МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
ХАРКІВСЬКИЙ НАЦІОНАЛЬНИЙ МЕДИЧНИЙ УНІВЕРСИТЕТ

CLASSIFICATION, STRUCTURE AND SIGNIFICANCE OF BIOLOGICALLY ACTIVE HETEROCYCLIC COMPOUNDS. STRUCTURE AND BIOCHEMICAL FUNCTIONS OF NUCLEOSIDES, NUCLEOTIDES AND NUCLEIC ACIDS

Methodical instructions for 1st year students' self-work
in Biological and Bioorganic Chemistry

КЛАСИФІКАЦІЯ, БУДОВА ТА ЗНАЧЕННЯ БІОЛОГІЧНО ВАЖЛИВИХ ГЕТЕРОЦИКЛІЧНИХ СПОЛУК. СТРУКТУРА ТА БІОХІМІЧНІ ФУНКЦІЇ НУКЛЕОЗИДІВ, НУКЛЕОТИДІВ ТА НУКЛЕЇНОВИХ КИСЛОТ

Методичні вказівки для самостійної роботи студентів 1-го курсу
з біологічної та біоорганічної хімії

Затверджено
Вченою радою ХНМУ
Протокол № 2 від 22.02.2018р.

Харків
2018

Classification, structure and significance of biologically active heterocyclic compounds. Structure and biochemical functions of nucleosides, nucleotides and nucleic acids : methodical instructions for 1st year students' self-work in Biological and Bioorganic Chemistry [electronic variant]/ compiled by G.O. Syrova, L.V. Lukianova, O.A. Zavada et al. – Kharkiv: KhNMU, 2018. – 26 p.

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Класифікація, будова та значення біологічно важливих гетероциклічних сполук. Структура та біохімічні функції нуклеозидів, нуклеотидів та нуклеїнових кислот : метод. вказ. для самостійної роботи студентів 1-го курсу з біол. та біоорг. хімії [електронний варіант]/ уклад. Г.О. Сирова, Л.В. Лук'янова, О.О. Завада та ін. − Харків: ХНМУ, 2018. − 26 с.

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Subject 7. CLASSIFICATION, STRUCTURE AND SIGNIFICANCE OF BIOLOGICALLY ACTIVE HETEROCYCLIC COMPOUNDS. STRUCTURE AND BIOCHEMICAL FUNCTIONS OF NUCLEOSIDES, NUCLEOTIDES AND NUCLEIC ACIDS

1. **Number of hours** 4

2. **Material and methodological support.**

Tables:

1. Classification, structure and role of biologically important heterocycles.
2. Names of ancestral structures.
3. The names of heterocycles.
4. Pyrrole and pyridine nitrogen in heterocycles.
5. Acid-basic properties of pyrrole and pyridine nitrogen.
6. Pyridinecarboxylic acids.
7. Derivatives of tryptophan.
8. Barbituric acid.
9. Anti-tuberculosis drugs.
10. Alkaloids (theobromine, theophylline, caffeine).
11. Uric acid.
12. Xanthine derivatives.
13. Some antineoplastic antibiotics.
14. Drugs based on pyrazole.
15. Structural formulas for heterocyclic drugs (Tiaminobromide (thiazole), diazolin, analgin, antipyrin, amidopyrin, anesthesin, streptocide, phenacetin, aspirin, etazol, validol).
16. Formation of DNA.
17. Nucleosides that make up RNA.
18. Primary structure of DNA.

1. Biological and Bioorganic Chemistry : in two books : Textbook. Textbook 1. Bioorganic Chemistry / B.S.Zimenkovsky, V.A.Muzychenko, I.V.Nizhenkovska, G.O.Syrova; edited by B.S.Zimenkovsky, I.V.Nizhenkovska. – K., AUP «Medicina», 2017. – 288 p.
2. Fundamentals of bioorganic chemistry: manual / A.O.Syrovaya, E.R.Grabovetskaya, V.N.Petiunina. – Kharkiv, KhNMU. – 2016. – p.
3. Biologically important classes of bioorganic compounds. Biopolymers and their structural components: workbook for self-work of first year students of medical and dentistry faculties/ draftsmen G.O.Syrovaya, V.M.Petunina, T.S.Tishakova et al.– Kharkiv: KhNMU, 2018. – 60 p.
4. Heterocyclic compounds. Nucleic acids and their structural components: methodical instructions for 1st year students' self-work in Biological and Bioorganic Chemistry (module 1) / compiled by A.O.Syrovaya, L.G.Shapoval, V.N.Petyunina et al. – Kharkiv: KhNMU, 2014. – 24 p.
5. Text of Lecture.

3. Motivational characteristic of the subject

High importance of heterocyclic compounds is that they are basis of many natural biologically active compounds and medicinal products. Alkylated pyrol rings are the base of important biologically active compounds: hemoglobin, chlorophyll and vitamin B_{12}. Heterocyclic rings (indole, imidasole etc.) are a part of some essential amino acids such as tryptophane, histidine etc. There are many medicinal products containing heterocyclic compounds: non-narcotic analgetics contain pyrazolone-5; vitamin PP and antituberculosis drugs which contain pyridine ring.

To know the structure and properties of biopolymers (nucleic acids) is necessary to understand the essence of normal processes and pathology, the origin of hereditary diseases and problems of vital activity regulation.

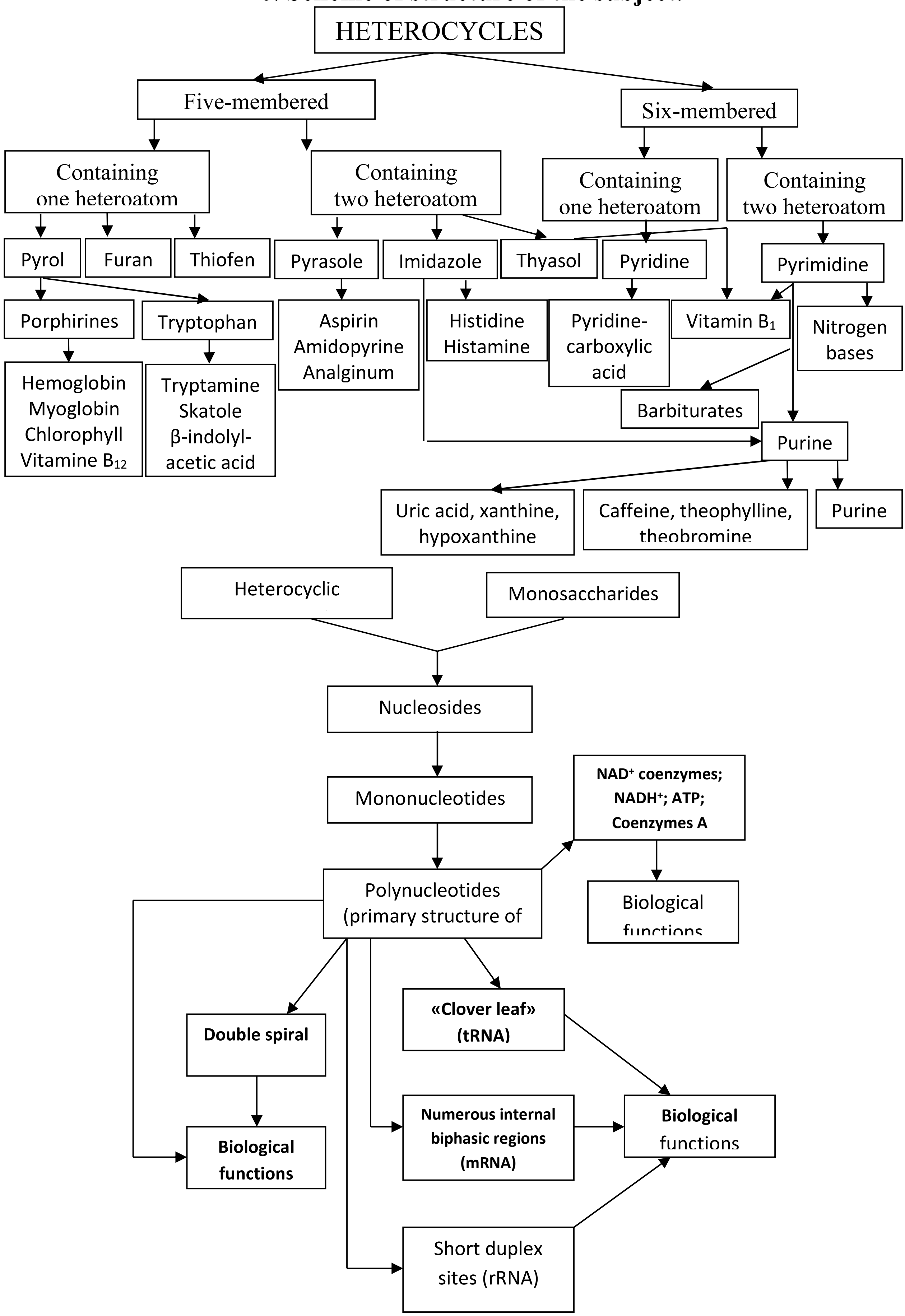
6. Objectives

To learn the structure and peculiarities of the chemical behavior of biologically active heterocyclic compounds.

