14/12/15

Biphasic Dosage Forms

Emulsion:- Emulsion is the biphasic liquid dosage form containing 2 immiscible liquids in which both the dispersed phase and dispersion medium (continous phase) are dispersed as a minute globules into the other.

- The dispersed phase (Internal phase) is finely subdivided (0.1 μ to 100μ) and disperses in the dispersion medium with the help of 3rd substance known as emulgents.

- The globule size varies from 0.25 to 25μ in dia. Emulsions having large globules are called coarse emulsions or macro emulsions while those having globules are 5μ are considered to be fine emulsion.

- Emulsions having globule size as small as 10nm are known as micro emulsions. Milk is the ideal, natural most perfect emulsion.

Advantages of Emulsions

- Medicines having an unpleasant taste and odour can be made more palatable for oral administration in the form of an emulsion.

  eg- castor oil, cod liver oil etc.

- Emulsion provides protection against the drugs which are prone to oxidation (or) hydrolysis

- Various external preparations such as creams, lotions and foam aerosols are formulated in emulsion.
- The sterile, stable intravenous emulsion containing fats, carbohydrates and vitamins can be administered to the patients who are unable to take them orally.
- Emulsions improves the absorption of oils when taken internally.
- Now-a-days radioopaque emulsions are used as diagnostic agents in X-ray examination.

Types of Emulsions:-

As there are 2 immiscible phases are present (aqueous & oily) are mainly two types of emulsions.

1) oil in water (o/w) :- Water is the external (or) continous phase and oils are dispersed phase. The oral emulsions usually are o/w type, here the disagreeable oily feel is masked.

2) water in oil (w/o):- Oil is the external (or) continous phase and water is dispersed phase. The emulsions for external use are w/o type (or) o/w type. The external preparations includes applications, lotions, Liniments these are semi-solid emulsions also.

3) Double emulsion (multiple emulsion):- It is the more modern in its origin which are described as

a) oil in water in oil (o/w/o)
b) water in oil in water (w/o/w)

d) Micro emulsions (Transparent):- It is the ~~most~~ more recent one. the property of transparency is due to the small particle size of the dispersed phase i.e. (0.05 μ). The transparency also results when the dispersed and continous phases have the same refractive index (RI). If two liquids have same refractive index but different optical dispersive property, a highly coloured (or) chromatic emulsions results.

15/12/15

Test For Identification of type of Emulsion:-

1) Dilutions Test:-

- Emulsion can be diluted only with the external phase

a) o/w type of emulsion diluted with water and remain stable but not with oil.

b) w/o type of emulsion diluted with oil and remains stable but not with water.

It is useful for liquid emulsion only.

2) Dye Test:-

- Water soluble solid dye amaranth tints coloured only in o/w type of emulsion but not in w/o.

• While sudan III (or) scarlet Red i.e oil soluble dye readily tints w/o type of emulsion but not o/w type of emulsion, means the dispersal gloubles appears colourless in the Red ground.

• This test may fail if Ionic emulgents are present

3) Conductivity Test :-

• Water conducts an electric current while oils donot, o/w emulsions conduct electric current while w/o do not.

• Because water is in the continous phase in case the bulb does not glow. The emulsion is w/o type of emulsion because oil is in the continous phase.

• The conductivity test fails in non-ionic o/w type of emulsions.

4) Flouresceence Test :-

• Many oils when exposed to the UV light fluorescence exhibits.

• o/w type of emulsion exhibit in dot pattern, while as w/o emulsion exhibit entire ~~filled~~ field fluorescence

• Certain fixed oils possess the physical properties of fluorescein in the presence of UV radiation.

5) $CoCl_2$ filter paper test

• Filter paper wetted with $CoCl_2$ dried (blue colour change to Pink colour) when o/w type of emulsion

is added.

6) Direction of Creaming Test

If the emulsion creams in upward direction the emulsion is o/w type of emulsion.

- If the emulsion creams in downward direction then it is w/o type. assumed that oil is lighter than water.

