PHARMACEUTICAL ANALYSIS

UNIT 1 NOTES

PHARMACEUTICAL ANALYSIS

- TYPES OF ANALYSIS
- METHODS OF EXPRESSING CONCENTRATION
- STANDARDS
- ERRORS
- ACCURACY & PRECISION
- SIGNIFICANT FIGURES

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PHARMACEUTICAL ANALYSIS

Pharmaceutical Analysis is a branch of Pharmaceutical Chemistry which deals with identification, determination, quantification and purification of pharmaceutical products / substances by using manual, chemical or instrumental methods.

TYPES OF PHARMACEUTICAL ANALYSIS

① Qualitative Analysis
② Quantitative Analysis
③ Semi - Quantitative Analysis

QUALITATIVE ANALYSIS

Qualitative Analysis deals with identification & presence or absence of various components in the given sample on the basis of physical & chemical properties.

QUANTITATIVE ANALYSIS

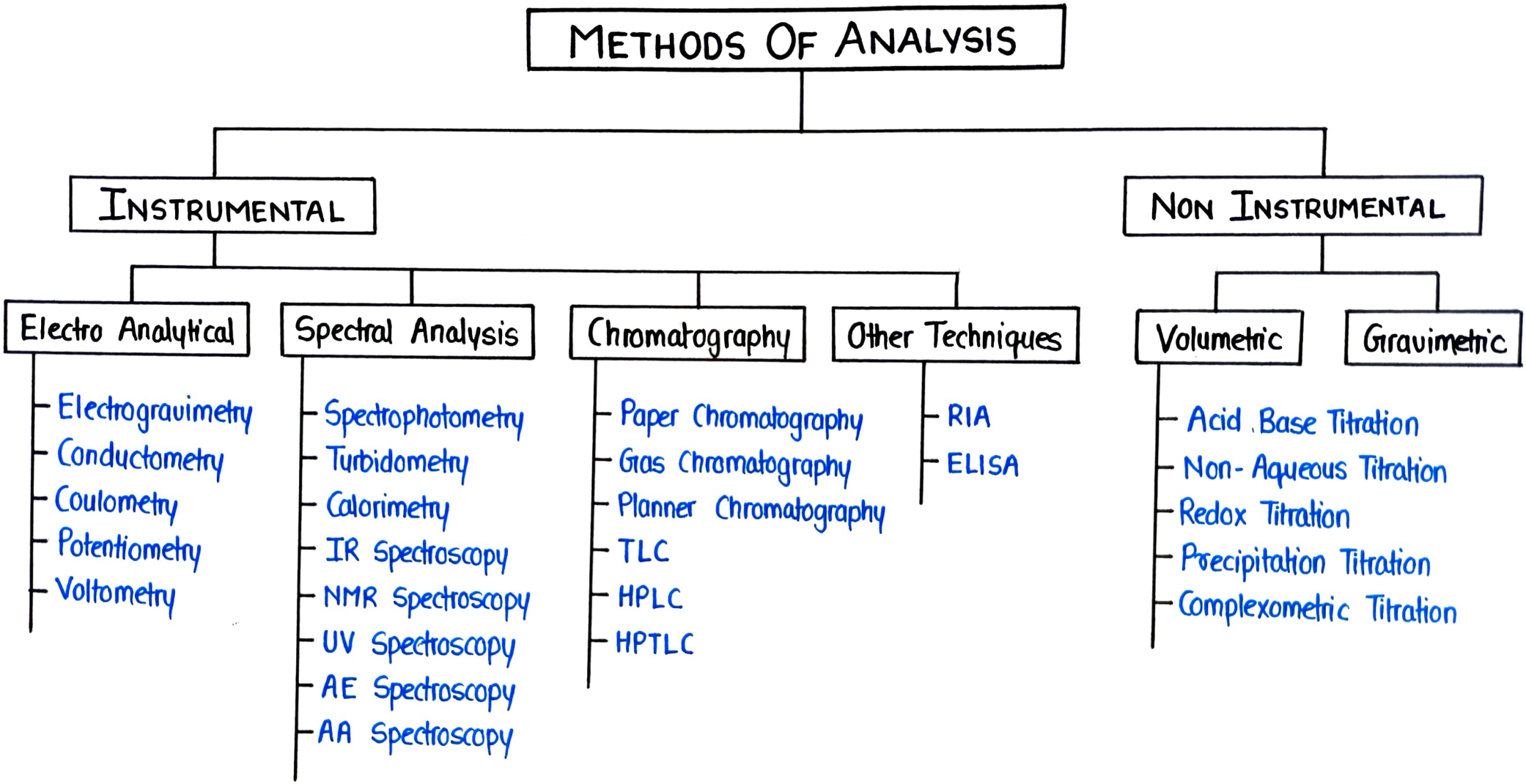
Quantitative Analysis deals with the determination of quantity of various substances that are present in the given sample.

