

Emulsion

Emulsion: a pharmaceutical preparation heterogeneous system consisting of two immiscible liquid usually water and oil, one of which is dispersed as small globules (droplet) in the other phase.

Thus the emulsion consist of

- Dispersed phase (internal phase)
- Dispersion media (external phase) or continuous media.

//// To prepare a stable emulsions add another substance called “emulsifying agent”. Emulsifying agents have the ability to stabilize the emulsion by one or more mechanism:

1/ prevent coalescence of particles.

2/ maintain the integrity of individual droplets of dispersed phase.

3/decrease interfacial tension between two liquids.

Types of emulsions:

1. Oil in water emulsion (O/W): The oil droplets are dispersed throughout the aqueous phase.
2. Water in oil emulsion (W/O): The water is dispersed throughout the oil phase.

The type of emulsion is determined by factors:

1. The ratio of the two immiscible phases.
2. The type of emulsifying agent used and its concentration. (Example acacia always give O/W emulsion)
3. The order of mixing of the two immiscible phases.
5. Presence of additive.

❖ Tests for identification of emulsion type

- 1. Miscibility test:** An emulsion will mix with a liquid that is miscible with its external phase. Therefore, O/W emulsion is miscible with water while W/O emulsion is miscible with oils.
- 2. Conductivity measurement:** Systems with aqueous external phases will readily conduct electricity, whilst systems with oily external phases will not.
- 3. Staining test:** Water-soluble and oil-soluble dyes are used. They will mix and stain the external phase of the emulsion.

❖ **Why emulsions?**

1. To enhance the palatability of oils and oil-soluble drugs.
2. To solve the issue of insolubility. i.e. when we have two liquids that are immiscible, we cannot form solution but emulsion
3. Emulsion can increase the absorption of oils and oil-soluble drugs through intestinal walls.
4. TPN (total parenteral nutrition) is feeding a person intravenously, bypassing the usual process of eating and digestion. The person receives nutritional formulae that contain nutrients such as glucose, amino acids, lipids and added vitamins and dietary minerals usually in a form of emulsion.

❖ **Uses of emulsions:**

1. Emulsions for internal use: Oral emulsions are stabilised O/W dispersions that may contain one or more active ingredient.
2. Emulsions for intravenous administration must also be of the O/W type. However, intramuscular injections can also be formulated as W/O products.
3. Emulsions for external use: Semisolid emulsions are termed creams and more fluid preparations are either lotions or liniments (liniments are intended for massage). Both W/O and O/W are available for external use.

❖ **Method of preparation of emulsion:**

- Dry gum method
- Wet gum method
- Nascent soap method or (Bottle method)
- Electrical method

❖ There are two main steps in the preparation of emulsion (dry and wet)

1) Preparation of primary emulsion which is thick, creamy and stable emulsion. Its consist of (oil, acacia, and water for primary emulsion).

2)Addition of other substances (Dilution)

Calculating quantities for primary emulsions:

Amount of acacia = $\frac{1}{4} \times$ amount of fixed oil.

Amount of acacia = $\frac{1}{2} \times$ amount of volatile oil.

Water is always double the amount of acacia (water = acacia \times 2).

If more than one oil is to be incorporated, the quantity of acacia for each one is calculated separately and the sum of the quantities is used.

1. Dry gum method

1. Triturate the oil with acacia powder in a dry mortar.
2. Measure water for the primary emulsion and immediately add all of it to the mortar with vigorous trituration in one direction until the mixture becomes thicker and the primary emulsion is formed. The primary emulsion is characterised by crackling (or clicking) sound.
3. Calculate the remaining vehicle: Final volume – (liquid ingredients).
4. Divide the remaining vehicle into 3 parts: 1st part for dilution of the primary emulsion, 2nd part for washing the mortar and pestle, and the 3rd part for completing the emulsion to its final volume.

2. Wet gum method

1. Here, the order of mixing is different: Water is added to acacia with quick trituration to form mucilage.
2. Oil is measured with a dry measuring cylinder and added to the mucilage in small portions (gradually). Continuous trituration in one direction is required after each addition until a thick primary emulsion is obtained.
3. Other steps are the same as continental method.

Which method?

□ Which method?

1. If we have one or more volatile oil □ dry gum method.
2. If we have one or more fixed oil □ wet gum method.
3. If we have a mixture of volatile and fixed oil □ dry gum method.

Notes:

- Soluble solid substances such as preservatives, stabilisers, colorants and flavouring agents are usually dissolved in the dilution part of the emulsion.
- Precipitate forming liquids (e.g. tincture of tolu) are added gradually to the centre of the primary emulsion with continuous trituration.
- Water-insoluble substances: are added to the primary emulsion
- Any substances that might interfere with the stability of the emulsion or emulsifying agent are added as near last as is practical. For example, alcohol has a precipitating action on acacia and therefore alcohol or alcohol-containing solutions are should not be added to the primary emulsion.
- Carbonate or hydroxide electrolyte of divalent or trivalent added after the formation of primary emulsion because it will react with FFA that present in the oil and form soap of w/o type that cause inversion and break emulsion , thus these substances should added after the formation of primary emulsion because acacia coat the droplet of emulsion.

R_x 1

Oil of turpentine ʒ ii (volatile oil)

P.W. qs. ʒ i

Calculation of 1^o E.

1. Oil ʒ ii = 8 ml

2. acacia = 1/2 the oil = 4 g

3. Water = 2 × acacia = 8 ml

4. 8 ml of water and 4 g of acacia will be used to form the primary emulsion.

5. Approximate volume of the remaining vehicle (water) = 30 – (8 + 8) = 14 ml.

6. $14 \div 3 = 4.66 \text{ ml}$ □ 4.66 ml for dilution, 4.66 ml for washing the mortar and pestle, and 4.66 ml for completing the emulsion to its final volume.

