CONCEPT OF ANALYSIS USED IN PHARMACY

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I. INTRODUCTION

Definition
- It is a branch of science of practical chemistry that involves a series of process for identification, determination, quantification & purification of compound, separation of the components of a solution or mixture or determination of structure or compound.
- The substance may be single or a mixture of compound & its it may be in any of dosage forms
- The sample to be analysed is called as analyse on the basis of the size of the sample they can be classified as; Macro (0.1 gm or more) Semi micro (0.000gm to 0.1 gm) Mirco (0.001gm to 0.001gm) sub macro (0.0001 gm to 0.001gm)

II. TYPE OF ANALYSIS

1. **Qualitative analysis (identification)**

- Analysis it is a performed to established composition of natural or synthesis substance.
- This test are performed as to indicate whether the substance is present in the sample or not
- These tests are detected by evolving gas, changing gas, boiling points , melting point range etc.

2. **Quantitative analysis (estimation)**

Quantitative analysical techniques are mainly used to quantity any compound or substance in the sample. these technique are based on

A) The quantification performance of suitable chemical reaction & either measuring the amount to reagent added to complete the reaction or measuring the amount of reaction product obtained.

B) The characterization movement of a substance throught a defined medium under controlled condition.

C) Electrical measurement

D) Measurement of some spectroscopic properties of compound.

III. VARIOUS TYPE OF QUALITATIVE ANALYSIS

1. **Chemical Method**
- Volumetric of titrimetric method

- Gravimetric method
- Gasometric titration
- Electrical method
- Instrumental method
- Biological & microbiological method

- **Chemical Method:** it involves reaction of substance to be determined with an appropriate reagent as a standard solution &volume of solution required to complete the reaction is determined.

  - **Various type of titrimetric method are used for** .
    - ➢ Acid base titration
    - ➢ Complexometric titration
    - ➢ Precipitation titration
    - ➢ Redox titration
    - ➢ Non aqueous titration

- **Gravimetric Method:** In this analysis a substance to be determine is converted into insoluble precipitation in pure form .which is collected an weight'. It is the time consuming process.

- **Gasometric Method** It involves measurement of the volume of gas evolve or absorb in a chemical reaction for eg : CO_2, helium, ethyileum etc.

2. **Electrical Method :**This type of analysis involves the measurement of electric current voltage or resistance in relation to the contraction of saline species in the solution It include
   - Potentiometry
   - Conductometry
   - Polarography
   - Voltametry
   - Amperometry

3. **Instrumental Method:** It involve measurement of some physical properties of the compound or substance. This method are employed for determination of minor or trace contraction of element in the sample. These are the preferred due to their selectivity , high speed , accuracy & simplicity of analysis

   Spectroscopic method of analysis depend upon the measurement of amount of reagent energy of particular wavelength emitted by the sample
   Example:- ultraviolent (UV), infrared (IR), Nuclear magnetic, Resonance (NMR) and Mass, spectroscopy.

4. **Biological & Microbiological Method:** These method are used when potency of a drugs or its derivative cannot be properly determined by any physical or chemical method are bio assay. Microbiological are used to observe patency of antibiotic or anti microbial agents

IV. APPLICATION

Manufacturing industries required both qualitative and quantitative analysis for raw material and final product. Most of the industrial processes give rise to pollutants which may cause health relative problems so quantitative analysis of AIR , water and soil .sample should be carried out to determine the level of pollution.

1. **Factor Affecting the Choice of Analytical Technique**

   These are various factor which are important for the selection of analytical technique these are

   - Nature of the sample ex. Acid or Base nature for acid – base titration , oxidizing or reducing sample for redox titration.
   - Type of analysis required for sample ex. Volumetric , spectroscopic & chromatographic analysis.
   - Physical state of the sample play major role for the solution of analytical technique ex. Solid liquid & gaseous state.
   - Presence of impurities affects the selection of analytical methods are not sensitive towards impurities present in the sample.
   - Selection of analytical technique in affected by the concentration range of the analyte. because some analytical technique are more sensitive.
   - Accuracy of the different analytical technique varies
   - Availability of instruments for selected analytical technique play major role
   - Amount of the sample available is an important role for the solution of analytical technique
   - Cost of the analysis is also play an important role

2. **Method of expressing concentration :**In all the technique of qualitative analysis the use of solution require some bases for the expression of solution concentration.

   Normality: the normality of the solution is defined as " the no of gram equivalent present in per litre of the solvent.

   $$N = \frac{No.of\ gram\ equivalent}{solvent\ (litre\ )}$$

   Molarity: The molar concentration of the solution is the no. of moles of solute per litre of the solution.

   $$M = \frac{No,.of\ moles\ of\ solute}{solution\ (per\ litre\ )}$$

   Molality: Molality is a measure of the number of moles of solute in a solution corresponding to 1 kg or 1000 g of solvent. This contrasts with the definition of molarity which is based on a specified volume of solution.P

   Parts per million:-it is frequently use to express the concentration of very dilute solution it is dinote as (ppm).

