CHAPTER 7

Complexometric Titrations

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During the last two decades, a new method has been developed for the determination of metal ions, which has markedly improved the ease and accuracy of this type of analysis. (The technique involves titrating metal ions with a complexing or chelating agent and is commonly referred to as a
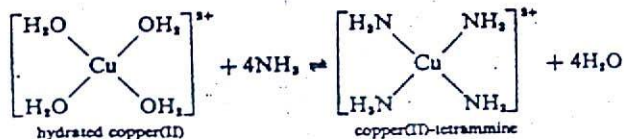
complexometric titration. This procedure represents an analytical application of a complexation reaction; that is, a simple ion is transformed into a complex ion and the equivalence point determined by a suitable method. Various other names, such as chelometric titration, chelometry, chelatometric titration, and EDTA titration, have been used to describe this method. [It should be recognized that all these terms refer to the same analytical technique; they have resulted from the use of EDTA (ethylenediaminetetraacetic acid) and other chelons as titrants and from the fact that these chelons react with metal ions to form a special type of complex known as a chelate.])

7.1 INTRODUCTION TO COMPLEXOMETRIC TITRATIONS

A. COMPLEXES AND CHELATES

(Metal ions in solution are always solvated; that is, a definite number of solvent molecules (usually two, four, or six) are firmly bound to the metal ion. However, these bound molecules are replaced by other molecules or ions during the formation of a metal complex or metal coordination compound. Molecules or ions which displace the solvent molecules are called *ligands.*) (Ligands or complexing agents can be any electron-donating entity which has the ability to bind with a metal ion producing a complex ion.) Such ligands are Lewis bases and can bind protons as well as metallic cations;) thus the pH of the solution plays an important role in complexation.

An example of a complexation reaction, between copper(II) ion and four ammonia molecules in an aqueous solution, may be expressed by the equation

$$\begin{bmatrix} H_2O & OH_2 \\ & Cu & \\ H_2O & OH_2 \end{bmatrix}^{2+} + 4NH_3 \rightleftharpoons \begin{bmatrix} H_3N & NH_3 \\ & Cu & \\ H_3N & NH_3 \end{bmatrix}^{2+} + 4H_2O$$

hydrated copper(II)   copper(II)-tetrammine

Nearly all metals of the periodic table form chelates or complexes. Numerous ligands are known; however, the donor atoms which combine with the metals are few. These atoms are strongly nonmetallic elements such as N, O, and S. (By Lewis' definition,[1] complexation is an acid-base reaction between the ligand, a Lewis base or electron donor, and the metal ion, a Lewis acid or electron acceptor. The nature of the chemical bond between the metal ion and the ligand may vary from covalent to ionic. Regardless of the precise character of the metal-ligand bond, the major function of the ligand is to donate electrons to the metal ion.)

(There is a specific number of ligands that are bound to each metal ion. This is termed the coordination number and usually is a characteristic for each metal ion. Some metals and their coordination numbers are listed in Table

7.1. There are times when a metal ion can have more than one coordination number, depending upon the valence state of the metal and the nature of the ligand.) The metal ions discussed here will usually have coordination numbers of four or six.

TABLE 7.1: Coordination Numbers of Some Metal Ions

Metal ion	Coordination number
Silver(I)	2
Copper(I)	2
Mercury(I)	2
Mercury(II)	2 or 4
Silver(II)	4
Copper(II)	4
Magnesium(II)	4 or 6
Zinc(II)	4 or 6
Cobalt(II)	4 or 6
Nickel(II)	4 or 6
Aluminum(III)	6
Calcium(II)	6
Strontium(II)	6
Barium(II)	6
Lead(IV)	6
Iron(II)	6
Iron(III)	6
Manganese(II)	6

Ligand molecules are bound to the metal ion in a specific pattern which is characteristic of the metal. Metals with a coordination number of four bind ligand molecules in such a way as to produce either a tetrahedral (I) or square-planar (II) structure. These structures arise from the spatial arrangement of the ligand molecules about the metal ion. An octahedral structure (III) is usually formed by metal ions with a coordination number of six.

Ligands are classified according to the number of sites in the molecule which attach to the metal ion. When a single site on the ligand is involved in the formation of the complex, the ligand is called *unidentate*. Halide ions, cyanide ion, water, and ammonia are common examples of unidentate ligands.

Molecules or ions that contain two or more donor groups that attach to a metallic ion are given the general term *multidentate* ligands. Such ligands can also be classified more specifically according to the actual number of donor groups in the molecule, such as *bidentate* (two donor atoms), *tridentate* (three), *quadridentate* (four), etc. When a multidentate ligand attaches to a metal at more than one site, a ring structure is formed. These ring compounds are called *chelates*. Thus, a chelate can be described as a heterocyclic ring structure in which a metal atom is a member of the ring.) The stability of

(I)
tetrahedral

(II)
square-planar

(III)
octahedral
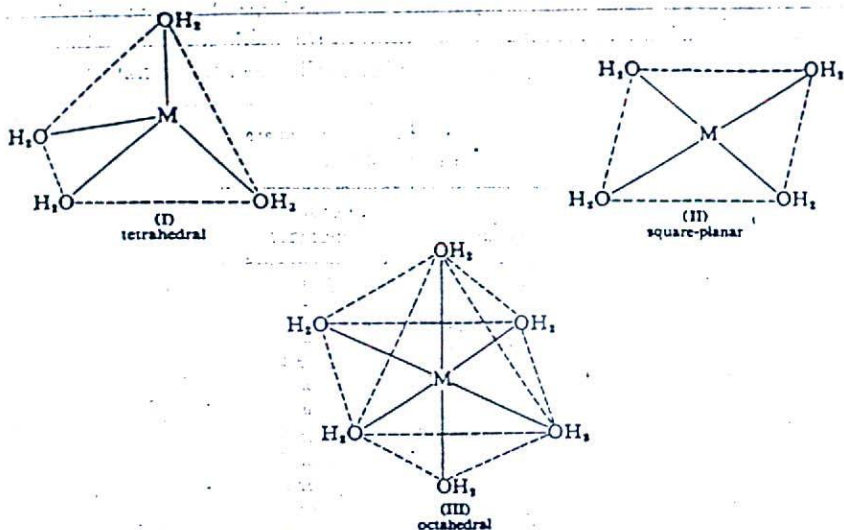
a chelate is usually much greater than that of a corresponding unidentate-metal complex. That is, a chelate is less dissociated than the complex ion. Examples of some multidentate ligands and their chelates are listed in Table 7.2.

Usually, when chelation takes place through oxygen or nitrogen atoms, 5- or 6-membered rings are formed. In some instances, rings of other sizes are formed, but the 5- and 6-membered rings are generally the most stable.

(Ligands which form water-soluble chelates are commonly termed *sequestering agents*. One of the most common sequestering agents is ethylenediaminetetraacetic acid (EDTA) (IV), whereas 8-hydroxyquinoline (V), or oxine, is a well-known chelation agent which forms insoluble chelates with many metals. Each of these chelating agents is used as a reagent in analytical chemistry. Sequestering agents are employed to titrate or solubilize metal ions. The agents which form water-insoluble chelates are used to remove the metal ions from solution by precipitation.)

EDTA (IV)

oxine (V)
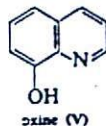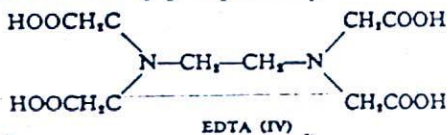
√ B. STABILITY OF CHELATES AND COMPLEX IONS

The law of mass action defines the concentrations of all species in equilibrium chemical processes. An example of an equilibrium process is the dissociation of the weak acid (HA), and it is described by reaction (7.1).

$$HA + H_2O \rightleftharpoons A^- + H_3O^+ \qquad (7.1)$$

TABLE 7.2: Examples of Some Multidentate Ligands

Ligand	Type	Chelate
Ethylenediamine	Bidentate	
Glycine	Bidentate	
Oxalate ion	Bidentate	
Diethylenetriamine	Tridentate	
N-hydroxyethylethylenediamine	Tridentate	
Nitrilotriacetic acid	Quadridentate	

TABLE 7.2 (continued)

Ligand	Type	Chelate
Triaminotriethylamine	Quadridentate	
Ethylenediaminetetraacetic acid	Sexadenatate	

Concentrations of the individual species at equilibrium are calculated by the equation

$$K_a = \frac{[A^-][H_3O^+]}{[HA]} \qquad (7.2)$$

where the concentrations are in moles per liter and K_a is the equilibrium constant or, in this case, the dissociation constant. The pK_a (negative logarithm of K_a) is often used as a more convenient form of the dissociation constant.