Procedure

1. Triturate 8 ml of turpentine oil with 4 g of acacia powder in a dry mortar.
 2. Measure 8 ml of water and add all of it at once to the mortar with immediate vigorous trituration in one direction until the mixture becomes thicker and the primary emulsion is formed.
 3. Add 4.66 ml of water gradually to the mortar with mixing to dilute the primary emulsion.
 7. Transfer to a measuring cylinder and wash the mortar with 4.66 ml of water.
Add this part to the cylinder.
 8. Complete the volume to 30 ml with the last 4.66 ml of water.
 9. Transfer to a suitable container and label.
- This emulsion is O/W and used externally as rubefacient and muscle relaxant.

R_x 2

Castor oil ʒ ii (fixed oil)

P.W. qs. ʒ i (vehicle)

Calculation of 1^o E.

1. Oil ʒ ii = 8 ml
2. acacia = ¼ the oil = 2 g
3. Water = 2 × acacia = 4 ml
4. 4 ml of water and 2 g of acacia will be used to form the primary emulsion.
5. Approximate volume of the remaining vehicle (water) = 30 – (8 + 4) = 18 ml.
6. $18 \div 3 = 6$ ml □ 6 ml for dilution, 6 ml for washing the mortar and pestle, and 6ml for completing the emulsion to its final volume.

□ Procedure

1. Weigh 2 g of acacia and place it in the mortar.
 2. Measure 4 ml of water and add it to the mortar with trituration to form mucilage.
 3. Measure 8 ml of castor oil and add it gradually (part by part) to the mucilage in the mortar with continuous trituration in one direction until the mixture becomes thicker and the primary emulsion is formed.
 4. Dilute the primary emulsion with 6 ml of water with continuous trituration.
 5. Transfer to a measuring cylinder and wash the mortar with 6 ml of water. Add this part to the cylinder.
 6. Complete the volume to 30 ml with the last 6 ml of water.
 7. Transfer to a suitable container and label.
- This emulsion is O/W and used as laxative (purgative).

R_X 4

Castor oil ℥ ii (fixed oil)

Bismuth carbonate gr X (water-insoluble solid –divalent)

P.W. qs. ℥ i (vehicle)

□ Bismuth carbonate is water insoluble diffusible solid and added or spread over the surface of the primary emulsion.

□ Castor oil is purgative agent and bismuth carbonate is a protective used for GIT ulcer.

R_x 5

Turbene ʒ iss (volatile oil)
Almond oil ʒ IV (fixed oil)
Tincture of tolu ʒ ii (precipitate forming liquid)
Tincture of ipecac ʒ ii (water miscible liquid)
P.W. qs. ʒ IV (vehicle)
mitte ʒ i

Calculation of 1^o E.

Turbene $1.5 \times 4 \times \frac{1}{4} = 1.5 \text{ ml}$

Almond $4 \times 4 \times \frac{1}{4} = 4 \text{ ml}$

Acacia $(1.5 \times \frac{1}{2}) + (4 \times \frac{1}{4}) = 1.75 \text{ gm}$

Water $1.75 \times 2 = 3.5 \text{ ml}$

Mix oil → Dry gum.

$30 - (1.5 + 4 + 3.5 + 2 + 2) = 17 \text{ ml}$

Tincture of tolu is a precipitate forming liquid □ added gradually to the center of the primary emulsion with continuous trituration.

□ Tincture of ipecac is water soluble and can be added with the dilution part.

□ almond oil is nutritive. The tincture of tolu is expectorants. Tincture of ipecac in low dose used as expectorant and in large dose as emitting agent.

3. Nascent soap method

soap act as emulsifying agents and some are prepared by mixing the oily phase containing a fatty acid such as olive oil and an equal volume of aqueous phase containing the alkali such as $\text{Ca}(\text{OH})_2$ or NaOH solution placed in wide mouth bottle with agitation of mixture FFA of the oil react with alkali to form soap which act as E.A this soap forms at time of mixing (so called nascent soap) or in situ soap.

- The preparation of emulsion in this method used for external use and does not require the preparation of primary emulsion.

- The method may be used to prepare either O/W or W/O depending on whether monovalent or polyvalent hydroxide employed.

Ca soap \rightarrow w/o E \rightarrow **divalent**

Na soap \rightarrow o/w E \rightarrow **monovalent**

Note: Soap are an ionic E.A they may produce irritant and laxative action in intestinal tract consequently they are not used in orally administration.

R_x

Castor oil 10ml

Oleic acid 5ml

Calcium hydroxide solution Q.S 30 ml

Ft. Emulsion

Sig: as directed

Procedure:

- 1) Take clear dry bottle
- 2) Mix castor oil (FFA) 10ml + oleic acid (FFA) 5ml, shake them well for about 1 min (volum=15ml).
- 3) Add to them 15ml of $\text{Ca}(\text{OH})_2$ sol. from supernatant.
- 4) Shake vigorously for about 1min to obtain W/O emulsion.

FFA+alkali \rightarrow Soap(E.M) w/o

$\text{Ca}(\text{OH})_2$ divalent alkali so calcium oleate soap is produce so w/o emulsion.

Lime water is $\text{Ca}(\text{OH})_2$

This Rx is used externally as emollient.

R_x Liquid paraffin emulsion

Liquid paraffin		10ml
oleic acid		5ml
Sodium Hydroxide solution	Q.S	30ml.

Sig. as directed

Liniments:

They are liquid or semiliquid preparation of an alcoholic or oily preparation, they are used and applied externally with massage and friction. It may contain substances possessing analgesic, rubefacient, soothing and stimulant properties, it should not be applied to broken skin, it causes vasodilation to relieve muscle spasm.

