2.7. GRAVIMETRIC ANALYSIS

A quantitative analysis involving weight is known as **gravimetric analysis** in which the substance to be analysed is converted into an insoluble precipitate. This precipitate is collected, weighed, and assayed using a suitable method. For isolation of the desired constituent from the sample solution, **precipitation** is the most suitable technique which employs formation of a precipitate not soluble in the solution. This is achieved by adding a suitable reagent that converts the desired entity into an insoluble compound without affecting the other constituents of the sample. The precipitate formed is separated by filtration, washed to remove the soluble impurities, dried or ignited to evaporate water, and weighed.

Certain substances that may transform to gaseous compounds are separated based on this particular property. **For example**, in determination of carbonate in a mineral analysis the sample is treated with an acid and as a consequence carbon dioxide is liberated. A weighed quantity of a solid alkaline reagent absorbs this gas, thus, the increase in weight of the absorbent indicates the amount of carbon dioxide present.

Some of the selected **examples** of gravimetric analysis are given in **table 2.6**:

Table 2.6: Gravimetric Analysis of Some Drugs

Analyte	Precipitant
Penicillin G and P	1-ethylpiperidinium
Piperazine Adipate Tablets BP	Picric acid
Piperazine Phosphate BP	Picric acid
Piperazine Phosphate Tablets BP	Picric acid
Progesterone Injection BP	2,4-dinitrophenylhydrazine

2.7.1. Principle

The underlying principles of gravimetric analysis are:
1) Law of mass action and reversible reactions,
2) Principle of solubility product, and
3) Common ion effect.

## 2.7.1.1. Law of Mass Action and Reversible Reactions

Several chemical reactions participating in quantitative analysis lies in the category of reversible reactions. Under certain experimental conditions, these reactions proceed towards completion, while under other conditions they achieve equilibrium prior to completion. Results are affected by errors for a pharmaceutical substance under study. Therefore as a priority, experimental conditions are designed first so that the reactions proceed forward towards completion and fulfil the objective in quantitative assays.

Three cardinal experimental parameters to be investigated rigidly to know the reversal processes and attain completion of a reaction are:
1) Formation of very slightly ionised molecules,
2) Formation of an insoluble gas, and
3) Formation of a sparingly soluble solid.

According to the **law of mass action**, the rate of a reaction is directly proportional to the product of molecular concentrations of the reacting substances.

For example:

$$BaCl_2 + H_2SO_4 \rightleftharpoons BaSO_4 + 2HCl$$
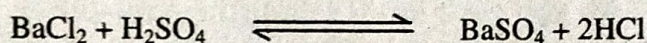
In the above reaction the rate of reaction of barium chloride with sulphuric acid is designated by the following expression:

i) **Forward Reaction**

$$\text{Rate} = [BaCl_2] \times [H_2SO_4] \times k \quad\quad\quad ..... (1)$$

Where, k = Constant that corrects for all factors which affect the rate other than concentration.

ii) **Opposing Reaction**

Likewise, in the opposing reaction:

$$\text{Rate} = [BaSO_4] \times [HCl] \times k_1 \quad\quad\quad ..... (2)$$

Where, k_1 = Another constant.

At equilibrium the rates of the forward **equation (1)** and opposing **equation (2)** are equal. Hence,

$$[BaCl_2] \times [H_2SO_4] \times k = [BaSO_4] \times [HCl] \times k_1 \quad\quad\quad ..... (3)$$

On rearranging **equation (3)**:

$$\frac{[BaCl_2] \times [H_2SO_4]}{[BaSO_4][HCl]} = \frac{k}{k_1} = K \quad\quad\quad ..... (4)$$

As k and k_1 are constants, their quotient K is also a constant known as the **equilibrium constant**.

In **equation (4)**, K is the equilibrium constant with a fixed value at a definite temperature, regardless of the concentrations of other components present. By increasing the concentration of sulphuric acid all other concentrations are altered respectively. So $BaCl_2$ concentration should be lower, whereas $BaSO_4$ and HCl concentration should be proportionately more for maintaining the equilibrium constant. This shifts the equilibrium towards the right. Many quantitative analyses allow adding one entity invariably to precede the reaction more close to completion.