SEMI - QUANTITATIVE ANALYSIS

It mainly describes whether the quantity of impurity present in the sample is above or below the standard limit.

Scope Of Pharmaceutical Analysis

- Examination of Raw Materials
- Examination of Soil & Rocks
- Examination of Radioactive Compounds
- Examination of Various Drug Substances
- In Food Industry
- In Bio Medical Application
- In Environmental Study



CONCENTRATION

- The term concentration is simply defined as amount of solute present in the given amount of solvent.
- Concentration of a solution can be expressed in different concentration terms.

METHODS OF EXPRESSING CONCENTRATION

It can be expressed in different concentration terms as follows :

- Molarity
- Molality
- Normality
- Formality
- Percent Concentration
- Parts Per Million

MOLARITY

- Molarity of a solution is defined as no. of moles of solute dissolved per litre of solution.
- It is denoted by M.

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

Molality

- Molality of a solution is defined as no. of moles of solute dissolved per kg of solvent.
- It is denoted by m.

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

Normality

- Normality of a solution is defined as no. of gram equivalent of solute dissolved / present per litre of solution.
- It is denoted by N.

$$N = \frac{\text{No of Gram Equivalent}}{\text{Volume of Solution (in L)}}$$

Formality

- Formality of a solution is defined as no. of Formoles of solute/ ionic compound present per litre of solution.
- It is denoted by F

$$F = \frac{\text{No of Formoles}}{\text{Volume of Sol. (In L)}}$$

Percent Concentration

Generally solution concentration is expressed in terms of percent (%).
This percent concentration is expressed in different concentration terms :

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

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

- $\%\ W/V = \frac{\text{Mass of Solute}}{\text{Volume of Solution}} \times 100$

Parts Per Million

- Parts per million is generally used to express the concentration of very dilute solution.
- It is represented by Cppm.

$$C_{ppm} = \frac{\text{Mass of Solute}}{\text{Mass of Solution}} \times 10^6$$

STANDARDS

- Standards are defined as very pure reagents.
- Concentration of standard solutions are accurately known.
- We can express them with definite numbers & proper units.

USES OF STANDARDS

- To provide a reference using which we can determine the concentration of an unknown solution.
- Standardization of volumetric solution
- To calibrate an instrument.

TYPES OF STANDARDS

Standards are mainly classified into two types :

① Primary Standards
② Secondary Standards

PRIMARY STANDARDS

- Primary Standards are defined as reagents with accurately known concentration and very high purity.
- When Primary Standards are dissolved to a known amount of solvent gives Primary Standard Solution.

PROPERTIES

- It should be 100 %. pure.
- It should be stable at atmospheric conditions.
- It must have molecular & equivalent weight.
- It must have high stability & low reactivity.
- It should be non- hygroscopic and non- toxic.
- It must be inexpensive & readily available.

COMMONLY USED PRIMARY STANDARDS

Some commonly used primary standards are as follows :

- **Acid- Base Titration** : Sodium Carbonate, Oxalic Acid, Succinic Acid, Benzoic Acid
- **Redox Titration** : Potassium Bromate, Sodium Oxalate, Copper Sulphate
- **Precipitation Titration** : Silver Nitrate, Sodium Chloride, Potassium Chloride
- **Complexometric Titration** : Metallic Zinc, Zinc Chloride, Magnesium Chloride

Secondary Standards

- Secondary Standards are those chemical compounds that are standardized against a primary standard for use in a specific analysis.
- They are mainly used in standardization process and for calibrating instruments.
- They are prepared because of limited numbers of Primary Standards.

Properties

- They are less pure than Primary Standards.
- They are less stable compare to primary standards.
- They are more reactive than primary standards.
- They are titrated against primary standards.
- They are hygroscopic in nature.