R_x White liniment (Emulsion type liniment)

Ammonium chloride	12.5g
Dilute ammonia solution	45ml
Oleic acid	83.3ml
Turpentine oil	250ml
Water	625ml
Ft. emulsion	

Procedure:

1. Mix turpentine oil and oleic acid in clean dry wide mouth bottle.
2. In another flask add equal vol. of warm H₂O to dilute ammonia solution and add this diluted solution step by step to oily liquid , shaking vigorously after each addition.
3. Dissolve NH₄Cl in the rest of H₂O and added to the bottle gradually with shaking.

- In this liniment turpentine oil is emulsified with NH_4 oleate produced from oleic acid and diluted ammonium solution, ammonium oleate is o/w emulsion (monovalent soap), but the preparation also contains NH_4Cl which due to **common ion** effect depresses the ionization of the soap and decreases the solubility in water, this together with a huge % of turpentine oil in the liniment causes **phase inversion**, producing w/o emulsion.

- **Hydrophilic lipophilic balance (HLB):**

One of the desirable properties of an emulsifying agent is that it undergo strong adsorption at the interface between the hydrophilic (Water soluble) and the lipophilic (Oil soluble) tendencies of the surfactant. If the E.A is predominantly hydrophilic, it tend to form an o/w emulsion. If its predominantly lipophilic, it favor to form an w/o emulsion.

- ❖ **HLB Scale:**

HLB number usually between 1-20 represent the relative proportion of the lipophilic and hydrophilic parts of the molecule. **High no. (8-18)** indicates a hydrophilic molecule and produce **o/w** emulsion. **Low no. (3-6)** indicates a lipophilic molecule and produce **w/o** emulsion.

- ❖ Two or more surfactant can be combined to achieve a suitable HLB value and often give better results than one surfactant alone.
- ❖ The HLB method (special for non ionic E.A) e.g polysorbate (Tween) and sorbitan ester (span).

The blend of emulsifiers contributes one or several actions:

1/ it provides the proper hydrophilic-lipophilic nature.

2/ it establishes a stable film at the interface.

3/ it supplies the desired consistency.

4/ contributes certain other properties such as emolliency, spreading and deflocculating.

R_x

Required HLB

Liquid paraffin	35g	12
Wool fat	1g	10
Cetyl alcohol	1g	15
Emulsifier	5g	
Water	Q.S	100gm

the total amount of oil phase $35+1+1=37$

The proportion of each oil ingredients.

Liquid paraffin $35/37=0.946$

Wool fat $1/37=0.027$

Cetyl alcohol $1/37=0.027$

The total required HLB (RHLB)

$0.946 \times 12 = 11.4$ Liquid paraffin

$0.027 \times 10 = 0.3$ Wool fat

$0.027 \times 15 = 0.4$ Cetyl alcohol

So total **RHLB** **12.1**

High value so o/w emulsion

Emulsifying agent blend (span 80 +tween 80),

HLB of span=4.3

HLB of tween=15

Assume that span 80 +tween 80=1

Let x= amount of span 80 in mixture

Then 1-x = amount of tween 80

$$4.3X + 15(1-X) = 12.1 \text{ RHLB}$$

$$X = 0.275 \text{ span 80}$$

$$1-x = 1-0.27=0.73 \text{g tween 80}$$

The total amount of mixed emulsifier in R_x is 5gm

$$X = 5 \times 0.27 = 1.35 \text{g Span 80}$$

$$1.35 \div (\text{sp gr. } 0.88) = 1.53 \text{ml}$$

$$5 \times 0.73 = 3.65 \text{g tween 80}$$

$$3.65 \div (\text{sp. gr. } 1.09) = 3.35 \text{ml}$$

- **Procedure:**

1. Mix the oil phase together (consist liquid Paraffin + cetyl alcohol + wool fat + span 80 it is lipophilic E.A) Warm to about 70°C in W.B
 2. Mix tween 80 with water($100-(35+1+1+5)=58$ g water) in another beaker, and heat to ($2-3^{\circ}\text{C}$) more the oily phase to prevent crystallization of waxes.
 3. Add water phase to oily phase gradually and mixing by electrical stirrer Until get o/w em \rightarrow we get white color emulsion no yellow color of oil which is disappeared due to emulsification by E.A.
- The type of em. is o/w (since it depend on HLB value)

Suppositories

Are solid medications intended for insertion into body cavities such as rectal and vaginal for local or systemic action. They disintegrate in the body cavity either by melting or by dissolution

It contain : active ingredient & base

Reasons for the Rx of Supp. :

- 1- To exert a direct action on the rectum and on the vagina such as hemorrhoid, constipation, and infection.
- 2- To promote evacuation of the bowel
- 3- To provide a systemic effect

• *Systemic treatment by the rectal route is of particular value for :*

- 1) Treating patients who are unconscious , mentally disturbed or unable to treat by oral medications because of vomiting or pathological condition of the GIT
- 2) Administrating drugs such as (aminophylline) that cause irritation , ibuprofen , Indomethacin & aspirin especially if the patient has ulcer or GIT disturbance
- 3) Treating Infants
- 4) Drugs that are affected by the pH of the stomach or the intestine , so they are preferred to be used in Supp. dosage form

- *Properties of the Ideal Base*

- 1) It should melt at body temp. or dissolve or disperse in body fluids
- 2) It should release any medication readily
- 3) It should keep its shape when handled
- 4) It should be non-toxic and non-irritant
- 5) It should be stable on storage
- 6) It should be compatible with any additives and medications
- 7) It should be stable if heated above its melting point
- 8) It should be easily molded and do not adhere to the mold
- 9) Solidify quickly after melting

- *Types of Supp. Base :*

1) Fatty Base these are melted at body temp. ex:
Theobroma oil

2) Water soluble or water miscible bases , either
dissolve or disperse in rectal secretions ex:
Glycerogelatin base and Macrogols (PEG)

- **Method of preparation of the Supp. :** By
(Mold or Hand)

- ❖ Mold Method is either by (Compression or
Fusion)

- *Fusion Method (Hot process)*

- 1) Melting a suitable Base

- 2) Incorporate the prescribed amount of finely powdered medicaments

- 3) Pouring the mixture into the mold

- *Compression method (Cold process)*

The drug incorporated with unmelted base and the resulting mass shaped either by hand or compression in a metallic mold.