Complexation is also an equilibrium process which can therefore be defined by the law of mass action. A complex, ML_n, is formed by the reaction

$$M + nL \rightleftharpoons ML_n \qquad (7.3)$$

where M is the metal ion, L the ligand, and n the number of ligand molecules reacting with the metal ion. The concentrations, in moles per liter, of these various species at equilibrium are defined by the equation

$$K_s = \frac{[ML_n]}{[M][L]^n} \qquad (7.4)$$

where K_s is the equilibrium constant or, in this instance, the stability constant. This term describes the affinity betweeen a ligand and a metal ion. By

examination of Eq. (7.4), it can be seen that, as the magnitude of K_s increases, the stability of the complex is greater and the concentration of the unbound metal ions and ligand, at equilibrium, is decreased. Since the stability constants of many complexes are large numbers, pK_s, the negative logarithm of K_s, is commonly used.

Recently, it has been recognized that metal complexes form in a stepwise fashion. Stepwise complex formation can take place as shown by the general equations

$$M + L \rightleftharpoons ML \tag{7.5}$$

$$ML + L \rightleftharpoons ML_2 \tag{7.6}$$

The final step is

$$ML_{n-1} + L \rightleftharpoons ML_n \tag{7.7}$$

An equilibrium constant for each of these steps can be written

$$K_1 = \frac{[ML]}{[M][L]}, \quad K_2 = \frac{[ML_2]}{[ML][L]}, \cdots, \quad K_n = \frac{[ML_n]}{[ML_{n-1}][L]} \tag{7.8}$$

$$K_1 K_2 \cdots K_n = K_s \tag{7.9}$$

The product of the stability constants for each individual step is the over-all stability constant K_s, as given in Eq. (7.4).

There is no experimental method universally employed in studying complex ion equilibria, but many methods have been successfully used. These methods determine the combining ratios of metal and ligands in the metal complex, as well as produce data used to calculate the stability constants.[1] Since chelation changes many of the characteristics of the unbound metal, some of these alterations, such as spectrophotometric properties, redox potential, and pH changes in solution, are more commonly used to measure quantitatively the complex equilibria.

A detailed discussion of the methods employed in the determination of stability constants for a complex is beyond the scope of this book.

C. TITRATIONS BASED ON COMPLEX FORMATION

According to Lewis' definition, the titration of a metal ion by a complexing agent is an acid-base reaction. Thus, many principles of acid-base titrimetry are employed in complexometry. However, it should be noted that complexometric reactions are more complicated than a simple acid-base reaction.

For any reaction to be used as the basis of a titration, a reacting species must be disappearing from the solution. This disappearance must be rapid and detectable by a suitable method; the reaction must be stoichiometric. For example, in the titration of an acid by a base the proton is the disappearing species, and in a complexometric titration the free metal ions disappear as they are changed into complex ions.

If in the titration of an acid by a strong base, the neutralization reaction is followed by measuring pH as base is added, there is a sudden increase in pH at the equivalence point (in Fig. 7.1). This sudden pH change is caused by the rapid depletion of the free hydrogen ion concentration. The end point can be detected potentiometrically or, more commonly, by a pH-sensitive indicator. A similar situation takes place during the titration of a metal by a chelon, such
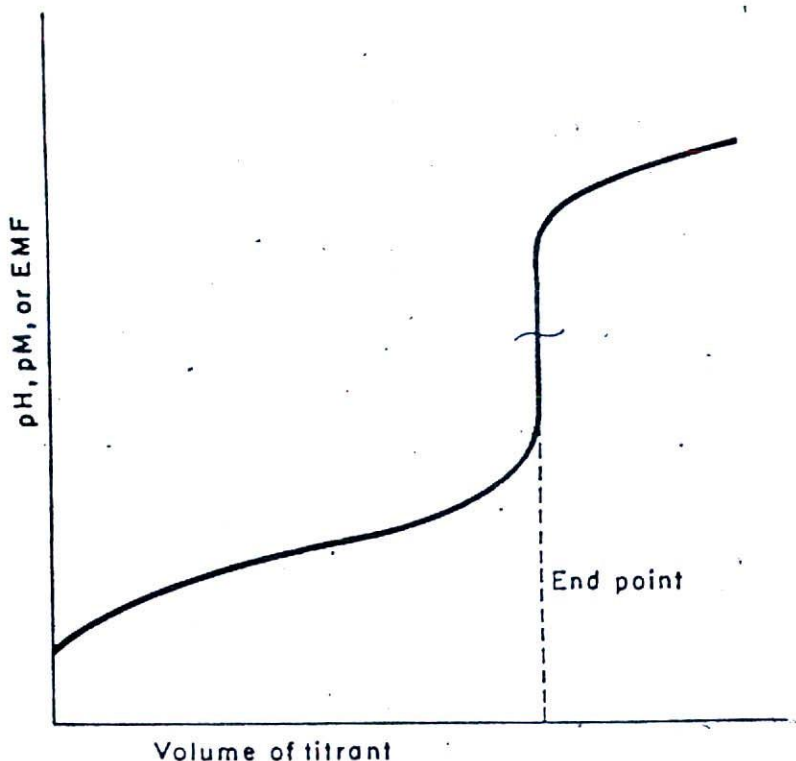

FIGURE 7.1: A typical titration curve for an acid-base or a metal-chelon reaction.

as EDTA. If the course of the complexometric titration is followed by measuring pM (negative logarithm of metal ion concentration) as the EDTA is added, at the end point the pM rapidly increases. This sudden pM rise results from removal of the last traces of free metal ion from solution by EDTA. Any method which can determine this sudden disappearance of free metal ion can be used for detecting the equivalence point or end point in a complexo-metric titration.

During the titration of a metal ion by a complexing agent which forms a soluble complex, two parameters are important in determining the magnitude

of the break in the titration curve at the end point: the stability of the complex formed, and the number of steps involved in the complex formation. The greater the stability constant for the complex formed, the larger the change in
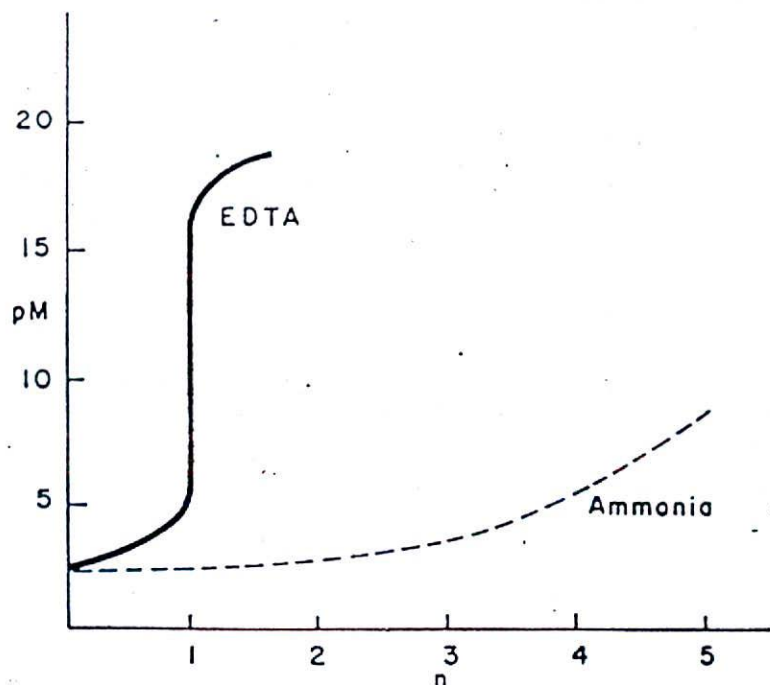

FIGURE 7.2: Comparison of the titration curves for Zn(II) with ammonia and EDTA. Solid line represents the EDTA titration and the broken line represents the ammonia titration. n is the number of moles of titrant per mole of Zn(II).

the free-metal ion concentration (pM) at the equivalence point and the more perceptible the end point.

