Discipline "General Pharmaceutical Chemistry"

Authenticity of medicinal products of an inorganic nature

Lecture 1

Features of pharmaceutical analysis

Pharmaceutical analysis is the science of chemical characterization and measurement of biologically active substances at all stages of production: from the control of raw materials to the assessment of the quality of the obtained medicinal substance, the study of its stability, the establishment of shelf life and standardization of dosage forms.

Pharmaceutical analysis has its own specific features that distinguish it from other types of analysis :

- **substances of various chemical nature (inorganic, organoelement, radioactive, organic compounds) are analyzed;**
- **extremely wide range of concentrations of the analyzed substances;**
- **The objects of analysis are not only individual medicinal substances (substances), but also mixtures containing a different number of components.**

Features of pharmaceutical analysis

The purpose of the study of medicinal substances is to establish the suitability of a medicinal product for medical use, that is, its compliance with the regulatory document for this drug.

Pharmaceutical analysis methods need to be systematically improved in connection with the creation of new medicines and the continuous increase in quality requirements.

Pharmaceutical analysis, depending on the tasks set, includes various aspects of quality control of medicinal substances :

1. Pharmacopoeia analysis
2. Step-by-step control of the production of medicines
3. Analysis of individually manufactured medicines
4. Express analysis in a pharmacy setting
5. Biopharmaceutical analysis

Quality assurance of medicines is a widespread concept that includes a set of measures that affect the quality of the finished product and ensure that it meets the requirements of regulatory documentation.

Features of pharmaceutical analysis

Pharmaceutical analysis of medicinal substances is a study of their suitability for use in medical practice.

Pharmaceutical analysis of medicinal substances, regardless of their chemical nature, consists of three parts :

- ✓ determining the authenticity of the test substance;
- ✓ determination of the presence of impurities of foreign substances and their maximum permissible content;
- ✓ quantitative determination of the test substance.

Previously, the authenticity of some medicinal substances can be determined by color, smell and other characteristics.However, the most reliable test method is a chemical study or a physico-chemical test.

Features of pharmaceutical analysis

In order to consider the identity of a substance to be reliably proven, it is necessary to conduct two or three reactions or tests. In this case, as a rule, reactions should be specific and, if possible, sensitive.

The term "sensitivity" is considered obsolete, and currently the sensitivity of the reaction is characterized by a lower detection limit and a limit dilution. These two characteristics are related by the formula:

$$D = P/ (V \times 10^6), [g/ml]$$

where D is the maximum dilution characterizing the minimum concentration of the substance at which a positive reaction is possible;

P is the lower limit of detection of the substance for this reaction (in % rel. or in fractions per million - ppm);

V is the volume of the solution in which the reaction takes place, ml.

Features of pharmaceutical analysis

Qualitative reactions can be carried out on a slide, on filter paper, in a microprobe, in a test tube and on a slide under a microscope.

The choice of technique depends on the amount of the substance, the lower detection limit and the dilution limit. Obviously, at low concentrations, the reaction can be negative.

Therefore, it is better to use a small volume of solution, but with a high concentration of the substance. To carry out a drip reaction on a slide, 0.03 ml of solution is enough, 0.01 ml of solution is enough to carry out the same reaction under a microscope, and up to 5 ml of solution is usually used in a test tube.

It should be noted that the sensitivity of the reaction is relevant in cases where a substance with high pharmacological activity and a low dosage is analyzed.

Methods of identification of medicinal substances

Currently (according to the State Pharmacopoeia), numerous physical, chemical and physico-chemical analysis methods are used to establish the authenticity of medicinal substances (appearance characteristics, solubility, melting point, distillation temperature limits, specific rotation, pH value, specific absorption index, chemical reactions to cations, anions or functional groups).

Chemical methods for the qualitative determination of medicines are based on chemical reactions.

An indispensable condition for an objective test is the identification of those ions or functional groups included in the structure of molecules that determine pharmacological activity.A large number of medicinal substances contain the same ion or the same functional group.

This made it possible to create unified methods for their identification using chemical reactions and combine them into a common pharmacopoeia article "General reactions to authenticity".

The regulatory documentation provides a combination of group and specific chemical reactions for the identification of medicinal substances.

Methods of identification of medicinal substances

The general pharmacopoeia article "General authenticity reactions" describes methods for detecting frequently occurring structural parts, indicating the limits of the content of the structural part in the sample of the analyzed sample, allowing for a distinct analytical effect taking into account dilution.

In this case, the pharmacopoeia article only provides links to the general pharmacopoeia article.

Inorganic drugs are electrolytes, and therefore are in solution in the form of simple and complex ions. In this form, they are available for pharmaceutical analysis, which ensures the quality (authenticity, goodness and quantitative content) of medicines.

The identification of inorganic medicinal substances consists in establishing authenticity based on the detection by chemical reactions of cations and anions that make up their molecules.

Identification of inorganic medicinal substances

To establish the authenticity of inorganic medicinal substances, they use:

1. Reactions of precipitation of anions and cations with the formation of substances insoluble in water, which can be characterized by color, solubility (in acids, alkalis, organic solvents), the ability to form complex compounds soluble in excess of reagents, etc.

