

will not migrate toward either electrode, predominates. The isoelectric point is then a characteristic property of each amino acid.

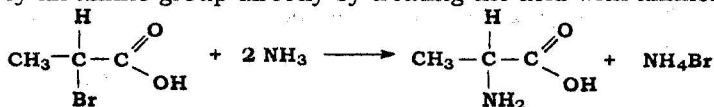
Mixtures of amino acids is based on the charge of an amino acid at a given pH.

Electrophoretic separation of proteins is an important tool in clinical laboratories. Because proteins have a number of different charges and molecular weights, they move at different rates in the electrophoretic apparatus. The most common use electrophoresis in the analysis of blood serum.

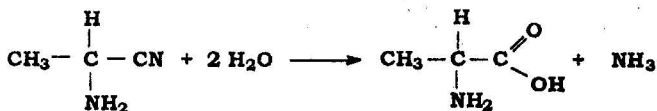
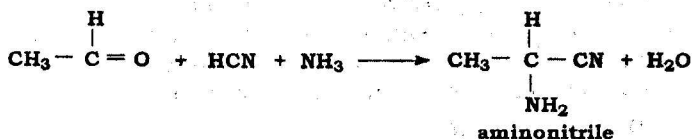
### Synthesis of amino acids

#### A. Direct. Amination of $\alpha$ -Halogen acids

In this method the halogen atom of an  $\alpha$ -halo acid is replaced by an amino group directly by treating the acid with ammonia



#### B. The hydrolysis of $\alpha$ -amino nitriles (Strecker Synthesis). In the Strecker synthesis of an amino acid, an aldehyde is treated with ammonium cyanide (ammonia and hydrogen cyanide). The aminonitrile that results from this reaction then is hydrolyzed to the amino acid

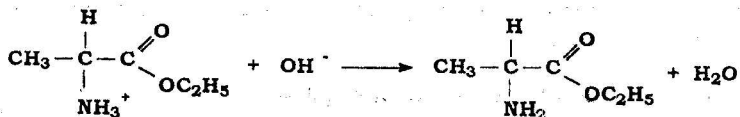
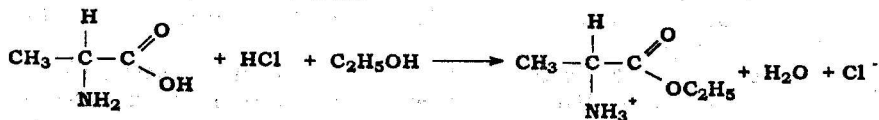


Any synthesis of amino acids (except glycine) leads to a racemic mixture and must be followed by resolution if the natural form of the amino acid is required.

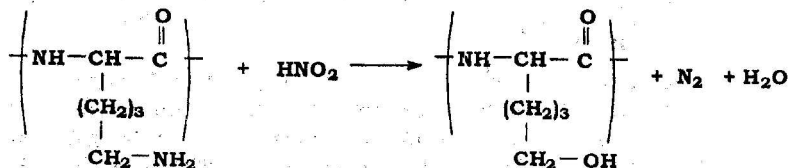
### Reactions of the amino acids

The reactions of amino acids are, in general, reactions characteristic of both carboxylic acids and primary amines.

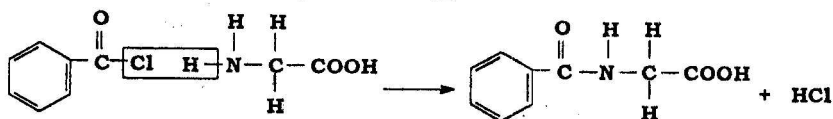
A. Esterification. All amino acids can be esterified Emil Fischer utilized this reactions.



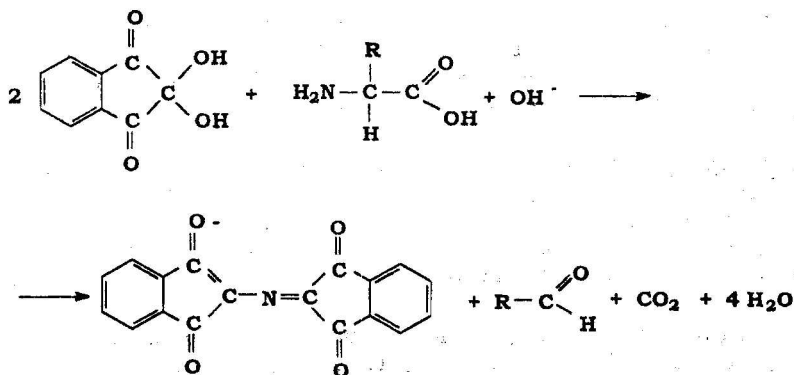
B. Reaction with nitrous acid. The amino acids, with the exception of proline, react with nitrous acid to liberate nitrogen gas. This reaction is the basis for the Van Slyke method for determining "free" amino groups (uncombined amino groups) in protein material.



C. Reaction with acid halides or acid anhydrides. The amino group of amino acids is readily converted to an amide by reaction with an acid halide to anhydride. Thus glycine reacts with benzoyl chloride to produce hippuric acid.

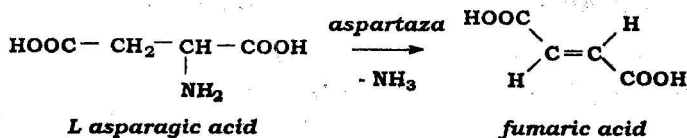


D. Reaction with ninhydrin. Amino acids react with a ninhydrin solution (triketonydrindene hydrate) to produce purple compounds. The reaction is of value in the assay of protein material and can be used for quantitative determination of amino acids. The following sequence of reactions illustrates how ninhydrin converts an amino acid into an aldehyde and carbon dioxide

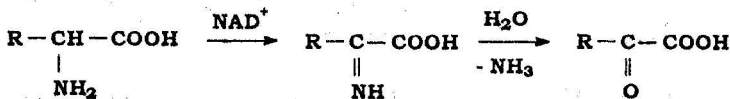


E. Desamination reactions are: oxidative and unoxidative.

Loss of  $\text{NH}_3$  without the presence of oxygen takes place by the influence of enzymes with formation of  $\alpha$ ,  $\beta$ -unsaturated acids:



Oxidative desamination reactions take place with participation of enzymes oxidase and coenzyme  $\text{NAD}^+$  and with formation of  $\alpha$ -ketoacids.  $\text{NH}_3$  enters in the urine synthesis



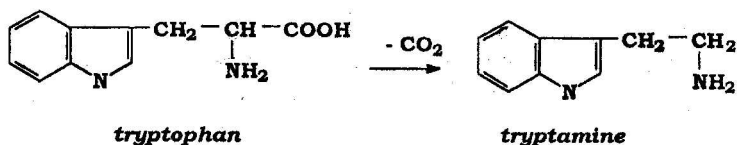
F. Transamination a chemical reaction, catalysed by any aminotransferase (transaminase) enzyme, in which the  $\alpha$ -aminogroup of the aminoacid is transferred to the  $\alpha$ -carbon of an  $\alpha$ -oxo acid. As a result, the  $\alpha$ -oxo acid is transformed into an amino acid, and the aminoacid that donated the aminogroup is converted to the corresponding  $\alpha$ -oxo acid:



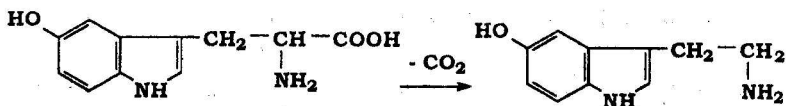
Transamination plays an important role in the catabolism of aminoacids, in which the amino group is eventually (to form aspartate) or to  $\alpha$ -oxoglutarate (to form glutamate). Pyridoxal phosphate is an important coenzyme of aminotransferases.

G. Decarboxylation the act or process of removing the carboxyl group from a carboxylic acid as carbon dioxide. The reaction may be enzyme - catalysed by a **decarboxylase** or, in some instances, particularly with 2-oxo acids, it may be spontaneous - **decarboxylate**.

**Tryptamine** (3-(2-aminoethyl) indole - biogenic amine, formed by enzymic decarboxylation of tryptophan. Of widespread occurrence in mammalian tissues, it is found also in plants and is a product of microbial degradation of proteinaceous material.

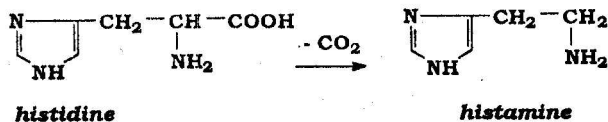


**Serotonin** 5-hydroxytryptamine, a monoamine neurotransmitter occurring in the peripheral and central nervous systems, also having hormonal properties. It is formed from tryptophan, after hydroxylation to 5-hydroxytryptophan, by tryptophan 5-monoxygenase followed by decarboxylation by aromatic-L-aminoacid decarboxylase:



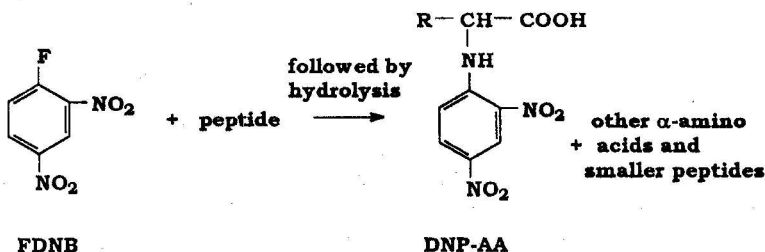
**Histamine** 2-(4-imidazolyl) ethylamine; a compound formed by the decarboxylation of L-histidine and present in many mammalian tissues, with especially high concentrations in lung, skin, and intestine. It is a potent vasodilator, also increases capillary permeability, causes contraction of smooth muscle, plays a role in the regulation of gastric secretion, and anaphylactic conditions. Histamine forms from histidine by histidine decarboxylase. A pyridoxal phosphate serves as coenzyme at this reaction.





### Sequence of amino acids in peptides

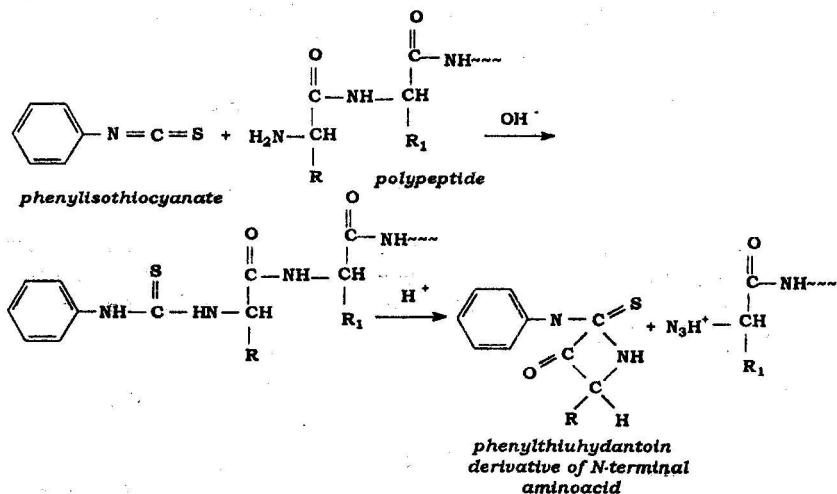
The N-terminal group of peptide is "tagged" by reaction with Sanger's reagent, 2,4 - dinitrofluorobenzene, or with dansyl chloride (5 - dimethyl amino-1-naphthalenesulfonyl chloride) before the peptide is hydrolyzed.



The tagged amino acid is liberated by hydrolysis. Since it is colored it is easily distinguished from the other amino acids that comprise the peptide structure.

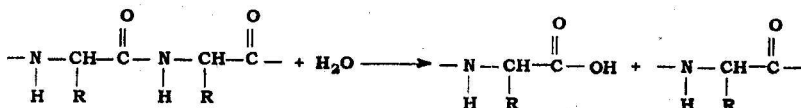
The advantage of the dansyl chloride procedure, which is chemically similar to the Sanger method, is that it yields easily detected fluorescent products and, thus, is about 100 times more sensitive as the Sanger method.

A third procedure, called Edman degradation, may be used, not only for the identification of N-terminal groups but also for the establishment of the sequence of amino acids in the polypeptide chain by a stepwise cleavage of the amino acid from the N-terminus. The reagent used is phenylisothiocyanate.

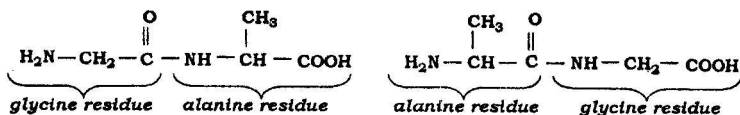


The process can be repeated to remove the new N-terminal amino acid and has been automated to permit the rapid determination of sequences of up to 20 amino acids by sequential removal and identification of amino acids.

Proteins consists of hundreds of amino acids bonded by peptide bonds. The components of the protein are called amino acid residues hydrolysis of protein yields a mixture of its constituent amino acids.



Peptides are lower-molecular weight materials containing fewer amino acids than proteins. A peptide containing two amino acid units is called a dipeptide; one containing three amino acids, a tripeptide; and one containing a large number, but less than 50, a polypeptide. Peptides are named by combining the names or abbreviations of the individual amino acids. The name starts with the amino acid whose amino group is free (the N-terminal amino acid) and ends with that whose carboxyl group is free (the C-terminal amino acid). Two examples of this nomenclature are

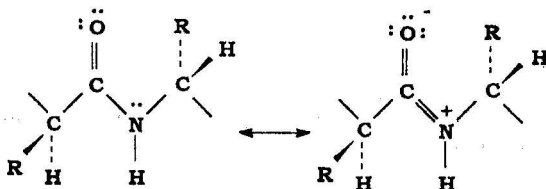


Although there are only two dipeptides possible from a given pair of amino acids (see above), the number of possible isomers increases rapidly with more amino acids.

The number of isomers peptides containing one molecule each of  $n$  different amino acids is equal to  $n!$ , where  $n! = 1 \times 2 \times 3 \dots \times (n-1) \times n$ . Each protein has a specific sequence of amino acids which are assembled under the direction and control of nucleic acids.

### The peptide bond

The peptide bond is the strongest and most important bond in a protein. There are restricted rotation about the carbon-nitrogen bond of amides. The restricted rotation is the result of some double bond character which is pictured in resonance forms



Peptides tend to exist in trans conformation about the carbon-nitrogen bond.