2.7.1.2. Principle of Solubility Product

At a given temperature and in a saturated solution of a difficultly soluble salt, the product of the concentration of the constituent ions is constant. Upon dissociation of one molecule of the salt, each concentration is raised to the power equal to the relative number of ions provided by it.

The principle of solubility product is **applicable to:**
1) Difficultly soluble salts in their saturated solutions,
2) Occurrence of precipitation,
3) Prevention of precipitation, and
4) Dissolution of a substance.

For example, a difficult soluble salt ApBq on dissociation provides a relative number of p cations and q anions. Thus, we have:

$$ApBq \rightleftharpoons pA^+ + qB^-$$
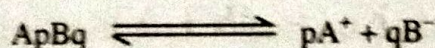
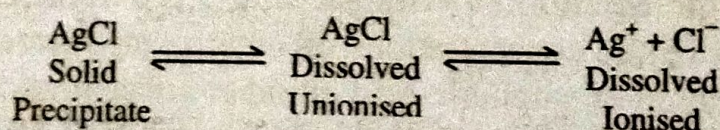Hence, solubility product $ApBq = [A^+]^p \times [B^-]^q$

Where, [ ] are generally used to express the molar concentrations.

Table 2.7 contains the solubility products of certain difficult soluble salts generally encountered in pharmaceutical analysis:

Table 2.7: Solubility Products of Important Inorganic Salts

Name of Substance	Temp. °C	Ions Involved	Solubility Product
Aluminium hydroxide	25	$Al^{3+} + 3OH^-$	1×10^{-33}
Barium sulphate	25	$Ba^{2+} + SO_4^{2-}$	1.1×10^{-10}
Calcium oxalate	25	$Ca^{2+} + C_2O_4^{2-}$	2.6×10^{-9}
Lead sulphate	18	$Pb^{2+} + SO_4^{2-}$	1.1×10^{-8}
Magnesium oxalate	18	$Mg^{2+} + C_2O_4^{2-}$	8.8×10^{-5}
Mercuric sulphide	25	$Hg^{2+} + S^{2-}$	1×10^{-50}
Silver chloride	25	$Ag^+ + Cl^-$	1.5×10^{-10}
Silver thiocyanate	25	$Ag^+ + SCN^-$	1.2×10^{-12}

The reaction of $AgNO_3$ and $NaCl$ forms $AgCl$ with slight solubility in water, approximately 0.00001 ml litre^{-1}, i.e., 1.5 mg litre^{-1}. Above this concentration, the AgCl precipitates and equilibrates with the dissolved AgCl. **At equilibrium,** a saturated solution of clear supernatant is found, and the precipitation rate of the dissolved salt is equal to the dissolution rate of the solid. This establishes the following **equilibria:**

$$\underset{\substack{\text{Solid} \\ \text{Precipitate}}}{AgCl} \rightleftharpoons \underset{\substack{\text{Dissolved} \\ \text{Unionised}}}{AgCl} \rightleftharpoons \underset{\substack{\text{Dissolved} \\ \text{Ionised}}}{Ag^+ + Cl^-}$$

Hence, the **ionisation equilibrium** may be expressed as follows:

$$\frac{[Ag^+] \times [Cl^-]_{ionized}}{AgCl_{unionized}} = K \qquad \qquad \dots (5)$$

Where, K = Ionisation constant.

On considering the following **two assumptions**:
1) At a given temperature, a saturated solution of AgCl is produced, and
2) Unionised AgCl has constant concentration, thus, the product K × [AgCl] will also be constant.

This concludes that the product of the molecular concentration of the ions of a sparingly soluble salt is constant in a saturated solution containing the salt.

2.7.1.3. Common Ion Effect

The solubility of a slightly soluble salt is decreased if excess of either of its ions are added. **For example**, the slightly soluble salt, BA gets dissociated as:

$$BA_{(S)} = B^+ + A^-$$
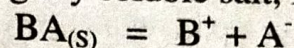
$$And \quad K_{sp} = [B^+][A^-]$$

Equilibrium condition is achieved at this point. If excess of either B^+ or A^- are added as another salt having solubility more than that of BA, the product of ionic concentrations $[B^+][A^-]$ will exceed the solubility product, thus, precipitating BA. This is because the product of ionic concentrations $[B^+][A^-]$ will get more than the solubility product. The common ion effect suggests concentration management for the ions liberated by a weak electrolyte.

