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DEPARTMENT OF PHARMACEUTICAL, ORGANIC
AND BIOORGANIC CHEMISTRY

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PHARMACEUTICAL CHEMISTRY

ANALYSIS OF MEDICINES OF THE HORMON GROUP

Section 2.3

Study and methodical Guide

for 4th year students of the specialty "Pharmacy, Industrial Pharmacy"

Zaporizhzhia
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S53

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CONTENTS

INTRODUCTION

Pharmaceutical chemistry is studied according to the Model curriculum for training specialists of the second (master's) level of higher education in the field of knowledge 22 "Health Protection" in higher educational institutions of the Ministry of Health of Ukraine in specialty 226 "Pharmacy" educational qualification "Master of Pharmacy" as of 26.07.2016.

Most of the drawings were developed by the authors of this study guide.

According to the order, pharmaceutical chemistry is studied in III, IV and V courses. In the fourth year (VII-VIII semesters) the discipline program is structured into 2 meaningful blocks:

Block 1 - "Pharmaceutical Analysis"

Block 2 - "Special Pharmaceutical Chemistry"

Block 2 consists of three sections:

Section 1 – "Analysis of medicines that affect the central nervous system. General characteristics, classification, relationship of structure with pharmacological action, extraction, methods of analysis, application".

Section 2 - "Analysis of medicines that affect the central and peripheral nervous system. General characteristics, classification, relationship of structure with pharmacological action, extraction, methods of analysis, application".

Section 3 - "Analysis of medicines of the hormones group. General characteristics, classification, relationship of structure with pharmacological action, extraction, methods of analysis, application".

The present Pharmaceutical chemistry guide for 4th year students of the specialty " Pharmacy, Industrial Pharmacy" complies with curriculum and cover most of topics of 8th semester.

Lecture plan

of pharmaceutical chemistry for 4th year students of the Faculty of Pharmacy (8th semester)

No.	Lecture topics	Number of hours
1	Analysis of psychotropic drugs. Medicines for the treatment of parkinsonism. General characteristics, classification, relationship between structure and pharmacological action, methods of preparation, methods of analysis, application in medicine.	**2**
2	Analysis of peripheral vasodilators. General characteristics, classification, relationship between structure and pharmacological action, methods of preparation, methods of analysis, application in medicine.	**2**
3	Analysis of narcotic analgesics. Vomiting and antiemetic drugs. General characteristics, classification, relationship between structure and pharmacological action, methods of preparation, methods of analysis, application in medicine.	**2**
4	Analysis of thyroid hormones, antithyroid drugs. General characteristics, classification, relationship between structure and pharmacological action, methods of preparation, methods of analysis, application in medicine.	**2**
5	Analysis of steroid hormones and their analogues. General characteristics, classification, relationship between structure and pharmacological action, methods of preparation, methods of analysis, application in medicine.	**2**

PLAN

of laboratory practicals and seminar classes on pharmaceutical chemistry for 4th year students of the Faculty of Pharmacy (8th semester)

No.	Lesson topics	Number hours
1.	Analysis of psychotropic drugs: neuroleptics, sedative drugs.	**3**
2.	Analysis of psychotropic drugs: antidepressants, analeptics.	**3**
3.	Analysis of psychotropic drugs: psychostimulants. Medicines for the treatment of parkinsonism.	**3**
4.	**Control lesson from the section.**	**2**
5.	Analysis of peripheral vasodilators.	**3**
6.	Analysis of narcotic analgesics and their analogues. Emetics and antiemetics.	**3**
7.	Analysis of means acting on cholinergic processes. Part 1. Cholinomimetics, anticholinesterase drugs.	**3**
8.	Analysis of means acting on cholinergic processes. Part 2. Cholinergic blockers, ganglioblockers.	**3**
9.	Analysis of agents acting on adrenergic processes: adrenomimetics, adrenoblockers, sympatho mimetics, sympatholytics.	**3**
10.	**Control lesson from the section.**	**2**
11.	Analysis of adrenal medulla hormones (catecholamines), thyroid gland, antithyroid drugs and pancreatic hormones. Synthetic analogues of pharmacological action.	**3**
12.	Analysis of drugs from the steroid hormone group: adrenal cortical hormones (corticosteroids). Synthetic analogues of pharmacological action.	**3**
13.	Analysis of sex hormones: progestogens, estrogens, androgens, anabolic steroids and their analogues. Birth control. Estrogens of nonsteroidal structure.	**3**
14.	**Control lesson from the section.**	**3**

SPECIFIC GOALS:

"Analysis of medicines of the hormones group. General characteristics, classification, relationship of structure with pharmacological action, extraction, methods of analysis, application»

- Learn the properties of drugs from the group of hormones.
- Know the main sources and methods of obtaining drugs from the group of hormones.
- To propose and carry out the selection of physical, physicochemical and chemical methods of quality analysis of drugs from the group of hormones in accordance with the requirements of the SPhU and other regulatory documentation, as well as Quality Control Methods (QCM).
- Explain the peculiarities of the analysis of drugs from the group of hormones using physical, physicochemical and chemical methods.
- Interpret the results of studies of the proposed drugs from the group of hormones, obtained using physical, physico-chemical and chemical methods.
- Explain the peculiarities of storage of drugs from the group of hormones, based on their physical and chemical properties.

Theoretical material

**** Hormones**(Greek. "Hopmaino" - set in motion, excite) - biologically active substances produced by endocrine glands or specialized endocrine cells that enter the body's internal environment directly, capable of exerting a specific chemical effect on specific cells and tissues in extremely small concentrations , organs (target cells, target organs), causing changes in metabolism and energy, structure and function of organs and tissues.*

Humoral regulation is a type of biological regulation in which information is transmitted with the help of biologically active chemicals that are carried around the body by blood or lymph, as well as by diffusion into the intercellular fluid.

Today, the following types of classification of hormonal drugs are known:

by nature of biological action:

- hormones that have a hormonal or hemocrine effect (that is, an effect at a considerable distance from the place of formation);
- - "- *isocrine*, or local effect (when a chemical substance synthesized in one cell acts on a cell located in close contact with the first, and the release of this substance is carried out into the interstitial fluid and blood);
- - "- *neurocrine*, or *neuroendocrine* (synaptic and non-synaptic) action (when the hormone, released from nerve endings, performs the function of a neurotransmitter or neuromodulator, i.e. a substance that changes (usually enhances) the action of a neurotransmitter);
- - "- *paracrine* action - a type of isocrine action, but at the same time, the hormone produced in one cell enters the intercellular fluid and affects a number of cells located in the immediate vicinity (the action of the hormone is perceived by neighboring cells, i.e. paracrine action of cells - stimulating neighboring cells action);
- - "- *juxtacrine* effect - a type of paracrine effect, when the hormone does not enter the intercellular fluid, and the signal is transmitted through the plasma membrane of another cell located nearby;
- - "- *autocrine* effect, when the hormone released from the cell affects the same cell, changing its functional activity;
- - "- *solinocrine* effect, when a hormone from one cell enters the lumen of the duct and thus reaches another cell, exerting a specific effect on it (for example, some gastrointestinal hormones).

by producing glands:

Hormone	Place of production
Dopamine	Central nervous system
Growth hormone, or somatotropin (GR, STH)	Pituitary gland and its anterior

Hormone	Place of production
	lobe
Prolactin (PRL)	Pituitary gland and its anterior part
Adrenocorticotropic hormone, or adrenocortico-tropin (ACTH)	
β-lipotropin and enkephalins	
Follicle stimulating hormone (FSH)	
Lutein-stimulating hormone (LSH)	
Thyroid stimulating hormone (TSH)	
Vasopressin (antidiuretic hormone - ADH) Oxytocin	The posterior part of the pituitary gland, hypothalamus
Melanocyte-stimulating hormone (MSH)	The intermediate part of the pitui-tary gland
Thyrotropin-releasing hormone (TRH)	Hypothalamus, central nervous system
Gonadotropin-releasing hormone	
Somatostatin	
Corticotropin-releasing hormone (CRH)	
Somatocrinin	
Melatonin, adrenoglomerulotropin, etc.	Epophysis
Thyroxine, Triiodothyronine	Thyroid
Parathyroid hormone, or parathyroid hormone (PTH)	Parathyroid glands
Calcitonin	C-cells of the thyroid gland
Thymosin	Subthoracic gland
Adrenalin	The medulla of the adrenal glands
Norepinephrine	CNS, medulla of the adrenal glands
Glucocorticoids	Adrenal cortex
Aldosterone	
Metabolites of cholecalciferol (vitamin D)	Liver, kidneys
Angiotensin (A II, A III)	Blood (from the predecessor), CNS
Insulin	β- Pancreatic islet cells
Glucagon	α- Pancreatic islet cells
secretin	Digestive organs
Cholecystokinin (HCC)	
Gastrin	
Gastric inhibitory peptide (GIP)	

Hormone	Place of production
Placental lactogen (PL)	Placenta
Chorionic gonadotropin (HCG)	Placenta
Estrogens (E2, E3)	Ovaries, placenta
Progesterone (P)	Yellow body, placenta
Testosterone (T)	Seminal glands
Dihydrotestosterone (DHT)	Testosterone-sensitive tissues

biochemical classification of hormones according to Yudayev:

- peptide nature (vasopressin, oxytocin, glucagon, calcitonin, etc.);
- simple proteins (prolactin, somatotropin, insulin);
- complex proteins, in particular glycoproteins (thyroid-stimulating hormone, follicle-stimulating hormone (FSH), luteinizing hormone (LH));
- derivatives of amino acids (phenylalkylamines, mainly tyrosine amino acids (precursors of biosynthesis) (thyroxine, adrenaline, norepinephrine, melatonin, etc.);
- steroid hormones (hormones of the adrenal cortex: gluco- and mineralocorticosteroids; sex hormones: andro- and estrogens)
- prostaglandins (derivatives of polyunsaturated fatty acids: vitamins of group D).

chemical classification of hormones:

1. *protein-peptide*
   - peptide (somatotropic hormone, prolactin, parathyroid hormone, insulin, calcitonin, etc.);
   - protein or glycoprotein (thyroid-stimulating hormone, follicle-stimulating hormone (FSH), lutein-stimulating hormone (LSH), thyroglobulin, etc.);
   - oligopeptides (adrenocorticotropic hormone, glucagon, etc.).

   2. steroid
   - pregnane derivatives (gluco- and mineralocorticosteroids, progestogens);
   - androstane derivatives (androgens);
   - - "- estran (estrogens);
   - - "- eicosan (cholestane);

   3. derivatives of amino acids.

V.G. Belikov gives a mixed classification, that is, he divides hormones into chemical groups and indicates the place of their formation:

I. Hormones of amino acids and their derivatives:

a) thyroid hormones and their synthetic analogues;
b) hormones of the medulla of the adrenal glands and their synthetic analogues;

II. Hormones that have a steroid structure:

a) hormones of the cortical layer of the adrenal glands (corticosteroids) and their synthetic analogues;
b) progestogen (lutein) hormones and their semi-synthetic analogues;
c) androgenic hormones and their semi-synthetic anabolic preparations;
d) estrogen hormones and their semi-synthetic analogues, and synthetic drugs of non-steroidal structure.

III. Hormones, polypeptides and proteins:

a) pituitary hormones;
b) thyroid hormones;
c) gastrointestinal hormones and others.

Hormone analysis methods. There are no general methods for identifying hormones and their synthetic analogues, unlike other groups of drugs. Thus, qualitative reactions are based on the individuality of their chemical structure, the nature of functional groups, depending on which they give certain reactions. Today, physicochemical methods based on the absorption of light energy (spectroscopy in the ultraviolet and infrared part of the spectrum) and biological methods (hormones, polypeptides and proteins) are also used to identify hormones.

Important indicators of the quality of hormones, from the group of polypeptides and proteins, are toxicity, sterility, pressor effect, which are established by biological means.

The methods of quantitative determination of hormones used today in pharmaceutical analysis are divided into biological, physicochemical (spectroscopy in the UV and IR region of the spectrum), chemical (titrimetric) and gravimetric.

Methods of biological standardization of hormones. The activity of hormones is determined by comparing the effect of the researched drug with a biological standard sample (biological standard samples are the relevant international standards and standard drugs established by the World Health Organization (WHO)). The specific activity of a weighted amount of a standard drug, equivalent in terms of biological activity to 1 IU of a certain hormone, is taken as a unit of action (U) of hormones. Conventional units of action are expressed in IU/ml or IU/mg, that is, the number of IU contained in 1 ml of solution or 1 mg of the drug.

Thyroid hormones and their synthetic analogs.

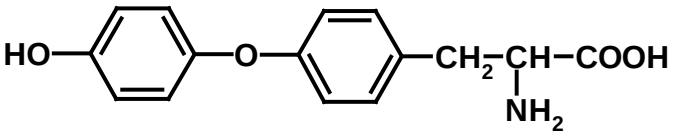
Thyroid – one of the most important glands of internal secretion. Violation of its normal function leads to delayed growth, mental development (cretinism),

metabolic disorders, etc. It was noted that taking drugs extracted from the thyroid gland of slaughter animals normalized these processes.

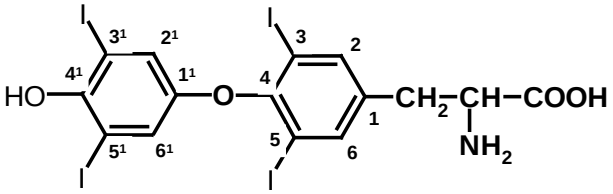
Iodized derivatives of thyronine have biological activity in the thyroid gland.

In 1919, Kendall isolated from the thyroid glands of animals a tetraiodo- derivative of thyronine, the structure of which was determined in 1927 and named thyroxine.

Thyroxine



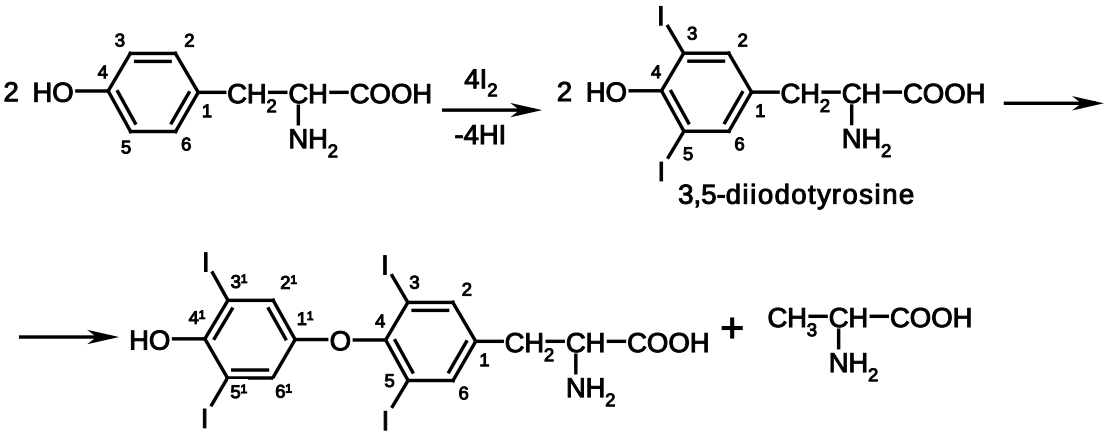
Thyronine



The asymmetric carbon atom indicates the presence of 2 isomers (optical), while L(-)-thyroxine is 10 times more active than the d(+) isomer.

Experiments conducted in 1952-1955 showed that not only tetraiodo derivatives, but also tri- and diiodo derivatives of thyronine have hormonal activity in the thyroid gland.

The biosynthesis of these hormones in the body is carried out from the amino acid tyrosine and iodine, which enter the body with water and food. First, the process of iodination takes place, then two molecules of diiodotyrosine condense to form thyroxine.



3,5-diiodotyrosine

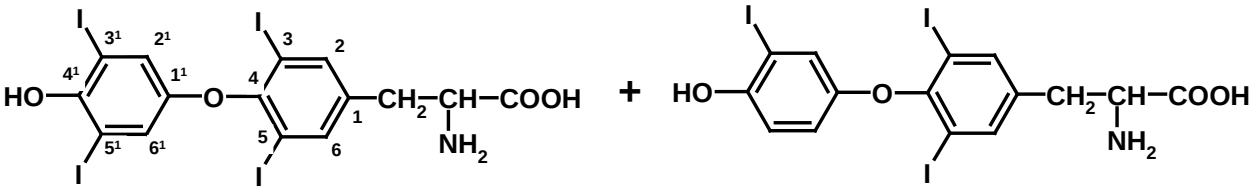
3,5,31,51-tetraiodothyronine (thyroxine)

α-alanine (α-aminopropionic acid)

According to this scheme, the biosynthesis of other hormones in the thyroid gland takes place. In medical practice, synthetic drugs are used: SPhU - liothyronine sodium salt (triiodide derivative) and levothyroxine sodium salt (tetraiodide

derivative), as well as thyroidin - obtained from defatted and dried glands of slaughter animals.

Thyreoidinum (Thyroidin)



3,5,31,51-tetraiodothyronine (thyroxine) 3,5,31-triiodothyronine

SPhU: (2S)2-amino-3{4-(4-hydroxy-3,5-diiodophenoxy)-3,5-diiodophenyl}propanoic acid (thyroxine).

The drug has biological activity of the thyroid gland due to the presence of two hormones in it: tetraiodothyronine (thyroxine) and triiodothyronine, which have a left rotation.

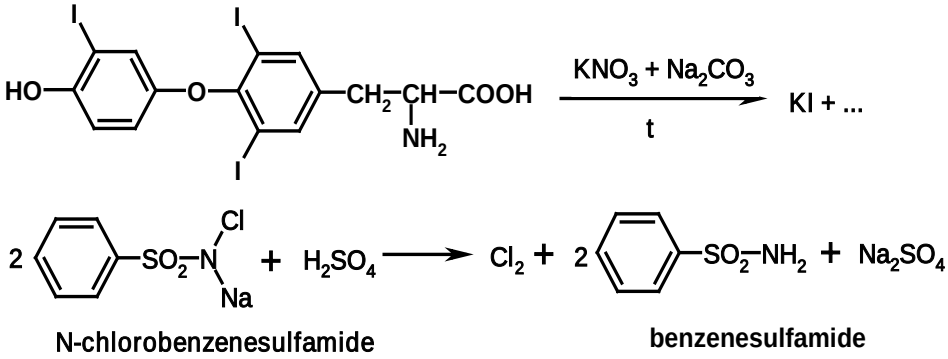
Properties. Yellowish-gray powder with a faint odor characteristic of dried animal tissues. Not soluble in water, alcohol, other solvents.

Thyroidin has amphoteric properties: acidic due to phenolic hydroxyls and carboxyl groups, therefore they dissolve in alkalis and carbonates, basic due to amino groups (weak), therefore they dissolve in acids.

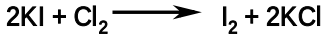
Identification: 1. The presence of protein is detected by reaction with sodium hydroxide. The preparation is heated with sodium hydroxide solution, a yellow color appears. After adding sulfuric acid, the solution becomes colorless and a colloidal precipitate falls out.

2. The second reaction – detection of organically bound iodine (covalently bound). First, organically bound iodine must be converted into an ionogenic state.

To do this, the substance is mineralized by roasting with a mixture of potassium nitrate and sodium carbonate. The formed iodides are dissolved in water, filtered and identified in the filtrate by their oxidation reactions. For example, with chloramine in an acidic environment in the presence of chloroform, which is colored red-violet due to iodine.



N-chlorobenzenesulfamide benzenesulfamide



3. Methods of converting an organic (covalently bonded) halogen into an ionogenic state:

A) burn the drug in a flask with oxygen. As a result, iodine is released, which colors the absorbing mixture blue.

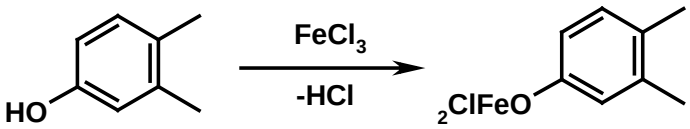
The absorbent mixture includes a starch solution and a 0.2% solution of sulfaminic acid.

B). Various methods are used to destroy organic compounds:

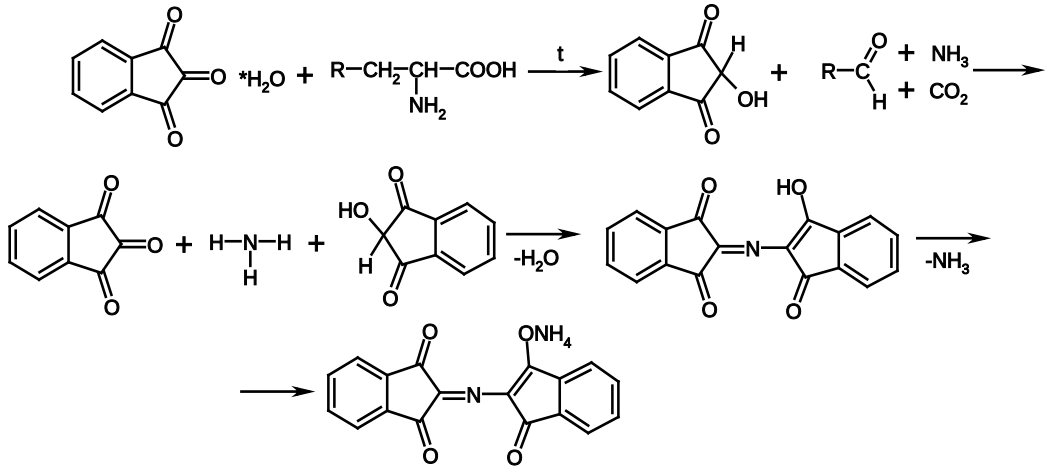
1. Oxidation reactions: with liquid oxidants: a mixture of nitric acid and potassium permanganate $HNO_3 + KMnO_4$, a mixture of nitric acid and sulfuric acid $HNO_3 + H_2SO_4$, a mixture of sulfuric acid and potassium dichromate $H_2SO_4 + K_2Cr_2O_7$ and others, with gaseous oxygen. Oxidize by fusing with dry oxidizers: a mixture of potassium hydroxide KOH and salt petre; sodium peroxide; a mixture of soda, potash and saltpeter and others.

2. Hydrogenation in the presence of a nickel catalyst, decomposition when heated with lime; decomposition when heated with metal (potassium, sodium) and others.

4. Reactions to phenolic hydroxyl with iron (III) chloride.



5. The amino group in the amino acid residue is determined using a reaction with ninhydrin.



Ammonium salt of diketohydrindenketohydrinamine - blue-violet color

6. Amino acids give stable complex salts with copper salts of dark blue color.

Impurities:1. Absence of iodides. The drug is shaken with water and filtered. In the filtrate, iodides are determined by oxidation with chlorine water or chloramine. The chloroform layer should not be colored. There should be no iodides.