The peptide unit is rigid and planar a feature that is important in the overall structure of proteins. In contrast, the bond between the  $\alpha$ -carbon atom is a single bond that is rotationally free. Similarly, the single bond between the nitrogen atom and the  $\alpha$ -carbon atom is also rotationally free. Thus a protein chain consists of rigid peptide units connected to one another by freely rotating single bonds. There is, in addition, free rotation about the bond between the  $\alpha$ -carbon atom and R group. Both the rigidity and flexibility of portions of protein chain are important in determining its conformation

### Structure of proteins

The unique biological activity of proteins is dependent on the three-dimensional shape of the molecule.

Protein structure may be described at four levels called primary, secondary, tertiary, and quaternary

### Primary structure

The sequence of amino acids in a protein and location of disulfide bonds is called its primary structure

### Secondary structure

The specific spatial arrangement of amino acid residues that are close to one another in the polypeptide chain is called the secondary structure. Recall that there is free rotation of bonds separating the planar and rigid peptide units. These peptide units are oriented at angles to each other and can exist in a variety of conformation. Many proteins consist of chain coiled into a spiral known as a helix. Such a helix may be either right - or left-handed, as in the case of screws. For proteins consisting of L-amino acids the right-handed (or  $\alpha$ ) helix is more stable than the left-handed helix. The spiral is held together by hydrogen bonds between the proton of the N-H group of one amino acid and oxygen of the C=O group of another amino acid in the next turn of the helix. There is another secondary structure -  $\beta$ -pleated sheet. The intermolecular hydrogen bonds between the chains of proteins cause a regular -pleated or partially folded structure

### Tertiary structure

The tertiary structure refers to the spatial arrangement of amino acid residues that are far apart in the polypeptide chain.

The spatial arrangement is the result of the three - dimensional shape of the protein.

The three-dimensional folded shape of a globular protein is the result of its primary and secondary structures, which together make possible the long-range interaction between amino acids.

### Quaternary structure

The quaternary structure of a protein is the organisation or the association of several protein chains or subunits into a closely packed arrangement. Each of the subunits has its own primary, secondary, and tertiary structure. The subunits fit together because of their shape and are held together by noncovalent interactions. Single-chain proteins have no quaternary structure.

## HETEROFUNCTIONAL ORGANIC COMPOUNDS, THAT PARTICIPATE IN METABOLISM PROCESSES

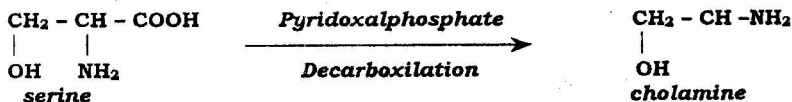
### Amino - alcohols



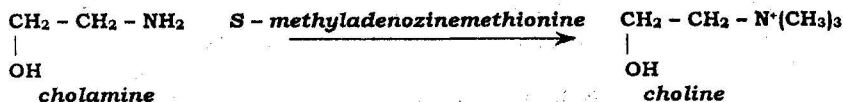
Amino-alcohols are compounds, containing in the same molecule the amino and hydroxi groups connected on a different carbon's atom.

The aminoalcohols appear in a number of compounds of potent physiological activity. The main representants are cholamine, choline, 3,4-dihidroxyphenylalanine (DOPA), epinephrine, adrenaline, noradrenaline.

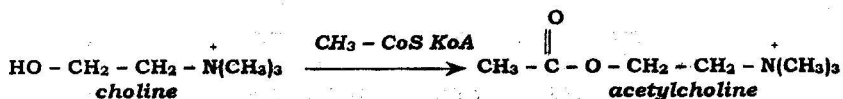
Cholamine appears in organism at the decarboxilation of aminoacid - serine,



Choline obtains at methylation of cholamine.

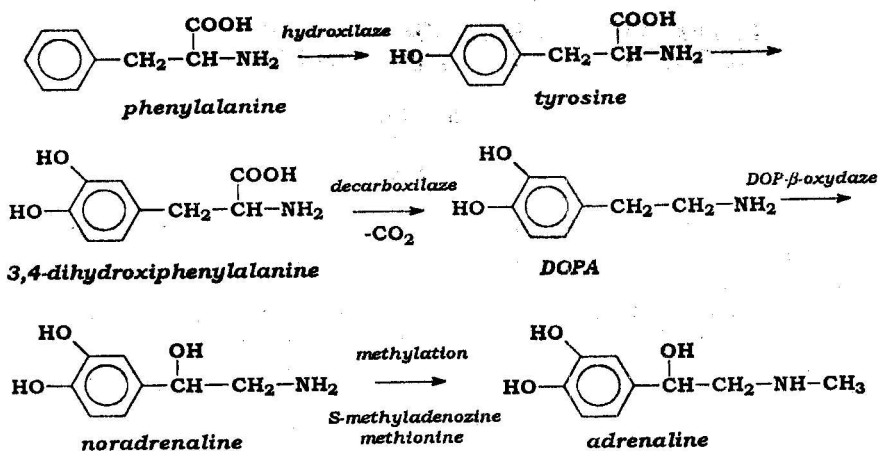


Choline appears in lecithin with glycerol as a mixed ester of phosphoric acid and fatty acids. Acetylated choline, or acetylcholine, plays a vital role in the generation and conduction of nerve impulses in the body:



The important role in organism have aminoalcohols: DOPA, catecholamines (adrenalin and noradrenaline).

The initial substance in biosynthesis of catecholamines is essential aminoacid - phenylalanine:



Epinephrine or adrenaline is a hormone secreted by the adrenal medulla and a neurotransmitter secreted by neurons in the brainstem. It is synthesized by the methylation of norepinephrine. It is an agonist for adrenoceptors, through which it has powerful glycogenolytic and lipolytic effects and also affects the activity of smooth muscle (notably of the cardiovascular system and bronchi) and glandular tissue.

### Hydroxi- and aminoacids



In dependence of reciprocal place of hydroxi- or aminogroups and carboxylic group we distinguish  $\alpha$ -,  $\beta$ -,  $\gamma$ -,  $\delta$ - and s.o. hydroxi and aminoacids.

Those two groups of organic compounds are biologically important, because they take part in many vital processes.

The property of hydroxi- and aminoacids are determined by different functional groups.

On carboxylic group – the formation salts, esters, anhydrides, amide, can lose carbon dioxide ( $\text{CO}_2$ ).

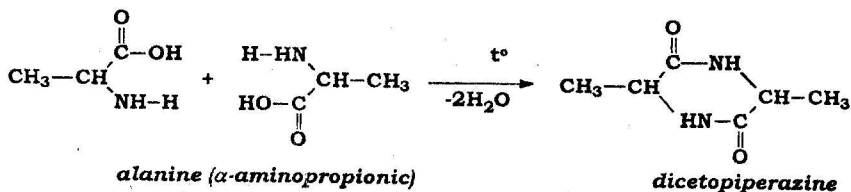
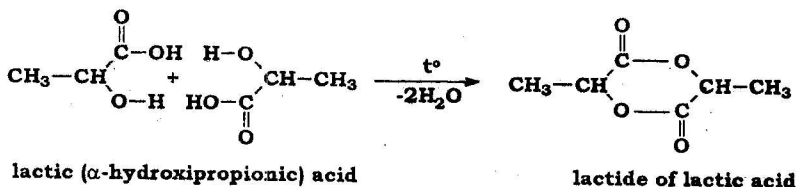
On hydroxyl groups – the formation of esters, oxidation with formation of aldehydes and ketoacids.

On aminogroups - take place alkylation and acetylation reactions

The specific properties of hydroxi- and aminoacids are conditioned by reciprocal influence of groups to it other.

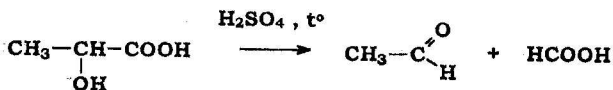
### $\alpha$ -hydroxi- and $\alpha$ -amino-acids

At heating of those compounds take place intermolecular dehydration with formation of six heterocycles - lactides and dicetopiperazines:

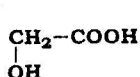


Lactides and dicetopiperazines represent corresponding cyclic esters or amides, therefore in condition of acidic or basic catalyst the compounds subject to hydrolyze with formation of initial hydroxi- or amino acids.

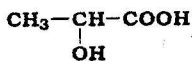
The particularly property of  $\alpha$ -hydroxiacids presents decomposition on heating in the presence of mineral acids with formation of carbonilic compounds and formic acid:



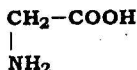
**The best important representatives of  $\alpha$ -hydroxi- and  $\alpha$ -aminoacids**



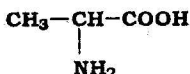
Glycolic acid – may be determined in many plants, grapes, beetroot



Lactic acid- one of the important hydroxiacids, form from lactic fermentation of lactose. Lactic acid is oxidated with formation of piruvic acid



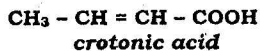
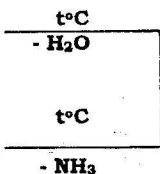
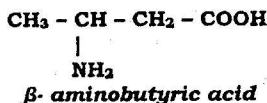
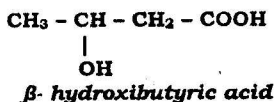
*glycine*



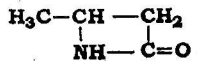
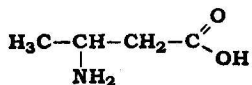
*alanine*

Glycine, alanine others present  $\alpha$ -aminoacids, that enter in composition of proteins

**$\beta$ -hydroxi and  $\beta$ - amino acids**



The easiness of these reactions is caused by high CH-acidity at  $\alpha$ -carbon. In this case it may take place the cyclisation reaction with formation of cycle of  $\beta$ -lactam.

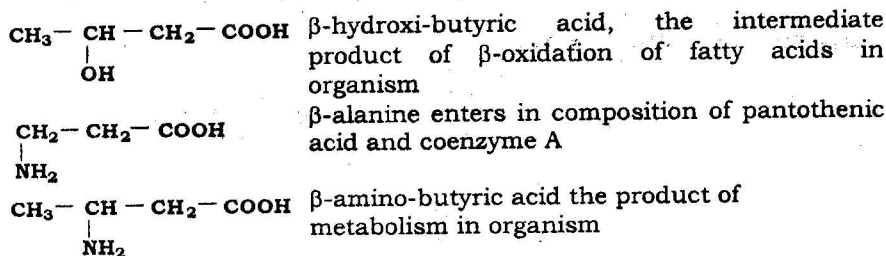


*$\beta$ -lactame*

But practical this reaction can not take place, because the tetrycycle is unsteady. But in some case tetrycycle can meet in penicillin, which easy hydrolysis, therefor penicillin, is impossible to sterilize in aquatic solution.

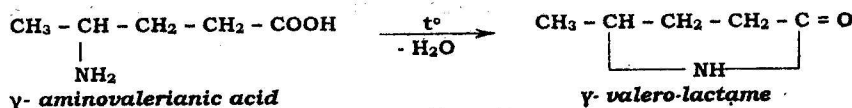
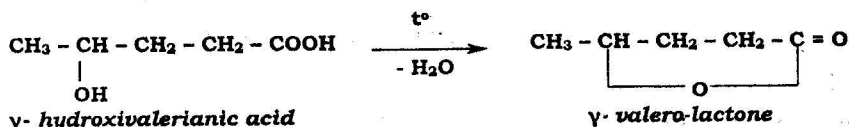


## The important representatives of $\beta$ -hydroxi and $\beta$ -aminoacids

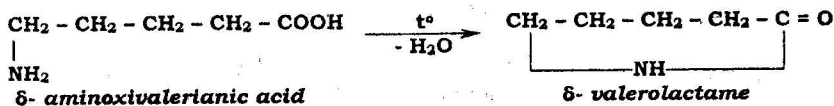
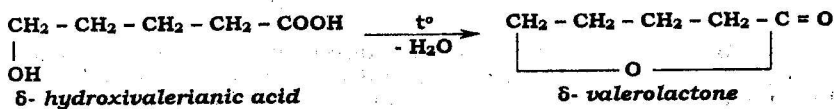


## Properties $\gamma$ -hydroxi- and $\gamma$ - amino acids

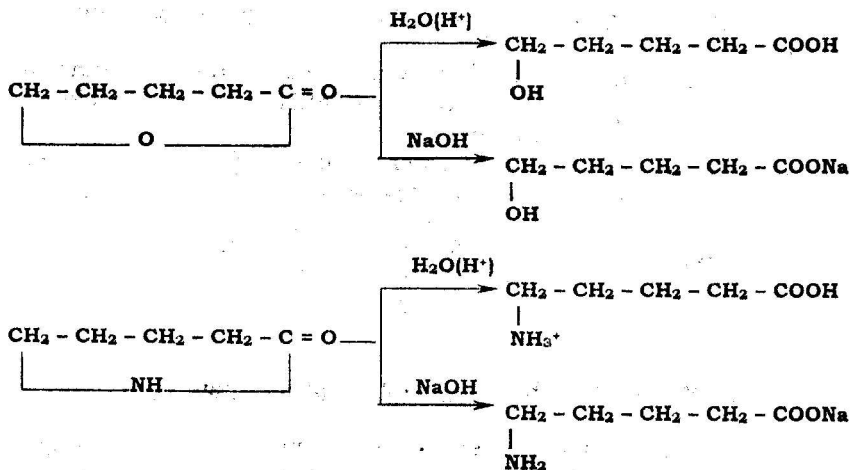
These acids at high temperature suffer intermolecular changes with formation of pentaheterocycles  $\gamma$ -hydroxiacids form cyclic esters - lactones but  $\gamma$ -aminoacids - cyclic amide - lactames.



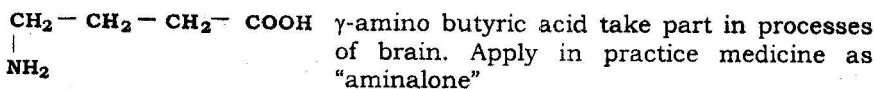
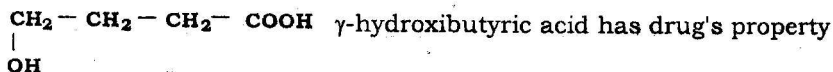
Analogous transformation suffer  $\delta$ -hydroxi- and aminoacids, form sixty cycles  $\delta$ -lactones and  $\delta$ -lactames:



Lactones and lactames in acidic and basic conditions suffer hydrolise reactions with formation of hydroxi- and aminoacids.

