Analytical methods for confirming the structure of synthesized drugs: qualitative and quantitative analysis

Substance analysis

- Substance analysis is the experimental acquisition of data on the chemical composition of a substance by any methods – physical, chemical, physico-chemical.
- The method of substance analysis is a brief definition of the principles underlying the analysis of a substance.
- Analysis methodology – a detailed description of all conditions and operations that provide regulated characteristics

Qualitative analysis

- **Qualitative analysis** is a process for identification of a substance, which allows to determine what chemical elements are included into the sample tested, what ions, functional groups or molecules are in its composition.
- **The purpose of qualitative analysis** is to detect the components of the analyzed sample, as well as to identify certain compounds.

Tasks of qualitative analysis

- Detection of all chemical elements that make up the substance (elemental analysis);
- Identification of molecules in the sample(molecular analysis);
- Analysis of simple or complex substances in the composition of the mixture (material analysis);
- Identification of individual phases of a heterogeneous system (phase analysis)

Qualitative analysis

- **Fractional analysis** – detection of an ion or substance in the analyzed sample using a specific component in the presence of all reagents of the mixture.
- **Systematic analysis -** this is the separation of the mixture analyzed ions by analytical groups, followed by the detection of each ion.

Quantitative analysis

- Quantitative analysis of a substance is an experimental determination (measurement) of the concentration (quantity) of chemical elements (compounds) or their forms in the analyzed substance, expressed as the boundaries of a confidence interval or a number indicating the standard deviation.

The task of quantitative analysis

- Obtaining the necessary quantitative data on the individual components of the system, i.e., in the quantitative determination of the content of the main component, components or impurities in the analyzed sample.

Principles of quantitative definitions

- Measurement of the physical properties of substances or products of their chemical reactions
- Measurement of the amount of the product of a chemical reaction of a substance with a reagent (by the mass of the precipitate, the volume of the gas). Using the law of equivalents.
- Measurement of the volume of the reagent (gas or reagent solution) required for reaction with the analyzed substance.

Classification of quantitative analysis methods

- Chemical methods of analysis (gravimetric (weight) and titrimetric (volume) methods);
- Physico-chemical and physical (instrumental) methods of analysis (optical, chromatographic, electrochemical methods);
- Biological methods of analysis.

Principles of quantitative definitions

- Measurement of the physical properties of substances or products of their chemical reactions. By measuring the intensity of the property, there fore,a quantitative determination of the substance can be carried out.
- Measurement of the amount of the product of the chemical reaction of a substance with any reagent (by sediment mass, gas volume). Using the law of equivalents.
- Measurement of the volume of the reagent (gas or reagent solution) consumed for chemical interaction with the substance to be determined

Characteristics of quantitative analysis

- Specificity
- Sensitivity
- Accuracy
- Stoichiometry
- The speed of the chemical reaction

Gravimetric methods of analysis

- ***Gravimetric methods*** are based on the precise mass measurement of the analyzed component of a sample, separated from the other components of the system, in the elemental form (i.e., in the stable form of a given chemical element) or in the form of a compound with a precisely known composition.
- ***Gravimetric methods*** are simple to perform, highly accurate, and reproducible, but are quite time-consuming and time-consuming.

Methods by the method of separating the component to be determined, a distinction is made between

- Methods of precipitation
- Distillation
- Separation
- Thermal gravimetric methods (thermogravimetry)

Thermogravimetric methods

- These methods are based on the determination of the mass of analyzed substance during its continuous heating within the specified temperature range (more often from room temperature to specified one). Measurements are usually carried out in special devices — derivatographs equipped with special thermal balance providing continuous weighing, an electrical furnace for sample heating, thermometer thermocouples, the standard of reference and recorder that continuously records variations in the mass of a heated substance.

Titrimetric methods of analysis

- ***Titrimetric methods*** are based on the measuring of the volume or mass of the reagent (titrant) required for the reaction with the analyzed substance (analysis is based titration).
- The methods are simple, highly accurate, and reproducible, but in the cases indicators are required to determine the endpoint of the titration.

Requirements for reactions in quantitative analysis

- Reactions must proceed quickly, to the end, if possible, at room temperature.
- Initial substances undergoing the reaction must react in exactly determined quantitative ratios (stoichiometrically) and without side processes.
- Impurities must not interfere with the quantitative analysis.
- The reaction must allow determining endpoint precisely and conveniently.

Titrimetric analysis

- **A titrant** is a solution containing the active reagent T, which is used to perform titration.
- **Titration** is usually performed by adding titrant from a calibrated burette to a titration flask with the analyzed solution. An aliquot fraction of the analyzed solution is placed in the flask before titration.

Titrimetric analysis

- **An aliquot fraction(aliquot)** is a precisely known part of the analyzed solution sampled for analysis. It is often sampled using a calibrated pipette, and its volume is commonly denoted by symbol Vn.