2. Fats. They are extracted with ether, the ether is distilled off, the residue is dried, then weighed. Fats should be no more than 2%.

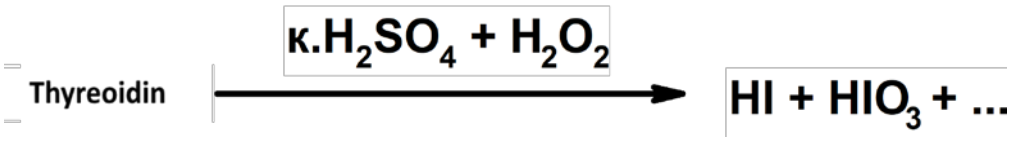
3. Should not have heavy metals.

<u>QUANTITATIVE DETERMINATION</u>:

Iodometric method.

The content of organically bound iodine is established in teroidin.

Mineralization is carried out with perhydrol in the presence of concentrated sulfuric acid. Iodides and their partial oxidation to iodates are formed.



Next, all iodides are oxidized to iodates with a solution potassium permanganate.

$5HI + 6KMnO_4 + 9H_2SO_4 = 6HIO_3 + 6MnSO_4 + 3K_2SO_4$

$I^- + 3H_2O - 6e \rightarrow IO_3^- + 6H^+$

$\underline{MnO_4^- + 8H^+ + 5e \rightarrow Mn^{2+} + 4H_2O}$

$5I^- + 5MnO_4^- + 18H^+ \rightarrow 5IO_3^- + 6Mn^{2+} + 9H_2O$

$2KMnO_4 + 5NaNO_2 + 3H_2SO_4 = 2MnSO_4 + 5NaNO_3 + K_2SO_4 + 3H_2O$

$2NaNO_2 + H_2SO_4 \rightarrow 2HNO_2 + Na_2SO_4$

$2HNO_2 + CO(NH_2)_2 = 2N_2 + CO_2 + 3H_2O$

$HIO_3 + 5HI = 3I_2 + 3H_2O$

$I_2 + 2Na_2S_2O_3 = 2NaI + Na_2S_4O_6$

Excess potassium permanganate is removed using sodium nitrite. A possible excess of nitrites is destroyed by with the help of urea. Only one oxidant remains in the solution - iodic acid in an amount equivalent to the iodine content in a measure of thyroidin. A solution of potassium iodide is added and the released iodine is titrated with sodium thiosulfate.

The drug should contain 0.17-0.23% of organically bound iodine.

Application. The two hormones that are part of the drug have a multifaceted effect on the body, increase tissue demand for oxygen, enhance energy processes, stimulate tissue growth, affect the functional state of the nervous and cardiovascular system, liver, kidneys and other organs and systems, strengthen absorption of glucose and its utilization.

The effect of thyroid hormones can vary depending on the dose.

In relatively small doses, they are prescribed for insufficient function of the thyroid gland, which leads to diseases - myxedema, hypothyroidism, cretinism, obesity, endemic goiter, thyroid cancer.

Larger doses thyroidin cause the breakdown of protein and reduce the function of the thyroid gland.

Historical reference. Thyroxine, entering the blood, combines with proteins and is transferred to cells, where metabolism is accelerated. In regions where the soil and drinking water contain insufficient amounts of iodine, the population suffers from hypothyroidism or cretinism (an acute form of hypothyroidism).

In 1820, only 10 years after the discovery of the iodine element, it was discovered that a daily intake of several milligrams of iodine prevents the development of cretinism, and later it was recommended to add small amounts of sodium iodide to table salt.

This was recommended by biochemists, and doctors objected on the grounds that iodine in large quantities is toxic (a lethal dose of 2-3 g). This led to a 100-year delay in the use of iodized salt.

Release form. Powder and tablets of 0.05 g, coated tablets of 0.1; 0.2 g

Storage. In well-stoppered glasses made of dark glass.

For children, doses should be appropriate for the child's age.

It is also known that triiodotyrosine is 3-5 times more effective than thyroxine (a tetraiodo derivative) and acts faster, because it binds less to blood proteins and is transformed into the blood mainly in free form and penetrates faster through the cell membrane.

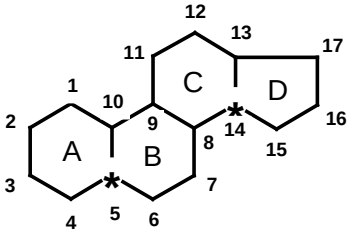
Therefore, triiodothyronine is now obtained synthetically and is used as an independent medical drug (SPhU).

CORTICOSTEROIDS.

Adrenal glands are paired glands that consist of two layers: cortical and medulla. The brain layer produces adrenaline and norepinephrine. But they are well described in your textbooks, so we will focus on the hormones of the adrenal cortex. The cortical layer of the adrenal glands produces a large number of steroid hormones (more than 40). They are called corticosteroids.

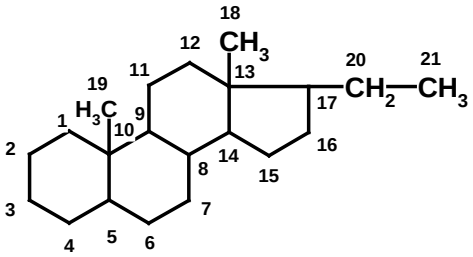
The structure of these compounds is based on a condensed system consisting of fully hydrogenated phenanthrene and cyclopentane - cyclopentaneperhydrophenanthrene.

Cyclopentaneperhydrophenanthrene



Corticosteroids are based on pregnane.

Pregnane



Angular methyl groups (angulus - angle), connected to a tertiary carbon atom and usually located above the plane of the rings, i.e. in - configuration (solid line, cis-configuration).

Hormones of the cortical layer of the adrenal glands are essential for human and animal life.

Animals die a few days after removal of the adrenal glands.

Based on the effect on metabolism, the main corticosteroids are conditionally divided into 2 groups:

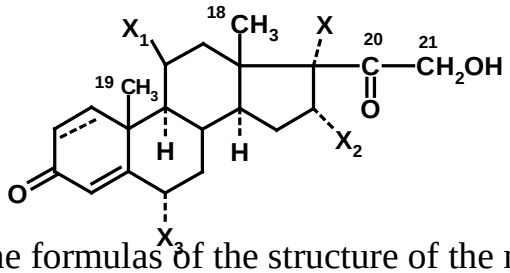
1. Mineralocorticosteroids (mineralocorticoids).

2. Glucocorticosteroids (glucocorticoids).

The main representative of the 1st group is aldosterone and deoxycorticosterone - these hormones actively affect the exchange of electrolytes (salt K and sodium) and water. In medical practice, deoscorticosteroid acetate (DOXa) is used.

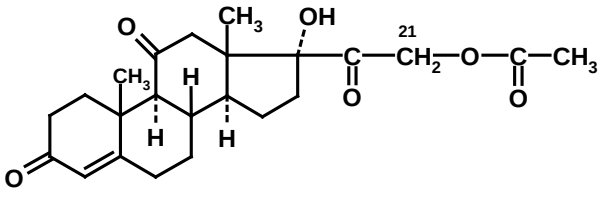
2nd group - regulates carbohydrate and protein metabolism. They contribute to the accumulation of glycogen in the liver, increase the sugar content in the blood, contribute to the excretion of nitrogen in the urine, and have anti-inflammatory activity. Important representatives of glucocorticoids are cortisone and hydrocortisone and their analogues: prednisone, prednisone and others, as well as halogenated hormones.

The general formula of the structure of corticosteroids and their synthetic analogues



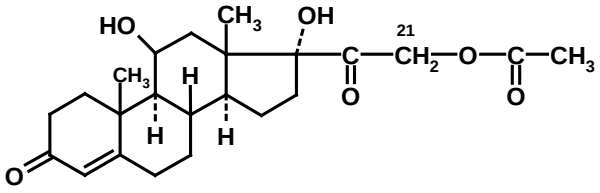
Let's consider the formulas of the structure of the main glucocorticoids.

Cortisoni acetas



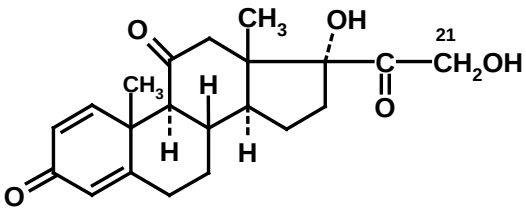
Pregnene-4-diol-17α,21-trione-3,11,20-acetate-21-

Hydrocortisoni acetas



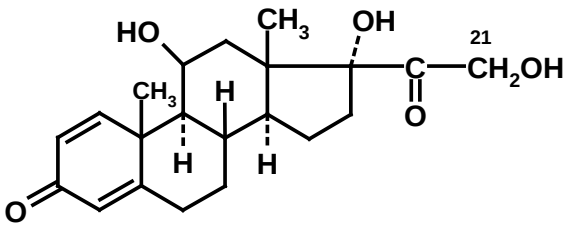
Pregnene-4-triol-11β,17α,21 dione-3,20-acetate-21

Prednisone



Pregnadiene-1,4-diol-17α,21- trione-3,11,20

Prednisolone



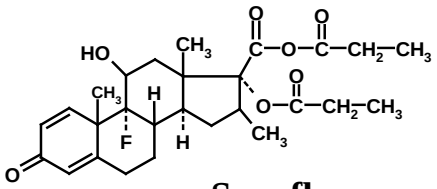
Pregnadiene-1,4-triol-11β,17α,21- dione-3,20

All glucocorticoids contain a steroid cycle, a carbonyl (keto) group in the 3rd position, and have one or two double bonds. And they can also be esters. What are the differences? Cortisone acetate and its analog prednisone - with different number of double bonds, cortisone acetate is a complex ester. Hydrocortisone acetate and its analogue prednisolone also have different number of double bonds, hydrocortisone acetate is a complex ester. Cortisone and hydrocortisone differ in that one has a carbonyl group in the 11th position, and the other has a hydroxyl group.

Let's consider several formulas of halogen-containing drugs. As we can see, they are analogues of hydrocortisone. They differ in that they have a halogen in the composition and different substituents in the 17th position.

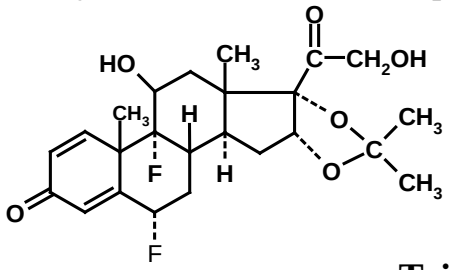
Betamethasone dipropionas

9α-fluoro-11β-hydroxy-16β-methyl-3,20-dioxopregna-1,4-diene-17,21-diyl dipropionate

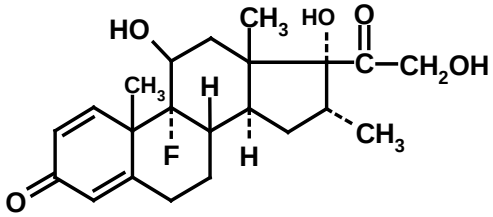


Synaflanum

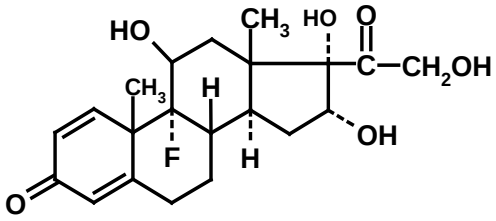
6α,9α-difluoro-16α,17α-dioxyacetonide-11,21-dioxopregnadiene-1,4-dione-3,20



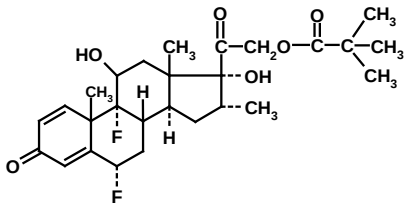
Dexamethasone



Triamcinolone



Flumetasone pivalate



The production of adrenal hormones is under the control of the central nervous system and is closely related to the function of the pituitary gland. Adrenocorticotropic hormone (ACTH) is a physiological stimulator of the adrenal cortex, ACTH enhances the formation and release of glucocorticosteroids.

The source for obtaining corticosteroids is the adrenal glands of slaughter cattle or natural substances of a steroid structure, such as cholesterol, which is a precursor of corticosteroids in the body, as well as ergosterol, bile acids, steroidal saponins: for example: diosgenin, solasodin.

For example: cortisone acetate and progesterone are extracted from solasodin (glucoalkaloid aglycone from nightshade).

Physical and chemical properties. Corticosteroids and their semisynthetic analogues have a similar structure. Therefore, they are all white crystalline substances with a yellowish or creamy shade without an odor. Practically not soluble in water, hardly or slightly soluble in most organic solvents.

Corticosteroids and their semisynthetic analogs are dextrorotatory optical isomers. They absorb radiation in the UV spectrum due to the chromophore of the A ring.

According to their chemical properties, they are reducing agents due to α-ketol or dioxyacetone groups in the 17-position.

All identification reactions are divided, depending on the structure, into:

1. Reactions to the steroid cycle;
2. Reactions on α-ketol or dioxyacetone groups;
3. Reactions on the carbonyl group in the 3rd position.
4. Reactions to the ester group.

Let's consider all these reactions, which will be characteristic of all corticosteroids and their analogues.

1. **Reactions to the steroid cycle**:

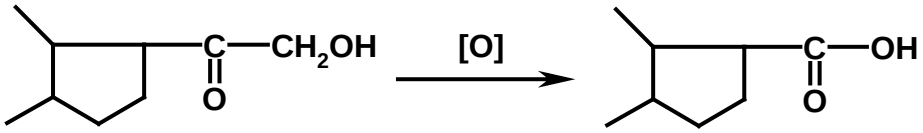
- ✓ With concentrated sulfuric acid
- ✓ Bascott reaction: concentrated acetic acid CH_3COOH and 88% solution of phosphoric acid H_3PO_4

All substances give a general group reaction with concentrated sulfuric acid, but it can also be called individual, because each preparation has its own color:

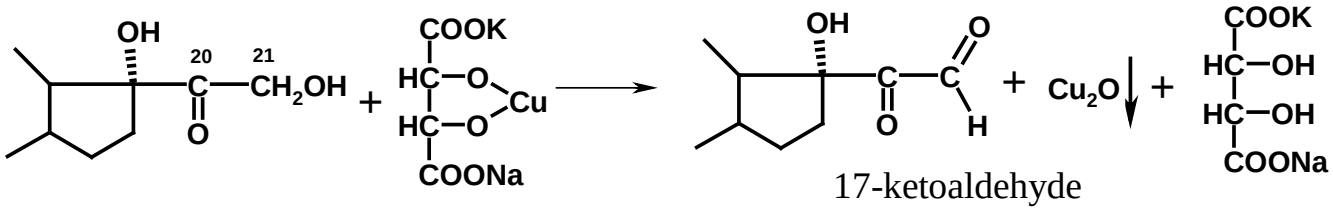
Thus, deoxycorticosterone has a cherry color with green-brown fluorescence; cortisone - yellow color; hydrocortisone - yellow color with green fluorescence; prednisolone - red color.

2. **Reactions on the alpha-ketol or dioxyacetone group**.

All corticosteroids, having alpha-ketol or dioxyacetone groups in their composition, show reducing properties, so they are easily oxidized. Moreover, depending on the strength of the oxidant, different products are formed. Yes, under the influence of weak oxidants17-ketoaldehyde or a carboxyl group are formed:

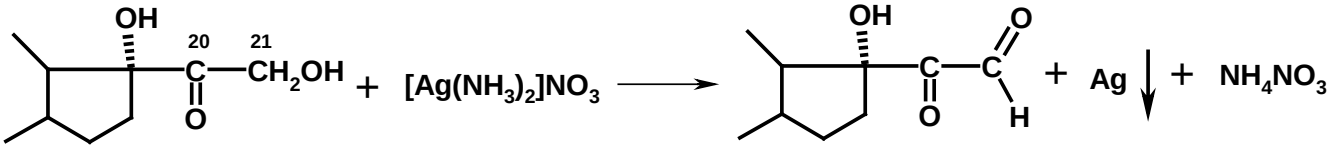


A) with Fehling's reagent:

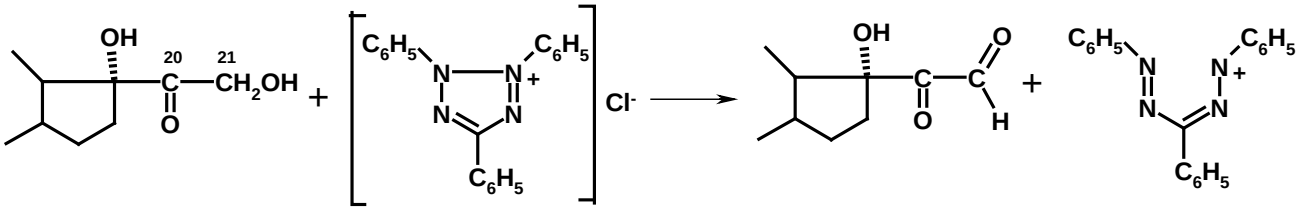


17-ketoaldehyde

b). Ammonia solution of silver nitrate



c). A solution of 2,3,5-triphenyltetrazolium chloride (Georig reaction):

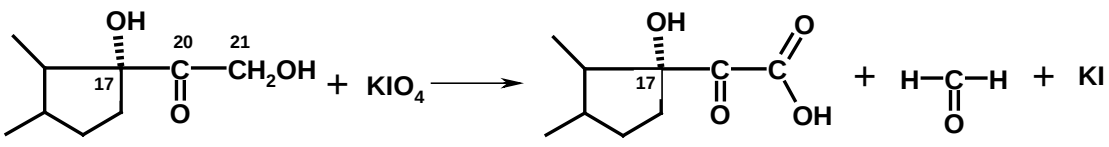


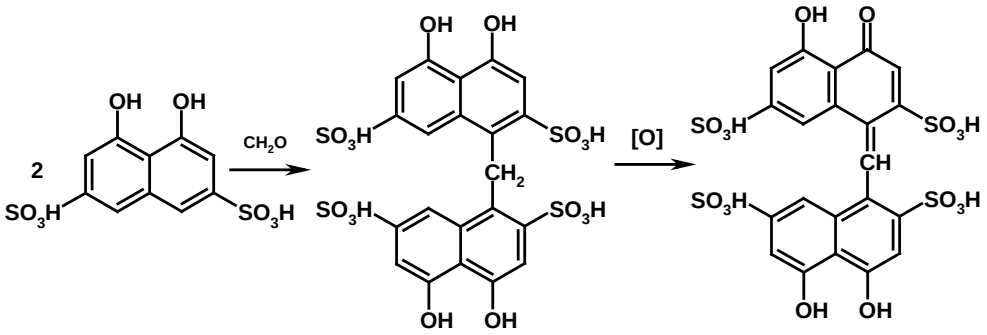
Red pharmazone

The tetrazolium salt is reduced to red pharmazone and the cycle is opened.

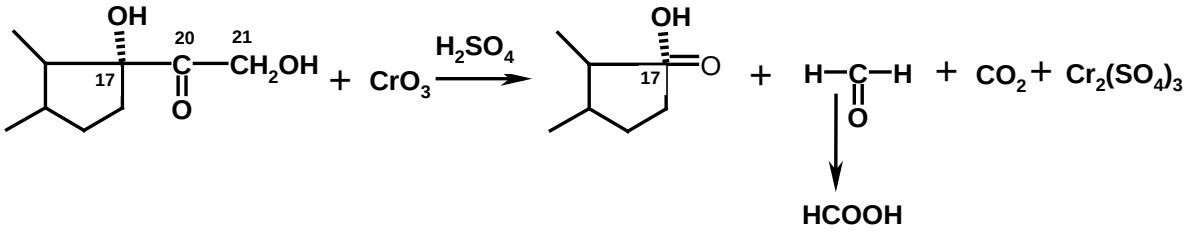
This reaction is used by all foreign pharmacopoeias for the quantitative determination of corticosteroids (photoelectrocolorimetry).

d). With a solution of potassium periodate, perchloric acid or phosphoromolybdic acid, 17-carboxylic acid and formaldehyde are formed, which can be combined with chromotropic acid (a purple auric dye is formed).



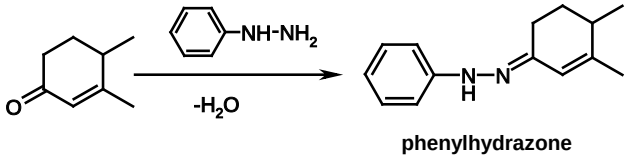


d) Under harsh conditions with strong oxidants: for example, with chromic anhydride, oxidation to 17-ketosteroid, decarboxylation and release of formaldehyde, which is easily oxidized to formic acid, occurs.

