UNIT-II

★ P'ceutical Calculations :-

→ To have a complete understanding of various type of calculations, which are involved in dispensing, it is desirable that the Pharmacist should have a through knowledge regarding weights and measures which are used in calculations.

→ There are two System of weights and Measures.

1. The Imperial System
2. The metric System

1. Imperial System :-

- Imperial System is an old System of weight and measures.
- Type. (i) Avoirdupois System
  (iii) Apothecaries system

(a) Avoirdupois System :-

In this System the pound is the standard unit for weighing and all measures of Mass are derived from the Imperial Standard pound (Lb).

(b) Apothecaries :-

- This System is also known as Troy System
- The grain is the standard unit in this System and all other weights are derived from it.

① Avoirdupois System :-

- primary unit of weight is pound (lb)

- 1 pound (lb) = 16 ~~ounce~~ ounce (oz)
- 1 pound = 7000 grains
- 1 ounce (oz) = 7000/16 = 437.5 grains

Here only weight is primarly used for Compounding.

437.5 grains = 1 oz = 28.35 gm

7000 grain = 1 Lb = 16 oz = 454 gm

1 kg = 2.2 lb

1 gr = 6.8 mg

② Apothecary System :-

- Comprised both volume and weight. In this System weight is measured in grain and volume in Minim.

(i) Volume :-

1 teaspoonful = 5 ml = 1 dram = 5 Cubic centimtr (cc)

1 tabespoonful = 15 ml

29.57 ml = 1 fluid ounce (fl oz)

473 ml = 1 pint (pt) = 16 fluid ounce (fl oz)

946 ml = 1 quad = 2 pints

3784 ml = 1 gallon = 8 pints = 128 fl oz

(ii) Weight :-

1 grain = 64.8 mg

1 ounce = 31.1 gm = 480 grain

② Metric System :-

- Metric System is used in the Indian pharmacopoeia for the measurment of weight and Capacity.
- It was implemented in India 1st April, 1964 in pharmacy profession.

- Measurment of weight in metric System :-

- A kilogram is the standard unit for measurment of weight and all other measures are derived from it.

- Measurment of Capacity in metric System :-

- A litre is the standard unit for measurment of Capacity and all measures of capacity are derived from it.

> 1 litre (Lt) = 1000 milliliters (ml)

- Measur of weight :-

1 kilogram	=	1000 gms
1 hectogram	=	100 gms
1 dectagram	=	10 gms
1 decigram	=	0.1 gms
1 Centigram	=	0.01 gms
1 Milligram	=	0.001 gms
1 microgram	=	0.000,001 gms

☆ Calculation involving percentage :-

percent Solution :-

→ Among the ways to describe the Concentration of a Solution is by its percent Solute Content in a Solvent.

→ one of two methods can be used to determine the percent.

→ Calculating the mass ratio of the Solute and the Solution.

– The ratio is Calculated by dividing the volume of the Solute by the volume of the Solution.

mass percent :-

The mass percent is the number of grams of Solute per 100 grams of the Solution when the Solute in a Solution is Solid.

$$\% \text{ Mass} = \frac{\text{Mass of Solute}}{\text{Mass of Solution}} \times 100\%$$

∴ Indicate % (m/m)

percent by volume :-

$$\% \text{ Volume} = \frac{\text{Volume of Solute}}{\text{Volume of Solution}} \times 100$$

∴ Indicated % (v/v)