2.7.2. Types of Gravimetric Analysis

Four fundamental gravimetric analysis types are described below that differ from each other with respect to sample preparation prior to weighing of the analyte:

1) **Physical Gravimetry:** It is the commonest of all the types and is used in environmental engineering. Environmental samples carry matter that is physically separated and categorised on the basis of volatility and particle size. Common analytes include total solids, suspended solids, dissolved solids, surfactants, oil, and grease.

2) **Thermogravimetry:** In this technique, a substance is kept at a controlled temperature system and its mass is measured with respect to temperature. This technique is used extensively in many disciplines like pharmacy, foods, polymer science, glasses, and volatile solids.

3) **Electro-deposition:** In this technique, the electrochemical reduction and simultaneous deposition of metal ions occurs at cathode. Before starting the electrolysis and after the process ends, the cathode is weighed. Difference in the weight corresponds to the mass of analyte that was initially present in the sample. This technique is applicable to environmental engineering analysis.

4) **Precipitative Gravimetry:** This technique causes chemical precipitation of an analyte. Precipitation methods attract the concern of analysts working with gravimetric analysis. In a gravimetric method, precipitation is the major chemical reaction as it could be a highly selective means for separating the desired component from the matrix.

2.7.3. Method of Gravimetric Analysis

Gravimetric analysis involves several steps for accurate quantitative estimation. These steps are as follows:

1) **Sampling:** The sample withdrawn from the bulk material is considered to be ideal if it represents all the properties of the bulk material. Nature of materials used, testing expenditure, product value, the end use of products, and accuracy of test method chosen are taken into account.

2) **Precipitation:** Precipitant is considered to be ideal when it reacts with the analyte and produces an easily filterable precipitate with low solubility and more stability. This precipitate should allow its washing to remove the contaminants, and after drying should bear a fixed known composition.

   Reaction occurring in a liquid forms a solid known as **precipitate**. When the solid is compacted through centrifuge, it is named as **pellet**. The liquid which remains above the solid in either case is called the **supernate** or **supernatant**.

3) **Purity of Precipitate (Co-Precipitation & Post-Precipitation):** Even if a precipitate is formed from a solution, it may not be completely pure. The substances soluble in mother liquor may also contaminate the precipitate. This is known as **co-precipitation** which is concerned with adsorption occurring at the surface of the particles in the solution and occlusion of foreign substances during the crystal growth from primary particles. Maximum adsorption occurs in gelatinous precipitates, while minimum occurs for microcrystalline precipitates.

   Co-precipitation is of two types, the first type involves surface adsorption of the particles exposed to the solution; and the second type involves occlusion of foreign materials during crystal growth from the primary molecules.

   Surface adsorption will be more for gelatinous precipitates and least for macrocrystalline precipitates. Precipitates with ionic lattices follow the **Paneth-Fajans-Hahn adsorption rule**. According to this rule, the ion forming the least soluble salt is most strongly adsorbed by an ionic substance (crystal lattice).

   Post-precipitation is a precipitation occurring on the surface of the initially formed precipitate. This precipitation may result in errors. Sparingly soluble substances forming supersaturated solutions show post-precipitation which occurs when the substances have an ion common with the primary precipitate. Precipitation occurring on the surface of the primary precipitate is enhanced with increase in contact time.

4) **Digestion:** Digestion of precipitate or **Ostwald ripening** is a process in which larger crystals grow at the expense of the smaller ones when a precipitate is allowed to stand in the presence of mother liquor.

5) **Ageing:** It is a process which under suitable conditions improves the crystal lattice structure to some extent of perfection. Impurities from the solution attached on to the precipitates for many reasons. Digestion allows these impurities to return to the solution by dissolving smaller particles.

6) **Filtration:** In the process of filtration, the mother liquor is separated from the **precipitate** using a different variety of filter media. The process involving separation of an insoluble solid from a liquid-solid mixture using a porous material such as a filter paper is known as **filtration**. The filter paper used retains the solid which is termed as the **residue** and allows the liquid to pass through it which is collected below and is called the **filtrate**. The way in which filter paper is fitted into the funnel influences the filtration. The rate of filtration can be enhanced by using a funnel with a large stem and placing it at an angle as nearly as 60°.