7. Practical skills

1. To be able to explain dependence of the reactivity of heterocyclic compounds on their structure.
2. To be able to simulate laboratory synthesis with the aim of preparation of medicinal products and also biosynthesis in the organism.
3. To be able to explain the mechanisms of participation of heterocyclic compounds as a part of vitamins, hormones and coenzymes in different biochemical transformations.
4. To be able to analyze the importance of mononucleotides in the formation of nucleic acids and actions of nucleotide coenzymes.
5. To be able to explain the mechanisms of participation of vitamins in the formation of coenzymes catalyzing biochemical transformations in the organism.

6. **Scheme of structure of the subject.**



7. **Plan of students' work.**

№	Stage	Time, min	Training and visual aids	Location
1.	Motivational characteristic and plan of subject. Questions and answers	35	Manual, self-study guide for the 1st year students	Class room
2.	Incoming control	20	Tests (Incoming control)	
3.	Independent work of students with methodological literature, the solution of educational problems, filling of self-study guide	35	Methodical instructions for students, text of lecture, manual for students' self-work, self-study guide, reference data, tables	
4.	Discussion of procedure of laboratory work	10	Text-book (work-book)	
5.	Performing of laboratory work and recording	35	Reagents, chemical utensils	
6.	Defence of laboratory work	15		
7.	Final control	25	Tests	
8.	Analysis and conclusions	4		
9.	Home-work	1		

8. **Tasks for self-work:**

- list of questions to be studied:

1. Classification of heterocycles classified according to the size of the heterocyclic ring and the nature and number of the heteroatoms.
2. Aromaticity of heterocycles.
3. Biologically important five-membered heterocycles.
4. Biologically important six-membered heterocycles.
5. Nucleic acids are biopolymers that store information, transfer genetical information and take part in protein biosynthesis.
6. Composition and structure of components of nucleic acids: nitrogen bases, monosaccharides.
7. Nucleosides and nucleotides – products of incomplete hydrolysis of nucleic acids. Structure of nucleotides.
8. Structure and significance of 3*,5* - cAMP.
9. Structure and biochemical functions of DNA.

10. Types of RNA, their structural organization and their biological role. Differences in structure, location and functions of DNA and RNA.

11. Phosphorylated derivatives of nucleotides. Biological role of ADP, ATP.

12. Participation of nucleotides in the formation of coenzymes. Mechanism of action of NAD^+.

Educational tasks and standards of their solution

Task 1. What are heterocyclic compounds? Give the examples of the most extended heterocyclic compounds?

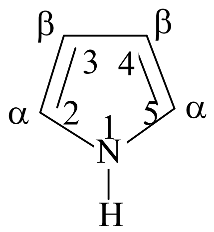
Solution. Molecules of heterocyclic compounds contain cycles, in the formation of which beside carbon atom take part atoms of other elements (more often nitrogen, oxygen, sulfur), which are named as heteroatoms.

One or several the same or different heteroatoms can be present in heterocycles.

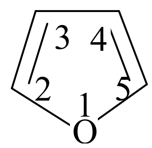
Five- and six-membered heterocycles are the most stable and therefore the most abundant.

According to the composition and chemical structure heterocycles are very diverse. They are often classified according to the ring size and number of heteroatoms on the following main groups:

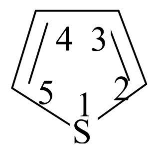
five-membered with one heteroatom:



Pyrrole

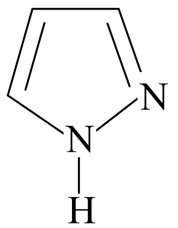


Furan

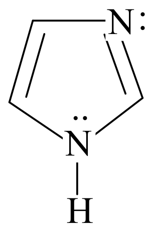


Thiophene

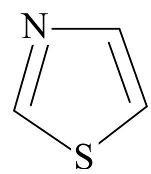
five-membered with two heteroatoms:



Pyrazole

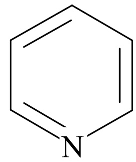


Imidazole



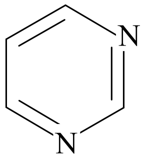
Thiazole

six-membered with one heteroatom:



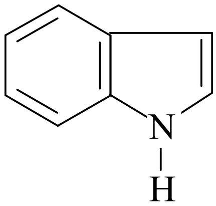
Pyridine

six-membered with two heteroatoms:

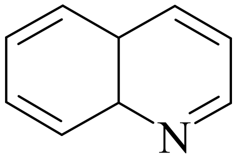


Pyrimidine

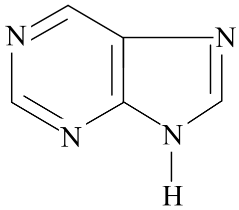
condensed heterocycic systems:



Indole



Quinoline

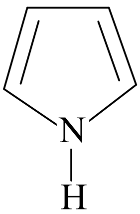


Purine

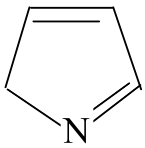
Nitrogen-containing heterocycles display basic properties. In addition heterocycles like benzene have aromatic nature; rings of heterocyclic compounds are in the basis of many biologically active substances and drugs.

Task 2. In what biologically important systems does pyrrole ring occur? Role of these systems in the life.

Solution. Tetrapyrrol compounds containing four pyrrole rings where two of them are in the isoform, have biological significance:

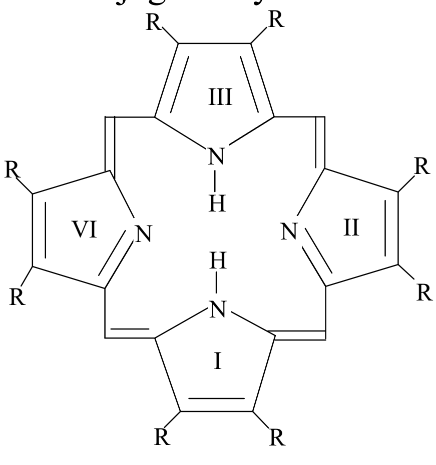


Pyrrole



Isopyrrole

These four rings form closed conjugated system called porphyrin:



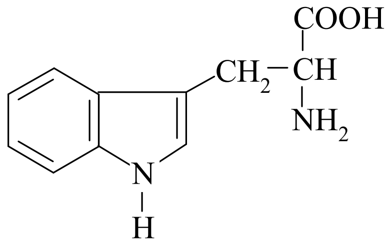
Porphyrine

Porphin contains 26 delocalized electrons. All rings are in the plane and have considerable stability not destroying even at heating to 350°C.

Porphines containing substituents in pyrrole rings are called porphyrines. Example of porphrines is protoporphyrin where sustituents are methyl- and vinyl-groups and remains of propionic acid.