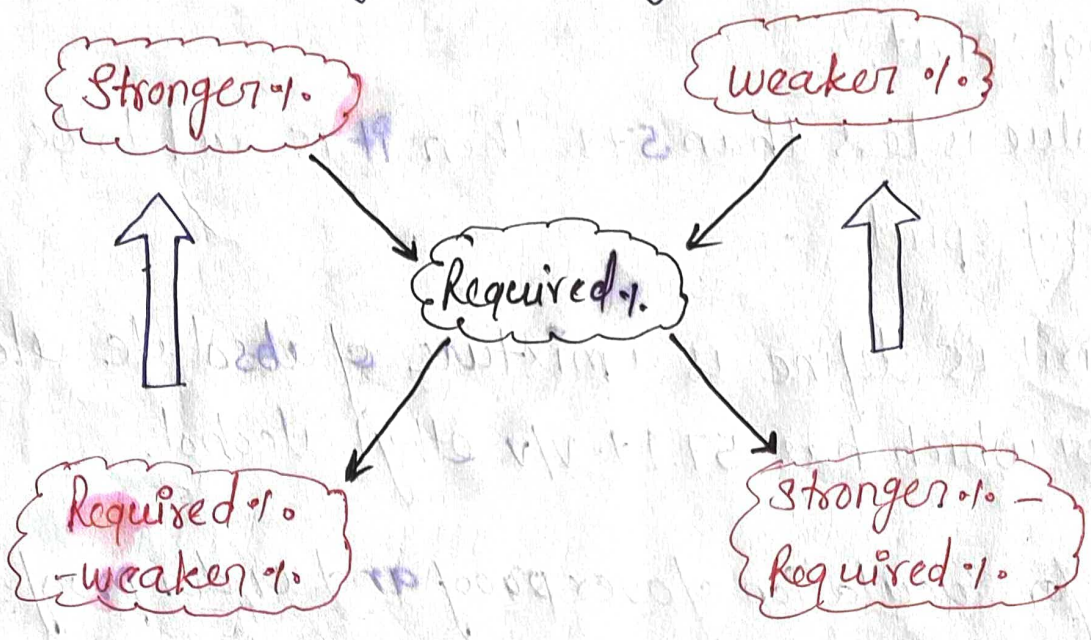
molality (m) =

A unit for Concentration.

$$m = \frac{\text{Moles of Solute (mol)}}{\text{kilogram of Solvent (kg)}}$$

★ Alligation :-

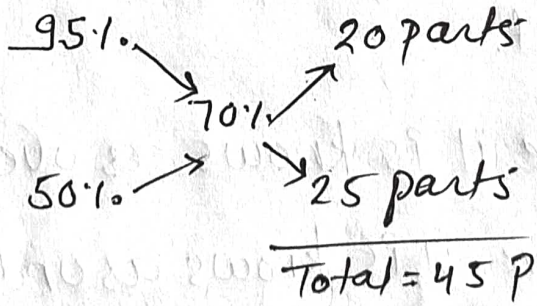
When the Calculation involves mixing of two similar preparation of different strenghts, to produce a preparation of intermediate strength, the alligation method is used.



Example :-

How much 95% alcohol and how much 50% alcohol will be needed to attain 450 ml of 70% alcohol? (based on alligation method)

Solution :-



Volume of 95% alcohol required is $20 \times \frac{450}{45} = 200$ ml

Volume of 50% alcohol required is $25 \times \frac{450}{45} = 250$ ml

☆ Proof spirit :-

→ The strength of alcohol is Calculated in proof degress.

→ The Indian standard of 100% proof spirit is equal to 57% v/v of ethyl alcohol.

i.e. 100% p.s = 57% v/v ethyl alcohol

→ If the value is more than 57% then it is said to be as over proof spirit.

→ If the value is less than 57% then it is said to be as under proof spirit.

→ Proof spirit is define as a mixture of absolute alcohol and water which has 57.1% v/v ethyl alcohol.

Formula for Calculation of over proof and under proof :-

- 57.1% v/v alcohol = 100 volume of proof spirit.

  Therefore, 1% v/v alcohol = 100/57.1 = 1.753 volume of proof sprit.

- So Multiply the given % Strength of alcohol by 1.753 and deduct from the product.
- If the result is positive it is knows as over proof.
- If the result is negative, it is knows as under proof.

Example :-

Find out the proof strength of alcohol which is 90% v/v and 30% v/v.

Solution :-

90% v/v = 90 x 1.753 = 157.77

Thus proof Strength = 157.77 - 100 = 57.77° op (over proof)

30% v/v = 30 × 1.753 = 52.59.

Thus proof strength = 52.59 - 100 = -47.41

i.e 47.41° U/P (under proof)

Example-2

Find out the % strength corresponding to 40° op and 25° op U/P.

Solution:- $40°\,O/P = \frac{100+40}{1.753} = 79.86\%\ v/v$

$25°\,O/P = \frac{100-25}{1.753} = 42.79\%\ v/v$

☆ Isotonic Solution based on freezing point and Molecular weight

- Isotonic Solution are which have same osmotic pressure or equal Solute Concentrations.
- 0.9% Sodium Chloride Solution is Considered to passes the same osmotic pressure and hence it is a standard Solution which is Isotonic with blood plasma.

→ Any Concentration above this (0.9%) is Considered is hypertonic and below this (0.9%) is Considered as hypotonic

Isotonic Adjustment
- Molecular Concentration method
- White Vinsent method
- NaCl Equivalent method
- Cryoscopic method.

① Freezing point method / cryoscopic method:-

$$\% \text{ w/v of adjusting Substance needed} = \frac{0.52 - PSM * a}{b}$$

where -

PSM = % Strength of medicament

a = Freezing point of the unadjusted Solution

b = Freezing point of a 1% w/v Solution of a adjusting substance.