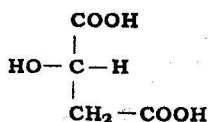


### The important representatives of $\gamma$ -hydroxi- and $\gamma$ -aminoacids

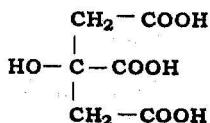


## MANYBASIC HYDROXILACIDS

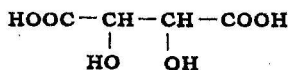
The representants of many basic hydroxyacids are malic, citric, and tartar acids.



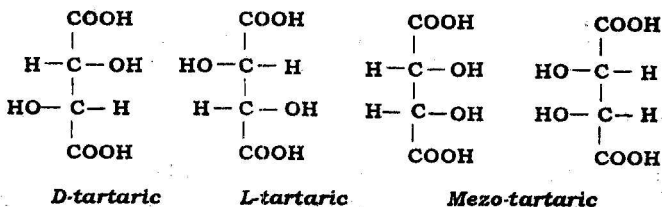
**Malic acid** is contained in green apples, ashberry, fruits juices. It forms in cycle Krebs from fumaric acid. The salts of malic acid are named malates.



*Citric acid* is contained in fruits of citric trees, grapes, gooseberry. The salts of citric acid are named citrates. Citric acid is an intermediate substance of the main biological process, which takes place in all living cells, named cycle or of citric acid (cycle Krebs)

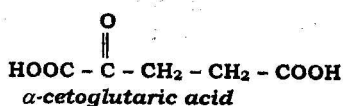
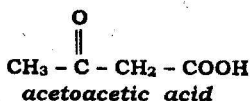
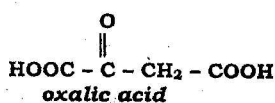
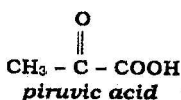
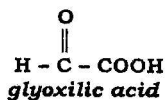


A tartaric's acids is contained two asymmetric carbon's atoms of carbon, which are formed stereoizomers.

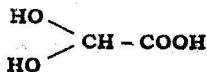


The equal concentrations of D- and L- tartar acids are named racemic mixture – tartaric acid. The racemic mixture, DL-tartaric acid, sometimes occurs during wine manufacture; it was originally known as paratartaric acid. Mezo-form of tartaric acid is optic inactive because has a symmetric plane.

#### Oxo-acids (aldehyde and ceto-acids)

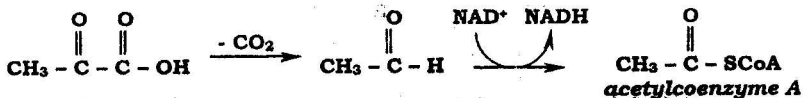


The simplest oxoacid is glyoxilic acid. It contains in unripe fruits and usually is hydratated

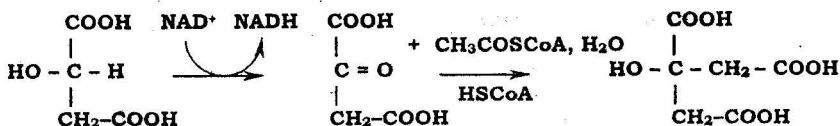


The important role in biochemist processes play ceto-acids

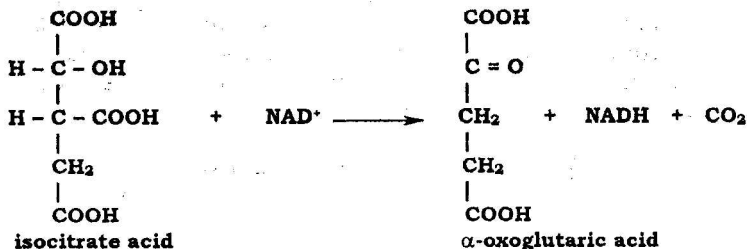
Piruvic acids:  $\text{CH}_3-\text{CO}-\text{COOH}$  It is key product in the metabolism of protein, fats and carbo-hydrates. At the oxidative decarboxilation piruvate transform in acetyl CoA



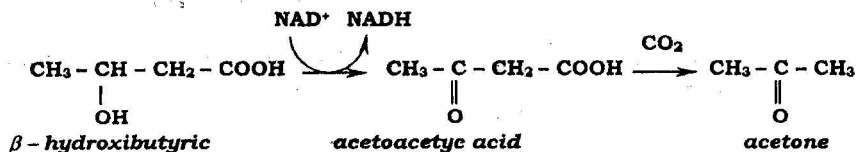
Later on acetylcoenzyme A participates at the same time belong to  $\alpha$ - and  $\beta$ -ketoacids. It forms from malic acid, and then on condensation with acetyl coenzyme A transforms in citric acid.



$\alpha$ -oxoglutaric acid:  $\text{HOOC}-\text{CO}-\text{CH}_2-\text{CH}_2-\text{COOH}$  is precursor for important aminoacids – glutamic and  $\gamma$ -aminobutyric. It results in cycle Krebs from isocitric acid:



Acetoacetic acid  $\text{CH}_3-\text{CO}-\text{CH}_2-\text{COOH}$ , forms in organism as result of oxidation of fatty acids, the concentration increased considerably on sugary diabetes. Decarboxylation of acetoacetic acid form acetone.



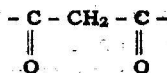
Genetic, these substances connect it others and are named "ketone bodies".

The big role in theoretical and practice biochemistry has ethylic ester of acetoacetic acid. On that compound firstly was show the ceto- and tautomerie.



This type of isomerism is called tautomerism, and the isomers are known as tautomers.

Ceto-enol tautomerism is observed at compounds in the presence of two carbonilic groups in  $\beta$ -position:



In this case is considerable increased CH-acidity that causes formation of enol-form.

Ceto-enol-tautomerism is characteristic for acetoacetic acid:



Increasing of stability of enol-form, connects with appearance of long chain with thermodynamic stability of acid molecule.

We may mention, that many reactions, including formation and transformation of carbonilic compounds, as will show in future, proceed across intermediate enol form or derivative's of these forms.

## PHYSIOLOGICAL ACTIVE DERIVATIVES OF HETEROCYCLIC SUBSTANCES.

### Heterocyclic and heteroatomic compounds

The ring systems of cyclic compounds, studied up to this point, have those in which only carbon atoms are joined together. Such ring systems are called **carbocyclic**.

Rings that contain, in addition to carbon, one or more atoms in the ring are called **heterocyclic**. The **heteroatoms** that occur most frequently in heterocyclic rings are nitrogen, sulfur, and oxygen.

Heterocyclic compounds, like carboxylic compounds may be saturated, unsaturated, or aromatic. You will note that numbering of the ring atoms begins with the heteroatom. Others ring atoms are often designated in nonsystematic nomenclature as  $\alpha$ ,  $\beta$  and  $\gamma$ . The  $\alpha$ -atom in the ring is members adjacent to the heteroatom.

### Five - membered heterocycls, contained only one heteroatom.

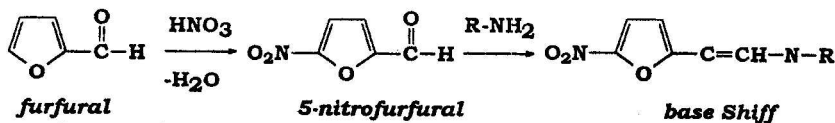
Five-membered heterocycls are: furan, thiophene, and pyrrole. All of then take to aromatic  $\pi$ -surplus systems.

#### Furan

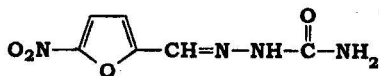


Mainly important derivatives of furan can be considerate **furfural**

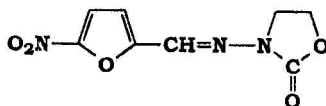
After nitration and amination of furfural can be obtained 5-nitro-derivative of furfural which possesses bactericides properties.



Largest interest have furathylene and furazolidone, which are affective substances in abscesses.

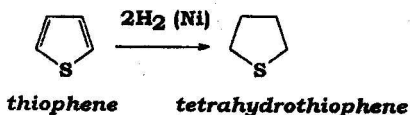


*furathylene*

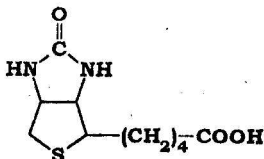


*furazolidone*

### Thiophene



The derivative of tetrahydrothiophene is **biotine** (vit. H)



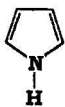
Biotine participates in reactions, which transfer carboxylic groups

### Pyrrole:

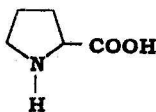


Pyrrole enters in terapyrroles substances - vitamin B<sub>12</sub>, chlorophyll-a, heme.

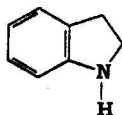
The derivatives of hydrated pyrrole is  $\alpha$ -iminoacid **proline** and heterocycles **indole**



*pyrrole*



*proline*

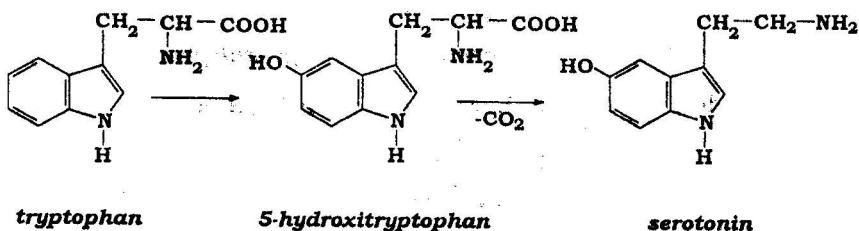


*indole*

We meet indole in tryptophan, strychnine, reserpine, and serotonin.

Tryptophan in mammals it is an essential  $\alpha$ -aminoacid, enters in composition of proteins and is glycogenic. We know that from tryptofphan was obtained serotonin. Serotonin (5-hydroxytryptamine) a monoamine neutrotransmitter occuring in the peripheral and central nervous systems, also having hormonal properties; it is also found in mast cells, platelets, brain, and the enterochromaffin cells of the gastrointestinal tract and is capable of causing vasoconstriction

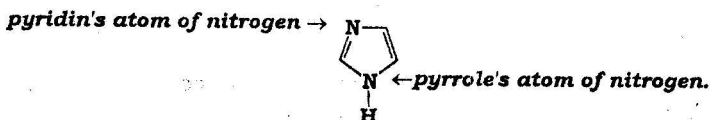
increasing vascular permeability, and contraction of smooth muscle. It is formed from tryptophan, after hydroxylation to 5-hydroxytryptophan, by tryptophan 5-monooxygenase.



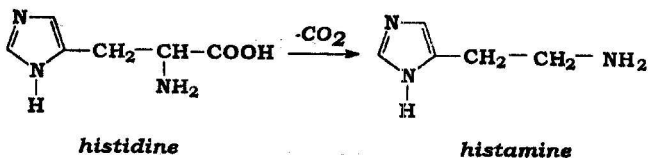
### Five - membered heterocycls wich contained two heteroatoms

Imidazol - aromatic substance, which is stronger base then pyridine, possesses amphoteral properties.

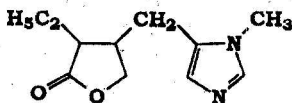
#### Imidazol



A mainly important derivative is  $\alpha$ -aminoacid **histidine** - and product at decarboxilation - **histamine**.

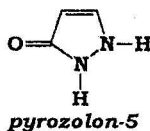
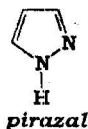


Imidazolic cycle was met in alkaloid - **pilocarpin** - used in treatment of eye diseases

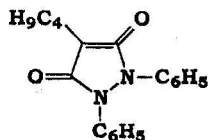
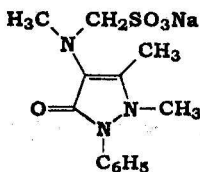
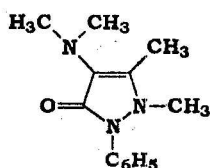
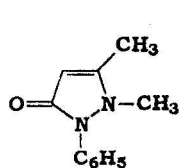




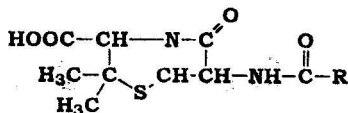
**Pyrazole** - aromatic compound, isomer of imidazol, are not known yet derivatives of pyrazole in nature.. A largely known derivative is pyrozonol -5.



A special importance have the derivatives of pyrozonol-5: antipirine, amidopirine, analgin, butadion, used in medicine as anti-fevers, sedative and anti-inflammation preparats (drugs).

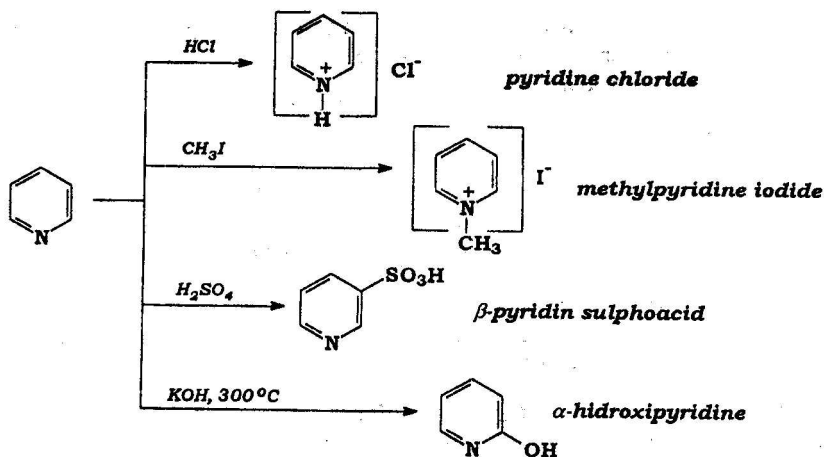


**Thiazole** - aromatic compound, weak base. Thiazole's cycle enters in composition of vitamin B<sub>1</sub> (thiamine), coenzyme of cocarboxilase, sulphanilamide and s.o. Reduced cycle of thiazole - thiazolidine - is the structure's component of antibiotics - penicilium.



