B. Pharmacy 1st Semester - Pharmaceutical Analysis Notes

UNIT – 1

(a) Introduction of Pharmaceutical Analysis 📊

Points to be covered in this topic

➞ DEFINITION & SCOPE OF PHARMACEUTICAL ANALYSIS
➞ TECHNIQUES IN PHARMACEUTICAL ANALYSIS
➞ METHODS OF EXPRESSING CONCENTRATIONS ANALYSIS
➞ PREPARATION AND STANDARDIZATION OF VARIOUS MOLAR AND NORMAL SOLUTIONS

PHARMACEUTICAL ANALYSIS 🔬

DEFINITION & SCOPE OF PHARMACEUTICAL ANALYSIS

Pharmaceutical analysis is a branch of chemistry which involves the application of analytical procedures to ensure the purity, quality and safety of pharmaceutical products. It involves qualitative and quantitative analysis that consists of series of procedures for the identification, determination, quantitation and purification.

➤ PRECISION 🎯

Precision is defined as, "the degree of agreement between various results of the same quantity". In other words, it is the reproducibility of result.

For example, if a result of an analysis is 6.18 when it was performed for the first time. If the analysis is repeated four times, and the values obtained are 6.17, 6.19, 6.18 and 6.17, then the precision is calculated by comparing the values with each other. The closeness of the values decide the precision of the method.

SIGNIFICANT FIGURES 🔢

Significant figures – While recording the values measured in analysis, some errors do happen if the figures are not properly recorded.

The number of significant figures can be defined as, "the number of digits necessary to express the results of a measurement consistent with the measured precision".

Each digit denotes the actual quantity that it specifies. The proper manner of expressing a result or observations is to retain such number of figures that all are known with certainty except the last.

It should be clear that, zeroes are employed to denote the significant part of measurement – to denote tens, hundreds, thousands etc or merely to locate the decimal point.

Thus, zeroes within a number like 25.05 and 1350 are significant as they express the exact quantity, while zeroes in figures like 0.0234 only show the magnitude of the other digits.

Significant figures rules 📏

- All non-zero digits are significant.
- Captive zeros are significant.

- Trailing Zeros are only significant if there is a decimal point or a bar above a zero.
- Leading zeros are never significant.
- Exact numbers have an infinite amount of sig digs.

ROUNDING OFF FIGURES 🔄

In number of observations or measurements or in calculations, sometimes data is spread in large numerical. It is necessary for accuracy and in calculations that rounding off the figures is done.

Examples:

- 12 → 10, 1,344 → 1,340
- 114 → 110, 1,488 → 1,490
- 58 → 60, 99 → 100

In rounding off the quantities, the correct number of significant figures should be retained, e.g., when adding 128.126, 018 & 0.2678, it should be written as 128.12 + 6.00 + 0.27.

Likewise, in multiplication or division, a similar rounding off of the figures are carried out as in multiplication of 112 × 2301 × 0.5786, the values used for calculations are 1.12 × 230 × 0.58.

The rounding off the figures thus is essential to curtail lengthy and tedious calculations.

It is very common in analytical work to get dissimilar results, and no analysis is complete until all the results are collected, calculated and

properly reported.

In quantitative analysis, when numerical data and results are collected, it is generally observed that the results obtained by various methods or of series of determinations differ among themselves to a varying extent.

There is a general tendency to find an average value of a series of measurements to be taken as the true value. It should be always remembered that the average value may not be the true value.

(c) Pharmacopoeia, Sources of Impurities & Limit Test 📚

Points to be covered in this topic

➤ PHARMACOPEIA

- INDIAN PHARMACOPOEIA
- INDIAN PHARMACOPOEIA 2022
- MONOGRAPHS
  ➤ SOURCES OF IMPURITIES
  ➤ LIMIT TEST
- LIMIT TESTS OF CHLORIDE
- LIMIT TESTS OF SULPHATE
- LIMIT TESTS OF IRON
- LIMIT TEST OF HEAVY METALS
- LIMIT TEST OF LEAD
- LIMIT TEST OF ARSENIC

PHARMACOPEIA 📖

INTRODUCTION 🌟

The term Pharmacopoeia is derived from the Greek word "pharmakon" which means a drug or medicine and "poieo" is to make. Drugs manufactured in India have to be labeled with the mandatory non-proprietary name with the suffix "I.P".

It provides a collected list of drugs and medicinal substances along with directions for making preparation from them.

A quality specification is a compilation of a set of appropriate tests that ascertain the amount of the active substance in the product and confirm the identity, purity and performance characteristics of the product. Reference standards are employed in such testing to ensure the quality of medicines.

The compilation covers starting materials, excipients, intermediates and finished pharmaceutical products (FPPs). It also covers the General requirements related to quality of medicines such as analytical methods, microbiological purity, dissolution testing stability, etc.

International standards are provided in the International Pharmacopoeia (Ph. Int.) issued by WHO. The pharmacopoeia is a common tool to be used by the public. It comprises of the recommended procedures for analysis and specifications for the determination of pharmaceutical substances, excipients and dosage forms and thus maintains the quality of medicines.

Most of the pharmacopoeias consist of a general part which includes tests, methods and general requirements for pharmaceutical substances and a specific part which is designed in the form of monographs for pharmaceutical substances.

INDIAN PHARMACOPOEIA IN

Indian Pharmacopoeia is published by the Indian Pharmacopoeial Commission (IPC), Government of India, Ministry of Health & Family Welfare. The Indian Pharmacopoeia (IP) is published according to the requirements of the Drugs and Cosmetics Act, 1940.

IP is published to contribute to the development of public health through ensuring the quality, safety and efficacy of medicines. It is published at regular and shorter intervals.

IP provides well-defined procedures for analysis and specifications for the determination of the quality of pharmaceutical substances, excipients and dosage forms.

The monograph in IP for an official substance or preparation comprises of the article's definition, description, identification, packaging, storage, specifications, impurities, assay and specific tests, analytical procedures, acceptance criteria, other requirements etc.

History of Indian Pharmacopoeia 📜

In 1833, East India Company's Dispensary committee recommended the publication of a Pharmacopoeia. Thus, Bengal Pharmacopoeia, was published in 1844.

The first IP published in 1868 covered both the drugs of British Pharmacopoeia (BP) 1867 and indigenous drugs used in India with a supplement published in 1869 incorporating the vernacular names of indigenous drugs and plants. However, from 1885 the BP was made official in India.

In 1927, Government formed a Drugs Enquiry Committee that recommended the publication of a National Pharmacopoeia. Later, the Indian Pharmacopoeia Committee was constituted in 1948, which published the IP in 1955, followed by a Supplement in 1960.