② Molar (or) Molecular Concentration :-

$$\% \text{ w/v of adjusting Substance required} = \frac{0.03M}{N}$$

where - M = gram molecular weight

N = no. of ions into which the Substance is ionised.

✱ Powders :-

Pharmaceutical powders are solid dosage forms of medicament in which one or more drugs are dispensed in finely divided state with or without excipients.

→ Powder are the simplest dosage forms and the basis of many other solid dosage forms such as, TABLET, CAPSULE etc.

→ They are available in crystalline or amorphous form.

Classification :-

1. Bulk powder for internal use
2. Bulk powder for external use
3. Simple and Compound powder for internal use
4. powders enclosed in Cachets and Capsule.
5. Compressed powders (~~tablets~~).

Advantages :-

→ It is used both internally and externally.
→ It is more stable than Liquid dosage form.
→ It is convenient for the physician to prescribe a specific amount of powder.
→ on set of action is faster as compared to tablet, Capsules, because it is easily in dissolved in body fluids.
→ Easy to carry
→ Easy to administration to the patient orally by dissolving

- in suitable liquid.

Disadvantage :-

→ Drugs have bitter taste, nausea and unpleasant taste can't be administered in powder form.

→ Deliquescent and hygroscopic drug cannot be dispensed in powder form they are packed in double wrapping.

→ Drugs which get affected by atmospheric condition are not suitable for dispense.

→ ~~Quan~~ quantity less than 100 mg cannot be weighed conveniently.

✱ Simple & Compound powder :-

Simple powder :-

- In Simple powder contain only one ingredient either in crystalline form or amorphous form.

→ If powder present in crystalline form then it is reduced to fine powder, weighed the powder & divided into number of doses & wrapped as individual dose.

Example :- Dispensed Six Powder of Aspirin each powder contains 300 mg of aspirin.

Rx. Aspirin · 300mg

Procedure :- Powder the aspirin & weigh the required quantity of aspirin, weigh 300 mg of aspirin for each powder & wrap each powder in individual powder paper.

Direction: one powder to be taken after every eight hours.

Compound powder:-

- Compound Powder Contain two or more than two Substance which are mixed together.
- Then divided into desired number of individual doses.
- Then dispensed into each powder paper.

Ex.:- Dispense eight powder of A.P.C each powder Contains 500 mg of A.P.C.

℞, Aspirin -300 mg.
Paracetamol-150 mg
Caffine -50 mg

Procedure:- Weigh ~~accurately~~ accurately of each powder & Mix them as per ascending order of their weight.
- weigh 500 mg of the mixed powder for each powder & Wrap each dose individual in powder paper.

Dusting powder :-

→ A powder is used on skin to relieve irritation or absorb moisture and to keep skin soft and Comfortable.

→ Dusting powders are use externally for local application not intended for systemic action.

→ They are applied to various part of body as lubricant, protectants, absorbents, antiseptics, astrigent and antifungal.

→ Dusting powder always should be dispensed in a very fine state of subdivision to enhance effictiveness and minimize irritation.

→ When necessary they may be passed through 80, 100, number sieves.

Characteristics of dusting powder :-

(i) Dusting powder should be homogeneous in nature.
(ii) It should have non-irritable property.
(iii) It should ~~should~~ have good spredibility.
(iv) powder should have good & adsorption and absorption property.
(vi) Dusting powder usually Contains substance as zinc oxide, starch, $MgCO_3$, light megnesium oxide, boric acid, tale, kaolin etc.
(vi) Dusting Powder should not be applied to broken skin.
(vii) It should be free flowing.

Formula :-

Rx Zinc oxide - 20 gm
Salicylic acid - 5 gm
Starch - 25 gm
Tale - 50 gm.

Labelling - For External use only

☆ Effervescent powder :-

- These type of powder are prepared for internal use.
- In that, Medicament mixed with Citric acid, tartaric acid, Sodium bicarbonate with Sweetening agents also present.
- When Contact with water they release of Carbon dioxide to Mask the bitter & Saline taste of drug.

→ Also, Carbon dioxide Stimulates the flow of gastric juice & help in the absorption of medicament. Ex ENO

methods of preparation of Effevecent Granules :-

① Heat Method
② Wet Method

① Heat Method :-

- Firstly, porcelain dish Make hot on water bath before transferring the powder.

→ Then, transfer the Medicament with Citric acid & other Ingredients.
→ In that Stage Citric acid liberates the water & produce dump mass.
→ Heating Stage takes 1 to 5 mint
→ Then damp mass pass through Sieve & dry in hot air oven at 60°C.
→ Than finally packed in air tight Container.