Also, the fewer the number of steps required in the formation of a complex, the greater the break in the titration curve at the equivalence point. This larger break in the curve results from the elimination of lower complexes that cause rapid changes in the free metal ion concentration during the initial portions of the titration and the decreased tendency of the complex to dissociate on dilution. The importance of these parameters is illustrated in Fig. 7.2. In this figure the titration curves for Zn(II) with the unidentate ligand, ammonia, and the multidentate ligand, EDTA, are compared. Four

steps are required for the formation of the Zn(II)-ammonia complex:

$$Zn^{2+} + NH_3 \rightleftharpoons Zn(NH_3)^{2+} \qquad \log K_1 = 2.3 \qquad (7.10)$$

$$Zn(NH_3)^{2+} + NH_3 \rightleftharpoons Zn(NH_3)_2^{2+} \qquad \log K_2 = 2.3 \qquad (7.11)$$

$$Zn(NH_3)_2^{2+} + NH_3 \rightleftharpoons Zn(NH_3)_3^{2+} \qquad \log K_3 = 2.4 \qquad (7.12)$$

$$Zn(NH_3)_3^{2+} + NH_3 \rightleftharpoons Zn(NH_3)_4^{2+} \qquad \log K_4 = 2.0 \qquad (7.13)$$

The over-all reaction and stability constant can be described by Eq. (7.14).

$$Zn^{2+} + 4NH_3 \rightleftharpoons Zn(NH_3)_4^{2+} \qquad \log K_s = 9.0 \qquad (7.14)$$
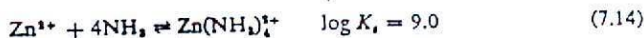
With ammonia as the titrant there is no detectable pM change at the equivalence point. However, when EDTA is used as the titrant, a one-step complexation reaction takes place, and a very stable chelate is formed. As a result the equivalence point is easily detectable.

$$Zn^{2+} + EDTA^{2-} \rightleftharpoons Zn\text{-}EDTA^{2-} + 2H^+. \qquad \log K_s = 19.0 \qquad (7.15)$$
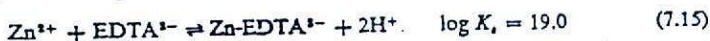
Chelating agents, such as EDTA, which are commonly employed as metal ion titrants, usually form metal complexes that are normally more stable than the complexes formed by unidentate ligands. This difference in stability between multidentate and unidentate ligands is commonly referred to as the *chelate effect*.[3]

During a complexometric titration the pH must be kept constant by the use of a buffer solution. Control of the pH is essential, since the hydrogen ions play an important role in chelation. Most ligands are bases and bind hydrogen ions throughout a wide pH range. Some of these hydrogen ions are frequently displaced from the ligand by the metal during chelate formation. Equation (7.16) illustrates the competition between the metal ion and the hydrogen

$$M^{2+} + H_2\text{-}EDTA^{2-} \rightleftharpoons M\text{—}EDTA^{2-} + 2H^+ \qquad (7.16)$$

ion for the ligand. Therefore, the stability of the metal complex is pH-dependent. The lower the pH of the solution the more hydrogen ions are available to compete with the metal ion for the ligand, and the equilibrium of Eq. (7.16) shifts to the left, causing a decrease in the stability of the complex. Only metals that form very stable complexes with titrants can be titrated in acidic solutions; conversely, metals forming weak complexes can only be effectively titrated in alkaline solution.

The attraction between the metal and the ligand at any particular pH is a function of the over-all stability constant of the complex and the stability constant for the protonated form of the ligand. The stability constant for a protonated ligand is the reciprocal of its dissociation constant (K_a value). The effective stability constant (K_e) defines the tendency for reaction between the metal and ligand at any particular pH value:

$$K_e = \frac{K_s}{\alpha} \qquad (7.17)$$

K_s is the over-all stability constant for the complex and α designates the pH-dependent term first introduced by Reilly et al.[4] This term α describes the amount of ligand present in the system that is available for complexation with the metal. In an acidic solution, α is large since the ligand is mostly undissociated; thus the K_s is small. As the pH increases, α decreases in magnitude as the ligand ionizes and the magnitude of K_s approaches that of the K_s:

$$\alpha = \frac{\text{total ligand in the system}}{\text{total ligand in complexing form}} \qquad (7.18)$$

D. TITRANTS EMPLOYED IN CHELOMETRIC TITRATIONS

Chelon is the general term given to reagents that are commonly employed as titrants for metal ions. The agents include polyamines and polyamino-carboxylic acids that form soluble, stable chelates (usually 1:1) with metal ions. Some of the most frequently used chelons, their common abbreviations, and their chemical structures are listed in Table 7.3.

Polyamines form stable chelates with only a few metal ions, for example, Zn, Co, Hg(II), Cu(II), and Ni, and are therefore used for the selective titration of these ions. Of the numerous polyamines available, only the two listed in Table 7.3, triethylenetetramine (trien) and tetraethylenepentamine (tetren), have been employed to any extent as metal ion titrants. These reagents form highly colored complexes with Cu(II) and are successfully used as titrants for this ion when the end point is determined photometrically. Because of the intense color of the polyamine-copper complex, traces of copper interfere with the analysis of other metal ions. Until recently, only technical grades of the polyamines were commercially available, and these were not of sufficient purity to be used as analytical reagents. Now that more pure materials are available, these agents may be used to a greater extent in metal ion analysis.

The polyaminocarboxylic acids are a closely related group of reagents. Chelates formed by these compounds are similar in structure and stability; thus there are only slight differences in the use of the materials as titrants. Polyaminocarboxylic acids are more versatile titrants than are the poly-amines, because they form stable chelates with a greater number of metal ions and are therefore more widely employed. The most commonly used polyaminocarboxylic acid is ethylenediaminetetraacetic acid, also known as (ethylenedinitrilo)tetraacetic acid, and conveniently abbreviated EDTA. Because of the low water solubility of the "free" acid form of this compound (0.2 g/liter), the water-soluble disodium salt (dihydrate) is the reagent of choice in metal titrations. Analytical grades of both the disodium EDTA dihydrate and the acid form are commercially available.

Since EDTA is the major titrant used in metal ion analysis, all further discussion concerning complexometric titrations will be based upon the use of this reagent.

TABLE 7.3: Common Chelons Used in Metal Ion Analysis

Chelon	Abbreviation	Structure
Nitrilotriacetic acid	NTA	$N-(CH_2COOH)_3$
Ethylenediaminetetraacetic acid	EDTA	$(HOOCH_2C)_2 N-CH_2-CH_2-N(CH_2COOH)_2$
Ethylene glycol-bis-(β-amino ethyl ether)-N-N'-tetraacetic acid	EGTA	$(HOOCH_2C)_2 N-CH_2-CH_2OCH_2CH_2OCH_2CH_2N(CH_2COOH)_2$
Diethylenetriaminepentaacetic acid	DTPA	$(HOOCH_2C)_2 N-CH_2-CH_2-N-CH_2-CH_2-N(CH_2COOH)_2$ with CH_2COOH on central N
Cyclohexanediaminetetraacetic acid	CDTA	cyclohexane ring bearing $-N(CH_2COOH)_2$ and $-N(CH_2COOH)_2$
N-Hydroxyethylenediamine triacetic acid	HEDTA	$(HOOCH_2C)(HOCH_2H_2C)N-CH_2-CH_2-N(CH_2COOH)_2$
Ethyletherdiaminetetraacetic acid	EEDTA	$(HOOCH_2C)_2 NCH_2CH_2-O-CH_2CH_2N(CH_2COOH)_2$
Triethylenetetramine	Trien	$NH_2CH_2CH_2NHCH_2CH_2NHCH_2CH_2NH_2$
Tetraethylenepentamine	Tetren	$NH_2-(CH_2-CH_2NH)_3-CH_2-CH_2NH_2$

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E. TYPES OF COMPLEXOMETRIC TITRATIONS

Complexometric titrations are based upon the reaction between a metal ion and a chelon. There are several types of metal titrations which are classified according to the manner in which these reagents are mixed and the titration performed: (1) direct titration; (2) back titration; (3) replacement titration; (4) indirect methods.

1. Direct Titration

Direct titration is the simplest and most convenient method used in chelometry. In this procedure the standard chelon solution is added to the metal ion solution until the end point is detected by a suitable method. This procedure is analogous to a simple acid-base titration.

Numerous problems may be encountered with direct titration of some metals, such as precipitation of the metal as a result of side reactions, a slow complexation reaction, or interferences of various types caused by the presence of other ions. Many of these problems can be overcome by alternate titration procedures.
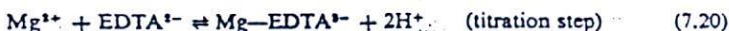
2. Back Titration

Back titration involves addition of an excess of a standard chelon to the metal being determined, and the excess is back titrated with a standard solution of a second metal ion to a suitable end point. An example of this procedure is the determination of Mn(II). This metal cannot be directly titrated with EDTA in alkaline solution, owing to precipitation of the manganese hydroxide. An excess of EDTA is added to an acidic solution of the manganese salt, an ammonia buffer is used to adjust the solution pH to 10, and the excess EDTA remaining after chelation is titrated with a standard Zn(II) solution using Eriochrome Black T as the indicator.[5] Again, this method is analogous to the well-known back-titration method encountered in acidimetry.

There are times when the difficulties, previously described, cannot be simply overcome by the use of a back titration. It is then advantageous to employ an alternate procedure, termed a replacement titration.

