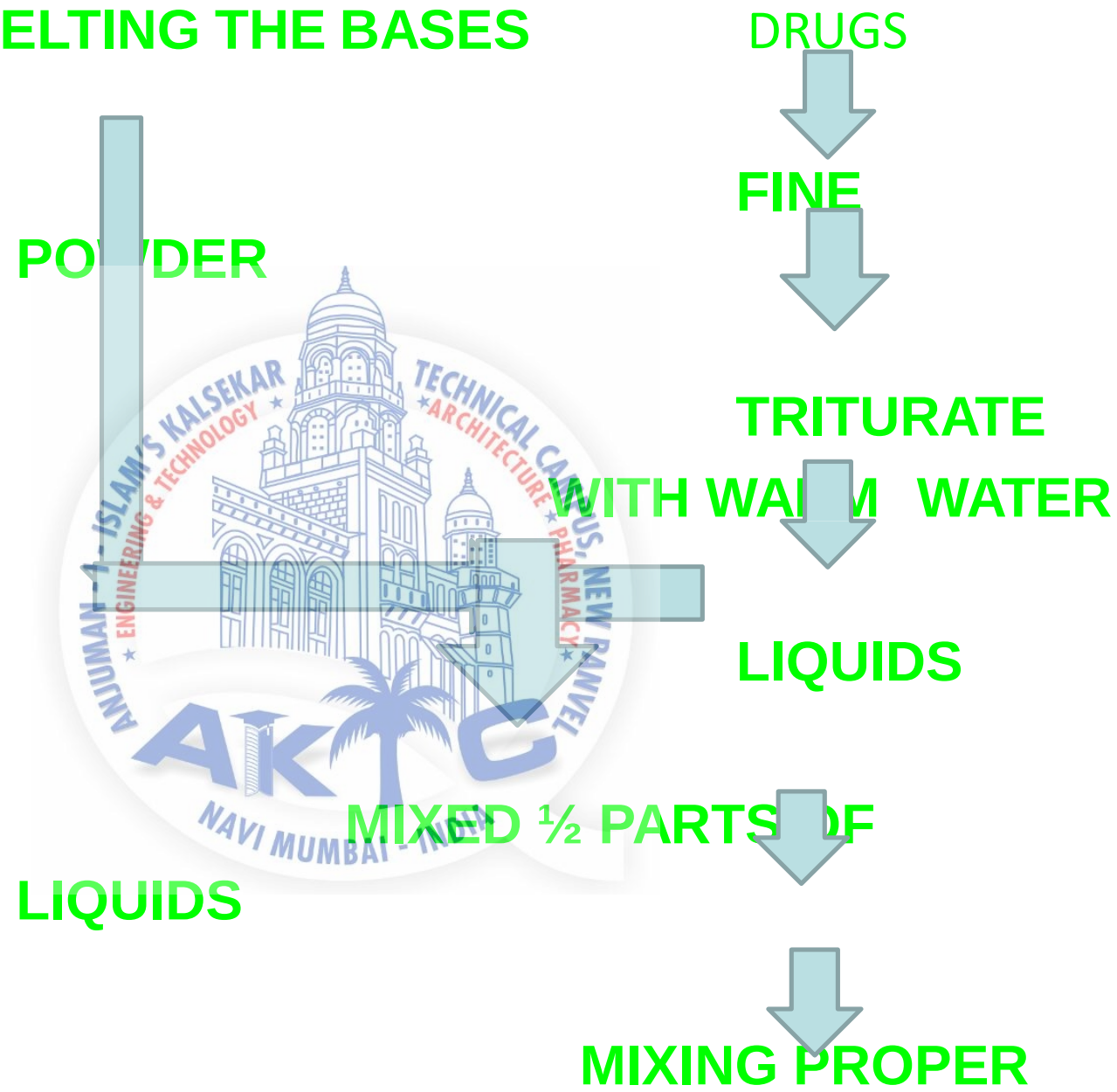
- These above liquid are mixed in melted bases in half amount after mixing , then added remaining liquid in bases.

ϖ FILLING OF MOLDS-

- ϖ First the lubricants are apply in molds.
- ϖ Then the above masses are introducing in molds.
- ϖ During introducing the masses in molds the stirring should be done to prevent the sedimentation of insoluble solids ,if they present.
- ϖ Overfilling is required to prevent the depression in suppositories.

ϖ COOLING AND COLLECTION OF SUPPOSITORIES

- ϖ After the2-3 min . the mass just sets. Then remove the excess mass with warm spatula.
- ϖ Cool the suppositories for 10-15 min. in refrigerators.
- ϖ Then open the mold and collect the suppositories and packed.


MELTING THE BASES
DRUGS
FINE
POWDER
TRITURATE
WITH WARM WATER
LIQUIDS
MIXED ½ PARTS OF
LIQUIDS
MIXING PROPER

CONT.....


APPLY THE LUBRICANTS IN MOLD
OVERFILLING OF MASSESIN MOLDS
REMOVE THE EXTRA MASSES
COOLING (10-15MIN)
OPEN MOLDS
PACKED
STORED

PACKING OF SUPPOSITORIES

- (1) DISPOSABLE MOLDS-
  - These are meant for

cs

(2) MODERN PACKING MACHINE

It is consist of roll of packing material which cut in the required size and rolled around each suppositories.

- **STORAGE CONDITION**

ϖ **It is stored at 10-15 0c**

ϖ **Used air tight container**

ϖ **The suppositories with cocoa butter stored at < 30 0c.**

ϖ **The suppositories with glycero-gelatin stored at < 35 0c.**

EVALUATION OF SUPPOSITORIES

- Test of appearance(size , shape)
- Test of physical strength
- Test of dissolution rate
- Test of melting range
- Test of softening time
- Test of uniformity of drug content

STABILITY PROBLEMS OF SUPPOSITORIES

- **BLOOMING-**
- **During storage , cocoa butter suppositories sometimes show deposition of white powder on the surface.**
- **This result in suppositories of disagreeable appearance.**
- **HARDENING-**
- **During storage , the suppositories made of fatty bases become hard.**
- **I is occurs due to crystallization of bases.**
- **This also effect the melting and rate of absorption of drugs.**

References:

- "The Theory & Practice Of Industrial Pharmacy" by Leon Lachman
- , H.A.Lieberman.
- Remington's "The Science & Practice Of Pharmacy" 21st Edition, Volume-I.

Review questions to ensure attainment of TLOs/ Cos

1) Define suppository and describe advantages and disadvantages for same
2) Elaborate on bases of suppositoryMethod of manufacturing of aerosol
3) Packaging material used for aerosol
4) Evaluation tests for suppository