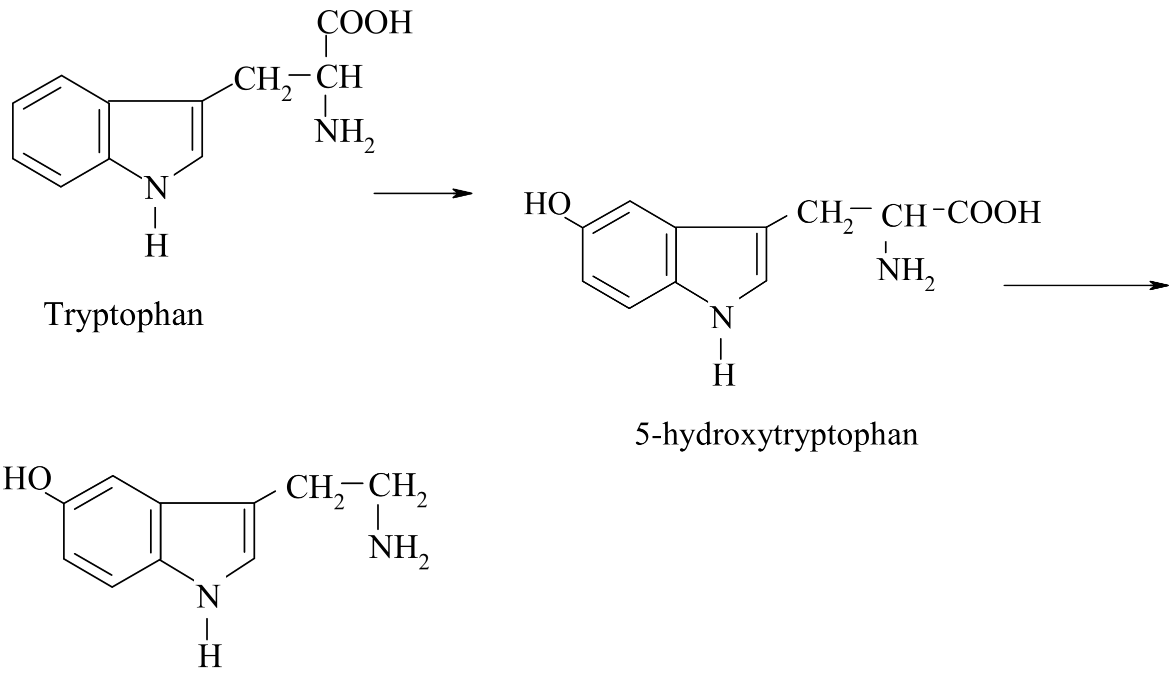
In nature porphyrines form complexes with metals. If Fe^{2+} is complexing agent then porphyrin is called heme and is nonprotein part (prosthetic group) of haemoglobin.

Condensed system from benzene and pyrrole rings (indole) is a constituent of essential amino acid – tryptophan.



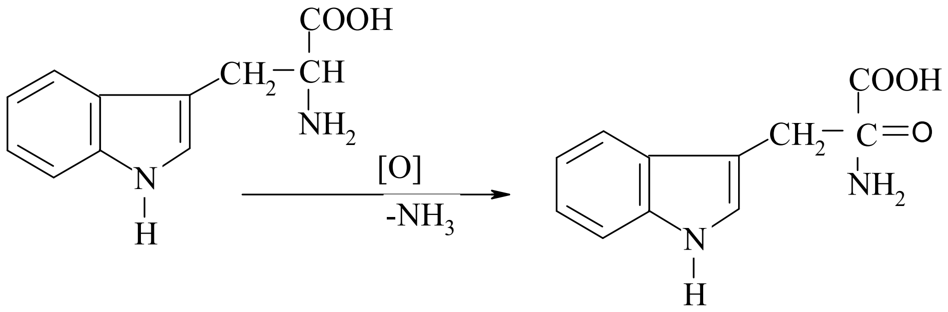
Tryptophan

First mode of biochemical transformations of tryptophan is hydroxylation with formation of 5-hydroxytryptophan which further undergoes decarboxylation giving 5-hydroxytryptamine (serotonin).

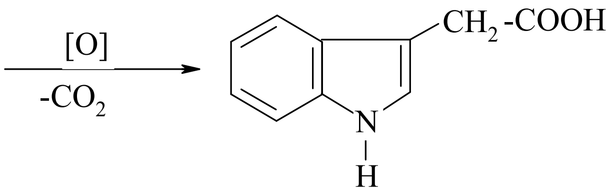


5-hydroxytryptamine (serotonin)

Another mode of tryptophan metabolism is conversion into the β - indoleacetic acid:



oxidative deamination

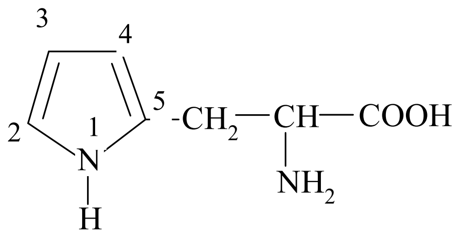


β - indoleacetic acid (heteroauxin)

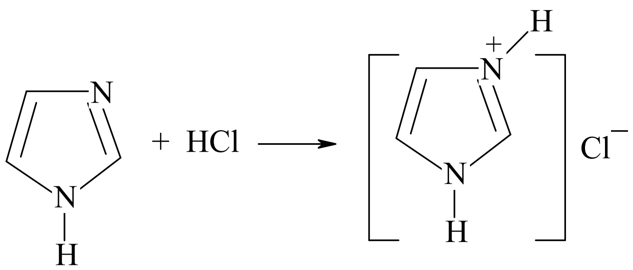
Heteroauxin is a growth hormone of plants. It influences greatly on the development of rootage.

Task 3. What physiologically relevant systems does imidazole comprise? Amphoterism of imidazole.

Solution. Imidazole ring is a constituent of histidine which is one of amino acid forming proteins.

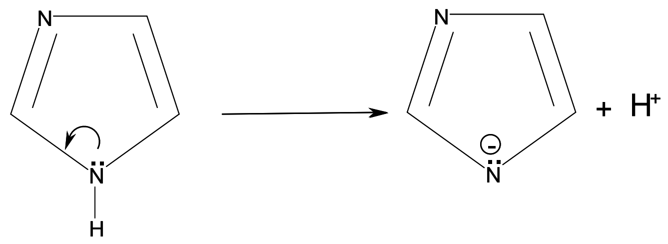


In the organism imidazole takes part in a number of enzymatic reactions being donor-acceptor of protons. Such its property is stipulated with different state of atoms entering the imidazole ring. One of them (I) – pyrrole unshared electron pair of which conjugates with π-electrons of ring. Second (II) – pyridine takes part in conjugation with one p-electron and can protonate at the expense of paired electrons exhibiting basic properties. Imidazole forms salts both with mineral and with some organic acids:



Imidazolinium chloride

Imidazole exhibits acidic properties due to pyrrole nitrogen as N-H bond is polarized and proton abstraction is possible (N-H-acidity). Imidazole is stronger acid than pyrrole so long as pyridine nitrogen acts as electron-withdrawing substituent increasing polarization of N-H bond:

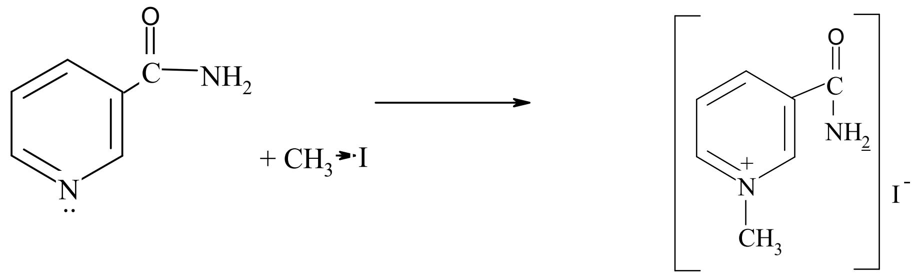


Amphoteric character of imidazole provides its reacting as anion or cation i.e. ability acts as donor and acceptor of proton.

Substituted heterocyclic rings of pyrimidine and thiazole are structural components of thiamine (vitamin B_1). In the organism thiamine diphosphate is a coenzyme (cocarboxylase), taking part in decarboxylation of pyruvic acid.