② Wet Method :-

- In this Method, the Ingredients are Mixed with alcohol to produce Coherent mass.
- Produce mass pass through Sieve no 10 or 8 & dry in hot air oven at 60°C.
- Then dried granules are again passed through Sieve to break the lumps which may be formed during drying.
- Finally, the prepared granules are packed in air tight Containers.

#Formula :-

Sodium bicarbonate	– 35 gm
Citric acid	– 25 gm
Tartaric acid	– 15 gm
Anhydrous Sodium Carbonate	– 25 gm

* Efflorescent and hygroscopic powders :-

Efflorescent powders :-

- Some Crystalline Substance liberates water of Crystallisation Wholly or partly on exposure to humid atmosphere.

e.g. citric acid, Caffeine, ferrous Sulphate etc.

- So the problem overcome by mixing or incorporate with inert Substance or using anhydrous slat.

hygroscopic powder :-

- Absorb the moisture from atmosphere are called hygroscopic powder.

E.g. Ammonium chloride, ammonium Citrate, pepsin, Phenobarbitone, Sodium iodide etc.

- Such Substance are usually provide in granular form in order to expose Less Surface area to atmosplere & avoid Convert into fine powder.

Eutectic mixtures :-

- When two or more Substance are mixed together they liquefy due to the lowering of melting point than their Individual melting point. Such Substance

are called as eutectic Substance.

Ex. Paracetamol-urea, griseofulvin - urea, menthol, — thymol, phenol, aspirin.

✱ Geometric Dilution :-

Geometric dilution is a p'ceutical process that thoroughly mixes a small amount of a drug with an appropriate amount of dilvent, an inert substance that thins or binds the drug.

→ The method used depends on the types of substances used, such a fluid or powder, and the form, such as an ointment or tablet of the compound.

→ Two Commonly used Method -

① **Trituration** :- which involves reducing a substance to particle size, requires the use of a mortar and pestle to grind together equal part of substance in small-batch quantity.

② **Liquid aliquot** :- It involves dissolving a quantity of the drug in a small ~~qual~~ quantity of an appropriate solvent often water or alcohol, to reach a desired volume, according to the UNC Eshelman School of pharmacy.

✡ Liquid dosage forms:-

- Dosage forms are essentially pharmaceutical products in the form which involves a mixture of active drug components and non drug Compants (excipients).

→ Liquid form of a dose of a drug used as a drug or medication intended for administration or consumption.