Commonly Used Secondary Standards

Some commonly used secondary standards are as follows :

- **Acid - Base Titration** : Hydrochloric Acid, Sulphuric Acid, Sodium Hydroxide
- **Redox Titration** : Potassium Permanganate, Sodium Thiosulphate
- **Precipitation Titration** : Potassium Thiocynate, Ammonium Thiocynate
- **Complexometric Titration** : Disodium Edetate, Lead Nitrate

Preparation And Standardization

Here, we have to study about Preparation and Standardization of various Molar & Normal solutions as follows :

① Oxalic Acid
② Sodium Hydroxide
③ Hydrochloric Acid
④ Sodium Thiosulphate
⑤ Sulphuric Acid
⑥ Potassium Permanganate
⑦ Cerric Ammonium Sulphate

Oxalic Acid

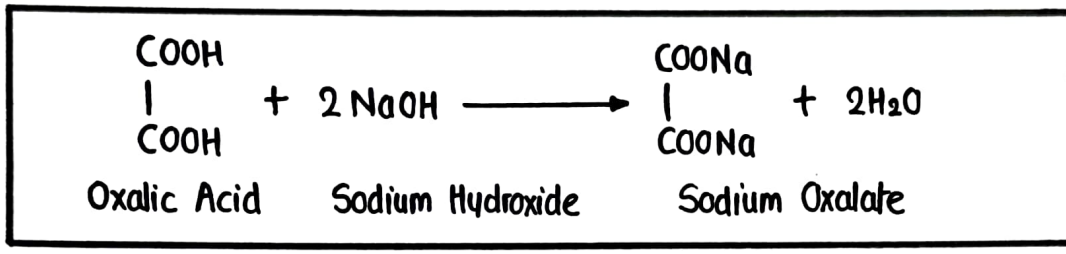
Chemical Formula : $C_2H_2O_4 \cdot 2H_2O$ (Dihydrated Form)
Molecular Weight : 126 g/mol

Preparation Of 0.1 N Oxalic Acid

- Take about 100 ml of distilled water in clean & dried volumetric flask of 1000 ml capacity.
- Add about 6.3 g of oxalic acid.
- Now make up the volume to 1000 ml (1 Litre) with distilled water.
- keep the solution aside for sometime and carry out the standardization.

Standardization Of Oxalic Acid

- Oxalic Acid is a primary standard hence it doesn't required to be standardized.
- Although we can standardized it using 0.1 N NaOH solution that can be prepared by dissolving 4 gram NaOH in 1 Litre solution.
- Standardization is based on following reactions :

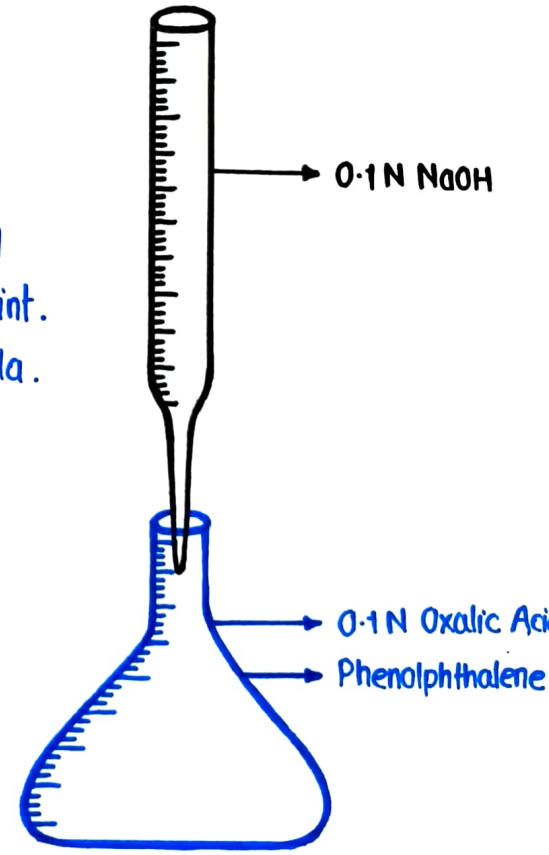


Procedure

- Add 0.1 N NaOH solution to the burette.
- Take 10 ml 0.1 N oxalic acid in a flask.
- Add 2-3 drops of phenolphthalene
- Now titrate the oxalic acid solution with NaOH until pink colour appears that indicates end point.
- Calculations are performed by using given formula.

$$N_1V_1 = N_2V_2$$

Here
- N_1 = Normality of NaOH
- V_1 = Volume of NaOH
- N_2 = Normality of Oxalic Acid
- V_2 = Volume of Oxalic Acid