- ❖ Supp. formulated in different shapes and sizes (usually 1-4 g)
- ***Mold calibration:*** the mold generally made of metal in two halves which are clamped together by screw. The capacity of the mold is confirmed by filling the mold with chosen base. The total Wt. calculated and a mean Wt. obtained.

- *Water Soluble or water miscible bases*

1) Glycerol –Gelatin base

This is a mixture of glycerol and water made into a stiff jelly by adding gelatin. Supp. and pessaries , the proportion being adjusted to the purpose for which the preparation is intended

The mass for glycerol-gelatin sup. (B.P): This contain about 14% w/w gelatin and 70% w/w glycerol (for use in hot climate up to 18% w/w of gelatin may be included)

Stiffer masses containing a higher proportion of gelatin are also used when the product contain more than about 20% of semi liquid or liquid, because such addition makes the mass too soft.

- Glycerogelatin base supps. are less often used than fatty base supps. Because of its **disadvantages** which are:
 - 1) They have physiological action (Glycerin sup. B.P is used as laxative)
 - 2) They are more difficult to prepare and handle
 - 3) Their dissolution time depends on the content and the quality of the gelatin and the age of the base
 - 4) They are hygroscopic (cause dehydration of the rectal mucosa and irritation)
 - 5) Gelatin is incompatible with protein precipitants agents such as tannic acid
 - 6) Because of the water content, microbial contamination is more likely than fatty base so preservatives may require to be added to the product

1) Macrogols PEG

- ***The characteristics that commend their use for this purpose are***
:
- 1) The mixture generally has a melting point 42°C above the body temp.
- 2) Because of this m.p they do not melt in the body but gradually dissolve and disperse releasing their medication slowly and providing longer action than fatty bases with no medical properties
- 3) Their physical properties can be varied by suitable mixture of high and low polymers
- 4) High polymers give hard product that dissolve and release their drug slowly
- 5) Softer , less brittle preparations that disperse and liberate their drug more quickly are obtained by mixing high with either medium or low polymers by adding plasticizers
- 6) They are not prone to microbial contamination

- *Their Disadvantage include :*

- 1) They are hygroscopic and have consequent disadvantages of glycerol gelatin base
- 2) It has good solvent properties that can result in retention of the drug in the liquefied base , with consequent reduction in the therapeutic activity
- 3) Product sometimes fracture on storage particularly if they contain water
- 4) Crystal growth of certain medications may occur
- 5) They are incompatible with bismuth salts , tannic , phenol (may lose its antimicrobial activity) , iodine ,pot. Iodide and sorbitol
- 6) They become brittle if cooled quickly also on the storage

- **Preparations**

R_x Glycerogelatin supp. B.P

Glycerin		70g
Gelatin		14g
PW	qs.	100 g

Mitt 5 supp.

Ft supp. of 2 gm

- We do the calculation for 7 supp. Each with 2 gm = 14 gm (total wt.)

Glycerin = 9.8 gm (in 14gm total wt.)

Gelatin = 1.96 gm (in 14gm total wt.)

$14 - (9.8 + 1.96) = 2.24 = \text{approximately } 3 \text{ ml of PW}$

Method of Preparation:

Add the gelatin to about 3 ml of PW heated nearly to boiling , then add the glycerin previously heated to 100C for 15 min or until dissolution is completed , adjust the wt of the product to 14 gm by the addition of the hot p.w (if less) or by evaporation (if exceeded), then pour into a suitable mold of 2 gm (which is previously lubricated with liquid paraffin) then cool it by ice bath.

Note: 1/avoid over heating because gelatin is protein so undergo denaturation

2/avoid over stirring to prevent air bubble

3/glycerogelatin sup. does not necessary to over fill the mold and this type of product does not require to be trimmed

R_x Glycerin supp. (U.S.P)

Glycerin 91 gm
Sodium stearate 9 gm (Solidifying agent)
PW 5 gm

Ft supp.

Mitt 5 supp.

We use a mold of 1 gm , calculation for 7 supp. , $7*1=7$ gm (total Wt.)

Glycerin = $6.06 / \text{sp.gr.} = 4.84$ ml

Sod. Stearate = 0.6 gm

PW = 0.34 gm of water

Method of preparation:

Put 4.84 ml of glycerin in a beaker, heat in water bath up to 120 C , add 0.6 gm of sod. Stearate to the glycerin with gentle stirring, then add 0.34 ml of PW with continuous heating until you get a suitable mixture (homogenous) , adjust the total weight to 7 gm then pour it into a (1 gm) mold which is previously lubricated with liquid paraffin and cool it in ice bath

R_x

PEG 4000 33%

PEG 6000 47%

Water 20%

Ft supp. Of 2 gm

Mitt 5 supp.

We do calculations for 7 supp. * each with 2 gm = 14 gm final weight

Method of Preparation:

Put PEG6000 in the beaker and melt it in water bath, then add PEG4000 and melt it with continuous stirring then add water , mix well and pour the product to the mold which is previously lubricated

Note1: we add an excess of the product to the mold surface to compensate for the shrinkage in volume due to cooling by ice then after cooling we cut (with a sharp tool) the edge and get the supp.

Note2: we always start with the higher molecular weight and then the lower molecular weight , knowing that as the molecular wt. **increase** the melting point **increase** , the stability **increase** , the solubility **decrease** and the release is **decreased** .

Note3: PEG with molecular wt. 300,400,600 are clear colorless liquid , while with molecular wt. more than 1000 it is wax like solid (increasing mol.wt. increases the hardness)

Note4: PEG is synthetic protein so don't undergo contamination and growth of M.O

R_x

PEG 400 4% sp.gr =1.12

PEG 1000 96%

Ft supp.

