Unit - I
Pharmaceutical Analysis

Greek word → Pharma + Ceutical   Analysis

Pharmakon ↓ Drug

Pharma ↓ Drug

Ceutical ↓ Carrier

Analysis → Qualitative ↓ Quality of Drug

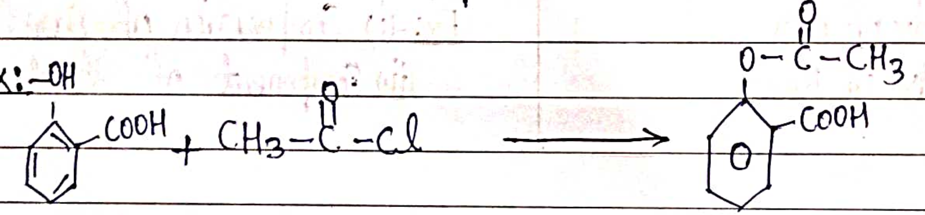
Analysis → Quantitative ↓ Quantity of Drug

* Pharmaceutical Analysis is the analysis of drug.

⇒ Pharmaceutical analysis is defined as the study of drug where complex substances of drug is dissociate into simpler form and analysis them.

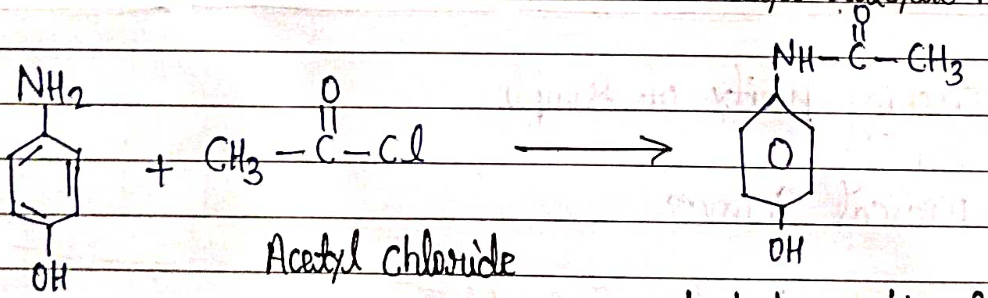
Ex:-

(i)



Salicylic Acid + Acetyl chloride → (Aspirine) ↓ Acetyl Salicylic Acid

(ii)



p-hydroxy Aniline + Acetyl chloride → p-hydroxy phenyl acetanilide (Paracetamol).

Scope of Pharmaceutical Analysis

→ Quality of Raw material
→ In process Control
→ Quality of finished product.

The quality of product should be in according with INDIAN PHARMACOPOEIA.

The quality of product should follow the standards related with safety, potency & efficacy.

Types of Pharmaceutical Analysis

(1.) Qualitative Analysis
(2.) Quantitative Analysis

S.No.	Qualitative Analysis	Quantitative Analysis
1.	Study of nature & quality of component present in sample. Ex:- (i) Quality of Air (ii) Quality of Blood	1. Study of number and their composition of component present in sample. Ex:- (i) Composition of Air (ii) Component of Blood

SIGNIFICANCE OF QUANTITATIVE ANALYSIS IN QUALITY CONTROL

(1.) In checking purity of Sample
(2.) In farming
(3.) In Medical Sciences

(1.) In checking the purity of Sample :-

(i) This is to perform to check the quality of sample in form of Raw material or finished product.

Ex:- Ⓐ % of purity (90%)   Ⓑ % of purity (40%)

(ii) In raw material there may be some Impurity present in a sample which make cause side effect and that may be analysed during quantitative analysis.

(2) Detection of Pollution :-

(i) Quantitative analysis is helpful to check the quality of air and quality of water etc.

(ii) If the concentration of O_2 is more than the concentration of CO_2 then the quality of air is good. and when the concentration of O_2 is less than the concentration of CO_2 then the quality of air is bad.

Air Composition:-

N_2 – 78%
O_2 – 21%
other gases & CO_2 – 0.1%

(iii) In case of water pollution wastage coming out from industrial effluent, sewage coming out from home, chemical fertilizers etc. are responsible for water pollution and the concentration of impurity are determined by quantitative analysis.