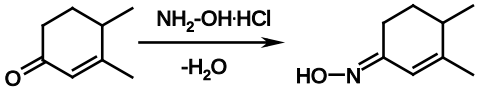


3. **Reactions on the carbonyl group in the 3 position.**

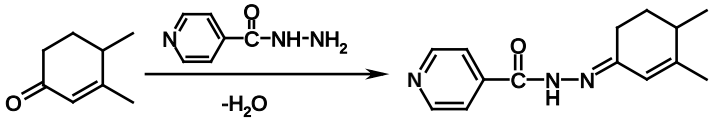
These reactions are the addition of hydroxylamine (oximes are formed), hydrazine derivatives: phenylhydrazine, semicarbazide, thiosemicarbazide, and others - hydrazones (usually colored) are formed.



phenylhydrazone

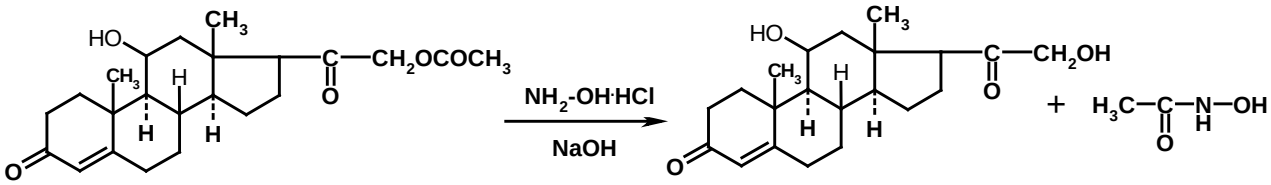


ketoxime

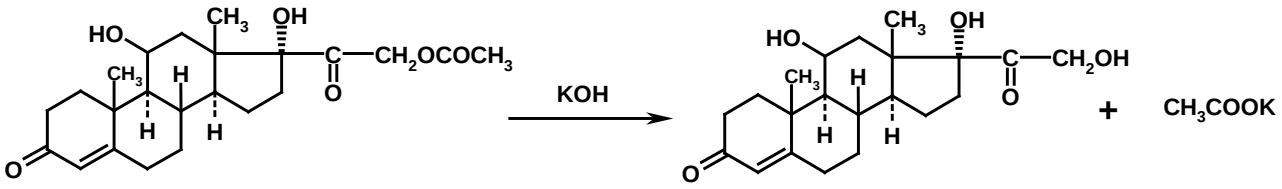


isonicotinoylhydrazone
yellow color

4. The ester group is determined using the hydroxam test:

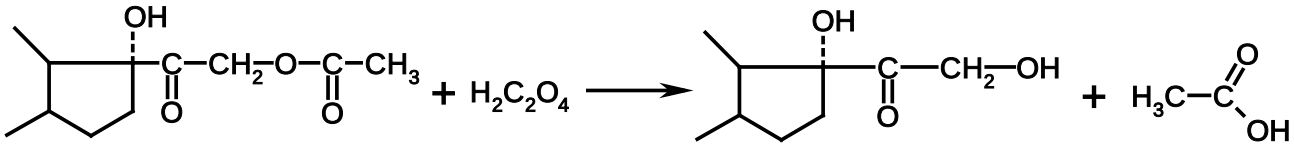


Or with the help of hydrolytic cleavage, (on the example of hydrocortisone acetate) in the presence of an alcoholic solution of potassium hydroxide. As a result, potassium acetate is formed, and when concentrated sulfuric acid is added, ethyl acetate is formed (ester – smell)



$$2CH_3COOK + H_2SO_4 + 2C_2H_5OH \longrightarrow 2CH_3COOC_2H_5 + K_2SO_4 + 2H_2O$$

SPhU offers to determine acetates (if they are included in the preparation) as follows: a) $H_2C_2O_4$ (oxalic acid) is added to the preparation, the smell of acetic acid appears. And this acid can also be determined by adding alcohol and concentrated sulfuric acid. The smell of the second complex ether - ethyl acetate will appear.



$$CH_3COOH + C_2H_5OH \xrightarrow{k.H_2SO_4} CH_3COOC_2H_5 + H_2O$$

odour

b). SPU Another reaction to acetates. With a solution of lanthanum (III) nitrate in the presence of I_2 and NH_4OH solution, a blue color or a blue precipitate is formed at to (the basic salt of lanthanum acetate adsorbs iodine):

$$La^{3+} + 3CH_3COO^- + 2H_2O \xrightarrow{I_2} La(OH)_2(CH_3COO) + 2CH_3COOH$$

c). SPhU. This reaction can be used to determine acetates in a neutral solution. When adding a solution of iron (III) chloride, a red-brown color appears

$$8CH_3COO^- + 3Fe^{3+} + 2H_2O \rightarrow [Fe_3(OH)_2(CH_3COO^-)_6]^+ + 2CH_3COOH$$

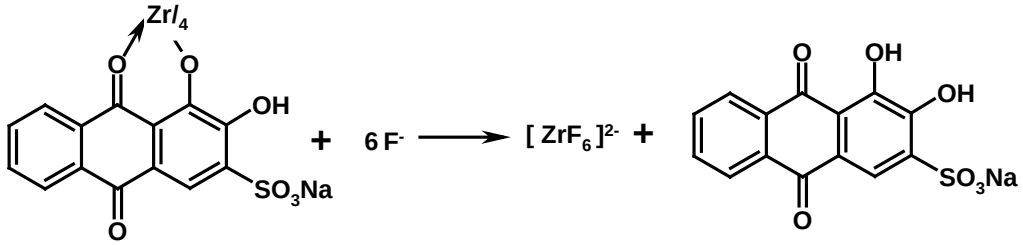
When mineral acids are added, the color disappears:

$$\mathbf{[Fe(OH)_2(CH_3COO^-)_6] + 8H^+ \rightarrow FeCl_3 + 6CH_3COOH + 2H_2O}$$

5. **Prove the presence of covalently bound fluorine** in fluorine-containing medicinal products, such as betamethasone, dexamethasone, sinaflan and others, it is possible only after the transfer of covalently bound fluorine to the ionogenic state. This can be done by the methods we have already talked about before: combustion in a flow of oxygen, mineralization, the action of oxidizing agents

or reducing agents, and other methods. And then prove its content with such reactions as:

6). SPhU: reaction with zirconium - alizarin complex, which consists of a mixture of alizarin solution and zirconyl nitrate (has a red color). Everything is mixed and equalized with the blank solution, which has a red color. And our solution is yellow (alizarin). I will give an example of the determination of betamethasone by SPU. The medicinal product is burned with magnesium oxide in a crucible, cooled, add 1 ml of water, 1-2 drops of phenolphthalein and 1 ml of hydrochloric acid until decolorization, filter. A mixture consisting of alizarin and 0.1 ml of zirconyl nitrate solution is added to the filtrate.



b). Or the fluoride ion is determined with calcium salts, which give a white precipitate of calcium fluoride.

$$Ca^{2+} + 2F^{-} = CaF_2$$

c). After burning in a flow of oxygen, the fluoride ion is absorbed by a solution of hydrogen peroxide, which will decolorize iron(III) thiocyanate, which has a red color.

$$Fe(CNS)_3 + 6F^{-} \rightarrow [FeF_6]^{3-} + 3SCN^{-}$$

METHODS OF QUANTITATIVE DETERMINATION

1. **Spectrophotometric methods** (by SPhU)

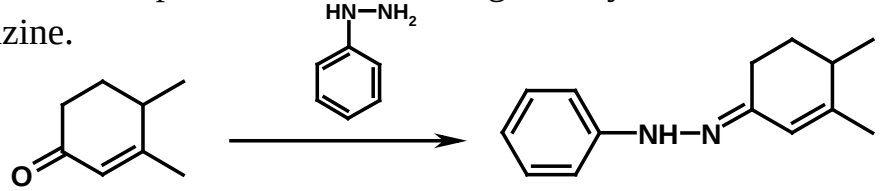
According to SPU determine hydrocortisone alcohol solution at = 241 nm, $\boldsymbol{A}_{1\text{см}}^{1\%}$ = 393

Prednisone alcohol solution at = 243.5 nm, $\boldsymbol{A}_{1\text{см}}^{1\%}$ = 415

$$\mathbf{C\%}=\frac{\boldsymbol{A_x * V_k \ldots}}{\boldsymbol{A_{1\text{см}}^{1\%} * m * V_{\text{п}} * l_{\text{см}}}}$$

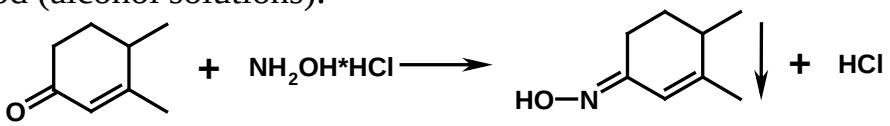
2. **Photoelectrocolorimetric** a method by which it is possible to determine colored solutions that are formed when interacting with concentrated sulfuric acid, or hydrazones, farmazones, etc. are formed.

For example: cortisone acetate gives a yellow color with phenylhydrazine.



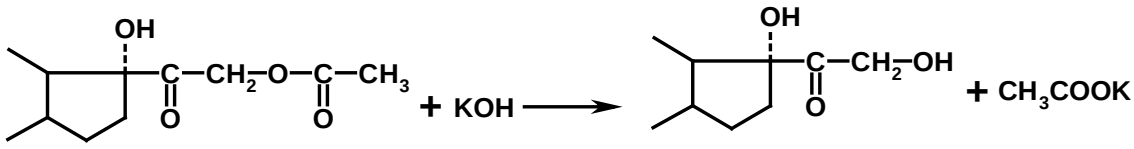
Color reactions with 2,3,5-triphenyltetrazolium (Goryog reaction) and others.

3. Oxime method (alcohol solutions).



$$HCl + NaOH \longrightarrow NaCl + H_2O \qquad f=1$$

4. Acid-base titration of esters. An excess of an alcoholic solution of potassium hydroxide is added, which is then titrated with hydrochloric acid.



$$KOH + HCl \longrightarrow KCl + H_2O \qquad f=1$$

5. **Weight (gravimetric) method. There are 2 ways** determination of concentration by this method: when an insoluble substance is obtained (oxime, base, hydra zone, etc.) and then a formula with a gravimetric factor is used.

$$C\% = \frac{a * F * 100\%}{m}$$

where

a – the weight of the sediment after drying, g

m – the weight of the drug, g

F – the gravimetric factor, which is equal to the molecular weight of the drug divided by the molecular weight of the precipitate obtained after the reaction.

$$F = \frac{\text{М.м. } \boldsymbol{substance\ to\ be\ determined}}{\text{М.м. } \boldsymbol{obtained\ substance}}$$

Or use a drug that does not dissolve in water. It is weighed(m), dried to constant mass, weighed again and quantified according to the formula:

$$X\% = \frac{a * 100\%}{m}$$

Impurities determined by HPLC or TLC.

Application. Corticosteroids or glucocorticoids affect carbohydrate and protein metabolism, but are less active in relation to water and salt metabolism. Contribute to the accumulation of glycogen in the liver, increase the content of glucose in the blood, and increase the excretion of nitrogen in the urine.

Glucocorticoids have anti-inflammatory, desensitizing and anti-allergic effects, have anti-shock and anti-toxic effects.

The high therapeutic activity of cortisone and hydrocortisone is accompanied by a number of undesirable side effects: a violation of water-salt and nitrogen metabolism, swelling, and an increase in blood sugar. Long-term use leads to suppression of the function of the adrenal cortex.

In order to reduce side effects, strengthen anti-inflammatory, desensitizing and antihistamine effects, a number of synthetic analogues of cortisone and hydrocortisone were obtained - these are prednisone and prednisone. Yes, prednisone (an analogue of cortisone) is 3-5 times more active than cortisone.

By introducing fluorine and chlorine atoms, drugs with minimal mineralocorticoid activity were obtained, but their anti-inflammatory activity is 20-40 times higher than the activity of hydrocortisone, and some (flumetasone pivalate, sinaflan) have very high activity - 150-300 times the activity of hydrocortisone. However, they are practically not absorbed when applied topically and therefore, unlike other corticoids, do not cause side effects. But recently it became known that with long-term use, dystrophic changes appear on the surface of the skin.

Thus, corticosteroids are used for replacement therapy, as well as for rheumatism, polyarthritis, bronchial asthma, leukemia, neurodermatitis, eczema and various allergic diseases. And recently - for the treatment of COVID-19.

It should be remembered that with long-term use of corticosteroids, it is not possible to cancel abruptly, but only gradually, reducing the dose.

Produced in powders and pills of 0.025; 0.05 g, in bottles of 5-10 ml of suspension (25 mg in 1 ml). Hydrocortisone acetate is more active than cortisone acetate, so its doses are 2/3 of the dose of cortisone. 1-2.5% ointment, 0.5-2.5% suspension, 0.5% eye ointment are produced.

Prednisone is produced in tablets of 0.005 g, prednisolone - 0.005 g, ampoules of 0.03 g and ointment 0.5%.

Storage: In a place protected from light in a well-closed container, because they oxidize easily.

GESTAGENS

Pregnane derivatives include progestogenic hormones (hormones of the corpus luteum) and their semi-synthetic analogues, so we will consider them.

Female sex hormones are formed in the ovaries, starting with the onset of puberty (12-15 years) and end up being formed during the period when their function declines.

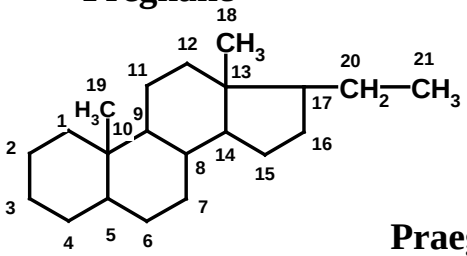
The ovaries secrete two main types of hormones into the blood: estrogens (follicular hormones) and progestins (hormones of the corpus luteum).

Estrogens are produced in the cells of a mature follicle (bubble), in which the egg is maturing. After maturation, the follicle bursts, ovulation occurs. On the site of the destroyed follicle, a yellow body (corpus luteum) is formed, which

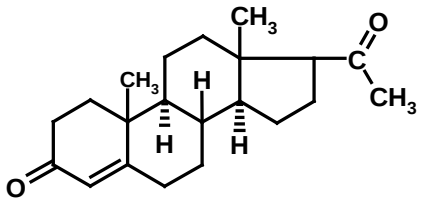
produces luteinizing hormones (or luteinizing hormones). The hormones of the corpus luteum regulate the normal course of pregnancy. Their action was first proved by Corner and Allen in 1933 year.

Of the luteinizing hormones, progesterone and its synthetic analogues are used as medicines: pregnin, oxyprogesterone capronate, norcalut, levonorgestrel (Postinor) and others. Their structure is based on a pregnane nucleus, as in the case of corticosteroids.

Pregnane

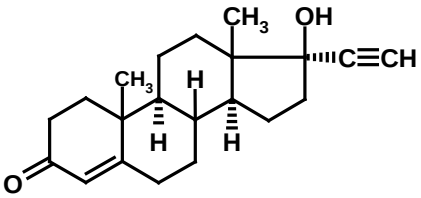


Progesteroneum



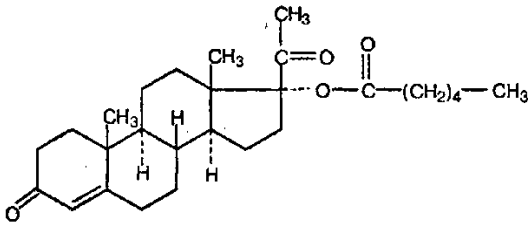
Pregnene-4-dione 3,20

Praegninum



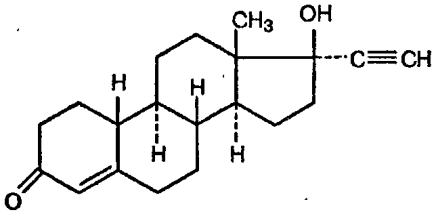
Pregnen-4-yn-20-ol-17β-one-3 or 17α-ethynyltestosterone

Oxyprogesterone capronate



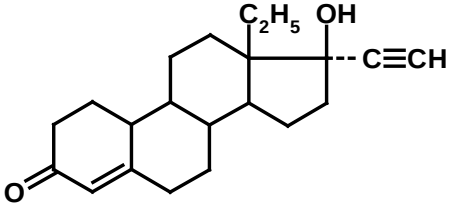
Pregnene-4-ol-17α-dione-3,20-capronate, or 17α-oxy-4-pregnene-3,20-dione 17-hexanoate, or 7α-hydroxypregn-4-ene-3,20-dione hexanoate

Norethisterone (Norethisterone)

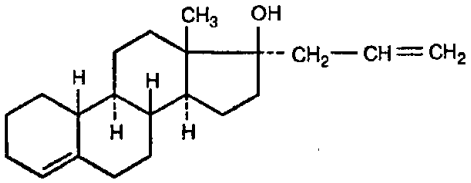


17α-Ethynyl-17β-oxy-4-estren-3-one, or 17α-ethynyl-19-nortestosterone

Levonorgestrel (Levonorgestrel, Postinor)

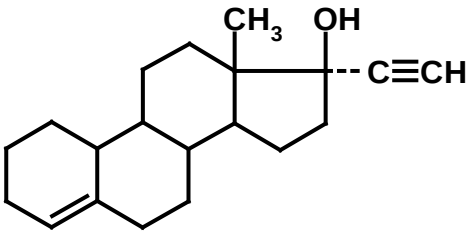


Allylestrenol (Allylestrenol)



17a-Allyl-4-estren-17β-ol

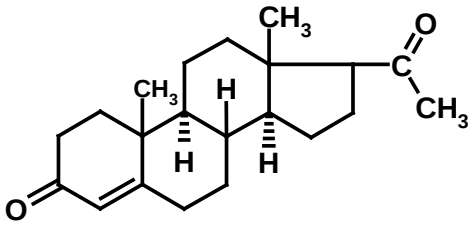
Lynestrenol (Lynestrenol)



But there are some differences in the structure of progestogens and estrogens. Progestogenic hormones (hormones of the corpus luteum) and their semisynthetic analogues, as well as corticosteroids, in most cases have methyl groups in positions 10 and 13, a keto group in position 3 and an unsaturated bond in position 4. But, unlike corticosteroids, in position 17, instead of a ketol group, they have acetyl (progesterone) or oxy- and ethynyl (acetylenic) groups (pregnin).

Consider progesterone.

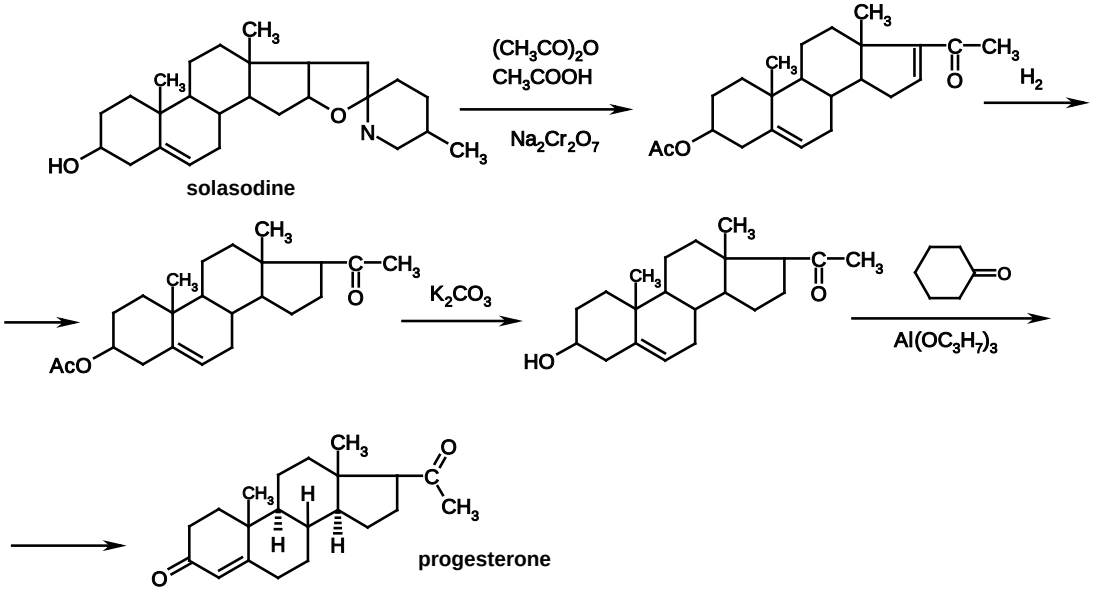
Progesteroneum

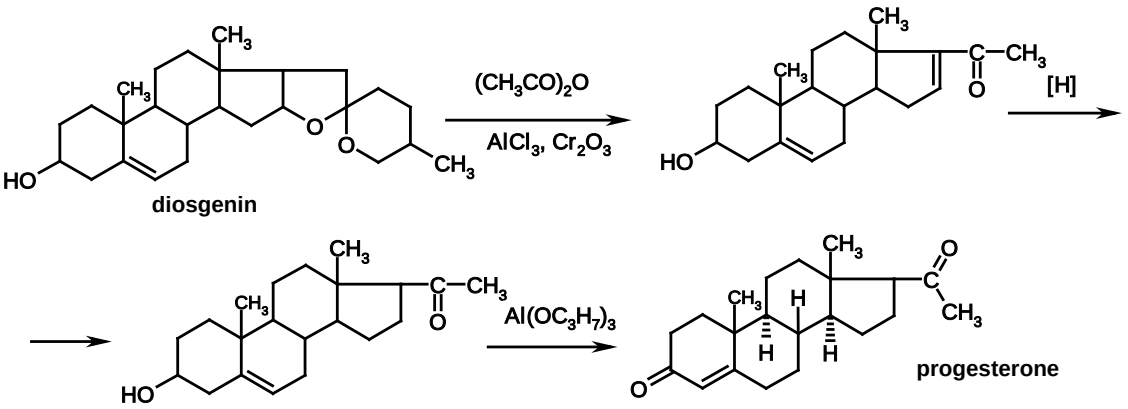


Pregnene-4-dione 3.20

Progesterone is extracted from the corpus luteum of pigs, and in a semi-synthetic way from solasodin (glycone from nightshade - a glycoside) or from diosgenin as an intermediate product in the production of cortisone.

Synthesis of progesterone





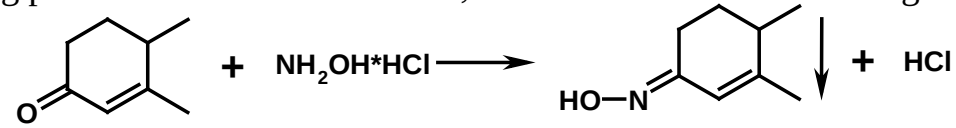
PHYSICAL-CHEMICAL PROPERTIES. Progesterone is a white with a yellowish tinge, fine crystalline powder, practically insoluble in water, soluble in oils and chloroform.

It has a carbonyl group in the 3rd position and a double bond in the 4th position. Due to this chromophore, light is absorbed in the ultraviolet range of the spectrum at 240 nanometers. Progesterone is optically active. According to its chemical properties, it is a reducing agent.

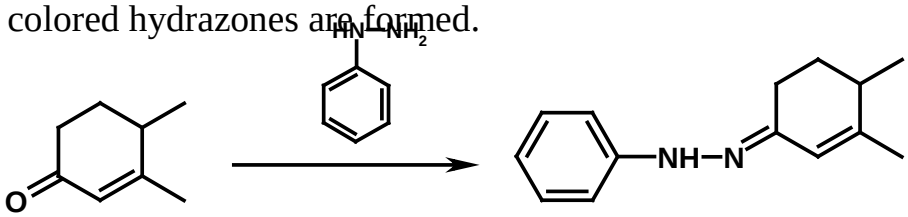
Identification. 1. Reaction as for corticosteroids, on a steroid cycle with concentrated sulfuric acid. A yellow color with green fluorescence appears. After adding chloroform, the color disappears. This reaction is both general and specific, because each drug has its own color (pregnin gives crimson fluorescence).

Bascott's reaction: a mixture of concentrated acetic acid and 88% phosphoric acid solution is added. Blue fluorescence appears (greenish-violet in pregnin).

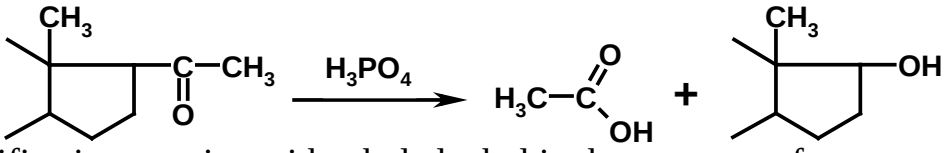
2. Reactions on the carbonyl group in the third position. For progestogens that have a carbonyl group, it is possible to conduct a reaction with hydroxylamine (a white precipitate of oxime is formed, which has no calories), and the melting point of oxime is determined, which is different for all drugs.