Mitt 5 supp. using 1g mold

R_x

PEG 4000 25%

PEG 1000 75%

Ft supp.

Mitt 5 supp. using 2g mold

2/ Fatty Bases

Theobroma oil (cocoa butter). It is a mixture of the glycerol esters of stearic , palmitic , oleic and other fatty acids.

It has valuable characteristics:

- 1) A melting point range of 30-36 °C , it is solid at normal temp but it melt in the body
- 2) It is readily liquefies on warming and solidify on cooling rapidly.
- 3) Miscibility with many ingredients
- 4) Blindness therefore no irritation occurs.

- The disadvantages:

- 1) Polymorphism

- 2) Adherence to the mold due to slightly shrinkage

- 3) Melting point too low for hot climate

- 4) Melting point reduced by soluble ingredients (add bees wax)

- 5) Slow deterioration during storage(oxidation of unsaturated glyceride) use witepsol instead.

- 6) Poor water absorbing capacity

- 7) Relatively high cost

- **#Polymorphism** : the crystal arrangement has the same chemical properties but different in physical properties. If theobroma oil melted at not more than 36°C and slowly cooled it forms stable beta crystal with normal melting point but if over heated it may produce on cooling unstable gamma crystal which melt about 15°C or alpha crystal which melt about 20°C . These unstable form eventually return to the stable condition but this may take several days and the suppository may not set at room temperature or if set by cooling may remelted in the warmth of patient home. This lowering of M.P can also lead to sedimentation of the suspended solid . The β is the most stable one , its melting point is higher than α and δ , it is the only one to be used .The α and δ has a much lower melting point than β so it cannot be used as a base , and if used and left for several days it will convert to the β type .

- *Displacement Value*

The volume of the suppository from a particular mold is uniform but its weight will vary because the density of the medicaments usually differs from the density of the base.

The DV of a drug is the number of grams of drug which displace one gram of the base

R_x

Bismuth subnitrate 0.5 gm

Cocoa butter qs to fill 2 gm mold

Ft supp.

Mitt 8 supp.

Calculations

We do calculations for 10 supp.

$0.5 * 10 = 5$ gm wt of Bismuth subnitrate

Displacement value for Bismuth subnitrate is (4)

Wt. of the base displaced by drug = wt. of drug / DV

$$= 5 / 4 = 1.2 \text{ gm displaced Base}$$

$10 \text{ supp.} * 2 \text{ gm. (mold)} = 20 \text{ gm. weight of Base}$

$20 \text{ gm} - 1.2 \text{ gm} = 18.8 \text{ gm of Base used}$

So For 10 suppositories they will contain 18.8 gm. base and 5 gm of drug

$18.8 + 5 = 23.8 \text{ gm wt. of 10 supp.}$

$23.8 / 10 = 2.38 \text{ gm wt. of each supp.}$

D.V

4

R_x

D.V

Bismuth subgallate	0.2 gm	2.6
Resorcinol	0.06 gm	1.3
Zinc oxide	0.13 gm	4.8
Oil of Theobroma	to fill	2gm mold

Fit. Supp.

Mitt 3 supp.

Calculation :

3 supp+2= 5 suppositories

0.2 gm *5 =1 gm of bismuth subgalate

0.3*5= 1.5 gm resorcinol

0.13 *5= 0.65gm zinc oxide

$D.V \ 1 \setminus 2.6 = 0.38$ (base displaced by bismuth)

$1.5 \setminus 1.3 + 1.15$ (base displaced by resorcinol)

$0.65 \setminus 4.8 = 0.135$ (base displaced by zinc)

Wt. of the base required to prepare 5 unmediated suppositories using 2 gm mold:

$$2 * 5 = 10 \text{ g}$$

The total amount of the displaced base:

$$0.38 + 1.15 + 0.135 = 1.665$$

Wt of the base used to prepare 5 medicated suppositories:

$$10 - 1.67 = 8.33$$

- Method of Preparation
 - Mix the powders by geometric dilution
 - Calculate the amount of the base displaced by each active ingredient , sum it together to get the total amount of the base displaced by all ingredients
 - Then follow the same procedure .

R_x **Phenobarbital suppositories**

Phenobarbital 20 mg

Cocoa butter q.s

Ft sup

Mitt 3 supp. Using 1 gm mold

D.V 1.1

Rx Chloral hydrate suppositories

Chloral hydrate 0.25 gm

Cocoa butter q.s

Mitt 3 supp. using 1 gm mold

D.V 1.5

General Method of Preparation (with fatty base)

1) supp. containing insoluble solids:

A) Calculate the quantities required (take the DV into account) , excess must be made because of the waste during preparation

B) Shred the fat and weigh the required amount

C) The drug must be finely powdered

D) Mix the powders on the Slap with Spatula (geometric dilution)

E) Place the base on the water bath until about $\frac{2}{3}$ of the content has melted then remove from the heat, the rest will melt with stirring using spatula , remove to the edge of the beaker

F) pour about half of the melted base on the mixed drug to make a smooth dispersion by levigation with spatula on the slap

G) transfer the dispersion to the beaker and stir to form a homogenous mixture , continue the stirring until the mixture become thick then fill each cavity in the mold (delay in pouring until the mass is about to become solid is essential to prevent sedimentation of the insoluble material)

H) Keep it in a cool place for 10-15min

Note: 1 - the mold is lubricated with glycerin

2 - insoluble solids ex: zinc oxide , tannic acid, bismuth subgallate

3- Suppositories containing soluble solid , this will result in lowering the Melting point and the supp. will be too soft, so we add Bees wax (M.P 62-64 C) Ex: Phenol , chloral hydrate

Semisolid Dosage form

Ointment

Are greasy semisolid preparation for external application often anhydrous and containing dissolved or dispersed medicament ,ointment may be medicated or non-medicated . The non medicated referred to as ointment base and used for their emollient , protective and lubricating effect , or as vehicle for preparation of medicated one .