After filtration, the solution should undergo a test to ensure complete precipitation of the analyte. The precipitation is said to be incomplete if a precipitate forms on adding a few drops of the precipitating reagent to the solution.......

7) **Washing of Precipitate:** The filtered precipitate contains some impurities on its surface that needs to be washed off. An ideal washing solution does not affect the precipitate but dissolves out the foreign matter. Water is not always used to wash the precipitates. Certain precipitates are washed using washing solution.

Washing with pure water is preferred, provided that it does not dissolve the precipitate in significant amounts. If the precipitate is soluble in water, a common ion should be added which decreases the solubility of an electrolyte in a dilute solution containing one of its ions compared to that in pure water.

8) **Drying and Ignition of Precipitate: Drying** facilitates conversion of the precipitate into a form having a constant composition which can be easily weighed. This process removes water and the adsorbed electrolyte from washing solution. **Ignition** employs heating using an appropriate burner or placing the crucible in an electrically heated muffle furnace. Ash-free filter papers are employed to make the ignition step easy. For temperature below 250°C, **drying** is preferred; whereas **ignition** is used for temperatures above 250°C and below 1200°C.

9) **Weighing and Calculations:** The residue obtained after drying is cooled in **desiccators** at room temperature. Thereafter, an analytical balance is used to accurately weigh the dried form of precipitate.

$$\% \, A = \frac{A(g)}{Sample(g)} \times 100$$

Where, A= Grams of analyte.

Modern balances weigh samples directly and masses from several grams to a few micrograms accurately and rapidly. Generally in a gravimetric method, a precipitate is weighed which is used to estimate the weight of the analyte contained in the sample. This calculation involves **Gravimetric Factor** (GF) which is the weight of analyte per unit weight of the precipitate. It is the ratio of the formula weight (f) of the analyte to the precipitate weight multiplied by the moles of analyte per mole of precipitate given by each moles of analyte. The GF is given by:

$$GF = \frac{f \, wt \, anlyate(g/mol)}{f \, wt \, precipitate \, (g/mol)} \times \frac{a}{b} (mol \, analyte/mol \, precipitate) \quad .....(1)$$

$$= g \, analyte/g \, precipitate$$

2.7.4. Applications

Gravimetric methods are applied in the following areas:

1) **Analysis of Standards:** This is required during testing and/or instrument calibration.

2) **Analysis Requiring Accuracy:** These analyses can be conducted using gravimetry which being time-consuming allows only a few determinations.

3) **Pharmacopoeial Analysis:** It is applied for the analysis of the following:

   i) **Chloride as Silver Chloride:** The aqueous chloride solution is acidified with dilute nitric acid so that the precipitation of other silver salts (like phosphate and carbonate) which might occur in neutral solution is prevented.

   The solution is also acidified to produce an easily filterable precipitate. Silver nitrate solution is added in slight excess, so that silver chloride is precipitated:

   $$Cl^- + Ag^+ = AgCl$$
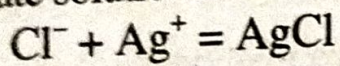
   At first the precipitate is colloidal which coagulates into curds by heating the solution. When the suspension is stirred vigorously, a clear supernatant liquid is obtained. The precipitate is collected in a filtering crucible and dilute nitric acid is used for washing it to prevent colloid formation. The washed compound is dried at 130-150°C and the residue is weighed as AgCl.

   ii) **Lead as Chromate:** This method has less application due to insolubility of chromates. However, this method helps in gaining experience in gravimetric analysis. The best results are obtained by precipitating from homogeneous solution using the homogeneous generation of chromate ion produced by slow oxidation of chromium (III) by bromate at 90-95°C in the presence of an ethanoate buffer.

   iii) **Nickel as Dimethylglyoximate:** Dimethylglyoxime (DMG) produces a red complex with alkaline solution of nickel in the presence of an oxidising agent (bromine).

   The Ni-DMG complex of red colour has nickel in higher oxidation state (probably (III) and also (IV)). The absorption range of complex is 445nm. The colour intensity varies with time; therefore, absorbance measurement is important within 10 minutes of mixing. Under the experimental conditions, cobalt (II), gold (III) and dichromate ions interfere. So their presence in analyte sample is undesirable.