Discipline
"General pharmaceutical Chemistry"

Quantitative assessment of medicines. Gravimetry

Lecture 5

METHODS OF QUANTITATIVE ANALYSIS OF MEDICINAL SUBSTANCES

FOUR GROUPS OF METHODS ARE USED FOR THE QUANTITATIVE ANALYSIS OF MEDICINAL SUBSTANCES :

- ✓ CHEMICAL;
- ✓ PHYSICAL;
- ✓ PHYSICO-CHEMICAL;
- ✓ BIOLOGICAL.

GENERAL REQUIREMENTS FOR QUANTITATIVE DETERMINATION METHODS

1. HIGH SENSITIVITY AND SPECIFICITY OF THE MAIN REACTION.
2. SIMPLICITY AND ACCESSIBILITY OF THE METHODOLOGY.
3. AVAILABILITY OF REAGENTS USED IN PRACTICE.
4. SPEED OF EXECUTION.
5. THE INTERACTION OF THE ANALYZED SUBSTANCE WITH THE TITRANT SHOULD PROCEED STOICHIOMETRICALLY, TO THE END.
6. THE POSSIBILITY OF FIXING THE EQUIVALENCE POINT.
7. MINIMUM CONSUMPTION OF REAGENTS AND SAMPLE.
8. THE ACCURACY OF THE METHOD.
9. NO INFLUENCE OF IMPURITIES, FILLERS, SOLVENTS IN THE ANALYSIS.

QUANTITATIVE ANALYSIS OF MEDICINAL SUBSTANCES

Quantitative determination is based on the physico-chemical and biological properties of medicines.

In this regard, the methods of analysis are divided into:

- ✓ physical;
- ✓ chemical;
- ✓ physico-chemical;
- ✓ biological.

QUANTITATIVE ANALYSIS OF MEDICINAL SUBSTANCES

The first group of methods is based on measuring the physical properties of substances – radioactivity, viscosity, density, etc.

The most common physical methods of quantitative analysis include: refractometry, X-ray spectral and radioactivity analysis.

The second methods are based on the measurement of the physico-chemical properties of the substance being determined.

These include :

- optical (spectrophotometry, spectral analysis, colorimetry);
- chromatographic (gas-liquid chromatography, ion exchange, distribution);
- electrochemical (conductometric titration, potentiometric, coulometric, electroweigh analysis, polarography).

Biological methods are based on the use of living organisms as analytical indicators.

Chemical methods are based on the chemical properties of the substance under study, chemical reactions.

CHEMICAL METHODS OF QUANTITATIVE ANALYSIS

Chemical methods are classified into:

- ✓ weight analysis (gravimetry) – based on accurate weighing;
- ✓ volumetric analysis (titration) – based on accurate measurement.

Gravimetric and titrimetric are of the greatest importance. They are called classical methods of chemical quantitative analysis.

Gradually, classical methods give way to instrumental ones. However, they remain the most accurate.

The relative error of these methods is only 0.1-0.2%, and that of the instrumental ones is 2-5%.

CHEMICAL METHODS OF QUANTITATIVE ANALYSIS (GRAVIMETRY)

Gravimetric analysis (gravimetry, weight analysis) is a quantitative chemical analysis method based on the accurate measurement of the mass of a substance.

In this case, it uses the law of conservation of mass of substances during chemical transformations.

The analytical signal in gravimetry is mass.

GRAVIMETRIC METHOD OF QUANTITATIVE DETERMINATION

The technique of quantitative analysis by gravimetry includes the following stages of the study :

1. **Precipitation of the compound** that contains the substance of interest.
2. **Filtration of the resulting mixture** to extract sediment from the filler liquid.
3. **Washing the sediment** to eliminate the settling fluid and remove impurities from its surface**.**
4. **Drying** at low temperatures to remove water or at high temperatures to transfer the sediment into a suitable weighing form.
5. **Weighing the resulting sediment.**
6. **Calculation of gravimetric analysis results**.

GRAVIMETRIC METHOD OF QUANTITATIVE DETERMINATION

Precipitation is usually carried out from hot solutions, their high temperature contributes to the formation of a coarse-crystalline precipitate.

The precipitator solution is mostly poured in a small stream, stirring continuously.