The Indian Pharmacopoeia Committee was reconstituted in 1978 considering the growth of Pharma Industries. In the Pharmacopoeia of India 1985, and in its Addenda 1989 and 1991, the inclusion of the traditional system of drugs was limited.

A new Indian Pharmacopoeia Commission established in the year 2005 focuses on those drugs and formulations related to National Health Care Programmes and the National Essential Medicines such as antiretroviral, anticancer, Antituberculosis and herbal drugs to be included in the IP 2007.

Biotechnological and Veterinary preparations are also included in IP 2007. 72 new monographs had been incorporated in Addendum 2008 to the IP 2007.

To establish transparency in setting standards for this edition, the contents of new monographs, revised appendices and other information have been publicized on the website of the IPC, besides following conventional approach of obtaining comments. Thus, the history continues and recent IP was published in 2018.

INDIAN PHARMACOPOEIA 2022 🆕

IPC releases IP 2022, 92 new monograph, 27 APIs added. In a bid to promote the highest standards of drugs for use in humans and animals, the Indian Pharmacopoeia Commission (IPC) has released Indian Pharmacopoeia 2022 containing:

- **92 new monographs**
- **21 vitamins, minerals, amino acids, fatty acids**
- **27 active pharmaceutical ingredients (APIs)**

The Indian Pharmacopoeia which is likely to be effective from December 1, 2022, also includes:

- 3 new biotechnology derived therapeutic products
- 2 herbs & herbal products
- 2 blood & blood related products
- 33 dosage forms (chemicals)
- 4 vaccines and immunosera for human use
- 12 new general chapters

Key Historical Facts:

- First pharmacopoeia publishes as "Bengal pharmacopoeia" in 1844.
- First Indian Pharmacopoeia Committee in 1948, Chairman – Dr. B. N. Ghosh.

Evolution of Indian Pharmacopoeia Editions 📊

Edition	Supplement	Features
1st – 1955	1960	• Covers 986 monographs • Titles of monograph in Latin language • Weight and measure in metric system
2nd – 1966	1975	• Titles of monograph in Latin language to English • Name of drugs first came • New analytical technique added
3rd – 1985 (2 Volume)	1989 and 1991	• Dissolution technique had been added • Microbial limit test prescribed for liquid preparation • Flame photometry, electrophoresis, fluorometry added
4th – 1996 (2 Volume)	2000, 2002 and 2005	• Computer generated formulae are used • IR and UV spectrophotometry test added • Contain 1149 monographs and 123 appendices
5th – 2007 (3 Volume)	2008	• Volume one contain general notice, structure of IPC • Volume two three contain general monographs

IPC Commission

The Indian Pharmacopoeia Commission (IPC) has been formed under the Ministry of Health and Family Welfare's Resolution in the year 2008. It is comprising of the General Body of 25 members, Governing Body of 13 members and scientific body of 15–23 members from different related scientific fields.

The Secretary, Ministry of Health and Family Welfare, is the Chairman and the Chairman-Scientific Body is the Co-Chairman of the Commission. The Secretary-cum-Scientific Director is the Chief Scientific and Executive Officer of the Commission.

Mission 🎯

The mission of the IPC is to promote public health in India by bringing out authoritative and officially accepted standard for quality of drugs including active pharmaceutical ingredients, excipients and dosage forms, used by health professionals, patients and consumers.

Objectives of IPC 📋

✓ To develop comprehensive monographs for drugs to be included in the Pharmacopoeia, including active ingredients, aids, dosage forms, devices, and to keep them updated by revision.

✓ To develop monographs for herbal drugs.

✓ To accord priority to monographs of drugs included in the National Essential Medicines List.

✓ To take note of the different levels of sophistication in analytical testing/ instrumentation available while framing the monographs.

✓ To accelerate the process of preparation, certification and distribution of IP Reference Substances.

✓ To collaborate with pharmacopoeias like the Ph Eur. BP, USP, JP, ChP and International Pharmacopoeia with a view to harmonizing with global standards.

✓ To review existing monographs periodically.

✓ To organize educational programs and research activities.

✓ To publish the National Formulary of India.

General Chapters of Indian Pharmacopoeia 📚

IP consists of the following general chapters:

1. General Notices, which includes:

- General Statements
- Name
- Official and Official Articles
- Official Standards
- Added Substances
- Alternative Methods
- Meanings of Terms
- Provisions Applicable to Monographs and Test Methods
- Expression of Contents
- Expression of Concentrations
- Abbreviated Statements
- Weights and Measures

2. Test Methods, which includes:

- Apparatus
- Biological Methods

- Chemical Methods
- Physical and Physicochemical Methods
- Pharmaceutical Methods
- Tests on Herbal Products
- Tests on Vaccines
- Tests on Blood and Blood-related Products

3. Reference Data

4. Reagents and Solutions

5. General Tests

6. Containers

7. Tables

MONOGRAPHS 📄

General Monographs 📖

General monographs on dosage forms include requirements of general application and apply to all preparations within the scope of the Introduction section of the general monograph, except where a preamble limits the application.

1. Production: In this section, the instructions which are mandatory related to manufacturing process are provided for manufacturers. The mandatory instructions are related to various stages such as raw materials,

the process of manufacturing, in-process methods, testing, storage, validation procedures etc.

2. Manufacture of Drug Products: The opening definitive statement in certain monographs for drug products is given in terms of the active ingredient only. Any ingredients other than those included in the statement, must comply with the general notice on Excipients and the product must conform to the Pharmacopoeial requirements.

3. Excipients: Any substance added in preparing an official preparation shall be innocuous, shall have no adverse influence in the therapeutic efficacy of the active ingredients and shall not interfere with the tests and assays of the Pharmacopoeia. Care should be taken to ensure that such substances are free from harmful organisms.

Individual Monographs 📋

Drug products which are mentioned in the individual monograph are also required to comply with the tests given in the general monographs. This includes the following sections:

➤ Titles:

For any drug substance, the main title is the International Non-proprietary Name (INN) approved by the World Health Organization. In addition to INN, synonyms or subsidiary names may also have been provided. However, generally in practice, the main titles of drug products are recognized.

➤ Chemical Formulae:

For an official substance, if the chemical structure is known or it is generally accepted, the graphic, molecular formulae and molecular weight are normally given at the beginning of the monograph. This information refers to the chemically pure substance, however it is not indicating the purity of the official substance.

For the official substances, if absolute stereo chemical configuration is to be specified, The IUPAC R/S and E/Z systems of designation have been used.

