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Quality control of drugs

Significant Figures

Errors

Analytical Chemistry

- Analytical chemistry is the science of obtaining, processing, and communicating information about the **composition and structure of matter.**
- In other words, **it is the art and science** of determining what matter is and how much of it exists.

- Analytical chemists use their knowledge of chemistry, instrumentation, computers, and statistics to solve problems in almost all areas of chemistry and for all kinds of industries.
- For example, their measurements are used to assure the **safety and quality** of food, pharmaceuticals, and water; to assure compliance with environmental and other regulations; to support the legal process; to help physicians diagnose diseases.
- Analytical chemists often work in service-related jobs and are employed in industry, academia, and government.
- They conduct basic laboratory research; perform process and product development; design instruments used in analytical analysis; teach; and work in marketing and law.
- Analytical chemistry can be a challenging profession that makes significant contributions to many fields of science.

Different types of chemical analysis may be classified as:

(i)Proximate Analysis: the amount of each element in a sample is determined with no concern as to the actual components present.

(ii)Partial analysis: deals with the determination of selected constituents in the sample,

(iii)Trace constituent analysis: a specialized form of partial analysis in which determination of specified components present in very minute quantity,

(iv)Complete Analysis: when the proportion of each component of the sample is determined.

Role of pharmaceutical analysis in pharmaceutical industry

- Pharmaceutical analysis may be defined as the application of analytical procedures used to determine the **purity, safety and quality of drugs and chemicals.**
- Pharmaceutical analysis rely upon both **qualitative and quantitative chemical analysis** to ensure that the raw material used meet all the desired specifications, and also to check the quality of the final product.
- The examination of raw material is carried out to ensure that there is no unusual substance present which might deteriorate the manufacturing process or appear as a harmful impurity in the final product.
- The quantity of required ingredient in raw material is determined by a procedure known as **Assay.**

- In the modern practice of medicine, the analytical methods are used in the analysis of chemical constituents found in the human body whose altered concentrations during disease states as diagnostic aids and also used to analyse the medicinal agents and their metabolites found in biological system.
- The term “quality” as applied to a drug product has been defined as the sum of all factors which contribute directly or indirectly to the safety, effectiveness and reliability of the product.
- These properties are built into drug products through research and during the manufacturing process by procedures collectively referred to as **quality control.**
- Quality control guarantees within reasonable limits that a drug products

i. is free of impurities
ii. is physically and chemically stable
iii. contains the amount of active ingredients as stated on label and
iv. provides optimal release of active ingredients when the product is administered.

- The quality of pharmaceutical products depends on the correct performance of al manufacturing operations and must be built in from the beginning of the manufacturing process.
- The principles of quality control procedures that should be applied to drug manufacturing practices are designated **Good Manufacturing Practices (GMP)** in the manufacture and quality control of drugs.
- The quantitative analytical methods such as assays are very much essential to find out the % purity, the active content of the pharmaceutical product etc.
- The choice and selection of the assay methods will depend on the type of substance to be estimated to find out its purity of the pharmaceutical product.

Some specific use of analysis is under mentioned:

(i)Quantitative analysis of air, water and soil samples is carried out to determine the level of pollution.

(ii)Chemical analysis is widely used to assist in the diagnosis of illness and in monitoring the condition of patients.

(iii) In farming, nature of soil and level of fertilizer application is analyzed

(iv) In geology, composition of the rock and soil is carried out.

In general analysis is divided into two major part:

(a) Qualitative analysis (what substances are present in the given sample)

(b)Quantitative analysis (to determine the quantity of each component in the given sample)

Different Techniques of Analysis

The main techniques are based upon:

1. The quantitative performance of suitable chemical reactions

2. Appropriate electrical measurements

3. Measurement of certain optical properties and

4.Combination of optical and electrical measurement followed by quantitative chemical reaction. Eg. Amperometry

1. Methods Based on Chemical Analysis: These are based on traditional method of analysis and may be divided as:

(a) Titrimetry

(b) Gravimetry

(c)Titrimetric Analysis (also termed as volumetric analysis) in this technique the substance to be determined is allowed to react with an appropriate reagent added as a standard solution, and the volume of solution needed for completion on reaction is determined. Following are the types of titrimetric analysis:

- **(i)** Neutralization (acid-base) reactions
- **(ii)** Complexometric titrations
- **(iii)** Precipitation titrations
- **(iv)** Oxidation-reduction titrations

(d)Gravimetric Analysis in this technique substance under determination is converted into an insoluble precipitate which is collected and weighed.

In a special case of gravimetric analysis, electrolysis of the substance is carried out and the material deposited on one of the electrodes is weigh, this technique is called as **electrogravimetry**

2. Electrical Methods of Analysis: These involve the measurement of current voltage or resistance in relation to the concentration of a certain species in a solution. These methods are of following types:

i.Voltametry: It is the measurement of current at a microelectrode at a specified voltage.

ii.Coulometry: It is the measurement of current and time needed to complete an electrochemical reaction or to generate sufficient material to react completely with a specified reagent.

iii.Conductometry: It is the measurement of electrical conductivity of a solution. The ionic reactions in which there is a sudden change in conductance after completion of reaction, can act as a basis of conductometric titration method.

iv.Potentiometry: It is the measurement of the potential of an electrode in equilibrium with an ion to be determined..