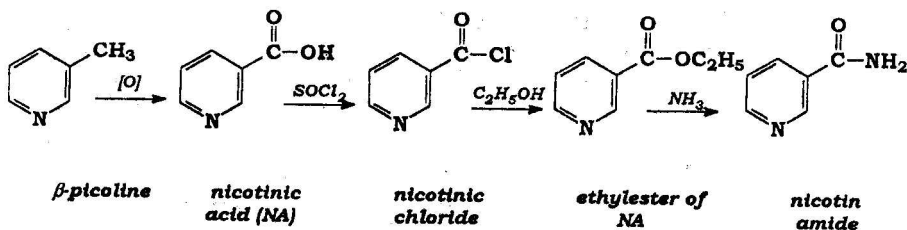
### Six-membered heterocycles contained only one heteroatom

Pyridine - aromatic compound, possesses basic properties, and changes by following the reactions:

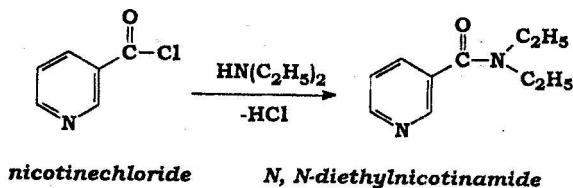


### Medical importances of pyridin derivatives.

**Nicotinic acid and its derivatives.** Nicotinic acid was obtained from  $\beta$ -picoline and was known as vitamin PP, used in medicine for treatment of pellagra.

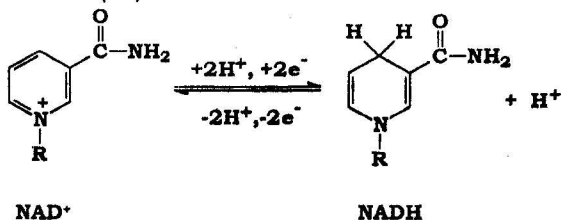


Cordiamine - diethylamide of nicotinic acid is effective stimulator of central nervous system

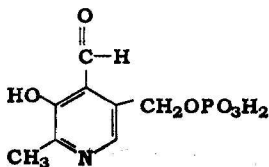


The active centers of nicotinamide in composition of enzymatic systems, participated in oxidoreducing processes of organism.

Chemical reaction based on coenzyme action  $\text{NAD}^+$  consists in adding of hydride-ion ( $\text{H}^-$ ).

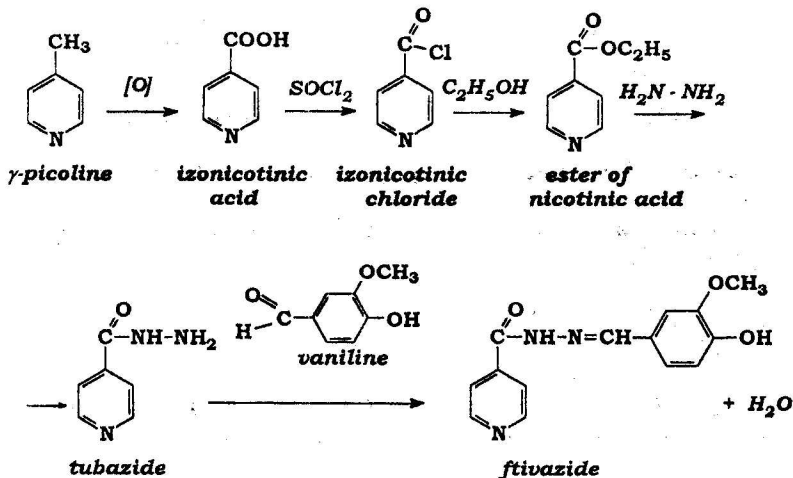


Another derivative of pyridine is coenzyme pyridoxal phosphate which is participating in nitrogen metabolism



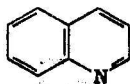
**Pyridoxal phosphate**

Isonicotinic acid - formed to oxidation of  $\gamma$ -picoline. Anti-tuberculosis preparation was synthesis - from nicotinic acid: **tubazide**, **ftivazide**.

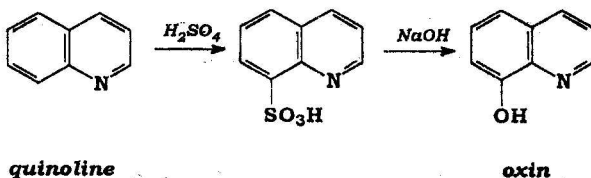


## Quinoline and its derivatives

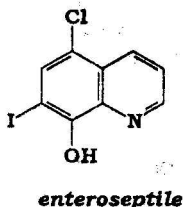
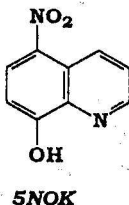
**Quinoline** by properties is the same as pyridine. The nucleus of quinoline enters in composition of alkaloids and drugs.



The sulphonation of quinoline produces 8-quinoline sulphoacid, which was transformed in 8-hydroxyquinoline (Oxin), used as an antiseptic drug.



Bactericides effect possesses 8-hydroxi-5-nitroquinoline (SNOK) and, also 8 hydroxi-7-iodide-5chloridquinolin (Enteroseptole). On the base of the action of this drugs lies their ability to form firm chelate compounds with ions of any biometalls.



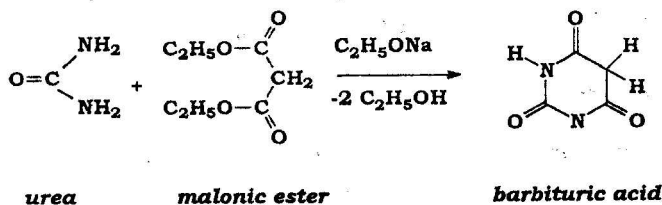
## Six-members heterocycls, containing two heteroatoms.

**Pyrimidine** - aromatic compound, possesses weaker basic properties then pyridine.

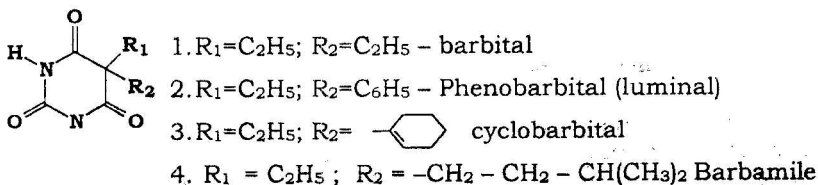


Aspecially important hydroxi-and aminoderivatives of pyrimidine, entered in composition of nucleic acid.

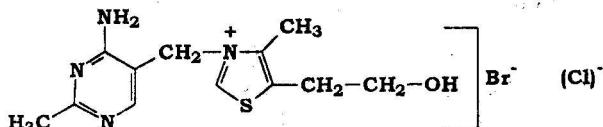
From derivatives of pyrimidine, which have drug's importance we note barbituric acid and barbiturate. Barbituric acid presents cyclic ureide of malonic acid.



On the base of barbituric acid were obtained many of sleeping pills, drugs, and anti-convulsing preparations. For example soporific property has 5,5 - disubstituents of barbituric acid.

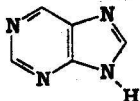


### Thiamine (vitamine B<sub>1</sub>)

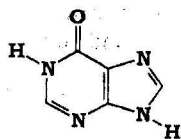


### Condensated heterocycles

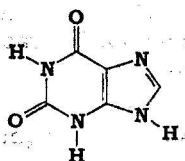
**Purine** - the product of condensation of pyrimidine and imidazole.



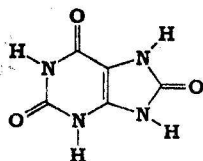
The very important hydroxi- and amino-purines, which are active substances and participate in different vital processes. Hydroxypurines form in organism as result of nucleic acid degradation



*hipoxantin*

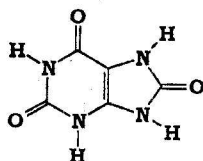


*xantin*

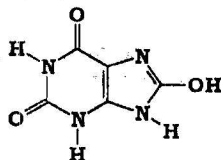


*uric acid*

For hydroxypurines was known lactim-lactam tautomeria, for example



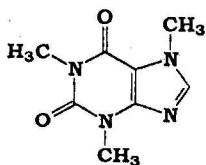
*lactam form*



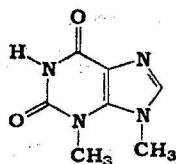
*lactim form*

Uric acid presents in organism as final product of degradation of purines in organism. The salts of acid uric was named urates. Urate of ammonium enters in composition of uric stones.

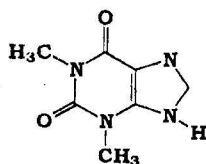
At alkaloids of purine's row belong derivative's of xantin – coffeine (1,3,7-trimethylxantine), theophylline (1,3-dimethylxantine), and theobromine (3,7 – dimethylxantine). The natural sources of those products are leaf of tea, coffee and cocoa beans.



*1,3,7 trimethylxantine  
coffeine*



*1,3 dimethylxantine  
theophylline*



*3,7-dimethylxantine  
theobromine*

Coffeine may be obtained from methylation of xantine, theophylline and theobromine with methyl iodide.

Coffeine – effective preparation exciting central nervous system and stimulating hart's work. Theophylline and theobromine are the competitive inhibitor of cyclic AMP phosphodiesterase. They have diuretic and cardiac stimulatory action, and relax smooth muscle, they are a bronchodilators.

## CARBOHYDRATES. MONOSACCHARIDES.

Carbohydrates are everywhere in nature; they occur in every living organism and are essential for life. The sugar and starch in food and the cellulose in wood, paper, and cotton are nearly pure carbohydrate. Modified carbohydrates form part of the coating around living cells; other carbohydrates are found in DNA, which carries genetic information; and still other are invaluable as medicines.

### Classification and Nomenclature

The word carbohydrate derives historically from the fact that glucose, the first simple carbohydrate to be obtained pure, has the molecular formula  $C_6H_{12}O_6$  and was originally thought to be a "hydrate of carbon"  $C_6(H_2O)_6$ . This view was soon abandoned, but the name persisted. Today the term *carbohydrate* is used to refer loosely to the broad class of polyhydrated aldehydes and ketones commonly called sugars.

The carbohydrates may be subdivided conveniently into three principal classes: monosaccharides, oligosaccharides, and polysaccharides.

**Monosaccharides** include all sugars that contain a single carbohydrate unit – that is, one incapable of producing a simple carbohydrate on further hydrolysis. Most of the monosaccharides are five – and six – carbon structures.

The five – carbon – carbon monosaccharides are called **pentoses**, and those of six – carbons are called **hexoses**. Monosaccharides are further classified as either **aldoses** or **ketoses**. The – ose suffix is used as the family – name ending for carbohydrates, and the ald- and ket- prefixes identify the nature of the carbon group (aldehyde or ketone). The number of carbon atoms in the monosaccharide is indicated by using tri-, tet-, pent-, hex-, and so forth in the parent name. For example, glucose is an *aldohexose*, a six-carbon aldehyde-sugar, fructose is a *ketohexose*, a six-carbon keto-sugar; and ribose is *aldopentose*, a five carbon aldehyde-sugar. Most of the commonly occurring simple sugars are either aldopentoses or aldohexose.

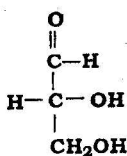
**Oligosaccharides** consist of two or more (ten in maximal number) monosaccharide units joined by acetal linkages between the aldehyde or ketone group of one simple sugar and a hydroxy group of another.

This kind of coupling in sugar chemistry gives rise to what is called a **glycosidic** linkage.

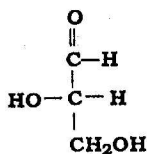
**Polysaccharides** consist of hundreds or even thousands of monosaccharide units joined together through glycosidic linkages to form macromolecules, or polymers.

### Stereochemistry of monosaccharides.

Glyceraldehyde has one chiral carbon atom and thereform has two enantiomeric (mirror-image) forms, but only the dextrorotary enantiomer occurs naturally. That is, a sample of naturally occurring glyceraldehyde placed in a polarimeter rotates plane - polarized light in clock wise direction, denoted (+). Since (+) - glyceraldehyde is known to have the R configuration at C<sub>2</sub>, it can be represented as bellow.

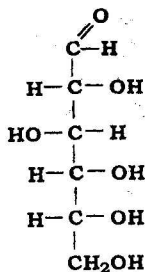


**D-Glyceraldehyde**  
[(R) - (+) - Glyceraldehyde]

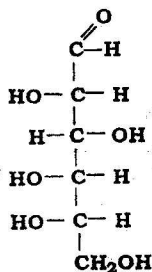


**L-Glyceraldehyde**  
[(S) - (-) - Glyceraldehyde]

Glucose, fructose, ribose, and most other naturally occurring monosaccharides have the same stereo chemical configuration as D-glyceraldehyde at the chiral carbon atom furthest from the carbonyl group. In Fischer projections, therefore, most naturally occurring sugars have the hydroxyl group at the lowest chiral carbon atom refferent to as D-sugars.



**D-glucose**



**L-glucose**

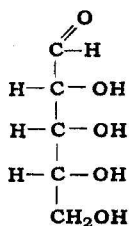
In contrast to the D-sugars, all L sugars have the hydroxyl group at chiral center farthest from the carbonyl group on the left in



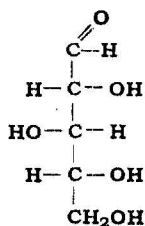
Fischer projections. Thus, L sugars are mirror images (enantiomers) of D sugars.