3. Replacement Titration

The method of replacement titration involves the quantitative displacement of a second metal (M_{II}) from a complex by the metal (M_I) being determined. The freed second metal is then directly titrated by a standard chelon solution. From these data one can calculate the concentration of M_I in the system. An example of this type of analysis is determination of manganese(II). As we have previously mentioned, this ion cannot be satisfactorily titrated directly

with an EDTA solution, when Eriochrome Black T is used as the indicator.[6] However, if an excess quantity of a Mg-EDTA chelate is added to the manganese solution, the magnesium is quantitatively displaced from the EDTA chelate. This displacement takes place because the manganese forms the more stable complex with EDTA. The freed Mg ions are then directly titrated with a standard EDTA solution and are equivalent to the amount of Mn(II) originally in the solution:

$$Mn^{2+} + Mg-EDTA^{2-} \rightleftharpoons Mg^{2+} + Mn-EDTA^{2-} \quad \text{(replacement step)} \quad (7.19)$$

$$Mg^{2+} + EDTA^{2-} \rightleftharpoons Mg-EDTA^{2-} + 2H^{+} \quad \text{(titration step)} \quad (7.20)$$
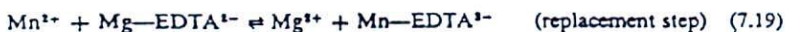
4. Indirect Titration

An indirect titration procedure can be used in the determination of ions, such as anions, which do not react with a chelon. For example, barbiturates do not react with EDTA but are quantitatively precipitated from alkaline solution by mercuric ion as 1:1 complexes,[7] After precipitation with an excess of Hg(II), the complex is removed by filtration and redissolved in an excess of a standard EDTA solution. A standardized Zn(II) solution can be employed as the titrant for the excess EDTA, using an appropriate method for the detection of the end point. This procedure determines the Hg(II) concentration by a back titration and the barbiturate concentration is found by an indirect method since it is equivalent to the Hg(II). The reactions are described by the scheme shown in Eqs. (7.21) to (7.23).

$$\underset{\substack{\text{barbiturate} \\ \text{anion}}}{B^{-}} + Hg^{2+} \rightleftharpoons Hg\text{-}B \text{ complex} \downarrow \quad (7.21)$$

$$Hg\text{-}B \text{ complex} + xs\text{-}EDTA^{2-} \rightleftharpoons B^{-} + Hg\text{-}EDTA + EDTA^{2-} \quad (7.22)$$

$$EDTA^{2-} + Zn^{2+} \rightleftharpoons Zn\text{-}EDTA^{2-} + 2H^{+} \quad (7.23)$$
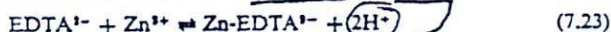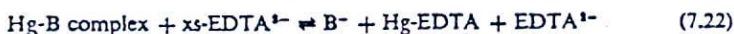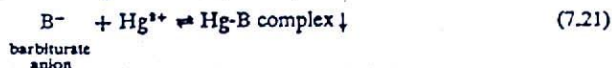
Another approach is precipitation of the anion with an excess of an appropriate metal and titration of the excess metal in the filtrate with a standardized EDTA solution. For example, sulfate can be determined by precipitation with an excess of Ba(II), and the excess Ba(II) in the filtrate titrated with a standard EDTA solution.[8]

From this short discussion of the various titration methods it can be seen that, even though complexometric titrations are based on the simple reaction between a metal ion and a chelon, the different procedures used in mixing the reagents have provided the analyst with a valuable tool for the determination of many elements of the periodic table. The elements which can be determined by chelometry are summarized in Tables 7.4 and 7.5, and are categorized by groups, as they are in the periodic table.

TABLE 7.4: Elements Directly Estimated by EDTA Titration

Group Ib	Group IIa	Group IIb	Group IIIa
Copper	Magnesium	Zinc	Aluminum
	Calcium	Cadmium	Gallium
	Strontium	Mercury	Indium
	Barium		Thallium
Group IIIb	**Group IVa**	**Group IVb**	**Group Va**
Scandium	Tin	Titanium	Antimony
Yttrium	Lead	Zirconium	Bismuth
Lanthanoid series		Hafnium	
(most members)			
Actinoid series			
(most members)			
Group Vb	**Group VIb**	**Group VIIb**	**Group VIII**
Vanadium	Chromium	Manganese	Iron
	Molybdenum		Cobalt
	Tungsten		Nickel
			Palladium

TABLE 7.5: Elements Indirectly Estimated by EDTA Titration

Group Ia	Group Ib	Group IVa	Group Va
Sodium	Silver	Carbon	Nitrogen
Potassium	Gold		Phosphorus
			Arsenic
	Group VIa	**Group VIIa**	
	Sulfur	Fluorine	
	Selenium	Chlorine	
		Bromine	
		Iodine	

F. METHODS OF END-POINT DETECTION

The rapid development of complexometric titration analysis during the last few years, can be attributed primarily to suitable new methods of end-point detection. These methods can be divided into two classes, visual and instrumental.

1. Visual Methods

a. Metal or Metallochromic Indicators. The simplest and most convenient method of metal analysis is the direct titration of a metal ion with a standardized chelon solution using a visual color change of a metal indicator to detect

the end point. Metal indicators, or metallochromic indicators, are substances, usually dyes, which produce one color in the presence of free metal ions and a different color (or no color) when they are absent. Many of these substances also have typical properties of acid-base indicators, and color changes are the result of the displacement of hydrogen ions by a metal ion. Although there are numerous compounds which give color reactions with metal ions, few are satisfactory as visual metal indicators for complexometric titrations. Several general requirements must be met before a compound can be considered a useful and practical metal indicator. It must be remembered, however, that these requirements must be met under the conditions which are encountered during a titration.

(1) The compound must be chemically stable during storage and through-out the titration procedure.

(2) The metal indicator should form a 1:1 complex which must be weaker than the metal-chelon complex, otherwise the end point is obscure.

(3) The metal indicator must have sufficient stability to withstand dilution and still give an adequate color change at the end point.

(4) The colors of the metal-complexed indicator and free indicator must be sufficiently different and intense enough to allow visual detection of the end point with a minimum amount of indicator.

(5) The color reaction should be selective for the metal being titrated and relatively free of interferences caused by other substances in the solution.

The sequence of reactions between the metal M, the indicator I, and the chelon EDTA, leading to the detection of the end point in a direct titration can be qualitatively described by the following steps. At the onset of the titration the buffered reaction medium contains the metal-indicator complex (MI) that has formed, and excess metal ions. This equilibrium process is defined by the law of mass action and the stability constant of the metal indicator complex (K_{MI}). When EDTA, the titrant, is added to the system a competitive reaction takes place between the free metal ions and the EDTA, which can be described by Eq. (7.26), and the stability constant K_s. Since, the

$$M + I \rightleftharpoons MI \tag{7.24}$$

$$K_{MI} = \frac{[MI]}{[M][I]} \tag{7.25}$$

metal-indicator complex is weaker than the metal-EDTA chelate ($K_s > K_{MI}$), the EDTA which is being added to the system during the course of the titration

$$M + EDTA \rightleftharpoons M\text{-}EDTA \tag{7.26}$$

$$K_s = \frac{[M\text{-}EDTA]}{[M][EDTA]} \tag{7.27}$$

is progressively chelating the free metal ions in solution at the expense of the metal-indicator complex. Finally, at the equivalence point, EDTA removes the last traces of metal from the indicator, and the indicator changes from its

complexed color to its metal-free color. The over-all reaction can be represented by Eq. (7.28).

$$\underset{\substack{\text{Colored}\\\text{complex}}}{MI} + \underset{\substack{\text{free}\\\text{metal}}}{M} + \underset{\text{titrant}}{EDTA} \rightleftharpoons \underset{\text{chelate}}{M\text{-}EDTA} + \underset{\substack{\text{free}\\\text{indicator}}}{I} \tag{7.28}$$

Numerous compounds have been tried as indicators for complexometric titrations. These metal indicators can be classified according to the chromophore groups responsible for the color. The more common substances which have been employed are usually from one of the structural classes (1) triphenylmethane dyes, (2) phthalines and substituted phthalines, (3) azo dyes, (4) phenolic compounds, and (5) anthraquinone dyes.