Filtration and washing of sediment – filtered through a paper filter, as well as through funnels with a porous bottom.

Sludge washing is carried out by decantation method.

Sludge drying is carried out in a drying cabinet in buckets (glass flasks with a lid).

Calcination of the sediment is performed in porcelain crucibles, using a muffle furnace for this purpose.

Calcination is carried out several times until the sediment mass becomes constant.

GRAVIMETRIC METHOD OF QUANTITATIVE DETERMINATION

The resulting sediment is weighed on analytical scales, which are a sensitive physical device.

In order for the scales not to spoil and weighing to give an accurate result, certain rules are strictly observed.

The substance to be determined should be deposited almost completely in the form of slightly soluble precipitation, precipitation should not contain noticeable amounts of impurities.

GRAVIMETRIC METHOD OF QUANTITATIVE DETERMINATION

The compound in which the component being determined is precipitated from the solution is called the precipitation form.

So, for example, during the precipitation of iron (III), the precipitation form is Fe(OH)3, and during the precipitation of chloride – AgCl :

$$FeCl3 + 3NH4OH \rightarrow Fe(OH)3\downarrow + 3NH4Cl;$$
$$AgNO3 + HCl \rightarrow AgCl + HNO3.$$

After filtration and washing, the precipitate is dried and calcined to a constant mass, and then weighed.

The compound in which the weighing is performed is called the gravimetric form.

Chemical processes can occur during drying and calcination of precipitation, for example:

$$2Fe(OH)3 \rightarrow Fe2O3 + 3H2O.$$

Thus, the deposition form and gravimetric form may differ in composition, or they may coincide (for example, in the case of AgCl).

GRAVIMETRIC METHOD OF QUANTITATIVE DETERMINATION

Gravimetric analysis is used to determine the main components of the analyzed material contained in it in large and medium quantities.

Gravimetric methods are the most reliable, but are currently rarely used.

The disadvantages of the gravimetric method of quantitative analysis are the duration of determination and non-selectivity (precipitating reagents are rarely specific). Therefore, a preliminary separation is necessary.

GRAVIMETRIC METHOD OF QUANTITATIVE DETERMINATION

Currently, the gravimetric analysis method is used to determine the mass loss during drying, total ash and sulfate ash.

The mass loss during drying is usually determined by drying a sample of the substance in a drying cabinet to a constant mass at a specified temperature.

In some cases, other drying methods are used, especially for thermolabile objects: desiccation over phosphorus pentoxide at normal pressure and room temperature, drying over phosphorus pentoxide in vacuum, drying over phosphorus pentoxide in high vacuum (0.1kPa).

GRAVIMETRIC METHOD OF QUANTITATIVE DETERMINATION

Determination of ash. Ash is an indicator of the quantitative content of inorganic substances in animal or vegetable raw materials.

To determine the total ash, the sample sample of the raw material is first burned in a crucible on a grid.

The burning is carried out so that there is no flame.

Then the residue is placed in a muffle furnace and calcined at about 500 °C to a constant mass.

GRAVIMETRIC METHOD OF QUANTITATIVE DETERMINATION

To determine the *ash insoluble in hydrochloric acid diluted*, the ash in the crucible is treated with hydrochloric acid diluted (15 ml), heated in a water bath for 10 minutes, 5 ml of purified hot water is added and filtered through an ashless filter.

The filter is placed in the same crucible, burned on a grid, then placed in a muffle furnace and calcined to a constant mass.

Sulfate ash is determined in organic substances according to approximately the same scheme. The required amount of substance is placed in the crucible, 1 ml of concentrated sulfuric acid is added, carefully heated on a grid until sulfuric acid vapor is removed, then calcined in a muffle furnace to a constant mass.

CLASSIFICATION OF GRAVIMETRIC METHODS

Gravimetric methods are divided into methods:

- ✓ deposition;
- ✓ distillation;
- ✓ isolation ;
- ✓ thermogravimetric methods (thermogravimetry).

Deposition methods are of the greatest importance.

CLASSIFICATION OF GRAVIMETRIC METHODS

Deposition methods. The determined component of the solution reacts chemically with the added precipitating reagent, forming a slightly soluble precipitate product, which is separated, washed, dried (calcined if necessary) and weighed on analytical scales.