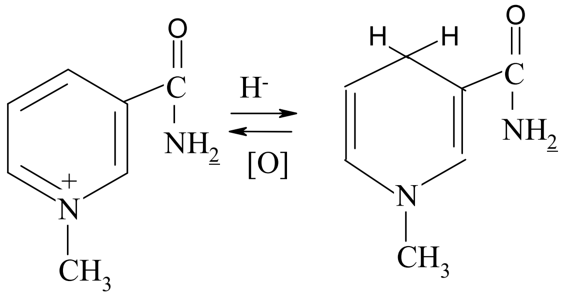
Task 4. What is the role of pyridine derivatives in the oxidation-reduction reactions in the organism?

Solution. Among pyridine derivatives pyridine carboxylic acids are very important. β-pyridine carboxylic acid (nicotinic acid) and its amide (nicotinamide) are known as two forms of vitamin PP, lack of which in the organism causes pellagra. Nicotinamide is a constituent of coenzyme NAD^+ catalyzing oxidation-reduction processes. Its catalytic action connects with nucleophilic properties of pyridine ring. Thus, quaternary salts of methylpyridinium are formed under the action of haloalkyles on pyridine and nicotinamide:



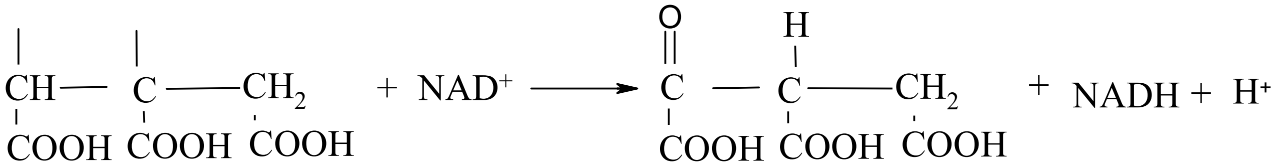
Activated form of α-aminoacid – methionine is methylating agent in the organism.

Forming cation becomes more electron-deficient at the expense of positive charge on the nitrogen atom and least electron density is in a position 4 of pyridinium ring. Under the interaction with hydride-ion nucleophilic attack takes place in this position:



As a result of this reaction cation attaches electron pair of hydride-ion. At that ring looses aromaticity passing into higher energy state. Under the reverse reaction oxidation is performed and released energy is expended for biochemical processes.

Oxidation of hydroxyl-containing compounds (for example, isocitric acid into oxalo- succinic acid in Krebs cycle) occurs in the organism with the involvement of NAD^+.

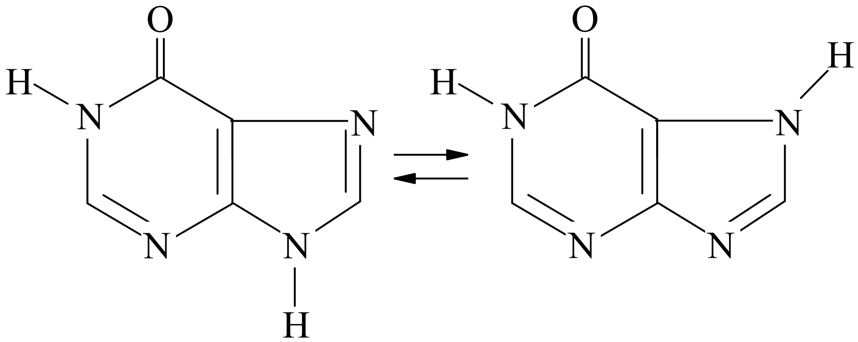


In this case dehydrogenation is realized with separation of hydride-ion and proton. Hydride-ion attaches to NAD^+ forming reduced form NADH.

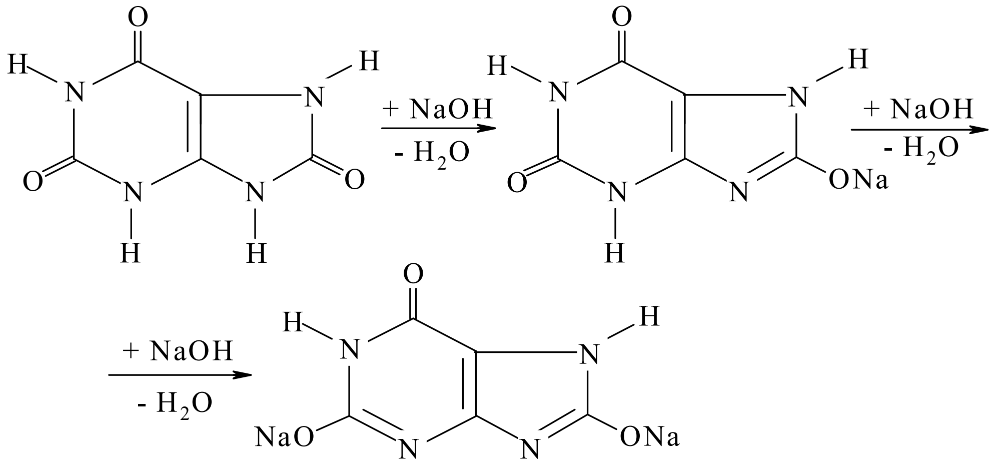
Task 5. What tautomeric forms are known for uric acid? Biological role of uric acid.

Solution. Uric acid is the final product of purine metabolism in humans. It excretes in urine in a quantity of 0,5-1 g per day.

Oxy-oxotautomerism is characteristic for all hydroxyl-derivatives of purine:



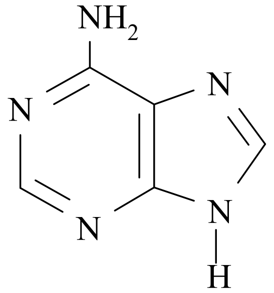
Uric acid is slightly soluble in water. It is dibasic acid and hence can form acid and neutral salts:



Salts of uric acid are called urates. Neutral salts of alkali metals are freely soluble in water, acid salts (except lithium salts) are poorly soluble.

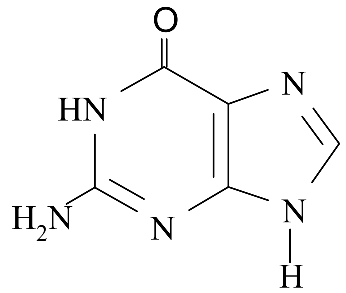
Salts of uric acid are deposited in the joints causing gout in some disorder in the human body and also in the bladder, kidneys, urinary tracts in the form of "urinary stones".

Purine is a condensed heterocyclic system, consisting of pyrimidine and imidazole rings. Purine is a founder of a large group of biologically important compounds. Purine bases, adenine and guanine, are components of nucleic acids:



Adenine

6-aminopurine



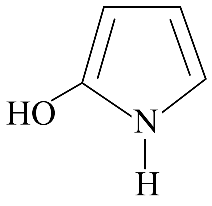
Guanine

2-amino-6-oxopurine

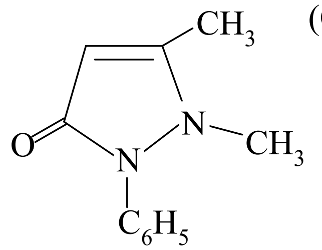
These compounds are formed under the decomposition of nucleic acids. Enzymes, catalyzing processes of purine ring destruction, are absent in humans.

Exercise 6. What imidazole-related medicinal preparations do you know?

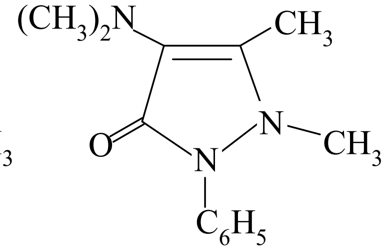
Example of solution. Ring of imidazole derivative (pyrazolone-5) is in the base of group of nonnarcotic analgetics: antipyrine, amidopyrine, analgin, butadione:



Pyrazolone-5



Antipyrine



Amidopyrine

These compounds are applied as ingredients of analgesic, antipyretic and anti-inflammatory medicines.

Task 7. What biologically active compounds where is quinoline do you know?

Solution. Derivatives of 8-hydroxyquinoline (oxyn) represent important group of medicinal products.