It is beyond the scope of this book to discuss in detail the individual indicators. A list of some of the more common metal indicators is given in Table 7.6.

b. pH Indicators. When a divalent or polyvalent metal ion is added to a solution of an EDTA salt, two hydrogen ions are liberated:

$$M^{2+} + (H_2\text{-}EDTA)^{2-} \rightleftharpoons (M\text{-}EDTA)^{2-} + 2H^+ \tag{7.29}$$

In a nonbuffered solution, the liberated acid can be titrated with standard base using an acid-base indicator to detect the end point. This method was the original end-point-detecting technique, but because of several disadvantages and the fact that the metal indicators are more accurate and much easier to use, the method is seldom employed today.

c. Redox Indicators. This method is very limited and can be applied only to special systems. In these systems, the metal ion must be a component of a redox couple. That is, the metal, such as iron, must be able to exist in two different oxidation states which are in equilibrium in the solution. Usually, EDTA forms stronger chelates with the oxidized state of the metal than with the reduced state. So, as the titrant is added to the system, the oxidized form of the metal is preferentially complexed and at the end point, the redox equilibrium is destroyed, which causes the indicator to be reduced and to change color. The indicator, Variamine Blue B (VI), is used in the titration of iron(III) by EDTA and at the end point the violet-blue shade becomes colorless.[9]

$$H_3CO-\!\!\!\!\bigcirc\!\!\!\!-NH_2-\!\!\!\!\bigcirc\!\!\!\!-NH_2$$

(VI)
Variamine Blue B
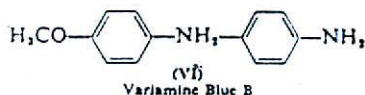
2. Instrumental Methods

The end point of most complexometric titrations is detected by the use of visual metal indicators. However, such a method can be inaccurate in highly colored or dilute solutions. Under the same experimental conditions, an instrumental method, such as a potentiometric or photometric technique, can frequently be employed to detect the end point without difficulty.

TABLE 7.6: Some Commonly Used Metal Indicators

Name	Other common names	Structure	Color changes	Metals detected
Eriochrome Black T	Solochrome Black T, Eriochromeschwarz T		Red $\xrightarrow{pH\ 6-7}$ blue Blue $\xrightarrow{pH\ 11-12}$ orange	Mg, Zn, Cd, Sr, Ba
Pyrocatechol	Catechol Violet		Red $\xrightarrow{pH\ 1-2}$ yellow Yellow $\xrightarrow{pH\ 6-7}$ violet Violet $\xrightarrow{pH\ 8-10}$ red-violet	Bi, Ni, Co, Mn, Zn, Cd, Ca
Xylenol Orange			Yellow $\xrightarrow{pH\ 5-7}$ red	Bi, Zn, Hg^{2+}, Co, Cd

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Metalphthalein

O-Cresolphthalein complexon

Phthalein Purple

Colorless $\xrightarrow{\text{pH 6-7}}$ rose

Rose $\xrightarrow{\text{pH 10-11}}$ red

Alkaline earth metals

HOOCH$_2$C $-$ N $-$ CH$_3$
HOOCH$_2$C

CH$_3$COOH
CH$_3$ $-$ N $-$ CH$_2$COOH

OH CH$_3$

CH$_3$

HO CH$_3$
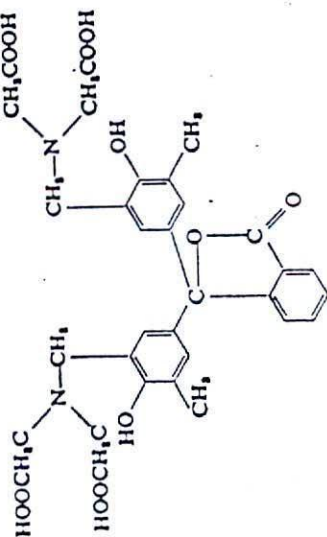
Muroxide — Ammonium purpurate

$NH_4^{\oplus}$
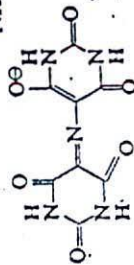
Red-violet $\xrightarrow{\text{pH 6-7}}$ violet

Violet $\xrightarrow{\text{pH 11}}$ blue-violet

Ca

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5. Potentiometric Methods. The course of some complexometric titrations can be followed by measuring the change of potential at an indicator electrode, immersed in the solution being analyzed, as the titrant is being added. The end point of the titration is indicated by a large and rapid change of potential.

In chelometry, two types of potentiometric titrations are important, and each employs a specific electrode system. In one method, a platinum electrode is used to measure redox potential changes associated with metal-EDTA complex formation.[10] In the other, more versatile, method a mercury electrode measures potential changes accompanying the replacement reaction between the metal being titrated and mercury(II) present as a mercury(II)-EDTA chelate.[11]

The indicator electrode most commonly employed in redox titrations is a platinum wire. The potential of the electrode is a function of the ratio of the two oxidation states of a metal in the same solution. An equilibrium exists for the electron transfer between the oxidized and reduced forms of a metal, as for example, ferrous and ferric iron:

$$Fe^{2+} \rightleftharpoons Fe^{3+} + e \qquad (7.30)$$

The potential at the platinum electrode is given by the Nernst equation:

$$E = E_0 - \frac{0.0591}{n} \log \frac{[Fe^{3+}]}{[Fe^{2+}]} \qquad (7.31)$$

where E_0 is the standard potential of the system, 0.0591 is a temperature-dependent coefficient, and n is the number of electrons transferred.

The platinum and calomel (reference electrode) electrode system has been employed in both direct and indirect titrations of metal ions. A direct titration is rather limited, since the electrode measures redox potential and can be used only in the determination of metal ions forming a reversible redox couple under the conditions of the titration. Copper(II), zinc, and iron(III) are examples of metals which can be titrated in this manner. The equivalence point is indicated by a marked change in the titration curve, when potential is plotted versus volume of titrant added to the solution, as in Fig. 7.1.

Back-titration procedures, using the platinum electrode system, have been developed for the determination of metals which do not form redox couples. An excess of EDTA is added to the solution containing the metal being determined, and the excess is back-titrated with an appropriate metal solution, especially iron(III). The metal ion used as the titrant must form a reversible redox couple, and the end point is detected in the same manner as for a direct titration.

The mercury electrode system can be used to detect the end point in the titration of almost all metal ions. When the electrode is immersed in a solution containing a mercury(II) salt the following equilibrium is established:

$$Hg^0 \rightleftharpoons Hg^{2+} + 2e \qquad (7.32)$$

The potential of the electrode is given by Eq. (7.33). When the potential of

$$E = E_0 - \frac{0.0591}{2} \log [Hg^{2+}] \tag{7.33}$$

the system is measured, the standard potential E_0 is known, and the concentration of free mercury(II) ion is calculated by Eq. (7.33).

In the titration procedure using this electrode system, the electrode is immersed in the solution containing the metal ion to be titrated and a small quantity of a mercury(II)-EDTA chelate (usually a few drops of a 0.01 M solution). Mercury(II) is displaced from the mercury(II)-EDTA chelate by the metal ion (that is, a divalent ion M^{2+}), and the following exchange equilibrium results:

$$M^{2+} + Hg\text{-}EDTA^{2-} \rightleftharpoons Hg^{2+} + M\text{-}EDTA^{2-} \tag{7.34}$$
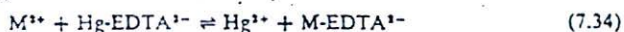
From this equilibrium it can be seen that the concentration of M^{2+}, which is in excess of the Hg-EDTA^{2-} at the start of the titration, determines the amount of free mercury(II) in solution; thus the potential of the mercury electrode depends upon the ratio $[M^{2+}]/[M\text{-}EDTA^{2-}]$. During the early part of the titration with EDTA, the ratio $[M^{2+}]/[M\text{-}EDTA^{2-}]$ changes only slightly; however, in the vicinity of the end point this ratio undergoes its largest changes and the potential of the mercury electrode changes accordingly. As in all potentiometric titrations, the equivalence point is indicated by a sharp inflection in the titration curve.

b. Photometric Methods. A photometric technique may be used when it is difficult to locate visually the end point of an EDTA titration. Under various circumstances it is advantageous to use a photometric titration procedure for (1) dilute solutions, (2) when large amounts of indicator are required, (3) when indicator color is of low intensity, (4) when color changes are not easily detectable, and (5) when the indicator does not form a stable complex with the metal being titrated. Two types of photometric titrations are commonly employed in chelometry: In one, a photometer or spectrophotometer is used to follow the formation of a metal-EDTA chelate when this complexation is associated with changes in the absorbance of the solution; in the other, a metal indicator is added to the solution and the absorbance changes of the indicator are followed in a similar manner. These absorbance changes may be in the ultraviolet, visible, or near-infrared regions of the spectrum.