Classification of Emulsions

There are various methods for classification of emulsion from dispensing point of view and its mode of administration. Emulsions can be classified as follows

A) Classification of Emulsion in accordance to type of emulsifying agent used in the preparation of Emulsion. Emulsions are classified as follows

1) Emulsion containing natural gums

eg:- Gum acacia, Tragacanth & Mucilages of Irishmoss

2) Emulsions containing Gum substitutes:-

eg:- cellulose and its derivatives and salts of Alginic acid.

3) Emulsions containing various soaps

4) Emulsions containing saponins

16/12/15

B) Accordance to their mode of administration

a) For oral administration:-

Usually there are o/w type of the emulsions and are used to adminster oils having medicinal value eg- castor oil, olive oil, almond oil, cod liver oil and liquid paraffin

b) Emulsions for External use:-

Either o/w type of emulsions (or) w/o type of emulsions however o/w type of emulsion are preferred over w/o type

c) For parenteral use only:-

It is used to administer fat soluble vitamins such as A, D, E and oil soluble hormones because their absorption in this form is very rapid.

d) for Rectal use only:-

These are used in the form of anemas for evacuation of Bowel. starch mucilage is generally used in the preparation of anemas.

Formulation of Emulsion

1) Emulsifying agent:-

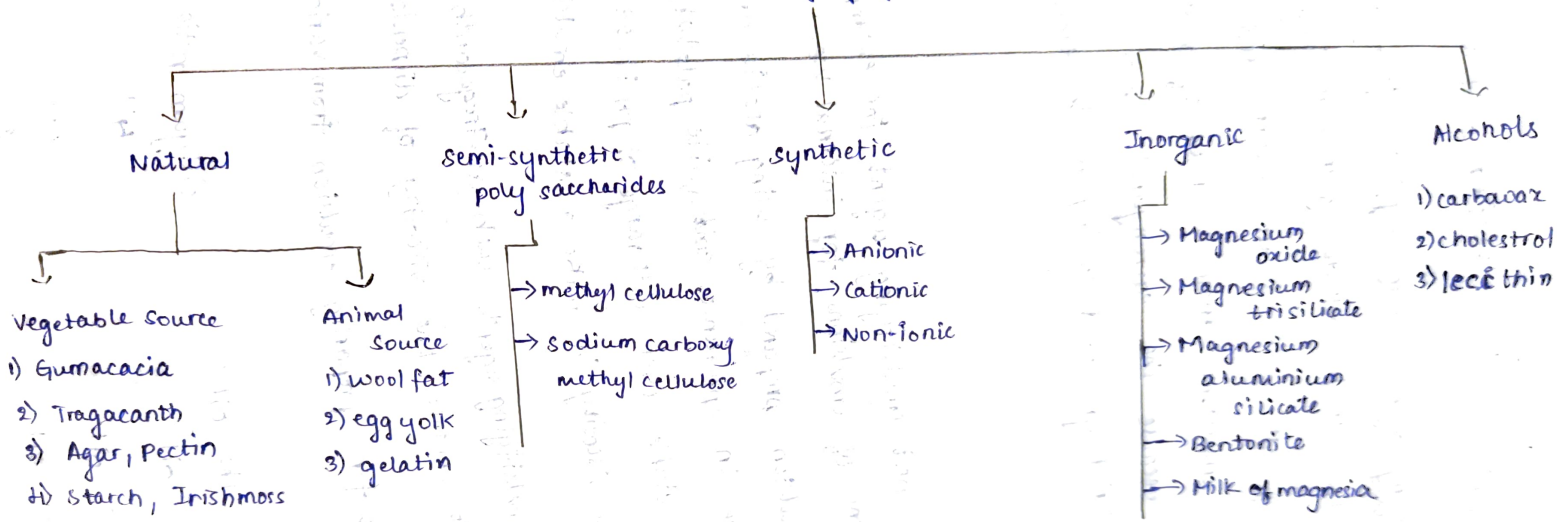
- Emulsifying agents reduce the interfacial tension between 2 phases i.e oily phase & aqueous phase and thus make them miscible with each other and to form a stable emulsion.
- Emulsifying agents are also known as emulgents (or) Emulsifiers.

