National University –SUDAN

Faculty of Clinical and Industrial Pharmacy

Second Year (**Batch-PA-14**)-Semester Four

Professional Skills-2- Laboratory Skills-1

(**PA-SKILL-221**)

Course Coordinator: Us. Maria M. Elamin Hamid,

M.Sc. Pharmaceutical Analysis and Quality Control

Email: chocoroy991@gmail.com

Phone Number (**00249-913714903**)

Standardization and Titration

Practical, No-4

Objectives

By the end of this lesson the student is expected to understand

1- To define standard solutions

2- To demonstrate Acid-Alkali titrations

3- To calculate concentrations of solution in volumetric analysis

4- To practice on writing a laboratory report on volumetric analysis

Standardization of sodium hydroxide NaOH solution with standard solution of hydrochloric acid HCl

Features of an accurate quantitative process

- The key features of an accurate quantitative process are as follows…
- To perform an accurate quantitative analytical process first of all we need two thing, they are –
- A representative sample &
- An appropriate methodology.

How Do We Express Concentrations of Solutions?

- Molarity (M)= moles/liter or mmoles/mL
- Normality(N) = equivalence/liter or meq/mL
- Formality(F)= is identical to molarity
- Molality(m) = moles/1000g solvent

Expression of Analytical Results
So Many Ways

- **Solid Samples:**
- %(wt/wt) = (wt analyte/wt sample)x 10^2 %
- ppm(wt/wt) = (wt analyte/wt sample)x 10^6 ppm
- ppb(wt/wt) = (wt analyte/wt sample)x 10^9 ppb
- **Liquid Samples**
- %(wt/vol) = (wt analyte/vol sample mL)x 10^2 %
- ppm(wt/vol) = (wt analyte/vol sample mL)x 10^6 ppm
- ppb(wt/vol) = (wt analyte/vol sample,mL)x 10^9 ppb

Example
Percentage weight in sample

- How many grams of dextrose are required to prepare 4000 ml of a 5% solution?
- Solution
- $5/100 \times 4000 = 200g$

EXAMPLE
Volume in Volume

- How many milliltres of liquified phenol (2.5%) in 240 ml of Calamine lotion should be used in compounding prescription for eye drop?
- Solution
- Volume of liquified phenol=2.5/100x240=6ml

Percent weight in weight

- How many grams of phenol should be used to prepare 240 gram of a 5% (w/w) solution in water?
- Solution
- 5/100x240=12.0g

Name	Defining Units
Molarity (e.g. 0.1200 M)	moles of solute/liter (solutions), or millimoles/milliliter (solutions)
Percent (e.g. 23.45 %)	(grams of substance/grams of sample) x 100%
Parts per million (e.g 2.34 ppm, 2.34 mg/L)	milligrams/liter (solutions), or micrograms/milliliter (solutions) milligrams/kilogram (solids), or micrograms/gram (solids)
Parts per billion (e.g. 0.45 ppb, 0.45 ug/L)	micrograms/liter (solutions), or nanograms/gram (solids)

Calculation of equivalent weight

- For HCl
- HCl+NaOH=NaCl+H2O
- HCl=NaOH=H
- 36.47=1000MLN1
- Sodium carbonate
- $Na2CO_3$+2Hcl= 2NaCl +CO2+H2O
- 106=2000ML, N1Hcl
- 53=1000ml

- **Calculate the number of equivalents in 220 grams of H_3PO_4**
- [the gram molecular weight of H_3PO_4 =98 gmw
- [Divide the gmw by the valence (which is 3 due to the +3 charge on the 3 H's)
- $\frac{98\text{ g}}{3\text{ eq}}$ = 32.6 g/Eq
- **equivalents** $\frac{220\text{ g}}{32.6\text{ g}}$ = ***6.74 eq***

- **What is the normality of a solution containing 149 grams of H_2SO_4 in 900 ml**
- the gram molecular weight of H_2SO_4 =98 gmw
- Divide the gmw by the valence (which is 2 due to the +2 charge on the 2 H's)
- Equivalent= $\frac{98\ g}{2\ Eq}$ = 49 g/Eq
- Figure out how many equivalents are in 149 grams of H_2SO_4
- No. of equivalents= $\frac{149\ g}{49\ g/eq}$ = 3.04 eq
- Normality = $\frac{\text{equivalents}}{\text{liters}}$ **(Don't forget to change ml to liters!!)**
- Normality = $\frac{3.04\ eq}{0.9\ L}$ = ***3.38 N***

Dilutions
Preparing the Right Concentration

- The millimoles taken for dilution will be the same as the millimoles in the diluted solution.
- $M_{stock} \times mL_{stock} = M_{diluted} \times mL_{diluted}$

Preparation of standard solution of Na_2CO_3 (0.IN):

1- Weigh out accurately 1.325gm of A.R. Na_2CO_3.