These term also employed to express concentration in pharmaceuticals.

$$ppm = \frac{\text{mass of solute (in grm)}}{\text{mass of solvent (in grm)}} \times (10)^6 \text{ ppm}$$

Percent concentration: The concentration is many a type express in terms of percentage (parts per 100)
For example :- percentage composition of a solution can be expressed as-

$$percent \frac{w}{w} = \frac{\text{weight of solute}}{weight\ of\ solvent} \times 100$$

Preparation of 10% w/w NaCl solution
(10% of NaCl will be dissolved in 90gm distilled water)

3. **Primary and secondary standard:**

- Very pure reagent used for standardization.
- A solution with accurately known concentration is called standard solution.
- Highly pure reagent or chemicals are used to prepare standard solution which doesn't require further standardization is known primary standard solution.

- **Properties**

  ➢ Primary standard solution should be easily available purified & dry.
  ➢ These substance should be 100% pure if impurities are present then the magnitude of it should be known to analyse the limit should not exceed (0.001 to 0.02%)
  ➢ It should be stable at normal atmospheric condition.
  ➢ Equivalent weight two molecules weight should be used.
  ➢ Equivalent point & practical end point should be equal.

- **Secondary standard:** Secondary standard should used for the standardization & whose concentration has been determined by comparison with the primary standard"
  For example

  ➢ An unknown solution of HCl can be determined by two methods.
  ➢ By using analytical grade NA_2CO_3 (primary standard).
  ➢ By using standard solution of NAOH (secondary standard))

V. PREPARATION AND STANDARDIZATION OF VARIOUS MOLAR AND NORMAL SOLUTIONS.

1. **Oxalic acid**

   Aim: To prepare 0.1 N oxalic acid standard solution .

   Requirement: Oxalic acid , volumetric flask, & distilled water,

   Procedure: Preparation of 0.1N oxalic acid
   It is primary standard substance so it does not require standardization
   Molecular formula of oxalic acid is $c_2h_2o_4.2h_2o$

Molecular weight of oxalic acid is 126

$$normality = \frac{\text{Molecular weight}}{\text{B/A}} \quad 126/2 = 63$$

Example 63 gm/ lit oxalic acid for 1N so for
0.1 N Oxalic acid required
0.1 N= 63/10 = 6.3n/lit
> Taken a 100ml volumetric flask and transfer the accurate amount i.e. 63 gm of oxalic acid & dissolved in 100 ml of water make a final volume upto 1000ml with water.
Normality of the prepared oxalic acid will be 0.1 N

2. **Sodium hydroxide:**

   Aim: To prepare & standardization 0.1N NAOH solution by using 0.1N HCl.

   Requirement: concentrated HCL, NaOH, Distilled water, Methyl orange, Burette, pipette, volumetric flask, beaker, funnel, Na_2Co_3.

   Principle:
   Step 1: Standardization of HCL

   Titration between HCL and Na_2CO_3 is based on the principal of strong acid & strong base titration.

   $$2HCL + NA_2CO_3 \rightarrow 2Nacl + Co_2 + H_2O$$
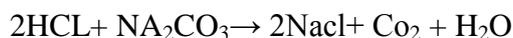
   Step 2: Standardization of NaOH

   Titration between NaOH and standardization HCL is based on the principle of strong acid and strong base titration.

   $$NaOH + HCl \rightarrow NaCl + H_2O$$

VI. **EXPERIMENTAL METHODOLOGY:**

   Taken 200 to 300 ml of distilled water into a 1000ml volumetric flask then, slowly added 8.7 ml of concentration hydrochloric acid drop wise in the volumetric flask & make up the volume upto 1000ml with distilled water. The normality of the prepared solution will be approximately 0.1 normal.

   Taken 5.3 gm sodium carbonate in a volumetric flask and added 100 ml of distilled water and dissolved .then make up the volume up to 1000ml with distilled HCl normality of the prepared solution 0.1 normal because sodium carbonate is a primary standard substance.
   Taken 4 gm of sodium hydroxide in a volumetric flask & added 100ml of distilled H_2O & dissolved , finally make up the volume upto 1000ml of distilled water normality of prepared solution will be 0.1 N which need standardization because sodium hydroxide (NaOH) is secondary standard substance.

Perform standardization of 0.1 N HCL with sodium carbonate solution.

1. **Standardization of 0.1N NaOH:** Transfer 10ml of prepared NaOH solution with the pipette to a conical flask then, added 10 drop of phenopthalein indicator to this solution. Taken the standardization HCL in a burette and added gradually with continue swirling of the solution to the conical flask near the end point HCl was added drop by drop continue the addition of the HCl until the colour of the solution turn from colourless to pink.

   Repeat the experiment 3 times for consecutive results, taken the precise reading for calculation of actual normality.

Sl.no	Start point	End point	Volume consumed

   Calculation :-
   $$N_1V_1 = V_2N_2$$

   N_1= Calculated normality of HCl
   N_2= Normality of NaOH
 V_1= Volume of HCl consumed.
   V_2= Volume of NaOH taken

   Result: NaOH solution was prepared and standardization with the standard 0.1N HCl and normality of the prepared NaOH solution was found to be……..