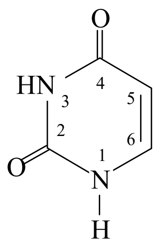
Enteroseptol (5-chloro-7-iodo-8-hydroxyquinoline) is poorly absorbed from the gastrointestinal tract, that's why it has antibacterial action in the intestine and is applied for dysentery and colitis treatment.

Nitroxoline (5-nitro-8-oxyquinolin) is absorbed from the gastrointestinal tract rapidly and it is excreted by the kidneys. For this purpose it is applied under kidney and urinary tract infections.

Ability to form chelate complexes with some metal ions (cobalt, magnesium) is in the base of biological action of 8-hydroxyquinoline related medicinal preparations. Thus, binding of microelement, necessary for bacterial activity, occurs.

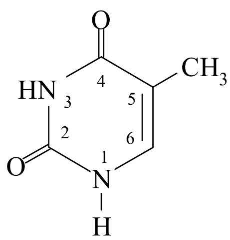
Task 8. Write the structure of the heterocyclic bases, which contain nucleic acids. What tautomeric transformations are possible for uracil and guanine? Write complimentary interaction between two nucleic bases: thymine-adenine, cytosine-guanine.

Solution. Heterocyclic bases of pyrimidine family – uracil (in RNA), thymine (in DNA) and cytosine (both DNA and RNA) and purine family- adenine, guanine (in DNA and RNA) are structural components of nucleic acids. They are also called nucleic bases.



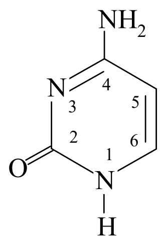
Uraci

2,4-dioxopyrimidin



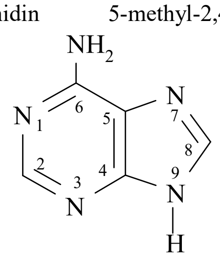
Thymine

5-methyl-2,4-dioxopyrimidine



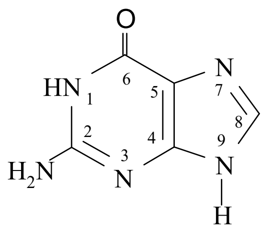
Cytosine

4-amino-2-oxopyrimidine



Adenine

6-aminopurine

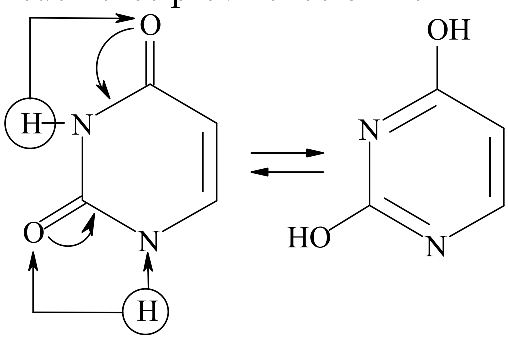


Guanine

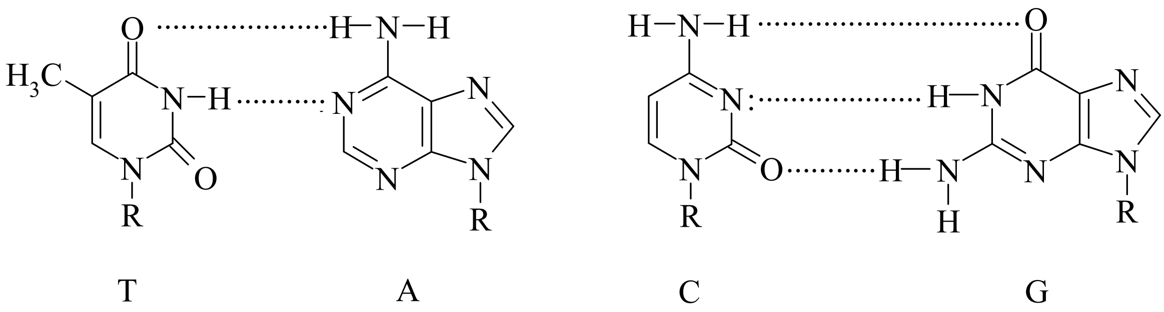
2-amino-6-oxopurine

Nitrogen bases show lactim-lactam tautomerism which is caused by that nitrogen atom exhibits great basicity, i.e. greater proton affinity than oxygen atom.

Thereby migration of one or two protons from oxygen atom to the corresponding nitrogen atoms is possible. In such case prevalence of lactam form takes place:



Complementarity interaction between two nucleic bases is caused by the occurrence of hydrogen bondigs: between oxygen atoms of oxo group; between hydrogen atom of pyrrole nitrogen of one base and unshared electron pair of pyridinium nitrogen of the other base. One of the nucleic bases, forming complementary pair, is a nitrogen base of purine family, other is a pyrimidine family:



(two hydrogen bonds) (three hydrogen bonds)

Planar configuration of complementary pairs allows them to pack one above the other like in stack.

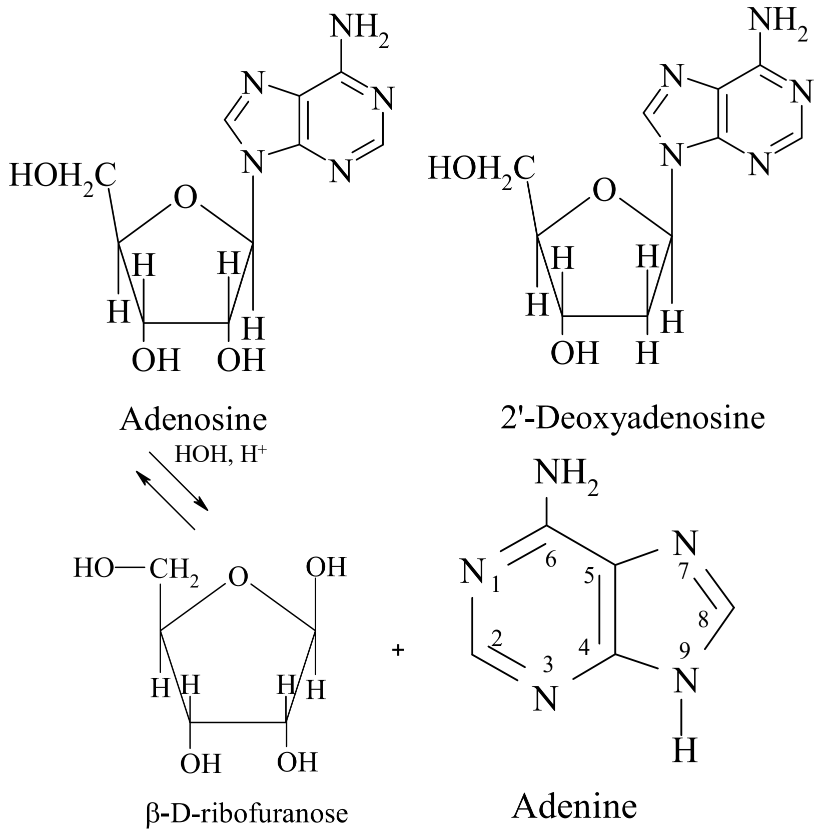
Task 9. Write the structure of N-glycosides: nucleoside adenosine and deoxycytidine. Write the equation for the hydrolytic decomposition of adenosine as characteristic reaction for glycosidic linkage.

Solution. Nucleosides are N-glycosides, formed with nucleic bases with ribose or deoxyribose. Depending on the nature of the carbohydrate residue names of nucleosides is formed from trivial name of the corresponding nucleic bases with ending –idine for pyrimidine family and –osine for purine family:

cytosine + deoxyribose → deoxycytidine;

adenine + ribose → adenosine.