3. Optical Methods of Analysis: The optical methods of analysis depend upon:

i. Measurement of the amount of radiant energy of a particular wavelength absorbed by the sample.

ii. The emission of radiant energy and measurement of the amount of energy of a particular wavelength emitted.

- Several analytical techniques have been developed which involve the measurement of radiant energy. These are:
    - i. Emission spectrography
    - ii. Colorimetry
    - iii. Fluorimetry
    - iv. Turbidimetry & Nephelometry
    - v. Spectrophotometry
    - vi. Flame photometry
    - vii. Atomic absorption spectroscopy
    - viii. Polarimetry

The optical methods are basically of two types:

i. Absorption methods

ii. Emission methods.

Absorption methods are usually classified according to wavelength involved:

i. Visible spectrophotometry

ii. Ultraviolet spectrophotometry

iii. Infrared spectrophotometry

iv. Atomic absoption spectroscopy

- In **emission** method sample is subjected to heat or electrical treatment so that the atoms are raised to excited states causing them to emit-energy; and the intensity of this emitted energy is measured.
- The emission spectroscopy includes flame photometry and fluorimetry as common excitation techniques.

4. Other Methods: the others methods of analysis like

Chromatography,

Radioactivity,

Kinetic methods,

Mass spectrometry,

Thermal method of analysis,

NMR spectroscopy and

X-ray diffraction analysis etc.

Significant Figures

- A figure of digit denotes any one of the ten numerals (0,1,2,3,4,5,6,7,8,9). A digit alone or in combination serves to express a number.
- A significant figure is a digit having some practical meaning, *i.e.* it is a digit, which denotes the amount of the quantity in the place in which it stands.
- For example in 0.456, 4.56 and 456 there are three significant figures in each number.
- Zero may or may not be a significant figure. A zero is a significant figure except when it serves to locate the decimal point, while it is a significant figure when it indicates that the quantity in place in which *i.e.* in 1.3680 and 1.0082, zero is significant but in 0.0035, zeros are not the significant figures as they serve only to locate the decimal point. Thus, first two numbers contain five but the third one contains two significant figures.

Computation Rules

- **Rule 1 →** In expressing an experimental measurement, never retain more than one doubtful digit. Eliminate all the digits that are not significant.
- **Rule 2 →** Retain as many significant figures in a result or in any data as will give only one uncertain figure. *e.g. a* volume between 30.5 ml and 30.7 ml should be written as 30.6 ml. and not as 30.60 as it would be between 30.59 and 30.61.
- **Rule 3 →** Two rules are given for rejecting superfluous digits.
- 1. When the last digit dropped is greater than 5, the last digit retained is increased by one. e.g. in rejecting the last digit in 8.947, the new value will be 8.95 as 7 is greater than 5. But when 4.863 is rounded up to two digits, it gives 4.9 as the first digit discarded is 6 which is greater than 5. This is known as rounding up.
- 2. If the first digit discarded is less than 5, leave the last digit unchanged. It is known as rounding down. e.g. when the number 5.64987 is rounded to two digits, we get 5.6 as the first digit, discarded is 4, which is less than 5. Rounding never changes the power of 10. Thus, it is better to express numbers in exponential notation before rounding. e.g. in rounding 57832 to four figures, result 5.783×10^4

- **Rule 4.** In addition or subtraction, there should be in each number only as many significant figures as there are in the least accurately known number. e.g. sum of three values 35.6, 0.162 and 71.41 should be reported only to the first decimal place as the value 35.6 is known only to the first decimal place. Thus, the answer 107.172 is rounded to 107.2
- **Rule 5.** In multiplication or division, retain in each factor one more significant figure than is contained in the factor having the largest uncertainty. The percentage precision of a product or quotient cannot be greater than the percentage precision of the least precise factor entering into the calculation. e.g. the product of the three figures 0.0121, 25.64 and 1.05782 is 0.0121 X 25.6 X 1.06 = 0.328
- In a product or quotient of experimental numbers, the final result will have only as many significant figures as the factor with smallest number of significant figures.

e.g. in the calculation, $\frac{(0.0181057)\,(197.15)\,(0.218)}{0.4970}$,least number of significant figures (3) is in 0.218. Thus, the answer should also be expressed in three significant figures.

- When a calculation involves both addition or subtraction and multiplication or division, addition is done first so as to determine the number of significant figures in the answer.
- **Rule 6** Computation involving a precision not greater than one fourth of 1 % should be made with a 10-inch slide rule. For greater precision, logarithm tables should be used.
- Slide rule is a good method for checking the calculations made by logarithms. Use of logarithms has been recommended where a large number of multiplications and divisions are to be made.