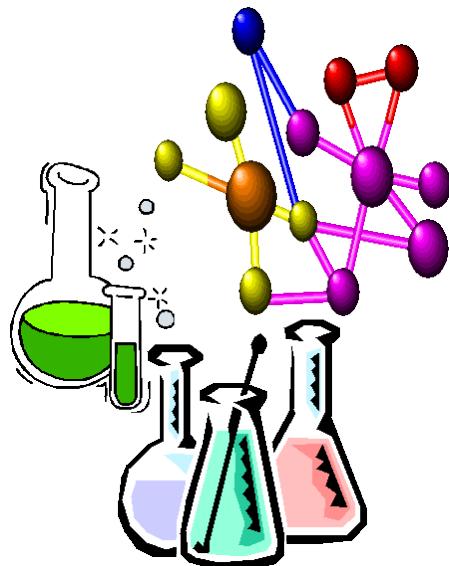


# Practical Medicinal Chemistry

Third year



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## Analytical chemistry

1. **Qualitative:** study and determine the type of materials
2. **Quantitative:** study the quantity of materials

### Types of analytical methods

1. **Volumetric analysis:** the volume of the solution of known concentration is measured that required to react with the analyte.
2. **Gravimetric analysis:** the weight of the reagent is measured.
3. **Coulometric :** the reagent is direct electrical current needed to react completely with the analyte. The time required to complete the electrochemical reaction is measured.

**Standard solution:** is the solution of known normality or molarity.

**Primary standard:** is ultra pure compound that serve as reference material in the titration analysis and its properties are:

1. Highly pure
2. stable atmospherically
3. has no water of hydration
4. low cost
5. good solubility in the titration medium
6. reasonable molecular weight to avoid weighing error

**Secondary standard:** is a compound whose purity has been established by chemical analysis and can serve as reference material in the titremetric analysis.

**Titration:** is the process of adding slowly the standard reagent to the analyte until the reaction is judged to be complete.

**Equivalent point (theoretical):** is the point in the titration when the amount of the standard reagent is equivalent to the amount of the analyte.

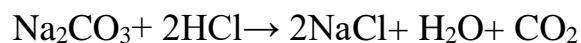
**End point** (experimental or practical): is the point in the titration when physical change occurs that is associated with chemical equivalence.

## Experiment No.1: Preparation and standardization 0.1N Hydrochloric acid

### Introduction:

Standardized solution is a solution of known normality and molarity. Standardization is a process (titration with standard solution) used to determine the normality or molarity of solution.

### Chemical equations:



### Procedure:

Preparation of 0.1N HCl: Dilute 2.2 ml of HCl to 250 ml.  
Standardization of 0.1N HCl: Fill the burette with 0.1N Na<sub>2</sub>CO<sub>3</sub> (primary standard solution which is prepared by weighing exactly 1.325g of Na<sub>2</sub>CO<sub>3</sub> and dilute it to 250ml of distilled water in a volumetric flask). Transfere 10 ml of the prepared HCl solution into a conical flask then add 2 drops of methyl orange as indicator. Orange color is obtained. Titrate with Na<sub>2</sub>CO<sub>3</sub> standard solution drop wise with mixing after each addition until a yellow color is obtained.

### Calculation:

How to prepare 250ml of 0.1N HCl?

$$N(HCl) = \frac{s.g * \% \frac{W}{W} * 1000}{Eq\ wt\ of\ HCl}$$

s.g of conc. HCl= 1.18

M.wt of HCl= 36.5g

The %w/w of HCl from the reagent bottle

NV( conc. HCl)= NV(dil. HCl)

Determination of the normality of the prepared HCl solution:

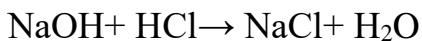
NV(HCl)= NV(Na<sub>2</sub>CO<sub>3</sub>)

## **Experiment No. 2: Preparation and standardization of 0.1N Sodium hydroxide**

### **Introduction:**

NaOH Is hygroscopic substance, can't be prepared as primary standard solution.

### **Chemical equations:**



### **Procedure:**

Preparation of 0.1N NaOH: Dissolve 0.4g of sodium hydroxide in 100 ml distilled water, the solution is standardized with previously prepared standardized hydrochloric acid.

Standardization of 0.1N NaOH: 10 ml of the prepared 0.1N NaOH solution is transferred to conical flask then add 2 drops of phenolphthalein indicator the color becomes pink then titrate with standardized 0.1N HCl solution until colorless solution is obtained.