- Very difficult for the selection of emulsifying agents because of their properties hence it is required to use more than one emulsifying agent.
- Every emulsifying agents having the number of HLB-scale. Emulgents with higher number from 8-18 indicates hydrophilic properties. and to produce o/w type of emulsion.
- Emulgents with lower number i.e. from 3-6 represents liphophilic properties and to produce w/o type of emulsion.

Ideal properties of Emulsifying agents:-

1) It should be capable of reducing the interfacial tension between two inmiscible liquids.
2) It should be compatible with other ingredients of the preparation.
3) It should be non-toxic.
4) It should be capable to produce and maintain the required consistency of the emulsion.
5) It should be chemically stable.
6) It should be capable of keeping the globules of dispersion liquid distributed indefinitely through-out the dispersion medium.

Classification of Emulsifying Agents



28/12/15

Emulsifying agents may be classified as follows:-

1) Natural emulsifying agents from vegetable sources:- These are carbohydrates which includes gums & mucilegenous substances. They are in nature and produces o/w type of emulsions. There is need of addition of preservatives because the carbohydrates act as medium for the bacterial growth. Following are the emulsifying agents:-

1) Acacia:-

- It is a best emulsifying agent for extemporaneous preparations of emulsions for internal use
- The emulsion prepared by using acacia are attractive in apperance, ~~exist~~ quite palatable and relatively stable over wide range of pH i.e. 2 to 10 and have low viscosity to make a stable emulsion.
- Other emulsifying agents such as Tragacanth (or) pectin to enhance the viscosity of dispersion media
- The ratio for preparing emulsion from various types of oil

Name of the oil	oil: gum ratio
Fixed oil	4:1
Volatile oil	2:1
Mineral oil	3:1

Tragacanth

- Alone can be used rarely because it produces very coarse and thick emulsion.

Agar

- It is not a good emulsifying agent as it forms very coarse and viscous emulsion.
- By preparing 2% of mucilage, dissolve in boiling water and cool to 45°C.

Pectin

- It is used as an emulsifying agent by preparing 1% mucilage in water.
- It is incompatible with alkali, strong alcohols, tanic acid and salicylic acid.

Starch

- It forms very coarse emulsion and used to prepare enemas.

Irish moss (Chondrus):-

- It is used as a thickening agent along with the acacia for the emulsification of cod liver oil to mask unpleasant odour & taste of the oil.
- Its 3% of solution is used to emulsify and equal volume of oil.

29/12/15

2) Natural Emulsifying agents from Animal Sources:-

a) Wool Fat:-

- It is generally used in emulsions which are meant for external use.
- They produces o/w type of emulsions and can absorb about 50% of water

b) Egg Yolk:-

- It is used in the extemporaneous preparations meant for Internal use. because it gets spoilt during the transportation hence emulsion must be stored in a cool place.
- It is used as an emulsifying agent in the concentration of 12 to 15%.

c) Gelatin:-

- It is used in conc of 1% for emulsification of liquid paraffin.
- Emulsion prepared with gelatin is quite white and needs proper preservation.

3) Semi Synthetic poly saccharides

a) Methyl cellulose:-

- It is synthetic derivative of cellulose

used as a suspending, thickening and emulsifying agent in the conc of 2%.
. It is used for emulsification of mineral oil and vegetable oil. but gets precipitated in presence of electrolytes.

b) Sodium CMC:-
. It is used as a emulsion stabilizer in conc of 0.5 - 1%.
. It is soluble in both hot and cold water.

ii) Synthetic Emulsifying agents:-
• Anionic, Cationic and Non-ionic surface active agents are used as a emulsifying agents.

a) Anionic:-
. Various alkali soaps, sulphated alcohols and sulphonates are used as anionic emulsifying agents.
• Used for External applications.
• SLS (Sodium Lauryl Sulphate) used as a emulsifying agent among sulphated alcohols produces o/w type of emulsion.

b) Cationic:-
• Qutarnery ammonium compounds such as Benzlkonium -chloride, Benzethionium chloride, cetrimide used as a cationic emulsifying agent.
• These bear positive charge on them and mainly

used in preparation for external ~~lotti~~ used as skin lotions & creams.

c) Non-ionic:-

- Glyceryl esters such as Glyceryl monostearate, sorbitan, fatty acid esters such as sorbitan mono palmitate.
- The emulsions prepared with non-ionic surfactants are stable for a wide range of pH changes.