When the absorption of the free metal and its EDTA chelate are sufficiently different, the end point may be located without the use of a metal indicator. In such a system, as the free metal is titrated, complex formation is accompanied by a change in the absorbance of the solution. The end point is characterized by a sharp inflection in the titration curve, when absorbance is plotted versus volume of titrant added to the solution. Typical titration curves for systems without an added indicator are shown in Fig. 7.3. Curve 1

represents the direct titration of iron(III) with an EDTA solution.[12] After each addition of titrant, the absorbance of the solution increases as the chelate forms, and the end point is detected by the sharp break in the curve. When copper, in an ammonia buffer, is titrated with EDTA, the resulting titration curve is represented by curve 2.[12] During this titration, the absorbance of the solution decreases, owing to the color change from an intense
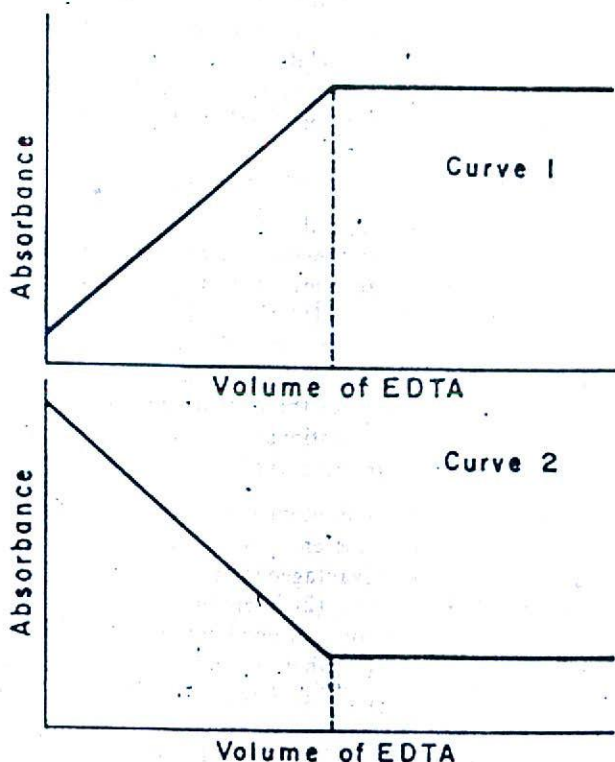
FIGURE 7.3: Typical titration curves for a metal solution without an added indicator.

deep blue of the copper(II)-tetraamine complex to the less intense light-blue color of the copper(II)-EDTA chelate. The end point is detected when the absorbance does not change upon the addition of more titrant.

In a photometric titration with an added metal indicator, the photometer or spectrophotometer is used to detect the absorbance changes of the indicator at the end point, rather than to follow the changes accompanying metal-EDTA complex formation. Thus, only the absorbance readings in the region of the end point are of importance. Figure 7.4 represents a typical titration curve with an added indicator.

c. Other Instrumental Methods. Several other instrumental methods have been successfully employed in detection of the end point in complexometric titrations. It is beyond the scope of this book to discuss, in any detail, these lesser-used methods: (1) amperometric titrations, (2) conductometric titrations, (3) coulometric titrations, and (4) high-frequency titrations.
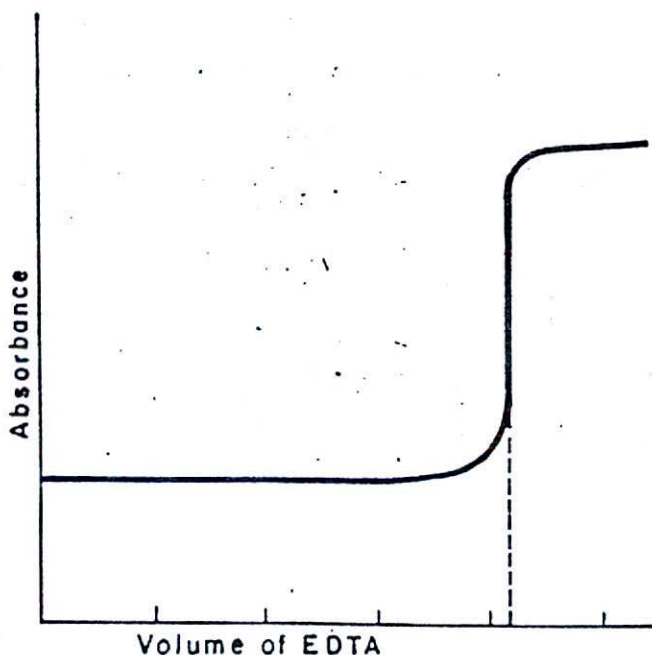
FIGURE 7.4: A typical titration curve with an added indicator.

G. TITRATION SELECTIVITY AND MASKING REAGENTS

Chelons are very unselective titrants because stable chelates are formed with a great number of metal ions. When several metal ions are present in a solution, the titration data usually give the total metal content. Thus, it is necessary to find practical methods which increase the selectivity of the titrant.

Several methods have been devised to titrate selectively individual metal ions in mixtures: (1) pH adjustment of the reaction medium, (2) the use of selective metal indicators, (3) the use of selective precipitants, and (4) the addition of masking agents to the reaction medium.

The formation of a metal chelate is dependent on the pH of the reaction medium. In weakly acidic solution the chelates of many metals, such as the

alkaline earths, are completely dissociated, whereas chelates of bismuth, iron(III) or chromium readily form. Thus, in acidic solution, bismuth can be effectively titrated with a chelon in the presence of the alkaline earth metals. This method is based upon the differences in stability of the chelates formed between the metal ions and the chelon.

A second method involves the use of selective metal indicators. These indicators are metal complexing agents which preferentially react with different metal ions under various conditions. Numerous selective metal indicators have been employed in volumetric analysis; however, since for individual metal ion mixtures, the indicator and titration system is more or less specific, we shall briefly describe only one such system.

Pyrocatechol Violet (Table 7.6) is a well-known example of a selective metal indicator. This substance preferentially reacts with bismuth in acidic solutions (pH 2 to 3). Bismuth can be directly titrated with a chelon in the presence of lead, calcium, or zinc.[13] When bismuth and zinc are present in a mixture, the bismuth is directly titrated in an acidic solution using Pyrocatechol Violet as indicator. At the completion of this titration, an ammonia buffer is added to adjust the pH to 10 and the system is again titrated to the Pyrocatechol Violet end point with the chelon solution. The volume of titrant employed in the second part of the titration is used to calculate the zinc concentration. The effect of pH on chelation has previously been discussed. We now have an example of how the pH of the reaction medium alters the specificity of the indicator.

Another approach to increase the specificity of the titrant involves the use of precipitating agents which separate out interfering metal ions, or groups of metal ions. Numerous precipitants have been successfully employed. Some of the more common agents are oxalate for removal of calcium ions, sulfide for the heavy metals, fluoride for aluminum, and hydroxide for some transition metals, iron, and magnesium. These procedures are based upon the classical separation methods of qualitative and quantitative analysis.

The most widely used method for the elimination of the interfering metal ions in complexometric titration involves the addition of a masking agent to the reaction medium. These substances are usually auxiliary chelating or complexing compounds, which selectively react with the interfering metal ions forming more stable complexes than does the chelon. Therefore, these interfering ions are said to be masked and are not titrated by the chelon. Needless to say, the masking agent must not form stable complexes with the metal ion being titrated. Some of the more common masking agents are listed in Table 7.7. Since masking a cation in solution is an equilibrium process, it is possible to reverse this reaction by the addition of suitable demasking agents; thereby, a series of metal ions can be titrated in one solution. One example of the use of masking and demasking reagents in chelometry is the analysis of a mixture of three metals: copper, cadmium, and calcium. Direct titration of the mixture with EDTA gives the sum of the three metals. Copper

TABLE 7.7: Common Masking Agents Employed in Chelometry

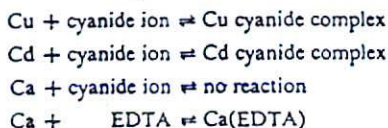| Masking agent	Metals masked
Cyanide	Nickel, cobalt, zinc, cadmium, copper, iron(II)
Iodide	Mercury
Ascorbic acid	Iron(III), copper
Triethanolamine	Iron(III), aluminum, manganese
BAL (2,3-dimercapto-1-propan-1-ol)	Tin, antimony, cadmium, mercury, zinc
Tiron (disodium catechol-3,5-disulfonate)	Aluminum, iron(III)

and cadmium may be masked with the addition of cyanide to the solution, leaving only the calcium ion titratable. When formaldehyde or chloral hydrate is added to the cyanide-containing mixture, only the cadmium is demasked, and the EDTA titrates the sum of the calcium and cadmium. In this manner the concentrations of all three ions are determined by three individual titrations. The reaction sequences involved in the various steps of this titration procedure are represented in Fig. 7.5.

