ANALYSIS METHODS

Analysis methods can be examined in two groups, qualitative and quantitative analysis methods.

QUALITATIVE ANALYSIS

It is used to determine which element, ion or functional groups a sample consists of (see: Pharmaceutical Chemistry Practices I).

QUANTITATIVE ANALYSIS

It is used to determine the amount of components in a sample.

Quantitative Analysis Methods are classified into two groups according to the method used and the substance to be analyzed.

*Quantitative Analysis Methods according to the substance to be analyzed

- Organic Quantitative Analysis
- Inorganic Quantitative Analysis

*Quantitative Analysis Methods according to the Method Used

- Gravimetric Analysis
- Titrimetric Analysis
- Instrumental Analysis

Gravimetric Analysis

It is a separation method based on the weight.

Separation of the substance to be analyzed from the mixture can be done by three different methods as described below.

a- Separated by simple physical methods, cleaned, dried and weighed.

b- The substance to be analyzed is precipitated by converting it into a water-insoluble compound. The precipitate is separated off, purified and weighed.

c- Volatile substances can be absorbed into a suitable compound.The increase in the weight of the absorbing agent gives the amount of substance.

Gravimetric analysis in pharmacy is most commonly used in the determination of ash, water, chloride, sulfate, magnesium and calcium ions.

Titrimetric Analysis

It is based on the measurement of the volume, so it is also called volumetry. However, because the volume measurement process is mostly done by titration, the titrimetry name is preferred.

Titration: It is the process of finding an unknown concentration of a solution in a given volume, by treating the concentration with a known substance solution containing the substance that is equivalent to the amount of unknown substance in the solution.

"Titration, also known as titrimetry, is a common laboratory method of quantitative chemical analysis that is used to determine the concentration of an identified analyte. Since volume measurements play a key role in titration, it is also known as volumetric analysis. A reagent, called the titrant or titrator is prepared as a standard solution. A known concentration and volume of titrant reacts with a solution of analyte or titrand to determine concentration. The volume of titrant reacted is called titration volume."

- The solutions in certain concentrations used in titrations, called Adjusted or **Standard Solution,**

-The point of completion of the titration is called **Equivalence Point (End point),**

- Auxiliary substances added to the environment for the determination of the Equivalence Point is called **Indicator.**

The equivalence point, or stoichiometric point, of a chemical reaction is the point at which chemically equivalent quantities of bases and acids have been mixed. In other words, the moles of acid are equivalent to the moles of base, according to the equation (this does not necessarily imply a 1:1 molar ratio of acid:base, merely that the ratio is the same as in the equation). It can be found by means of an indicator, for example phenolphthalein or methyl orange.

The endpoint (related to, but not the same as the equivalence point) refers to the point at which the indicator changes color in a colorimetric titration.

The number of milliequivalents (meq) of fully reacted substances are equal. This rule constitutes the basis for quantification methods

* "valence factor" (n factor,"n") is determined as follows:

Class of Compound ,	"Valence factor" (n factor,"n")
Acid,	n is the number of acidic H in case of an acid
Base,	n is the number of OH in case of a base
Salt,	n is the (number of cations x valency of cation) in case of a salt.
Redox Substance,	n is the number of electrons lost or gained in case we are dealing with a reducing agent or oxidizing agent respectively.

So you can convert from molarity to normality simply by knowing the n .

N = M x “n”

HCl	H_2SO_4	NaOH	$Ba(OH)_2$	$CaCl_2$	CH_3COOH	Benzoic acid
“n”=1	“n”=2	“n”=1	“n”=2	“n”=2	“n”=1	“n”=1

For $KMnO_4$; As a salt “n”= 1

In acidic media “n”= 5
In basic media “n”= 3
In strong basic media “n”= 1

meq= m/(MA/”n”) **meq=N x V**

Reactions Based on Titrimetric Analysis Methods

Titrimetric Analysis Methods are divided into two according to their reactions. Combinations of ions or electron transfer reactions.

1- Titrimetric analysis based on the combination of ions

a- Titrations based on the formation of a non-ionizing compound (eg acid-base / neutralization titrations)

b- Titrations based on precipitation (eg, Arjantimetry)

c- Titrations based on complex formation (eg Complexometry)

2- Titrimetric analysis based on electron transfer

a- Adjusted solution of a suitable oxidation agent of a reducing agent, titration of an oxidizing agent with an adjusted solution of a suitable reducing agent (Oxido-reduction titrations), (eg, Permanganimeter, Serimetry, Bromometry, Titanometry, Iodometry, Bromometry, Nitritometry)

b- Titrations based on halogenation (eg Bromometry).

**In order for a compound to be quantified, it must show the following properties.

1-Both substances should be react to the end (quantitative).

2-The reaction should be extremely fast. If the reaction is not fast enough, back titration is carried out (the substance in which it reacts is added in advance, the residue being added is titrated with another solution).

3-No side reactions, uniform reactions.

4-Standard solution should not be react with additives or other substances,

5-Indicator selection should be appropriate.

Indicators

Indicators are divided into two as internal and external indicators.

a- *Internal indicators*; are the indicators added to the reaction medium from the outside during the reaction,

b- *External indicators;* are the process by which the reaction medium is treated with an indicator outside the reaction medium (eg, the outer starch paper used in nitriteometric titrations is an external indicator).