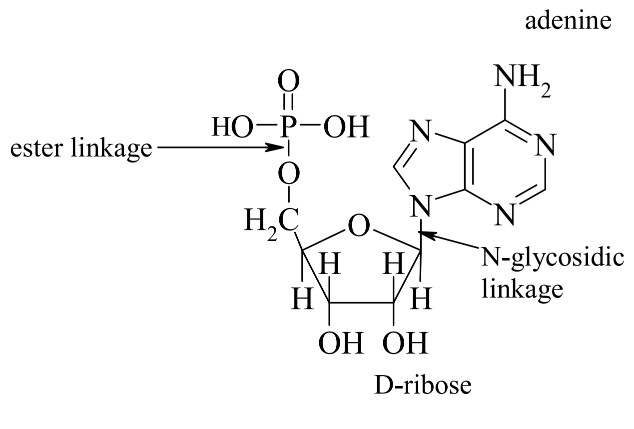
Formation of glycosidic linkage is realized through $C_1^{'} - N_1$ for pyrimidine bases and through $C_1^{'} - N_9$ for purine bases.



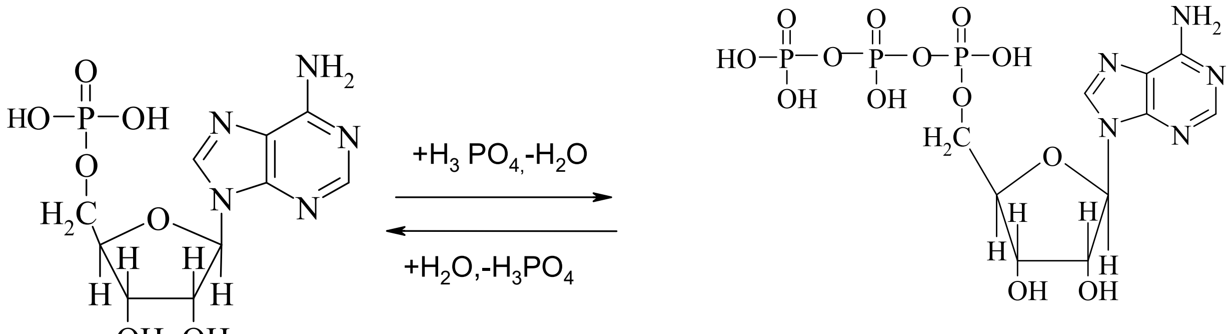
Nucleosides decompose in acidic medium but they are resistant to hydrolysis in alkalescent medium.

Task 10. Write the scheme of adenosine triphosphoric acid (ATP) formation, which is a motive force of biochemical processes in the organism.

Solution. Nucleotides are phosphorylated nucleosides. Usually hydroxyl group is etherified in nucleosides near C-5’ or C-3’ of pentose cycle. This is a nucleophilic substitution reaction.



New compound with ester linkage – nucleotide-adenosine-5’-phosphate (ATP) was formed. Under the construction of ATP from AMP energy-rich bonds are formed and energy storage occurs (31,2 kJ/mol).

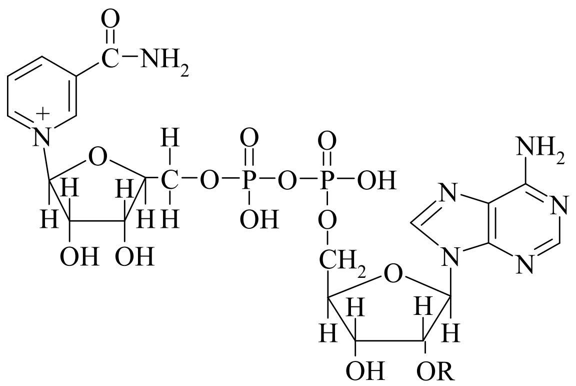


ATP

Under the hydrolytic decomposition energy release occurs and it is used in the organism for other energy processes. Remains of phosphoric acid are used for other compounds phospholyration.

Task 11. Write the scheme of lactic acid transformation into pyruvic acid using coenzyme NAD^+.

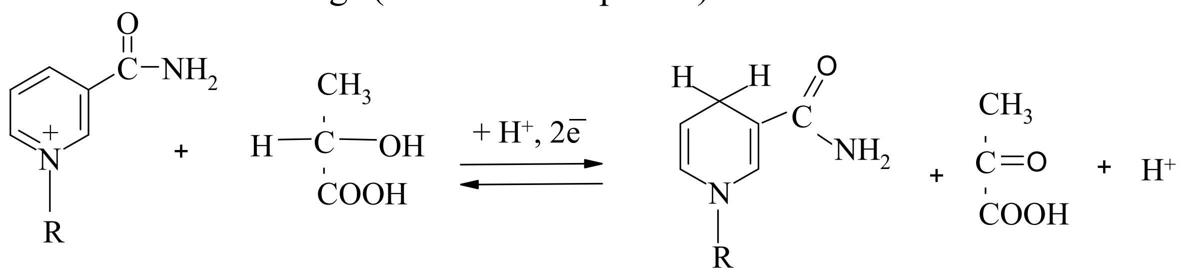
Solution. Nucleotides are structural components of many coenzymes. Nicotinamide-adenine dinucleotide (NAD^+) and connected with it nicotineamide-adenine dinucleotide phosphate ($NADP^+$) can be used as example. They transfer hydrogen.



$NAD^+ \rightarrow R = H$

$NADP^+ \rightarrow R = PO_3H_2$

Lactic acid transformation into pyruvic acid using NAD^+ is an example of oxidation-dehydrogenation reaction. Removal of two hydrogen atoms from substrate takes place: one of them (hydride-ion) reacts with pyridinium cation but other remains in the surroundings (in the form of proton).



NAD^+ NADH

Then reductive coenzyme NADH can take part in reduction reaction as electron donor.

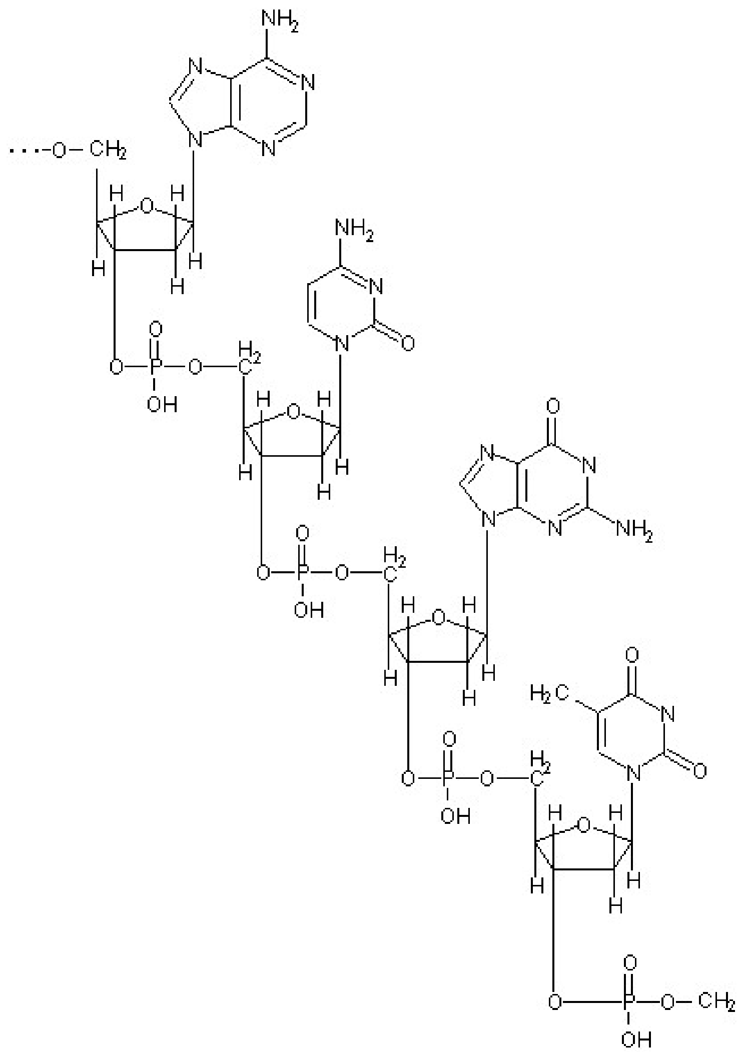
Task 12. Give the definition of primary structure of nucleic acids. Write the structure of DNA fragment with ACGT consequence.