Sodium Hydroxide

Chemical Formula : NaOH

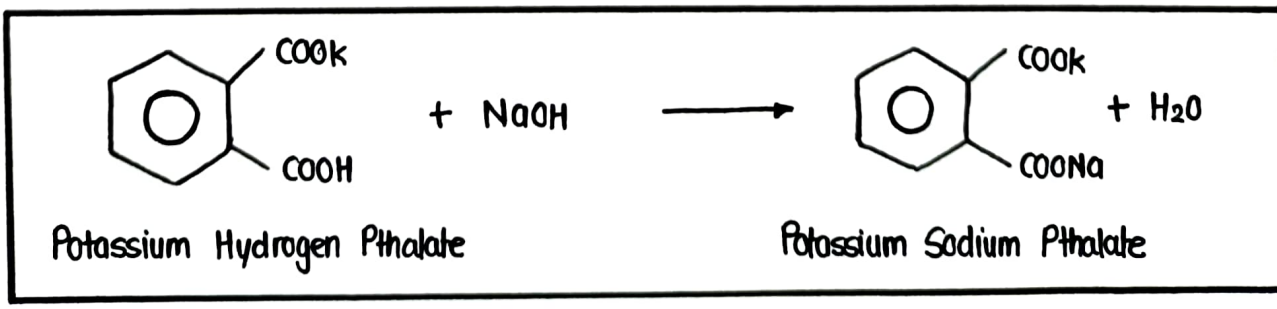
Molecular Weight : 40 g/mol

Preparation Of 0.1 N NaOH

- Take about 100 ml of distilled water in clean & dried volumetric flask of 1000 ml capacity.
- Add about 4 gram of NaOH in it.
- Now make up the volume to 1000 ml with distilled water.
- keep the solution for atleast 1 hour and carry out the standardization.

Standardization

- NaOH can be standardized using standard Potassium Hydrogen Pthalate solution.
- For this first we have to prepare 0.1 N standard solution of potassium hydrogen pthalate by dissolving 20.424 gram of KHP solution in 1 Litre water.
- Standardization is based on following reactions :

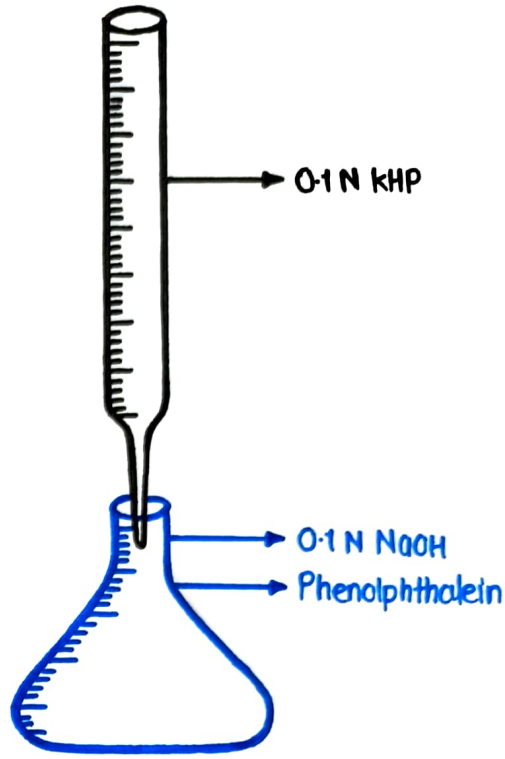


Procedure

- Add 0·1 N Potassium hydrogen pthalate in burette.
- Take 10 ml 0·1 N NaOH in flask.
- Add 2-3 drops of Phenolphthalein.
- Now titrate the NaOH solution with kHP until the colour change from Pink to colourless that indicates the end point.
- Calculations are performed using given formula :

$$N_1V_1 = N_2V_2$$

Here
- V_1 = Volume of NaOH
- N_1 = Normality of NaOH
- N_2 = Normality of kHP
- V_2 = Volume of kHP



Hydrochloric Acid

Chemical Formula : HCl

Molecular Weight : 36.5 g/mol

Preparation Of 0.1 N HCl

- Take about 100 ml of distilled water in a clean and dried volumetric flask of 1000 ml capacity.
- Add about 8.3 ml of HCl stock solution (37%) into it.
- Now make up the volume to 1000 ml with distilled water.
- Keep the solution for atleast 1 hour and then carry out the standardization.