➤ Atomic and Molecular Weights:

The atomic weight or molecular weight is shown, as and when appropriate at the top right hand corner of the monograph.

➤ Definition:

The official definition of the drug product or preparation or article forms the opening statement of a monograph.

➤ Statement of Content:

The limits of content stated are those determined by the method described under Assay.

➤ Category:

In this section, the basis of the substance or article is provided for information. The statement of category is indicative of the medical or pharmaceutical basis for recognition in the Pharmacopoeia.

➤ Dose:

Doses of the substance or article in monograph are provided just for general guidance.

➤ Usual Strength:

The usual strength of the preparation marketed is provided in the individual monograph for information of the pharmacist and the medical practitioner.

➤ Description:

Description of an article or preparation in the individual monograph may help in preliminary evaluation of the integrity of the preparation.

➤ Solubility:

Statements on solubility are not to be considered as official requirements: They are intended as information on the appropriate solubility at a temperature between 15 and 30% unless otherwise stated.

SOURCES OF IMPURITIES 🚫

➤ WHAT IS IMPURITIES? ❓

It is define as foreign particle that affects the purity of the substance.

➤ WHAT IS PHARMACEUTICAL IMPURITIES? 💊

Impurities in pharmaceuticals are the unwanted chemicals that remain with the active pharmaceutical ingredients (API), or develop during formulation. The presence of these unwanted chemicals even in small amounts may influence the efficacy and safety of the pharmaceutical products.

➤ Source And Effect Of Impurities In Pharmacopoeial Substances 🔍

The substances are used in pharmaceutical field must be pure so that they can be used safely. But it is very difficult to obtain an almost pure substance.

❖ Sources of impurities 📍

- Materials employed in manufacture.
- Method or the process used in manufacture.
- Chemical processes and the plant materials employed in the processes.
- Storage conditions.
- Decomposition.

❖ EFFECT OF IMPURITIES ⚠️

Almost pure substances are difficult to get and some amount impurity is always present in the material. So the impurities which are present in the substances may have the following effects:

- Impurities may bring about incompatibility with other substances.
- Impurities may lower the shelf life of the substances.
- Impurities may cause difficulties during formulations and use of the substances.
- Sometimes Impurities changes the physical and chemical properties of the substances.
- Therapeutic effect can be decreased.

- Shows toxic effect after a certain period.
- Injurious when present above certain limits.
- It may change odour, colour, taste of the substance

To prevent these impurities many test such as limit test are carried out to lower the impurities to make the pharmaceuticals safer.

How we can minimize Pharmaceutical Impurities 🛡️

- Evaluating starting material purity.
- Minimizing impurity levels in synthesis and manufacturing processes.
- Identifying impurity structures.
- Isolating and synthesizing impurities for qualification in toxicity studies.
- Monitoring the stability of APIs and DPs to detect degradation products.
- Storage and Stability Analysis.

TEST FOR PURITY ✅

Pharmacopoeias of all countries prescribe 'tests for purity'. The tests for purity means detecting impurities in the substances and pharmacopoeias fix the limits of tolerance for these impurities, these tests is to determine how much impurity is likely to be harmful, or to bring about technical and other difficulties, when the substance is used.

Insoluble Residue 💧

Pure substance gives a clear solution in a given solvent. When insoluble impurities are present in a substance, the solution appears cloudy, or

shows opalescence. The measurement of turbidity or opalescence helps to determine the amount of insoluble impurity present in the substance.

Ash, Water Insoluble Ash 🔥

Determination of ash in crude vegetable drugs, organic compounds, and some inorganic compounds, gives a good indication about the extent of impurities of heavy metals or minerals in nature.

Colour, Odour and Taste 👁️ 👃 👅

The description of taste, odour, colour etc. is given in the pharmacopoeias. Though they have limited value, they are useful in determining whether the substance is reasonably pure, hygienic etc.

✓ Physico-chemical Constants 🔭

Solubility of the substance in various solvents, determination of melting and boiling points for organic substances, optical rotation for optically active substances and refractive index for liquids, are some values which tell us about the purity of substance.

✓ Acidity, Alkalinity and pH 🧪

Substances that are prepared from chemical reactions involving acids and alkalis often contain considerable amounts of the acid or alkali, as an impurity. Thus, the tests for acidity or alkalinity are a great help to estimate the extent of the impurity.

✓ Anions and Cations ⚡

A large number of synthetic inorganic and organic drugs are prepared using strong acids like hydrochloric, sulphuric, nitric etc. The presence of chloride and sulphate ions is thus common impurity.

LIMIT TEST 🔬

➤ WHAT IS LIMIT TESTS? ❓

Limit tests are quantitative tests which are designed to detect and limit small quantities of impurities present in the substance. All the limit tests that are prescribed in the pharmacopoeias are based on the comparison of standard turbidity or colour with that of the sample under test.

➤ IMPORTANCE OF LIMIT TEST ⭐

✓ To find out the harmful amount of impurities.
✓ To find out the avoidable/unavoidable amount of impurities.

LIMIT TESTS OF CHLORIDE 🧂

PRINCIPLE 📖

Limit Test for Chloride is based upon the chemical reaction between silver nitrate and soluble chloride in the presence of dilute nitric acid to give opalescence of silver chloride. The opalescence produced is compared with the standard solution. If the opalescence is less than the standard, it passes the test. If it is more than the standard, it fails the test.

CHEMICAL REACTION ⚗️

$$AgNO_3 + Cl^- \rightarrow AgCl + NO_3^-$$

PROCEDURE 📋

Test Solution	Standard Solution
Dissolve the given sample in 20 ml of water and transfer to a Nessler's cylinder.	Transfer 100 ml of standard chloride solution (25 ppm) in to a Nessler's cylinder and add 5 ml water.
Add 10 ml of dilute nitric acid, dilute to 50 ml with water.	Add 10 ml of dilute nitric acid, dilute to 50 ml with water.
Add 1 ml of 0.1 M silver nitrate solution.	Add 1 ml of 0.1 M silver nitrate solution.
Stir immediately with a glass rod and allow to stand for 5 min, protected from light and viewed transversely against a black background.	Stir immediately with a glass rod and allow to stand for 5 min, protected from light and viewed transversely against a black background.

OBSERVATION 👁️

The opalescence produce in sample solution should not be greater than standard solution. If opalescence produces in sample solution is less than the standard solution, the sample will pass the limit test for chloride and vice-versa.

LIMIT TESTS OF SULPHATE 🧪

PRINCIPLE 📖

Limit test of sulphate is based on the reaction of soluble sulphate with barium chloride in presence of dilute hydrochloric acid to form barium sulphate which appears as solid particles (turbidity) in the solution. The turbidity produced is compared with the standard solution.

