Subject Name: Pharmaceutical Analysis

Topic Cover

1. **Importance of quality control in pharmacy**
2. **Acid-base titrations**

Definitions of acids & bases according to Arrhenius & Lewis theory. Definitions of normality, molarity, molality, & equivalent weight. Primary & secondary standards with examples & differences between them. Standardization of strong acids & bases using primary & secondary standards. Preparation of standard solutions of & calculations of equivalent weights of oxalic acid, potassium acid phthalate, calcium chloride dihydrate, & sodium carbonate. Calculation of factors involved in standardization of sodium hydroxide, hydrochloric acid, & oxalic acid. Direct, back & differential titrations. Application of direct & back titrations to preparations like boric acid & borax in a mixture, ammoniated mercury, milk of magnesia, & zinc oxide ointment.

Law of mass action, acid-base equillibria, pH scale, pH & hydronium ion concentrations in aqueous systems, calculations of pH for weak acids & weak bases. Use & applications of pH meter. Hydrolysis of salts. Strengths of acids & bases, dissociation constant.

Theory of acid –base indicators. Neutralization [titration] curves. Definition, different types of buffers [chemical & biological], & their composition. Buffer capacity, buffered isotonic solutions. Calculations involving preparation of various buffer capacity solutions. Biological & pharmaceutical applications of buffers.

3. **Non-aqueous titrations**

Acid-base definitions according to Lowry-Bronsted, Lewis & Arrhenius concept. Factors affecting strengths of acids & bases. Intrinsic structure & surrounding environment. Protophilic, protogenic, amphiprotic & aprotic solvents. Acid-base equillibria in non- aqueous media. Titrants & indicators used for assay of acidic & basic substances. Preparation of perchloric acid, formation of onium ion. Assay of 1o, 2o, 3o amines & amine hydrochlorides using perchloric acid & the reactions involved in it. Standardization of sodium ethoxide solution. Assay of phenols & phenobarbitone. General applications of non-aqueous titrations

4. **Oxidation- reduction titrations**

Definition of oxidation, reduction, oxidizing & reducing agent. Equivalent weight, concept of half reactions. Systematic balancing of half reactions with respect to: a. Oxalic acid-$KMnO_4$, b. $FeSO_4$-ceric nitrate, & c. I_2-sodium thiosulphate solution titrations. Calculation of equivalent weight of oxalic acid, $KMnO_4$, $FeSO_4$, permangnate & I_2 from half reactions. Calculation of factors for titrations mentioned in a, b & c.

a) Redox itrations: $KMnO_4$ as self indicator, it's preparation, standardization, & use in the assay of ferrous gluconate tablets, H_2O_2, & $NaNO_2$ solution.

b) Iodimetric & iodometric titrations. Definitions & difference between iodimetry & iodometry. Preparation, standardization of iodine solution. Assay of ascorbic acid & sulphur ointment by iodimetry. Assay of copper sulphate & ferric chloride by iodometry.

c) Bromometric titrations.

d) Iodate titrations. Definition. Preparation, standardization & use of KIO_3 in the assay of ascorbic acid & KI.

e) Cerimetric titrations. Preparation, standardization & use of ceric solutions in the assay of paracetamol tablets. It's advantages over permanganate solutions.

f) Bromine titrations. Preparation, standardization & use of bromine solution in the assay of phenol & isoniazide tablets. g) Potassium dichromate titrations. Preparation, standardization & use of potassium dichromate solution in the assay of ferrous ammonium sulphate.

5. **Precipitation titrations**

Principle of solubility product & sparingly soluble salts. Titrants & indicators used in Mohr's, Volhard's, & Fajan's methods. Preparation & standardization of silver nitrate & ammonium thiocyanate solutions. Assay of sodium chloride by Mohr's method, use of nitrobenzene in the assay of halides, ammonium chloride, & thiourea by Volhard's method. Calculation of factors in argentimetric titrations. Titration curve method. General applications of precipitation titrations.

6. **Complexometric titrations**

Difference between double salts & co-ordinate compounds. Definitions of co-ordination number of metal ions, ligands- uni-, bi-, & multidentate. Complexing, chelating, & sequestering agents with respective examples. Structure of complexes of platinum with ammonia. Ethylene diamine tetraacetate [EDTA] as a multidentate ligand in complexometry. Co- ordinate compounds of EDTA with bi-, tri-, & tetravalent metal ions. Stability of complexes & factors affecting it, use of buffers in EDTA titrations. Selective analysis of ions based on pH adjustments, use of masking & demasking agents, pM or metal ion indicators. Standardization of EDTA solution, titration curves, and examples of assays carried out by direct & back titrations & by replacement of one complex by the other. Applications of complexometry in the assays of calcium gluconate, milk of magnesia, zinc undecenoate ointment, & aluminium hydroxide gel. Assay of NaF by indirect titration.

7. **Gravimetry**

Principles of gravimetry. Factors affecting precipitation, formation, & properties of precipitate. Colloidal state. Impurities in precipitate, conditions of precipitation. Precipitation from homogenous solutions, washing, drying, & ignition of precipitate.

Experimental techniques of drying & ignition. Applications of gravimetry in pharmacy.

8. Extraction techniques Liquid-liquid extraction, separation of mixtures by extraction. Distribution law. Successive & multiple extraction [Craig method], continuous counter- current extraction. Effect of temperature & pH on extraction. Inert solute, associate ion pair formation, emulsion problem in extractions. Applications in pharmacy.