Or reactions are carried out with hydrazine, phenylhydrazine, 2,4-dinitrophenyl hydrazine, isoniazid - isonicotinoyl hydrazide, semicarbazide and others. In this case, colored hydrazones are formed.



3. Progesterone differs from pregnin, as well as from corticosteroids, the substituent in the 17th position is the presence of an acetyl residue, which is determined using phosphate acid, when added, acetic acid is released. It is determined by the smell, or blue litmus paper will turn red, or by the reactions we already know about acetic acid:



A) Esterification reaction with ethyl alcohol in the presence of concentrated sulfuric acid produces ethyl acetate, which has a specific fruity smell

$$CH_3COOH + C_2H_5OH \xrightarrow{k.H_2SO_4} CH_3COOC_2H_5 + H_2O$$

odour

B) With lanthanum nitrate in the presence of iodine and ammonia solution when heated, a blue precipitate or blue color appears (the basic salt of lanthanum acetate adsorbs iodine):

$$La^{3+} + 3CH_3COO^- + 2H_2O \xrightarrow{I_2} La(OH)_2(CH_3COO) + 2CH_3COOH$$

B) This reaction can be used to determine acetates in a neutral solution. When adding a solution of iron (III) chloride, a red-brown color appears.

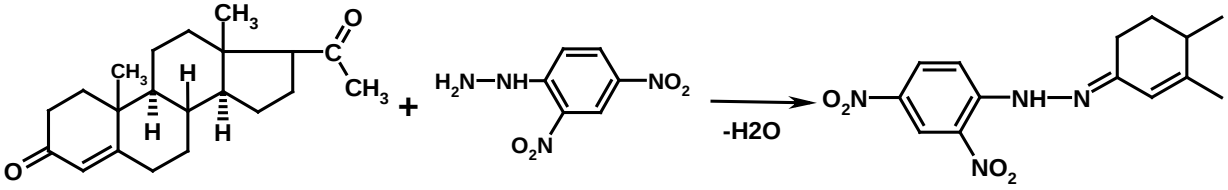
When mineral acids are added, the color disappears:

$$8CH_3COO^- + 3Fe3+ + 2H_2O \rightarrow [Fe_3(OH)_2(CH_3COO^-)_6]+ + 2CH_3COOH$$

$$[Fe(OH)_2(CH3COO^-)_6] + 8H+ \rightarrow FeCl_3 + 6CH_3COOH + 2H_2O$$

4. Progesterone with m-dinitrobenzene forms a pink color, which turns into red-brown.

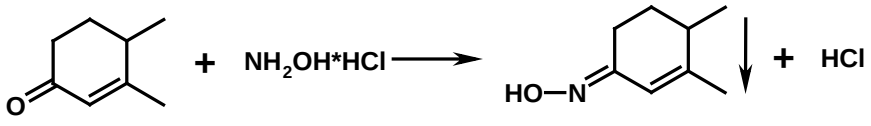
Quantitative definition.1. Gravimetry by products of interaction with 2,4-dinitrophenylhydrazine.



$$C\% = \frac{a * F * 100\%}{m}$$

2. Spectrophotometry in ethanol solution at 241 nanometers.

3. Oxime method



$$HCl + NaOH \longrightarrow NaCl + H_2O \qquad f=1$$

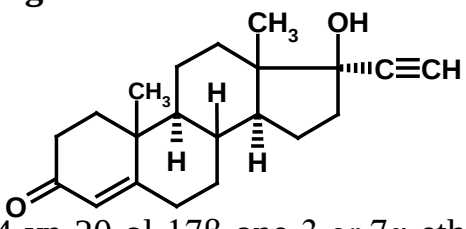
4. Photoelectrocalorimetry, high-performance liquid chromatography and other physical and chemical methods.

Application. Progesterone is used in replacement therapy as a progestogen drug for ovarian dysfunction associated with corpus luteum deficiency, which leads to painful menstruation, infertility, miscarriages and other diseases associated with corpus luteum deficiency. Progesterone is prescribed in the form of 1% or 2,5% solutions in oil for injections for intramuscular administration.

Storage. In a well-closed container, protected from light

Pregnin is a synthetic analogue of progesterone.

Praegninum **Ethisterone***



Pregnen-4-yn-20-ol-17β-one-3 or 7α-ethynyltestosterone

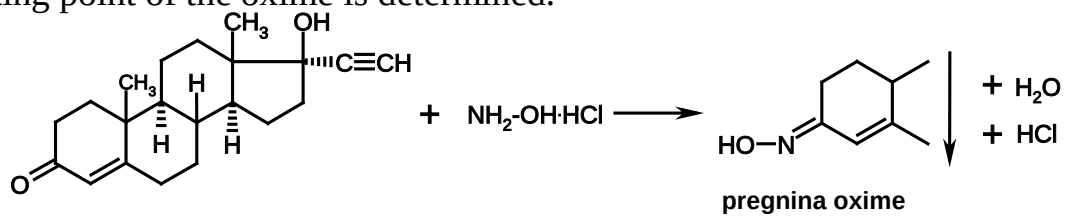
PHYSICAL-CHEMICAL PROPERTIES. Pregnin is a white with a yellowish tinge, fine crystalline powder, practically insoluble in water, very slightly soluble in ethanol and ether, slightly soluble in chloroform.

It has a carbonyl group in position 3 and a double bond in position 4. Due to this chromophore, light is absorbed in the ultraviolet range of the spectrum at 240 plus minus 2 nanometers. Pregnin is optically active. Pregnin differs from progesterone in the presence of an acetylene group in the 17th position. According to its chemical properties, it is a reducing agent, and due to the remaining acetylene, it has acidic properties

Identification. 1. Reaction, as for corticosteroids, to a steroid cycle with concentrated sulfuric acid. A crimson color with green fluorescence appears. After adding chloroform and stirring, the lower layer turns orange, the upper layer is almost colorless. This reaction is both general and specific, because each drug has its own color (progesterone gives a yellow color with green fluorescence).

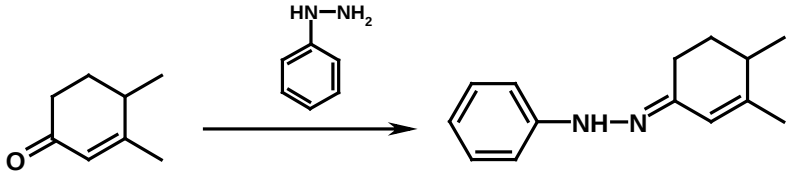
Bascott's reaction: a mixture of concentrated acetic acid and 88% phosphoric acid solution is added. Greenish-violet fluorescence appears in pregnin (progesterone is blue)

2. The keto group reacts with hydroxylamine (a precipitate is formed). The melting point of the oxime is determined.

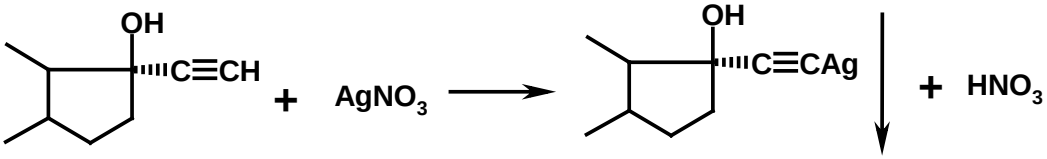


pregnina oxime

3. Gives color reactions with amino-derivative hydrazides, forming hydra zones.



4. Reaction to the ethynyl residue in pregnin.



A white precipitate of silver acetanilide

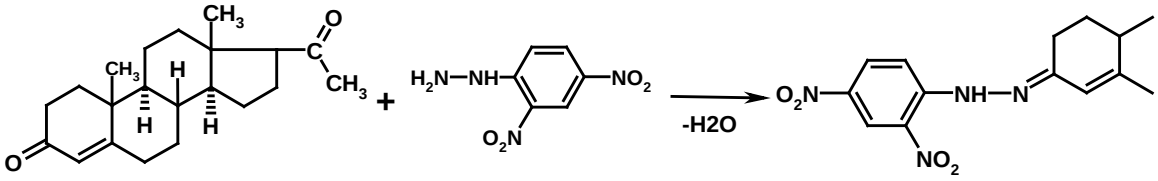
Quantitative definition.

1). Spectrophotometric determination of pregnin in powder and tablets

Gram content $$\frac{A_x * V_k \dots * P_{лек.формы}}{A^{1\%}_{1см} * m * V_п * l_{см} * 100\%}$$

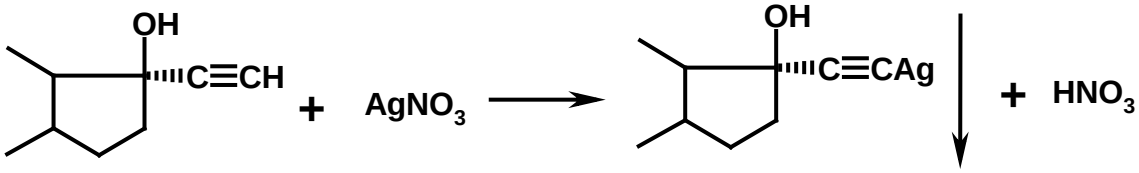
C%= $$\frac{A_x * V_k \dots}{A^{1\%}_{1см} * m * V_п * l_{см}}$$

2). Weight method of determining progesterone (Gravimetry).



C%= $$\frac{a * F * 100\%}{m}$$

3. Alkalimetric determination of pregnin by substitution. Indicator is Bromocresol green or potentiometric.



4. Spectrophotometry of the alcohol solution at 241 nanometers according to the standard sample.

$$C\% = \frac{A_x * C_{0\ g/1ml} * 100\%}{A_0 * l_{cm}}$$

5. Other methods are possible: oxide method, photoelectrocalorimetry, high-performance liquid chromatography and others.

Application. Pregnin, like progesterone, is used in replacement therapy as a progestogen drug for ovarian dysfunction associated with corpus luteum insufficiency, which leads to painful menstruation, infertility, discharges and other diseases associated with corpus luteum insufficiency. Pregnin is 5-6 times less active than progesterone, but it retains its activity when administered orally (under the tongue).

Storage. In a well-closed container, it should be stored away from light.

LESSON No. 1

1. TOPIC: Analysis of adrenal medulla hormones (catecholamines), thyroid gland, antithyroid drugs and pancreatic hormones. Synthetic analogues of pharmacological action.

2. PURPOSE: To master the methods of analysis of medicinal products from the group of adrenal medulla hormones (catecholamines), thyroid gland, antithyroid drugs and pancreatic hormones.

3. TARGETS:

3.1. To study the structure, nomenclature, synonyms, physicochemical properties, sources and methods of obtaining medicines from the group of adrenal medulla hormones (catecholamines), thyroid gland, antithyroid drugs and pancreatic hormones.

3.2. To study the methods of analysis of the considered group of medicinal products according to the SPhU, QCM.

3.3. Propose and justify possible methods of identification and quantification, based on the structure of drugs of the studied group.

3.4. To study specific impurities, as well as testing methods for the purity of this group of substances.

3.5. Consider the peculiarities of the analysis of drugs from the group of adrenal medulla hormones (catecholamines), thyroid gland, antithyroid drugs and pancreatic hormones, physicochemical and chemical methods.

3.6. To learn how to analyze the quality of the considered group of medicines using physical, physico-chemical and chemical methods.

3.7. Interpret and give a correct assessment of the received analysis results, draw a conclusion about the quality of the analyzed substances.

3.8. Explain the peculiarities of storage of medicines from the group of adrenal medulla hormones (catecholamines), thyroid gland, antithyroid drugs and pancreatic hormones, based on their physicochemical properties.

3.9. Learn and follow the rules of safe work in a chemical laboratory.

4. TASKS FOR STUDENT SELF-TRAINING:

4.1. Repeat the theoretical material from organic and analytical chemistry courses on this topic.

4.2. Study the program material on the subject of the lesson according to the questions below.

Educational questions for self-training of students

1. General characteristics of hormones. Classification. The role of hormones in human and animal life. Sources of hormones.
2. Chemical structure, Latin name, synonyms of medicinal substances from the group of hormones.
3. Characterization of the physicochemical properties of drugs of this group, as well as justification of hormone identification methods, based on the characteristics of the chemical structure. Chemistry of reactions.
4. Thyroid hormones - thyroxine, thyroidin, levothyroxine and liothyronine sodium salts. Methods of obtaining, analysis and application in medicine. Indicate which qualitative reactions can be used to confirm the presence of covalently bonded halogen in the given preparations. Antithyroid drugs (mercazolil, methylthiouracil).
5. Medicinal products substituted with phenylethylamine derivatives: adrenaline hydrochloride and tartrate, norepinephrine hydrotartrate, mesaton, isoprenaline hydrochloride (izadrine), methyldopa (methyldopa), levodopa, etc. Methods of synthesis. Redox properties, the problem of stability, identification and quantitative analysis, application features.
6. Explain the origin and definition of specific impurities:
   - adrenaline and norepinephrine into adrenaline tartrate;
   - liothyronine and other concomitant impurities in levothyroxine sodium salt;
   - levothyroxine and other concomitant impurities in liothyronine sodium salt.
7. To justify the use of chemical and instrumental methods in the quantitative determination of medicinal substances and medicinal preparations of this group.
8. Hormones, polypeptides and proteins. Approaches to the analysis of the quality of this group of hormones. Insulins. Application and release form.
9. Assessment of biological activity of hormones.
10. Application of hormones and their synthetic analogues in medicine. Relationship between structure and biological action in a number of hormones and their synthetic analogues. Ways of introduction into the body. Storage.

4.3. Test tasks:

#

1) Indicate which method is recommended for the quantitative determination of thyroidin:

- permanganatometric
- iodochlormetric
- iodometric
- spectrophotometric
- acidimetric

#

2) In the control and analytical laboratory, in order to identify thyroidin, it was processed with the capture of transformation products. The blue color of the absorbent starch solution was observed. The method used was:

- burning
- oxidation
- mineralization
- alkaline hydrolysis
- acid hydrolysis

#

3) Specify the drugs whose amino acid derivatives are used in medical practice for insufficient thyroid gland function:

- alanine
- tyrosine
- methionine
- glycine
- tryptophan

#

4) What drug is used for hypofunction of the thyroid gland?

- thyroidin
- isadrin
- mercazolil
- norepinephrine
- adrenalin

#

5) What drug is used for hypofunction of the thyroid gland?

- norepinephrine
- isadrin
- mercazolil
- liothyronine sodium salt
- adrenalin

#

6) What drug is used for hyperfunction of the thyroid gland?

- triiodothyronine
- mercazolil
- isadrin
- adrenaline tartrate

#

7) What drug is used for hyperfunction of the thyroid gland?

- triiodothyronine
- thyroidin
- methylthiouracil
- adrenaline tartrate

#

8) Which of the following groups of compounds are part of thyroidin:

- thyroxine, tyrosine
- tyrosine, triiodothyronine
- thyroxine, triiodothyronine
- diiodotyrosine, thyroxine
- triiodothyronine, diiodotyrosine

#

9) The QCM for mercazolyl substance requires determining the loss in mass during drying. To do this, the analyst must dry the weight of the medicinal substance to a constant weight in the control and analytical laboratory. The analyst may consider constant mass to be achieved if the difference between the two following weighings does not exceed:

- 0.0005 g
- 0.01 g
- 0.007 g
- 0.00001 g
- 0.5 g

#

10) What is the pharmacological action of Mercazolil?

- analgesic
- anti-inflammatory
- antithyroid
- antipyretic
- antiseptic

#

11) Medicinal products containing the imidazole ring in their structure include:

- adrenalin
- diphenhydramine hydrochloride (diphenhydramine)
- metamizole sodium salt (Analgin)
- nitrofural (furacilin)
- mercazolil

#

12) Which of the listed methods is used for the quantitative determination of mercazolylum [Mercazolylum]:

- alkalimetry by proxy
- permanganatometry (reverse titer)
- acidimetry (direct titration)
- nitritometry
- complexonometry

#

13) Specify the pharmacopoeial preparation of thyroid hormones:

- liothyronine sodium salt

- mercazolil
- thyroidin

#

14) Specify the pharmacopoeial preparation of thyroid hormones:
- adrenalin
- levothyroxine sodium salt
- thyroidin

#

15) Thyroid hormones, which are included in the preparation of thyroidin - thyroxine and thyronine, are:
- levorotatory optical isomers
- dextrorotatory optical isomers
- racemates
- optically inactive substances

#

16) When thyroidin is heated with concentrated sulfuric acid, the following is observed:
- Release of violet vapors of iodine
- Yellow color of the solution
- Precipitation of a white crystalline precipitate, insoluble in nitric acid
- The release of ammonia is detected by the smell or by the turning of litmus paper

#

17) According to the requirements of the SPhU, the quantitative determination of levothyroxine and liothyronine sodium salts is carried out by the method:
- liquid chromatography
- non-aqueous titration in the medium of a protogenic solvent
- non-aqueous titration in the medium of a protophilic solvent
- Kjeldahl
- alkalimetry in an aqueous medium

#

18) According to the requirements of the SPhU, a specific impurity is determined in the preparation of levothyroxine sodium salt:
- liothyronine and related impurities
- 3,5-diiodotyrosine and related impurities
- tyrosine
- thyronine

#

19) According to the requirements of the SPhU, a specific impurity is determined in the preparation of liothyronine sodium salt:
- levothyroxine and related impurities
- 3,5-diiotyrosine and related impurities

- tyrosine
- thyronine

#

20) One of the express methods of determining covalently bound iodine in the structure of thyroid hormones (levothyroxine and liothyronine sodium salts, thyroidin) is to introduce several grains of the drug into the colorless flame of the burner, which turns bluish-green. This method is called:

- Belshtein tests.
- hydroxam sample
- lignin sample
- Van Urck reactions
- Zincke reactions

#

21) The content of organically bound iodine in thyroidin, according to the requirements of the SPhU, should be within the limits of:

- 0.17-0.23%
- 17.0-23.0%
- 8.6-9.1%
- 4.0-5.0%
- 10.5-11.5%

#

22) One of the non-pharmacopoeial methods of quantitative determination of thyroidin is the determination of organically bound iodine in the preparation by the combustion method. Iodine is connected to the organic part of the molecule, while oxidizing:

- oxygen
- chloramine
- potassium dichromate
- chlorine
- a mixture of one volume of nitric acid and three volumes of hydrochloric acid

#

23) The SPhU regulates the content of chloride impurities in liothyronine sodium salt in terms of NaCl and dry matter (no more than 2%). Specify the method by which this impurity is determined:

- direct argentometry with potentiometric termination
- Moreau's method
- Folgard's method
- Fayance method
- mercurometry

#

24) The general method of identification of thyroid hormone preparations (levothyroxine and liothyronine sodium salts) is the reaction to naturalα- amino acids. At the same time, the reagent is used:

- ninhydrin
- bromine water
- alkaline solution of hydroxylamine hydrochloric acid
- sodium nitrite solution, hydrochloric acid, followed by the addition of an alkaline solution of β-naphthol
- hydrogen peroxide solution, sulfuric acid

#

25) In the control and analytical laboratory, it is necessary to conduct an analysis of thyroidin - a drug from the group of thyroid hormones. When identifying it, the analyst must react to:

- nitro group
- aromatic amino group
- organically bound iodine
- ester group
- steroid cycle

#

26) Thyroidin analysis is performed in the laboratory of the State Inspection for Quality Control of Medicines. After boiling it with a solution of sodium hydroxide, a yellow color is formed, which disappears when dilute sulfuric acid is added, which is also accompanied by the precipitation of a colloidal precipitate. This test confirms the presence of thyroidin:

- carboxyl group
- amide group
- molecular iodine
- squirrel
- phenolic hydroxyl

#

27) The starting material for obtaining mercazolil is:

- ethanol
- glycerin
- tyrosine
- 3,5-diiodotyrosine
- picric acid (2,4,6-trinitrophenol)

#

28) Mercazolil, a drug from the group of antithyroid drugs, must be analyzed in a control and analytical laboratory. When identifying it, the analyst must perform a reaction with:

- silver nitrate
- sodium nitrite and hydrochloric acid
- concentrated sulfuric acid

- potassium dichromate and sulfuric acid
- sodium acetate

#

29) According to the value of the specific rotation, they analyze:
- anesthesin
- Mercazolil
- thyroidin
- sodium benzoate

#

30) Epinephrine and norepinephrine are hormones of the medulla of the adrenal glands. Common for these hormones is an identification reaction with a reagent:
- iodine solution
- sulfuric acid
- hydrochloric acid
- sodium hydroxide
- iron (III) chloride

#

31) Quantitative analysis of adrenaline tartrate is carried out in the control and analytical laboratory. According to the requirements of the SPhU, the method of quantitative determination is used:
- reverse bromatometry
- acidimetry in an aqueous medium
- acidimetry in acetic acid
- substitute iodometry
- alkalimetry in a non-aqueous medium

#

32) A pharmacist-analyst conducts an express analysis of eye drops containing adrenaline hydrotartrate. After adding a solution of iron (III) chloride, an emerald-green color appeared, which indicates the presence of adrenaline in the molecule:
- phenolic hydroxyl groups
- aldehyde groups
- aromatic amino groups
- ester groups

#

33) You can distinguish adrenaline hydrotartrate from norepinephrine hydrotartrate by:
- oxidation reactions at different pH values
- reaction with a solution of iron (III) chloride
- solubility in water
- reactions with general alkaloid reagents

#

34) To identify the hydrotartrate ion in the hydrotartrate adrenaline molecule, the pharmacist-analyst used potassium chloride as the main reagent. A positive result should be considered:

- precipitation of a white precipitate
- the appearance of a red color
- release of gas bubbles
- the appearance of a characteristic smell

#

35) The pharmacist-analyst determines the quantitative content of adrenaline tartrate in accordance with the requirements of the SPhU, by the method of acid-base titration in a non-aqueous medium. As a titrant, he uses a solution:

- perchloric acid
- hydrochloric acid
- sodium hydroxide
- sodium methylate

#

36) Sodium metabisulfite as an antioxidant is used to stabilize injection solutions

- glucose
- insulin
- adrenaline hydrochloride
- morphine hydrochloride
- novocaine

#

37) Injectable solutions are not subjected to thermal sterilization:

- glucose
- hexamethylenetetramine
- adrenaline hydrotartrate
- novocaine hydrochloride

#

38) Due to which groups in the structure of adrenaline hydrotartrate, the main properties are expressed:

- primary aliphatic amino group
- secondary aliphatic amino group
- primary aromatic amino group
- secondary aromatic amino group
- amide group

#

39) The natural metabolite of the body is:

- dopamine
- isadrin
- ephedrine

- salbutamol
- adrenalin

#

40) Which of the following drugs is a naturally occurring catecholamine?