Barium sulphate reagent contains barium chloride, sulphate free alcohol and small amount of potassium sulphate. Alcohol prevents super saturation and more uniform turbidity develops.

CHEMICAL REACTION ⚗️

$$BaCl_2 + SO_4^{2-} \rightarrow BaSO_4 + 2Cl^-$$

OBSERVATION 👁️

The opalescence produce in sample solution should not be greater than standard solution. If opalescence produces in sample solution is less than the standard solution, the sample will pass the limit test for sulphate and vice-versa.

REASONS 💡

- Hydrochloric acid helps to make solution acidic.
- Potassium sulphate is used to increase the sensitivity of the test by giving ionic concentration in the reagent
- Alcohol helps to prevent super saturation.

LIMIT TESTS OF IRON 🔴

PRINCIPLE 📖

Limit test of Iron is based on the reaction of iron in Ammoniacal solution with thioglycollic acid in presence of citric acid to form iron thioglycolate which is pale pink to deep reddish purple in color.

Ferric iron is reduced to ferrous iron by the thioglycollic acid and the compound produced is ferrous thioglycolate. Citric acid forms a soluble complex with iron and prevents its precipitation by ammonia as ferrous hydroxide.

The colour develops only in the presence of alkali. The colour is due to the formation co-ordination compound, ferrous thioglycollate which is stable in the absence of air but fades in air due to oxidation. Therefore, the colour should be compared immediately after the time allowed for full development of colour is over.

CHEMICAL REACTION

Fe^{3+} + Thioglycollic acid + NH_3 → Fe-thioglycolate complex (Purple color)

OBSERVATION

The purple color produce in sample solution should not be greater than standard solution. If purple color produces in sample solution is less than the standard solution, the sample will pass the limit test of iron and vice versa.

REASONS

1. Citric acid helps precipitation of iron by ammonia by forming a complex with it.
2. Thioglycolic acid helps to oxidize iron (II) to iron (III).
3. Ammonia to make solution alkaline

LIMIT TEST OF HEAVY METALS ⚫

PRINCIPLE 📖

The limit test for heavy metals is based on the reaction of metallic impurities with hydrogen sulfide in acidic medium; the reaction product will be the sulphides of the respective metals.

In acidic media, it produces reddish / black colour with Hydrogen sulphide which is compared with standard lead nitrate solution. The metallic impurities in substances are expressed as parts of lead per million parts of the substance. The usual limit as per Indian Pharmacopoeia is 20 ppm.

Metals that response to this test are lead, mercury, bismuth, arsenic, antimony, tin, cadmium, silver, copper, and molybdenum.

CHEMICAL REACTION ⚗️

$M^{2+} + H_2S \rightarrow MS + 2H^+$ (where M = heavy metal)

OBSERVATION 🧿

The color produce in sample solution should not be greater than standard solution. If color produces in sample solution is less than the standard solution, the sample will pass the limit test of heavy metals and vice versa.

LIMIT TEST OF LEAD 🔘

PRINCIPLE 📖

Limit Test for Lead is based upon the chemical reaction between lead and diphenyl thio carbazone (Dithizone) in an alkaline solution to form lead

Dithizone, which is red.

Dithizone itself is green in colour and the lead Dithizone formed is violet in colour. Thus, the net resultant colour of the solution becomes red. To avoid interference by other metals and make the pH optimum, reagents like ammonium citrate, KCN, and $NH_2OH.HCl$ is employed.

CHEMICAL REACTION ⚗️

Pb^{2+} + Dithizone → Pb-Dithizone complex (Red color)

OBSERVATION 👁️

The intensity of the color of the complex depends on the amount of lead in the solution. The color produces in the sample solution should not be greater than the standard solution.

LIMIT TEST OF ARSENIC ☠️

PRINCIPLE 📖

The principle is based on Gutzeit Test wherein, all arsenic present is duly converted into arsine gas (AsH_3) by subjecting it to reduction with zinc and hydrochloric acid.

Limit test of Arsenic is based on the reaction of arsenic gas with hydrogen ion to form yellow stain on mercuric chloride paper in presence of reducing agents like potassium iodide. The intensity of the stain is proportional to the amount of arsenic present. The stain is compared with that produced from a known amount of arsenic.

The IP prescribes the limits for the presence of arsenic (NMT 2 ppm) as an impurity in various pharmaceutical substances. Apparatus used for arsenic limit test is called Gutzeit apparatus.

CHEMICAL REACTION ⚗️

$As^{3+} + Zn + HCl \rightarrow AsH_3 + ZnCl_2 + H_2$

$AsH_3 + HgCl_2 \rightarrow$ Yellow stain

OBSERVATION 👁️

If the sample show stain lesser intensity than that of the standard stain, the sample passed the limit test for arsenic as per IP.

REASONS 💡

1. Stannous chloride is used for complete evolution of arsine.
2. Zinc, potassium iodide and stannous chloride is used as a reducing agent.
3. Hydrochloric acid is used to make the solution acidic.
4. Lead acetate pledger or papers are used to trap any hydrogen sulphide which may be evolved along with arsine.

📚 SUMMARY

This comprehensive unit covers the fundamental aspects of pharmaceutical analysis including:

- **Definition and scope** of pharmaceutical analysis and its importance in healthcare

- **Various analytical techniques** including qualitative and quantitative methods
- **Methods of expressing concentrations** in pharmaceutical analysis
- **Primary and secondary standards** and their properties
- **Preparation and standardization** of various molar and normal solutions
- **Types and sources of errors** in pharmaceutical analysis
- **Accuracy, precision, and significant figures** in analytical measurements
- **Pharmacopoeia** and its role in maintaining drug quality standards
- **Sources of impurities** and their effects on pharmaceutical products
- **Limit tests** for various impurities including chloride, sulphate, iron, heavy metals, lead, and arsenic

Understanding these concepts is crucial for ensuring the quality, safety, and efficacy of pharmaceutical products in the healthcare industry. 🎯 Scopes of Pharmaceutical analysis** 🎯

Career Requirements: A Career in Pharmaceutical Analysis Requires a Certain Level of Education. To become a Pharmaceutical Analyst, students must possess knowledge in the following areas: biology, chemistry, physics, and mathematics.

Educational Qualifications: The ideal candidate for the position of Pharmaceutical Analyst will possess a degree in Pharmaceutical Analysis, Pharmacology, Chemistry, or any related subject. For higher positions,

companies may prefer candidates with postgraduate degrees or doctorates in a related field and work experience.