### **Calculation:**

How to prepare 100ml of 0.1N NaOH?

$$N = \frac{wt}{Eq. wt} \times \frac{1000}{Vol}$$

Determination of the normality of the prepared NaOH solution:

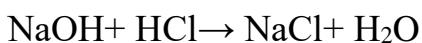
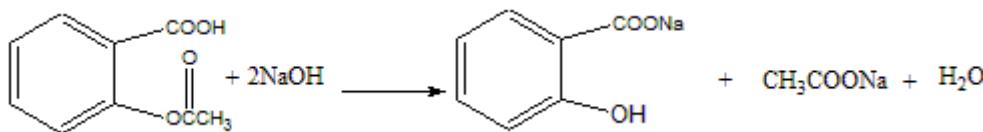
$$NV(\text{NaOH}) = NV(\text{HCl})$$

## Experiment No. 3: Assay of Aspirin

### Introduction:

Aspirin is acetylsalicylic acid  $\text{CH}_3\text{COOC}_6\text{H}_4\text{COOH}$  used as analgesic, antipyretic, and anti-inflametory agent, also used as antiplatelet to prevent clot formation within blood vessel. M. wt 180.1g

### Chemical equations:



### Procedure:

Weigh accurately 1.5g of the aspirin sample, add 50ml of 0.5N NaOH standard solution (secondary standard), boil gently for 10 minutes and cool. Titrate the excess of NaOH with 0.5N HCL using phenol red as indicator, the color changes from pink to colorless, the difference between the two volumes represents the alkali required for hydrolysis of aspirin.

## Calculation:

Calculate weigh of aspirin in the sample

Each ml of 0.5 N NaOH is equivalent to 0.04504g of aspirin.

## Experiment No. 4: Assay of Borax

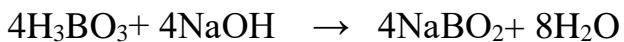
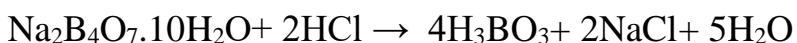


### Introduction:

*Mannitol*

Borax is sodium tetra borate,  $\text{Na}_2\text{B}_4\text{O}_7 \cdot 10 \text{H}_2\text{O}$ . is either pure or contaminated with sodium carbonate and with free boric acid. M. wt 381.4g, Medicinally used as antiseptic.

### Chemical equation and principle:



Titrate the Borax with 0.5N HCl using methyl red as indicator, boric acid is librated which is very weak acid and the indicator would not work. Mannitol is added to complex the boric acid which will increase the acidity so it can directly be titrated with NaOH. The solution should be boiled to remove  $\text{CO}_2$  (in the presence of  $\text{CO}_2$  the end point might be not sharp).

### Procedure:

Weigh accurately 1 g of Borax, dissolve in 20 ml water, titrate with 0.5N HCl using 2 drops of methyl red as indicator, the color changes from yellow to pink. Record the volume required, (this volume required to convert Borax to boric acid) boil and cool the solution, add 5g of mannitol and titrate with 1N sodium hydroxide using phenolphthalein as indicator.

### **Calculation:**

Calculate weigh of Borax in the sample

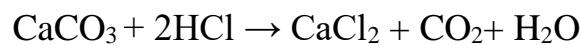
Each ml of 1N sodium hydroxide is equivalent to 0.09534g of  $\text{Na}_2\text{B}_4\text{O}_7 \cdot 10\text{H}_2\text{O}$ .

## **Experiment No. 5: Assay of Calcium carbonate tablet**

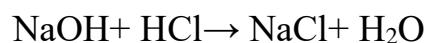
## Introduction:

Calcium carbonate  $\text{CaCO}_3$  is water insoluble. M.wt 100.4g, is used medicinally as calcium supplement and antacid.  $\text{CaCO}_3$  is the main cause of water hardness.

## Chemical reactions:



(water insoluble) (water soluble)



## Procedure:

Grind to fine powder and weigh accurately 2g, add to the powder 100 ml of distilled water then add 50 ml of 1N HCl, boil to remove  $\text{CO}_2$  then cool and filter the solution. Titrate the excess of acid with 1N NaOH using methyl orange solution as indicator, the color changes from red to yellow after reaching the end point.

## Calculation:

Calculate weight of  $\text{CaCO}_3$  in the sample

Each ml of 1N HCl is equivalent to 0.05004g of  $\text{CaCO}_3$ .

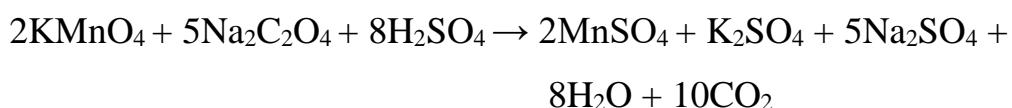
# Experiment No. 6: Preparation and standardization of 0.1N Potassium permanganate

## Introduction:

Potassium permanganate  $KMnO_4$  is strong oxidizing agent widely used in the experimental lab for this purpose.  $KMnO_4$  readily oxidizes any organic material present in the water. Medicinally used as antiseptic, it has antibacterial and antifungal properties.