- adrenalin
- isadrin
- ephedrine
- chloramphenicol
- methyldopa

#

41) What derivative of phenylalkylamine is used in medicine as a hormonal agent?

- isadrin
- anaprilin
- adrenaline hydrotartrate
- hexamethylenetetramine
- Mercazolil

#

42) Medicinal product, which is characterized by a reaction with iron (III) chloride:

- adrenaline hydrotartrate
- procaine hydrochloride
- magnesium oxide
- diphenhydramine
- anesthesin

#

43) Is an α-amino alcohol:

- adrenalin
- levodopa
- anesthesin
- diiodotyrosine
- liothyronine

#

44) Specify the pharmacopoeial drug that has an adrenomimetic effect:

- adrenaline tartrate
- dibazole
- anesthesin
- methyldopa
- mesatone

#

45) Catecholamine drugs have the following properties:

- amphoteric
- sour

- the main ones

#

46) Specify the starting compound for the synthesis of adrenaline and norepinephrine:

- pyrocatechin
- glycerin
- benzene
- 3,5-diiodotyrosine
- picric acid (2,4,6-trinitrophenol)

#

47) Indicate by which method, in accordance with the requirements of the SPhU, the determination of the specific admixture of adrenaline in the preparation of adrenaline tartrate is carried out:

- photometrically
- polarimetric
- chromatographically
- by reaction with iron (III) chloride
- not conducted

#

48) Indicate the method by which, in accordance with the requirements of the SPhU, the specific admixture of norepinephrine in the adrenaline tartrate preparation is determined:

- by the method of thin-layer chromatography
- photometrically
- polarimetric
- by reaction with iron (III) chloride
- not conducted

#

49) According to the SPhU, to identify the substance adrenaline tartrate, the reaction of the formation of adrenochrome at pH 3.56 with a solution is used:

- sodium nitroprusside
- iron (III) chloride
- ninhydrin
- iodine
- glyoxalhydroxyanil

4.4. Situational tasks:

1. Specify the characteristic reactions that can be used in the analysis of adrenaline tartrate and norepinephrine hydrotartrate. Justify your answer and illustrate the chemistry of the reactions.

2. Give examples of chemical reactions that confirm that adrenaline tartrate, mesaton, and isadrin are salts of nitrogenous bases.
3. Describe possible methods for quantitative determination of adrenaline tartrate. Give a rationale for using the methods. Write the reaction equations.
4. Describe possible methods for quantitative determination of levodopa. Give a rationale for using the methods. Write the reaction equations.
5. Explain whether the general identification reaction for tartrates with resorcinol in concentrated sulfuric acid can be used to reveal the tartrate in adrenaline tartrate.
6. Justify the possibility of using the iodometric titration method for the quantitative determination of drugs that stimulate the function of the thyroid gland (sodium salts of levothyroxine and liothyronine). Give the reaction equations and the formula for calculating the quantitative content.
7. Suggest methods for proving the presence of covalently bound halogen in thyroid preparations.
8. State the biochemical prerequisites for the creation of drugs from the phenylalkylamine group based on the metabolism of the amino acid tyrosine.

4.5. Tasks:

1. Calculate the mass of a test of norepinephrine hydrotartrate (M.w. 337.29), if 4.95 ml of a 0.1 M solution of perchloric acid (C_a = 1.0030) was spent on its titration, its percentage content in the preparation is 99.5%, the percentage of water is 5% and the volume of the titrant in the control experiment is 0.30 ml.
2. Determine the mass fraction of adrenaline hydrotartrate (M.w. 333.30) in the medicinal product, if 5.04 ml of 0.1 M perchloric acid solution was spent on the titration of 0.1685 g of adrenaline hydrotartrate (C_a = 1.0004).
3. Calculate the volume interval of 0.01 M sodium thiosulfate solution (C_a = 1.0000), which will ensure the quality of thyroidin in quantitative determination by the unified iodometric method, if the weight of the drug is 0.5000 g, and the iodine content in it should be from 0.17% to 0.23%. 1 ml of 0.01 M sodium thiosulfate solution corresponds to 0.0002115 g of I.
4. Calculate the content of epinephrine (adrenaline tartrate) in the injection solution, if 5 ml of the drug is diluted with water in a 100 ml volumetric flask. Iron-citrate reagent is added to 10 ml of the obtained solution and the value of the optical density is determined on a spectrophotometer in a cuvette with a layer thickness of 10 mm. The optical density of the standard solution is 0.245, the optical density of the test solution is 0.240. 1 ml of standard sample solution contains 0.00091 g of epinephrine (adrenaline tartrate). The content

of medicinal substances in 1 ml of solution for injection should be from 0.0016 to 0.0020 g.

5. Justify the pharmacopoeial method of quantitative determination of adrenaline tartrate in a substance. Make a conclusion about the quality, if 6.20 ml of titrant (0.1 mol/l) with C_a = 1.0000 was consumed during titration of 0.2025 g of medicinal substance. The content of epinephrine (adrenaline tartrate) should be from 98.5% to 101.0%. M.w. epinephrine (adrenaline tartrate) 333.30.
6. Justify the non-aqueous titration method for the quantitative determination of methyldopa (methyldopa) in a substance. What a daremedicinal substance should be taken so that 11.85 ml of a titrant solution (0.1 mol / l) with C_a = 1.0000 is spent on titration? The content of methyldopa (methyldopa) in the drug is 98.8%. M.w. methyldopa (methyldopa) 211.21.
7. Calculate the percentage of mesatone (M.w. 203.67) in the preparation, if 16.10 ml of 0.1 M sodium thiosulfate solution (C_a = 1.0000) was spent on the titration of a weight of 0.1120 g, the loss in weight during drying - 0.5% and the volume of the titrant in the control experiment - 48.50 ml.
8. Calculate the distance from the starting line to the center of the methylthiouracil spot if Rf = 0.82 and the distance traveled by the solvent is 10.0.
9. Calculate the volume of a 0.1 M solution of perchloric acid (C_a = 1.0009), which was spent on the titration of 0.1598 g of mesatone (M.w. 203.67). The percentage content of mesatone in the preparation is 98.64%, the weight loss during drying is 0.52%, and the titrant volume in the control experiment is 0.12 ml.
10. Calculate the percentage content of mercazolil (M.w. 114.17) in the preparation, if 8.64 ml of 0.1 M sodium hydroxide solution (C_a = 1.0000) was spent on the titration of a weight of 0.1009 g, the loss in weight during drying is 0 , 48%.
11. Calculate the weight of mercazolil measurement (M.w. 114.17), if 10.20 ml of 0.1 M sodium hydroxide solution (C_a = 1.0015) was spent on its titration, its percentage content in the preparation is 99.21%.

5. LABORATORY WORK

During laboratory work it is necessary to strictly follow the safety rules in the chemical laboratory.

Each student individually carries out reactions of identification of samples of drug substances under the instruction of the teacher and draws up the test report.

LESSON No. 2

1. TOPIC: Analysis of drugs from the steroid hormone group: adrenal cortical hormones (corticosteroids). Synthetic analogues of pharmacological action.

2. PURPOSE: To master the methods of analysis of medicinal products from the group of adrenal cortical hormones (corticosteroids).

3. TARGETS:

3.1. To study the structure, nomenclature, synonyms, physicochemical properties, sources and methods of obtaining medicines from the group of adrenal cortical hormones (corticosteroids).

3.2. To study the methods of analysis of the considered group of medicinal products according to the SPhU, QCM.

3.3. Propose and justify possible methods of identification and quantification, based on the structure of drugs of the studied group.

3.4. To study specific impurities, as well as testing methods for the purity of this group of substances.

3.5. Consider the peculiarities of the analysis of drugs from the group of adrenal cortical hormones (corticosteroids), physicochemical and chemical methods.

3.6. To learn how to analyze the quality of the considered group of medicines using physical, physico-chemical and chemical methods.

3.7. Interpret and give a correct assessment of the received analysis results, draw a conclusion about the quality of the analyzed substances.

3.8. Explain the peculiarities of storage of medicines from the group of adrenal cortical hormones (corticosteroids), based on their physicochemical properties.

3.9. Learn and follow the rules of safe work in a chemical laboratory.

4. TASKS FOR STUDENT SELF-TRAINING:

4.1. Repeat the theoretical material from organic and analytical chemistry courses on this topic.

4.2. Study the program material on the subject of the lesson according to the questions below.

Educational questions for self-training of students

1. General characteristics of steroid hormones. Classification, role in the body.
2. Chemical structure, Latin name, synonyms of medicinal substances from the group of hormones.

3. Characterization of the physicochemical properties of drugs of this group, as well as justification of hormone identification methods, based on the characteristics of the chemical structure. Chemistry of reactions.
4. Corticosteroids and their medicinal preparations. Mineralocorticosteroids (deoxycorticosterone acetate, spironolactone). Physico-chemical properties, analysis, release form, application. Biological role and significance for medicine.
5. Glucocorticosteroids that do not contain halogen atoms in the molecule: hydrocortisone acetate, cortisone acetate. Properties, analysis, release form, application. What structural fragment of the corticosteroid molecule determines their restorative properties? Show it on a concrete example by writing reaction equations.
6. Semi-synthetic analogues of hydrocortisone and cortisone - prednisone, prednisone, methylprednisolone and others. Properties, analysis, release form, application.
7. Halogen-containing analogues of prednisolone: dexamethasone, betamethasone dipropionate, triamcinolone, sinaflan, flumethasone, beclomethasone and others. Effect of halogen on pharmacological properties. Properties, analysis by functional groups, release form, application. Methods of introducing and determining the covalently bonded fluorine atom.
8. Explain the origin and definition of concomitant impurities in hydrocortisone acetate, betamethasone dipropionate.
9. Assessment of biological activity of hormones.
10. Application of hormones and their synthetic analogues in medicine. Relationship between structure and biological action in a number of hormones and their synthetic analogues. Ways of introduction into the body. Storage.

4.3. Test tasks:

#

1) One of the substances is used as a starting point in the synthesis of cortisone acetate. Specify it:
   - β-picoline
   - progesterone
   - salt pot
   - thyroxine
   - anethole

#

2) One of the above reagents is specific for proving the presence of a steroid cycle in hormones. Specify it:
   - concentrated hydrochloric acid

А. concentrated sulfuric acid
Б. Fehling's reagent
В. hydroxylamine solution
- 2,4-dinitrophenylhydrazine

#

3) One of the above methods can be rationally used for quantitative determination of prednisolone. Specify it:
- acidimetric
- spectrophotometric
- iodometric
- fluorimetric
- permanganatometric

#

4) Specify the pharmacological effect most characteristic of synthetic analogues of prednisolone, which have a fluorine atom in the 6th and 9th positions in the molecule:
- anabolic
- analgesic
- antiphlogistic
- antioxidant
- cytostatic

#

5) One of these drugs belongs to corticosteroids and is included in DFU. Specify it:
- levothyroxine sodium salt
- testosterone propionate
- progesterone
- hydrocortisone acetate
- deoxycorticosterone acetate

#

6) One of the above methods can be rationally used for the quantitative determination of a solution of deoxycorticosterone acetate in oil. Specify it:
- spectrophotometric
- fluorimetric
- acidimetry in non-aqueous solvents
- gravimetric
- acidimetric

#

7) One of the above drugs has in the moleculeα-keto group, which is analytically confirmed by Fehling's reagent. Specify this drug:
- methyltestosterone
- deoxycorticosterone acetate
- diethylstilbestrol propionate

- methandrostenolone
- levothyroxine sodium salt

#

8) One of these substances is the starting point in the synthesis of deoxycorticosterone acetate. Specify it:
- folic acid
- anethole
- diosgenin
- β-picoline
- *p*- nitrotoluene

#

9) On the basis of one of these hormones, its synthetic analogue - prednisone - was obtained. Specify this hormone:
- hydrocortisone
- deoxycorticosterone
- testosterone
- estradiol
- progesterone

#

10) One of the listed drugs belongs to synthetic analogues of prednisolone and contains a fluorine atom in the steroid cycle. Specify it:
- phenobolin
- betamethasone dipropionate
- Dimestrol
- pregnane
- hydrocortisone acetate

#

11) One of the listed reagents is used in the pharmacopoeial analysis to prove the presenceα-ketol group in corticosteroids. Specify it:
- concentrated sulfuric acid
- Fehling's reagent
- sodium nitrite solution
- 2,4-dinitrophenylhydrazine solution
- sodium edetate solution

#

12) One of the following names corresponds to the steroid cycle, which is part of the corticosteroid hormones. Specify it:
- pregnane
- TV show
- eicosan
- cholestane
- androstane

#

13) One of the listed hormonal preparations has restorative properties and gives a positive reaction with Fehling's reagent. Specify it:
- retabolil
- liothyronine sodium salt
- octestrol
- cortisone
- methandrostenediol

#

14) Oxidizing-reducing properties of prednisone are due to the presence of:
- steroid cycle
- ketogroups
- α-ketoenol group
- ester group
- ethynyl group

#

15) What optical isomer is prednisolone:
- right-handed
- left-handed
- racemate

#

16) Cortisone can be distinguished from prednisolone:
- by reaction with an ammonia solution of silver nitrate
- by UV spectra
- by reaction with Fehling's reagent
- by reaction with sodium acetate

#

17) Cortisone can be distinguished from prednisolone:
- by reaction with an ammonia solution of silver nitrate
- by reaction with sodium nitrite in a hydrochloric acid environment
- by reaction with Fehling's reagent
- by reactionwith 2,4-dinitrophenylhydrazine

#

18) The presence of a keto group in prednisone is confirmed by the reaction:
- formation of esters
- hydroxam test
- with concentrated sulfuric acid
- with Fehling's reagent
- formation of hydrazones

#

19) When identifying deoxycorticosterone acetate, the drug is dissolved in concentrated sulfuric acid, resulting in a cherry color with greenish-brown fluorescence. With the help of this reaction, identify:
- keto group in position 3 of the steroid cycle

- steroid cycle
- dioxyacetone group
- ester group in position 21 of the steroid cycle

#

20) In the control and analytical laboratory, the identification of glucocorticoid hormones: prednisone and hydrocortisone acetate is carried out using the identification reaction for the dioxyacetone group. As a reagent, use:
- phenylhydrazine sulfate
- concentrated sulfuric acid
- sodium hydroxide solution
- Fehling's reagent
- Wagner reagent

#

21) In the control and analytical laboratory, identification of steroid hormones is carried out, which have hydroxyl groups in positions 3 and 17 of the steroid cycle. The reaction of the formation of complex esters is used, for which the following are determined:
- specific optical rotation
- refractive index
- specific absorption index
- the shape of the crystals
- melting point

#

22) The identification of steroid hormones and their synthetic analogues, which contain an ester group (acetates, propionates), is carried out. For this, the reaction is used:
- hydroxam sample
- murexide sample
- thalleiochin sample
- with sodium acetate
- with ninhydrin

#

23) Cortisone interacts with hydroxylamine due to the presence in the structure:
- steroid cycle
- keto group in the third position
- α-ketol group
- alcohol hydroxyl

#

24) The hydroxam sample can be used in the analysis of:
- ethyl alcohol
- dexamethasone
- doxa
- pregnane

- triamcinolone

#

25) Identifying cortisone acetate, a control and analytical laboratory specialist conducts a reaction with phenylhydrazine. The appearance of a yellow color confirms the presence in the molecule:
- ketogroups
- steroid cycle
- ester group
- β-ketol group

- #

26) α-Ketol group in the structure of corticosteroids reveals:
- amphoteric properties
- basic properties
- regenerative properties
- oxidizing properties

#

27) Corticosteroids react with Fehling's reagent to form:
- blue sediment
- red sediment
- red solution
- do not react with Fehling's reagent

#

28) Corticosteroids when interacting with silver nitrate solution form:
- black precipitate in an ammonia medium
- white precipitate in a nitric acid environment
- black precipitate in a nitric acid environment
- white precipitate in an ammonia medium

#

29) When halogens are introduced into the C6 and C9 positions of steroid compounds, the following occurs:
- solubility in organic solvents improves
- solubility in water improves
- increasing the activity of drugs
- side effects increase

#

30) The structure of steroid hormones is based on the cyclopentaneperhydrophenanthrene skeleton. Based on this, the general reaction to all steroid hormones and their synthetic analogues is a reaction with acid:
- concentrated sulfate
- diluted sulfate
- concentrated hydrogen chloride
- diluted hydrogen chloride
- concentrated nitrate

#

31) Specify the pharmacopoeial drug from the group of halogen-containing semi-synthetic analogues of corticosteroid hormones:

- betamethasone dipropionate
- triamcinolone
- beclomethasone
- dexamethasone
- sinaflan

#

32) Ester groups in steroid molecules are detected using the reaction:

- esterification
- formation of hydrazones
- hydroxam sample
- murexide sample

4.4. Situational tasks:

1. Suggest reagents to prove the presence of an alpha-ketol group in the hydrocortisone molecule.Write the chemistry of reactions.
2. Justify the possibility of quantitative analysis of corticosteroids using spectrophotometry.
3. Suggest reactions for the identification of deoxycorticosterone acetate by functional assay.
4. Name the functional groups present in the structure of cortisone acetate. Where possible, give the equations and indicate the conditions for the reactions that confirm their presence.
5. Name the main functional groups of corticosteroids used to identify these drugs. What physical and physicochemical properties are used in the analysis of corticosteroids?
6. What reactions can be used to confirm the presence of a carbonyl group in the 3rd position of corticosteroids? What is the basis of the use of these reactions for the identification of medicinal products?
7. What are the ways to convert a covalently bonded halogen into an ionogenic state?
8. What reactions can be used to confirm the presence of organically bound Fluorine in the dexamethasone molecule?
9. Suggest identification reactions of prednisone using functional analysis.

4.5. Tasks:

1. Calculate the value of the specific absorption index, if opticaldensity 0.001% solution of prednisolone in methyl alcohol at a wavelength of 242 nm in a cuvette with a layer thickness of 10 mm is equal to 0.705.
2. Calculate the volume of 0.1 M sodium hydroxide solution (C_a = 1.0013), which was used for the titration of 0.2018 g of cortisone acetate (M.w. 402.5),

determined by the oxime method. The percentage content of cortisone acetate in the preparation is 99.64%, the weight loss during drying is 0.42%.

3. Calculate the specific rotation and evaluate the quality of hydrocortisone acetate, if a weight of the drug weighing 0.4973 g was dissolved in dioxane in a 50 ml volumetric flask. The average angle of rotation of the obtained solution is equal to + 3.22°. The length of the cuvette is 2 dm. Specific rotation should be from +158° to + 167°.
4. Calculate the specific absorption index and evaluate the quality of cortisone acetate, if a weight of the drug weighing 0.0805 g was dissolved in a 100 ml volumetric flask, 1 ml of this solution was transferred to a 50 ml volumetric flask and brought up to the mark with ethanol. Average opticsdensityof the obtained solution at 238 nm is 0.483, the thickness of the cuvette is 10 mm. The content of cortisone acetate in the preparation is 99.1%. The specific absorption index should be 380-400
5. Calculate the percentage content of hydrocortisone acetate (M.w. 404.5) in the preparation determined by the oxime method, if 5.08 ml of 0.1 M sodium hydroxide solution (C_a = 1.0003) was spent on the titration of a weight of 0.2056 g.
6. Calculate the specific absorption index and evaluate the quality of prednisolone, if a weight of the drug weighing 0.1184 g was dissolved in a 100 ml volumetric flask in methanol, 0.5 ml of the resulting solution was transferred to a 50 ml volumetric flask and brought up to the mark with methanol. Average optics densityof the obtained solution at 242 nm is 0.482, the thickness of the cuvette is 10 mm. The content of prednisolone in the drug is 98.76%. The specific absorption index should be 400-430.
7. Calculate the quantitative content and evaluate the quality of prednisolone, if a weight of the drug weighing 0.1037 g was dissolved in a 100 ml volumetric flask in ethanol. 1 ml of this solution was transferred to a 100 ml volumetric flask and made up to the mark with ethanol. Average optics density at 242 nm is 0.483, the thickness of the cuvette is 10 mm. The specific absorption index is 460. The content of prednisolone in the drug should be at least 98.5%.
8. Calculate the weight of hydrocortisone acetate (M.w.404.5), determined by the method of acid-base titration by substitution, if 10.8 ml of 0.1 M hydrochloric acid solution (C_a = 1.0005) was spent on its titration, the percentage its content in the drug is 98.22%.
9. Calculate the specific absorbance and rate the quality of deoxycorticosterone acetate if the mean opticaldensity, measured on a spectrophotometer at 240 nm with a cuvette thickness of 10 mm, 0.001% solution equals 0.443. The specific absorption index should be from 440 to 450.

10. Calculate the gram content of prednisolone in the dosage form (prednisone tablets 0.001 g, average weight (P) equal to 0.042 g), if 0.075 g of powder of crushed tablets, dissolved in alcohol when heated, filtered and made up to a volume of 100 ml with the same solvent, give an opticaldensityon a spectrophotometer at a wavelength of 239 nm in a cuvette with a layer thickness of 1 cm is 0.78. As a control experiment, alcohol is used, the specific absorption index ($E_{1см}^{1\%}$) of prednisolone 432.

5. LABORATORY WORK

During laboratory work it is necessary to strictly follow the safety rules in the chemical laboratory.

Each student individually carries out reactions of identification of samples of drug substances under the instruction of the teacher and draws up the test report.

LESSON No. 3

1. TOPIC: Analysis of sex hormones: progestogens, estrogens, androgens, anabolic steroids and their analogues. Birth control. Estrogens of nonsteroidal structure.

2. PURPOSE: To master the methods of analysis of medicinal products from the group of sex hormones: progestogens, estrogens, androgens, anabolic steroids and their analogues.

3. TARGETS:

3.1. To study the structure, nomenclature, synonyms, physicochemical properties, sources and methods of obtaining medicines from the group of sex hormones: progestogens, estrogens, androgens, anabolic steroids and their analogues.

3.2. To study the methods of analysis of the considered group of medicinal products according to the SPhU, QCM.

3.3. Propose and justify possible methods of identification and quantification, based on the structure of drugs of the studied group.

3.4. To study specific impurities, as well as testing methods for the purity of this group of substances.

3.5. Consider the peculiarities of the analysis of drugs from the of sex hormones: progestogens, estrogens, androgens, anabolic steroids and their analogues, physicochemical and chemical methods.

3.6. To learn how to analyze the quality of the considered group of medicines using physical, physico-chemical and chemical methods.

3.7. Interpret and give a correct assessment of the received analysis results, draw a conclusion about the quality of the analyzed substances.

3.8. Explain the peculiarities of storage of medicines from the group of sex hormones: progestogens, estrogens, androgens, anabolic steroids and their analogues, based on their physicochemical properties.