Solution. Primary structure is a nucleotide sequence (alternation of nucleic bases). Formation of polynucleotide chain is realized by means of binding with phosphate esters link the 3'–OH of one ribose (or deoxyribose) with the 5'–OH of another.

DNA chains consist of such alternate fragments. The structure of RNA is similar to that of DNA with two exceptions: pentose residue in RNA is a D-ribose but in the set of heterocyclic bases is not thymine but uracil.

Genetic information, which must be transferred under the mitosis, is codified in nucleotide sequence of DNA. This is realized by a duplication (replication) of DNA molecules. At first two chains of double helix begin to split and new chain with complementary region forms along with every of them.

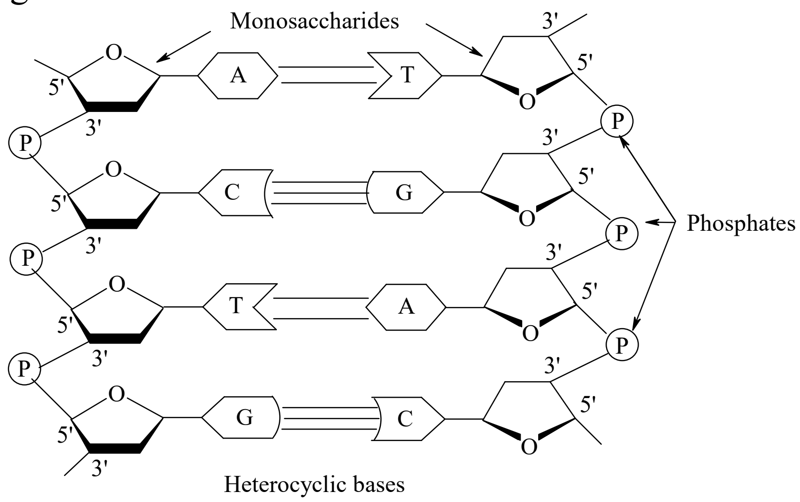
Thus, two DNA molecules identical to initial and each other form from one DNA molecule. Similarly replication of iRNA molecules takes place on despiralizated DNA molecule, nucleotide sequence of which determines amino-acid composition of proteins, synthesized in organism.



Task 13. What is the reason of existence of secondary structure of DNA? What is the difference between DNA and RNA structures?

Solution. Secondary structure of DNA is a helix consisting of two nucleotide chains coiled around a common axis in a double helix. Whole turn of double-stranded chain of DNA consists of 10 mononucleotides. Structure of double helix is maintained with Van der Waals' attractive forces, act between complementary bases: adenine (A) – thymine (T) and guanine (G) – cytosine (C). In one direction along with helix linkage between carbon and phosphate residues will be 3'-5' but in the other helix it will be 5'-3', i.e. they are anti-parallel.

Complementarity of the bases is in the base of regularities using which nucleotide component of DNA of different origin is submitted. These regularities were stated by Chargoff:



- the number of purine bases is equal to the number of pyrimidine bases, i.e. (A + G) = (C + T);

- the number of adenine is equal to the number of thymine (A = T), the number of guanine (G) is equal to the number of cytosine (C);

- the number of bases, comprising of amino-group in the position 4 of pyrimidine ring and position 6 of purine ring, is equal to the number of bases, comprising of oxo-group in the same positions:

$$A + C = G + T.$$

Chargoff's rules are not complied for RNA or they are complied with some approaches. In regard to secondary structure of transfer RNA model of "cloverleaf" is most probable. Secondary structure for matrix and ribosomal RNA is less known.

Revision exercises

№ 1

1. Write the structure of pyrazole, imidazole and pyrrole. Explain why they are aromatic compounds. Compare the behaviour of imidazole and pyrrole in acidic medium.

2. Write the structure of medicinal preparations, which contain a fragment of nicotinic acid amide – vitamin PP.

3. Write the equations for the reactions that take place with triptophane (β-indole – β-aminopropionic acid). Name the reaction products.

4. Write the structures for pyrimidine bases, comprising nucleic acids composition and name them.

5. Write the scheme for incomplete hydrolysis of 5'-adenylic acid, proceeding on ester linkage. Point conditions.

№ 2

1. Write the reaction for the equation of pyrrole sulfonation. What is the mechanism of the reaction?

2. Write the equation for the reaction of nicotinic acid decarboxylation. How to be sure, that reaction has passed?

3. Explain a process of lactam-lactim tautomerism for uric acid (write equation). What is the role of uric acid in a metabolism?

4. Write the structures for purine bases, comprising nucleic acids composition and name them. For one of the purine bases write tautomeric forms.

5. Write the scheme for incomplete hydrolysis of 5'-cytidylic acid. Name the products of the reaction.

№ 3

1. Write the mechanism of nitration for furan.
2. Characterize structure and application of nicotinic acid derivatives – tybazide and phtivazide.
3. Explain the reason of acidity of barbituric acid and its derivatives – barbital and phenobarbital. Give the examples of treatment by these medicines.
4. Write the structure of coenzyme NAD^+. Write the schemes of chemical reactions which underlie in the base of this coenzyme action in biological systems.
5. Write the scheme for the reaction of nucleotide hydrolytic degradation if it is known, that final products will be a phosphoric acid and thymidine (1:1). Name the initial product.

№ 4

1. Write the equation of qualitative reaction for antipyrine with a nitrous acid.
2. Write the structure of pyridine, pyrimidine and purine. Specify atomic numbering. Explain why these compounds are aromatic.
3. Give the examples of soluble and insoluble salts of uric acid.
4. Write the structures for nucleic bases, comprising DNA and name them.
5. Write a scheme of hydrolytic decomposition of ATP to ADP.

№ 5

1. Write the equation of qualitative reaction for antipyrine with a nitrous acid.
2. How to explain the ability of pyridine and pyrimidine interact with hydrochloric acid?

3. Write the structure of biogenic amines – tryptamine (β-indolylethylamine) and serotonin (5-oxytryptamine). What heterocyclic system is in their structure?

4. Write the structures for thymine, guanine and their complementary bases.

5. Write the scheme of chemical reactions which underlie the action of NAD^+ coenzyme.

№ 6

1. Write the equation for the reaction of antipyrine interaction with iodine. What is the mechanism of the reaction?

2. Write the equation for the reaction between pyridine and methyl bromide. What is the mechanism of the reaction?

3. Write the examples of xanthine (2,6-dioxopurine) tautomers. In what medicinal preparations xanthine nucleus is as a structural component?

4. Write the structures for nucleic bases, comprising RNA and name them.

5. Write the structure for compound under the heating of which at the presence of a mineral acid phosphoric acid, deoxyribose and guanine have been received in the ratio 1:1:1. Name compounds. Point out glycosidic and ester linkages.

№ 7

1. Write the formula of amidopyrine. What is the medical application of this medicine?

2. Write the equation for the reaction of nicotinamide formation from nicotinic acid. Nicotineamide application in medical practice.

3. Explain a process of lactam-lactim tautomerism for barbituric acid (write equation). What type of tautomerism does cause acid properties of barbituric acid?

4. Write the structures for thymine, guanine and their complementary bases.

5. Write the scheme for the reaction of nucleotide hydrolytic degradation if it is known, that phosphoric acid and thymidine (1:1) will be final products. Name initial product.

№ 8

1. What features of histidine do cause its acid-basic properties?

2. Write the equation for the reaction between nicotineamide and alkali solution under normal conditions and heating. What products can be formed?

3. Write the structure of indole. What biologically active compounds where indole is present in do you know?

4. Write the structure (lactam-lactim tautomerism) for pyrimidine bases.

5. Write the scheme for the reaction of deoxyguanylic acid formation from the corresponding nucleoside. Point out ester linkage.

№ 9

1. How to obtain amidopyrine from antipyrin. Write the scheme antipyrin formation $\xrightarrow{NO_2}$? $\xrightarrow{[H]}$? $\xrightarrow{2CH_3I}$?
2. What process is in the base of formation of coenzyme NAD^+? Write the scheme of the reaction.
3. Write the equations for the reactions, confirming quinoline basic properties.
4. Write the structures for thymine, guanine and their complementary bases.
5. Write the scheme for the reaction of deoxyguanylic acid formation from the corresponding nucleoside. Point out ester linkage.

