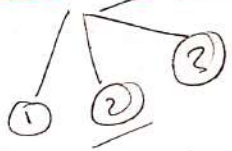
P. ANALYSIS → U-1

CHAPTER - 1st



⊙ Syllabus →

Pharmaceutical Analysis - Definition and scope, different techniques of analysis & methods of expressing concentration, primary and secondary standards,

- preparation and standardization of various molar and normal solutions - ① Oxalic acid, ② Sodium hydroxide, ③ hydrochloric acid, ④ sodium thiosulphate, ⑤ sulphuric acid, ⑥ potassium permanganate and ⑦ ceric ammonium sulphate,

⊙ Definition →

It is the branch of pharmaceutical chemistry which involves the process of identification, determination, quantification and purification of substances.

OR

It is the qualitative and quantitative determination of substances by using manual, chemical and instrumental methods.

⊙ It is of three types :- [diff. techniques]

i) Qualitative analysis → It involves the identification and purification of substance in any sample

(eg) identify functional group or elements in sample.

ii) Quantitative analysis → It involves the determination and quantification of substances.

(eg) conc^{n}/amount of solute present in sol^{n}.

iii) Semi-quantitative analysis → It involves the determination of impurity present in sample is below or above the specified limit (eg.) Limit tests..

⊙ Scope of Analysis

Pharmaceutical analysis play a major role in production of an effective, safe and pure drug.

- It is used in following fields :-

⊙ Quality control → to ensure the quality of raw materials, intermediate, and finished products.

⊙ Identification of compounds → to detect the presence or absence of one or more components in the drug.

⊙ determination of impurity → to determine the amount of impurities and the amount of pure components.

⊙ farming → to know the amount of essential nutrients for the plant growth.

⊙ Diagnosis → to diagnose the cause of any illness.

• others →

- food determination
- Biological sample determination
- Dairy product
- forensic, - soil study, - research etc..

• Different techniques of analysis →

It is of two types :-

i) Instrumental → In this instruments are used for analysis.
it further divided into several types.

ii) Non-Instrumental → In this instruments are not used for the analysis of sample. (classical methods)
It involves titrations and chemicals.
(eg) Titration & Gravimetry..

- Methods of expressing concentration
- These are those methods which are used to find out the concentration/amount of drug present in any solution.
- Concentration, is basically the amount of solute mixed with solvent.

- They are expressed by following terms :-
  - i) Molarity or Molar concentration.
  - ii) Molality or Molal concentration.
  - iii) Normality or Normal concentration.
  - iv) Formality or formal concentration
  - v) Mole fraction and mole percentage
  - vi) percentage calculation
  - vii) Parts per million (ppm)

i) Molarity →

Also known as molar concentration and denoted by capital ('M').

It is defined as, no. of moles of solute dissolved in one litre (1 ℓ) of solution.

$$M = \frac{\text{No. of moles of solute}}{\text{Volume of solution (1 L)}}$$

Unit = g/ℓ = $mole^{-1}$

- **Mole** → It is the fundamental unit which is used to measure the amount of substances (solute).

$$\text{mole} = \frac{\text{mass given}}{\text{molecular weight}}$$

ii) Molality →

Also known as molal concentration and denoted by small 'm'.

It is defined as, no. of moles of solute dissolved in one kg of solvent.

$$m = \frac{\text{No. of moles of solute}}{\text{weight of solvent (in kg)}}$$

iii) Normality →

Also known as Normal concentration, and denoted by capital ('N')

It is defined as, no. of gram equivalent of solute dissolve per litre of solution.

$$N = \frac{\text{No. of gram equivalent}}{\text{volume of solution (in L)}} \quad (L)$$

$$\text{Gram equivalent of solute} = \frac{\text{Molecular weight}}{\text{x [Acidity / Basicity]}}$$

→ H^+ or OH^- ions

$$\text{No. of Gram Equivalent} = \frac{\text{Weight of substance}}{\text{Equivalent weight}}$$

(eg) find out normality of H_2SO_4, 49g of H_2SO_4 present in 500 ml of soln.

mol. wt. (98) & acidity

→ Gr. Eq. weight = $\frac{98}{2} = 49$

No. of Gr. Eq. = $\frac{49}{49} = 1$

$N = \frac{1}{500} \times 1000$

$N = 2$ = 2N

iv) formality →

It is defined as, the no. of gram formula weight of solute dissolved in one litre of solution. ionic compounds

• It is denoted as 'f'

$$f = \frac{\text{No. of formula weight of solute}}{\text{Litre of solution}}$$

v) Mole fraction →

It is defins as, the ratio of no. of moles of solute to the total no. of moles of solute and solvent.

$$X_{solute} = \frac{\text{moles of solute}}{\text{moles of solute + moles of solvent}}$$

total moles

$$\text{Mole percentage} = \text{Mole fraction} \times 100$$

vi) Percentage Calculation →

Also known 'percentage concentration'.