5) Inorganic Emulsifying agents:-

- Several Inorganic salts such as:- ~~milk~~

Milk of magnesia (10-20%)
MgO (5-10%)
Mg Al Silicate (1%) - for coarse o/w emulsion
Bentonite (5%) - for o/w (or) w/o

6) Alcohols:-

a) Carbowaxes:- preparation of ointments and creams.

- Carbowaxes having molecular weight between 200-700 are viscous, light coloured, hygroscopic liquids
- Carbowaxes with mol.wt 1000 and above are wax like solids.

b) Cholestrol:-

- In this category cetyl alcohol, stearyl alcohol, glyceryl monostearate, cholestrol are used to stabilise the emulsion.

c) Lecithin:-

Which forms w/o emulsion and rarely used as an emulsifying agent because it darkens in colour. When exposed to light & gets easily oxidised.

Preservation of Emulsion

. To avoid cracking of emulsion and to avoid the growth of bacteria, fungi & moulds. Add

1) Benzoic acid (0.1 - 0.2 %)
2) Methyl paraben & propyl paraben (0.1 - 0.2 %)
3) chloroform (0.25 %)
4) cetrimide (0.002 to 0.01 %)
5) chloro cresol (0.1 %)
6) Phenyl mercuric nitrate (0.004 to 0.01 %)

. Antioxidants such as tocopherol, gallic acid, propyl gallate & ascorbic acid are added to avoid oxidation by atm O_2 of fats & emulsifying agents.

Flavours :-

. vanillin is used as good flavouring agent for liquid paraffin emulsion.

. Benzaldehyde is generally used for cod-liver oil emulsion.

Preparation of Emulsions :-

Following methods are used for the preparation of emulsion on a small scale :-

1) Dry gum method
2) Wet gum method
3) Bottle method
4) Other methods.

1) Dry gum methods :-

1) Measure the required qty. of oil in a dry measuring cylinder & transfer it to a dry ~~mortar~~ mortar.
2) Add calculated qty. of gum acacia into it & triturate rapidly to form uniform mixture.

3) Add required qty. of water & triturate vigorously till a clicking sound is produced and the product becomes white. The emulsion produced at this stage is known as primary emulsion.

4) Add water to produced required volume.

Sl.NO.	Type of oil	Examples	Ratio of o:w:gum
1)	Fixed oil	castor oil Almond oil Arachis oil Cod-liver oil	4:2:1
2)	volatile oil	Turpentine oil peppermint oil cinnamon oil	2:2:1
3)	Mineral oil	Liquid Paraffin	3:2:1

- Prepare and dispense 100ml of arachis oil emulsion

℞

Arachis oil - 50ml
Purified water - 200ml

- Arachis oil is fixed by dry gum method, the proportion of oil:water:gum is 4:2:1.

Then formula for primary emulsion is

Arachis oil - 50ml
water - 25ml
Acacia - 12.5gm
Total - 87.5ml

Emulsion ∴ volume of primary emulsion is 87.5ml

Total volume of emulsion is 200ml.

volume of water required - 200-87.5 = 112.5ml

1) Wet gum method:-

- In this method proportion of oil: water: gum will be same as in dry gum method.
- Calculate quantity of oil, water and gum required for preparing the primary emulsion.
- Powder the gum acacia into mortar, add water & triturate it with gum so as to form a mucilage
- Add required quantity of oil in small portions with rigid trituration until a clicking sound is produced and the product produced is white (or) nearly white. This is known as primary emulsion.
- Add more of water with trituration to produce the required volume

Prepare & dispense the following emulsion.