3.9. Learn and follow the rules of safe work in a chemical laboratory.

4. TASKS FOR STUDENT SELF-TRAINING:

4.1. Repeat the theoretical material from organic and analytical chemistry courses on this topic.

4.2. Study the program material on the subject of the lesson according to the questions below.

Educational questions for self-training of students

1. General characteristics of steroid hormones. Classification, role in the body.

2.Chemical structure, Latin name, synonyms of medicinal substances from the group of hormones.

3. Characterization of the physicochemical properties of drugs of this group, as well as justification of hormone identification methods, based on the characteristics of the chemical structure. Chemistry of reactions.

4. Estrogenic hormones and their medicinal preparations: estradiol and its esters, estrone, ethinylestradiol and estriol. Obtaining, properties, analysis, release form and application. Dependence between structure and biological action.

5. Estrogenic drugs of non-steroidal structure: sinestrol, diethylstilbestrol, dimestrol, phosphestrol, sigetin and others. Obtaining, properties, analysis, release form and application. What structural features determine their estrogenic effect?

6. Progestogenic hormones and their medicinal preparations: progesterone, pregnin and others. Obtaining, properties, analysis, release form, application.

7. Contraceptives (Non-Ovlon, Ovidon, Femodene, etc.) Their composition, properties, form of release, application.

8. Androgenic hormones: testosterone and its esters, methyltestosterone. Based on the structure, justify the analysis. Forms of release, application and storage. List reactions that may be common to androgenic drugs.

9. Anabolic medicinal substances, derivatives of testosterone and 19-nortestosterone: methandrostenolone, methylandrostenediol, phenobolin, retabolil. Prerequisites for the creation of these preparations. Physico-chemical properties, analysis, release form, application. Biological role and significance for medicine.

10. Antiandrogens (cyproterone acetate, finasteride, flutamide). The relationship between structure and biological action.

11. Assessment of biological activity of hormones.

12. Application of hormones and their synthetic analogues in medicine. Relationship between structure and biological action in a number of hormones and their synthetic analogues. Ways of introduction into the body. Storage.

4.3. Test tasks:

#

1) The identification of steroid hormones and their synthetic analogues, which contain an ester group (acetates, propionates), is carried out. For this, the reaction is used:
   - hydroxam sample
   - murexide sample
   - thalleiochin sample

- with sodium acetate
- with ninhydrin

#

2) The structure of steroid hormones is based on the cyclopentaneperhydrophenanthrene skeleton. Based on this, the general reaction to all steroid hormones and their synthetic analogues is a reaction with acid:
- concentrated sulfate
- diluted sulfate
- concentrated hydrogen chloride
- diluted hydrogen chloride
- concentrated nitrate

#

3) One of these drugs is an estrogen hormone. Specify it:
- testosterone propionate
- methylandrostenediol
- ethinylestradiol
- pregnane
- progesterone

#

4) One of the listed hormonal preparations corresponds to the following chemical name 17-α-ethynylestratriene-1,3,5(10)-diol-3,17β. Specify it:
- sinestrol
- progesterone
- ethinylestradiol
- prednisone
- methyltestosterone

#

5) One of the above preparations gives a positive reaction to phenolic hydroxyl with a solution of ferric ammonium alums. Specify it:
- pregnane
- methandrostenolone
- ethinylestradiol
- hydrocortisone acetate
- prednisone

#

6) Ethinyl estradiol dissolves in sodium hydroxide solution due to the presence in its structure:
- steroid cycle
- methyl group
- phenolic hydroxyl
- alcohol hydroxyl

#

7) Estrogenic hormones are steroids by chemical structure. A feature of their structure compared to other hormones is the presence of an aromatic ring with a substituent:
- keto group in position 3
- phenolic hydroxyl in position 2
- phenolic hydroxyl in position 3
- keto group in position 2
- methyl group in position 2

#

8) Estradiol dipropionate belongs to the group of estrogen hormones. Quantitative determination of this hormone by the method of alkalimetry (back titration) includes carrying out the reaction:
- saponification
- oxidation-reduction
- condensation
- esterification
- decomposition

#

9) Ethinylestradiol is part of combined oral hormonal contraceptives. Quantitative determination of this hormone in medicinal products is carried out by the method:
- Alkalimetry in the water environment
- Alkalimetry by deputy
- Alkalimetry in a non-aqueous environment
- Acidimetry in a non-aqueous environment
- Argentometry according to Folgard

#

10) The main source of synthesis of estrogenic hormones is:
- β-naphthol
- folic acid
- cholesterol
- bile acid

#

11) The method of indirect neutralization is used for the quantitative determination of:
- estrone
- ethinylestradiol
- estradiol
- estriol

#

12) To identify estrogenic hormone preparations, a reaction with:
- iron (III) chloride solution
- alcohol solution of ninhydrin

- ammonia solution
- hydrogen peroxide solution
- phosphoric acid

#

13) Specify the natural estrogen hormone:
- estriol
- testosterone
- sinestrol
- progesterone

#

14) In the quantitative determination of ethinyl estradiol by the method of indirect neutralization, the titrant is used:
- titrated solution of nitric acid
- titrated solution of silver nitrate
- titrated solution of hydrochloric acid
- titrated sodium hydroxide solution

#

15) One of the listed hormones belongs to non-steroidal estrogenic drugs and is a derivative of diphenylethane. Specify it:
- progesterone
- liothyronine sodium salt
- sinestrol
- prednisone
- retabolil

#

16) One of the above methods can be rationally used for the quantitative determination of progesterone. Specify it:
- gravimetry
- acidimetry
- cerimetry
- acidimetry in non-aqueous solvents
- argentometry

#

17) One of the following names corresponds to the steroid cycle, which is part of female (gestogens) sex hormones. Specify it:
- pregnane
- TV show
- eicosan
- cholestane
- androstane

#

18) Hormones of the corpus luteum are called progestogen hormones. They include:

- progesterone and testosterone
- progesterone and pregnane
- testosterone and pregnane
- phenobolin and testosterone
- phenobolin and pregnin

#

19) Progesterone and pregnin belong to steroid hormones. When identifying the steroid cycle, the substance is added to the solution:
- concentrated nitric acid and water
- concentrated hydrochloric acid
- water and acetic acid
- concentrated sulfuric acid and water
- water and nitric acid

#

20) Natural progestin hormone:
- postinor
- progesterone
- norethisterone
- mestranol

#

21) The method of indirect neutralization is used for quantitative determination
- progesterone and ethinylestradiol
- estradiol dipropionate and ethinylestradiol
- postinor and ethinylestradiol
- there is no right answer

#

22) For one of the medicinal substances, it is possible to carry out the acid-base titration method after carrying out the acylation reaction. Specify it:
- testosterone propionate
- diethylstilbestrol propionate
- sigetin
- hydrocortisone acetate
- sinestrol

#

23) One of the above substances is the starting point in the synthesis of sinestrol. Specify it:
- anethole
- citral
- diosgenin
- cholesterol
- salt pot

#

24) Indicate which of the listed drugs corresponds to the international name "Hexestrolum":
- octestrol
- progesterone
- ethinylestradiol
- sinestrol
- testosterone propionate

#

25) Indicate which method is recommended for quantitative determination of sinestrol after the acylation reaction:
- alkalimetry
- photoelectrocolorimetry
- cerimetry
- iodometry
- acidimetry in non-aqueous solvents

#

26) Synthetic estrogenic compounds sinestrol and diethylstilbestrol are used in medical practice for the treatment of:
- hypothyroidism
- thyrotoxicosis
- malignant neoplasms
- allergies
- rheumatism

#

27) Medicinal substances that have an estrogenic effect, the molecules of which do not include the steroid cycle, include:
- ethinylestradiol and diethylstilbestrol
- estradiol and diethylstilbestrol
- estradiol and sinestrol
- sinestrol and diethylstilbestrol
- estradiol and ethinylestradiol

#

28) The determination of the quantitative content of sinestrol in the oil solution of the drug, after extraction of the active substance with an aqueous solution of sodium hydroxide, is carried out by a specialist of the State Inspection for Quality Control of Medicines using the following method:
- acidimetry
- nitritometry
- bromatometry
- alkalimetry

#

29) Indicate which drug is used to identify the azo dye formation reaction:
- phenobolin

- retabolil
- ethinylestradiol
- testosterone propionate
- prednisone

#

30) One of the above reagents is specific for proving the presence of a steroid cycle in hormones. Specify it:

- concentrated hydrochloric acid
- concentrated sulfuric acid
- Fehling's reagent
- Hydroxylamine solution
- 2,4-dinitrophenylhydrazine

#

31) One of these drugs is a derivative of 19-nortestosterone and belongs to anabolic steroids. Specify it:

- methyltestosterone
- betamethasone dipropionate
- retabolil
- deoxycorticosterone acetate
- ethinylestradiol

#

32) One of the following names corresponds to the steroid cycle, which is part of the male sex hormones. Specify it:

- pregnane
- TV show
- eicosan
- cholestane
- androstane

#

33) Indicate which method of quantitative determination is the most rational to use for an oil solution of testosterone propionate:

- acidimetric
- spectrophotometric
- acidimetry in non-aqueous solvents
- polarimetric
- bromatometric

#

34) One of the listed drugs belongs to androgenic hormones. Specify it:

- pregnane
- dexamethasone
- methylandrostenediol
- testosterone propionate
- ethinylestradiol

#

35) One of the listed medicinal substances gives a positive reaction with a solution of 2,4-dinitrophenylhydrazine (orange-red precipitate). Specify it:

- levothyroxine sodium salt
- potassium orotate
- methandrostenolone
- adrenaline hydrotartrate
- ethinylestradiol

#

36) One of the above pharmacological actions is characteristic of the drug retabolil. Specify it:

- anti-inflammatory
- progestogenic
- anabolic
- estrogenic
- cytostatic

#

37) The presence of alcohol hydroxyl in methyltestosterone is confirmed by the reaction:

- formation of esters
- hydroxam test
- formation of hydrazones
- with Fehling's reagent
- oxime formation

#

38) Male gonads produce androgen hormones, which include:

- testosterone
- phenobolin
- methylandrostenediol
- progesterone
- pregnane

#

39) One of the ways to identify the androgenic hormone testosterone propionate is to determine the melting point of testosterone oxime obtained from testosterone propionate as a result of:

- alkaline hydrolysis
- acid hydrolysis
- mineralization
- dissolution in concentrated sulfuric acid
- interactions with hydroxylamine

#

40) It is a derivative of androstane

- cortisone acetate

- pregnane
- testosterone propionate

А. ethinylestradiol
Б. dexamethasone

#

41) The effect of testosterone becomes longer after:
- halogenation with fluorine
- esterification with fatty acids
- oxidation of the α-ketol group
- there is no correct option

#

42) Ester groups in steroid molecules are detected using the reaction:
- esterification
- formation of hydrazones
- hydroxam sample
- murexide sample

#

43) A semi-synthetic derivative of androgenic hormones is:
- methyltestosterone
- androstane
- dehydroandrosterone
- testosterone

#

44) Testosterone propionate upon interaction with hydroxylamine forms an oxime, which is identified by:
- specific rotation
- melting point
- characteristic color
- characteristic smell

#

45) Anabolic steroids include methylandrostenediol. To determine its content in the medicinal product, the following method is used:
- acid-base titration
- polarimetry
- refractometry
- gravimetry
- spectrophotometry

4.4. Situational tasks:

1. What reaction can distinguish diethylstilbestrol propionate from diethylstilbestrol? Write the reaction diagrams.

2. Describe the bromatometric method of quantitative determination of medicinal substances using sinestrol as an example. Give the reaction equations and the formula for calculating the quantitative content.
3. Describe the acetylation method for quantitative determination of diethylstilbestrol. Give the reaction equations and the formula for calculating the quantitative content.
4. Suggest reagents to prove the presence of a keto group in the pregnin molecule.Write the reaction schemes.
5. Justify the possibility of quantitative analysis of estrogenic drugs using spectrophotometry.
6. What reactions can be used to distinguish pregnane from progesterone? Write the reaction schemes.
7. What reactions can distinguish methyltestosterone from testosterone propionate? What are these reactions based on? Write the reaction schemes.
8. Name the methods of quantitative determination of drugs from the group of androgens. What functional groups in androgen molecules can be used for this purpose?
9. Suggest reagents to prove the presence of a keto group in a moleculemethyltestosterone. Write the reaction schemes.
10. Justify the possibility of quantitative analysis of androgens using spectrophotometry.

4.5. Tasks:

1. Calculate the percentage content and evaluate the quality of ethinyl estradiol, if 6.7 ml of 0.1 M sodium hydroxide solution (C_a = 0.9900) was spent on the titration of a weight of ethinyl estradiol weighing 0.2033 g. 1 ml of 0.1 mol/l sodium hydroxide solution corresponds to 0.029641 g of ethinyl estradiol, which should be at least 98.0% in the preparation.
2. Calculate the specific rotation and evaluate the quality of progesterone, if a weight of the drug weighing 0.1250 g was dissolved in alcohol in a 25 ml volumetric flask. The average angle of rotation of the obtained solution is equal to +1.94°. The length of the cuvette is 20 cm. The specific rotation should be from +186° to + 196°.
3. Calculate the percentage content of sinestrol (M.w. 270.37) in the preparation, if 4.00 ml of 0.5 M caustic soda solution (C_a = 1.0100) was spent on the titration of a weight of 0.4590 g and the amount of titrant in the control experiment - 10.50 ml.
4. Calculate the gram content of sinestrol in the dosage form (0.001 g tablets of sinestrol, the average weight (P) is 0.100 g) if 0.3000 g of the powder of crushed tablets dissolved in alcohol, filtered and made up to a volume of 100 ml with the same solvent gives an optical density 0.393 on a spectrophotometer at a wavelength of 280 nm in a cuvette with a layer thickness of 10 mm.

Alcohol is used as a control experiment. In parallel, the optical density of the solution of the standard sample with a concentration of 0.00003 g in 1 ml is determined, which is equal to 0.402.

5. Calculate the weight of the ethinyl estradiol sample (M.w. 296.41), if 9.10 ml of 0.1 M sodium hydroxide solution (C_a = 0.9898) was spent on its titration, its percentage content in the preparation is 98.94%. weight loss during drying - 0.44%.
6. Calculate the volume of 0.1 M sodium hydroxide solution (C_a = 1.0000), which was used for the titration of 0.2198 g of ethinyl estradiol (M.w.296.41). The percentage content of ethinylestradiol in the preparation is 99.02%, the weight loss during drying is 0.56%.
7. Calculate the mass of sinestrol sample (M.w. 270.37), if 5.00 ml of 0.5 M sodium hydroxide solution (C_a = 1.0041) was spent on its titration, the titrant volume in the control experiment was 10.20 ml, percentage its content in the drug is 99.12%.
8. Calculate the volume of 0.5 M sodium hydroxide solution (C_a = 0.9986), which was used for the titration of 0.2452 gsinestrol (M.w. 270.37),the volume of the titrant in the control experiment is 12.20 ml. Percentage content sinestrol in the preparation - 98.89%.
9. Calculate the specific absorption index and evaluate the quality of pregnin, if a weight of the drug weighing 0.0744 g was dissolved in a 100 ml volumetric flask in methanol, 0.5 ml of the resulting solution was transferred to a 50 ml volumetric flask and brought up to the mark with methanol. Average opticsdensityof the obtained solution at 241 nm is 0.382, the thickness of the cuvette is 10 mm. The content of pregnin in the preparation is 99.66%. The specific absorption index should be 500-520.
10. Calculate the gram content of pregnin in the dosage form (pregnin tablets 0.01 g, the average weight (P) is 0.10 g), if 0.1020 g of the powder of crushed tablets, dissolved in alcohol when heated, filtered and adjusted to a volume of 100 ml with the same solvent, 5 ml of the filtrate was transferred to a 50 ml volumetric flask and the optical density was measured on a spectrophotometer at a wavelength of 241 nm in a cuvette with a layer thickness of 10 mm, which is equal to 0.52. As a control experiment, alcohol is used, the specific absorption index ($E_{1см}^{1\%}$)pregnane 520.
11. Calculate the specific rotation and evaluate the quality of methandrostenolone, if the average angle of rotation of a 1% solution of the drug in chloroform is + 0.12°. The length of the cuvette is 20 cm. The specific rotation should be from 0° to +5°.

12. Calculate the gram content of methylandrostenediol in tablets when determined by the gravimetric method, if it is known that the weight of the crushed tablets is 0.5006 g, which was mixed with water, filtered, the sediment was dissolved in alcohol, the alcohol was driven off, the sediment was dried to a constant weight. The mass of the weighing form is 0.0505 g, the loss in mass during drying is 1.98%. The average weight of the tablet is 0.25 g.
13. Calculate the value of the specific absorption index, if the optical density of a 0.001% solution of methyltestosterone in methyl alcohol at a wavelength of 240 nm in a cuvette with a layer thickness of 10 mm is equal to 0.525.
14. Calculate the gram content of methyltestosterone in the dosage form (tablets of methyltestosterone 0.005 g, the average weight (P) is 0.10 g), if 0.0509 g of powder of crushed tablets dissolved in alcohol, filtered and made up to a volume of 50 ml with the same solvent, 10 ml of the filtrate was transferred to a 50 ml volumetric flask and the optical density was measured on a spectrophotometer at a wavelength of 241 nm in a cuvette with a layer thickness of 10 mm, which is equal to 0.530. As a control experiment, alcohol is used, the specific absorption index ($E_{1см}^{1\%}$) of methyltestosterone 535.
15. .Calculate the specific rotation and evaluate the quality of testosterone propionate, if the average angle of rotation of a 1% solution of the drug in alcohol is + 1.8°. The length of the cuvette is 20 cm. The specific rotation should be from 87° + 90°.
16. .Calculate the percentage content of methandrostenolone (M.w. 300.44) in the preparation determined by the oxime method, if 6.74 ml of 0.1 M sodium hydroxide solution (C_a = 0.9968) was spent on the titration of a weight of 0.2038 g, the loss in dry weight - 0.62%.
17. Calculate the weight of methyltestosterone (M.w. 302.46), determined by the oxime method, if 8.10 ml of 0.1 M sodium hydroxide solution (C_a = 0.9958) was spent on its titration, its percentage content in the preparation is 99.44% ,. weight loss during drying -0.18%.
18. Calculate the volume of 0.1 M sodium hydroxide solution (C_a = 1.0000), which was used for the titration of 0.3008 g of methyltestosterone (M.w. 302.46), determined by the oxime method. The percentage content of methyltestosterone in the preparation is 99.87%, the weight loss during drying is 0.36%.
19. Calculate the content of testosterone propionate in a 0.001% alcohol solution of the drug, if opticaldensityof the investigated solution - 0.240, opticaldensityof a standard 0.001% solution is 0.245, measured on a spectrophotometer in a cuvette with a layer thickness of 10 mm.

20. Calculate the specific index and evaluate the quality of methyltestosterone if the average angle of rotation of a 1% solution of the drug in alcohol is + 0.80 o. The length of the cuvette is 10 cm. Loss in mass during drying is 0.98%. Specific rotation should be from + 82º to +85º.

5. LABORATORY WORK

During laboratory work it is necessary to strictly follow the safety rules in the chemical laboratory.

Each student individually carries out reactions of identification of samples of drug substances under the instruction of the teacher and draws up the test report.

LESSON No. 4

1.THEME: Final lesson on theory and practice on the topic: «Analysis of medicines of the hormones group. General characteristics, classification, relationship of structure with pharmacological action, extraction, methods of analysis, application».

2.PURPOSE: To form systematic knowledge and consolidate practical skills in the analysis of the quality of the hormones group and their semi- & synthetic derivatives using physical, physico-chemical and chemical methods of analysis.

3. TARGETS:

3.1. Check and consolidate theoretical knowledge and practical skills in the use of physical, physicochemical and chemical methods to analyse the quality of of the hormones group and their semi- & synthetic derivatives.

3.2. Check the protocols of laboratory work and analyze the correctness of the analysis of medicines of the hormones group and their semi- & synthetic derivatives in accordance with the requirements of the State Medical Research Institute, the Ministry of Health.

4. TASK FOR SELF-PREPARATION OF STUDENTS FOR THE FINAL LESSON

4.1. Control questions

1. General characteristics of hormones. Classification. The role of hormones in human and animal life. Sources of hormones.
2. Chemical structure, Latin name, synonyms of medicinal substances from the group of hormones.
3. Characterization of the physicochemical properties of drugs of this group, as well as justification of hormone identification methods, based on the characteristics of the chemical structure. Chemistry of reactions.
4. Thyroid hormones - thyroxine, thyroidin, levothyroxine and liothyronine sodium salts. Methods of obtaining, analysis and application in medicine. Indicate which qualitative reactions can be used to confirm the presence of organically bound halogen in the given preparations. Antithyroid drugs (mercazolil, methylthiouracil).
5. Medicinal products substituted with phenylethylamine derivatives: adrenaline hydrochloride and hydrotartrate, norepinephrine hydrotartrate, me-

saton, isoprenaline hydrochloride (izadrine), methyldopa (methyldopa), levodopa, etc. Methods of synthesis. Redox properties, the problem of stability, qualitative and quantitative analysis, features of application.

6. Hormones, polypeptides and proteins. Approaches to the analysis of the quality of this group of hormones. Insulins. Application and release form.
7. General characteristics of steroid hormones. Classification, role in the body.
8. Androgenic hormones: testosterone and its esters, methyltestosterone. Based on the structure, justify the analysis. Forms of release, application and storage. List reactions that may be common to androgenic and corticosteroid drugs.
9. Anabolic medicinal substances, derivatives of testosterone and 19-nortestosterone: methandrostenolone, methylandrostenediol, phenobolin, retabolil. Prerequisites for the creation of these drugs. Physico-chemical properties, analysis, release form, application. Biological role and significance for medicine.
10. Antiandrogens (cyproterone acetate, finasteride, flutamide). The relationship between structure and biological action.
11. Estrogenic hormones and their medicinal preparations: estradiol and its esters, estrone, ethinylestradiol and estriol. Obtaining, properties, analysis, release form and application.
12. Estrogenic drugs of non-steroidal structure: Sinestrol, diethylstilbestrol, dimestrol, sigetin and others. Obtaining, properties, analysis, release form and application. What structural features determine their estrogenic effect?
13. Progestogenic hormones and their medicinal preparations: progesterone, pregnin and others. Obtaining, properties, analysis, release form, application.
14. Combined estrogen-gestagen preparations (oral contraceptives) and prerequisites for their creation. Non-ovlon, Ovidon, Femodene, Tri-regol, Continuin, Postinor, etc. Application and release form.
15. Corticosteroids and their medicinal preparations. Mineralocorticosteroids (deoxycorticosterone acetate, spironolactone). Physico-chemical properties, analysis, release form, application. Biological role and significance for medicine.
16. Glucocorticosteroids that do not contain halogen atoms in the molecule: hydrocortisone acetate, cortisone acetate. Properties, analysis, release form, application. What structural fragment of the corticosteroid molecule determines their restorative properties? Show it on a concrete example by writing reaction equations.