## Chemical reactions:

Potassium permanganate can be standardized by titrating it with sodium oxalate (reducing agent and primary standard).



## Procedure:

Preparation of 0.1N  $KMnO_4$  : Dissolve 3.3g of  $KMnO_4$  in 1000 ml of distilled water in stoppered flask. Standardization of 0.1N  $KMnO_4$  : Weigh 0.2g of sodium oxalate then transfer it to conical flask, add 250 ml of distilled water and 7 ml of concentrated  $H_2SO_4$ . Heat about 50 ml of 0.1N  $KMnO_4$  solution and filter it (using glasswool and funnel) directly to the burette, then start titration (sodium oxalate with potassium permanganate) until the color of  $Na_2C_2O_4$  solution changes from colorless to pink and

persists for at least 2 minutes (reaching the end point). The tempreture should be not less than 60C° during the titration.

## Calculation:

Preparation of 0.1N KMnO<sub>4</sub> solution:

$$N = \frac{wt}{Eq wt} \times \frac{1000}{V}$$

Standardization of 0.1 N KMnO<sub>4</sub> solution:

$$NV(\text{Na}_2\text{C}_2\text{O}_4) = NV(\text{KMnO}_4)$$

## Experiment No. 7: Assay of Ferrous sulfate

### Introduction:

Ferrous sulfate  $\text{FeSO}_4$  is a reducing agent, medicinally used in the treatment and prevention of iron deficiency anaemias. M.wt 151.91g

### Chemical equation:



### Procedure:

Weigh accurately 2 g of ferrous sulfate powder then add 20 ml of diluted sulfuric acid. Titrate with 0.1N potassium permanganate standard solution, color changes from colorless to pink at the end point.

### Calculation:

Calculate the weigh of ferrous sulfate in your sample

Each ml of 0.1N potassium permanganate is eqivalent to 0.01519g of  $\text{FeSO}_4$

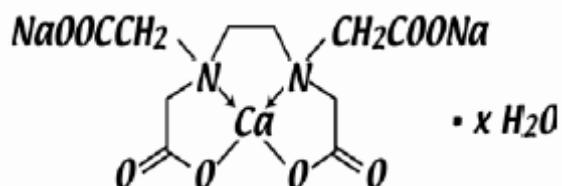
# Experiment No. 8: Determination of water hardness

## Introduction

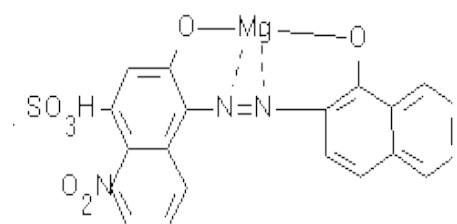
The determination of water hardness is a useful test that provides a measure of quality of water for households and industrial uses. Water hardness was defined as the measure of the capacity of the water to precipitate soap. Hard water is not a health hazard. Hard water does cause soap scum, clog pipes and boilers.

Soap scum is formed when calcium ion binds with the soap. This causes an insoluble compound that precipitates out producing the scum.

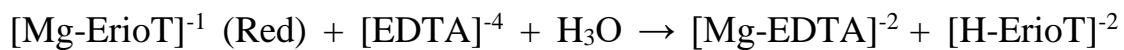
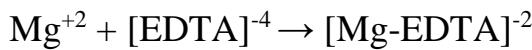
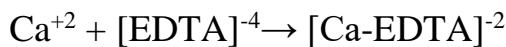
## Calcium disodium editate structure



## Magnesium-Eriochrome Black T complex



## **Chemical equation:**



(Blue) + H<sub>2</sub>O

## **Procedure**

Take 50 ml of tap water ( hard water) then add 5 ml of M/20 MgSO<sub>4</sub> and 10 ml of strong ammonia ammonium chloride solution, and titrate with M/20 of disodium editate using Eriochrome Black T as indicator (color changes from red to blue at the end point).

## **Calculation**

Calculate the amount of CaCl<sub>2</sub> in the water sample.

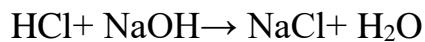
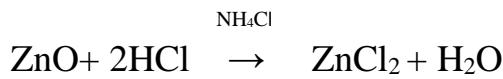
From the volume of M/20 disodium editate required subtract the volume of M/20 of MgSO<sub>4</sub> added, each ml of the remainder is equivalent to 0.01095g of CaCl<sub>2</sub>.6H<sub>2</sub>O.