Titrimetric analysis

- **Equivalent point (EP)** is a point (moment) during titration, at which the amount of added titrant T is equivalent to the amount of titrated substance X. Synonyms of EP are stoichiometric point, theoretic end point.

Titrimetric analysis

- **The end point** of titration (EPT) is a point (moment) of titration, at which a certain property of solution (for example, its color) changes noticeably (sharply). An EPT more or less corresponds to EP, but most commonly does not coincide with it.

Titrimetric analysis

- **An indicator** is a substance that exhibits a noticeable change at the EP or close to it. In the perfect case, the indicator is present in a sufficiently low concentration so that a significant amount of titrant T is not consumed in its transition range. A sharp noticeable change of indicator property (for example, its color) corresponds to EPT.

Titrimetric analysis

- **Indicator transition range** is the range of concentration of hydrogen ion, metal, or other ions, within which the human eye is capable of detecting a change in color shade, color intensity, fluorescence, or other property of a visual indicator caused by the change in the ratio of two corresponding forms of an indicator.

REAGENTS USED IN TITRIMETRIC ANALYSIS

- **Primary standard substance (primary standard)** is a high-purity substance used to determine titrant concentration (to standardize titrant), which is based on the stoichiometry of their interaction, or it can be used itself to prepare titrant solution with a precisely known concentration.

REAGENTS USED IN TITRIMETRIC ANALYSIS

- **Secondary standard substance (secondary standard)** is a substance used for standardization; the content of an active component in it is determined using the primary standard.

REAGENTS USED IN TITRIMETRIC ANALYSIS

- **A standard solution** is a solution with a known concentration of an active substance.
- **A primary standard solution** is a standard solution prepared from the primary standard substance, whose concentration is known by mass of this substance in a certain volume (or mass) of the solution.

REAGENTS USED IN TITRIMETRIC ANALYSIS

- **A secondary standard solution** is a solution whose concentration is determined by standardization or prepared according to the known mass of the secondary standard substance.

Titrimetric analysis

- **Standardization** is the process of determining the concentration of the active reagent in solution (most often by titration with standard solution).

TYPES OF TITRATION USED IN TITRIMETRIC ANALYSIS

- Direct titration
- Back titration
- Indirect titration, or titration with substituent (substitution titration)

Direct titration

- **Direct titration** is a type of titration during which the determined substance directly titrated with standard titrant solution or vice versa. The results of direct titration results are calculated similarly to the described above pipetting method

Back titration

- **Back titration (titration by residue)** is titration of unreacted substance, which has been added as a standard solution in excess to the analyzed solution. The precisely known volume V(T1) of standard substance T, solution with molar equivalent concentration c(1/zT,) is added to an aliquot of an analyzed solution with a volume of V(X)n. The determined substance X reacts with T, completely. Then, unreacted excess of substance T, is titrated with a standard solution of titrant T2.

Indirect titration

- **Indirect titration (substitution titration)** is titration, during which a determined substance does not react directly with a titrant, and is determined indirectly by using a stoichiometrically proceeding reaction leading to the formation of another substance that reacts with the titrant.

CLASSIFICATION OF TITRIMETRIC ANALYSIS METHODS

- **Acid-base titration (neutralization method)** is titration based on the reaction of proton transfer from one reacting particle to another in solution. It includes acidimetry and alkalimetry.

CLASSIFICATION OF TITRIMETRIC ANALYSIS METHODS

- **Oxidation-reduction (redox) titration (redoxometry)** is titration accompanied by a transition of one or more electrons from donor ion or molecule (reducing agent) to an acceptor (oxidizing agent).

CLASSIFICATION OF TITRIMETRIC ANALYSIS METHODS

- **Precipitation titration** is a type of titration, during which the titrated substance is precipitated from solution due to interaction with the titrant.

CLASSIFICATION OF TITRIMETRIC ANALYSIS METHODS

- **Complexometric titration** is titration of a substance with a compound solution that interacts with the titrated substance forming a weakly dissociating soluble complex.

METHODS FOR DETERMINING END POINT OF TITRATION

- There exist two groups of methods for determining EPT: **visual** and **instrumental**.

Visual methods for determining end point of titration

- **Visual methods**. The reaction is controlled visually by monitoring color change (or other property) of a specially added indicator.

Visual methods for determining end point of titration

- **In case of indicator visual methods**, an indicator is added to a titrated solution. Depending on the specifics of titrated solution and titrant, various indicators are used: acid-base, redox, precipitation, metalchromic, adsorption, metal fluorescent, fluorescent, chemiluminescent, screening, extraction. The most important of these indicators are considered below when describing different types and methods of titration.
- **Non-indicator visual methods** are based on color of titrant or titrated substance. EPT is determined by titrant coloration or titrated substance discoloration.

Instrumental methods for determining end point of titration

- **Instrumental methods.** EPT is determined by changing physical-chemical properties of a solution, such as fluorescence, optical density, potential, specific electrical conductivity, current strength, radioactivity, etc. Changes in physico-chemical properties are recorded using various instruments.