2. Redox reactions.

3. Reactions of neutralization and decomposition of anions (by smell, releaseof oxides and dioxides).

4. A change in the color of a colorless flame.

5. Changes occurring during heating and calcination of medicines.

Identification of inorganic medicinal substances

1. Precipitation reactions :

Sodium ions are precipitated with zincuranyl acetate:

$$Na^+ + Zn[(UO_2)_3(CH_3COO)_8] + CH_3COOH + 9H_2O \rightarrow$$
$$\rightarrow NaZn[(UO_2)_3(CH_3COO)_9] \cdot 9H_2O\downarrow + H^+$$

yellow

Potassium ions are precipitated with tartaric acid:

$$K^+ + HOOC — (CH_2OH)_2 — COOH \rightarrow HOOC — (CH_2OH)_2 — COOK\downarrow + H^+$$

white

Potassium ions can be precipitated with a solution of sodium hexanitrocobaltate (III):

$$2K^+ + Na_3[Co(NO_2)_6] \rightarrow K_2Na[Co(NO_2)_6]\downarrow + 2Na^+$$

yellow

Identification of inorganic medicinal substances

2. Redox reactions (accompanied by a change in the color of the resulting interaction products).

Bromide and iodide ions are oxidized with chlorine (chloramine, other oxidizing agents):

$$2Br^- + Cl_2 \rightarrow Br_2 + 2Cl^-$$

$$2I^- + Cl_2 \rightarrow I_2 + 2Cl^-$$

The released bromine turns the chloroform layer orange, and iodine turns purple.

Iodine is also detected by the blue staining of starch paste.

Identification of inorganic medicinal substances

Fluoride ions discolor the red color of the iron rhodanide solution :

$$[Fe(NCS)_6]^{3-} + 6F^- \rightarrow 6NCS^- + [FeF_6]^{3-}$$

Copper and silver ions are reduced from oxides and salts to free metals :

$$Ag_2O + HCOH \rightarrow 2Ag\downarrow + HCOOH$$

$$CuSO_4 + Fe \rightarrow Cu\downarrow + FeSO_4$$

Identification of inorganic medicinal substances

3. Decomposition reactions (accompanied by the formation of gaseous products that are organoleptically detected (odor, color).

Ammonium ions decompose under the action of hydroxide solutions (the smell of ammonia or a change in the color of red litmus paper):

$$NH_4^+ + NaOH \rightarrow NH_3\uparrow + Na^+ + H_2O$$

Carbonate ions form a white precipitate under the action of a saturated solution of magnesium sulfate, and bicarbonate forms a precipitate only when the mixture is boiled:

$$4Na_2CO_3 + 4MgSO_4 + 4H_2O \rightarrow 3MgCO_3 \bullet Mg(OH)_2 \bullet 3H_2O\downarrow + CO_2\uparrow + 4Na_2SO_4$$

Carbonate and bicarbonate ions form carbon dioxide gas under the action of mineral acids:

$$CO_3^{2-} + 2HCl \rightarrow CO_2\uparrow + H_2O + 2Cl^-$$

$$HCO_3^- + HCl \rightarrow CO_2\uparrow + H_2O + Cl^-$$

3. Decomposition reactions :

Nitrite ions, unlike nitrate ions, release nitrogen oxides under the action of acids (nitrogen dioxide has a red-brown color):

$$2NO_2^- + H_2SO_4 \rightarrow NO\uparrow + NO_2\uparrow + H_2O + SO_4^{2-}$$

4. Changing the color of a colorless flame :

It is possible to establish the presence of a number of elements in inorganic organoelement drugs by changing the color of the colorless flame of the burner.

Sodium salt introduced into the flame turns it yellow, potassium salt turns purple, calcium salt turns brick red, lithium turns carmine red.

Boron salts soaked in ethanol turn the flame rim green.

Identification of inorganic medicinal substances

5. Changes that occur during heating and calcination of medicines. Identification of organoelement drugs.

Elemental analysis is used to test substances containing atoms of sulfur, phosphorus, halogens, arsenic, bismuth, and mercury in a molecule.

Since the atoms of these elements in these medicinal substances are not ionized, preliminary mineralization is a necessary condition for testing their authenticity.

As a result, the organic part of the molecule is destroyed (the conversion of carbon, hydrogen and oxygen into CO2 and H2O), and the above atoms form the corresponding ions, which are identified by sedimentary reactions to inorganic ions.

Conclusions

1. Pharmaceutical analysis has its own specific features that distinguish it from other types of analysis.

2. The purpose of pharmaceutical analysis of medicinal substances is to establish the suitability of a medicinal product for medical use, that is, its compliance with the regulatory document for this drug.

3. Unified methods for the identification of medicinal substances using chemical reactions are combined in the general pharmacopoeia article "General reactions to authenticity".

4. The identification of inorganic medicinal substances is the establishment of authenticity based on the detection by chemical reactions of cations and anions that make up their molecules.

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