Professional Requirements: For a Pharmaceutical Analyst to succeed, he or she needs to possess extensive theoretical and practical knowledge.

Importance in Healthcare: Pharmaceutical analysis and quality control is vital in pharmaceutical industries as the pharmaceuticals have an important role in human health. Quality of drugs is vital and those which deviate in quality aspects are referred as sub-standard.

Quality Assurance: Quality of a product is an output of series of analysis starting from raw materials, in process during the conversion stage and extend till finished product. The quality should be ensured in every stage of manufacturing of product, thus, it can reach market with safety assurance. Hence, the manufacturing and quality of drugs should be in accordance with the standard protocols prescribed by Pharmacopoeia.

TECHNIQUES IN PHARMACEUTICAL ANALYSIS ⚗️

There are various techniques of pharmaceutical analysis which can be divided into two major categories:

1. Qualitative Analysis 🔍

This category of analysis involves various test procedures that are designed for the identification of compounds in the sample. These test results confirm the presence or absence of a compound in the sample to be analysed.

Examples include: Colour reaction tests, limit tests, melting point and boiling point determination for identification, precipitate formation etc.

2. Quantitative Analysis 📏

This category of analysis involves the quantitative determination of compounds in the sample. Generally, the quantitation has been done on the basis of some physical property of components.

➢ Quantitative analytical techniques are further classified as follows:

Category	Methods
Chemical Methods	(a) Volumetric, (b) Gravimetric, (c) Gasometric
Physico-chemical Methods	Instrumental Methods
Microbiological Methods	Bioassays for antibiotics
Biological Methods	Bioassays

Chemical Methods 🧪

1. Volumetric Methods 📊

In volumetric methods, measurement of volume of solution is taken as a parameter for assay. The volume of known strength of a solution that is required to react completely with the substance to be analyzed is measured. The quantity of analyte is determined from the volume of solution by calculation. The solution or reagent is called as titrant and the analyte to be analysed is termed as titrate.

Volumetric methods are classified into different types:

1. Neutralization titrations
2. Precipitation titrations
3. Complex metric titrations
4. Non-aqueous titrations
5. Oxidation-reduction titrations

2. Gravimetric Methods ⚖️

In Gravimetric analysis, quantitation is done on the basis of weight of compound. This process involves isolation and weighing of the compound of known composition, i.e. purest form. The analysis is carried out by various processes such as precipitation, volatilization, electro-analytical etc.

Process Steps: (a) Weighing the sample to be analysed
(b) Dissolving this sample in water
(c) Adding a suitable chemical to form a precipitate
(d) Filtering to collect the precipitate
(e) Repeated drying and weighing until a constant mass of precipitate is obtained

Precipitation and volatilization are widely employed methods. Gravimetric analysis is time-consuming compared to other techniques. It is useful for the examination of compounds for the presence of impurities.

3. Instrumental Methods 🔬

These methods involves the usage of instruments to measure the physical or physiochemical property of the compound to be analysed thus lead to

quantitation of the compound. Depending on the physical property of the compound various instruments have been used for the measurement.

Physical Properties	Instrumental Methods
Electrical potential	Potentiometer
Electrical conductance	Conductometry
Electrical current	Polarography and voltammetry
Absorption of radiation	Spectrophotometry, Colorimetry, Atomic absorption spectroscopy
Emission of radiation	Emission spectroscopy, Flame photometry, Fluorimetry
Scattering of radiation	Turbidimetric and Nephelometry
Refraction of radiation	Refractometry
Rotation of plane polarized light	Polarimetry, Optical rotatory dispersion
Thermal properties	Thermal method of analysis (DSC, DTA, TGA)
Mass to charge ratio	Mass spectrometry

4. Microbiological Methods

Microbiological methods are employed for compounds especially for antibiotics, for which the chemical methods are not useful. This method involves the determination of inhibition of growth of bacteria by the substances to be analysed in comparison with the standard compound.

5. Gasometrical Methods

In this method, the measurement of the volume of gases forms the basics of analysis. When a chemical reaction is carried out under the specific process, the volume of gas evolved or absorbed in the reaction is measured. The measured volume is corrected to standard conditions of temperature and pressure. Gas burettes or nitro-meters are used for the measurement of volume of gas.

Examples of gases measured: Cyclopropane, carbon dioxide, nitrous oxide, oxygen, octal nitrate, nitrogen, amyl nitrate, ethylene and helium.

6. Biological Methods 🧬

Biological assays are carried out to observe the biological effect of the drug on some type of living matter. They are also called as bioassays. These are recommended when the chemical or physical methods are not capable to estimate the potency of a drug.

METHODS OF EXPRESSING CONCENTRATIONS ANALYSIS 📈

There are so many methods of expressing concentrations in pharmaceutical analysis.

➤ Solution Concentration 💧

Solutions used in quantitative analysis require some basis for the expression of solution concentration. Generally, the expression of solution concentration involves similar basis in all systems with respect to weight relationships of solute and solvent. However actual method of expression of concentration should be of some convenient and specific form.

➤ Normality 🔢

The normality (N) of a solution is described as the number of equivalents of solute per litre of solution.

➤ Percent Concentration 📊

Generally solution concentration is expressed in terms of percent (%) (parts per hundred). This percent concentration is expressed in different ways for different solutions:

1. **Percent w/w (% w/w)** is used to describe the concentration of commercial aqueous reagents.
2. **Percent v/v** is used to denote the concentration of solution prepared by diluting pure liquid with another liquid.
3. **Percent w/v** is used to denote the concentration of solution which is prepared by dissolving solid reagents in solvents.

➤ Molar Concentration ⚗️

The molar concentration of the solution is defined as, 'the number of moles of solute per litre of solution'. In addition to above expression, Molarity is also expressed in number of millimoles of a solute per milliliter of solution.

Molarity of the solution is influenced by change in temperature. The reason is, molarity is the basic measure that involves volume of the solution, thus a change in volume due to changes in temperature affects the Molarity.

➤ Molal Concentration 🌡️

Molality of the solution is defined as, 'the number of moles of solute per 1000 g of solvent.' Molality is represented by 'm'.

➤ Formal Concentration 📝

When substances exist in ionic form in either solid or solution state, the molecular weight is not considered for preparation of solution. Instead, the formula weight is used for preparation of solution and its concentration is expressed in terms of formality. Formal concentration is expressed by 'F'.

Similar to molarity, formal concentrations are also influenced by changes in volume associated with temperature.