2- Dissolve in small quantity of distilled water and transfer quantitatively to 250ml measuring flask.

3- Complete to the mark and shake well.

4- Calculate the exact normality of Na_2CO_3 solution.

Weight required = Normality x eq.wt. x volume in liter.

Volumetric Analysis - Principles Standard Solutions

- "Primary Standard " –
  - highly purified compound used as a reference material in titrimetry
- Properties:
- High purity
- Stable
- Independent of relative humidity
- Readily available
- Reasonable solubility
- Large formula weight

Volumetric Analysis - Principles Standard Solutions

- "Secondary Standard"
  - do not meet requirements for a primary standard but are available with sufficient purity and properties to be generally acceptable
- Desirable properties of a Standard Solution:
- Prepared from primary standard
- Stable
- Reacts rapidly and completely with analyte
- Reacts selectively with analyte

Volumetric Analysis - Principles
Examples of Standard Materials

- **Primary**
- Potassium Acid Phthalate
- $KHC_8H_4O_4$ (FW 204.23)
- Benzoic Acid
- C_6H_5COOH (FW 122.12)
- Na_2CO_3
- Arsenious Oxide (As_2O_3)
- Sodium Oxalate ($Na_2C_2O_4$)
- KI , $K_2Cr_2O_7$, Fe(pure)

- **Secondary**
- NaOH , KOH , $Ba(OH)_2$
- HCl , HNO_3 , $HClO_4$
- Sulfamic Acid (HSO_3NH_2)
- $KMnO_4$, $Na_2S_2O_3$

Volumetric Analysis - Principles

- **Acid – Base**
- $HA + B \rightarrow BH^+ + A^-$
- **Precipitation**
- $M^{n+} + X^- \rightarrow MX_n$
- **Complexation**
- $M^{n+} + Q \rightarrow M(Q)^{n+}$ use standard Q solution
- **Oxidation-Reduction**
- $Red_1 + Ox_2 \rightarrow Ox_1 + Red_2$

- **Titrimetry**” – determination of **analyte** by reaction with measured amount of standard reagent. **Titration**” is the slow addition of titrant to analyte solution from a volumetric vessel (burrette).
- **titrant** $\rightarrow$ the reagent added to a solution containing the analyte
- **Types**
  - **<u>Acid – Base</u>**
  - **<u>Precipitation</u>**
  - **<u>Complexation</u>**
  - **<u>Oxidation-Reduction</u>**

TITRIMETRY

- **Requirements** for a useful titration procedure:
- reaction must have a large equilibrium constant (i.e., go to completion)
  reaction must proceed rapidly to a stable and well defined equivalence point.
  reaction must have an easily detectable end point
- The reaction should be nearly complete at the equivalence point. In other words, chemical equilibrium favours products.

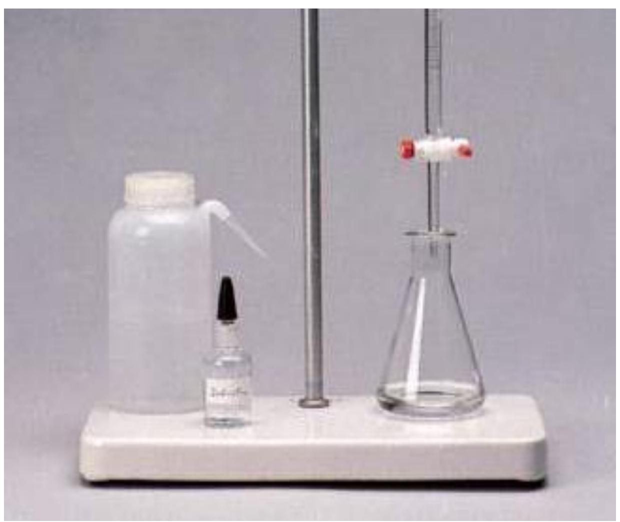
Volumetric Analysis - Principles

- "**Titrimetry**" – determination of **<u>analyte</u>** by reaction with measured amount of standard reagent
- "Standard Solution" (**<u>titrant</u>**) – reagent of known concentration
- "**Titration**" – slow addition of titrant to analyte solution from a volumetric vessel (burrette)
- "**Equivalence Point**" – reached when amount of added titrant is chemically equivalent to amount of analyte present in the sample.
- "**End Point**" – the occurrence of an observable physical change indicating that the equivalence point is reached. Might differ from Eq.Pt.!