Standardization

- HCl can be standardized using standard sodium carbonate solution :
- For this we have to prepare 0.1 N Na_2CO_3 solution by dissolving 5.3 g Na_2CO_3 in 1 Litre distilled water.
- Standardization is based on following reactions.

$$Na_2CO_3 + 2HCl \longrightarrow 2NaCl + H_2O + CO_2$$

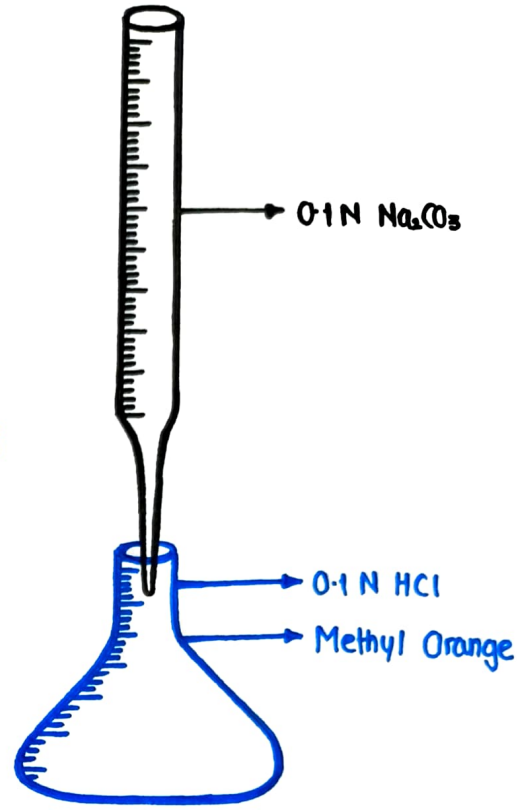
Sodium Carbonate — Sodium Chloride

Procedure

- Add 0·1 N Na_2CO_3 in burette.
- Take 10 ml 0·1 N HCl in flask.
- Add 2-3 drops of Methyl Orange as indicator.
- Titrate the HCl solution with Na_2CO_3 until the orange colour changes to pink that indicates the end point.
- Calculations are performed using given formula :

$$N_1V_1 = N_2V_2$$

Here
- N_1 = Normality of HCl
- V_1 = Volume of HCl
- N_2 = Normality of Na_2CO_3
- V_2 = Volume of Na_2CO_3



Sodium Thiosulphate

Chemical Formula : $Na_2S_2O_3 \cdot 5H_2O$ (Pentahydrated Form)

Molecular Weight : 248 g/mol

Preparation of 0.1 N Sodium Thiosulphate

- Take about 100 ml of water in a cleaned and dried 1000 ml volumetric flask.
- Add about 24.8 gm of sodium thiosulphate with continuous stirring.
- Add about 0.2 gm of sodium carbonate to it.
- Make up the volume to 1000 ml with water.

Standardization

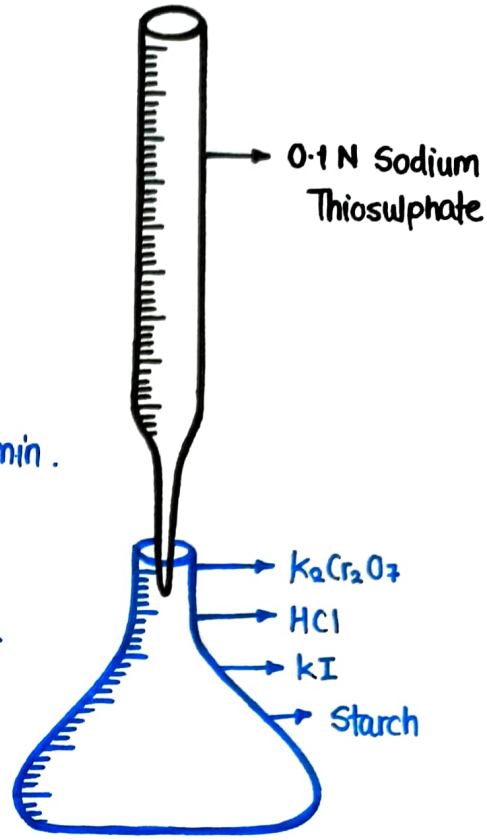
- Sodium thiosulphate solution can be standardized using Potassium Dichromate and potassium iodide that ultimately liberates iodine.
- Standardization is based on following principle.

$$\underset{\text{Potassium Dichromate}}{K_2Cr_2O_7} + \underset{\text{Potassium Iodide}}{6\,KI} + \underset{\text{Hydrochloric Acid}}{14\,HCl} \longrightarrow \underset{\text{Iodine}}{3I_2} + \underset{\text{Chromium Chlorate}}{2CrCl_3} + \underset{\text{Potass. Chloride}}{8\,KCl} + 7H_2O$$

$$\underset{\text{Sodium Thiosulphate}}{2\,Na_2S_2O_3} + \underset{\text{Iodine}}{I_2} \longrightarrow \underset{\text{Sodium Tetrathionate}}{Na_2SuO_6} + \underset{\text{Sodium Iodide}}{2\,NaI}$$