Methods of distillation. The component to be determined is isolated from the analyzed sample in the form of a gaseous substance and either the mass of the distilled substance (direct method) or the mass of the residue (indirect method) is measured.

The direct method is used, for example, to determine the water content in the analyzed samples.

Indirect distillation methods are widely used to determine the content of volatile substances: the mass of the analyzed sample is measured when it is dried in a thermostat (drying cabinet) at a fixed temperature.

CLASSIFICATION OF GRAVIMETRIC METHODS

Selection methods. The component to be determined is isolated (usually from a solution), for example, during electrolysis on one of the electrodes (electrogravimetric method).

Then the electrode with the released substance is washed, dried and weighed. By increasing the mass of the electrode, the mass of the released substance is found.

Thermogravimetric methods. They are based on measuring the mass of the analyzed substance when it is continuously heated in a given temperature range.

Measurements are usually carried out on special devices – derivatographs equipped with special thermal weights for continuous weighing, an electric furnace for heating the sample, thermocouples for measuring temperature, a reference standard and a recorder that continuously records the change in the mass of the heated substance.

CLASSIFICATION OF GRAVIMETRIC METHODS

The essence of gravimetric quantitative analysis is the isolation of the substance of interest in its pure form and its weighing.

The separation of the substance is most often carried out by precipitation.

In some cases, the component to be determined must be obtained in the form of a volatile substance (*distillation method*).

In this way, it is possible to determine, for example, the content of crystallization water in crystallohydrates.

The precipitation method determines silicic acid in the processing of rocks, iron and aluminum in the analysis of rocks, potassium and sodium, organic compounds.

CALCULATIONS OF THE RESULTS OF GRAVIMETRIC ANALYSIS

The result of the gravimetric analysis is calculated using the formula:

$$x = m^* [M(x)/M(g.f.)],$$

where x is the mass of the substance being determined;

m is the mass of the gravimetric shape;

M(x) and M(g.f.) are, respectively, the molar masses of the substance being determined and the gravimetric shape (g/mol).

The ratio M(x)/M(g.f.) = F is called a *gravimetric factor* (*gravimetric multiplier*) or a conversion factor.

Therefore,

$$x = m^*F$$

CALCULATIONS OF THE RESULTS OF GRAVIMETRIC ANALYSIS

When calculating the gravimetric factor, it is necessary to take into account the stoichiometric coefficients in the chemical formulas of the substance being determined and the gravimetric shape, so that the number of atoms of the component being determined in the numerator and denominator of the fraction is the same:

$$F = \nu1*M(x)/\nu2*M(г.ф.)$$

The numerical values of the conversion factors for most practically important definitions are calculated with high accuracy and are given in reference books.

Determination of humidity – the content of hygroscopic water in the analyzed substance (as a percentage) according to the formula:

$$X = ((A-B)/A)*100\% ,$$

where X is humidity, %;

A is the weight of the suspension before drying, g;

B is the weight of the weighing mold after drying, g.

CALCULATIONS OF THE RESULTS OF GRAVIMETRIC ANALYSIS

Determination of ash content – the content of the inorganic part of the analyzed substance (as a percentage) according to the formula:

$$X = (B/A)*100\%,$$

where X is the ash content, %;

A is the weight of the suspension before calcination, g;

B is the weight of the weight mold after calcination, g.

Determination of the element content in a substance during procedures according to the formula:

$$X = ((n*Ar*B)/(Mr*A))*100\%,$$

where X is the content of the element, %;

N is the number of atoms of an element in a substance;

Ar is the atomic mass of an element;

Mr is the molecular weight of a substance;

A – weight of the attachment, g;

B – weight of the weight form, g.

CALCULATIONS OF THE RESULTS OF GRAVIMETRIC ANALYSIS

The choice of the optimal method of chemical determination is determined, first of all, by its ability to evaluate a medicinal substance by the physiologically active part of the molecule.

The trends currently existing in the analysis of medicinal substances are somewhat different from the concept given in textbooks.

This is due to the bias of all analysis methods towards instrumentation and an increasing tendency to use physico-chemical methods in the quantitative determination of medicinal substances.


THANK YOU FOR ATTENTION!