Types of ointment base

- 1) Oleaginous ,Hydrocarbon base include fixed oil of vegetable origin or fat obtained from animal or semisolid hydrocarbon obtained from petrolatum. These are effective as occlusive dressing, and prolong time release of the drug.
- 2) Absorption base these have ability to absorb water and aqueous solution producing an O/W emulsion example hydrophilic petrolatum.
- 3) Emulsion base either O/W emulsion (aqueous cream)or W/O emulsion(oily cream) .
- 4) Water soluble base :it should not be hydrolyzed or support mold growth , they are washable ointment example PEG.

Method of preparation

Both in large scale or small scale , the semisolid dosage form are prepared by two general method

1) Incorporation or trituration method the active ingredient are incorporated into the non medicated vehicle.

a) By using slab and spatula (widely used)

b)Mortar and pestle this method is used when we have large quantity of ointment or when we want to prepare prescription containing large quantity of liquid.

- **General method of preparation using slab and spatula**

- 1) Any powders should be reduced to a fine state before weighing to avoid grittiness .If there are more than one ingredient they should finely powdered and mixed by geometric dilution method
- 2) Powder are placed on slab and rub with small quantity of the base until thoroughly distributed , so in this case we have concentrated ointment.
- 3) Incorporate the reminder of ointment base to the concentrated ointment gradually (ie make dilution).
- 4) Then any liquid present in the prescription can be incorporated to the base

• Notes

- a) When there is powder in the prescription we can make it or convert it to paste by mixing it with small quantity of either mineral oil or vegetable oil.
- b) If any liquid (aqueous liquid present in the Rx and to be incorporated into the ointment base the aqueous solution can be mixed with the absorption base or with emulsion base or water soluble base , but if we use oleaginous (hydrocarbon base) we have to displace a portion of the hydrophobic (hydrocarbon base) with hydrophilic one . Incorporate the solution into the hydrophilic base and then mix the product with the original base.
- c) If the Rx contain natural balsam in this case we mix this balsam with equal portion of castor oil and then incorporate it into the base.
 - ## in all cases we prefer to use stainless steel spatula except when there is iodine , mercury , phenol or salicylic acid in the Rx we will use hard rubber spatula to avoid the possibility of chemical reaction

2) Fusion method

The compounding of many semisolid preparation include the blending together of oily material , some of which are solid at room temperature e.g waxes ,paraffin , fatty alcohol and fatty acid. Fusion is necessary when these substances are included in the formula or when drug is soluble in the melted base . To prepare the ointment by fusion method:

- 1-Place the constituent in an evaporating dish or beaker in water bath and melt.
- 2-When all the ingredient are melted, remove the beaker from the water bath and gently stir until congeal.
- 3- If the medicament is soluble it should be added to the melted base before it congeal and stir.
- 4- Insoluble drug should be levigated with small quantity of the melted base and added after congeal.
- 5- Water and water miscible liquid should be heated to approximately the same temperature as the melted base before mixing to prevent separation and crystallization.

R_x Simple ointment B.P

Wool fat 50g

Hard paraffin 50g

Cetostearyl ester 50g

White or yellow soft paraffin 850g

Procedure

Mix the substance according to their melting point the high melting point to be melted first in the following order; hard paraffin, cetostearyl ester , wool fat and lastly soft paraffin. This Rx is used as vehicle for preparation of other medicated Rx. It is non medicated ointment.

R_x Zinc oxide ointment

Zinc oxide 150 g

Simple ointment 850 g

Mitt. 10g

Procedure: Weigh 8.5 g of the simple ointment you have prepared then incorporate zinc oxide following the general method using slab and spatula. Zinc oxide with portion of ointment to have concentrated ointment then mixes with the remainder of the base. Used as astringent and protective in various skin preparation.

R_x sulfur ointment

Precipitated sulfur 10%

Liquid paraffin 10%

White simple ointment 80%

Fit. Oint.

levigate precipitated sulfur with liquid paraffin
into small paste incorporate with white ointment.

R_x Zinc and castor oil ointment B.P

Zinc oxide	7.5 g
Castor oil	50g
Cetostearyl alcohol	2g
White bees wax	10g
Arachis oil	30.5g

Fit oint.

Procedure

Melt together the bees wax, cetostearyl alcohol and arachis oil.

Levigate the sifted zinc oxide with a suitable quantity of oil until smooth.

Transfer the mixture to a beaker containing the melted ingredient, mix well and then add the rest of castor oil and stir until cold

Uses: this ointment is used for napkin rash. It is an example of ointment prepared by fusion method containing an insoluble solid.

This product is ointment not cream but it has an appearance like cream.

R_x Compound Benzoic acid ointment (White field ointment)

Benzoic acid 6%

Salicylic acid 3%

Emulsifying ointment 91%

Emulsifying ointment is prepared as followed: للاطلاع

White soft paraffin 500g

Cetomacrogol emulsifying wax 300g

Liquid paraffin 200g

The components are mixed together and melt, stir until cold.

Pastes

Are ointments like preparation for external application they contain high percentage of solid ingredient than ointment so they are usually sifter and less greasy, they are more difficult to apply and removed but adhere well to the skin. Paste for their high powder content have slight drying action so they are used for acute lesion that are oozing (absorb exudates).

Medication incorporated in pastes are less readily absorb than from ointment and therefore have more superficial action. Pastes are not suitable for application to hairy parts (scalp)

The base and method of preparation are similar to those for ointment. However when a levigating agent is to be used to render the powder component smooth, a portion of the base is often used (melted) rather than liquid, which will soften the paste.

R_x compound zinc paste B.P

Zinc oxide	25g
Starch	25g
White soft paraffin	50g

Fit paste

Procedure

Melt the white soft paraffin , mix the required amount of zinc oxide and starch powder in a mortar and **triturate** with a little of the melted base until smooth ,gradually add the rest of the base and mix until cold.