➤ Parts per Million and Parts per Billion 🔬

Parts per Million is usually mentioned as ppm. It is used to describe the concentration of dilute solutions. For very dilute solutions, the concentration is expressed in parts per billion (ppb). These terms are also employed to express the concentration of impurities in pharmaceuticals.

Equivalent Weight ⚖️

The weight of a substance which contains or reacts with 1.0078 g of hydrogen or 8 g of oxygen, or 35.45 g of chlorine, is said to be equivalent weight of that substance. This concept is used while calculating the equivalent weight of the substances during reactions.

In Neutralization Reactions 🧪

When we consider a neutralization reaction in which an acid and base are involved, then the equivalent weight of an acid can be expressed as the

weight of the acid which contains 1 g atom of replaceable hydrogen, e.g. 1.0078 g of hydrogen.

Thus, the monobasic acids will have an equivalent weight of their molecular weight whereas the equivalent weight of a dibasic and a tribasic acid is ½ & 1/3 respectively of its molecular weight.

Similarly, equivalent weight of a base in a neutralization reaction, is expressed as the weight of the base which consists of one replaceable hydroxyl group.

In Complexation Reactions

If we consider the complexation reactions, the equivalent weight is expressed as the weight of the substance which consists of or reacts with 1 g atom of an univalent cation M^{+}, ½ g atom of a bivalent cation M^{+2}, ⅓ g atom of trivalent cation M^{+3} etc.

For cations, equivalent weight is the atomic weight divided by the valency of atom. The cation referred above is referred to the cation which is directly involved in the reaction and not necessarily the cation contained in the compound whose equivalent weight is being defined.

In Precipitation Reactions

In precipitation reaction, the equivalent weight of a salt is expressed as the ratio of gram molecular weight of the salt and the valency of the reacting ions.

In Oxidation-Reduction Reactions

Equivalent weight of a substance participating in oxidation and reduction reaction can be defined as, 'the weight of the substance which reacts or contains 1.0078 g of available hydrogen or 8.0 g of available oxygen'.

Equivalent weight can be calculated by:

- Ion-electron balance method
- Oxidation number method

(a) Ion-electron balance Method ⚡

Ion electron balance method is based on the following steps:
a) Ascertain the reactants and products of the reaction.
b) Determine oxidising agent. Write down partial equation for oxidising agent.
c) Determine reducing agent. Write down partial equation for reducing agent.
d) Add both partial equations and cancel out common substances after multiplying both partial equations by suitable coefficient.

(b) Oxidation Number Method 🔄

Oxidation and reduction are the processes involving the changes in the valency. Oxidation number (O.N.) indicates the amount of oxidation or reduction which is required to convert one atom of the element from free state to that in the compound.

If oxidation is taking place the oxidation number is positive, and if reduction is taking place oxidation number is negative.

Following general rules apply in determination of oxidation number:

1. Oxidation number of metal in combination is generally positive.
2. Oxidation number of radical or ion is equal to its electrovalency with correct sign.
3. Oxidation number of compound is zero and is determined by sum of O.N. of individual atoms.
4. Oxidation number of free or uncombined element is zero.
5. Oxidation number of hydrogen (except hydrides) is +1.
6. Oxidation number of oxygen except peroxides is -2.

What is Titer? ⚗️

The term Titer denotes the solution concentration in quantitative analysis, particularly the analysis in which volumetric method is involved. The titer gives the weight of some particular substance with which the solute in 1 ml of solution will react.

Titer of the solution can be calculated using the following formula: **Titer = (N × Equivalent weight) / 1000**

N represents normality of solution whereas equivalent weight denotes equivalent weight of the substance involved in the reaction and not to that of the solute. The titer of the solution changes with volume changes associated with temperature.

PRIMARY AND SECONDARY STANDARDS 📋

Volumetric Analysis 🧪

❖ **Definitions:**

Volumetric analysis is also called as titrimetric analysis. It involves determination of volume of solution as a basic parameter. In this reaction or titration, the substance in solution is analysed by reaction with a solution of accurately known concentration. The volume of solution required to react completely with the solution of substance to be analysed is determined and used for the calculation.

➤ **Titration** 📊

A titration is defined as 'the process of determining the quantity of a substance A by adding measured increments of substance B, the titrant, with which it reacts until exact chemical equivalence is achieved' (the equivalence point).

➤ **Titrate** 🧪

The substance to be analysed, which is allowed to react with the solution of known concentration by titration is called as Titrate. This solution is usually taken in the conical flask and titrated.

➤ **Titrant** 💧

The solution of known concentration, prepared by weighing accurately and dissolving in suitable solvent, and used for titration against titrate is called as Titrant. This solution is usually taken in burette during titration.

➤ **Standard solution** ⚖️

The solution of accurately known concentration is called as the Standard Solution.

➤ Equivalence point or stoichiometric end point 🎯

These are generally called as end point in practice which denotes the point at which the reaction of titrant and titrate is completed.

➤ Indicator 🌈

Indicator is defined as, "an auxiliary substance which is added with the titrate in a titration to indicate the equivalence point at the completion of reaction by showing clear visual changes". For example, colour change.

➤ Titration error ❌

Titration error denotes the small variation in the expected theoretical equivalence point or end point with the practical end point of a titration.

➤ Endpoint 🔴

The point at which the indicator changes color is called the endpoint.

➤ Points to be considered during Volumetric Methods ✅

- The selected titrant and titrate should react easy and completely without any interferences so that it should be able to produce end point suitably.
- The reaction should be effectively completed with short duration of time. Slow reactions will make the method more tedious.
- The reaction should not involve any side reactions which affect the end point determination.
- The reaction should be compatible with the selected indicators and produce sharp changes of physical or chemical property at the end

point.

- The method of indicating the end point should be simple like the sharp colour change in which the change of colour should have distinct difference with the colour before the end point.

➤ Classification of Volumetric Methods of Analysis 📊

1. **Neutralization (Aqueous acid-base) titrations:** It involves neutralization reaction in presence of water as solvent.
2. **Non-aqueous titrations:** It involves the reaction between acid and base in presence of non-aqueous i.e., organic solvents.
3. **Precipitation titrations:** It involves the reaction leading to precipitate formation. It includes the methods where the reacting substance and standard solution react to yield a precipitate or a slightly soluble salt as the primary reaction product.
4. **Complexometric titrations:** It includes all the methods wherein the reacting substance and the standard solution react to form a soluble but very slightly dissociated complex substance. In other words, it is based on complex formation reaction mainly EDTA titrations.
5. **Redox titrations:** These titrations involve simultaneous oxidation reduction reactions. It includes all the methods where in reacting substance is oxidized or reduced by the standard solution.