2. **Sulphuric Acid**

   Aim: To prepare and standardization 0.1N H_2So_4 solution by using primary standard 0.1 N Na_2Co_3.

   Principal: Titration between sulphuric acid & Na_2Co_3 is based on the principle of strong acid and strong base titration.
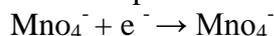   The reaction is as follow.
   $$Na_2Co_3 + H_2So_4 \rightarrow Na_2So_4 + Co_2 + H_2o$$
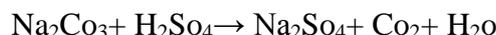
3. **Potassium Permagnate**:

   Aim: To prepare and standardization 0.1N $KMnO_4$ solution by using standard solution of 0.1N oxalic acid.

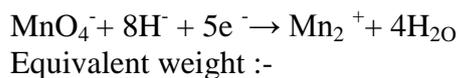   **Principle**: The Permagnate ions get reduce to different products depending upon the reactant condition..
   For example:- In basic medium.
   $Mno_4^- + e^- \rightarrow Mno_4^-$
   In neutral medium:--
   $Mno_4^- + 4H^+ + 3e^- \rightarrow Mno_2 + 2h_2O$
   Acidic medium

$MnO_4^- + 8H^- + 5e^- \rightarrow Mn_2^+ + 4H_2O$

Equivalent weight :-
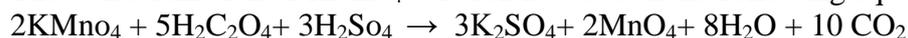
$$\frac{Molecular \ weight}{1} = 158/1 = 158$$

For neutral = 158/3 = 52.6
For acidic = 158/5 = 31.6
The standardization of $KMno_4$ solution is based on the following equation.
$2KMno_4 + 5H_2C_2O_4 + 3H_2So_4 \rightarrow 3K_2SO_4 + 2MnO_4 + 8H_2O + 10 \ CO_2$

VII. ERROR

Error is an action which means mistake in analytical chemistry the difference between true value, standard value / observe value is called error.

Example:- if a tablet contain 500gm of PCM and after analysis the analyst observe 490 milligram of PCM in the tablet. Then,

Absolute error = 500-490
= 10gm
Percent error = $100 - \frac{490}{500} x \ 100$
= 2% loss

1. **Source of Error:**
   - Sample preparation
   - Error by analyst
   - Equipment problem
   - Calibration (strength)
   - Reporting error (writing)
   - Calculation error
   - Error in method selection
   - Error during transport
   - Storage problem
   - Laboratory environment

2. **Types of Error**
   - Determination error:- systemic error are known to the analyst these are usually one sided and by pre-planning carefully working can be avoided on kept at minimum.
   - These are mainly six types
   - Personal error :- These type of error are caused due to personal mistake and carelessness of the analyst.
   - Instrumental error:- These are due to defects in instruments these are caused due to quality and un calibrated glassware apparatus and Instruments.
   - Reagent error:- These error are depend on the quality of individual reaent.
   - Additive / constant error:- Sometime the value of error is constant in a series determination and is independent amount of taken on analysis , these are termed as additive error.

- Proportional error:- In this type of error the magnitude of the error depends on the size.
- Error in method any error occurred during the method or selection of wrong method.
- **Indetermination/Random Error:-** These error are also known as systematic error or accidental error , sometime the cause of random error may or may not be known.

3. **Method of Minimizing Error :** Error can be minimized by the following technique.

- Calibration of apparatus:- By calibrating all the instruments error can be minimized and appropriate correction are applied to the original measurement.
- Central determination:- Standard substance is used in experiment in identical experiment condition to minimize the error.
- Blank determination:- by omitting sample is determination is carried out
- To maintain accuracy of result independent methods of analysis will be carried out.
- Parallel determination:- Instead of single determination duplicate or triplet determination is carried out to minimize the accidental error.

VIII. ACCURACY AND PRECISION

Accuracy is the degree of agreement between the measured value and the true value and absolute true value seldom is known as the accuracy value to true value or standard value.

Precision is defined as the degree of agreement between replicate measurement of the same quality .it is the repeatability of a result.
The precision may be expressed as the
For example :-

There are two analyst x24 , who determine the % of the PCM in the branch of tablet.
The standard value for PCM in tablet 100.00%
Where, ass they obtain following results

X= 99.8,99.9, 100.00, 99.30
Y= 99.75, 98.75, 98.80,98.80

Average value of $X = \dfrac{99.80+99.90+100.00+99.30}{4}$

$= 99.75$

Average value of $Y = \dfrac{99.75+98.75+98.80+98.80}{4}$

$= 98.775$

X error = 100 - 99.75= 0.25%
Y error = 100- 98.775= 1.225
The different observed value of analyst X differ quite among them, Hence the error is poor but accuracy is fairly good.