Cold cream

It is emulsion of W/O type they are called cold cream because of cooling effect produced by slow evaporation of water when this cream is applied to skin, cold cream is used as emollient.

R_x Cold cream USP

Spermaceti	125g
White wax	120 g
Mineral oil (liquid paraffin) 0.88)	560g (converted to ml by dividing on
Sodium borate	5g
P.W	190g

It is emulsion of w/o type since the percentage of water is 19% it is called cold cream due to cooling effect produced by slow evaporation of water when this cream is applied to the skin.

In cold cream the emulsifying agent is soap formed by the reaction between alkali (sodium borate) and the FFA in the wax

Procedure

- 1- Put spermaceti and white wax together and melt them on steam bath with mineral oil and raise the temperature until reach 70° C.
- 2- Dissolve the borax in water and heat the solution to 70°C.
- 3- Gradually add the warm water solution to the melted mixture and stir rapidly and continuously until it is congeal.

R_x Vanshing cream (American Pharmacy)

Stearic acid	15g
White wax	2g
White petrolatum	8g
Potassium hydroxide	1.5g
Propylene glycol	8g
P.W	65.5g

The percentage of water is 65.5 so o/w emulsion is produced.

Since cold and vanishing cream are example of soap emulsion therefore they are incompatible with acid or compound having acidic property because the acid destroys the soap and break the emulsion.

Gel

Is non greasy semisolid preparation for external use consisting of dispersion of small or large molecule in an aqueous liquid vehicle rendered jelly like by the addition of gelling agent. They are either medicated, or have lubrication effect. They are easily to apply and removed evaporation of water content produce cooling effect.

The residual film usually adheres well and gives protection, but it is easily removed by washing when the treatment is complete.

Examples of Gelling agent: Tragacanth, carbomer , sodum alginate , pectin ,starch , gelatin, clays, cellulose derivative like carboxymethylcellulose, hydroxypropyl methyl cellulose and methylcellulose .

R_x

Zinc oxide 10g

Glycerol 10g

Bentonite 10g

P.W q.s 100 g (Freshly boiled and cooled)

Procedure

Mix zinc oxide finely sifted with the bentonite in the mortar and triturate with glycerol . Add the water in small amount with constant stirring.

Powders

Are mixture of drugs and/or chemical preparations in a dry powder form, they are used internally or externally in various dosage forms such as : capsules , effervescent salts , dusting powders , powders used to make soap , powders used to make solution

Advantages of powders :

- 1) The Tablets , capsules and pills are difficult for children to swallow , powders or suspension often is desirable (easy to administer to patients such as infants)
- 2) Powders are economical and convenient form (except for suspension) liquid vehicle are not present so many incompatibility are avoided as well as deterioration in some cases
- 3) Small particle size will reduce irritation of the stomach so its suitable for Br, Cl⁻, and I⁻
- 4) Powders will give the physician free choice of the drug dose and bulk
- 5) The small particle size will result in large surface area which will lead to fast absorption resulting in a fast onset of action
- 6) To improve the stability of drug

Disadvantages of powders :

1. Powder not suitable for bitter ,corrosive drugs and those that change on exposure to the air e.g. Deliquescent and efflorescent drug.
2. Bulk powder not suitable for potent drug with low dose.
3. powder not suitable for drugs inactivated in the stomach, these should be presented as enteric coated tablet.

Mixing of Powders (Geometric dilution)

The mixing process of powders is based on the agitation produced by some method or device.

The general principle of mixing which should be observed in all cases is

1. To start with the smallest amount (or the most potent ingredient)
2. Add an equal amount of diluent or other ingredient and mix thoroughly
3. Add another ingredient which is equal in quantity to the bulk already mixed
4. Mix and repeat the process until all ingredients have been combined

This process result in a uniform distribution of each ingredient (so called ascending order of weight to ensure proper mixing)

Equipments for mixing

Motor method : used when the powders to be mixed are in a large quantity or in crystalline form or coarse powders that need trituration ,(this method has a disadvantage that powders may stick on the pestle or the wall of the mortar)

Spatula Method (using spatula and slab) : used for small quantity of ingredients which do not need trituration or for which trituration would produce too compact powder

Sifting Method (using kitchen type flour sifter)

Dispensing of powders: Powders are prescribed in:

- 1) **Bulk quantity** : used for non-toxic drugs that can be administered safely by the patient and for non-potent drugs (ex: Antacid)
- 2) **Dusting powder** : intended for external or local use which should be dispensed with a colored label indicating external or local use to distinguish it from oral powders
- 3) **Divided doses** : these are prescribed to make certain that the patient get the proper dose after mixing , used for potent drugs
- 4) **Insufflation** : used for medicated powders which are blown into regions such as ear, nose and throat using insufflator e.g sodium cromoglycate is now presented in this way because its rapidly absorbed from lung when inhaled as fine powder, but poorly absorbed after oral or topical administration.

- **The Method for divided powders**

- 1) The weighing method : used for potent drugs (very accurate method)
- 2) Block and divide method (not as accurate as weighing method)
- 3) Measures in special forms
- 4) Mechanical powder divider

- **Wrapping of powders**

- The minimum weight of an individually wrapped powder is (2 gr)(100mg) , dilution of the drug with diluent , usually lactose is often necessary to produce this weight
- Note: Lactose is preferred over sucrose because lactose is colorless, odorless, soluble, harmless and have a good flow properties, while sucrose absorb moisture causing caking and it is not suitable for diabetic patients so it is avoided.