9. Potentiometry Theory, ion selective electrodes, measurement of potential, red-ox titration curve, pH measurement, relation of pH to potential. Applications in pharmacy.

10. Miscellaneous methods of analysis Diazotization titrations. Kjeldahl nitrogen estimation. Karl Fisher titrations. Liquid gelenicals. Oxygen flask Determination of alcohol content in liquid gelenicals. Oxygen flask combustion method.

11. Calibration Calibration of instruments.

12. General principles of spectroscopy Wave-particle duality, wave properties, particulate properties. Line & band spectrum. Electromagnetic spectrum. Absorption & emission spectroscopy. Understanding of terms such as absorbance, transmittance, absorptivities, molar absorptivity, E 1cm 1%, λmax, effect of solvent & pH on λmax.

13. Ultraviolet-visible Spectrometry Different electronic transitions. Auxochromes & their effects, auxochromic, bathochromic & hypsochromic shifts [red & blue shifts]. Beer-Lambert law, its derivation, deviations in Beer's law. Single & double beam spectrophotometers covering sources of radiations, different monochromators, detectors such as barrier cell, photocell, photomultiplier tube. Photodiode array detector. Applications of this technique in qualitative & quantitative estimations giving emphasis on problem solving. Fieser-Woodward rules for calculations of theoretical λmax values.

14. Spectrofluorimetry Principle, definitions & types of luminescence. Mechanism of fluorescence & phosphorescence. Singlet & triplet states & intersystem crossing. Fluorescence yield & factors affecting it. Quenching of fluorescence & fluorescence quenchers. Structure & fluorescence. Brief discussion of instrumentation. Applications of fluorimetry in pharmacy.

15. Flame photometry & atomic absorption spectrometry Principle & instrumentation with emphasis on working & importance of different components. Temperature, flame absorption & emission profiles. Interferences & their avoidance. Quantitative estimations & applications.

16. Infrared spectrometry Infrared region in EM spectrum. Principle, different stretching & bending vibrations. Components [& their working] of a dispersive instrument. Fourier transform [FT] technique, FT instruments & their comparison with dispersive instruments. Sample handling techniques. Functional group & finger print regions in the spectrum. Functional groups identification & their use in characterization of compounds. Problems based on identification of functional groups from spectra of unknown compounds.

17. Proton nuclear magnetic resonance spectrometry Principle involved in the technique. Knowledge about fundamental terms involved such as quantized absorption, flipping of nucleus, spin number, magnetic moment, magnetogyric ratio, relaxation, etc. Equations relating these terms to frequency of radiation & magnetic field [without derivation of the equations]. Types of relaxation processes. Low & high resolution instruments. A brief discussion on the low resolution instrumentation [60 MHz]. Quantitative knowledge of relationship between MHz & magnetic field. An introduction to superconductivity magnets. Solvents & reference standards used. Setting up of a NMR scale. Sample preparation. Shielding & deshielding of a proton & it's effect on chemical shifts. Discussion on & importance of equivalent & non equivalent protons [number of signals], chemical shifts [position of signal] & their calculation from the spectrum, chemical shifts of different H's, splitting [multiplicity] of a signal, coupling constants [J values] , integration [area under the signal] . Importance of these terms in identification [or confirmation] of different functional groups. Significance & contribution of J value in stereochemistry. Prediction [expected theoretical values] of chemical shifts & multiplicities for all protons from simple structures containing up to 12-15 carbons. An introduction to FT-technique & its significance in 13C-NMR spectrometry.

18. Mass spectrometry Principle. Low & high resolution instruments. Components & importance of each in brief. Different types of mass spectrometric techniques. Brief knowledge of Chemical Ionization mass spectrometry. Calculations of hydrogen deficiency index [HDI] or unsaturation index [UI]. Base or parent peak, molecular ion, M + 1, M + 2 peaks. Calculations of molecular weight based on M +1 & M + 2 peaks. Formation of molecular ion & further fragmentation. Rearrangements in mass spectrometry. Major modes of fragmentations of hydrocarbons, hydroxyl

compounds, halogen compounds, aldehydes, ketones, carboxylic acids, and amines. Introduction [only] to recent advances in MS.

19. Polarography. Principle & instrumentation. Ilkovich equation [no derivation] & its importance. Dropping mercury electrode [DME], saturated calomel electrode. Liquid-liquid junction potential, polarographic cell. Explanation of origin of S-shaped C-V curve. Applications of this technique. Amperometric titrations, principles, instrumentation, & applications.

20. Nephelometry & Turbidimetry Principles, Tyndall effect. Duboscq turbidimeter. Eeel's nephelometer. Applications.

21. Chromatography. Principle, rate & plate theory, Van Deemter equation & the parameters affecting separation/band broadening. Classification of chromatography, retention factor. A detailed study of thin layer chromatography [TLC], preparative TLC, paper chromatography [PC], column chromatography, gas chromatography [GC / GLC]. Qualitative & quantitative applications of the above techniques. An introduction to high performance TLC [HPTLC], comparison of TLC & HPTLC. A brief introduction to high pressure / performance liquid chromatography [HPLC].

22. Miscellaneous An introduction to electrophoresis. An introduction to lasers & masers. Statistical treatment to experimental data. Sampling techniques & applications in pharmaceutical industry.