PRIMARY AND SECONDARY STANDARDS 🏆

➤ Standard Solutions 📋

Standard solutions are the solutions which are prepared with known strength. The accurate weight of very pure reagents of high stability is taken, dissolved and diluted to exact known volume and concentration is calculated on theoretical basis.

The calibration of other solutions and reagents depends upon the accurate strength of these solutions. Substances having typical characteristics are used to prepare the standard solutions and these substances are known as standard substances.

➤ There are two types of standard substances:

1. Primary standards
2. Secondary standards

➤ Primary Standards 🥇

Those substances which can easily be obtained in highly pure and crystalline form and used in preparation of standard solution are known as Primary Standard Substances. Accurately weighed quantities of these primary standards are used in the standardization of solutions of unknown strength.

➤ The commonly used primary standard substances are:

Titration Type	Primary Standards
Acid-base titrations	Sodium carbonate, potassium hydrogen phthalate, succinic acid, benzoic acid, oxalic acid and picric acid
Redox titrations	Potassium dichromate, potassium bromate, potassium iodate, Sodium oxalate, Arsenious oxide
Precipitation titrations	Sodium chloride, potassium chloride, potassium bromide, silver nitrate
Complexometric titration	Various pure metals such as zinc, magnesium, manganese and salts such as lead nitrate, calcium carbonate etc.

➤ Properties of Primary Standards ✨

- The reaction to be amenable to use simple indicator to determine the end point of the titration.
- There will not be any difference between end point and theoretical equivalence point.
- They do not have water of hydration so that the composition of the solid does not change with variation in relative humidity.
- They are readily soluble in experiment solvents.
- They are obtained easily in pure form and it is easy to purify, dry and preserve in pure state.
- The reaction with standard solution is stoichiometric and practically instantaneous.
- They are stable to atmospheric conditions and not decomposed by atmospheric condition. They are not hygroscopic or deliquescent in nature.

- They have a high equivalent weight in order to reduce the effect of weighing errors. In weighing a greater amount of substance, the relative error will be smaller than that for a small amount.

❖ Secondary Standards 🥈

These are the substances used for the standardization and whose concentration has been determined by comparison with the primary standard. As the number of primary standard substances is limited, a substance with less but known purity is used in standardization process. These substances are known as secondary standards.

➤ Properties of Secondary Standards 🔍

- Reaction might not be rapid or stoichiometric.
- They may not be available in pure form and may react with organic matter present in water.
- It is difficult to maintain these in pure state as drying is difficult due to low fusion point.
- The concentration of their solutions changes with time. They are prone to undergo photochemical decomposition or hydrolysis and they may be hygroscopic.
- Usually, they are not readily soluble in experiment solvent.

PREPARATION AND STANDARDIZATION OF VARIOUS MOLAR AND NORMAL SOLUTIONS 🧪

For preparation of standard solutions a known quantity of standard substances depending upon the requirement is dissolved in a known

amount of water and desired volume is made. Since, these substances have a constant weight, high purity, non-hygroscopic property, the solution obtained is of known and definite concentration.

Sodium Hydroxide 🧪

Preparation of N/10 NaOH Solution:

- Molecular weight of NaOH = 40
- Acidity (number of replaceable OH group) = 1
- Equivalent weight of NaOH = 40
- Therefore, 4 g of NaOH dissolved in one litre of solution will give N/10 NaOH solution.

✓ **Procedure:** Weigh accurately 4 g of NaOH in a beaker and dissolve it in distilled water. Weighing should be performed quickly as it is hygroscopic. Transfer the contents and the washings to a 1 litre volumetric flask. Cool and then make volume up to the mark. Shake well.

✓ **Standardization:** The N/10 NaOH prepared as per the above-mentioned procedure is standardized by titrating against N/10 oxalic acid using phenolphthalein as an indicator. 10 ml of N/10 oxalic acid is taken in conical flask to which 2-3 drops of phenolphthalein is added and mixed well. This solution is titrated slowly with constant stirring against N/10 NaOH taken in a burette. Titration is continued till the appearance of permanent pale pink colour as the end point.

Sulphuric Acid 🧪

Preparation of N/10 H_2SO_4:

- Equivalent weight of H_2SO_4 = 49 g
- Specific gravity = 1.84 g/ml
- So, volume of 49 g H_2SO_4 = 26.6 ml
- Concentrated H_2SO_4 (reagent grade) is about 97% pure

Therefore, actual amount of concentrated H_2SO_4 required for 1.0 litre of N/10 H_2SO_4 solution = (100/97) × 26.6 = 27.42 ml

Thus, for 1.0 litre of N/10 H_2SO_4 solution, 2.74 ml of concentrated H_2SO_4 is required.

Procedure: Take 2.74 ml Sulphuric acid in a beaker filled with small amount of distilled water. Transfer the contents of beaker to a volumetric flask of 1 litre capacity and make volume up to the mark with distilled water. Shake well.

Standardization: N/10 H_2SO_4 is titrated with 10 ml of 0.1 N Na_2CO_3 using mixed/ methyl orange as an indicator. Repeat the titration until at least three concordant readings are obtained.

Oxalic Acid

Preparation of N/10 Oxalic Acid: Oxalic acid $(COOH)_2 \cdot 2H_2O$ is to be dissolved in one litre of distilled water to get N/10 oxalic acid solution.

Procedure: Weigh accurately 6.3 g of oxalic acid [$(COOH)_2 \cdot 2H_2O$] and transfer it in to a volumetric flask (1 litre), half-filled with distilled water. Shake well and make the volume up to the mark. Label it as N/10 oxalic acid solution.

Note: If anhydrous oxalic acid $(COOH)_2$ is available, then dissolve 4.5 g of the acid in one litre of distilled water to get 0.1 N oxalic acid solution.

Potassium Permanganate

Preparation of N/10 $KMnO_4$ Solution:

- Molecular weight of $KMnO_4$ = 158 g/mol
- Equivalent weight of $KMnO_4$ is reaction specific. In acidic medium $KMnO_4$ is used as an oxidiser.
- So there will be 5 electrons gained by Mn atom.
- Hence, the equivalent weight of $KMnO_4$ = Molecular weight / Number of electrons gained in redox reaction = 158 / 5 = 31.6

So 3.16 or 3.2 g of $KMnO_4$ is weighed accurately and dissolved in 1 litre of distilled water to get N/10 $KMnO_4$ solution.

Procedure: In general, 3.2 g of $KMnO_4$ is accurately weighed and dissolved in one litre of distilled water. The solution is boiled for 10–15 minutes and then allowed to stand for few days and filtered through glass wool.