(3) In farming :-

- * Analysis of soil is used to determine the composition of essential nutrient element like N, P, K, Zn, Co, Mg, Pb, Fe etc.
- * Elements like N, P, K are required in larger quantity that's why they are known as MACRO NUTRIENT.
- * Elements like Zn, Co, Mg, Pb, Fe are required in smaller quantity that's why they are known as MICRO NUTRIENT.
- * Testing of soil to find the concentration of nutrient in soil is called soil profiling. The nutrient will be externally added on the suitability of soil.

(4) <u>In Medical field</u> :- * Quantitative analysis have utility in biomedical sciences for diagnosis of illness and monitoring the condition of patient.

* Some disease are identify after chemical examination of blood, urine, stool and sputum.
* Pharmaceutical analysis represent the role of Assay (Percentage purity) method in characteristics the quality of bulk drug.
* Immunoassay are bio analytical methods in which quantitation on analyte depends on the reaction of an antigen and antibody.

  Ex:- Diagnosis of disease, drug monitoring, clinical pharmacokinetic and bio equivalance in drug discovery and pharmaceutical industory.

Different techniques of Analysis :-

Techniques of Analysis

- Classical Method
  - Volumetric analysis
    - (a) → Neutralization Titration (Acid-Base titration)
      - → Aqueous
      - → Non-aqueous
    - (b) → Precipitation titration
    - (c) → Complexometric titration
    - (d) → Oxidation-Reduction titration
    - (e) → Diazatization titration
  - Gravimetric analysis
  - Gasometric analysis
- Instrumental Method
  - (1) Potentiometry
  - (2) Conductometry
  - (3) Amperometry

    (1)–(3): Electro analytical method
  - (4) Spectroscopic method
  - (5) Chromatographic method
  - (6) Mass spectroscopy.
  - (7) Polarometry / Polarography
  - (8) Thermal method.

Classical Method :- Mass and Volume are most common signal, and corresponding techniques are -

(1) Volumetric technique :- Volumetric technique are simple and accurate in comparison to gravimetric analysis these are further categorised in following methods.

(a) Neutralization Titration :- It involve reaction of substances (Acid or Base) to determined with the appropriate acidic or Basic reagent, and volume of solution required to complete the reaction which is determined by indicator.

Types of Acid - Base Titration.

(i) Non - aqeous titration :- * Take place in solvent other than water.

Ex:- (Glacial Acetic Acid (GAA), Polyethyline Glycol, Alcohal). This may be due to insolubility of drug in water.

(ii) Aqueous titration :- * Take place in water.

* Used for substances which dissociate completely & rapidly in water
* Determination of the end point is easy with the change of pH of the solution.

(b) Precipitation Titration :-

* It involves the titration between analyte and reagent resulting in the formation of precipitate.
* The most useful of these precipitating reagent is silver nitrate used for estimation of Halide salt, for

Ex:- estimation of sodium chloride with standard silver nitrate solution.

(c.) Complexometric Titration:-

- It involves the titration between cations and Complex forming reagent EDTA (Ethylene diamine tetra-acetic acid).
- The most useful of these complexing reagent or organic compound with several electron donor groups that can form multiple covalent bond with metal ion.

(d) Oxidation - reduction Titration :-

- It involves the oxidation - reduction reaction, hence known as redox titration.
- An oxidation occur when atom or ion loses electron.
- A reduction occur when atom or ion gain electron.

  Ex:- Titration of Iodide salt to determine Iodide salt Quantitatively.

(e) Diazotization Titration:-

- It involve the estimation of drug substances having primary amine group. (Aromatic group)
- Aromatic primary amine group :-

  Ex:- Sulpha drug is estimated by conversion into diazonium salt with standard sodium nitrate ($NaNO_2$) solution.

(2) Gravimetric Analysis :-

- In gravimetric analysis, a substance to be determine is converted into insoluble precipitate in the purest form which is then collected and weighed.

(3) Gasometric Analysis :-

- * Gasometric involves measurement of volume of gas evolve or absorbed in a chemical reaction. Some of the go
- * Some of the gases which are analysised are Carbon dioxide (CO_2), Di-nitrogen oxide (N_2O), Cyclopropane, amyl nitrite Nitrogenand Helium.