Indicators used in acid-base titrations

Indicators such as phenolftalein, methyl orange, bromphenol blue, bromine cresol green, methylene red are examples for this.

Indicator	*Color change pH range*
Methyl orange	3.1-4.4
Phenol ftalein	8.0-10.0
Methylene red	4.2-6.3

When selecting the indicator, it is necessary to select an indicator to give color change at the pH of about 0.1% before the equilibrium point.

Indicators used in redox titrations

KMnO4 (autoindicator)and starch are examples of these indicators.

Solutions Used in Titrimetry

Concentrations are expressed in terms of normality.

Molarity (M) is defined as the number of moles of solute per liter of solution. (Molarity is a measurement of the moles in the total volume of the solution)

molarity = moles of solute/liters of solution

Normality (N) is defined as the number of mole equivalents per liter of solution:

normality = number of mole equivalents/1 L of solution

Like molarity, normality relates the amount of solute to the total volume of solution; however, normality is specifically used for acids and bases.

How to calculate normality from molarity

The mole equivalents of an acid or base are calculated by determining the number of H+ or OH- ions per molecule:

N = “n” × M (where n is an integer)

For an acid solution, “n”(valence factor) is the number of H+ ions provided by a formula unit of acid.

Example:

**A 3 M H_2SO_4 solution is the same as a 6 N H_2SO_4 solution.

For a basic solution, “n” is the number of OH^- ions provided by a formula unit of base.

Example:

A 1 M $Ca(OH)_2$ solution is the same as a 2 N $Ca(OH)_2$ solution.

Note: The normality of a solution is NEVER less than its molarity!

% Solutions: a / a, a / h or h / h.

a / a: The amount in grams of 100 grams of solution,

a / h: amount in grams of 100 ml solution,

h / h: The amount in milliliters per 100 ml of solution.

Preparation of Standard Solutions

If the standard solution is pure, the solution can be prepared in full normality. To do this, we weight 1 Ekivalan grams to complete the desired volume, but cannot prepare a complete normal solution of when there are impurities. After preparation of solutions which have impurities, substances known as primary standards are used to find the true normality. The primary standard is a substance which is used as a reference substance in titrimetric methods and has a high purity. A certain amount of the primary standard is titrated with the prepared solution and the factor indicated by the normality regulator “f” is calculated.

Factor x normality = returns true normality. If “f “ is less than 1, the solution is more dilute than normal, and if “f” is greater than 1, the solution is more concentrated than normal.

The requirements for the primary standard are:

1- The molecular weight must be large (in order to reduce the error due to weighing),

2- The reaction with the solution to be adjusted should be known,

3- Quantitative (end to end) reaction with the solution to be adjusted,

4- It should be very pure.

Example; 0.5 g of the primary standard substance was dissolved in a suitable solvent and titrated with solution B to determine the factor; The amount of solution B that needs to be spent gives theoretical consumption.

(Molecular Weight of primary standard= 232, n factor =1)

If , 1 lt 1 N (B solution) *reacts with* 232 g (molecular weight/n factor)
primary standard substance

X ml 1 N (B solution) 0.5 g primer standard

X= **0.0021 lt** (2.1 ml) Solution B must be consumed **(Theoretical Consumption)**

The amount of solution B spent in titration is **2.2 ml (Practical Consumption),**

Factor (f)= **Theoretical Consumption** / **Practical Consumption**

f = 2.1 / 2.2

f = 0.9590

Factor Usage:

It will be used to determine the amount of matter. (% purity determination)

When weighing A g from substance Y and titrating with the "f" determined solution B, the solution is spent Z ml;

1 lt	**1 N** (B solution)	is equivalent to	**C g** (M.A/n) Y substance
Z ml	**1 Nx f** (B solution)	is equivalent to	**? g** Y substance.

? = **C g x Z mlx f**

If **? g** is pure of **A g** Y substance

X **100 g** Y substance

X= **Purity %**

Example: To calculate the true normality of 0.5 N HCl solution, take 0.50 g of full weight Na2NO3 (primary standard) and dissolve in 100 ml of water. In the indicator of methyl red, titrate up to pink with a 0.5 N HCl solution. Calculate the true normality of 0.5 N HCl solution as 10 ml is spent in titration. (C:12 O:16 Na:23 N:14)

Example: If 500 ml 0.2 N sodium nitrite solution has a factor of 0.9755, find the amount of sodium nitrite contained in this solution. (O: 16 Na: 23 N: 14)

Tablet Calculations

1 ml **b N** (solution A) is equivalent to **C g** (Molecular Weight / n) active substance of the tablet

X ml **b N** (solution A) is equivalent to **Z g** active substance of the tablet

1 Tablet weight (D gram) = Total tablet weight / number of tablets

1 Tablet weight	1 Tablette olması gereken etken madde miktarı
Y gram (Sizin tartımınız)	E gram Tablet etken maddesi içeriyorsa

1 Tablet weight amount of active ingredient which should be on one tablet

Y gram (Your weight) contains **E gram** Tablet active substance

Purity% :

E g	**Zg**
100	**X**

Question: It is known that the amount of active substance in the tablet is 500 mg. 10 of these aspirin tablets are weighed and it is 6.57 g. This 10 tablets powdered and 754 mg of sample is taken from this. 25 ml 0.5 N NaOH is added and titrated with 15 ml of 0.5 N HCl in the presence of phenol ftalein indicator. What is the purity of aspirin tablet according to this?