

# Contents

<i>Preface</i> .....	vii
<i>B. Pharm. Syllabus</i> .....	ix
<b>1. Theoretical Aspects of Quantitative Analysis</b> .....	<b>1-33</b>
1.1 Introduction .....	3
1.2 Importance of Quantitative Analysis in Quality Control.....	4
1.3 Different Techniques of Pharmaceutical Analysis.....	7
1.3.1 Volumetric Analysis	7
1.4 Computation of Analytical Results .....	8
1.4.1 Addition and Subtraction	9
1.4.2 Multiplication and Division	9
1.4.3 Rounding Numbers	9
1.4.4 Retention of as many Significant Figures	10
1.5 Preliminaries and Definitions.....	10
1.5.1 Statistical Validation	10
1.5.2 Validation of a Method	11
1.5.3 Titrimetric (Volumetric) Analysis	13
1.5.4 Instrumental Analysis	14
1.5.5 Sources of Errors in Weighing	15
1.5.6 Protein-Free Filtrates	16
1.5.7 Quality Control Chart (QCC)	16
1.5.8 True Value	17
1.5.9 Sample Size	18
1.5.10 Minimum Number of Samples	18
1.5.11 Precision	19
1.5.12 Sensitivity	19
1.5.13 Range (R)	20
1.5.14 Limit of Detection	20

1.5.15	Precision of a Result	21
1.5.16	Limit of Quantitation	21
1.6	Significant Figures	22
1.7	Types of Error <i>vis-a-vis</i> Concept of Error	22
1.7.1	Types of Errors	23
1.7.1.1	Determinate (Systematic) Errors	23
1.7.1.2	Indeterminate (Random) Errors	25
1.8	Mean (Average) Deviation	25
1.9	Standard Deviation	26
1.10	Statistical Treatment of Small Data Sets	26
1.11	Calibration of Analytical Instruments, Apparatus and Applying Necessary Corrections	27
1.12	Methods of Expressing Concentrations	29
1.12.1	Percent by Weight	30
1.12.2	Percent by Volume	30
1.12.3	Percent Weight/Volume (w/v)	30
1.12.4	Molarity (M)	30
1.12.5	Normality (N)	30
1.12.6	Formality (F)	30
1.12.7	Molality (m)	31
1.12.8	Mole Fraction	31
1.13	Primary and Secondary Standards	31
1.13.1	Primary Standard	31
1.13.2	Secondary Standard	32

## 2. Acid-Base (Neutralization) Titrations

34-77

2.1	Acid-Base Concepts (Theories)	35
2.1.1	Arrhenius Theory [ $H^+$ and $OH^-$ ]	36
2.1.2	Theory of Solvent Systems [Solvent Cations and Anions]	36
2.1.3	Bronsted-Lowry Theory [Taking and Giving Protons]	37
2.1.4	Lewis Theory [Taking and Giving Electrons]	38
2.2	Role of Solvent	39
2.3	Relative Strengths of Acids And Bases	42
2.3.1	Dissociation Constant	42
2.3.2	Autoprotolysis	43
2.3.3	Molar Equilibrium Constants	44
2.4	Law of Mass Action	45
2.5	Common Ion Effect [Shifting The Equilibria]	48

2.6	Ionic Product of Water [ $K_{H_2O}$ ]	49
2.7	pH [or The pH Scale]	50
2.8	Hydrolysis of Salts	52
2.9	Henderson-Hasselbalch Equation	54
2.10	Buffer Solution	54
2.11	Neutralization Curves [Titration Curves]	56
2.12	Acid-Base Indicators	58
2.13	Theory of Indicators	59
	2.13.1 Ionic Theory of Indicators	60
	2.13.2 Chromophore Theory of Indicators	61
2.14	Choice of Indicators	66
2.15	Mixed Indicators	67
2.16	Universal Indicators	69
2.17	Polyprotic System	71
2.18	Applications of Acid-Base Titrations	72
	2.18.1 Assay of Sodium Hydroxide [NaOH]	72
	2.18.2 Assay of Calcium Carbonate [ $CaCO_3$ ]	74
	2.18.3 Assay of Phosphoric Acid [ $H_3PO_4$ ]	75

### **3. Oxidation-Reduction Titrations** **78-121**

3.1	Concepts of Oxidation and Reduction	79
3.2	Reduction-Oxidation (Redox) Reactions	90
3.3	Standard Oxidation Potential	81
3.4	Strengths and Equivalent Weights of Oxidizing and Reducing Agents	82
	3.4.1 Strengths of Oxidizing and Reducing Agents	82
	3.4.2 Redox Equivalent Weights [Equivalent Weights of Oxidizing and Reducing Agents]	83
3.5	Nernst Equation [Effects of Concentrations on Potentials]	85
3.6	Theory of Redox Titrations	86
	3.6.1 Before the Equivalence Point	88
	3.6.2 At the Equivalence Point	88
3.7	Equilibrium Constants of Oxidation-Reduction Reactions	89
3.8	Side Reactions in Redox Titrations	91
3.9	Oxidation-Reduction Titration Curves [Redox Titration Curves]	92
3.10	Redox Indicators	98
3.11	Redox Cell Representations [Electrochemical Cells]	101