Instrumental Method

1. Electro analytical method.

(i.) Potentiometry :-

- * In potentiometry the difference between the potential of two electrode is measured.
- * The potential of One electrode (Indicator electrode) respond to the analyte's activity (Concentration) and other electrode (reference electrode) has fixed potential.

(ii.) Conductometry :-

- * The principle of Conductometry is based on one of the ion is replaced by other and invariably these two ions differ in ionic Conductance with result that Conductivity of the solution varies during the course of solution.

(iii.) Amperometry :-

- * In this method a ~~sample~~ there is detection of ion in a solution, based on electric current or change in diffusion electric current on addition of titrating reagent.

2. Spectroscopic Method :-

- * Spectroscopic method of analysis depends on measurement of radient energy of particular wavelength absorbed or emitted by the sample.
- * Method which include measurement of absorption of radiation or ultraviolet visible infrared atomic absorption, nuclear magnetic Resonance (NMR). These are called absorption spectroscopic.
- * Emmission Spectroscopic method involve heating of the sample show that the atom or raised to the excited state. The excited state is short lived and so return to the ground state with the emmission of Energy.

Ex:- Flame photometry
Fluorometry
Atomic emission spectroscopy

3. Chromatographic Method :-

Chromatography is a method of separation in which the components to be separated or distributed between two phases. One of which is stationery phase while the other is mobile phase.

4. Mass Spectrometry :-

Mass Spectrometry involves vapourization of sample using a high vaccum and the vapour is Bombarded by high energy electron beam. Vapours molecules undergo fragmentation to produce ions of differents size and mass.

5. Polarimetry / Polarography

Polarimetry is an instrumental method in which polarize light by optically acting substance is measured to know its concentration in a solution.

6. Thermal Method

Thermal method involves the measurement of physical parameter of a system has function of temperature.

Ex:- Thermogravimetric analysis (TGA).

Method of Expressing Concentration:-

(1.) Molarity (M) ⇒ $M = \frac{\text{No. of mole}}{\text{Volume of solution (l.)}}$

$= \frac{\text{wt/ molecular wt.}}{\text{Volume of solution (in litre)}}$

(2.) Normality (N) ⇒ $N = \frac{\text{No. of gram equivalent}}{\text{Volume of sol}^n\text{ (in lt.)}}$

$= \frac{\text{wt./Equivalent wt.}}{\text{Volume (lt.)}}$ → $\text{Eq. wt} = \frac{\text{Mol. wt}}{x \text{ factor}}$

(3) Molality (m) ⇒ $m = \frac{\text{no. of mole}}{\text{mass of solvent (kg)}} = \frac{\text{wt./molecular wt.}}{\text{Mass of solvent (kg)}}$

(4) Formality (F):- Formality is defined as number of formula weight of solute that are present in 1 litre of solution.

$F = \frac{\text{No. of formula wt.}}{\text{Volume of sol}^n}$

(5.) Percentage by Weight :- It refers to the no. of gram of solute present in 100gram of solution.

(6.) Percentage/Volume :- It refers to the no. of millilitres of solute present in 100ml of solution.

(7.) Percentage weight/volume :- It refers to no. of grams of solute present in 100ml of solution.

(8.) Mole fraction :- Mole fraction is the number of moles of a particular solute divided by total no. of moles in solution.

$$\text{Mole fraction of solute A} = \frac{\text{No. of mole of solute B}}{\text{No. of mole of solute A} + \text{No. of mole of solute B}}$$

(9.) Parts Per million :- (PPm) :- It is a unit of the measuring Concentration in very dilute solution.

For E.g:
→ Pollutants present in water & air.
It is defined as unit of solute present in 1million (10^6) unit of solution.

(10.) Relation b/w Normality and Volume of solution :-

$$N_1V_1 = N_2V_2$$

$$N \propto \frac{1}{V}$$

$$\frac{N_1}{N_2} = \frac{1}{V_1/V_2}$$

$$\frac{N_1}{N_2} = \frac{V_2}{V_1}$$

$$\boxed{N_1V_1 = N_2V_2}$$

Primary & Secondary Standard:-

Primary Standard :- Primary standard defined as substance of Known purity (Analytical grade reagent) whose Carefully weight quantity helps in the standardization an unknown ~~Sample~~ Solution. (N/M).