⊙ % by weight of solute i.e.

$$\%\ w/w = \frac{\text{wt. of solute}}{\text{wt of solution}} \times 100$$

⊙ % by volume of solute i.e.

$$\%\ v/v = \frac{\text{volume of solute}}{\text{volume of solution}} \times 100$$

⊙ % of weight of solute by vol. of solution.

$$\%\ w/v = \frac{\text{weight of solute}}{\text{volume of solution}} \times 100$$

vii) Parts per million (ppm) →

It is the parts of solute in one million parts of solution.

$$PPM = \frac{\text{mass of solute}}{\text{mass of solution}} \times 10^6$$

It is used for very less quantity conc substances.

- STANDARD SOLUTIONS →

These are those solutions which have accurately known concentration and which is highly pure and which further use for standardization

- Standardization – to make solution standards.
- It is of two types :-

i) Primary standards

ii) Secondary standards

i) Primary standards →

These are those solution which are prepared through highly pure reagents or chemicals and they have accurately known concentration.

- they do not required further standardization.

(eg) Sodium Carbonate, oxalic acid, silver nitrate etc..

- properties →

- Highly pure, less reactive and stable.
- Highly soluble, non-toxic and eco-friendly.

ii) Secondary standards →

These are those solution which are less stable and standardized by using primary standard solutions.

- they are mainly used for quantitative analysis.
- they are used for standardization of other substances.

- properties →

- less pure and more reactive than 1° standards
- less stable

(eg) Sulphuric acid (H_2SO_4), Potassium permanganate ($KMnO_4$), etc..

HCl (Hydrochloric acid)

- PREPARATION AND STANDARDISATION OF VARIOUS MOLAR AND NORMAL SOLUTIONS

⊙ Preparation → It is the process in which pre-weighed standard (solutes) (drugs) dissolved in (solvent)

⊙ Standardization → preparation of standard soln.

⊙ Molar solution → Molarity → No. Moles / V of soln

⊙ Normal solution → Normality → No. Gr. eq / Vo. of soln

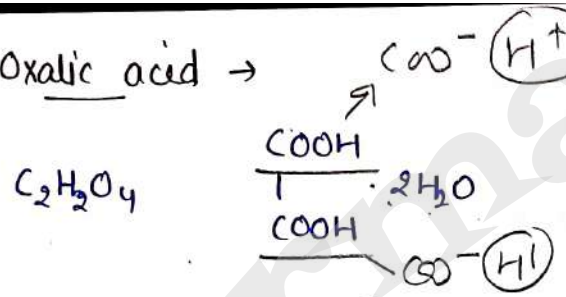
⊙ Molecular weight → total mass of all element of any compound.

(eg) NaOH → 23 + 16 + 1 = 40 g/mol

★ following compounds :—

i) Oxalic acid
ii) Sodium Hydroxide
iii) Hydrochloric acid
iv) Sodium thiosulphate
v) Sulphuric acid
vi) Potassium permanganate
vii) Ceric ammonium sulphate.

1) Oxalic acid →



$C_2H_2O_4$

Mol. weight 126 g/mol.

⊙ preparation of 0.1 M oxalic acid

M = moles / volume (1L)

∴ No. of moles = 126 g

1 M = 126 g dissolved in 1000 ml. So,

for 0.1 M, dissolved (12.6 g) oxalic acid into 1000 ml.

⊙ preparation of (0.1 N) oxalic (acid)

N = No. of (Gr. eq) / V of soln (in L), (Gr eq) = mol. wt / Basicity

= 126/2 = (63 g/mol)

for (1N) = dissolved 63g oxalic acid into (1000 ml.) so,

for 0.1 N = dissolve 6.3g oxalic acid into 1000 ml solvent.

No need of standardization (1° standards).

ii) Sodium Hydroxide → NaOH

Mol. wt → 40g/mol , Acidity → (1)

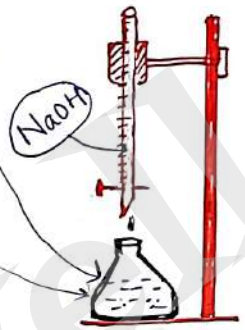
⊙ preparation of 0.1 M NaOH →

1 M = dissolved 40g NaOH in 1000 ml. so,

for 0.1 M = dissolved (4g (approx.) NaOH in 1000 ml.

⊙ standardization → through titration

- titration with potassium biphthalate and phenolphthalein used as indicator.