## Experiment No. 9: Assay of Zinc oxide

### Introduction:

Zinc oxide ZnO is water insoluble, M. wt 81.37g. It is astringent and it has antibacterial properties, used topically to relief skin irritation caused by e.g. diaper rash or minor burns.

### Chemical equation:



### Procedure:

Dissolve 1.5g accurately weighed and 2.5g ammonium chloride in 50 ml of 0.1N HCl and titrate the excess of acid with 0.1N NaOH using methyl orange solution as indicator.

### Calculation:

Each ml of 0.1N HCl is equivalent to 0.04068 of ZnO.

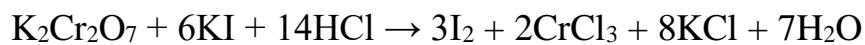
## Experiment No. 10: Preparation and standardization of 0.1N Sodium Thiosulphate solution

### Introduction

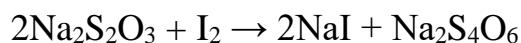
White granular compound M.wt is 248, freely soluble in water, medicinally used as antifungal.

### Chemical principle

Potassium dichromate is an oxidizing agent, it is reduced by excess KI in acidic media and an equivalent amount of iodine is formed. The liberated iodine is titrated with sodium thiosulphate solution using starch indicator. This indirect procedure is known as iodometry.



Excess



Sodium tetrathionate

### Procedure

Dissolve 26g of sodium thiosulphate and 200mg of sodium carbonate in 1000ml of recently boiled and cooled water.

#### Standardization

Weigh accurately about 200mg of primary standard potassium dichromate ( $\text{K}_2\text{Cr}_2\text{O}_7$ ) previously dried at  $120^\circ\text{C}$  for 4 hours and dissolve in 100 ml of

water in a glass stoppered flask, swirl to dissolve the sample, remove the stopper and quickly add 3g of potassium iodide, 2g of sodium bicarbonate and 5ml of concentrated hydrochloric acid. Stopper the flask and swirl to mix and allow to stand in dark place for 10 minutes, rinse the stopper and the inner wall of the flask with water and titrate the liberated iodine with sodium thiosulphate solution until the solution is faintly yellow in color, add starch mucilage and continue the titration to the discharge of the blue color.

## **Calculation**

Calculate the normality of sodium thiosulphate

$$N_1 V_1 = N_2 V_2$$

## **Experiment No. 11: The preparation and assay of aqueous Iodine solution (Lugol's solution)**

### **Introduction**

It contains 5% w/v  $I_2$  and 10% w/v KI, used in pre-operative treatment of thyrotoxicosis.

Lugol's Solution

Iodine	50g
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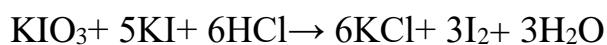
Potassium iodide	100g
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Purified water. Sufficient to produce 1000 ml

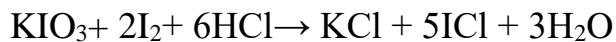
Dissolve the potassium iodide and the iodine in 100 ml of purified water and add sufficient purified water to produce 1000 ml.

### Chemical Principle

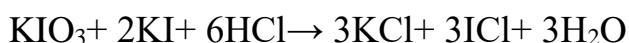
Potassium iodate is fairly strong oxidizing agent, it can react quantitatively with both iodide and iodine. If the concentration of hydrochloric acid does not exceed 1N the reaction between potassium iodate and potassium iodide stops when iodate is reduced to free iodine.



In the presence of concentrated HCl exceeding 4N, the iodine produced by the above reaction is further oxidized to iodine monochloride.



The reaction between Potassium iodate and potassium iodide in the presence of a high concentration of HCl (4N) is expressed by the following equation



### **Procedure**

Dilute 25 ml with water to 100 ml.

### **Assay of Iodine**

To 20 ml of the diluted solution add 10 ml of water and titrate with 0.1N Sodium thiosulphate. Each ml of 0.1N Sodium thiosulphate is equivalent to 0.01259g of iodine.

## **Assay of Potassium iodide**

To 10 ml of diluted solution add 20 ml of water and 40 ml of HCl and titrate with 0.05M Potassium iodate until the dark brown solution which is formed became pale brown, add 1 ml of amaranth solution and continue titration until the red color just changes to pale yellow. From the number of ml of 0.05M Potassium iodate subtract one quarter of the number of ml of 0.1 N Sodium thiosulfate required in the assay for iodine. Each ml of the remainder is equivalent to 0.0166g of KI.

## **Experiment No. 12: Assay of Copper Sulphate**

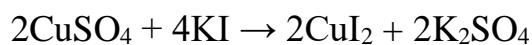
### **Introduction**

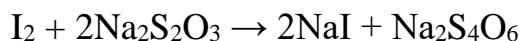
Copper sulphate CuSO<sub>4</sub>.5H<sub>2</sub>O used in Fehling and Benedict reagents. Medicinally used as antifungal and algeside. Mwt = 249.

