Ministry of Health of the Russian Federation

Volgograd State Medical University

Department of Pharmaceutical and Toxicological Chemistry

GENERAL PHARMACEUTICAL CHEMISTRY

Quantification of drugs. Gravimetry.

Lesson 11

V term

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QUESTIONS FOR THE LESSON

1. Methods of quantitative analysis of pharmaceutical substances.
2. Chemical methods of quantitative analysis.
3. Gravimetric method of quantification. Essence, stages of analysis.
4. Classification of gravimetric methods.
5. Equipment and chemical utensils for gravimetric analysis.
6. Calculations of the results of gravimetric analysis.

Quantitative analysis

Quantitative analysis (also termed quantitation or quantification) is intended to measure the exact concentration or the exact amount of the analyte in a given sample.

The quantification of a medicinal substance is the is the final step in pharmaceutical analysis. It is carried out after the test substance has been identified and the presence of an allowed amount of impurities has been determined.

Four ***groups of methods*** are used for the quantitative analysis of drugs:

- chemical,
- physical,
- physico-chemical
- biological.

Physical methods are based on the measurement of physical properties of substances - radioactivity, viscosity, density, etc. The most common physical methods of quantitative analysis are refractometry, X-ray spectroscopy and radioactivity analysis.

Physico-chemical methods are based on the measurement of the physico-chemical properties of the determined substance. These include:

- ✓ Optical (spectrophotometry, spectral analysis, colorimetry);
- ✓ Chromatography (gas-liquid chromatography, ion-exchange, distributive);
- ✓ Electrochemical (conductometric titration, potentiometric, coulometric, electroweights analysis, polarography).

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

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

General requirements for quantification methods:

1. High sensitivity and specificity of the main reaction.
2. Simplicity and availability of the methodology.
3. Availability in practice of the reagents used.
4. Promptness of procedure.
5. The interaction of the test substance with the titrant must proceed stoichiometrically to completion.
6. Ability to fix the point of equivalence.
7. Minimum consumption of reagents and sample.
8. Accuracy of method.
9. No influence of impurities, fillers, solvents in the analysis.

Quantitative chemical analysis methods

Chemical methods are divided into:

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

Titrimetric (volumetric) analysis

Titrimetric quantification is the accurate measurement of the volume of a reagent solution that is consumed in an equivalent interaction with an analysed substance. The concentration of the reagent used is determined beforehand. Given the volume and concentration of the reagent solution, the content of the analysed component is calculated.

Titration is the process of gradually adding a solution of known concentration to a specific volume of another solution. It continues until the substances have reacted completely with each other. This is called the point of equivalence and is indicated by a change in colouration of the indicator.

Methods of titrimetric analysis:

- Acid-base.
- Oxidation-reduction method.
- Precipitation.
- Complexometric.

Gravimetric method of quantification

Essence, steps of the analysis

Gravimetric analysis (gravimetry, weight analysis) is a method of quantitative chemical analysis based on the exact mass measurement of a substance. It uses the law of conservation of mass in chemical transformations. The analytical signal in gravimetry is mass.

The essence of gravimetric quantitative analysis is to isolate the test substance in its pure form and weigh it.

Classification of gravimetric methods

Gravimetric methods are divided into methods of

- precipitation;
- distillation,
- extraction,
- thermogravimetric methods (thermogravimetry).

Precipitation methods. The component of sampled solution reacts chemically with the added precipitant. This produces a poorly soluble product, the precipitate. The precipitate is separated, washed and dried (occasionally calcined) and weighed on an analytical balance.

Methods of distillation. The analysed component is extracted from the test sample as a gaseous substance. The next step is to measure either the mass of the distillate (direct method) or the mass of the residue (indirect method).

The *direct* method is used, for example, to determine the water content of the samples to be analysed.

Indirect distillation methods are widely used for the determination of volatile substances: The mass of the analysed sample is measured when it is dried in a thermostat (desiccator) at a fixed temperature.

Methods of extraction. The test compound is extracted (usually from a solution), for example by electrolysis on one of the electrodes (electrogravimetric method). The electrode with the excreted substance is then washed, dried and weighed. By increasing the mass of the electrode is the mass of the released material.

Thermogravimetric methods. Based on the measurement of the mass of the analysed substance when continuously heated over a given temperature range.

Precipitation method. Essence, steps of the analysis.

The methodology includes the following steps:

1. Precipitation of the compound which contains the analysed substance.
2. Filtration of the resulting mixture to extract the precipitate from the supernatant.
3. Washing the precipitate to remove the supernatant and removal of impurities from its surface.
4. Drying at low temperatures to remove water or at high temperatures to or at elevated temperatures to transform the precipitate into a suitable form for weighing.
5. Weighing the resulting precipitate.
6. Calculating the result of the gravimetric analysis.

Precipitation is usually carried out from hot solutions. Their high temperature promotes the formation of a coarse crystalline precipitate.

The precipitant solution is mostly injected in a small stream, stirring continuously.

The test substance shall precipitate almost completely as a low-soluble precipitate, the precipitation shall not contain appreciable quantities of impurities.