The mainest representations of sugars are:

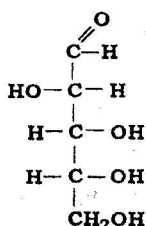
### Pentoses



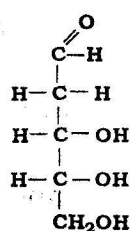
*D-Ribose*



*D-Xylose*

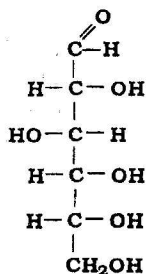


*D-Arabinose*

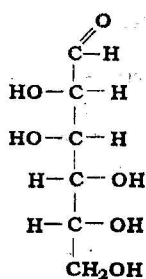


*D-Dezoxiribose*

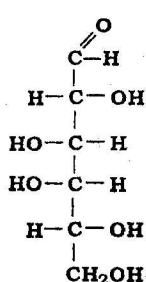
### Hexoses



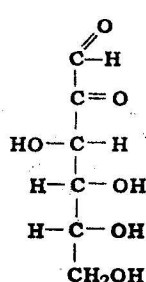
*D-Glucose*



*D-Mannose*

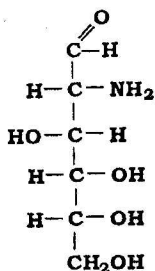


*D-Galactose*

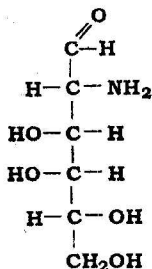


*D-Fructose*

Stereoisomers of monosaccharids, distinguished only with one of chiralic atom of carbon, named epimerons. For example D-glucose and D-mannose and s.o. In nature we can meet derivatives of monosaccharids, containing instead of hydroxi-group – amino-group. The important representatives of aminosugars are:



*D-Glucosamine*

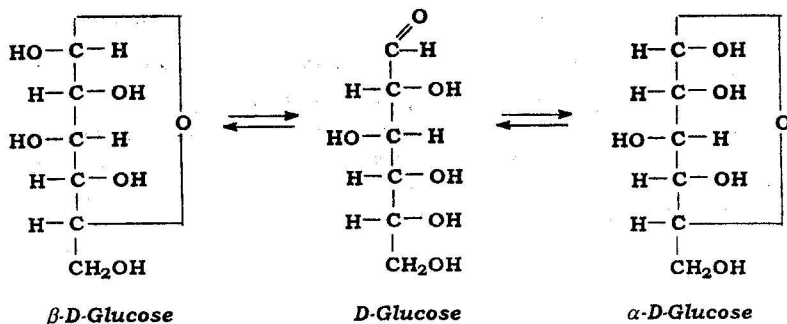


*D-Galactosamine*

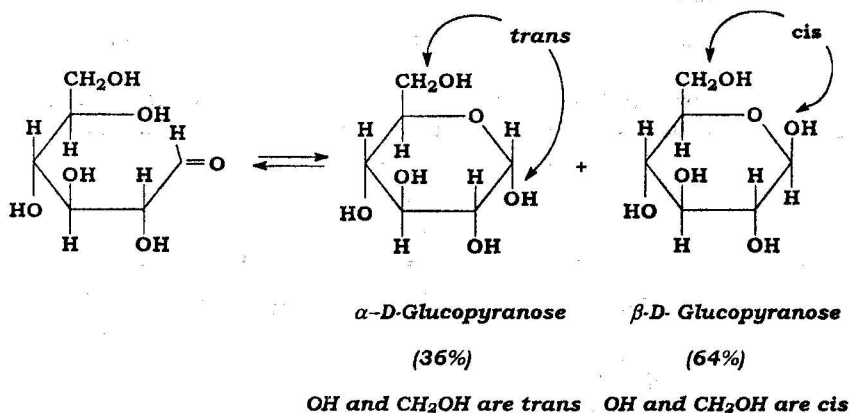
### Cyclic structures of monosaccharides: hemiacetal formation

Several properties of glucose are not explainable by the open chain formula. For example, when D-glucose is heated with methanol in the presence of hydrogen chloride, the expected dimethyl acetal is not obtained.

It both the hydroxyl and carbonyl group are in the same molecule, an intramolecular nucleophilic addition can take place, leading to the formation of a cyclic hemiacetal. Five- and six-membered cyclic hemiacetals form particularly easily, and many carbohydrates therefore exist in an equilibrium between open chain and cyclic forms. For example, glucose exists in aqueous solution primarily as the six-membered (pyranose) ring formed by intramolecular nucleophilic addition of the hydroxyl group at C<sub>5</sub> to C<sub>1</sub> aldehyde group.



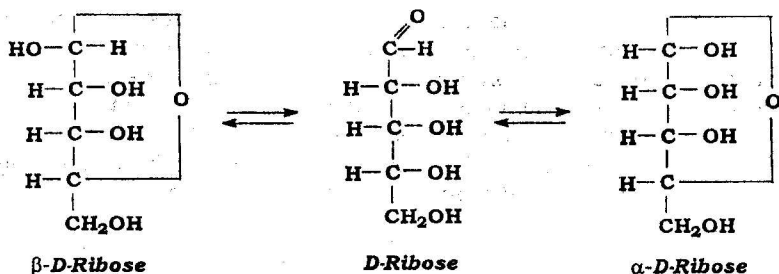
When an open-chain monosaccharide cyclizes to a pyranose form, a new chiral center is formed at what used to be the carbonyl carbon. Two diastereomers called anomers (an-oh-mers) are produced, with the hemiacetal carbon referred to as **the anomeric center**. Anomer- $\alpha$  a pyranose sugar whose hydroxyl group at c 1 is either up ( $\beta$ ) or down ( $\alpha$ ). For example, glucose cyclizes reversibly in aqueous solution to yield a 36:64 mixture of two anomers.



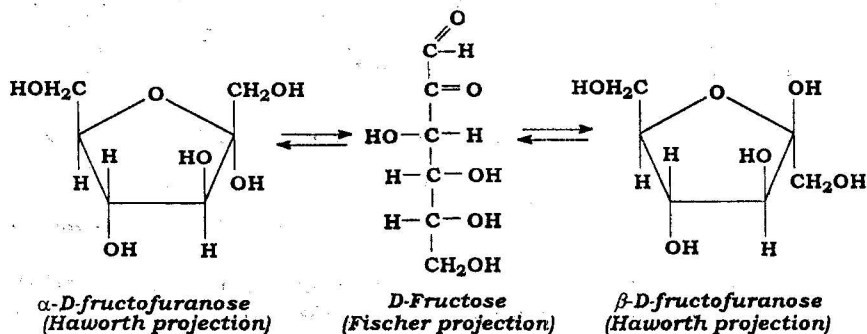
Both anomers of D-glucose can be crystallized and purified. Pure  $\alpha$ -D-glucose has a melting point of 146°C and a specific rotation  $[\alpha]_D$  of + 12,2°; pure  $\beta$ -D-glucose has a melting point of 148-155°C and a specific rotation of + 18,7°.

When a sample of either pure  $\alpha$ -D-glucose and  $\beta$ -D-glucose is dissolved in water, however, both optical rotation of the  $\alpha$ -anomer solution decreases from + 112,2° to 52,6°, and the specific rotation of the  $\beta$ -anomer solution increases from + 18,7° to + 52,6°. Known as a **mutarotation**, this phenomenon is due to the slow conversion of the pure  $\alpha$  and  $\beta$  enantiomers into the 36:64 equilibrium mixture.

Fructose, on the other hand, exists to the extent of about 20% as the five-membered (furanose) ring formed by addition of the hydroxyl group at C<sub>5</sub> to C<sub>2</sub> ketone. Pentoses form a five-membered ring, too.



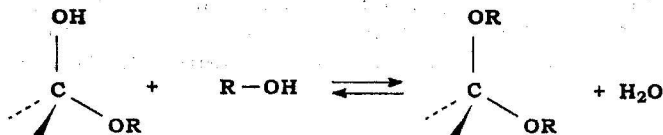
Pyranose and furanose rings are often represented using the **Haworth projections**. The equilibrium between oxo-form and cyclic form are known as cyclo-oxo-tautomerism.



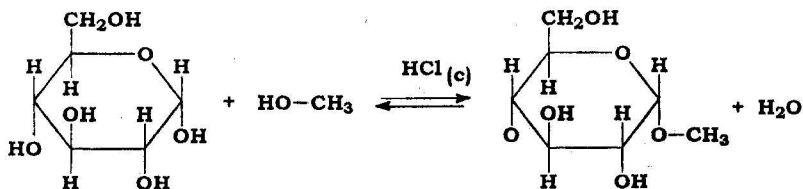
### Chemical properties of monosaccharides

#### 1. Glycoside formation

Treatment of a hemiacetal with an alcohol and acid catalyst yields an acetal.



For example, reaction of glucose with methanol gives methyl  $\beta$ -D-glucopyranoside:



In this case - CH<sub>3</sub> present unsugar part of glycoside, named *aglicone*.

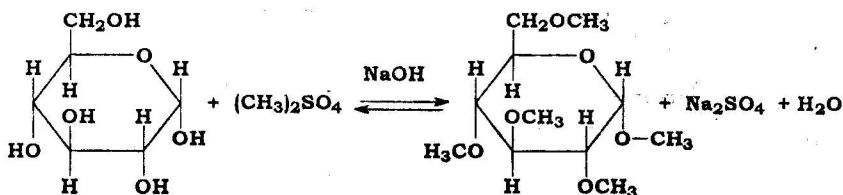
Carbohydrate acetals are called **glycosides**.

They are named by first citing the alkyl group and then replacing the -ose ending of sugar with -oside. Glycosides, like all acetals, are stable to water, but they can, be converted back to the free monosaccharide by hydrolysis with aqueous acid.

Glycosides are widespread in nature, and a great many biologically active molecules contain glycosidic linkages. For example, digitoxin, the active component of the digitalis preparations used treatment of heart disease consisting of a complex steroid alcohol linked to a trisaccharide.

## 2. Ester and ether formation

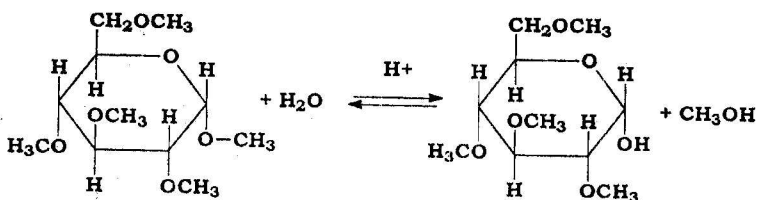
At reaction of monosaccharides with CH<sub>3</sub>I or (CH<sub>3</sub>)<sub>2</sub>SO<sub>4</sub> in base environment enter in reaction all hydroxyl groups and form esters (the products of full methylation of monosaccharides):



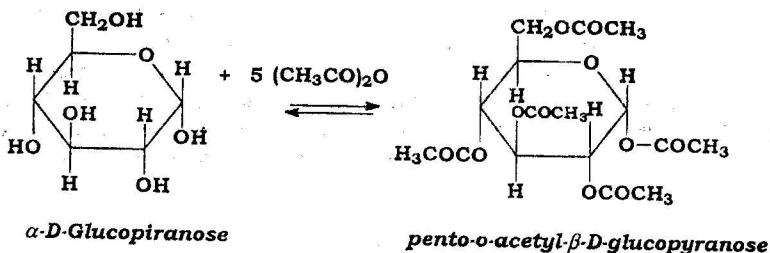
*α-D-glucopyranose*

*o-methyl-α-P-2,3,4,6-tetromethylglucopyranoside*

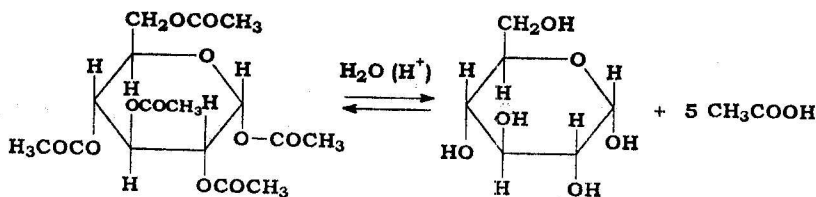
Esters of monosaccharides confirm its structure. Hydrolyses in acid environment are bringing to disintegration of glycozidic bond.



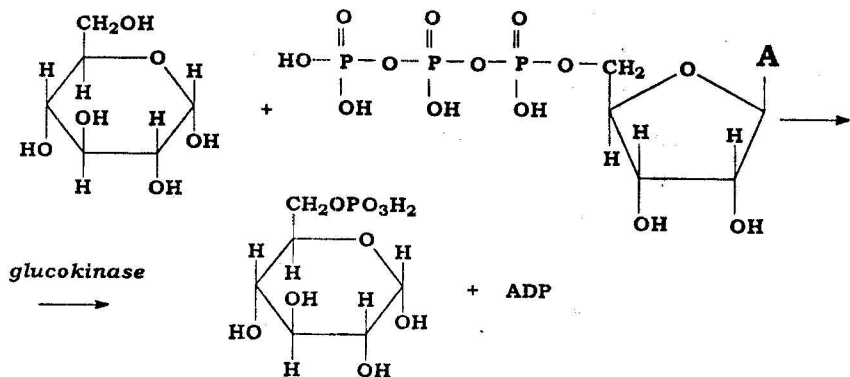
Esterification is carried out by treating the carbohydrate with an acid chloride or acid anhydride in the presence of a base. All the hydroxyl groups react, including the anomere one. For example,  $\beta$ -D-glucopyranose is converted into its pentacetate by treatment with acetic anhydride in pyridine solution.



The esters are easily hydrolyzed with formation of monosaccharides.

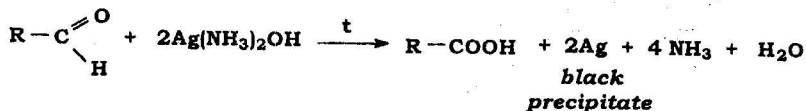
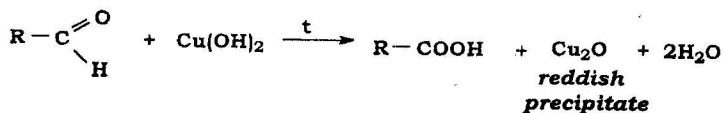


In organisms the main role has reaction of phosphate esters. Phosphorylation of glucose carries out with ATP participation.

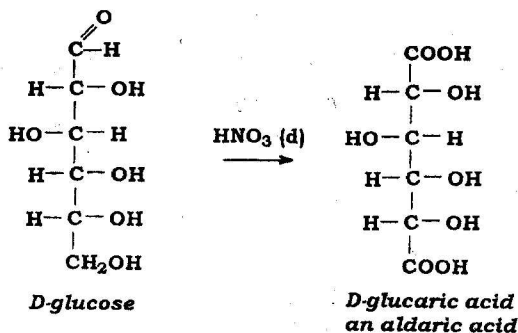


### 3. Oxidation of monosaccharides

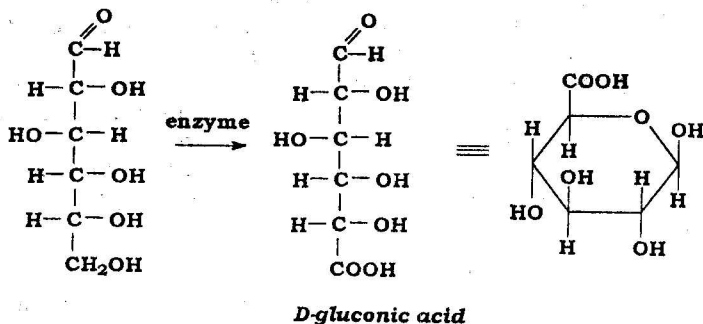
Like other aldehydes, aldoses are easily oxidized to yield carboxylic acids called **aldonic acids**. Aldoses react with Tollen's reagent ( $\text{Ag}^+$  in aqueous ammonia), Fehling's reagent ( $\text{Cu}^{2+}$  with aqueous sodium tartrate), and Benedict's reagent ( $\text{Cu}^{2+}$  with aqueous sodium citrate) to yield the oxidized sugar and a reduced metallic species. All three reactions serve as simple chemical tests for what are called reducing sugars (reducing because the sugar reduces the metallic oxidizing agent).