### **Chemical principle**

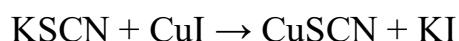
CuSO<sub>4</sub> is treated with excess potassium iodide in acidic media, cupric iodide is formed which is unstable and will break up in to iodide and iodine.

The liberated iodine is titrated with standard sodium thiosulphate solution.





The liberated iodine is adsorbed by the precipitated cuprous iodide. The addition of potassium thiocyanate near the end point forms coprous thiocyanate, and tend to free the adsorbed iodine.



## Procedure

Dissolve about 1g accurately weighed in 50ml of water, add 1.5g of potassium iodide, and 5ml acetic acid, and titrate the liberated iodine with 0.1N sodium thiosulphate using starch mucilage as indicator, and continue the titration until the blue color disappears.

## Calculation

Calculate the amount of  $CuSO_4$ ?

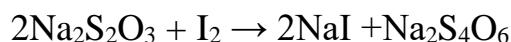
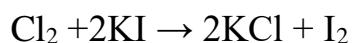
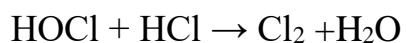
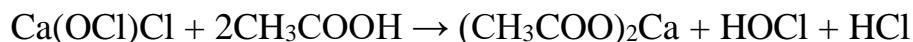
Each ml of 0.1N  $Na_2S_2O_3$  is equivalent to 0.0249g of  $CuSO_4 \cdot 5H_2O$

# Experiment No. 13: Assay of Chlorinated Lime Bleaching Powder, Calcium Chloro Hypochlorite $Ca(OCl)Cl$

## Introduction

It contains not less than 30% w/w available chlorine, white powder with characteristic oder. Used as disinfectant.

## Chemical Principle



Aqueous solution of the substance is treated with acetic acid in the presence of the excess KI. Acetic acid like other acids liberates chlorine from the chlorinated lime and the liberated chlorine displaces an equivalent amount of the iodine from potassium iodide, the iodine produced is titrated with 0.1N sodium thiosulphate using starch mucilage as indicator.

## Procedure

Treat about 4g accurately weighed with successive small quantities of water and transfer to a liter flask.

Dilute to 1000ml with water and shake thoroughly. Mix 100ml of this suspension with a solution of 3g of potassium iodide in 100ml of water, acidify with 5ml of acetic acid, and titrate the liberated iodine with 0.1N sodium thiosulphate.

## Calculation

Calculate the amount of the available chlorine?

Each ml of 0.1N sodium thiosulphate is equivalent to 0.003545g of the available chlorine.

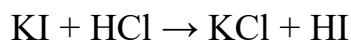
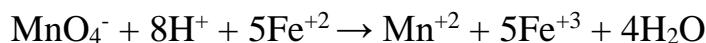
## Experiment No. 14: Assay of Ferric Ammonium Citrate

### Introduction

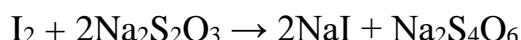
Ferric Ammonium Citrate or Iron Ammonium Citrate is a compound of iron, ammonia and citric acid of undetermined structure. It contains not less than 20.5% W/W and not more than 22.5% of Fe.

### Chemical principle

All the iron is oxidized to the ferric state. The ferric ion then liberates an equivalent amount of iodine from acidified potassium iodide solution.



The liberated iodine is titrated against standard sodium thiosulphate solution.



### Procedure

Dissolve about 0.5g accurately weighed in 15ml of water, add 1ml of sulphuric acid, and warm until the dark brown color becomes pale yellow. Cool to below 20°C and maintain this temperature throughout. Add 0.1N potassium permanganate, drop by drop, until a pink color persists for five

second. Add 15ml of hydrochloric acid and 2g of potassium iodide, set aside for three minutes, add about 60ml of water, and titrate with 0.1N sodium thiosulphate, using starch mucilage as indicator.

## **Calculation**

Calculate the amount of iron?

Each ml of 0.1N sodium thiosulphate is equivalent to 0.005585g of Fe.

# **Experiment No. 15: Assay of Alum**

## **Introduction**

Alum is either Potash Alum, Potassium aluminium sulphate,  $KAl(SO_4)_2 \cdot 12H_2O$ . Mwt =474.4, or Ammonia Alum, Ammonium Aluminium sulphate,  $NH_4Al(SO_4)_2 \cdot 12H_2O$ . Mwt = 453.3.

## Chemical principle

Compleximetric back titration method is an excess of standard disodium editate solution is added to the sample and the resulting solution is buffered to the desired PH and an excess of reagent (EDTA) is back titrated with standard metal ion solution, Lead nitrate solution.