Filtration and washing of the precipitate. Filtrate through a paper filter or porous-bottom funnel. The washing of the precipitate is done by decantation. The precipitate is dried in a desiccator in weighing bottles (glass flasks with a lid).

The precipitation is calcined. Carried out in porcelain crucibles using a a muffle furnace. The calcination is carried out several times until the mass of the precipitate becomes constant.

The resulting precipitate *is weighed* on an analytical scale.

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

Example 1, in chloride precipitation, the precipitation form is AgCl:

$$AgNO_3 + HCl \rightarrow AgCl + HNO_3$$

Example 2, when iron (III) is precipitated, the precipitation form is $Fe(OH)_3$:

$$FeCl_3 + 3NH_4OH \rightarrow Fe(OH)_3\downarrow + 3NH_4Cl$$

The compound as weighed is called **gravimetric form.**

When precipitates are dried and calcined, chemical processes may take place, for example:

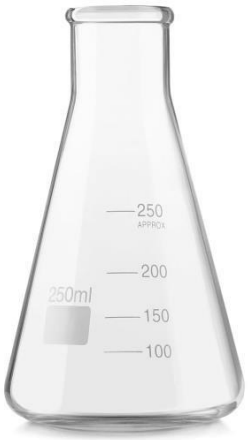
$$2Fe(OH)_3 \xrightarrow{t^\circ} Fe_2O_3 + 3H_2O$$

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

The disadvantages of the gravimetric method of quantitative analysis are the long detection time and the non-selectivity (the precipitating reagents are rarely specific).

Equipment and chemical utensils for gravimetric analysis

Chemical flasks and beakers. Chemical flasks and beakers are used to quickly heating or cooling of solutions. In gravimetric analysis, beakers of 100, 200 and 400 ml volume are used for precipitation from solutions.



Conical flask

Beaker

The watch glasses are used to take a sample or to cover beakers and flasks.

Watch glasses

Funnels are used for filtering and rinsing precipitations.

Funnels

Pissettes is used to rinse precipitate from the sides of the beaker, of the watch glass, filter, and blotter.

Pissettes

Glass sticks are used to stir liquids, for transferring liquids during filtration.

Glass sticks

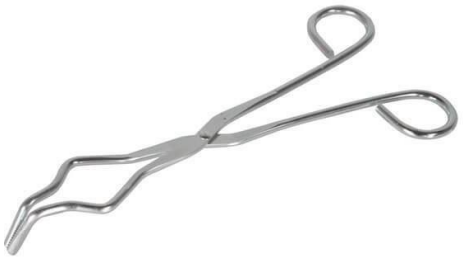
Weighing bottles are small beakers with a ground glass lid. They are used for determining the moisture of substances and for weighing solids and liquids.

Weighing bottle

Porcelain crucibles are used for calcining precipitation. A new crucible is always calcined in a muffle furnace for several hours to constant mass before use.

Porcelain crucible

Crucible tongs. The crucibles are transferred with special tongs, the ends of which are flat and curved upwards. Before using the tongs, the ends of the tongs are burned on a gas flame. The crucible is gripped by the edges with the tongs, not around it.



Crucible tongs

Desiccators. Desiccators are used to store substances that can absorb moisture from the air. Crucibles or vials containing dried or calcined substances dried are cooled in the desiccators to at room temperature.

Desiccator

Electric drying ovens are used for drying of chemical vessels, precipitates or test samples. The temperature is automatically regulated between 20 °C and 250 °C.

Electric drying oven

Electric muffle furnaces are used to calcine precipitation in crucibles. Temperatures of between 800 and 1200°C can be reached in these furnaces.

Figure 1Electric muffle furnace

Calculations of gravimetric analysis results

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

$$x = m\frac{M(x)}{M(\text{g. f.})}$$

x - mass of determined substance;

m - the mass of the gravimetric form;

M(x) - molar mass of the determined substance;

M(g.f.) - molar mass of gravimetric form.

The ratio *M(x)/M(g.f.) = F* is called the ***gravimetric factor.***

Therefore,

$$x=mF$$

When calculating the gravimetric factor it is necessary to consider the stoichiometric coefficients in the chemical formulae of the substance and gravimetric form.

$$F = \frac{\nu_1 M(x)}{\nu_2 M(\text{g. f.})}$$

For example if the substance to be determined is Fe_3O_4 and the gravimetric form Fe_2O_3, the gravimetric factor would be

$$F = \frac{2M(Fe_3O_4)}{3M(Fe_2O_3)}$$

Determination of moisture content - the hygroscopic water content of the analysed substance (in per cent) according to the formula:

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

where

X - moisture content, %;

A- mass of the sample before drying, g;

B mass of the weight form after drying, g.

Determination of ash content - Inorganic content of the substance to be analysed (percentage) by formula:

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

where

X - ash content, %;

A - mass of the sample before calcination, g;

B - mass of the weight form after calcination, g.

Determine the elemental content of the substance in the procedures using the formula:

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

Where:

X - element content, %;

n - number of atoms of the element in the substance;

Ar - atomic mass of the element;

Mr - molecular weight of the substance;

A - mass of the sample, g;

B - mass of the weight form, g.