If warm dilute nitric acid is used as the oxidizing agent, aldoses are oxidized to dicarboxylic acids called **aldaric acids**. Both the aldehyde carbonyl and the terminal  $-\text{CH}_2\text{OH}$  group are oxidized in this reaction.

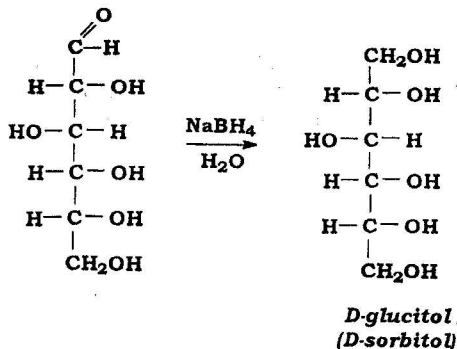


In animal organism we meet enzyme oxidation with oxidation of C<sub>6</sub> carbon atom to form uronic acids.



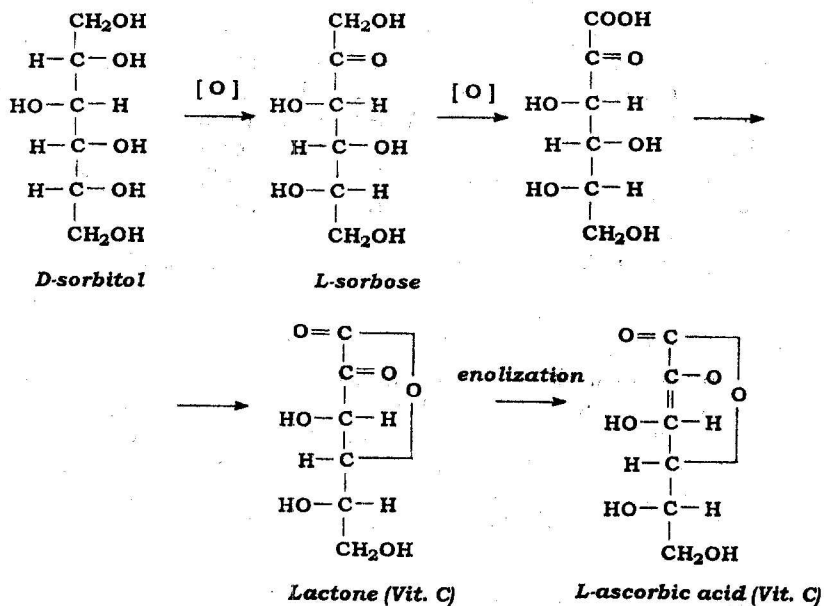
#### 4. Reduction of monosaccharides

Treatment of an aldose or ketose with borohydride reduces it to a polyalcohol called an alditol.





Reduction of glucose in D-sorbitol is one of reactions of obtain ascorbic acid (vit. C).



## OLIGOSACCHARIDES AND POLYSACCHARIDES

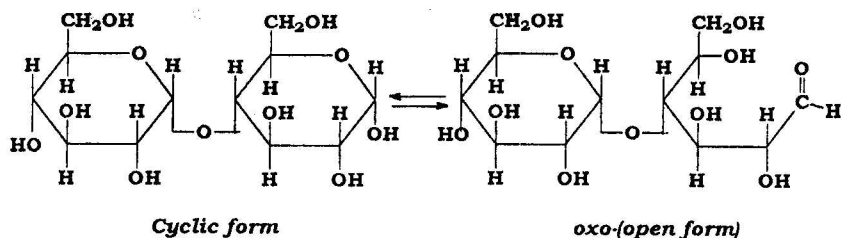
### I. Oligosaccharides.

Disaccharides, the most important of oligosaccharides, may be regarded as glycosides. Oligosaccharides consist of two or more (but a relatively small number) monosaccharide units joined by acetal linkages between the aldehyde or ketone group of one simple sugar and hydroxy group of another. This kind of coupling in sugar chemistry gives rise to what is called a glycosidic linkage. A glucosidic link between C1 of the first sugar and C4 of the second sugar, called a 1,4' link, is particularly common.

A glycosidic bond to the anomeric carbon can be either alpha or beta.

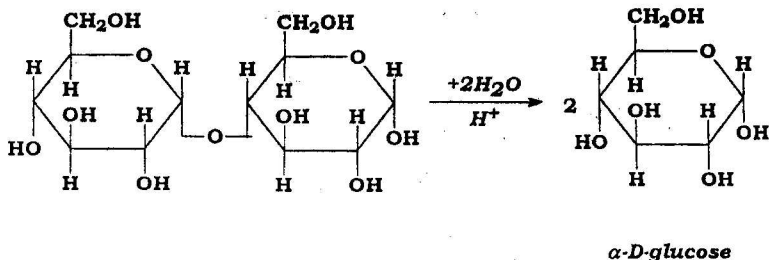
#### **1. Maltose.**

Maltose, or malt sugar, is disaccharide produced when starch is hydrolyzed by malt *diastase*. Another enzyme, *maltase*, selectively split the alpha-glycosidic link and completely hydrolyzes maltose to yield two D-glucose units. Maltose is *reducing* sugar. This chemical evidence suggests the presence of an aldehyde group either uncombined or in equilibrium with the hemiacetal form, as are shown below:



The structure of maltose is that of two glucose units in a "head-to-tail" arrangement joined through an  $\alpha$ -linkage from carbon (1) of one glucose unit to carbon (4) of a second glucose.

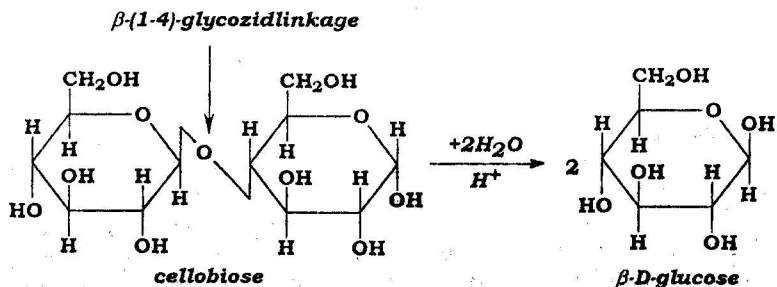
Maltose easily forms glucosides, esters and ethers. Maltose can reduce Tollens' or Fehling's reagent. In acid environment on heating enzymatically maltose can be hydrolysed to form two molecules of  $\alpha$ -D-glucose.



## 2. Cellobiose

Cellobiose is a disaccharide that is obtained by the hydrolysis of cellulose. It is a reducing sugar consisting of two glucose units joined as in maltose, but through a  $\beta$ -linkage.

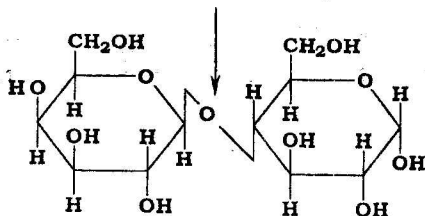
The enzyme maltase is incapable of hydrolyzing cellobiose. In all other respects the behavior of cellobiose is identical to that described for maltose. Cellobiose is also reducing sugar. On hydrolyzation cellobiose can produce two molecules of  $\beta$ -D-glucose:



## 3. Lactose.

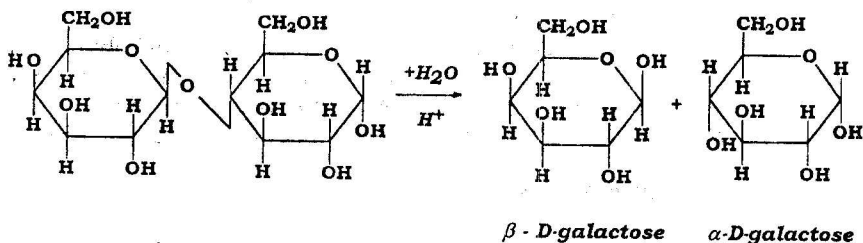
Lactose is known as a milk sugar because it is present in the milk of mammals. It is present in cows' milk to extent of about 5% and in human milk to about 7%. It is produced commercially as a by-product in the manufacture of cheese. Lactose is a reducing sugar, forms an osazone, and exhibits mutarotation. Lactose, when hydrolyzed by mineral acids or by the action of the enzyme *lactase*, produces equimolar quantities of D-glucose and D-galactose. Lactose is a  $\beta$ -galactoside in which the anomeric (1) carbon of galactose is joined through a  $\beta$ -linkage to the number (4) carbon of glucose in a "head-to-tail" arrangement. This is shown below.

***$\beta$ -{1-4}-glycosidlinkage***



***$\beta$ -D-galactopyranosyl-1,4- $\alpha$ -D-glucopyranose***

**Hydrolyzation of lactose**



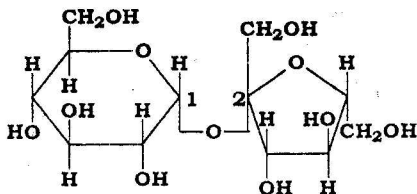
**4. Sucrose**

Sucrose, ordinary table sugar, is obtained from the juices extracted from sugar cane and sugar beets. Sucrose is a disaccharide that yields one equivalent of glucose and one equivalent of fructose on hydrolysis of its glycoside link. This 1:1 mixture of glucose and fructose is often referred to as *invert sugar* because the sign of optical rotation changes (inverts) during the hydrolysis from sucrose,  $[\alpha]_D = +66.5^\circ$ , to a glucose/fructose mixture,  $[\alpha]_D = -22^\circ$ .

Certain insects such as honey bees have enzymes called invertases that catalyze the hydrolysis of sucrose to glucose + fructose.

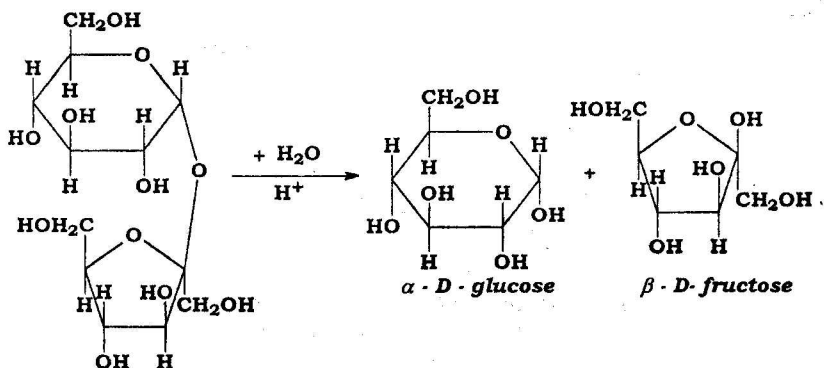
Honey, in fact, is primarily a mixture of glucose, fructose, and sucrose.

Unlike most other disaccharides, sucrose isn't a reducing sugar and doesn't exhibit mutarotation. These observations imply that sucrose has no hemiacetal groups, suggesting that the glucose and fructose units must both be glycosides. Structure of sucrose is shown below:



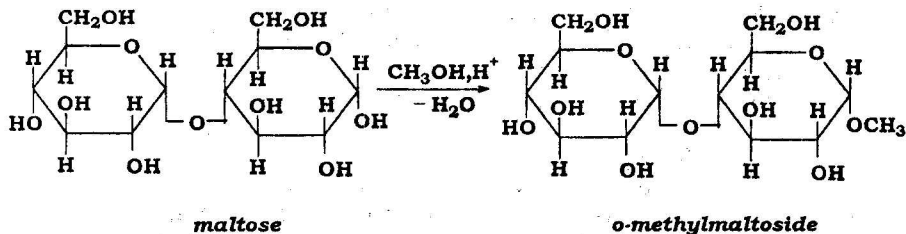
**Sucrose**  
 ***$\alpha$ -D-glucopyranosyl-1,2- $\beta$ -D-fructofuranoside***

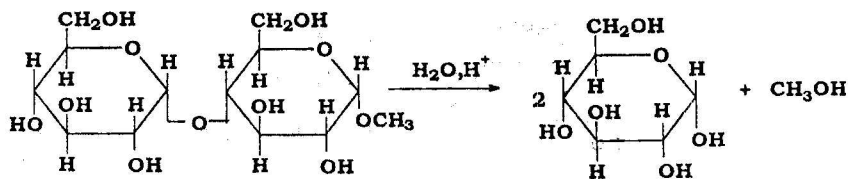
At acid's or enzymes' hydrolysis we can obtained one glucose and one fructose:



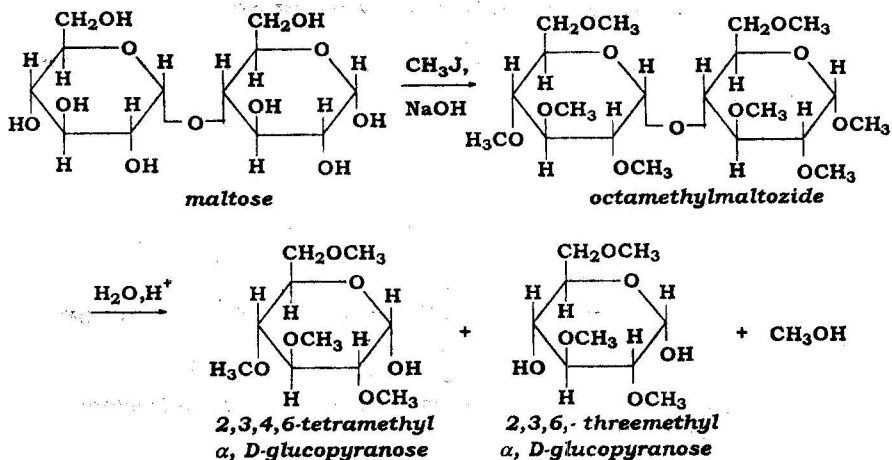
Disaccharides have the same properties as monosaccharides, for example, form esters and ethers, but maltose, cellobiose and lactose oxidate with reduce Fehling's solution and Tollens' reagent. Disaccharides form glycoside.