## Procedure

Dissolve about 1.7g accurately weighed in sufficient water to produce 100ml. To 20ml add 30ml of M/20 disodium editate and 100ml of water. Heat on water bath for 10 minutes and cool, then add 5g hexamine, and titrate with M/20 Lead nitrate, using 0.4ml of xylenol orange solution as indicator color will change to purple at the end point.

## Calculation

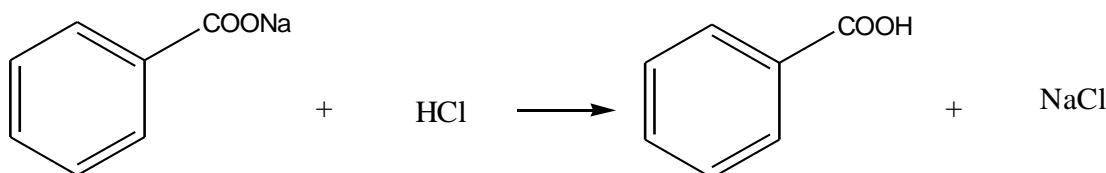
Calculate the amount of the Alum?

Each ml of M/20 EDTA is equivalent to 0.02372g of  $KAl(SO_4)_2 \cdot 12H_2O$  or 0.02267g of  $NH_4Al(SO_4)_2 \cdot 12H_2O$

# Experiment No. 16: Assay of Sodium Benzoate

## Introduction

Sodium benzoate is a salt of strong base and weak acid (alkaline salt). It is used as a preservative in acidic media.



**Sodium benzoate**

Salt of strong base and weak acid,  
Soluble in water and insoluble in organic solvents.

**Benzoic acid**

Weak organic acid,  
slightly soluble in water,  
highly soluble in organic solvents like ether

## Procedure

Dissolve about 3g in 50ml of water and neutralize the solution. If necessary with 0.1N HCl, using phenolphthalein solution as indicator, add 25 ml of solvent ether and few drops (5-6) of bromophenol blue solution and titrate with 0.5N HCl, with constant shaking, until the color of the indicator begins to change. Separate the lower layer, wash the ethereal layer with 10 ml of water, and to the separated aqueous layer add the washings and a further 10ml of solvent ether. Complete the titration with the 0.5N HCl, with constant shaking.

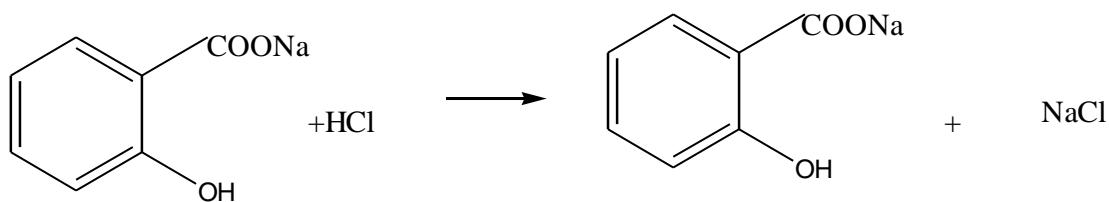
## Calculation

Amount of sodium benzoate?

Each ml of 0.5N HCl is equivalent to 0.07205g of benzoic acid.

## Experiment No. 17: Assay of Sodium Salicylate

Sodium Salicylate assay has the same chemical principle as the assay of sodium benzoate except there is no neutralization.



## Calculation

Each ml of 0.5N HCl is equivalent to 0.08005g of sodium salicylate.

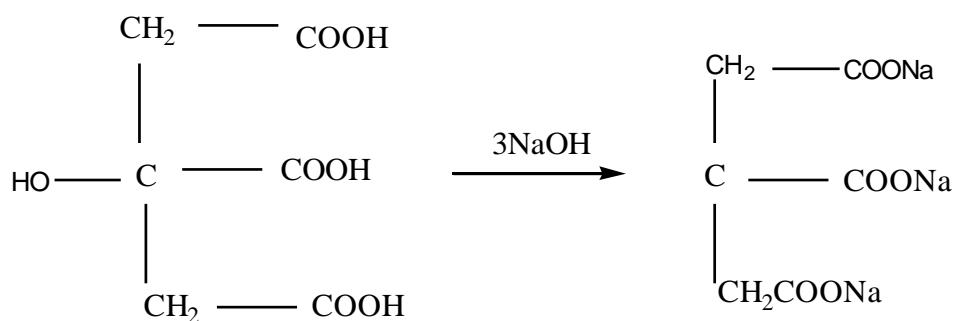
## Experiment No. 18: Assay of Citric acid

### Introduction

Citric acid is tribasic acid. Mwt = 210.1

### Chemical principle

Citric acid is titrated against a standard base like NaOH.