R_x

castor oil - 8ml

water upto - 30ml

Make an emulsion

Send - 120ml

Direction:- one tablespoonful to be taken before going to bed.

- Castor oil is a fixed oil.
- oil : water : gum
  - 4 : 2 : 1 for primary emulsion.

Formula for primary emulsion:-

Castor oil — 8ml X 4 = 32ml

water — 16ml

Gum acacia powder — 8gm

Total volume - 56ml

Total volume of emulsion - 120ml

= 120-50 = 64ml

So 64ml of water is needed to dilute the emulsion.

- Add Gum acacia, add water in mortar & prepare mucilage.
- Add castor oil in small portions with continous, rapid trituration to produce emulsion. This is called Primary emulsion.
- Add remaining quantity of water with trituration to produce the required volume

3) Bottle Method:-

- This method is used for preparation of emulsion of volatile and other non-viscous oils.
- This proportion of oil:water:gum is 2:2:1
- Measure the required quantity of oil & transfer into a large bottle. Add the required quantity of gum acacia
- Shake vigorously the bottle, until the oil & gum are mixed thoroughly.
- Add the calculated amount of water all at once
- Shake the mixture vigorously to form a primary emulsion
- Add more of water in small portions with constant

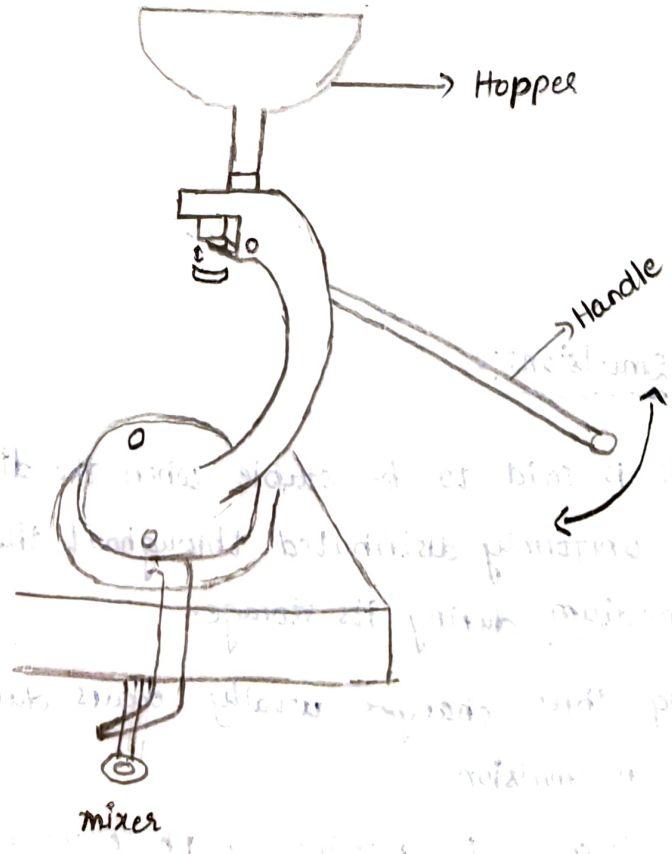
agitation to produce the required volume

ii) Other Methods:-

- various methods blenders & homogenisers are used to prepare emulsion.
- Silverson mixture, homogeniser, colloidal mill are used for the preparation of extemporaneous emulsions.
- These will help to breakdown of large globules into the fine in less than one