17. Semi-synthetic analogues of hydrocortisone and cortisone - prednisone, prednisone, methylprednisolone and others. Properties, analysis, release form, application.
18. Halogen-containing analogues of prednisolone: dexamethasone, betamethasone dipropionate, triamcinolone, sinaflan, flumethasone, beclomethasone and others. Effect of halogen on pharmacological properties. Properties, analysis by functional groups, release form, application. Methods of introducing and determining the covalently bonded fluorine atom.
19. Antitumor hormonal means. Estrogenic drugs (chlorotrianisen, phosphestrol, estracite). Anti-estrogens (tamoxifene and klomiphen citrates). Progestogenic drugs (hestonoron caproate, medroxyprogesterone acetate). Inhibitors biosynthesis corticosteroids (khloditan, aminoglute-tymid). Connection between structure and biological action.
20. To justify the use of chemical and instrumental methods in the quantitative determination of medicinal substances and medicinal preparations of this group.
21. Explain the origin and definition of specific impurities:
    - adrenaline and norepinephrine in adrenaline tartrate;
    - liothyronine and other accompanying impurities in levothyroxine sodium salt;
    - levothyroxine and other concomitant impurities in liothyronine sodium salt.
    - concomitant impurities in hydrocortisone acetate, betamethasone dipropi-onate;
22. Assessment of biological activity of hormones.
23. Application of hormones and their synthetic analogues in medicine. Rela-tionship between structure and biological action in a number of hormones and their synthetic analogues. Ways of introduction into the body. Storage.

4.2. Test tasks for the final lesson

#

1) Indicate which method is recommended for the quantitative determination of thyroidin:

- permanganatometric
- iodochlormetric
- iodometric
- spectrophotometric
- acidimetric

#

2) In the control and analytical laboratory, in order to identify thyroidin, it was processed with the capture of transformation products. The blue color of the absorbent starch solution was observed. The method used was:

- burning
- oxidation
- mineralization
- alkaline hydrolysis
- acid hydrolysis

#

3) Specify the drugs whose amino acid derivatives are used in medical practice for insufficient thyroid gland function:

- alanine
- tyrosine
- methionine
- glycine
- tryptophan

#

4) What drug is used for hypofunction of the thyroid gland?

- thyroidin
- isadrin
- mercazolil
- norepinephrine
- adrenalin

#

5) What drug is used for hypofunction of the thyroid gland?

- norepinephrine
- isadrin
- mercazolil
- liothyronine sodium salt
- adrenalin

#

6) What drug is used for hyperfunction of the thyroid gland?

- triiodothyronine
- mercazolil
- isadrin
- adrenaline tartrate

#

7) What drug is used for hyperfunction of the thyroid gland?

- triiodothyronine
- thyroidin
- methylthiouracil
- adrenaline tartrate

#

8) Which of the following groups of compounds are part of thyroidin:

- thyroxine, tyrosine
- tyrosine, triiodothyronine
- thyroxine, triiodothyronine
- diiodotyrosine, thyroxine
- triiodothyronine, diiodotyrosine

#

9) The QCM for mercazolyl substance requires determining the loss in mass during drying. To do this, the analyst must dry the weight of the medicinal substance to a constant weight in the control and analytical laboratory. The analyst may consider constant mass to be achieved if the difference between the two following weighings does not exceed:

- 0.0005 g
- 0.01 g
- 0.007 g
- 0.00001 g
- 0.5 g

#

10) What is the pharmacological action of Mercazolil?

- analgesic
- anti-inflammatory
- antithyroid
- antipyretic
- antiseptic

#

11) Medicinal products containing the imidazole ring in their structure include:

- adrenalin
- diphenhydramine hydrochloride (diphenhydramine)
- metamizole sodium salt (Analgin)
- nitrofural (furacilin)
- mercazolil

#

12) Which of the listed methods is used for the quantitative determination of mercazolylum [Mercazolylum]:

- alkalimetry by proxy
- permanganatometry (reverse titer)
- acidimetry (direct titration)
- nitritometry
- complexonometry

#

13) Specify the pharmacopoeial preparation of thyroid hormones:

- liothyronine sodium salt

- mercazolil
- thyroidin

#

14) Specify the pharmacopoeial preparation of thyroid hormones:
- adrenalin
- levothyroxine sodium salt
- thyroidin

#

15) Thyroid hormones, which are included in the preparation of thyroidin - thyroxine and thyronine, are:
- levorotatory optical isomers
- dextrorotatory optical isomers
- racemates
- optically inactive substances

#

16) When thyroidin is heated with concentrated sulfuric acid, the following is observed:
- Release of violet vapors of iodine
- Yellow color of the solution
- Precipitation of a white crystalline precipitate, insoluble in nitric acid
- The release of ammonia is detected by the smell or by the turning of litmus paper

#

17) According to the requirements of the SPhU, the quantitative determination of levothyroxine and liothyronine sodium salts is carried out by the method:
- liquid chromatography
- non-aqueous titration in the medium of a protogenic solvent
- non-aqueous titration in the medium of a protophilic solvent
- Kjeldahl
- alkalimetry in an aqueous medium

#

18) According to the requirements of the SPhU, a specific impurity is determined in the preparation of levothyroxine sodium salt:
- liothyronine and related impurities
- 3,5-diiodotyrosine and related impurities
- tyrosine
- thyronine

#

19) According to the requirements of the SPhU, a specific impurity is determined in the preparation of liothyronine sodium salt:
- levothyroxine and related impurities
- 3,5-diiotyrosine and related impurities

- tyrosine
- thyronine

#

20) One of the express methods of determining covalently bound iodine in the structure of thyroid hormones (levothyroxine and liothyronine sodium salts, thyroidin) is to introduce several grains of the drug into the colorless flame of the burner, which turns bluish-green. This method is called:

- Belshtein tests.
- hydroxam sample
- lignin sample
- Van Urck reactions
- Zincke reactions

#

21) The content of organically bound iodine in thyroidin, according to the requirements of the SPhU, should be within the limits of:

- 0.17-0.23%
- 17.0-23.0%
- 8.6-9.1%
- 4.0-5.0%
- 10.5-11.5%

#

22) One of the non-pharmacopoeial methods of quantitative determination of thyroidin is the determination of organically bound iodine in the preparation by the combustion method. Iodine is connected to the organic part of the molecule, while oxidizing:

- oxygen
- chloramine
- potassium dichromate
- chlorine
- a mixture of one volume of nitric acid and three volumes of hydrochloric acid

#

23) The SPhU regulates the content of chloride impurities in liothyronine sodium salt in terms of NaCl and dry matter (no more than 2%). Specify the method by which this impurity is determined:

- direct argentometry with potentiometric termination
- Moreau's method
- Folgard's method
- Fayance method
- mercurometry

#

24) The general method of identification of thyroid hormone preparations (levothyroxine and liothyronine sodium salts) is the reaction to naturalα- amino acids. At the same time, the reagent is used:

- ninhydrin
- bromine water
- alkaline solution of hydroxylamine hydrochloric acid
- sodium nitrite solution, hydrochloric acid, followed by the addition of an alkaline solution of β-naphthol
- hydrogen peroxide solution, sulfuric acid

#

25) In the control and analytical laboratory, it is necessary to conduct an analysis of thyroidin - a drug from the group of thyroid hormones. When identifying it, the analyst must react to:

- nitro group
- aromatic amino group
- organically bound iodine
- ester group
- steroid cycle

#

26) Thyroidin analysis is performed in the laboratory of the State Inspection for Quality Control of Medicines. After boiling it with a solution of sodium hydroxide, a yellow color is formed, which disappears when dilute sulfuric acid is added, which is also accompanied by the precipitation of a colloidal precipitate. This test confirms the presence of thyroidin:

- carboxyl group
- amide group
- molecular iodine
- squirrel
- phenolic hydroxyl

#

27) The starting material for obtaining mercazolil is:

- ethanol
- glycerin
- tyrosine
- 3,5-diiodotyrosine
- picric acid (2,4,6-trinitrophenol)

#

28) Mercazolil, a drug from the group of antithyroid drugs, must be analyzed in a control and analytical laboratory. When identifying it, the analyst must perform a reaction with:

- silver nitrate
- sodium nitrite and hydrochloric acid
- concentrated sulfuric acid

- potassium dichromate and sulfuric acid
- sodium acetate

#

29) According to the value of the specific rotation, they analyze:
- anesthesin
- Mercazolil
- thyroidin
- sodium benzoate

#

30) Epinephrine and norepinephrine are hormones of the medulla of the adrenal glands. Common for these hormones is an identification reaction with a reagent:
- iodine solution
- sulfuric acid
- hydrochloric acid
- sodium hydroxide
- iron (III) chloride

#

31) Quantitative analysis of adrenaline tartrate is carried out in the control and analytical laboratory. According to the requirements of the SPhU, the method of quantitative determination is used:
- reverse bromatometry
- acidimetry in an aqueous medium
- acidimetry in acetic acid
- substitute iodometry
- alkalimetry in a non-aqueous medium

#

32) A pharmacist-analyst conducts an express analysis of eye drops containing adrenaline hydrotartrate. After adding a solution of iron (III) chloride, an emerald-green color appeared, which indicates the presence of adrenaline in the molecule:
- phenolic hydroxyl groups
- aldehyde groups
- aromatic amino groups
- ester groups

#

33) You can distinguish adrenaline hydrotartrate from norepinephrine hydrotartrate by:
- oxidation reactions at different pH values
- reaction with a solution of iron (III) chloride
- solubility in water
- reactions with general alkaloid reagents

#

34) To identify the hydrotartrate ion in the hydrotartrate adrenaline molecule, the pharmacist-analyst used potassium chloride as the main reagent. A positive result should be considered:

- precipitation of a white precipitate
- the appearance of a red color
- release of gas bubbles
- the appearance of a characteristic smell

#

35) The pharmacist-analyst determines the quantitative content of adrenaline tartrate in accordance with the requirements of the SPhU, by the method of acid-base titration in a non-aqueous medium. As a titrant, he uses a solution:

- perchloric acid
- hydrochloric acid
- sodium hydroxide
- sodium methylate

#

36) Sodium metabisulfite as an antioxidant is used to stabilize injection solutions

- glucose
- insulin
- adrenaline hydrochloride
- morphine hydrochloride
- novocaine

#

37) Injectable solutions are not subjected to thermal sterilization:

- glucose
- hexamethylenetetramine
- adrenaline hydrotartrate
- novocaine hydrochloride

#

38) Due to which groups in the structure of adrenaline hydrotartrate, the main properties are expressed:

- primary aliphatic amino group
- secondary aliphatic amino group
- primary aromatic amino group
- secondary aromatic amino group
- amide group

#

39) The natural metabolite of the body is:

- dopamine
- isadrin
- ephedrine

- salbutamol
- adrenalin

#

40) Which of the following drugs is a naturally occurring catecholamine?

- adrenalin
- isadrin
- ephedrine
- chloramphenicol
- methyldopa

#

41) What derivative of phenylalkylamine is used in medicine as a hormonal agent?

- isadrin
- anaprilin
- adrenaline hydrotartrate
- hexamethylenetetramine
- Mercazolil

#

42) Medicinal product, which is characterized by a reaction with iron (III) chloride:

- adrenaline hydrotartrate
- procaine hydrochloride
- magnesium oxide
- diphenhydramine
- anesthesin

#

43) Is an α-amino alcohol:

- adrenalin
- levodopa
- anesthesin
- diiodotyrosine
- liothyronine

#

44) Specify the pharmacopoeial drug that has an adrenomimetic effect:

- adrenaline tartrate
- dibazole
- anesthesin
- methyldopa
- mesatone

#

45) Catecholamine drugs have the following properties:

- amphoteric
- sour

- the main ones

#

46) Specify the starting compound for the synthesis of adrenaline and norepinephrine:

- pyrocatechin
- glycerin
- benzene
- 3,5-diiodotyrosine
- picric acid (2,4,6-trinitrophenol)

#

47) Indicate by which method, in accordance with the requirements of the SPhU, the determination of the specific admixture of adrenaline in the preparation of adrenaline tartrate is carried out:

- photometrically
- polarimetric
- chromatographically
- by reaction with iron (III) chloride
- not conducted

#

48) Indicate the method by which, in accordance with the requirements of the SPhU, the specific admixture of norepinephrine in the adrenaline tartrate preparation is determined:

- by the method of thin-layer chromatography
- photometrically
- polarimetric
- by reaction with iron (III) chloride
- not conducted

#

49) According to the SPhU, to identify the substance adrenaline tartrate, the reaction of the formation of adrenochrome at pH 3.56 with a solution is used:

- sodium nitroprusside
- iron (III) chloride
- ninhydrin
- iodine
- glyoxalhydroxyanil

#

50) One of the substances is used as a starting point in the synthesis of cortisone acetate. Specify it:

- β-picoline
- progesterone
- salt pot
- thyroxine

- anethole

#

51) One of the above reagents is specific for proving the presence of a steroid cycle in hormones. Specify it:

- concentrated hydrochloric acid

Г. concentrated sulfuric acid

Д. Fehling's reagent

Е. hydroxylamine solution

- 2,4-dinitrophenylhydrazine

#

52) One of the above methods can be rationally used for quantitative determination of prednisolone. Specify it:

- acidimetric
- spectrophotometric
- iodometric
- fluorimetric
- permanganatometric

#

53) Specify the pharmacological effect most characteristic of synthetic analogues of prednisolone, which have a fluorine atom in the 6th and 9th positions in the molecule:

- anabolic
- analgesic
- antiphlogistic
- antioxidant
- cytostatic

#

54) One of these drugs belongs to corticosteroids and is included in DFU. Specify it:

- levothyroxine sodium salt
- testosterone propionate
- progesterone
- hydrocortisone acetate
- deoxycorticosterone acetate

#

55) One of the above methods can be rationally used for the quantitative determination of a solution of deoxycorticosterone acetate in oil. Specify it:

- spectrophotometric
- fluorimetric
- acidimetry in non-aqueous solvents
- gravimetric
- acidimetric

#

56) One of the above drugs has in the moleculeα-keto group, which is analytically confirmed by Fehling's reagent. Specify this drug:

- methyltestosterone
- deoxycorticosterone acetate
- diethylstilbestrol propionate
- methandrostenolone
- levothyroxine sodium salt

#

57) One of these substances is the starting point in the synthesis of deoxycorticosterone acetate. Specify it:

- folic acid
- anethole
- diosgenin
- β-picoline
- *p*- nitrotoluene

#

58) On the basis of one of these hormones, its synthetic analogue - prednisone - was obtained. Specify this hormone:

- hydrocortisone
- deoxycorticosterone
- testosterone
- estradiol
- progesterone

#

59) One of the listed drugs belongs to synthetic analogues of prednisolone and contains a fluorine atom in the steroid cycle. Specify it:

- phenobolin
- betamethasone dipropionate
- Dimestrol
- pregnane
- hydrocortisone acetate

#

60) One of the listed reagents is used in the pharmacopoeial analysis to prove the presenceα-ketol group in corticosteroids. Specify it:

- concentrated sulfuric acid
- Fehling's reagent
- sodium nitrite solution
- 2,4-dinitrophenylhydrazine solution
- sodium edetate solution

#

61) One of the following names corresponds to the steroid cycle, which is part of the corticosteroid hormones. Specify it:

- pregnane

- TV show
- eicosan
- cholestane
- androstane

#

62) One of the listed hormonal preparations has restorative properties and gives a positive reaction with Fehling's reagent. Specify it:

- retabolil
- liothyronine sodium salt
- octestrol
- cortisone
- methandrostenediol

#

63) Oxidizing-reducing properties of prednisone are due to the presence of:

- steroid cycle
- ketogroups
- α-ketoenol group
- ester group
- ethynyl group

#

64) What optical isomer is prednisolone:

- right-handed
- left-handed
- racemate

#

65) Cortisone can be distinguished from prednisolone:

- by reaction with an ammonia solution of silver nitrate
- by UV spectra
- by reaction with Fehling's reagent
- by reaction with sodium acetate

#

66) Cortisone can be distinguished from prednisolone:

- by reaction with an ammonia solution of silver nitrate
- by reaction with sodium nitrite in a hydrochloric acid environment
- by reaction with Fehling's reagent
- by reactionwith 2,4-dinitrophenylhydrazine

#

67) The presence of a keto group in prednisone is confirmed by the reaction:

- formation of esters
- hydroxam test
- with concentrated sulfuric acid

- with Fehling's reagent
- formation of hydrazones

#

68) When identifying deoxycorticosterone acetate, the drug is dissolved in concentrated sulfuric acid, resulting in a cherry color with greenish-brown fluorescence. With the help of this reaction, identify:
- keto group in position 3 of the steroid cycle
- steroid cycle
- dioxyacetone group
- ester group in position 21 of the steroid cycle

#

69) In the control and analytical laboratory, the identification of glucocorticoid hormones: prednisone and hydrocortisone acetate is carried out using the identification reaction for the dioxyacetone group. As a reagent, use:
- phenylhydrazine sulfate
- concentrated sulfuric acid
- sodium hydroxide solution
- Fehling's reagent
- Wagner reagent

#

70) In the control and analytical laboratory, identification of steroid hormones is carried out, which have hydroxyl groups in positions 3 and 17 of the steroid cycle. The reaction of the formation of complex esters is used, for which the following are determined:
- specific optical rotation
- refractive index
- specific absorption index
- the shape of the crystals
- melting point

#

71) The identification of steroid hormones and their synthetic analogues, which contain an ester group (acetates, propionates), is carried out. For this, the reaction is used:
- hydroxam sample
- murexide sample
- thalleiochin sample
- with sodium acetate
- with ninhydrin

#

72) Cortisone interacts with hydroxylamine due to the presence in the structure:
- steroid cycle

- keto group in the third position
- α-ketol group
- alcohol hydroxyl

#

73) The hydroxam sample can be used in the analysis of:
- ethyl alcohol
- dexamethasone
- doxa
- pregnane
- triamcinolone

#

74) Identifying cortisone acetate, a control and analytical laboratory specialist conducts a reaction with phenylhydrazine. The appearance of a yellow color confirms the presence in the molecule:
- ketogroups
- steroid cycle
- ester group
- β-ketol group

- #

75) α-Ketol group in the structure of corticosteroids reveals:
- amphoteric properties
- basic properties
- regenerative properties
- oxidizing properties

#

76) Corticosteroids react with Fehling's reagent to form:
- blue sediment
- red sediment
- red solution
- do not react with Fehling's reagent

#

77) Corticosteroids when interacting with silver nitrate solution form:
- black precipitate in an ammonia medium
- white precipitate in a nitric acid environment
- black precipitate in a nitric acid environment
- white precipitate in an ammonia medium

#

78) When halogens are introduced into the C6 and C9 positions of steroid compounds, the following occurs:
- solubility in organic solvents improves
- solubility in water improves
- increasing the activity of drugs
- side effects increase

#

79) The structure of steroid hormones is based on the cyclopentaneperhydrophenanthrene skeleton. Based on this, the general reaction to all steroid hormones and their synthetic analogues is a reaction with acid:

- concentrated sulfate
- diluted sulfate
- concentrated hydrogen chloride
- diluted hydrogen chloride
- concentrated nitrate

#

80) Specify the pharmacopoeial drug from the group of halogen-containing semi-synthetic analogues of corticosteroid hormones:

- betamethasone dipropionate
- triamcinolone
- beclomethasone
- dexamethasone
- sinaflan

#

81) Ester groups in steroid molecules are detected using the reaction:

- esterification
- formation of hydrazones
- hydroxam sample
- murexide sample

#

82) The identification of steroid hormones and their synthetic analogues, which contain an ester group (acetates, propionates), is carried out. For this, the reaction is used:

- hydroxam sample
- murexide sample
- thalleiochin sample
- with sodium acetate
- with ninhydrin

#

83) The structure of steroid hormones is based on the cyclopentaneperhydrophenanthrene skeleton. Based on this, the general reaction to all steroid hormones and their synthetic analogues is a reaction with acid:

- concentrated sulfate
- diluted sulfate
- concentrated hydrogen chloride
- diluted hydrogen chloride
- concentrated nitrate

#

84) One of these drugs is an estrogen hormone. Specify it:

- testosterone propionate
- methylandrostenediol
- ethinylestradiol
- pregnane
- progesterone

#

85) One of the listed hormonal preparations corresponds to the following chemical name 17-α-ethynylestratriene-1,3,5(10)-diol-3,17β. Specify it:

- sinestrol
- progesterone
- ethinylestradiol
- prednisone
- methyltestosterone

#

86) One of the above preparations gives a positive reaction to phenolic hydroxyl with a solution of ferric ammonium alums. Specify it:

- pregnane
- methandrostenolone
- ethinylestradiol
- hydrocortisone acetate
- prednisone

#

87) Ethinyl estradiol dissolves in sodium hydroxide solution due to the presence in its structure:

- steroid cycle
- methyl group
- phenolic hydroxyl
- alcohol hydroxyl

#

88) Estrogenic hormones are steroids by chemical structure. A feature of their structure compared to other hormones is the presence of an aromatic ring with a substituent:

- keto group in position 3
- phenolic hydroxyl in position 2
- phenolic hydroxyl in position 3
- keto group in position 2
- methyl group in position 2

#

89) Estradiol dipropionate belongs to the group of estrogen hormones. Quantitative determination of this hormone by the method of alkalimetry (back titration) includes carrying out the reaction:

- saponification
- oxidation-reduction

- condensation
- esterification
- decomposition

#

90) Ethinylestradiol is part of combined oral hormonal contraceptives. Quantitative determination of this hormone in medicinal products is carried out by the method:
- Alkalimetry in the water environment
- Alkalimetry by deputy
- Alkalimetry in a non-aqueous environment
- Acidimetry in a non-aqueous environment
- Argentometry according to Folgard

#

91) The main source of synthesis of estrogenic hormones is:
- β-naphthol
- folic acid
- cholesterol
- bile acid

#

92) The method of indirect neutralization is used for the quantitative determination of:
- estrone
- ethinylestradiol
- estradiol
- estriol

#

93) To identify estrogenic hormone preparations, a reaction with:
- iron (III) chloride solution
- alcohol solution of ninhydrin
- ammonia solution
- hydrogen peroxide solution
- phosphoric acid

#

94) Specify the natural estrogen hormone:
- estriol
- testosterone
- sinestrol
- progesterone

#

95) In the quantitative determination of ethinyl estradiol by the method of indirect neutralization, the titrant is used:
- titrated solution of nitric acid
- titrated solution of silver nitrate

- titrated solution of hydrochloric acid
- titrated sodium hydroxide solution

#

96) One of the listed hormones belongs to non-steroidal estrogenic drugs and is a derivative of diphenylethane. Specify it:

- progesterone
- liothyronine sodium salt
- sinestrol
- prednisone
- retabolil

#

97) One of the above methods can be rationally used for the quantitative determination of progesterone. Specify it:

- gravimetry
- acidimetry
- cerimetry
- acidimetry in non-aqueous solvents
- argentometry

#

98) One of the following names corresponds to the steroid cycle, which is part of female (gestogens) sex hormones. Specify it:

- pregnane
- TV show
- eicosan
- cholestane
- androstane

#

99) Hormones of the corpus luteum are called progestogen hormones. They include:

- progesterone and testosterone
- progesterone and pregnane
- testosterone and pregnane
- phenobolin and testosterone
- phenobolin and pregnin

#

100) Progesterone and pregnin belong to steroid hormones. When identifying the steroid cycle, the substance is added to the solution:

- concentrated nitric acid and water
- concentrated hydrochloric acid
- water and acetic acid
- concentrated sulfuric acid and water
- water and nitric acid

#

101) Natural progestin hormone:

- postinor
- progesterone
- norethisterone
- mestranol

#

102) The method of indirect neutralization is used for quantitative determination

- progesterone and ethinylestradiol
- estradiol dipropionate and ethinylestradiol
- postinor and ethinylestradiol
- there is no right answer

#

103) For one of the medicinal substances, it is possible to carry out the acid-base titration method after carrying out the acylation reaction. Specify it:

- testosterone propionate
- diethylstilbestrol propionate
- sigetin
- hydrocortisone acetate
- sinestrol

#

104) One of the above substances is the starting point in the synthesis of sinestrol. Specify it:

- anethole
- citral
- diosgenin
- cholesterol
- salt pot

#

105) Indicate which of the listed drugs corresponds to the international name "Hexestrolum":

- octestrol
- progesterone
- ethinylestradiol
- sinestrol
- testosterone propionate

#

106) Indicate which method is recommended for quantitative determination of sinestrol after the acylation reaction:

- alkalimetry
- photoelectrocolorimetry
- cerimetry
- iodometry

- acidimetry in non-aqueous solvents

#

107) Synthetic estrogenic compounds sinestrol and diethylstilbestrol are used in medical practice for the treatment of:

- hypothyroidism
- thyrotoxicosis
- malignant neoplasms
- allergies
- rheumatism

#

108) Medicinal substances that have an estrogenic effect, the molecules of which do not include the steroid cycle, include:

- ethinylestradiol and diethylstilbestrol
- estradiol and diethylstilbestrol
- estradiol and sinestrol
- sinestrol and diethylstilbestrol
- estradiol and ethinylestradiol

#

109) The determination of the quantitative content of sinestrol in the oil solution of the drug, after extraction of the active substance with an aqueous solution of sodium hydroxide, is carried out by a specialist of the State Inspection for Quality Control of Medicines using the following method:

- acidimetry
- nitritometry
- bromatometry
- alkalimetry

#

110) Indicate which drug is used to identify the azo dye formation reaction:

- phenobolin
- retabolil
- ethinylestradiol
- testosterone propionate
- prednisone

#

111) One of the above reagents is specific for proving the presence of a steroid cycle in hormones. Specify it:

- concentrated hydrochloric acid
- concentrated sulfuric acid
- Fehling's reagent
- Hydroxylamine solution
- 2,4-dinitrophenylhydrazine

#

112) One of these drugs is a derivative of 19-nortestosterone and belongs to anabolic steroids. Specify it:

- methyltestosterone
- betamethasone dipropionate
- retabolil
- deoxycorticosterone acetate
- ethinylestradiol

#

113) One of the following names corresponds to the steroid cycle, which is part of the male sex hormones. Specify it:

- pregnane
- TV show
- eicosan
- cholestane
- androstane

#

114) Indicate which method of quantitative determination is the most rational to use for an oil solution of testosterone propionate:

- acidimetric
- spectrophotometric
- acidimetry in non-aqueous solvents
- polarimetric
- bromatometric

#

115) One of the listed drugs belongs to androgenic hormones. Specify it:

- pregnane
- dexamethasone
- methylandrostenediol
- testosterone propionate
- ethinylestradiol

#

116) One of the listed medicinal substances gives a positive reaction with a solution of 2,4-dinitrophenylhydrazine (orange-red precipitate). Specify it:

- levothyroxine sodium salt
- potassium orotate
- methandrostenolone
- adrenaline hydrotartrate
- ethinylestradiol

#

117) One of the above pharmacological actions is characteristic of the drug retabolil. Specify it:

- anti-inflammatory
- progestogenic

- anabolic
- estrogenic
- cytostatic

#

118) The presence of alcohol hydroxyl in methyltestosterone is confirmed by the reaction:
- formation of esters
- hydroxam test
- formation of hydrazones
- with Fehling's reagent
- oxime formation

#

119) Male gonads produce androgen hormones, which include:
- testosterone
- phenobolin
- methylandrostenediol
- progesterone
- pregnane

#

120) One of the ways to identify the androgenic hormone testosterone propionate is to determine the melting point of testosterone oxime obtained from testosterone propionate as a result of:
- alkaline hydrolysis
- acid hydrolysis
- mineralization
- dissolution in concentrated sulfuric acid
- interactions with hydroxylamine

#

121) It is a derivative of androstane
- cortisone acetate
- pregnane
- testosterone propionate

B. ethinylestradiol

Г. dexamethasone

#

122) The effect of testosterone becomes longer after:
- halogenation with fluorine
- esterification with fatty acids
- oxidation of the α-ketol group
- there is no correct option

#

123) Ester groups in steroid molecules are detected using the reaction:
- esterification

- formation of hydrazones
- hydroxam sample
- murexide sample

#

124) A semi-synthetic derivative of androgenic hormones is:
- methyltestosterone
- androstane
- dehydroandrosterone
- testosterone

#

125) Testosterone propionate upon interaction with hydroxylamine forms an oxime, which is identified by:
- specific rotation
- melting point
- characteristic color
- characteristic smell

#

126) Anabolic steroids include methylandrostenediol. To determine its content in the medicinal product, the following method is used:
- acid-base titration
- polarimetry
- refractometry
- gravimetry
- spectrophotometry

4.3. Situational tasks:

1. Specify the characteristic reactions that can be used in the analysis of adrenaline tartrate and norepinephrine hydrotartrate. Justify your answer and illustrate the chemistry of the reactions.
2. Give examples of chemical reactions that confirm that adrenaline tartrate, mesaton, and isadrin are salts of nitrogenous bases.
3. Describe possible methods for quantitative determination of adrenaline tartrate. Give a rationale for using the methods. Write the reaction equations.
4. Describe possible methods for quantitative determination of levodopa. Give a rationale for using the methods. Write the reaction equations.
5. Explain whether the general identification reaction for tartrates with resorcinol in concentrated sulfuric acid can be used to reveal the tartrate in adrenaline tartrate.
6. Justify the possibility of using the iodometric titration method for the quantitative determination of drugs that stimulate the function of the thyroid gland (sodium salts of levothyroxine and liothyronine). Give the reaction equations and the formula for calculating the quantitative content.
7. Suggest methods for proving the presence of covalently bound halogen in thyroid preparations.

8. State the biochemical prerequisites for the creation of drugs from the phenylalkylamine group based on the metabolism of the amino acid tyrosine.
9. Suggest reagents to prove the presence of an alpha-ketol group in the hydrocortisone molecule.Write the chemistry of reactions.
10. Justify the possibility of quantitative analysis of corticosteroids using spectrophotometry.
11. Suggest reactions for the identification of deoxycorticosterone acetate by functional assay.
12. Name the functional groups present in the structure of cortisone acetate. Where possible, give the equations and indicate the conditions for the reactions that confirm their presence.
13. Name the main functional groups of corticosteroids used to identify these drugs. What physical and physicochemical properties are used in the analysis of corticosteroids?
14. What reactions can be used to confirm the presence of a carbonyl group in the 3rd position of corticosteroids? What is the basis of the use of these reactions for the identification of medicinal products?
15. What are the ways to convert a covalently bonded halogen into an ionogenic state?
16. What reactions can be used to confirm the presence of organically bound Fluorine in the dexamethasone molecule?
17. Suggest identification reactions of prednisone using functional analysis.
18. What reaction can distinguish diethylstilbestrol propionate from diethylstilbestrol? Write the reaction diagrams.
19. Describe the bromatometric method of quantitative determination of medicinal substances using sinestrol as an example. Give the reaction equations and the formula for calculating the quantitative content.
20. Describe the acetylation method for quantitative determination of diethylstilbestrol. Give the reaction equations and the formula for calculating the quantitative content.
21. Suggest reagents to prove the presence of a keto group in the pregnin molecule.Write the reaction schemes.
22. Justify the possibility of quantitative analysis of estrogenic drugs using spectrophotometry.
23. What reactions can be used to distinguish pregnane from progesterone? Write the reaction schemes.
24. What reactions can distinguish methyltestosterone from testosterone propionate? What are these reactions based on? Write the reaction schemes.
25. Name the methods of quantitative determination of drugs from the group of androgens. What functional groups in androgen molecules can be used for this purpose?
26. Suggest reagents to prove the presence of a keto group in a moleculemethyltestosterone. Write the reaction schemes.
27. Justify the possibility of quantitative analysis of androgens using spectrophotometry.

4.4. Tasks:

1. Calculate the mass of a test of norepinephrine hydrotartrate (M.w. 337.29), if 4.95 ml of a 0.1 M solution of perchloric acid (C_a = 1.0030) was spent on its titration, its percentage content in the preparation is 99.5%, the percentage of water is 5% and the volume of the titrant in the control experiment is 0.30 ml.
2. Determine the mass fraction of adrenaline hydrotartrate (M.w. 333.30) in the medicinal product, if 5.04 ml of 0.1 M perchloric acid solution was spent on the titration of 0.1685 g of adrenaline hydrotartrate (C_a = 1.0004).
3. Calculate the volume interval of 0.01 M sodium thiosulfate solution (C_a = 1.0000), which will ensure the quality of thyroidin in quantitative determination by the unified iodometric method, if the weight of the drug is 0.5000 g, and the iodine content in it should be from 0.17% to 0.23%. 1 ml of 0.01 M sodium thiosulfate solution corresponds to 0.0002115 g of I.
4. Calculate the content of epinephrine (adrenaline tartrate) in the injection solution, if 5 ml of the drug is diluted with water in a 100 ml volumetric flask. Iron-citrate reagent is added to 10 ml of the obtained solution and the value of the optical density is determined on a spectrophotometer in a cuvette with a layer thickness of 10 mm. The optical density of the standard solution is 0.245, the optical density of the test solution is 0.240. 1 ml of standard sample solution contains 0.00091 g of epinephrine (adrenaline tartrate). The content of medicinal substances in 1 ml of solution for injection should be from 0.0016 to 0.0020 g.
5. Justify the pharmacopoeial method of quantitative determination of adrenaline tartrate in a substance. Make a conclusion about the quality, if 6.20 ml of titrant (0.1 mol/l) with C_a = 1.0000 was consumed during titration of 0.2025 g of medicinal substance. The content of epinephrine (adrenaline tartrate) should be from 98.5% to 101.0%. M.w. epinephrine (adrenaline tartrate) 333.30.
6. Justify the non-aqueous titration method for the quantitative determination of methyldopa (methyldopa) in a substance. What a daremedicinal substance should be taken so that 11.85 ml of a titrant solution (0.1 mol / l) with C_a = 1.0000 is spent on titration? The content of methyldopa (methyldopa) in the drug is 98.8%. M.w. methyldopa (methyldopa) 211.21.
7. Calculate the percentage of mesatone (M.w. 203.67) in the preparation, if 16.10 ml of 0.1 M sodium thiosulfate solution (C_a = 1.0000) was spent on the titration of a weight of 0.1120 g, the loss in weight during drying - 0.5% and the volume of the titrant in the control experiment - 48.50 ml.

8. Calculate the distance from the starting line to the center of the methylthiouracil spot if Rf = 0.82 and the distance traveled by the solvent is 10.0.
9. Calculate the volume of a 0.1 M solution of perchloric acid (C_a = 1.0009), which was spent on the titration of 0.1598 g of mesatone (M.w. 203.67). The percentage content of mesatone in the preparation is 98.64%, the weight loss during drying is 0.52%, and the titrant volume in the control experiment is 0.12 ml.
10. Calculate the percentage content of mercazolil (M.w. 114.17) in the preparation, if 8.64 ml of 0.1 M sodium hydroxide solution (C_a = 1.0000) was spent on the titration of a weight of 0.1009 g, the loss in weight during drying is 0 , 48%.
11. Calculate the weight of mercazolil measurement (M.w. 114.17), if 10.20 ml of 0.1 M sodium hydroxide solution (C_a = 1.0015) was spent on its titration, its percentage content in the preparation is 99.21%.
12. Calculate the value of the specific absorption index, if opticaldensity 0.001% solution of prednisolone in methyl alcohol at a wavelength of 242 nm in a cuvette with a layer thickness of 10 mm is equal to 0.705.
13. Calculate the volume of 0.1 M sodium hydroxide solution (C_a = 1.0013), which was used for the titration of 0.2018 g of cortisone acetate (M.w. 402.5), determined by the oxime method. The percentage content of cortisone acetate in the preparation is 99.64%, the weight loss during drying is 0.42%.
14. Calculate the specific rotation and evaluate the quality of hydrocortisone acetate, if a weight of the drug weighing 0.4973 g was dissolved in dioxane in a 50 ml volumetric flask. The average angle of rotation of the obtained solution is equal to + 3.22°. The length of the cuvette is 2 dm. Specific rotation should be from +158° to + 167°.
15. Calculate the specific absorption index and evaluate the quality of cortisone acetate, if a weight of the drug weighing 0.0805 g was dissolved in a 100 ml volumetric flask, 1 ml of this solution was transferred to a 50 ml volumetric flask and brought up to the mark with ethanol. Average opticsdensityof the obtained solution at 238 nm is 0.483, the thickness of the cuvette is 10 mm. The content of cortisone acetate in the preparation is 99.1%. The specific absorption index should be 380-400
16. Calculate the percentage content of hydrocortisone acetate (M.w. 404.5) in the preparation determined by the oxime method, if 5.08 ml of 0.1 M sodium hydroxide solution (C_a = 1.0003) was spent on the titration of a weight of 0.2056 g.
17. Calculate the specific absorption index and evaluate the quality of prednisolone, if a weight of the drug weighing 0.1184 g was dissolved in a 100 ml volumetric flask in methanol, 0.5 ml of the resulting solution was transferred to a 50 ml volumetric flask and brought up to the mark with methanol. Aver-

age optics densityof the obtained solution at 242 nm is 0.482, the thickness of the cuvette is 10 mm. The content of prednisolone in the drug is 98.76%. The specific absorption index should be 400-430.

18. Calculate the quantitative content and evaluate the quality of prednisolone, if a weight of the drug weighing 0.1037 g was dissolved in a 100 ml volumetric flask in ethanol. 1 ml of this solution was transferred to a 100 ml volumetric flask and made up to the mark with ethanol. Average optics density at 242 nm is 0.483, the thickness of the cuvette is 10 mm. The specific absorption index is 460. The content of prednisolone in the drug should be at least 98.5%.
19. Calculate the weight of hydrocortisone acetate (M.w.404.5), determined by the method of acid-base titration by substitution, if 10.8 ml of 0.1 M hydrochloric acid solution (C_a = 1.0005) was spent on its titration, the percentage its content in the drug is 98.22%.
20. Calculate the specific absorbance and rate the quality of deoxycorticosterone acetate if the mean opticaldensity, measured on a spectrophotometer at 240 nm with a cuvette thickness of 10 mm, 0.001% solution equals 0.443. The specific absorption index should be from 440 to 450.
21. Calculate the gram content of prednisolone in the dosage form (prednisone tablets 0.001 g, average weight (P) equal to 0.042 g), if 0.075 g of powder of crushed tablets, dissolved in alcohol when heated, filtered and made up to a volume of 100 ml with the same solvent, give an opticaldensityon a spectrophotometer at a wavelength of 239 nm in a cuvette with a layer thickness of 1 cm is 0.78. As a control experiment, alcohol is used, the specific absorption index ($E_{1см}^{1\%}$) of prednisolone 432.
22. Calculate the percentage content and evaluate the quality of ethinyl estradiol, if 6.7 ml of 0.1 M sodium hydroxide solution (C_a = 0.9900) was spent on the titration of a weight of ethinyl estradiol weighing 0.2033 g. 1 ml of 0.1 mol/l sodium hydroxide solution corresponds to 0.029641 g of ethinyl estradiol, which should be at least 98.0% in the preparation.
23. Calculate the specific rotation and evaluate the quality of progesterone, if a weight of the drug weighing 0.1250 g was dissolved in alcohol in a 25 ml volumetric flask. The average angle of rotation of the obtained solution is equal to +1.94°. The length of the cuvette is 20 cm. The specific rotation should be from +186° to + 196°.
24. Calculate the percentage content of sinestrol (M.w. 270.37) in the preparation, if 4.00 ml of 0.5 M caustic soda solution (C_a = 1.0100) was spent on the titration of a weight of 0.4590 g and the amount of titrant in the control experiment - 10.50 ml.

25. Calculate the gram content of sinestrol in the dosage form (0.001 g tablets of sinestrol, the average weight (P) is 0.100 g) if 0.3000 g of the powder of crushed tablets dissolved in alcohol, filtered and made up to a volume of 100 ml with the same solvent gives an optical density 0.393 on a spectrophotometer at a wavelength of 280 nm in a cuvette with a layer thickness of 10 mm. Alcohol is used as a control experiment. In parallel, the optical density of the solution of the standard sample with a concentration of 0.00003 g in 1 ml is determined, which is equal to 0.402.
26. Calculate the weight of the ethinyl estradiol sample (M.w. 296.41), if 9.10 ml of 0.1 M sodium hydroxide solution (C_a = 0.9898) was spent on its titration, its percentage content in the preparation is 98.94%. weight loss during drying - 0.44%.
27. Calculate the volume of 0.1 M sodium hydroxide solution (C_a = 1.0000), which was used for the titration of 0.2198 g of ethinyl estradiol (M.w.296.41). The percentage content of ethinylestradiol in the preparation is 99.02%, the weight loss during drying is 0.56%.
28. Calculate the mass of sinestrol sample (M.w. 270.37), if 5.00 ml of 0.5 M sodium hydroxide solution (C_a = 1.0041) was spent on its titration, the titrant volume in the control experiment was 10.20 ml, percentage its content in the drug is 99.12%.
29. Calculate the volume of 0.5 M sodium hydroxide solution (C_a = 0.9986), which was used for the titration of 0.2452 gsinestrol (M.w. 270.37),the volume of the titrant in the control experiment is 12.20 ml. Percentage content sinestrol in the preparation - 98.89%.
30. Calculate the specific absorption index and evaluate the quality of pregnin, if a weight of the drug weighing 0.0744 g was dissolved in a 100 ml volumetric flask in methanol, 0.5 ml of the resulting solution was transferred to a 50 ml volumetric flask and brought up to the mark with methanol. Average opticsdensityof the obtained solution at 241 nm is 0.382, the thickness of the cuvette is 10 mm. The content of pregnin in the preparation is 99.66%. The specific absorption index should be 500-520.
31. Calculate the gram content of pregnin in the dosage form (pregnin tablets 0.01 g, the average weight (P) is 0.10 g), if 0.1020 g of the powder of crushed tablets, dissolved in alcohol when heated, filtered and adjusted to a volume of 100 ml with the same solvent, 5 ml of the filtrate was transferred to a 50 ml volumetric flask and the optical density was measured on a spectrophotometer at a wavelength of 241 nm in a cuvette with a layer thickness of 10 mm, which is equal to 0.52. As a control experiment, alcohol is used, the specific absorption index ($E^{1\%}_{1см}$)pregnane 520.

32. Calculate the specific rotation and evaluate the quality of methandrostenolone, if the average angle of rotation of a 1% solution of the drug in chloroform is + 0.12°. The length of the cuvette is 20 cm. The specific rotation should be from 0° to +5°.
33. Calculate the gram content of methylandrostenediol in tablets when determined by the gravimetric method, if it is known that the weight of the crushed tablets is 0.5006 g, which was mixed with water, filtered, the sediment was dissolved in alcohol, the alcohol was driven off, the sediment was dried to a constant weight. The mass of the weighing form is 0.0505 g, the loss in mass during drying is 1.98%. The average weight of the tablet is 0.25 g.
34. Calculate the value of the specific absorption index, if the optical density of a 0.001% solution of methyltestosterone in methyl alcohol at a wavelength of 240 nm in a cuvette with a layer thickness of 10 mm is equal to 0.525.
35. Calculate the gram content of methyltestosterone in the dosage form (tablets of methyltestosterone 0.005 g, the average weight (P) is 0.10 g), if 0.0509 g of powder of crushed tablets dissolved in alcohol, filtered and made up to a volume of 50 ml with the same solvent, 10 ml of the filtrate was transferred to a 50 ml volumetric flask and the optical density was measured on a spectrophotometer at a wavelength of 241 nm in a cuvette with a layer thickness of 10 mm, which is equal to 0.530. As a control experiment, alcohol is used, the specific absorption index ($E_{1cm}^{1\%}$) of methyltestosterone 535.
36. .Calculate the specific rotation and evaluate the quality of testosterone propionate, if the average angle of rotation of a 1% solution of the drug in alcohol is + 1.8°. The length of the cuvette is 20 cm. The specific rotation should be from 87° + 90°.
37. .Calculate the percentage content of methandrostenolone (M.w. 300.44) in the preparation determined by the oxime method, if 6.74 ml of 0.1 M sodium hydroxide solution (C_a = 0.9968) was spent on the titration of a weight of 0.2038 g, the loss in dry weight - 0.62%.
38. Calculate the weight of methyltestosterone (M.w. 302.46), determined by the oxime method, if 8.10 ml of 0.1 M sodium hydroxide solution (C_a = 0.9958) was spent on its titration, its percentage content in the preparation is 99.44% ,. weight loss during drying -0.18%.
39. Calculate the volume of 0.1 M sodium hydroxide solution (C_a = 1.0000), which was used for the titration of 0.3008 g of methyltestosterone (M.w. 302.46), determined by the oxime method. The percentage content of methyltestosterone in the preparation is 99.87%, the weight loss during drying is 0.36%.

40. Calculate the content of testosterone propionate in a 0.001% alcohol solution of the drug, if opticaldensityof the investigated solution - 0.240, opticaldensityof a standard 0.001% solution is 0.245, measured on a spectrophotometer in a cuvette with a layer thickness of 10 mm.
41. Calculate the specific index and evaluate the quality of methyltestosterone if the average angle of rotation of a 1% solution of the drug in alcohol is + 0.80 o. The length of the cuvette is 10 cm. Loss in mass during drying is 0.98%. Specific rotation should be from + 82^{o} to +85^{o}.

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