Standardization: 10 ml of N/10 oxalic acid is taken in a conical flask. Add 5 ml dilute Sulphuric acid, warm it to 60–70°C and titrate against $KMnO_4$ from the burette till a light pinkish colour appears. Repeat the titration until concomitant results are obtained.

Hydrochloric Acid

Preparation of N/10 HCl:

- Molar mass for HCl is 36.4611 g/mol.

- Since HCl has only one hydrogen ion, the equivalent mass will be 36.4611.
- Specific gravity for 1 litre volume of HCl is 1.189.
- For 1 litre volume, Grams of compound needed (0.1 N)(36.4611) (1 Litre) = 3.6461

So, 8.1774 ml of 37.5% concentrated HCl is dissolved in 1 litre of water to prepare 0.1 N HCl.

Procedure: Transfer exactly 20 ml of the approximately 0.1 M HCl solution into a 250 ml conical flask. Add 3 drops of phenolphthalein as indicator. Titrate against standard N/10 NaOH solution until a permanent pale pink colour is appeared.

Standardization: HCl is standardized against standard N/10 NaOH which is already standardized against N/10 oxalic acid using Phenolphthalein indicator.

Preparation of 0.1 N Sodium Thiosulphate Solution ($Na_2S_2O_3.5H_2O$)

Dissolve approximately 24.8 gm of sodium thiosulphate crystals in previously boiled and cooled distilled water and make the volume to 1000 ml. Store the solution in a cool place in a dark colored bottle.

Standardization: Weigh accurately about 5.0 gm of finely ground potassium dichromate which has been previously dried to a constant weight at 105 ± 2°C in to a clean 1.0 litre volumetric flask. Add sufficient distilled water to dissolve the content of volumetric flask and make up to

the mark with distilled water, shake thoroughly and keep the solution in dark place.

Pipette 25.0 ml of this solution into a clean glass stoppered 250 ml conical flask. Add 5.0 ml of concentrated hydrochloric acid and 15.0 ml of 10% potassium iodide solution. Allow to stand in dark for 5 minutes and titrate the mixture with the solution of sodium thiosulphate using starch solution as an indicator towards the end point. The end point is taken when blue color changes to green.

(b) Pharmaceutical Errors ❌

Points to be covered in this topic

➤ PHARMACEUTICAL ERRORS
➤ ACCURACY AND PRECISION
➤ SIGNIFICANT FIGURES
➤ ROUNDING OFF FIGURES

Pharmaceutical Errors 🚫

INTRODUCTION 📖

Error is the difference between the true result (or accepted true result) and the measured result. If the error in an analysis is large, serious consequences may result. As reliability, reproducibility and accuracy are the basis of analytical chemistry.

A patient may undergo expensive & even dangerous medical treatment based on an incorrect laboratory result because of an analytical error. Two

major categories of errors are known as absolute error and relative errors.

The difference between the experimental mean and a true value is known as 'absolute error.' Sometimes a term 'relative error' is used in analysis. The relative error is the value found by dividing the absolute error by the true value.

Relative Error = Absolute Error / True Value

The relative error is generally expressed as percent, that is, by multiplying the relative error by 100 or by expressing it as parts per thousand by multiplying the relative error by 1000.

SOURCE AND TYPE OF ERRORS 🔍

In pharmaceutical analysis, the variations or differences in the results are caused by errors of various sources and these errors are of different nature. Depending on the nature of errors which affects the accuracy or precision of a measured quantity, they are classified as two main classes:

1. **Determinate Errors**
2. **Indeterminate Errors**

➤ Determinate Errors 🎯

These are ascertainable errors that can be either avoided or corrected. The error may be constant as in the case of weighing with uncalibrated weights or in measuring a volume using burette or pipette. Such measurable determinate errors are categorized as systematic errors.

The determinate errors arise due to:

(a) Instrumental errors: These errors are caused by faulty equipments or low quality equipments which do not perform well.

(b) Personal errors: These errors occur by persons who are handling the method of analysis. The error may be resulted due to carelessness or ignorance and even by unskilled persons. This error is also called operative error.

(c) Chemical errors: These errors are resulted by using chemicals and reagents with impurities or contaminants which may interfere with the reactions, thus affects the results.

(d) Errors in the methodology: This is a most serious error in analysis as the error arises due to faulty method, e.g. co-precipitation of impurities, slight solubility of precipitate, incomplete reactions etc.

Errors of this category are usually detectable and can be eliminated to a large extent.

➤ Indeterminate Errors 🎲

Indeterminate errors are often called accidental or random errors. They are revealed by small differences in series of measurements made by the same analyst under identical conditions. They cannot be predicted and hence cannot be eliminated. Such accidental errors will follow a random distribution pattern and the mathematical laws of probability can be applied to get net conclusion regarding the results.

The random distribution of indeterminate errors of various magnitudes is shown in a graph. The magnitude of error and the frequency of deviation

have the shape of a normal frequency distribution curve or probability curve. This graph is also called as 'Curve of error'.

From the graph it will be seen that:

1. Very large errors are unlikely to occur
2. Smaller errors occur with greater frequency than large errors, and
3. The errors on positive and negative side occur with equal probability

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METHODS TO MINIMIZE ERRORS 🛠️

1. Personal Errors 👤

- Skilled persons should be employed or the knowledge of the operator to perform analysis is to be ensured prior to analysis.
- Regular reporting and monitoring of analysis can be done.

2. Instrumental Errors 🔧

- These errors can be minimized by checking thoroughly the equipments used for the analysis before starting of any analysis.
- Proper calibration should be performed to ensure the performance of equipments. Faulty equipments should be corrected by experts and rechecked for accuracy of results.

3. Chemical Errors 🧪

- Standard chemicals from authentic source without impurities must be used for the analysis. The quality of chemicals and reagents can be checked periodically as per the standard guidelines.

4. Errors in Methodology 📋

- These errors can be avoided by following the standard methods with proper references. Continuous monitoring of reactions by skilled persons can be employed to minimize these errors.

5. Indeterminate Errors ❓

- Since indeterminate errors are not predictable, the entire procedure of analysis should be carried out in a well-planned manner considering all factors which affect the accuracy and precision of the results.

ACCURACY AND PRECISION 🎯

➤ ACCURACY ✅

Accuracy is the degree of closeness of the measurements to the target or ref. value. Accuracy often referred as Bias error. Accuracy is measuring near the target or true or ref. value. ISO defines accuracy as describing a combination of both types of observational error above (random and systematic), so high accuracy requires both high precision and high trueness.

**➤