

THEORY OF ALKALIMETRY

Acidic substances are usually determined quantitatively by methods similar to those used for the quantitative determinations of bases. However, *two* methods are generally adopted for the assay of acidic substances, namely :

(a) **Direct Titration Methods** : It is accomplished by directly titrating an exact quantity of the acid, acid salt or other acidic substance with standard alkali solutions.

(b) **Residual Titration Methods** : It is carried out by the addition of an excess of the standard alkali solution and subsequently determining the amount in excess by residual titration with standard acid solution.

As a general principle, the following guidelines may be observed carefully, namely :

(i) the normality of the solution obtained by dissolving the acidic substance must be approximately the same as that of the titrant,

(ii) the liquid acidic substance to be titrated must be brought to room temperature (25°C) before titration, because many indicators offer different values at different temperatures, and

(iii) the quantity of acid to be taken should be calculated in such a manner that approximately 30 to 40 ml of the previously standardized base shall be utilized for the assay.

Inorganic Acids—for these either methyl red or phenolphthalein may be employed as indicators and the alkali must be standardized with the particular indicator used.

Organic acids—for these phenolphthalein is invariably used, but bromothymol blue, thymol blue and thymolphthalein are also employed as per specific requirements.

Besides, the aforesaid visual methods of assay *i.e.*, observing the change in colour of indicators used, alternative instrumental methods such as : potentiometric, amperometric, polarographic, conducto-metric methods are also employed in determining the end-point.

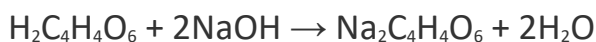
1. DIRECT TITRATION METHOD (DTM)

1.1. Tartaric Acid

Materials Required : 2 g of Tartaric acid ; 1 N sodium hydroxide.

Procedure : Place 2 g of previously dried and accurately weighed sample of tartaric acid in a conical flask. Dissolve it in 40 ml of DW, add a few drops of phenolphthalein indicator and titrate with standardized 1 N sodium hydroxide. Each millilitre of 1 N sodium hydroxide is equivalent to 75.04 mg of $C_4H_6O_6$.

Equation :



(150.09)

From the above equation it is evident that two moles of sodium hydroxide is needed to neutralize one mole of tartaric acid, therefore, the equivalent weight of tartaric acid is 75.04 g. Hence, each millilitre of 1 N sodium hydroxide is equivalent to 0.07504 g (*i.e.*, 1 meq) of tartaric acid.

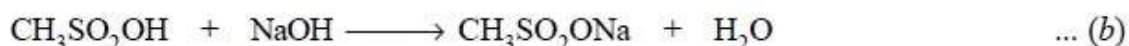
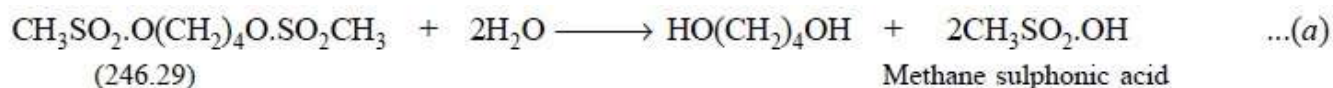
Thus, the percentage of tartaric acid present in the sample is given by :

$$\% \text{ Tartaric Acid} = \frac{\text{ml} \times 1 \times 0.07504 \times 100}{\text{wt. of sample}}$$

1.2. Busulphan

Materials Required : 0.25 g of Busulphan ; 0.1 N sodium hydroxide.

Procedure : Weigh accurately about 0.25 g of busulphan, add 25 ml of DW and boil gently under a reflux condenser for 30 minutes. Wash the condenser with a small quantity of DW, cool and titrate with 0.1 N sodium hydroxide using phenolphthalein solution as indicator. Each millilitre of 0.1 N sodium hydroxide is equivalent to 0.01232 g of $\text{C}_6\text{H}_{14}\text{O}_6\text{S}_2$.



Busulphan is first hydrolyzed by refluxing it with water and two moles methanesulphonic acid (from one mole of Busulphan) thus generated, titrated with 0.1 N sodium hydroxide employing phenolphthalein as indicator. Hence, the equivalent weight of busulphan is 123.145 g. Therefore, each millilitre of 0.1 N sodium hydroxide is equivalent to 0.01232 g of busulphan.

Thus, the percentage of busulphan present in the sample may be calculated as under :

$$\% \text{ Busulphan} = \frac{\text{ml} \times 0.1 \times 0.01232 \times 100}{\text{wt. of sample}}$$

Caution : Busulphan is extremely poisonous. Great care should be taken to avoid inhaling the particles of busulphan or exposing the skin to it.

1.3. Cognate Assays

Benzoic acid ; cellulose acetate phthalate ; chlorpropamide ; ibuprofen ; indomethacin ; nicotinic acid ; oxyphenbutazone ; phosphoric acid ; phenylbutazone and salicylic acid.