Hand Homogeniser:-

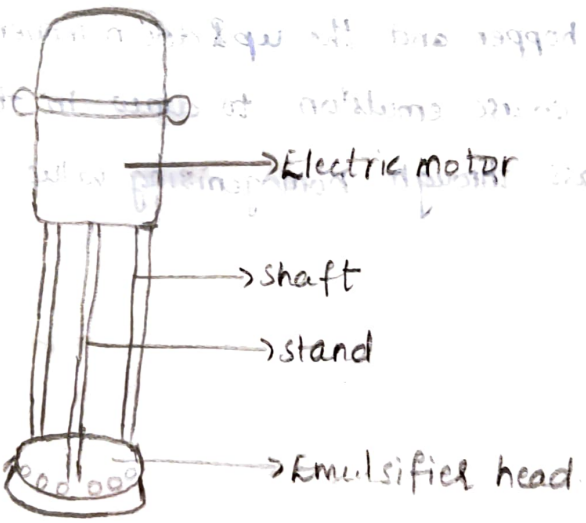
- It is the hand operated in which the emulsion is placed in the hopper and the up & down movement of the handle causes coarse emulsion to draw in through in let value and pass through homogenising value



Silverson mixer homogeniser

It consists of an emulsifier head which is covered with fine meshed stainless steel sieve. The emulsifier head consists of a number of blades which rotate at a very high speed in order to produce a powerful shearing action. The blades are rotated by using an electric motor fixed at top.

The emulsifier head is placed in a vessel containing immiscible liquids, in such a way that it should get dipped into it. When motor started, liquid gets sucked through the fine holes & oil reduced into fine globules & expelled out the fine emulsion.



Stability of Emulsions :-

- The emulsion is said to be stable when the dispersed globules are uniformly distributed throughout the dispersion medium during its storage.
- The following three changes usually occurs during the storage of an emulsion.

a) Cracking b) Creaming c) Phase inversion

Cracking:-

Cracking means the seperation of two layers of disperse & continous phase, due to the coalescence of disperse phase globules which are difficult to redisperse by shaking. Cracking may occurs due to the following reasons.

(i) By adding of emulsifying agent of opposite type:-

Soaps of monovalent metals produce o/w type emulsions where as soaps of divalent metals produce w/o type emulsions. But adding of monovalent soap to a divalent soap emulsion leads to cracking.

(ii) By decomposition (or) precipitation of emulsifying agents:-

- If acid is added to an alkali soap emulsion (Turpentine liniment) it causes decomposition of Emulsifying agent.
- When sodium chloride is added to sodium (or) pottasium soap emulsion leads to precipitation of Emulsifying agent and cracking of Emulsion takes place

(iii) By addition of Common solvents:-

- Common Solvent is added to an emulsion which is either miscible with (or) dissolve the dispersed phase, Emulsifying agent & continous phase, there is formation of one phase (or) a clear solution. Addition of alcohol to turpentine liniment leads to the formation of clear solution because turpentine oil, soft soap and water are soluble in alcohol.

(iv) By Microorganisms

If emulsion is not stored properly, may

develop bacterial and mould growth.

- This may lead to destruction of emulsifying agent and causes cracking of emulsion. Hence store emulsion property

(v) By change in temperature:-

When emulsions are stored for a long time, an increase in temperature, may reduce the viscosity of emulsion and causes creaming.

→ Emulsions are stored at a very low temperature

(vi) By Creaming:-

A creamy emulsion is more liable to crack.

B) Creaming:-

Creaming may be defined as the upward movement of dispersed globules to form a thick layer at the surface of the emulsion and it is temporary phase & gets re-distribu-ted by mild shaking.

→ Creaming leads to seperation of 2 phases.

(i) Radius of globules:-

→ It is directly proportional to the radius of globules.

→ larger the size of globules more will be creaming. And it is prevented (avoided) by reduction of globule size using homogeniser

(ii) Difference in density of disperse phase (or) continous phase

If greater the difference more will be creaming.

(iii) Viscosity of Dispersion medium:-

The rate of creaming is inversely proportional to the viscosity of dispersion medium.

- Viscosity can be increased by addition of tragacanth and methyl cellulose.
- But viscosity is more then difficult to pour from container & get settled down at bottom.

(iv) Storage Conditions:-

- Store in cool place but avoid freezing because it may lead to cracking.

c) Phase Inversion:-

- Phase Inversion means change of one type of emulsion into the other type means o/w changes to w/o type.
- This may be due to the Following Reasons:-

1) Addition of an electrolyte
2) By changing phase ÷ volume ratio
3) By temperature change
4) By changing Emulsifying agents.