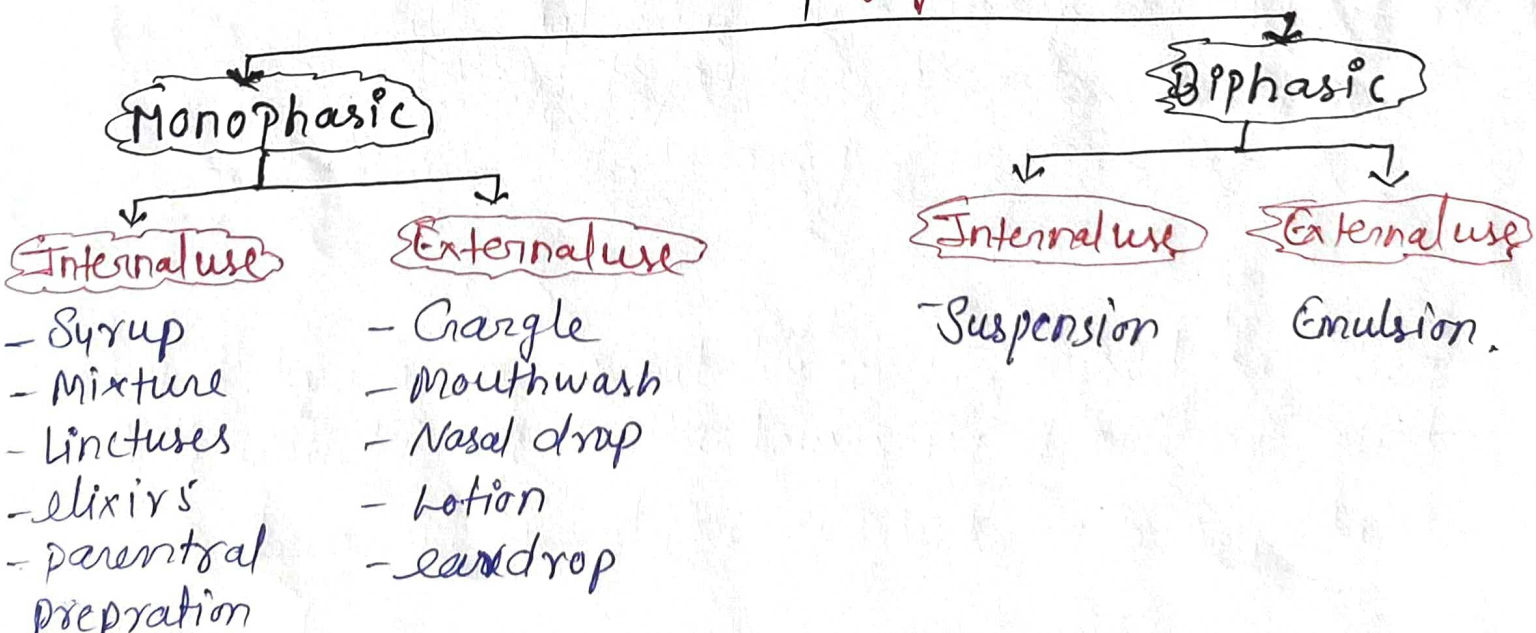
- Liquid dosage forms are prepared:-

a. By dissolving the active drug substance in an aqueous or non-aqueous (e.g. alcohol, ether, glycerin) solvent.

b. By Suspensing the drug in appropriate medium or

c. By incorporating the drug substance into an oil or water phases.

Classification:-



Advantage of LDF :-

→ Better for patients who have trouble Swallowing expiration than other.
→ Faster absorption than Solids.
→ More flexibility in achieving the proper dosage of Medication.
→ palatable
→ Best choice for childern and old age person.

Disadvantages of LDF :-

→ Shorter life than other dosage form.
→ Harder to measure accuracy,
→ Need special storage Condition
→ Easily affected by microorganism.
→ Measuring dose is requried.

☆ Excipients used in formulation of LDF :-

#Excipients :- An excipient is a pharmacologically inactive substance formulated along with the active pharmaceutical ingredient (API) of a medication.

① Solvent/co-solvent :-

Co-solvent are defined as water-miscible organic solvents that are used in liquid drug formulation to increase the solubility of poorly water soluble substance or to enhance the chemical stability of a drug.

② The Vehicle :-

The preferred and most commonly used vehicle in liquid dosage forms is purified water USP. due to:

- Low cost & toxicity
- Physical compatibility
- Good solubilizing powder

③ Buffers :-

- Buffers are employed within pharmaceutical solution to control the pH of the formulated product.

Ex. Acetates (acetic acid and Sodium acetate)
Citrates (citric acid and Sodium citrate)
Phosphates (Sodium phosphate and disodium phosphate)

④ Preservative :-

Preservative are used to Control microbial bio-burden of the formulation.

Example :- Benzoic acid and Salts (0.1 - 0.3 %)
Sorbic acid and its salts (0.05 - 0.2 %)

⑤ Antioxidants :-

Included to enhance the Stability of therapeutic agents that are Susceptible to Chemical degradation by oxidation.

Example :- - Sodium Sulphite
- Sodium metasulphite
- Sodium Formaldehyde
- ascorbic acid

⑥ Viscosity-enhancing agent :-

- Suspension Stabilizer : Prevent settling / sedimentation.

Example :-
- water-Soluble - Methylcellulose, or hydroxyethylcellulose
- water-insoluble - Microcrystalline Cellulose.

⑦ Sweeting Agent :-

Natural Sweetener -
- Sucrose : soluble in water (vehicle)
- Sorbitol - Lower Sweet than Sucros

Artifical Sweeteners :-
Ex. Saccharin and its Salt Aspartame.

⑧ Humectants :-

- To retard evaporation of aqueous vehicle of dosage form.
- To prevent drying of the product after application to the skin. Ex. propylene glycol, Glycerol, PEG.

☆ Solubility enhancement techniques :-

In liquid pharmaceutical solutions Sometime the active drug is poorly soluble or insoluble in desired solvent Could not able to achieve the required Concentration of formulation.

→ In Such Cases, it is required to increase the Solubility of that Material in the Solvent by a Suitable technique.

Different techniques :-

① Physical modification :-

(A) Particle Size reduction
1. Micronization
2. Nanosuspension

(B) Modification of the Crystal habit.
1. polymorphs
2. pseudopolymorphs

(C) Drug dispersion in Carriers
1. Eutectic mixtures
2. Solid Solutions

(D) Complexation.
use of Complexing agents

(E) Solubilization by Surfactants
. microemulsion

(ii) Chemical modification:-

1. Change in the pH
2. Use of buffer
3. Derivatization

(iii) other Methods

1. Co-crystallisation
2. Co-Solvency
3. Hydrotrophy.
4. Using Soluble prodrug.