S. No.	Name of Substance	Quantity Prescribed	Indicator Employed	Calculations
1.	Benzoic acid	2.5 g	Phenolphthalein	Each ml of 0.5 N sodium hydroxide \equiv 0.06106 g of $C_7H_6O_2$.
2.	Cellulose Acetate Phthalate (For phthalyl groups)	0.4 g	-do-	Phthalyl groups : $\frac{1.49b}{w} - 1.795 S\%$ where, b = ml of 0.1 N NaOH used, w = wt. in g of the sample, calcd. with reference to the anhyd. substance, S = %age of Free Acid.
3.	Chlorpropamide	0.5 g	-do-	Each ml of 0.1 N sodium hydroxide \equiv 0.02767 g of $C_{10}H_{13}ClN_2O_3S$
4.	Citric Acid	3.0 g	-do-	Each ml of 1 N NaOH \equiv 0.06404 g of $C_6H_8O_7$
5.	Frusemide	0.5 g	Bromothymol Blue	Each ml of 0.1 N NaOH \equiv 0.03308 g of $C_{12}H_{11}ClN_2O_5S$
6.	Glibenclamide	0.5 g	Phenolphthalein	Each ml of 0.1 N NaOH \equiv 0.0494 g $C_{23}H_{28}ClN_3O_5S$
7.	Ibuprofen	0.5 g	-do-	Each ml of 0.1 N NaOH \equiv 0.02063 g of $C_{13}H_{18}O_2$
8.	Indomethacin	0.45 g	-do-	Each ml of 0.1 N NaOH \equiv 0.03578 g of $C_{19}H_{16}ClNO_4$
9.	Nicotinic Acid	0.3 g	Phenol Red	Each ml of 0.1 N NaOH \equiv 0.01231 g of $C_6H_5NO_2$
10.	Oxyphenbutazone	0.5 g	Bromothymol Blue	Each ml of 0.1 N NaOH \equiv 0.03244 g of $C_{19}H_{20}N_2O_3$
11.	Phosphoric Acid	1.0 g	Phenolphthalein	Each ml of 1 N NaOH \equiv 0.049 g of H_3PO_4
12.	Phenylbutazone*	0.5 g	Bromothymol Blue	Each ml of 0.1 N NaOH \equiv 0.03084 g of $C_{19}H_{20}N_2O_2$
13.	Salicylic Acid	2.0 g	Phenol Red	Each ml of 0.5 N NaOH \equiv 0.06905 g of $C_7H_6O_3$

*It is almost insoluble in water, hence aqueous acetone is employed as the solvent which helps in reducing the apparent pKa of the acid.

2. RESIDUAL TITRATION METHODS (RTM)

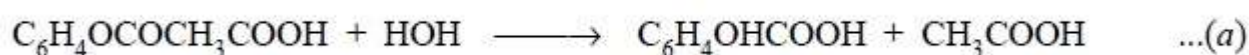
This method is mostly applicable to *official compounds* belonging to the class of esters, acid anhydrides, aldehydes and acid chlorides. In practice this method applies to such substances that normally react too slowly with the titrant because of their poor solubility which may be accomplished either by a heating process or by a precipitation method so as to convert the substance capable for reaction with the standard base.

2.1. Aspirin Tablets

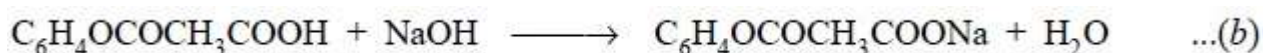
Materials Required : 20 Aspirin Tablets ; 0.5 N sodium hydroxide ; 0.5 N HCl.

Procedure : Weigh and powder 20 tablets. Accurately weigh a quantity of the powder equivalent to about 0.5 g of aspirin, add 30.0 ml of 0.5 N sodium hydroxide boil gently for 10 minutes and titrate with 0.5 N hydrochloric acid using phenol red solution as an indicator. Repeat the operation without the substance being examined, the difference between the titrations represents the amount of 0.5 N sodium hydroxide required by the aspirin. Each ml of 0.5 N sodium hydroxide is equivalent to 0.04504 g of $C_9H_8O_4$.

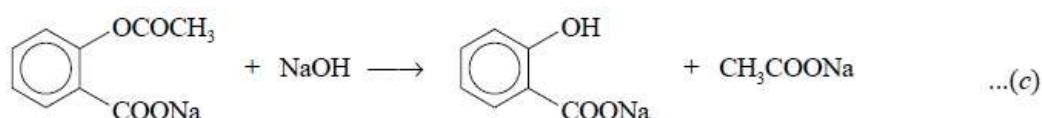
Equations : The aspirin is titrated with sodium hydroxide so as to neutralize any free acid formed by hydrolysis of the acetylsalicylic acid as shown by the following equation :



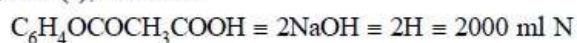
The carbonyl group present in acetylsalicylic acid is subsequently neutralized with NaOH to yield :



Further reaction of aspirin with excess of standard NaOH added followed by heating results in the saponification of the sodium acetylsalicylate as shown below :



From equations (b) and (c), we have :



or $0.04504 \text{ g } C_9H_8O_4 \equiv 1 \text{ ml of } 0.5 \text{ NaOH}$

2.2. Cognate Assays

Lactic acid ; Methyl salicylate ; Nicoumalone.

S. No.	Name of Substance	Quantity Prescribed	Indicator Employed	Calculations
1.	Lactic acid	0.2 g	Phenolphthalein	Each ml of 0.1 N NaOH $\equiv 0.009008 \text{ g of } C_3H_6O_3$
2.	Methyl Salicylate	0.5 g	Phenol Red	Each ml of 0.1 N NaOH $\equiv 0.01522 \text{ g of } C_8H_8O_3$
3.	Nicoumalone	0.6 g	Bromothymol Blue	Each ml of 0.1 N NaOH $\equiv 0.03533 \text{ g of } C_{19}H_{15}NO$