- Phase Inversion can be minimised by keeping concentration of disperse phase between 30% to 60%.

4/1/16

Suppositories

Suppositories:- Suppository is a medicated solid dosage form intended for administration via any of several body orifices with the exception of oral cavity.

- Orifices ordinarily employed are the rectum, vagina, urethra & used in nose & ear
- Suppositories are used for local (or) systemic effect.
- Their effect either by melting at body temperature (or) by dissolving in ~~Aq~~ Aq. secretions of mucous membrane and allowing release of active medicaments.

Size and shape of suppositories

Type	Shape	Size & wt
a) Rectal	cone (or) tropedo	2gm - Adult 1gm - children
b) Vaginal (known as pessaries)	ovi form [or] globular, conical	3-5gm
c) Urethral (called as bougies)	• Pencil shaped • Pointed at one end • thin cylindrical	For Males • 4 gm For Females • 10-15 cm long
d) Nasal Bougies	Thin & cylindrical	wt - 1gm. 9 to 10cm long
e) Ear cone (Aurinaria)	Thin, tong & cylindrical	1gm

Advantages of Suppositories:-

1) Gives local as well as systemic action as compared to oral dosage form.

2) It is useful where oral medication would not be retained (Nausea, vomiting), absorbed properly (or) decomposed in Gastro Intestinal (G-I) fluids.

3) It is also useful in unconscious patient, childrens, old persons who can't swallow the drug easily

4) Suppositories avoid first-pass metabolism by the liver, so no modification of therapeutic activity

5) The drugs are absorbed rectally more quickly & at therapeutically more effective liver than oral.

6) Gastric irritant drug (Aminophylline) can be administered in suppositories dosage form.

7) Useful in Infants. These are inserted into body cavity to produce local effect of the medicament.

Disadvantages

(8) These are inserted into rectum to promote evacuation of the bowel.

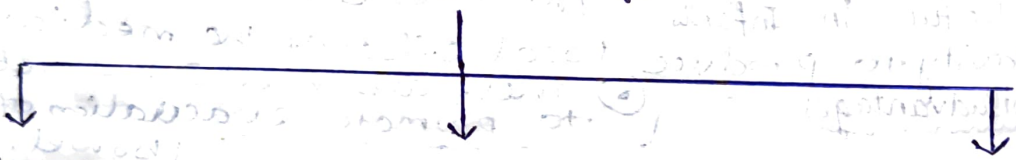
1) Discomfort to the patient, or embarrassment to the patient.
2) May irritate to mucous membrane
3) Leaking
4) Difficult to manufacture, store and use in tropical country.

Ideal Properties of Suppository Bases :-

- Melt at body temperature.
- Non-toxic, Non-irritating and Non-sensitising.
- Compatible with large variety of drugs.
- Shrinks sufficiently on cooling which make easy release from mould. Easily mouldable by pouring or cold compression.
- Has wetting & emulsifying properties.
- Stable on storage
- Easy Manufacturing.

- If it is vegetable (or) animal fat follows standard must comply.
  - → Acid value less than 3
  - → Saponification value - 200 to 245
  - → Iodine value - below 7.
- Releases Medicament easily & readily,
- Maintains shape when being handled.
- Stable if heated above its Melting Point.
- Must have water number high.

Suppository Bases Type



Oleganious - (fatty)

a) Cocoa Butter (Theobroma oil)

b) synthetic fats (synthetic triglycerides mixtures]
- Hydrogenated palm Kernel oil

Aqueous-Base (Hydrophylic)

a) glycerinated gelatin

b) Soap glycerin

c) Maccrogol (PEG)

Emulsifying Base (water dispersable)

a) Massaesterinum

b) Witepsol

c) Massupol

1) Oleaginous Base
- It includes
  - a) Cocoa Butter
  - b) Synthetic triglyceride mixture