- pink color indicates end point.

- Repeat till two concordant results.

$M = \frac{\text{wt in gm of Potassium biphthalate}}{0.20423 \times \text{NaOH soln mV}}$

⊙ preparation of 0.1 N NaOH →

1N = (40g) in 1000 ml [Gr.eq = 40g, (n-factor) acidity = 1]

for 0.1 N = 4g NaOH dissolved in 1000 ml

⊙ standardization → $N_1V_1 = N_2V_1$

- titration with 0.1 N oxalic acid [5ml]

- phenolphthalein indicator → faint pink color (end point)

iii) Hydrochloric acid → (HCl) Acid add in water (Not) water in acid ✗

Mol. wt (mass) → 36.46 g/ml , Basicity → (1)

⊙ preparation of (0.1 M HCl soln →

for (37%) of HCl soln, add 8.5 ml of con' HCl soln in 1000 ml of distilled water.

⊙ standardization → 0.1 M

By using (THAM), Bromocresol indicator, pale yellow endpoint.

⊙ standardization for 0.1 N HCl →

By using 5ml of 0.1 N of sodium carbonate, methyl orange indicator - faint red end point.

iv) Sodium thiosulphate →

$Na_2S_2O_3 \cdot 5H_2O$, Mol. wt → (248.18)

for 0.1 M = dissolve (25gm) of sodium thiosulphate in (1000 ml) of distilled water.

⊙ standardization → By using potassium iodate

⊙ for 0.1 N → dissolve 26 g sodium thiosulphate and 0.2 g of sodium carbonate in 1000 ml water.

v) Sulphuric Acid → H_2SO_4

Mol. wt → 98 g, Basicity → 2

⊙ preparation of 0.1 M H_2SO_4

Add 6ml of H_2SO_4 into 1000 ml of water.

⊙ Standardization

By using Sodium carbonate soln (0.2gm in 100ml), methyl red indicator, faint pink color end point.

⊙ preparation of 0.1 N H_2SO_4

Add appox. 3ml of H_2SO_4 in 1000 ml of distilled water.

⊙ Standardization

By using 0.1 N NaOH soln, phenophthalein indicator, end point - pink color.

vi) Potassium permanganate → $KMnO_4$ - 158g

⊙ for 0.02 M →

for 1M → 158 g in 1000 ml

for 0.02 M → 158 X 0.02 → 3.2 - 3.5 appox in 1000ml water

⊙ for 0.1 N →

add 3.2 gm of potassium permanganate in 1000 ml.

$KMnO_4$ → neutral salt.

vii) Ceric ammonium sulphate →

- 0.1 M → By applying gentle heat, about 65 gm of ceric ammonium sulphate is dissolve in mixture of 30ml of H_2SO_4 and 500 ml of water.

then volume upto 1000 ml.

- 0.1 N → same ↑

ERRORS

CHAPTER-2ND

- Syllabus :- Introduction, Sources, Types, Methods of minimizing errors, Accuracy and Precision, Significant figures, Identifying significant digits, Rounding-off digits, Rules for retaining significant figures.

- Errors :-

It is defined as, it is the difference between the standard/true value to the observed value.

Errors = Standard Value - Observed value.

$$\text{percentage Error} = \frac{\text{Standard value} - \text{Observed value}}{\text{Standard value}} \times 100$$

(eg) Paracetamol → 500 mg (standard)
during observation → 450 mg find.

Error → $500_{mg} - 450$ mg → 50 mg

$$\% \text{ error} = \frac{500 - 450}{500} \times 100 = \frac{50^{10}}{\cancel{500}} \times \cancel{100} = 10\%$$

- Sources of errors :-

- Error can be occured due to improper sampling or sample preparation.
- It can be occured by analyst, due to lack of knowledge and focus.
- Due to improper calibration in equipments.
- Due to incorrect observation and data.
- Due to wrong calculation.
- Due to any type of impurities present in sample.
- Due to wrong method selection.
- During transport and storage - Due to improper handling.

Types of Errors :-

It is mainly of three types :-

i) Systemic error (Determinate) — personal, Instrumental, methodic, Reagent
ii) Random error (Indeterminate)
iii) Gross errors — total

i) Systemic Errors → Determinate errors

These are those error, which occurs during analysis by analyst, due to wrong procedure or instruments.

These errors can be prevented or minimised.

(eg.) Incorrect formula used by analyst for calculation.

- These errors can be further divided into following types :-

⊙ Personal error → Those errors which occurs due to personal mistakes or carelessness of analyst. It may be due to lack of knowledge. (eg.) improper sampling, color blindness.

⊙ Instrumental error → It occurs due to defet in instrument.