Procedure

- Take about 0.16 - 0.22 g dried potassium dichromate (at 110°C for 30 minutes) into iodine flask.
- Add 25 ml distilled water.
- Add 5 ml concentrated HCl.
- Add 3 gm Potassium Iodide.
- Add 100 ml distilled water & leave for 10 min.
- Now add 1% starch solution as an indicator.
- Add 0.1 N sodium thiosulphate into burette
- Now start the titration until the blue colour changes to green.
- Calculations are performed using given formula :



$$N = \frac{\text{Wt. of } K_2Cr_2O_7}{\text{Volume of } Na_2S_2O_3 \times 0.04904}$$

Here N = Normality of $Na_2S_2O_3$

Sulphuric Acid

Chemical Formula : H_2SO_4

Molecular Weight : 98 g/mol

Preparation Of 0.1 N H_2SO_4

- Take about 100 ml of distilled water in a clean and dried conical flask of 1000 ml capacity.
- Add about 2.75 ml of H_2SO_4 (97%, 36.4 N) solution into it.
- Now make up the volume to 1000 ml with distilled water.
- Keep the solution aside for some time and continue the titration.

Standardization

- Sulphuric Acid solution can be standardized using standard sodium carbonate solution.
- For this first we have to prepare 0.1 N Na_2CO_3 solution by dissolving 5.3 g sodium carbonate in 1 Litre water.
- Standardization is based on following principle :

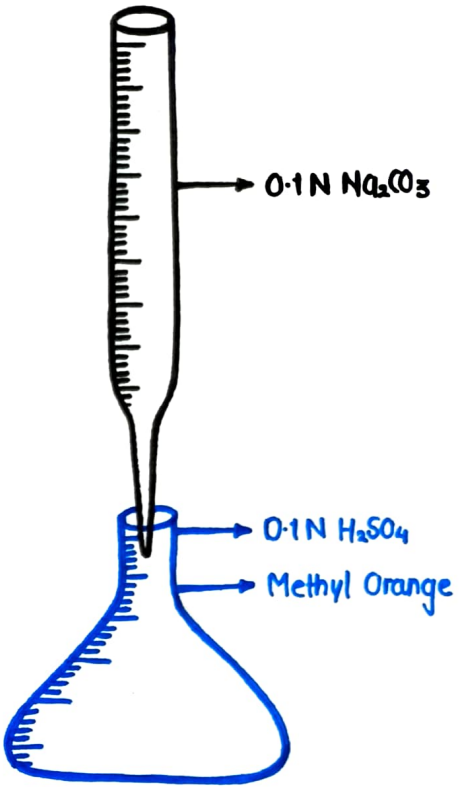
$$\underset{\text{Sulphuric Acid}}{H_2SO_4} + \underset{\text{Sodium Carbonate}}{Na_2CO_3} \longrightarrow \underset{\text{Sodium Sulphate}}{Na_2SO_4} + \underset{\text{Water}}{H_2O} + \underset{\text{Carbon Dioxide}}{CO_2}$$

Procedure

- Take 10 ml 0·1 N H_2SO_4 in flask.
- Add 0·1 N Na_2CO_3 in burette.
- Add 2-3 drops of Methyl Orange indicator.
- Titrate the H_2SO_4 with Na_2CO_3 until the red colour changes to orange or yellow that indicates the end point of the titration.
- Calculations are performed using given formula :

$$N_1V_1 = N_2V_2$$

Here
- N_1 = Normality of H_2SO_4
- V_1 = Volume of H_2SO_4
- N_2 = Normality of Na_2CO_3
- V_2 = Volume of Na_2CO_3



Potassium Permanganate

Chemical Formula : $KMnO_4$

Molecular Weight : 158 g/mol

Preparation of 0.1 N $KMnO_4$

- Take about 100 ml distilled water in a clean and dried volumetric flask of 1000 ml capacity.
- Dissolve 3.16 - 3.2 gram potassium permanganate into it.
- Now make up the solution to 1000 ml with distilled water.
- Heat the solution on water bath for 1 hour.
- Allow the solution to stand for 2 days and filter through glass wool.
- Standardize the solution in the following manner.