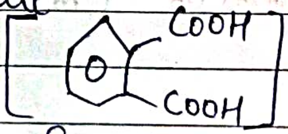
for e.g:- To prepare & standardize Sodium hydroxide solution using 0.1 N Oxalic Acid Solution.

→ Here it is oxalic Acid.

→ In Actual practice any solution where Concentration is unknown is standardized by titration against a substance of Known purity (primary standard).

Eg:- (1) Strong Acid Solution :- They are normally standardize against a variety of pure basic Chemical Compound, Such as -
Na_2CO_3, Borax ($Na_2B_4O_7$) etc.

(2) Strong Basic Solution:- They are normally standardize against pure acidic chemical Compound Such as - Potassium pthalate



→ Primary standard must have five basic criteria to be fulfilled -

(i) It must be 100% pure, although an impurities ranging 0.01 to 0.002 % in fairly tolerable.
(ii) It must be thermostable at the drying temperature.
(iii) It should not be too expensive to use in Analytical laboratory.
(iv) It must have relatively high formula weight.
(v) It is meant to be employed in a specific titration.

Secondary Standard:- Secondary standards refers to another standard solution of less purity than that of primary standard solution. It is also implied for standardization of an unknown solution.

→ Alternatively, secondary standard is not a in a sufficiently pure form and a solution is usually prepared to produce nearly the desired concentration (0.1N) and is standardize by titrating against a weighed quantity of primary standard.

Eg:-(1)- To prepared 0.1N NaOH solution never represent a standard solution by the virtue of the fact that NaOH is not pure sufficiently. Hence, the prepared NaOH solution is standardize by titrating a primary standard acid (eg:- Oxalic acid):

(2) Prepared 0.1N HCl solution never represent a standard solution. Hence, It is standardized by titrating with a primary standard base.
e.g;- Na_2CO_3 (Analytical Grade)

ERRORS

Errors :- Errors are defined as the difference between observed valve and true value.

Source of Errors :- Common source of errors are –

(i) Instrumental Error
(ii) Gross Error / Human Error
(iii) Environmental Error
(iv) Procedurer Error

Types of Errors :-

(i) Determinate Error (Systematic Error)
(ii) Indeterminate Error (Random Error)

(i) **Determinate Error :-** Those errors which are determinable and can be corrected.

The determinate error arrises due to -

- Instrumental Error
- Operative, chemical Errors
- Errors in Methodology.

- Use of faulty Instrument / Equipment.

- Operative Errors made by person in operating analysis.

- Chemical Error → Errors due to impurities in chemical solvent of reagent.

- Methodology Error → This is most serious error in analysis because this arises due to applying wrong method / procedure.

(ii) Indeterminate Error:-

~~Indeterm~~ Indeterminate Errors are called as Accidental or Random Error.
These errors are due to small differences observed in series of measurement made by same person under Identical Condition.

Methods of Minimizing Errors:-

(i) Use of Correct or Precise instrument to measure.
(ii) Improve the experimental technique.
(iii) Take the average by the repeating the experiment several times.
(iv) Take the measurement carefully to avoid the Gross Error (Human Error).
(v) Adjust the zero of instrument properly.
(vi) Take the reading of experiment by the standing straight to the instrument and not from the side.

Accuracy and Precision :-

Accuracy :- Accuracy is closeness of measurement to a specific value called True value.

→ The term accuracy refers to agreement of experimental measured value with the true value and is expressed in terms of error.

Precision :- Precision is closeness of measurement to each other or one another.
→ Precision refers to the degree of agreement ~~expert~~ between various results of the same experiment and is expressed in the term of reproducibility of result.