⊙ Methodic error → sometimes, analyst choose wrong method which cause errors.

⊙ Reagents error → It occurs due to any impurities in reagents.

ii) Random Errors → Indeterminate errors

These are those errors, which occurs randomly, and which are unpredictable and difficult to identify.

- Analyst has no control over these types of error, so elimination and prevention of these types of error may not possible

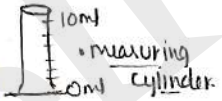
(eg.) Error occurs due to temp° and humidity

◉ METHODS OF MINIMIZING ERRORS

Errors can be minimized by following methods :-

1) Calibration of Instruments / apparatus →

Calibration is the process by which we check the correctness of instruments and apparatus by using standard reading and value.



- By using calibration, we minimised those determinants errors which occurs due to instruments or apparatus (glasswares etc.).

2) Blank determination →

In this, analysis is performed with or without sample to identify impurities in reagents and solvents and minimize them.

3) Control determination →

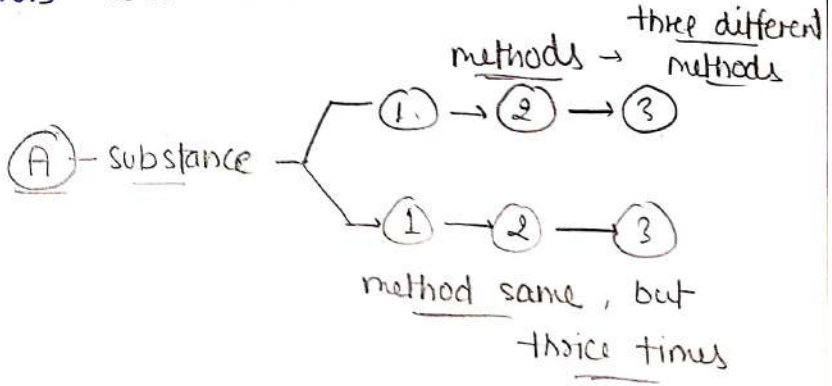
In this, standard solution are used for analysis and compared with the normal determination.

4) Independent methods →

In this, we perform the analysis of any substances by two or more different-2 methods and then compare to find error and minimize them.

5) Parallel determination →

In this, we perform the analysis of any substances more than two times and then compare to find errors and minimize them.



⊙ ACCURACY AND PRECISION

These are those processes which tell us about the correctness of observation of any analysis.

1) **Accuracy** :- It is defined as, it is Near to true value the closeness or correctness of the measured value to the standard or true value

2) **Precision** :- It is defined as, it is the Repeated Value repeated value of measurement or closeness of multiple observation to each other.

- They can decreases the chances of error:
- Example :-
  One tablet - have to measure the conc^{n} of drug present in it.
  - Seven students perform this experiments their observations are :-

① 490 mg
② 495 mg
③ 490 mg
④ 505 mg
⑤ 502 mg
⑥ 490 mg
⑦ 499 mg — Accuracy — error ↓

① to ⑥ — precision

Now, the standard value / true value is 500 mg i.e. Paracetamol 500 mg. standard Value

Accuracy i.e. closeness → 499 mg
Precision i.e. repeatness → 490 mg

⊙ SIGNIFICANT FIGURES

These are those numbers or digits which are used to express the observation and results.

- It is mainly based on decimal system and used to define the degree of accuracy.

eg. 2000 → (1)
2.0 → (2)
2.00 → (3)
} significant figures

•) Rules for Identifying significant digits

① All Non-Zero digits are considered as significants. eg. 123, 1.23, 345 etc (3)

② Zeroes between two non-zero digits are significants. eg. 1001 (4), 1.001, 2.04 (3)

③ All leading zeroes are non-significants (insignificants) eg. 005 (1), 0.0025 (2)
initial

④ Trailing Zeroes / Ending zeroes are significant, if occurs, after decimal only.

eg. 2.70 (3), 2.700 (4)

others - 270 (2), 27000 (2), 2700 (2)

⑤ 10^n or 10^{-n} are non-significants.

eg. 1.3×10^4 (2) 250×10^6 (2)

2.50×10^6 (3)

•) Rounding-off digits

It required when we required answer in fixed digits.

eg. 2.45689 → 2.4569 → 2.457

$\pi = 3.14$

2.5 ← 2.46

•) Rules for Retaining significant figures

for addition or substraction, match the decimal.

eg.
$$\begin{array}{r} 2.4 \\ 3.57 \\ +\ 4.60 \\ \hline 10.57 \end{array} \qquad \begin{array}{r} 11.50 \\ -\ 2.65 \\ \hline 8.85 \end{array}$$