Standardization

- Potassium permanganate solution can be standardized using standard oxalic acid solution.
- For this, first we have to prepare 0.1 N standard solution of oxalic acid by dissolving 6.3 gram into 1 Litre water.
  Standardization is based on following reaction :

$$2\,KMnO_4 + 5\,H_2C_2O_4 + 3\,H_2SO_4 \longrightarrow K_2SO_4 + 2\,MnSO_4 + 8H_2O + 10\,CO_2$$

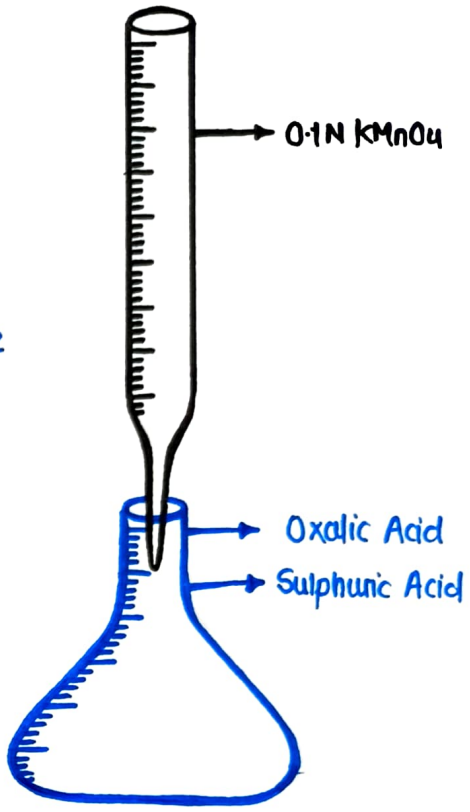
Potassium Permanganate	Oxalic Acid	Sulphuric Acid	Potassium Sulphate	Manganese Sulphate	Water	Carbon Dioxide

Procedure

- Take 0.1 N potassium permanganate in burette.
- Add 20 ml 0.1 N oxalic acid into the flask.
- Now add 5 ml concentrated H_2SO_4 into it & swirl the content & warm the mixture at 70° C.
- Titrate the warm solution against $KMnO_4$ until the pink colour appears (that retained for atleast 30 seconds) that indicates the end point.
- Calculation is based on following formula :

$$N_1V_1 = N_2V_2$$

Here
- N_1 = Normality of $KMnO_4$
- V_1 = Volume of $KMnO_4$
- N_2 = Normality of Oxalic Acid
- V_2 = Volume of Oxalic Acid



ERRORS

- Errors are simply defined as 'Mistake'
- In Pharmaceutical Analysis the difference between True / Standard Value and Observed value is known as Error.
- Large errors can have serious consequences.
- A Patient may undergo expensive and even dangerous medical treatment based on incorrect laboratory result because of an analytical error.

$$\text{ERROR} = \text{STANDARD VALUE} - \text{OBSERVED VALUE}$$

$$\%\ \text{ERROR} = \frac{\text{STANDARD VALUE} - \text{OBSERVED VALUE}}{\text{STANDARD VALUE}} \times 100$$

SOURCES OF ERRORS

There can be various sources of errors as follows :

- Error By Analyst
- Error Due To Equipments
- Error During Sample Preparation
- Experimental Error
- Error in Method Selection.

Error By Analyst

Error May occur by the analyst if he is not well qualified / experienced or having some personal inability i.e., Colour Blindness.

Error Due To Equipments

Error may occur if the equipments used in the analysis is defective or they are not properly calibrated.

Error During Sample Preparation

Error may occur during sampling if proper sampling techniques not followed or using wrong concentration of solution.

Experimental Error

Error may occur if suitable laboratory environment and favourable conditions is not available for particular experiment.

Error in Method Selection

Error may occur if the analyst performing experiment select wrong method or not followed the proper steps of procedure.

Types Of Errors

Errors are basically divided into two categories :

- Determinate or Systematic Error
- Indeterminate or Random Error

① Determinate Errors

- Determinate Errors are also known as Systemic Errors.
- These types of errors generally occurs due to the fault in analytical procedure or in the instruments.
- Cause or sources of these errors are generally known to the analyst and can be avoided by preplanning and careful working.

Types Of Determinate Errors

Determinate Errors can be further subdivided into following sub types.

- Personal Errors
- Instrumental Errors
- Reagent Errors
- Additive Errors
- Error in Method

Personal Errors

- These error occurs by the persons who are handling and performing the analysis.
- These errors arise due to personal mistakes or carelessness of analyst or due to inability of individual i.e. colour blindness.

Instrumental Errors

- These error occurs due to defect in the equipment or use of uncalibrated glasswares, apparatus or instruments.

Reagent Errors

- These errors depends on the quality of individual reagent.
- Many reagents and compounds are not present in pure form & contain impurities.

Additive Errors

- Sometimes errors are constant throughout the analysis and independent of amount of sample.
- Example : 10·1, 20·1, 30·1 (0·1 ml of error independent of amount)

Error In Method

- These type of errors caused due to selection of wrong or improper method.