### Procedure

Dissolve about 3 g accurately weighed in about 100ml of water and titrate with 1N NaOH, using phenolphthalein as indicator.

### Calculation

Calculate the amount of citric acid.

Each ml of 1N NaOH is equivalent to 0.07005g of citric acid.

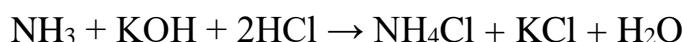
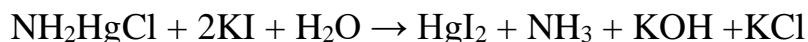
# Experiment No. 19: Assay of Ammoniated mercury $\text{NH}_2\text{HgCl}$

## Introduction

$\text{NH}_2\text{HgCl}$  is also called mercuric chloride, it is present as a white precipitate, odorless, insoluble in water Mwt 252.1. Medicinally used as antiseptic and disinfectants.

## Chemical principle

Ammoniated mercury is assayed by treating a weighed sample with an excess of potassium iodide in water, the total alkali liberated as a result of the reaction is titrated with standard HCl using mixed indicator for the end point detection.



## Procedure

Mix about 0.25g accurately weighed with 50ml of  $\text{H}_2\text{O}$  in a stoppered flask, add 2g of potassium iodide, and shake, until the solution is complete then titrate with 0.1N HCl, using methyl orange – xylene cyanol FF solution as indicator.

## Calculation

Calculate the amount of the Ammoniated mercury?

Each ml of 0.1N HCl is equivalent to 0.0126g of  $\text{NH}_4\text{HgCl}$ .

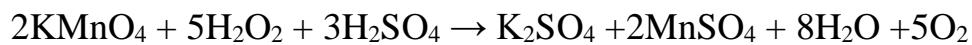
## Experiment No. 20: Assay of Hydrogen peroxide solution

### Introduction

It is an aqueous solution of  $\text{H}_2\text{O}_2$ , colorless, odorless liquid, medicinally used as antiseptic and deodorant.

### Chemical principle

Hydrogen peroxide solution is titrated with potassium permanganate solution in acidic medium at room temperature



### Procedure

Dilute 10ml to 200ml with water, to 20ml of the diluted solution add 5ml of sulphuric acid (50%W/V) and titrate with 0.1N potassium permanganate.

### Calculation

Calculate the amount of hydrogen peroxide?

Each ml of 0.1N potassium permanganate is equivalent to 0.001701g of  $\text{H}_2\text{O}_2$ .

## Experiment No. 21:Nonaqueous titration

Nonaqueous titration is the titration of substances dissolved in nonaqueous solvents. It is the most common titrimetric procedure used in pharmacopoeial assays. The most commonly used procedure is the titration of organic bases with perchloric acid in anhydrous acetic acid.

### Advantages of Non Aqueous Solvent over Aqueous Solvent

- 1) Organic acids and bases that are insoluble in water are soluble in non-aqueous solvent.
- 2) It is suitable for the titration of very weak acids and very weak bases and when the end point is difficult to be detected.
- 3) By the proper choice of the solvents or indicator, the biological ingredients of a substance whether acidic or basic can be selectively titrated.
- 4) Non aqueous titrations are simple and accurate, examples of non aqueous titration are:

Ephedrine preparations, codeine phosphate, tetracycline, Anti- histamines and various piprazine preparations.

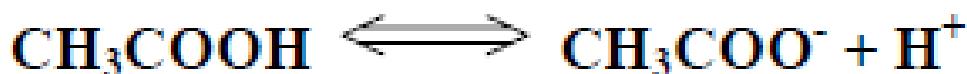
### Solvents for Non Aqueous Titrations

**1. Aprotic Solvents:** Aprotic solvents include those substances, which may be considered chemically neutral, and virtually un-reactive under the conditions employed. Carbon tetrachloride and toluene come in this group; they possess low dielectric constants, do not cause ionization in solutes and do not undergo reactions with acids and bases. Aprotic solvents are frequently used to dilute reaction mixture.

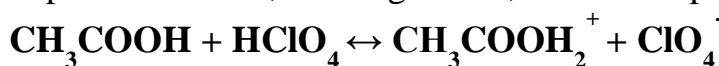
**2. Protophilic Solvents:** Protophilic solvents are the substances that possess a high affinity for protons.  $\text{HB} + \text{S} \leftrightarrow \text{SH}^+ + \text{B}^-$   
The equilibrium in this reversible reaction will be generally influenced by the nature of the acid and the solvent. Weak acids are normally used in the presence of strongly protophilic solvents as their acidic strengths are then enhanced and then become comparable strong acids; this is known as the **levelling effect**.