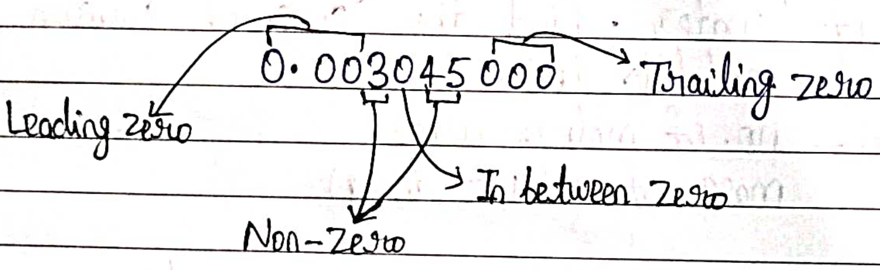
$$\boxed{\text{Relative Error} = \frac{\text{Mean value} - \text{True Value}}{\text{True Value}}}$$

Significant figures :-

Significant figures can be defined as the number of digits necessary to express the results of measurement consistant with the measured precision.

Leading Zero ⊗

always signified
- Non-zero ✓
- In between zero ✓
- Trailing zero ✓
  - Significant only when placed after decimal



Q. How many significant figure are present in following digit.

(i) 0.0050400
S.f → 5

(ii) 1500
S.f. → 2

(iii) 6.04×10^{-3}
S.f. → 3

(iv) 015.04320
S.f. → 7.

(v) 16070
S.f. → 4.

(vi) 15.8 + 5.00 + 83 = 103.80
S.f. → 4.

(vii) 780000000
S.f. → 2.

(viii) 7.09×10^{-8}
S.f → 3

(ix) 0.00418
S.f. → 3

Q. Questions on Methods of Expressing Concentration

Q. What is the molarity of a solution in which 211g $NaHCO_3$ is dissolved in 10 l. solution.

Solve:- $M = \frac{\text{no. of mole of solute}}{\text{Volume of solution in (l.)}}$

$= \frac{211/84}{10}$

$= \frac{211}{84 \times 10} = \frac{211}{840}$

$= 0.251\ M$ Ans.

Q. A solution is prepared by dissolving 10.2 gm of glucose in 405 gm of water. Find the conc. of solution in term of molality (m).

Solution:- $m = \frac{\text{no. of mole of solute}}{\text{mass of solvent (in kg)}}$

Q. Calculate the normality of solution obtained by dissolving 0.321 gm of Na_2CO_3 in 250 ml water.

Solve:- $N = \frac{\text{wt./Equ wt}}{\text{Vol. (l.)}}$

$= \frac{0.321/53}{0.25}$

$= \frac{0.321}{0.25 \times 53}$

$= \frac{0.321}{0.25 \times 53} = \frac{0.321}{13.25}$

$= 0.024N$ Ans

Q. what is the normality of $0.0521\ M\ H_3PO_4$.

Solve:- $N = \text{Molarity} \times x \text{ factor}$

$= 0.0521 \times 3$

$= 0.1563\ N.$ Ans.

Relation between Molarity & Normality:-

$$M = \frac{wt./mol.wt.}{Volume} = \frac{wt.}{mol.wt. \times Volume}$$

$$N = \frac{wt./Equ.wt.}{Volume} = \frac{wt.}{Equ.wt. \times Volume}$$

$$\frac{M}{N} = \frac{1/mol.wt.}{1/Equ.wt.} = \frac{Equ.wt.}{mol.wt.}$$

$$\frac{N}{M} = \frac{mol.wt.}{Equ.wt.} = x \text{ factor}$$

$$\boxed{N = \text{Molarity} \times x \text{ factor}}$$

Q. In the following reaction calculate the normality of $1M\ H_3PO_4$.

Solve:. $H_3PO_4 + 2NaOH \longrightarrow Na_2HPO_4 + 2H_2O$

$N = \text{molarity} \times x \text{ factor}$

$= 1 \times 2$

$= 2N\ H_3PO_4.$ Ans.

Q: How many mili litres of $5M\ CuSO_4$ solution are needed to prepare 0.35 litre of $0.5M\ CuSO_4$.

Solve:- $5M\ CuSO_4 = 0.35\ Lt.$ of $0.5\ CuSO_4$.

$M_1V_1 = M_2V_2$

$5 \times V_1 = 0.5 \times 0.35$

$= \frac{0.5 \times \cancel{0.35}^{0.07}}{\cancel{5}}$

$= 0.035\ Lt. = 35\ ml.$ Ans