In a ***titration*** a solution of accurately known concentration is added gradually added to another solution of unknown concentration until the chemical reaction between the two solutions is complete.

Equivalence point – the point at which the reaction is complete

Indicator – substance that changes color at the **endpoint** (hopefully close to the equivalence point)



Slowly add base to unknown acid

UNTIL

The indicator changes colour

- The endpoint is approached directly but cautiously, and finally the titrant is added dropwise from the buret in order that the final drop added will not overrun the endpoint. The quantity of the substance being titrated may be calculated from the volume and the normality or molarity factor of the titrant and the equivalence factor for the substance given in the individual monograph.

Acidimetry and Alkalimetry

General Concepts

Acid-base titration neutralization titration

Acid–base titrations are routinely used for both qualitative and quantitative measurements in pharmaceutical analysis. Titration methods are also utilized to determine fundamental physical constants, such as the equilibrium constants and molecular weights of acids and bases.

THEORY OF ACIDIMETRY

- Acidimetry, essentially involves the direct or residual titrimetric analysis of alkaline substances (bases)
- employing an aliquot of acid and is provided usually in the analytical control of a large number of substances
- included in the various *official compendia. Examples :*
- (*a*) ***Organic substances : urea, sodium salicylate, diphenhydramine, emetine hydrochloride,*** meprobamate, paramethadione, pyrazinamide etc., and
- (*b*) ***Inorganic substances : sodium bicarbonate, milk of magnesia, ammonium chloride, calcium***
- hydroxide, lithium carbonate, zinc oxide etc.
- The *two methods, namely : direct titration method and residual titration method are briefly discussed*

(I) Determination of the normality of hydrochloric acid by a standard solution of sodium carbonate (0.IN).

Theory:

Sodium carbonate reacts with hydrochloric acid according to the following equation:

$Na_2CO_3 + 2HCl = 2NaCl + CO_2 + H_2O$

In other words, to neutralize all the carbonate, two equivalent of HCl should be used and as such the equivalent weight of sodium carbonate = M.wt/2 =53 When one equivalent of HCl is added to the carbonate it is transformed into bicarbonates.

$Na_2CO_3 + HCl = NaHCO_3 + NaCl$ ph.ph.

And the pH of the solution changes form 11.5 (alkaline) to 8.3. When phenolphthalein is used, it changes to colorless at the end of this stage as its color range falls within the same zone. ph.ph (8.3-10).

When another equivalent of HCl is added to the solution of bicarbonate, complete neutralization takes place and it is transformed into sodium chloride and CO_2 gas is evolved.

$NaHCO_3 + HCl = NaCl + H_2O + CO_2$ M.O.

The pH of solution changes from 8.3 to 3.8, which is near enough to the color range of M.O. (3.1-4.4). If methyl is used at this stage, the color of the solution changes from yellow to red. It thus follows that ph.ph. is used in the neutralization of HCl with sodium carbonate, the volume of acid used will be equivalent to half of the carbonate, when methyl orange is used in this titration the volume of acid used will be equivalent to all carbonate. Methyl orange is generally used in this as ph.ph. is sensitive to carbon dioxide.

Materials:

Sodium carbonate solution (standard).

HCl solution of unknown normality.

Procedure:

Transfer 10 ml of the sodium carbonate solution with a pipette to a conical flask then add one or two drops of M.O. to this solution.

Add the acid (HCl) from the burette gradually with continuous stirring of the solution in the conical flask, and near the end point, the acid is added drop by drop. Continue the addition of the acid till the color of the solution passes from yellow to orange.

Repeat the experiment three times and tabulate your results then take the mean of the three readings.

Repeat the experiment using ph.ph. which changes its color from red to the colorless at the end point. Compare the results in this case with those in the case of M.O.

Calculations:

In case of M.O.

Suppose that the volume of HCl is V_1 and its normality is N_1 while V_2 is the volume taken from sodium carbonate and N_2 is its normality.

The volume of HCl (from burette) ≡ all carbonate = V_1

$$N_1 V_1(HCl) = N_2 V_2(Na_2CO_3)$$

Or $$N_1 = N_2 V_2/V_1$$

In case of ph.ph.

The volume of HCl (from burette) ≡ 1/2 carbonate

The volume of HCl ≡ all carbonate = $2V_1$

$$N_1 2V_1 = N_2 V_2$$

Or $$N_1 = N_2 V_2 / 2V_1$$

And as the strength in gm/L = normality x eq. wt.

Strength of HCl = $N_1 \times 36.5$ *g/L*

For more Information watch video P-4