№ 10

1. Write the porphine nucleus. In what biologically important compounds porphine is present in?
2. Write the equation for the reaction of pyridine reduction. Name the reaction product. What medicines with hydrogenated pyridine as a structural component do you know?
3. Write the structures of medicinal preparation, in which 8-oxyquinoline is a structural component. What is the medical application for these medicines?
4. Write tautomeric forms for uracil, thymine and name them.
5. Write the scheme for dephospholyration of 5'-deoxyadenylic acid.

№ 11

1. Write the equation for the reaction of tryptophan decarboxylation.
2. Write the structure of phtivazide. At what diseases it can be used?
3. Write the tautomeric forms of hypoxanthine. Number atoms in the ring.
4. Write the structure for complementary bases UA and CG.
5. Write the scheme of complete hydrolysis for 5’-thymidylic acid.

№ 12

1. What derivatives of pyrazole have found application in medicine. Write their structures.
2. Write the equation for the reaction of methylpyridinium iodide formation and reaction for its interaction with hydride ion. What is the significance of this reaction?
3. Write the lactam form of uric acid. What is the role of uric acid in organism physiology?
4. Write the structure for N-glycosides (nucleosides of D-ribose and 2-deoxy-D-ribose with nucleic bases) and write the reaction for their hydrolytic degradation.
5. Characterize tautomeric transformations of thymine. What tautomer does prevail in equilibrium system?

№ 13

1. Write the equation of qualitative reaction for antipyrine, what is its application.
2. Write the scheme for the reaction of isonicotinic acid hydrazide formation; what is the application of the compounds.
3. Write the structures of pyrimidine bases where pyrimidine is as a structural component. Write the formulas for these bases. Number atoms in the ring.
4. Write the structure for nucleotides comprising DNA composition of deoxyadenylic acid, thymidylic acid.
5. Write the structure of ATP and scheme of the chemical reactions underlying the action of this compound in biological systems.

№ 14

1. Write the equation for the reaction of complete and incomplete pyrrole hydrogenation. What is the mechanism of the reaction?
2. Write the equation for the reaction between pyridine and hydrochloric acid.
3. Write the equation for the reaction of barbituric acid formation. Write the structures of medicinal preparations, in which barbituric acid is a structural component. What is the application of these preparations?
4. Write the structure of deoxyguanylic acid and deoxycytidylic acid comprising DNA.
5. Write the scheme of the chemical underlying the action of coenzyme NAD^+ in biological systems.

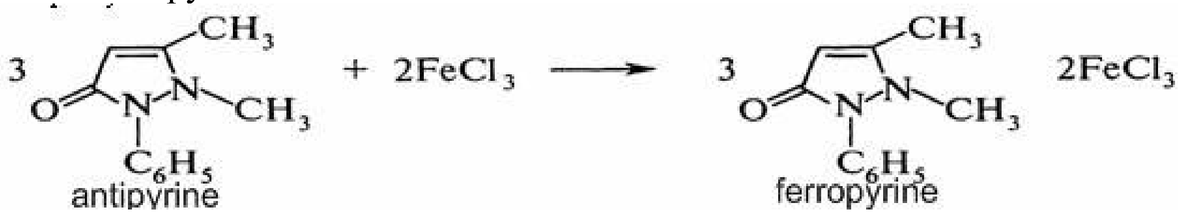
№ 15

1. Write the equation for the reaction of thiophen sulfonation. What is the mechanism for this reaction?
2. Write the equation for the reaction of methylpyridinium iodide formation. What compound pyridine or methylpyridinium cation does undergo a reaction of nucleophilic addition (S_N) easier and why? Write the structure of coenzyme consisting of alkylpyridinium ion?
3. Write the structures of nucleic bases where purine is a structural component. Number atoms in ring.
4. Write the structures for pyrimidine bases, comprising nucleic acids composition and name them.
5. Write the scheme for incomplete hydrolysis of 5’-adenylic acid, proceeding on ester linkage. Point conditions.

Laboratory work

Experiment 1. Interaction of antipyrine and amidopyrine with iron (III) chloride

In a test tube dissolve a few crystals of antipyrine in 2 drops of distilled water. To the received solution add 1 drop of 1 % solution of iron (III) chloride and observe appearance of the intensively orange color, predefined by the formation of complex compound – ferropyrine.



1-phenyl-2,3-dimethyl-pyrazolone-5

For comparison in the second test tube dissolve a few crystals of amidopyrine in 2 drops of water and add 1 drop of 1 % solution of iron (III) chloride. Observe appearance of the blue color that quickly disappears. Then in a test tube add again 3 drops of 1 % solution of iron (III) chloride. Flaky brown precipitate forms. Upon the further acidification of the tube content by 2 drops of diluted chloride acid the precipitate dissolved, and the solution becomes intense blue-violet; the color dose not disappear (distinctive reaction between amidopyrine and analgin).

amidopyrine, dioxyamidopyrine
4-dimethylamino-antipyrine

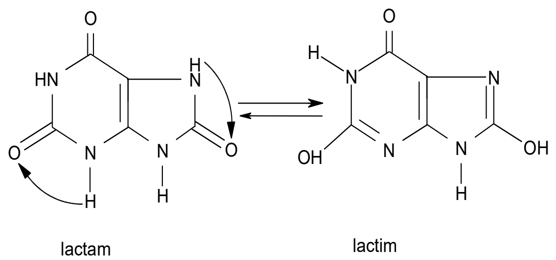
Experiment 2. Interaction of antipyrine and amidopyrine with nitrous acid

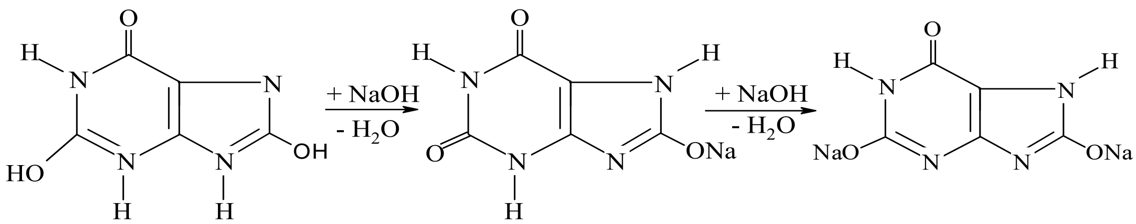
In a test tube dissolve a few crystals of antipyrine in 2 drops of distilled water. To the received solution add 1 drop of 10 % solution of sulfuric acid and 1 drop of 5 % solution of sodium nitrite. Observe appearance of emerald-green color, predefined by the formation of 4-nitrozoantipyrine.

For comparison in the second test tube dissolve a few crystals of amidopyrine in 2 drops of distilled water. To the received solution add 1 drop of 10 % solution of sulfuric acid and 1 drop of 5% solution of sodium nitrite.

Experiment 3. Solubility of uric acid and its sodium neutral salt in water

Place a small amount of uric acid into a test tube. Add water dropwise shaking the test tube. Pay attention to bad solubility of uric acid in water. To the received solution add 1 drop of 10 % NaOH solution and keep this solution for the next experiments.





SUGGESTED READINGS

1. Biologically important classes of bioorganic connections. Biopolymers and their structural components: Theoretical course of biological and bioorganic chemistry, Module 1 / A. O. Syrovaya, E. R. Grabovetskaya, N. M. Tkachuk, L. G. Shapoval, V. N. Petiunina, S. A. Nakonechnaya. – X.: «Цифровая типография № 1». – 2013. – 183 p.

2. Zurabyn S. E. Fundamentals of Bioorganic Chemistry. – M.: GEOTAR-MED, 2003. – 320 p.

Навчальне видання

Класифікація, будова та значення біологічно важливих гетероциклічних сполук. Структура та біохімічні функції нуклеозидів, нуклеотидів та нуклеїнових кислот

Методичні вказівки для самостійної роботи студентів 1-го курсу з біологічної та біоорганічної хімії

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