**3. Protogenic Solvents:** Protogenic solvents are acidic in nature and readily donate protons. Because of these, they enhance the strength of weak bases. Such as hydrogen fluoride and sulphuric acid.

**4. Amphiprotic Solvents:** Amphiprotic solvents consist of liquids, such as water, alcohols and weak organic acids, which are slightly ionized and combine both protogenic and protophilic properties in being able to donate protons and accept protons. Ethanoic acid (acetic acid) displays acidic properties as donating proton:



But in presence of perchloric acid, a stronger acid, it will accept a proton:



The  $\text{CH}_3\text{COO}^-$  ion can very readily give up its proton to react with a base, so basic properties of a base is enhanced, so titrations between weak base and perchloric acid can often be accurately carried out using ethanoic acid as solvent.

\* **Levelling Solvents:** In general, strongly protophilic solvents are important to force equilibrium equation to the right. This effect is so powerful that, in strongly protophilic solvents, all acids act as of similar strength. The converse occurs with strongly protogenic solvents, which cause all bases to act as they were of similar strength. Solvents, which act in this way, are known as **Levelling Solvents**.

## Preparation and standardization of 0.1N perchloric acid $\text{HClO}_4$

### Procedure:

Dissolve 8.5 ml of 72%  $\text{HClO}_4$  in about 900 ml glacial acetic acid with constant stirring, add about 30 ml acetic anhydride and make up the volume (1000 ml) with glacial acetic acid and keep the mixture for 24 hour. Acetic

anhydride absorbed all the water from  $\text{HClO}_4$  and glacial acetic acid and makes the solution anhydrous.  $\text{HClO}_4$  must be well diluted with glacial acetic acid before adding acetic anhydride because reaction between  $\text{HClO}_4$  and acetic anhydride is explosive.

Standardization of the prepared 0.1N  $\text{HClO}_4$  with Potassium acid Phthalate.



To 500 mg of potassium acid phthalate add 25 ml of glacial acetic acid and add few drops of 5% w/v crystal violet indicator. This solution is titrated with 0.1  $\text{HClO}_4$ . The color changes from blue to blue green.

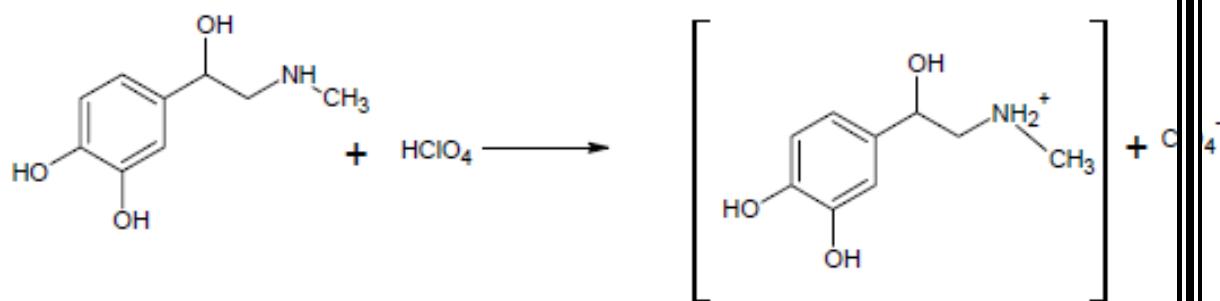
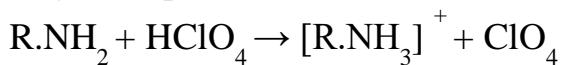
## Calculation

$$N_1 V_1 \text{Potassium acid phthalate} = N_2 V_2 (\text{HClO}_4)$$

Mwt of potassium acid Phthalate = 204

## **Assay of Adrenaline**

The reaction-takes place between a secondary amine and perchloric acid may be expressed as follows:



## Procedure:

Weigh accurately about 0.3 g of sample into a flask; add 50ml glacial acetic acid, warm gently, if necessary. Cool and titrate with 0.1 N perchloric acid using crystal violet as indicator.

### **Calculations:**

The amount of adrenaline present in the sample is given by:

Hence, 183.2 g of  $C_9H_{13}NO_3 \equiv 1000 \text{ ml } 1\text{N of HClO}$

$\rightarrow 0.01832 \text{ g of } C_9H_{13}NO_3 \equiv 1 \text{ ml of } 0.1 \text{ N HClO}_4$

Each ml of 0.1N HClO<sub>4</sub> is equivalent to 0.01832g of adrenaline

## **Assay of Propranolol**

Apply the same as the previous procedure; calculate the amount of propranolol in the sample.

Propranolol ( $C_{16}H_{21}NO_2$ ) Mwt= 259.3