- **Sometimes we need double wrapping or wrapping using wax paper for**

- 1) Volatile substance (ex: thymol & menthol)
- 2) Hygroscopic substance to avoid air (ex : ammonium citrate potassium citrate , iron and NaCl)

- **Rule in Mixing**

- 1) Avoid fracture of grain
- 2) allow for at least one extra pack
- 3) Reduce the particle size of the ingredients which are crystalline
- 4) Dilute the ingredients of smallest quantity with the other, mixing them in ascending of weight to ensure proper mixing

Note: the smallest amount that can be weighed is 1 gr (50 mg) and the least weight for a packet that can be dispensed is 2 gr (100 mg), if it weigh less the powder should be diluted with lactose

So we need **Dilution** when the packet weighs less than 2 gr (100 mg) but the weight of active ingredient (after multiplying by the number of packets) is mor than 1 gr (50 mg)

Sometimes we need **double dilution** when the active ingredient (after multiplying by the number of packets) weighs less than 1 gr (50 mg) and so that the packet weighs will be less than 2 gr (100 mg) , both cases in one prescription

Note: on Dispensing all pack must have the same weight, size and color

R_x

Phenacetin IV gr

Caffeine I gr

Ft Pulv

Mitt 10 packet

We do calculations for 11 packs

($11 * 4 = 44$ gr and $11 * 1 = 11$ gr)

Phenacetin = $4 * 1/15 * 11 = 2.933$ gm

Caffeine = $1 * 1/15 * 11 = 0.733$ gm

$2.933 + 0.733 = 3.66$ gm

((we do not need dilution))

Procedure:

Put caffeine in mortar triturate well then mix it with phenacetin in ascending order of weight , triturate and mix well then make 10 packs by weight method since we have potent drug each pack should have 0.332 gm then wrap it and label it.

Caffeine: CNS stimulant

Phenacetin: non-Narcotic analgesic and cause damage to the kidney in large doses , it is used for mild to moderate pain associated with the musculoskeletal system .

R_x

Bismuth carbonate	}	aa	1 gm
Calcium carbonate			
Light magnesium oxide			
Peppermint oil			0.1ml (1 drop)
Sodium Bicarbonate	qs		6 gm
Ft Pulv			
Sig: as directed			

Procedure:

((we do not need dilution))

Weigh 1gm of Bismuth carbonate, put it in a mortar, triturate it well then add 1gm of calcium carbonate, mix well then add 1gm of light Mg oxide, mix well then with trituration add one drop of peppermint oil, then add 3gm of NaHCO₃ and mix well, put the powder in a clean dry bottle and label it.

R_x

Codeine phosphate 1/6 gr

Ft pulv.

Mitt XI packs

$$1/6 * 12\text{packet} = 2 \text{ gr} * 0.065 = 0.13 \text{ gm}$$

PS: we multiplied by 12 packets to avoid fractures of grain

((we need dilution))

$$2 \text{ gr (the smallest wt. for packet to be dispensed)} * 12 \text{ packet} = 24 \text{ gr}$$

24 gr – 2 gr (wt. of codeine) = 22 gr (140 mg) wt. of Lactose that must be added

Procedure:

Weigh 0.13 mg of codeine phosphate, triturate it in a clean dry mortar, add to it nearly the same weight found in a mortar and so on, so mix by ascending order of weight to ensure proper mixing, divide the powder into packs with weight equal to 100 mg each

R_x

Phenobarbitone 1/8 gr

Caffeine 1/4 gr

Ft pulv

Mitt 9 packs

We do calculations for 10 packets

$$1/8 * 10 = 1.25 \text{ gr}$$

$$1/4 * 10 = 2.5 \text{ gr}$$

$$2 \text{ gr (the smallest wt for pack to be dispensed)} * 10 \text{ packet} = 20 \text{ gr}$$

$$20 - (1.25 + 2.5) = 16.25 \text{ gr of lactose added for dilution}$$

Procedure:

Weigh the caffeine then add to it phenobarbitone then add lactose by geometric dilution method in ascending order of weight to ensure proper mixing then make 9 packets by weighing method since we have potent drug, each pack has 100mg weight

Double Dilution Method

Sometimes we may need double dilution when the amount of active ingredient after multiplying by the number of packs is less than 1 gr and the weight of one pack is less than 2 gr.

Note (we may increase the number of packs more than one to avoid fractions of grain)

R_x

Hyoscine hydrobromide 1/150 gr

Ft Pulv.

Mitt 12 pack

We do calculations for 15 packets to avoid fractions of grain

((we need double dilution))

15 packet * 1/150 gr = 0.1 gr

<u>Drug</u>	<u>Drug+Lactose</u>	
0.1 gr	1gr	
1gr	x	X = 10 gr

So 1 gr drug + 9 gr Lactose = 10 gr total wt.

(PS: 1 gr of this mixture contain 0.1 gr Drug)

2 gr (the smallest wt for pack to be dispensed) * 15 packet = 30 gr

30 gr – 1gr = 29 gr of lactose added to 1 gr of the previous mixture containing 0.1gr of drug, mix well

So:

Take 1 gr (0.065gm) of drug (the smallest amount that can be weighed) and 9 gr (0.6gm) of lactose, mix well then take 1 gr of this mixture and add it to 29gr (1.93gm) lactose

Mix by geometric dilution method in ascending order of weight to ensure proper mixing then make 12 packets by weighing method since we have potent drug, each packet has 2gr weight

R_x

Codeine phosphate 0.3 mg

Ft Pulv.

Mitt 9 packets

We do calculations for 10 packets

((we need double dilution))

10 pack * 0.3mg = 3mg

Drug

Drug+Lactose

3mg

50mg (the smallest amount can be weighed)

50mg

x

X = 833mg

So 50mg drug + 783mg Lactose = 833mg total wt.

(PS: 50mg of this mixture contain 0.3mg Drug)

100mg (the smallest wt. for packet to be dispensed) * 10 packet = 1000mg

1000mg – 50mg = 950mg of lactose added to 50mg of the previous mixture containing 0.3mg of drug

Mix by geometric dilution method to ensure proper mixing then make 9 packets by weighing method since we have potent drug, each packet has 100mg weight