3.12	Measurement of Electrode Potentials [or Half-Reaction Potentials] .....	103
3.13	Titrations Based on Redox Reactions .....	105
3.13.1	Iodimetry and Idometry 105	
3.13.2	Permanganate Titrations 108	
3.13.3	Potassium Dichromate [K <sub>2</sub> Cr <sub>2</sub> O <sub>7</sub> ] Titrations 111	
3.13.4	Ceric Sulphate Titrations [Cerimetry; Oxidation by Ce <sup>4+</sup> Ions) 112	
3.13.5	Titrations with Potassium Bromate [KBrO <sub>3</sub> ] 113	
3.13.5.1	Assay of Mephenesin 113	
3.13.5.2	Phenol 114	
3.13.6	Titrations with Potassium Iodate [KIO <sub>3</sub> ] 114	
3.13.6.1	Assay of Benzalkonium Chloride 116	
3.13.6.2	Assay of Potassium Iodide [KI] 116	
3.13.7	Reduction By Ti <sup>3+</sup> Ions [Titanometry] 117	
3.13.7.1	Direct Titration with TiCl <sub>3</sub> 117	
3.13.7.2	Residual Titration with TiCl <sub>3</sub> 117	
3.13.8	Sodium-2, 6-dichlorophenolindophenol 119	

#### **4. Precipitation Titrations**

**122-139**

4.1	Introduction .....	123
4.2	Principle of Precipitation Titrations .....	123
4.3	Precipitation Reaction Chemistries .....	125
4.4	Solubility Product [K <sub>sp</sub> ] .....	125
4.5	Influence of Acids (pH), Stoichiometry, Stability and Common-Ion Effect <i>vis-a-vis</i> Solubility of Precipitate .....	128
4.5.1	Influence of Acids (pH) on Solubility of Salts 128	
4.5.2	Stoichiometry <i>vis-a-vis</i> Solubility 130	
4.5.3	Stability 130	
4.5.4	Common-Ion Effect 130	
4.6	Profile of Precipitation Titrations: Involving .....	131
4.6.1	Silver Nitrate 131	
4.6.2	Ammonium or Potassium Thiocyanate 131	
4.6.3	Mercuric Nitrate 132	
4.6.4	Barium Sulphate 133	
4.7	Specifically Named Precipitation Titrations .....	133
4.7.1	Gay-Lussac's Method 133	
4.7.2	Mohr's Method [or Indicator Method] 135	
4.7.3	Volhard's Method 136	
4.7.4	Fajan's Method 138	

<b>5. Gravimetric Analysis</b>	<b>140–183</b>
5.1 Introduction .....	141
5.2 Theory [or Fundamentals] .....	142
5.3 Precipitation Techniques .....	145
5.3.1 Solution Preparation	145
5.3.2 Precipitation	146
5.3.3 Digestion	148
5.3.4 Filtration	149
5.3.5 Washing	151
5.3.6 Ignition [Incineration or Drying]	152
5.3.7 Weighing to Constant Weight	152
5.4 Solubility Products .....	152
5.5 The Colloidal State .....	152
5.6 Coprecipitation and Factors Affecting Coprecipitation .....	155
5.6.1 Effect of the Adsorbent Area	157
5.6.2 Effect of Concentration	157
5.6.3 Effect of Temperature	157
5.6.4 Effect of Nature of Adsorbed Ions	157
5.6.5 Effect of Precipitation Conditions	159
5.7 Post-Precipitation .....	159
5.8 Precipitation from Homogeneous Solution .....	160
5.9 Choice of Precipitants [or Precipitating Reagents] .....	160
5.9.1 Ideal Organic Precipitants	160
5.9.2 Organic Reagents for Chelate Formation in Metal Analysis	161
5.10 Requirements for the Precipitated Form .....	163
5.11 Amount of Precipitation Reagents [Precipitants] Required .....	164
5.12 Salt Effect .....	166
5.13 Factors Affecting Completeness of Precipitation .....	168
5.13.1 Effect of Temperature upon Completeness of Precipitation	168
5.13.2 Effect of pH ( $H^+$ Ion Concentration) upon Completeness of Precipitation	170
5.13.2.1 Precipitation of Sparingly Soluble Metal Hydroxides	170
5.13.2.2 Precipitation of Sparingly Soluble Salts of Weak Acids	171
5.13.2.3 Precipitation of Sparingly Soluble Salts of Strong Acids	172
5.14 Thermal Degradations and Thermogravimetric Analysis [TGA] .....	173
5.14.1 Static Thermogravimetric Analysis	173
5.14.2 Dynamic Thermogravimetric Analysis	174

5.15	Pharmaceutical Applications of Gravimetric Techniques .....	175
5.15.1	Sulphate [ $\text{SO}_4^{2-}$ ] as Barium Sulphate [ $\text{BaSO}_4$ ] 175	
5.15.2	Aluminium [ $\text{Al}^{3+}$ ] as Aluminium Oxide [ $\text{Al}_2\text{O}_3$ ] 177	
5.15.3	Calcium [ $\text{Ca}^{2+}$ ] – as Calcium Oxalate [ $\text{CaC}_2\text{O}_4$ ] 177	
5.15.4	Magnesium [ $\text{Mg}^{2+}$ ] – as Magnesium Pyrophosphate [ $\text{Mg}_2\text{O}_7\text{P}_2$ ] 179	
5.16	Applications of Gravimetric Analysis in Assay of Drugs .....	180
5.16.1	Assay of Papaverine Hydrochloride Tablets 180	
5.16.2	Assay of Amodiaquine Hydrochloride 181	

**185–199****Appendices (I to IV)****185-200**

Appendix I	– International Atomic Masses	185
Appendix II	– Formula Weights	189
Appendix III	– Compounds for Preparing Standard Solutions	191
Appendix IV	– Acronyms And Abbreviations of Significance in Pharmaceutical Analysis	193

**Index****201–212**