Formation and hydrolyzation of glucoside are shown bellow:





Formation and hydrolyzation of esters:



## II. Polysaccharides

The polysaccharides are high molecular weight (25 000-15 000 000) natural polymers in which hundreds (or even thousands) of pentose or hexose units have been joined through glycosidic linkages. The polysaccharides divide in two groups: homopolysaccharides and heteropolysaccharides. The unit of homopolysaccharides is one of monosaccharides, but heteropolysaccharides have different monosaccharides as structural units. The most important polysaccharides are starch, glycogen and cellulose.

### 1. Starch, Glycogen.

Starch is the carbohydrate of most plants. It comprises the major part of all cereal grains and most plant tubers, where it is stored. Starch is used as a principal food source throughout the

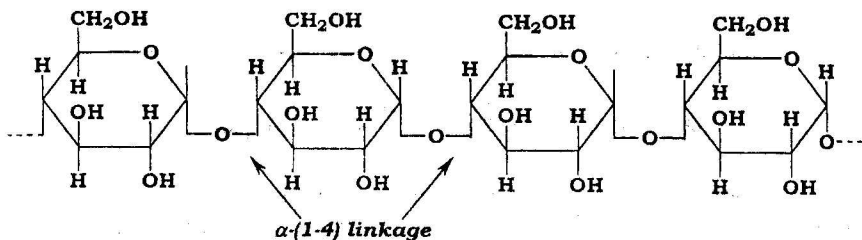
world. Glycogen is the reserve of carbohydrate of animals, and a relatively small amount is stored in the liver and muscles. Structurally starch and glycogen are similar.

Both have the empirical formula  $(C_6H_{10}O_5)_n$ , and both, when completely hydrolyzed, yield glucose.

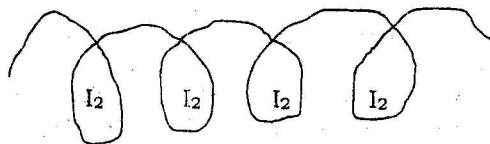
Starch and glycogen are only partially hydrolyzed to maltose by the enzyme amylase.

When a paste made of starch and water is heated, two fractions may be separated. One called the **amylose fraction**, is water-soluble and has a molecular weight range of 20 000-225 000. A second fraction, called amylopectin, is water-insoluble and has a molecular weight range of 200 000-1 000 000.

Amylose can be hydrolyzed almost completely to maltose by the enzyme  $\beta$ -amylase. This hydrolysis indicates that the maltose units arise from glucose units joined through  $\alpha$ -1-4 linkage.



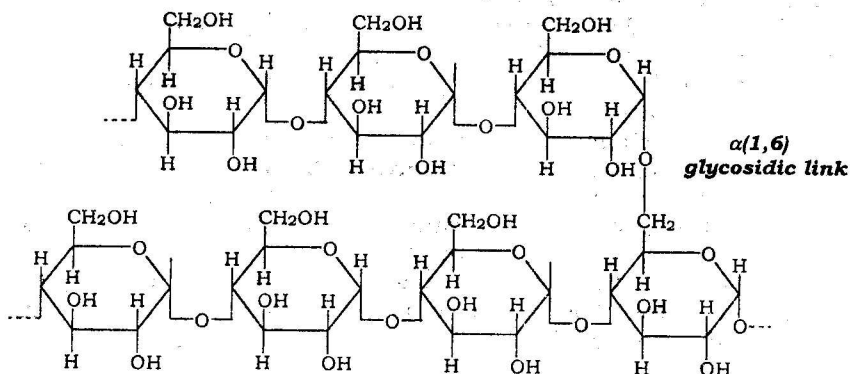
The second structure of amylose presents an unbranched chain, in which rests of glucose twist in spirals' form, in which six glucose enter in one coil.



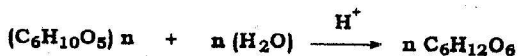
The emptiness, formed in such form of chain, can contain the molecules of blue iodine that bring to formation of blue complex substance – the qualitative reaction on starch.

Amylopectin, on the other hand, is hydrolyzed to maltose to a much lesser degree by the same enzyme. Chemical evidence indicates that considerable branching occurs in the amylopectin fraction of the starch molecule. Such branches are formed from glucose units linked through carbon atom (1) and (6). The glycosidic link at these positions

resists hydrolysis by  $\beta$ -amylase. A segment of a branched starch molecule is shown:



Complete acid hydrolysis of starch yield  $\alpha$ -D-glucose:



Glycogen is the emergency polysaccharides of animal and human organism. On chemical structure glycogen is the same as chemical structure of amylopectin, but branching meet more often and molecule of glycogen considerable bigger on dimensions.

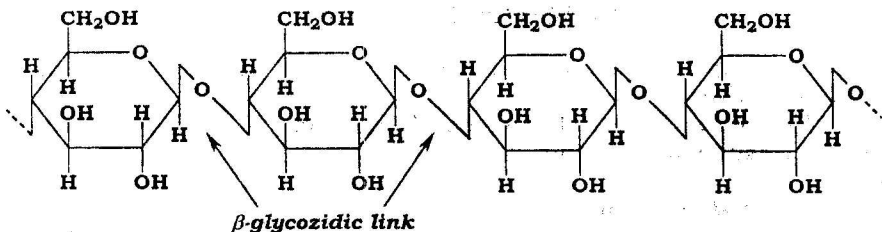
## 2. Cellulose.

Cellulose comprises the skeletal material of plants and is the most abundant organic substance found in nature. It is the chief constituent of wood and cotton. Cotton, almost pure cellulose, is the principal source of cellulose used as fiber for fabrics. The cellulose content of wood is approximately 50 per cent. The separation of cellulose from other plant components is an important commercial process upon which the textile, paper, and plastic industries are largely dependent.

The general formula for cellulose, like that for starch, may be written  $(\text{C}_6\text{H}_{10}\text{O}_5)_n$  but the numerical value of  $n$  in the formula for cellulose is much larger than that for starch, is largely unbranched.

Complete hydrolysis of cellulose produces  $\beta$ -D-glucose. Partial hydrolysis produces cellobiose, cellotriose, and higher oligosaccharides. The presence of  $\beta$ -glycosidic linkages establishes the structure of cellulose as.

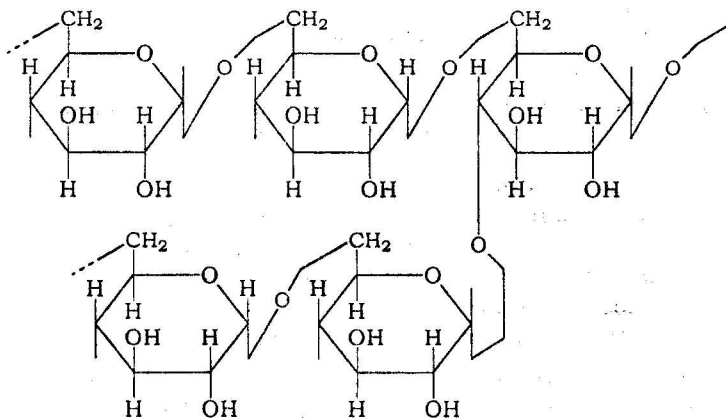




Humans are incapable of utilizing cellulose for food because their digestive juices lack enzymes capable of hydrolyzing the  $\beta$ -glycosidic linkage. Ruminants (cud-chewing animals) are able to digest cellulose because certain microorganisms present in their compartmented stomachs cause a preliminary hydrolysis of cellulose before it reaches the intestine. Certain lower orders of animals (snails, termites) having similar assistance also are able to feed upon cellulose.

### 3. Dextranes

Dextranes represents polysaccharides formed as result of microorganism activity. The fragment macromolecule of dextrane we can see below:



Chemical evidence indicates that considerable branching occurs in the dextrans. Solutions of dextrans after partial acid hydrolyzes using as substitute for blood plasma.

### III. Heteropolysaccharids

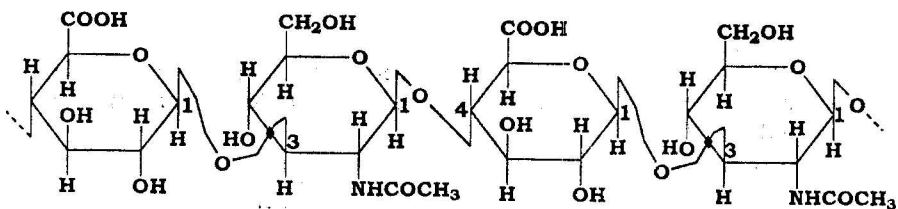
Heteropolysaccharids consists from two monosaccharids or their derivatives.

The representants of heteropolysaccharids are: hyalunoric acid, hondroitinsulphats, heparin.

#### 1. Hyalunoric acid

The main importance of hyalunoric acid is to hold together water to regulat the penetration of tissue and to protection of microbes penetrating.

By chemical structure of hyaluranic acid represents unbranching polymer, consists from two disaccharides:  $\beta$ -d-glucuronic acid and N-acetyl- $\beta$ -D-glucosamine, joined by  $\beta$  (1-3) glycozidic linkage.



*repeated disaccharid*

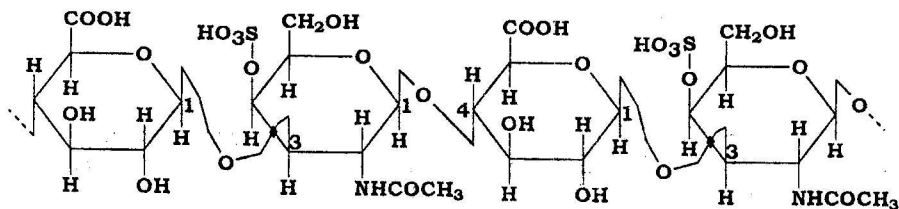
*repeated disaccharid*

*Hyaluronic acid*

#### 2. Hondroitinsulphats:

Hondroitinsulphats are similar by structure with hyaluronic acid and consist from repeated disaccharided units, formed from  $\beta$ -D-glucuronic acid and N-acetyl- $\beta$ -D-galactoseamine, joined each with oter  $\beta$ (1-3) glycozidic linkage.

The fragment hondroitin-4-sulphate, is shown bellow:



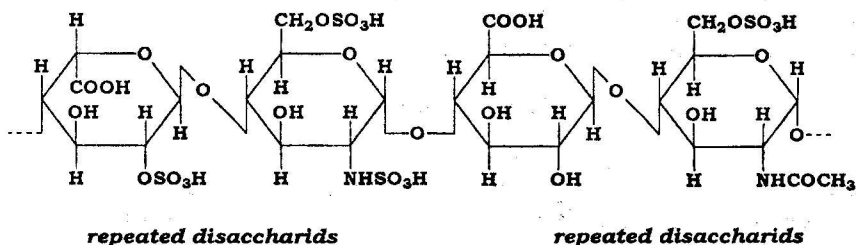
*Hondroitin-4-sulphate*

Hondroitin-4-sulphate in big quantity is meeting in cartilage, bone's tissue and play a main role in calcification of tissue.

### 3. Heparin

Heparin any member of a group of glycosaminoglycans found mainly as an intracellular component of mast cells, and act as inhibitors of blood clotting by activating antithrombin III. In connection with that fact heparin is largely used in practical medicine as drug for delayed trombose formation and other as stabilizer of blood transfusion.

Macromolecule of heparin consists from disaccharids' repeated units, formed from sulphate's  $\alpha$ -D-glucosamine rest and two uronic acids-D-glucuronic and L-iduronic, joined  $\beta(1-4)$  glycozidic link.



As resulting from heparin's structure  $\text{SO}_3\text{H}$  groups gives to macromolecule of heparin strongly negative charge, that increases polyanion's and anticoagulation's properties.

## THE NUCLEIC ACIDS

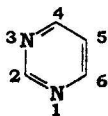
The nucleic acids are high molecular weight natural polymers found in the nuclei and cytoplasm of all living cells, where they play a highly specialized role in the chemistry. The nucleic acids, deoxyribonucleic acid (DNA) and ribonucleic acid (RNA), are the chemical carriers of a cell's genetic information. Coded in a cell's DNA is all the information that determines the nature of the cell, controls cell growth and division, and directs biosynthesis of the enzymes and other proteins required for all cellular function.

Just as proteins are polymers made of amino acid units, nucleic acids are polymers made up of individual building blocks called **nucleotides** linked together to form a long chain. Each nucleotide is composed of a nucleoside plus phosphoric acid,  $H_3PO_4$ , and each nucleoside is further composed of a simple aldopentose sugar plus a heterocyclic amine base.

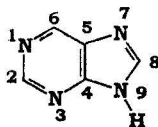
### Heterocyclic amine

The basic portion of nucleic acids are derivatives of two heterocyclic structures, purine and pyrimidine, and are the parts of nucleic acids responsible for the storage and transmission of genetic information.