Step 1. *All three metals titrated:*

$$
\begin{array}{c}
Cu \\
Cd \\
Ca
\end{array} + EDTA \rightleftharpoons
\begin{array}{c}
Cu(EDTA) \\
Cd(EDTA) \\
Ca(EDTA)
\end{array}
$$
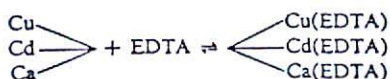
Step 2. *Only calcium titrated (Cu and Cd masked by cyanide):*

$$Cu + \text{cyanide ion} \rightleftharpoons Cu \text{ cyanide complex}$$
$$Cd + \text{cyanide ion} \rightleftharpoons Cd \text{ cyanide complex}$$
$$Ca + \text{cyanide ion} \rightleftharpoons \text{no reaction}$$
$$Ca + \quad EDTA \rightleftharpoons Ca(EDTA)$$

Step 3. *Calcium and cadmium titrated (Cu masked):*

$$
Cd \text{ cyanide complex} + \underset{\substack{\text{demasking} \\ \text{agent}}}{CH_2O} \rightleftharpoons Cd + \overset{O^-}{\underset{}{CH_2CN}}
$$

$$Cu \text{ cyanide complex} + CH_2O \rightleftharpoons \text{no reaction}$$

$$
\begin{array}{c}
Cd \\
Ca
\end{array} + EDTA \rightleftharpoons
\begin{array}{c}
Cd(EDTA) \\
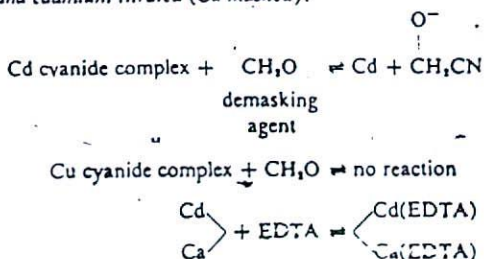Ca(EDTA)
\end{array}
$$

FIGURE 7.5: The three reaction steps involved in the titration of a mixture of copper, calcium, and cadmium ions in one solution.

7.2 PRACTICAL SECTION

A. WATER

The water used in the preparation of reagent or sample solutions may contain trace amounts of metal ions. These trace metals, such as calcium, magnesium, or ·copper, are often found in distilled water and can interfere with the EDTA titration by consuming the titrant or inactivating the indicator. Deionized distilled water should. be used whenever possible in the preparation of reagent and sample solutions.

A simple test can be run on a sample of distilled water to determine whether it is of sufficient purity to be used in the preparation of volumetric solutions. Take 100 ml of the water, and add 2 ml of an ammonia buffer and 1 drop of Eriochrome Black T indicator. Add 1 drop of a 0.1 M EDTA solution and, if a blue color develops, the water can be used. When the color remains red, a new source of water should be found or the water deionized before use by passing it through a column of a strong cation exchange resin.

B. PREPARATION OF INDICATORS

I. Eriochrome Black T

This indicator is also known as Solochrome Black, Eriochromeschwarz T, and mordant black.

Triturate 1 part of Eriochrome Black T with 500 parts of sodium chloride, or potassium sulfate or chloride, until a fine powder is obtained. Use about 100 mg of this powder for each titration. This mixture is indefinitely stable if kept dry and in a closed container.

Aqueous or alcoholic solutions of this indicator are stable for only a few weeks because of polymerization and oxidation.

A solution of Eriochrome Black T can be prepared by dissolving 200 mg of the indicator and 2 g hydroxylamine hydrochloride in 50 ml of methanol. The hydroxylamine hydrochloride, a reducing.agent, is present in the solution to stabilize the indicator from oxidation. However, fresh solutions should be prepared every few weeks.

2. Xylenol Orange

Dissolve 100 mg of Xylenol Orange in 100 ml of water or dilute alcohol. This solution is stable except for the tendency of mold growth.

3. Murexide

Triturate 400 mg of the indicator with 40 g sodium chloride, or potassium sulfate or chloride. Use 40 mg of this powder for each titration.

Aqueous solutions of murexide are not stable and must be prepared daily. Solutions prepared in alcohol or some glycols are stable for several weeks.

4. Hydroxy Naphthol Blue Indicator

Dissolve 300 mg in 100 ml of water, add 10 ml of sodium hydroxide T.S. and 1 ml of calcium chloride solution (1 in 200), and dilute to 165 ml. The solution is reddish pink in color. Upon the addition of 1.0 ml of 0.05 M EDTA, the solution becomes deep blue in color.

C. PREPARATION OF BUFFER SOLUTIONS

1. Ammonia Buffer

Dissolve 54 g of ammonium chloride in 100 ml of distilled water, add 350 ml of ammonium hydroxide solution, and dilute to 1000 ml with distilled water.

2. Acetate Buffer

Dissolve 136 g of sodium acetate trihydrate in 500 ml of water; add 29 ml of glacial acetic acid and sufficient water to make 1 liter.

D. PREPARATION OF 0.1 M EDTA SOLUTION

Both the free-acid form of EDTA and its disodium salt dihydrate can be commercially obtained as analytical reagents and can serve as primary standards. For most purposes the solutions prepared from these reagents are sufficiently accurate to be used as titrants.

To prepare a 0.1 M EDTA solution, dissolve 37.22 g of the disodium EDTA dihydrate in water. When solution is complete, dilute to 1 liter.

This solution may be standardized against pure calcium carbonate by the following procedure. Dissolve an accurately weighed quantity (200 to 400 mg) of calcium carbonate in 100 ml of water with the aid of a minimum amount of hydrochloric acid. Adjust the pH of the solution to about 12 with a freshly prepared 0.1 N sodium hydroxide solution. Add 40 mg of murexide powder and 3 ml of Naphthol Green B indicator; titrate to a deep-blue color with EDTA solution. Calculate the molarity by the formula

$$M_{EDTA} = \frac{W_{CaCO_3}}{MW_{CaCO_3} \times Vol_{EDTA}}$$

where W_{CaCO_3} is the weight of calcium carbonate sample, MW_{CaCO_3} the molecular weight of calcium carbonate (100.1), and Vol_{EDTA} is the volume, in milliliters, of EDTA solution required for the titration.

The EDTA solution should be standardized against the metal ion for which it is to be used as titrant and under the conditions of the actual titration. For example, if zinc is to be determined, the EDTA solution should be standardized by titrating a zinc solution prepared from pure zinc, and the titration should be carried out in a manner similar to that to be used in the assay.

To prepare more dilute EDTA solutions, the 0.1 M EDTA solution may be appropriately diluted with water or the solution may be made from the disodium salt dihydrate.

Solutions of EDTA are stable indefinitely when stored in clean polyethylene containers. The titers of standardized solutions slowly change when they are stored in glass bottles. This titer change is caused by the "leeching" of metal ions from the surface of the glass. Soft-glass containers should never be used for storage of EDTA solutions, and borosilicate-glass containers should not be used for prolonged storage.

E.   PREPARATION OF 0.1 M METAL SALT SOLUTIONS

1. Magnesium Sulfate Solution

Dissolve 24.65 g of magnesium sulfate heptahydrate or 12.04 g of anhydrous magnesium sulfate in a sufficient quantity of water to make 1 liter.

To standardize this solution, accurately pipette a 20-ml aliquot into a suitable titration vessel, add 5 ml of ammonia buffer and a few drops of Eriochrome Black T indicator solution. Titrate with the standardized 0.1 M EDTA to a deep-blue end point. The molarity of this solution is calculated by the equation:

$$M_{MgSO_4} = \frac{M_{EDTA} \times Vol_{EDTA}}{20}$$

where M_{MgSO_4} is the molarity of the magnesium sulfate solution, M_{EDTA} the molarity of the standard EDTA solution, and Vol_{EDTA} the volume, in milliliters of the EDTA solution consumed during the titration.

2. Lead Nitrate Solution

Dissolve 33.12 g of lead nitrate in sufficient water to make 1 liter. Standardize this solution by accurately pipetting a 20-ml sample into a suitable titrating vessel and adding 5 ml of acetate buffer and a few drops of Xylenol Orange indicator solution. Titrate with the 0.1 M EDTA solution to a purple-yellow end point. Calculate the molarity of the lead nitrate solution as described for the magnesium sulfate solution.

3. Zinc Sulfate Solution

Dissolve 16.14 g of anhydrous zinc sulfate in a sufficient quantity of water to make 1 liter.

This solution can be standardized by the procedure described for either magnesium sulfate or lead nitrate solutions. The calculation of molarity would be the same as for the other metal salt solutions.

F. DETERMINATION OF ALUMINUM

Aluminum forms EDTA complexes slowly and is best determined by a back-titration procedure. The pH of the solution must remain acidic to avoid the formation of hydroxo-aluminum compounds which interfere with the titration.

Dissolve an accurately weighed sample of the aluminum-containing substance, equivalent to about 100 mg of Al^{3+}, in water with the aid of a few drops of hydrochloric acid, if necessary. Dilute the solution to 100 ml with water. To 25 ml of this solution, add 25 ml of the standardized 0.1 M EDTA solution and 25 ml of water. Heat the solution on a water bath for 30 min, add 10 ml of acetate buffer, and titrate with lead nitrate or zinc sulfate solution using a few drops of Xylenol Orange as indicator. At the end point, the indicator changes from a lemon-yellow color to red. The volume of 0.1 M EDTA solution consumed by the aluminum is found by subtracting the volume of lead nitrate or zinc sulfate from the total volume of EDTA added to the system. Each milliliter of 0.1 M EDTA is equivalent to 2.698 mg of aluminum.