② INDETERMINATE ERRORS

- Indeterminate errors are also known as Random Errors.
- Generally cause of random error is not known, Analyst has no control over it.
- These errors cannot be eliminated even after using high quality reagents and apparatus.

METHODS OF MINIMIZING ERRORS

Errors can be minimized by following methods given below :

- Calibration of Apparatus
- Independent Method of Analysis
- Running a Blank Determination
- Running a Control Determination
- Running a Parallel Determination

Calibration of Apparatus

By calibrating all instruments (weights, Flask , Burettes, Pipettes) and applying appropriate corrections errors can be minimized to very much extent.

Independent Method of Analysis

In this , we perform the analysis for a particular substance by two or more different methods and compare the results.

Running A Blank Determination

By carrying out a separate determination without sample under exactly same conditions as for actual analysis , we can find out error occured due to presence of impurities in the reagents.

Running A Control Determination

In this, we use standard substances and perform the analysis in the identical conditions and compare it with normal / actual analysis.

Running A Parallel Determination

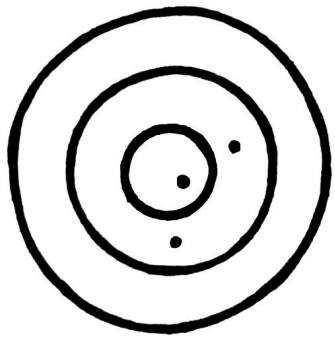
In this, we basically perform the analysis for the particular analyte more than two or three times so that we can get more accurate results.

ACCURACY

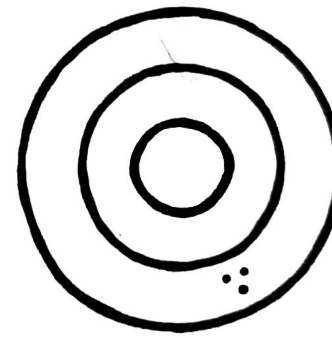
- Accuracy is defined as closeness of measurment to the true value.
- Accuracy refers to correctness of measurment.
- Accuracy is inversely proportional to error, higher the accuracy lower the error.

PRECISION

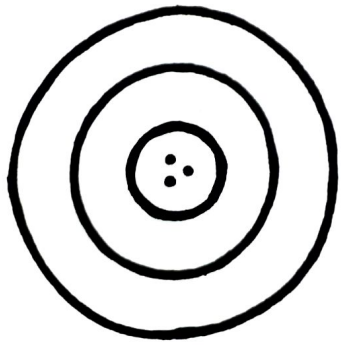
Precision is defined as closeness of multiple / several observations to one another.
It can also be defined as repeatability or reproducibility of measurments.



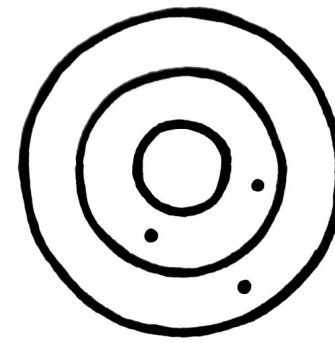
Accuracy Without Precision



Precision Without Accuracy



Accuracy & Precision



No Accuracy No Precision

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Significant Figures

- Significant Figures are the number of digits in a value that defines the degree of accuracy of value.
- There are certain rules that helps to identify the number of significant figures in a value as follows :

Rule No. 1

All non-zero digits are significant

example
- 2.133 (4 significant figures)
- 4.46 (3 significant figures)
- 552 (3 significant figures)

Rule No 2

All zeroes between two non zero / two significant figures are significant figures.

example
- 4.03 (3 significant figures)
- 1.004 (4 significant figures)
- 506 (3 significant figures)

Rule No 3

Ending zeroes are significant only if they appear after decimal.

example
- 3.000 (4 significant figures)
- 2.460 (4 significant figures)
- 2350 (3 significant figures)

Rule No. 4

Initial zeroes are always insignificant.

example
- 0.0042 (2 significant figures)
- 0.1034 (4 significant figures)
- 007 (1 significant figures)

Rule No 5

Power of 10 / order of magnitude is never significant.

example
- 2.4×10^6 (2 significant figures)
- 346×10^7 (3 significant figures)
- 4.8×10^5 (2 significant figures)

Rule No 6

Constant numbers have infinite significant figures.

example
- π (∞ significant figures)

THANK YOU

FOR CHOOSING IMPERFECT PHARMACY AS YOUR STUDY PARTNER

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