This procedure is similar to the BP assay for alum and aluminum hydroxide.[14]

G. DETERMINATION OF CALCIUM

Calcium ions may be determined by four various titrimetric procedures: a direct titration with an EDTA solution, a direct titration after the addition of a known quantity of a magnesium salt, a back titration, and a replacement titration.

1. Direct Titration

Dissolve an accurately weighted sample of the calcium salt, equivalent to about 100 mg of calcium, in 50 ml of water with the aid of a few drops of hydrochloric acid, if necessary. When solution is complete, dilute the sample with water to volume in a 100 ml volumetric flask and mix thoroughly. Accurately pipette 50 ml of the sample solution into a suitable titration vessel containing 50 ml of water, adjust the pH of the solution to 12 with a freshly prepared 1.0 N sodium hydroxide solution, add 300mg Hydroxy Naphthol Blue indicator, and titrate rapidly with 0.1 M EDTA until the color changes to a deep blue. Each milliliter of the titrant is equivalent to 4.008 mg of calcium.

The solution must be titrated rapidly because carbon dioxide from air reacts with calcium ion forming calcium carbonate, which tends to precipitate from highly alkaline solutions.

This procedure is similar to the official USP assay for some calcium-containing compounds.[15]

2. Direct Titration in the Presence of a Magnesium Salt

Prepare the sample solution as described under the direct titration procedure. Pipette 50 ml of the solution into a titration vessel containing 50 ml of water; add by means of a pipette 2 ml of 0.1 M magnesium sulfate solution, 5 ml of ammonia buffer, and a few drops of Eriochrome Black T indicator. Titrate with 0.1 M EDTA solution to a deep-blue color.

The volume of 0.1 M EDTA consumed by the calcium is calculated by substracting the volume of 0.1 M magnesium sulfate, in milliliters, from the total volume of 0.1 M EDTA required to obtain the deep-blue color at the end point. Each milliliter of titrant is equivalent to 4.008 mg of calcium.

Both calcium and magnesium are directly titrated in this procedure. The magnesium salt is added to the system to improve the sharpness of the color change at the end point.

It should be noted that this is essentially the same procedure as is used to determine the total hardness of water. The total hardness is the amount of calcium and magnesium ions in parts per million calculated in terms of calcium carbonate.

This titrimetric procedure is similar to the BP assay for some calcium-containing substances.[14]

3. Back Titration

Prepare a sample solution as previously described. Pipette 50 ml of the solution into a suitable vessel, add by means of a pipette 50 ml of 0.1 M EDTA solution, add 5 ml of ammonia buffer, and a few drops of Eriochrome Black T indicator. Titrate with 0.1 M magnesium sulfate solution until the color changes from blue to wine-red.

The difference in volume between the 0.1 M EDTA solution and the magnesium sulfate solution is the volume of 0.1 M EDTA solution consumed by the calcium. Each milliliter of this solution is equivalent to 4.008 mg of calcium.

4. Replacement Titration

The replacement titration procedure involves the addition of an excess of a Mg-EDTA chelate to the solution of calcium ion being analyzed. Since calcium forms more stable chelates with EDTA than does magnesium, the calcium displaces the magnesium from the chelate and the freed magnesium is

then titrated directly. A solution of Mg-EDTA, equivalent to 50 mg/ml of the chelate is prepared by dissolving 19.90 g of $MgSO_4 \cdot 7H_2O$ and 30.1 g of Na_2-EDTA$\cdot 2H_2O$ in water and diluting to 1 liter.

Prepare the sample solution as previously described. Pipette 50 ml of the sample solution into a titration vessel containing 50 ml of water; add 25 ml of Mg-EDTA solution, 5 ml of ammonia buffer, and a few drops of Erio-chrome Black T indicator. Titrate to a deep blue with 0.1 M EDTA solution. Each milliliter of titrant is equivalent to 4.008 mg of calcium.

Since magnesium is added to the system as the EDTA chelate, no correction of titrant volume is required.

H. DETERMINATION OF LEAD

Dissolve an accurately weighed sample, equivalent to about 250 mg of lead, in sufficient water to make 100 ml. Pipette 50 ml of the sample solution into a suitable vessel, add 5 ml of acetate buffer, a few drops of Xylenol Orange indicator, and titrate with 0.1 M EDTA solution to a purple-yellow end point. Each milliliter of titrant is equivalent to 20.72 mg of lead.

This procedure is similar to the BP assay for lead acetate.[14]

I. DETERMINATION OF MAGNESIUM

Dissolve an accurately weighed sample, equivalent to about 75 mg of mangesium, in sufficient water to make 100 ml. Pipette 50 ml of this solution into a suitable vessel containing 50 ml of water; add 5 ml of ammonia buffer, and a few drops of Eriochrome Black T indicator. Titrate to a deep blue color with 0.1 M EDTA solution. Each milliliter of titrant is equivalent to 2.432 mg of magnesium.

This procedure is similar to the BP assay for magnesium stearate and sulfate.[14]

J. DETERMINATION OF ZINC

Dissolve an accurately weighed sample of zinc salt, equivalent to about 200 mg of zinc, in sufficient water to make 100 ml. Pipette 50 ml of the sample solution into a vessel containing 50 ml of water, and add 5 ml of acetate buffer and a few drops of Xylenol Orange indicator. Titrate to a purple-yellow end point with 0.1 M EDTA solution. Each milliliter of the titrant is equivalent to 6.538 mg of zinc.

This procedure is similar to the BP assay for zinc sulfate and zinc undecylenate.[14] The official USP assay for zinc stearate involves the direct titration of the ammonia-buffered sample solution with 0.1 M EDTA solution using Eriochrome Black T indicator.[15]

QUESTIONS

Q7.1. Why does chelation take place through oxygen or nitrogen atoms rather than through other atoms present in a ligand molecule?

Q7.2. Why are multidentate ligands more commonly employed as titrants than unidentate ligands?

Q7.3. How does hydrogen ion concentration effect chelate formation?

Q7.4. Why are most metal ions titrated in an alkaline solution?

Q7.5. Define the following terms:
    (a) stability constant,
    (b) dissociation constant,
    (c) association constant.

Q7.6. Describe and compare a metal ion-ligand titration and an acid-base titration.

Q7.7. Describe the chemical equilibria involved in the color change of an indicator at a complexometric titration end point.

Q7.8. Describe several methods for increasing the selectivity of a titrant.

Q7.9. What are masking agents?

Q7.10. Devise a method for determining the quantity of zinc undecylenate present in an ointment.

REFERENCES

1. Lewis, G. N., *Valence and the Structure of Atoms and Molecules*, The Chemical Catalog Publ. Company, New York, 1923.

2. Chaberek, S., and A. E. Martell, *Organic Sequestering Agents*, Wiley, New York, 1959, Chaps. 3 and 4.

3. Schwarzenbach, G., *Helv. Chim. Acta*, **35**, 2344 (1952).

4. Reilley, C. N., R. W. Schmid, and F. S. Sadek, *J. Chem. Educ.*, **36**, 555 (1959).

5. Biedermann, W., and G. Schwarzenbach, *Chimia (Aarau)*, **2**, 1 (1948).

6. Flaschka, H., A. M. Amin, and R. Zaki, *Chemist-Analyst*, **43**, 67 (1954).

7. Kurpiel, I., J. Mojejko, and L. Przyborawski, *Acta Polon. Pharm.*, **18**, 221 (1961); *C.A.*, **56**, 8844g (1962).

8. Schwarzenbach, G., *Complexometric Titrations* (H. Irving, translator), Wiley (Interscience), New York, 1957.

9. Flaschka, H., *Mikrochim. Acta*, 1954, 361.

10. Přibil, R., Z. Koudela, and B. Mateyska, *Collection Czech. Chem. Commun.*, **16**, 80 (1951); *C.A.*, **45**, 10120d (1951).

11. Schmid. R. W., and C. N. Reilley, *J. Am. Chem. Soc.*, **78**, 2910 (1956).

12. Sweetser. P. B., and C. E. Bricker, *Anal. Chem.*, **25**, 253 (1953).

13. Malát, M., V. Suk, and O. Ryba, *Chem. Listy*, **48**, 203, 533 (1954).

14. *British Pharmacopoeia*, The Pharmaceutical Press, London, 1963.

15. *Pharmacopeia of the United States*, 17th rev., Mack Publishing Co., Easton, Pa., 1965.