Although there are a number of minor, but important, bases, five constitute the major bases found in nucleotides. Two of these, adenine and guanine, are purines and are found in both RNA and DNA. The other three, thymine, cytosine and uracil, are pyrimidines. DNA contains thymine, and RNA contains uracil. Cytosine is common to both nucleotides



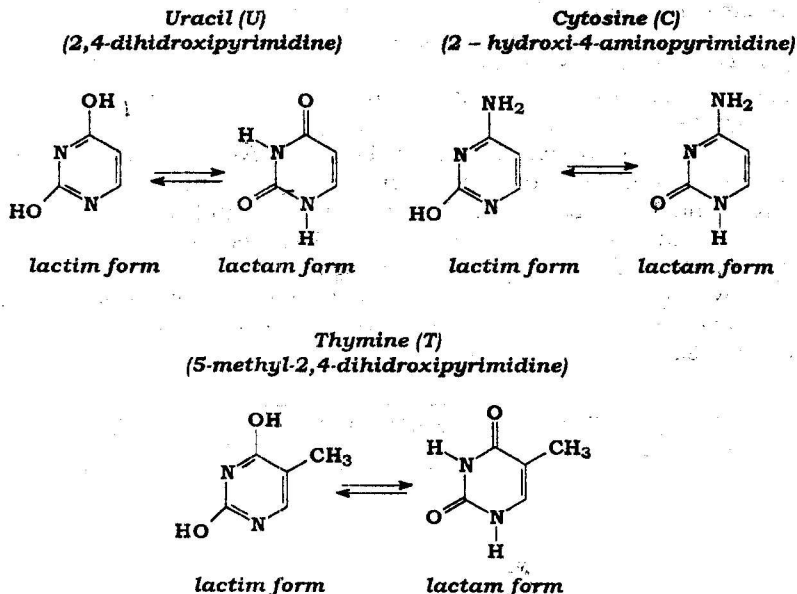
*pyrimidine*



*purine*

## Pyrimidine bases

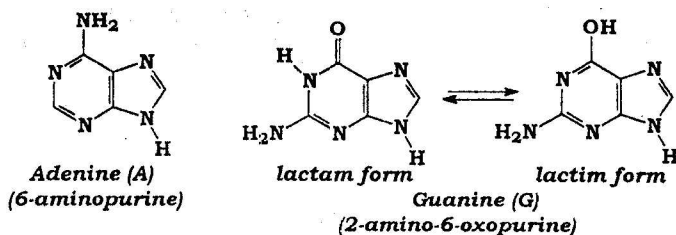
Pyrimidine bases uracil, thymine and cytosine. They have two tautomeric forms: lactim – lactam:



The steadyest is lactam form, because in this form we have conjugated system. It is founded that in composition of nucleic acids we meet lactam form of basic portions

## Purine base

The structure of purine bases are shown bellow:



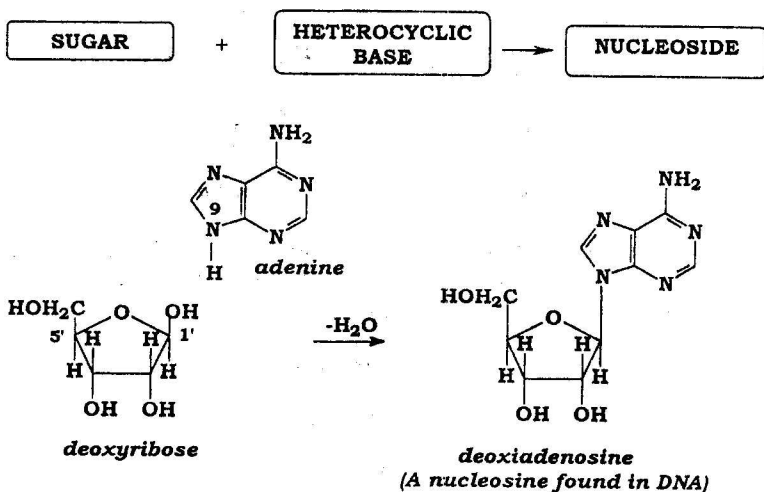
## Nucleotides and nucleosides

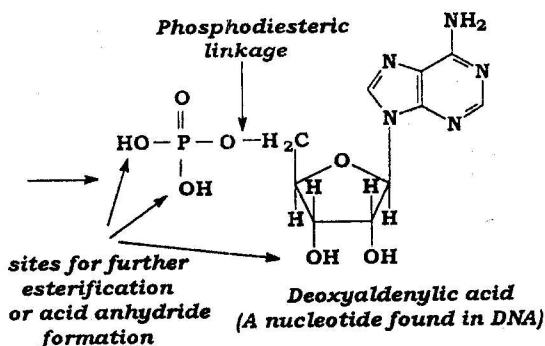
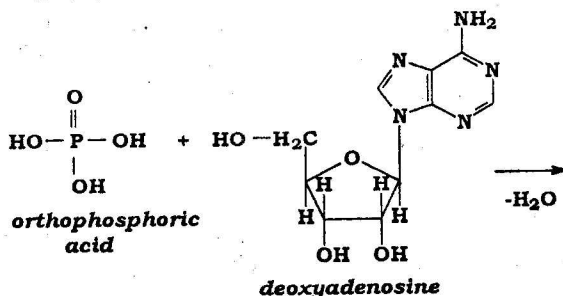
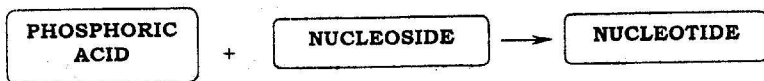
The structural units in both RNA and DNA are called nucleotides and are phosphate esters of substituted pentose, the substituent being either a purine or a pyrimidine derivative attached at carbon atom number 1' of the sugar ring.

In order to distinguish between two different ring systems present within a nucleic acid, primed numbers will henceforth be used to designate position in the sugar, unprimed numbers to designate ring position in the heterocyclic base.

The point of attachment in the heterocyclic base is at position 1 in the pyrimidine and at position 9 in the purine. The 1' position of sugar and 1 or 9 positions of bases are link with N-glycosidic bond.

A nucleoside is only the substituted sugar portion of a nucleotide and structurally is analogous to a glycoside, except that here we have a nitrogen atom instead of an oxygen atom bonded at carbon 1'. Examples of both nucleoside and nucleotide formation are illustrated bellow:





The name of a nucleotide incorporates that of its nitrogen base using the suffix -ylic and followed by acid as a separate word. The name of nucleoside is similar to that given to a nucleotide with the same sugar and base except that the name ends with the suffix -idine if the base portion is a pyrimidine with -osine if the base portion is a purine. Of course the word acid does not apply. Names of structural units found in RNA and DNA are given in follow table.

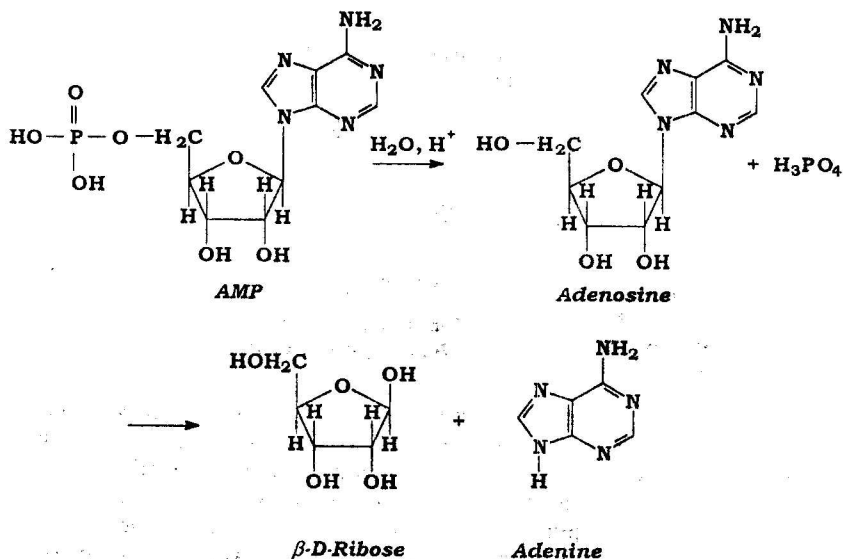
Table. Some nucleosides and nucleotides

	Base	Pentose	Nucleoside	Nucleotide
<b>Purines</b>	Adenine	Ribose	Adenosine	Adenylic acid
	Guanine	Deoxyribose	Deoxyguanosine	Deoxyguanylic acid
<b>Pyrimidines</b>	Uracil	Ribose	Uridine	Uridylic acid*
	Thymin	Deoxyribose	Deoxythymidine	Deoxythymidinic acid**
	Cytosine	Deoxyribose	Deoxycytidine	Deoxycytidilic acid

\* - Found only in RNA

\*\* - Found only in DNA

Nucleotides maintain two linkages. N-glycosidic and phosphodiesteric, therefore they can hydrolysed steply:



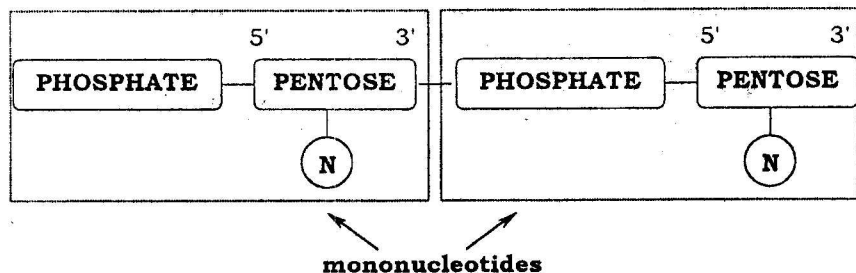
### Structure of nucleic acid.

There are two families of nucleic acids: **ribonucleic acid** (RNA), it contains sugar D-ribose. RNA are found largely in the cytoplasm, and **deoxyribonucleic acid** (DNA), its sugar is 2-deoxy-D-ribose. DNA - is the constituent of genetic material in the cell nucleus. DNA are found largely in nucleu.

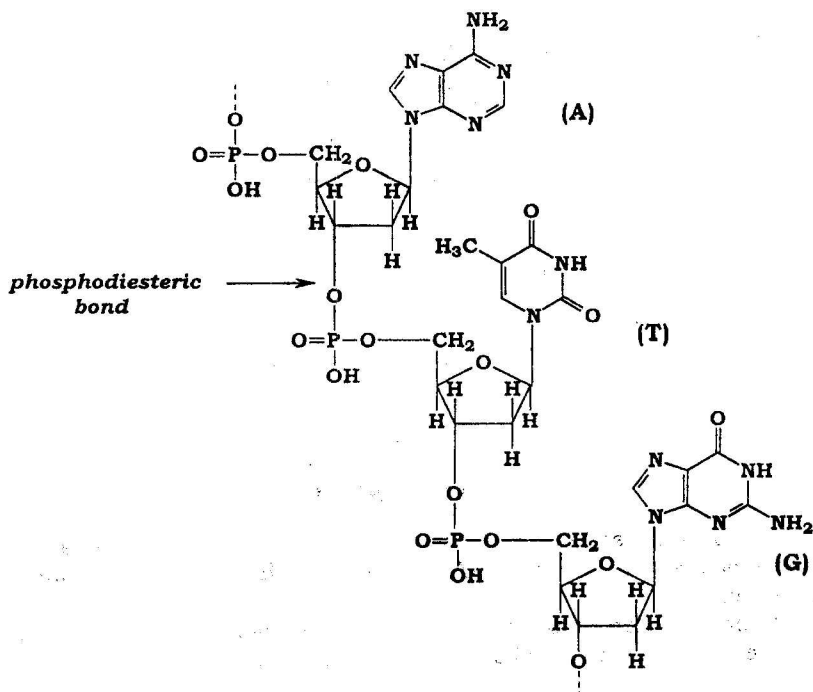


The primary structure of nucleic acid polymer actually is a polyester structure in which phosphoric acid-sugar units are repeated over and over.

The structure of nucleic acid we can show as repeated mononucleotides, linked by 3' → 5' phosphodiesteric bond

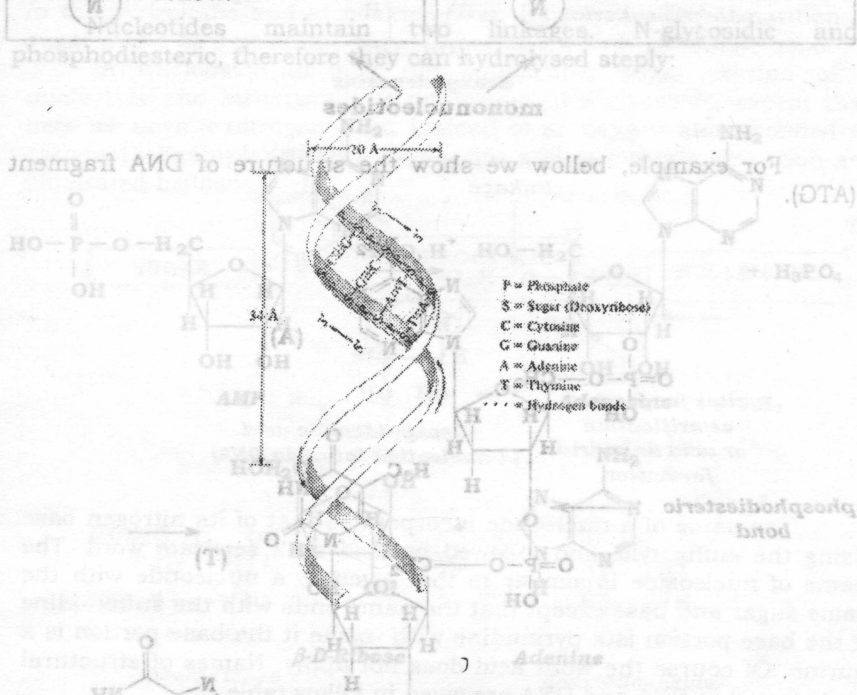


For example, bellow we show the structure of DNA fragment (ATG).



The *secondary* structure of DNA presents a *double helix* and was proposed by Watson-Crick.

The Watson - Crick model was based upon measurements and calculations made from X-ray diffraction data obtained by M. Wilkins from crystallographic studies on a prepared sample of DNA polymer. A double helix structure would allow nitrogen bases in each DNA stand to be projected toward the center. Uniform intermolecular (hydrogen) bonding would then be possible between adenine in one strand and also between cytosine in one strand and guanine in the other. The hydrogen bonding capabilities of complementary base pairs are shown below:



### The structure of RNA

The primary structure of RNA differs that of DNA mainly nature of the nucleosides esterified. RNA incorporates the base uracil instead of thymine.

Another different between DNA and RNA lies in their sugar; in structure of RNA we meet ribose instead of deoxyribose.

Difference between DNA and RNA lies in their secondary structure, too. RNA molecules exist mainly as single strands, rather than in the form of double helices.

Three different types of RNA molecules appear to be involved in the vital business of protein synthesis. One of these, **ribosomal RNA** (r-RNA), is of the greatest molecular weight and is associated with the ribosomes, or nucleoprotein particles, in cytoplasm. A second type of RNA, called **messenger RNA** (m-RNA) is a polynucleotide of lower molecular weight than r-RNA and carries the transcribed genetic code from the DNA in the nucleus of the cell to the ribosomes. A third type of RNA is called **transfer RNA** (t-RNA). Transfer RNA by weight is the smallest of polynucleotides.

The function of t-RNA is to select and to carry the amino acids required for a specific protein to the correct m-RNA-ribosome site.

### **Nucleic acids and heredity**

A DNA molecule is the chemical repository of an organism's genetic information. What Crick has termed the central dogma of molecular genetics says that the function of DNA is to store information and pass it to RNA. The function of RNA, in turn, is to read, decode, and use the information received from DNA to make proteins.

Each of the thousands of individual genes on a chromosome contains the instructions necessary to make a specific protein needed for a specific biological purpose.

Three fundamental processes take place in the transfer of genetic information

**DNA  $\longrightarrow$  RNA  $\longrightarrow$  proteins**

**Replication** is the process by which identical copies of DNA are made, forming additional molecules and preserving genetic information.

**Transcription** is the process by which information in the DNA is read and decoded by RNA.

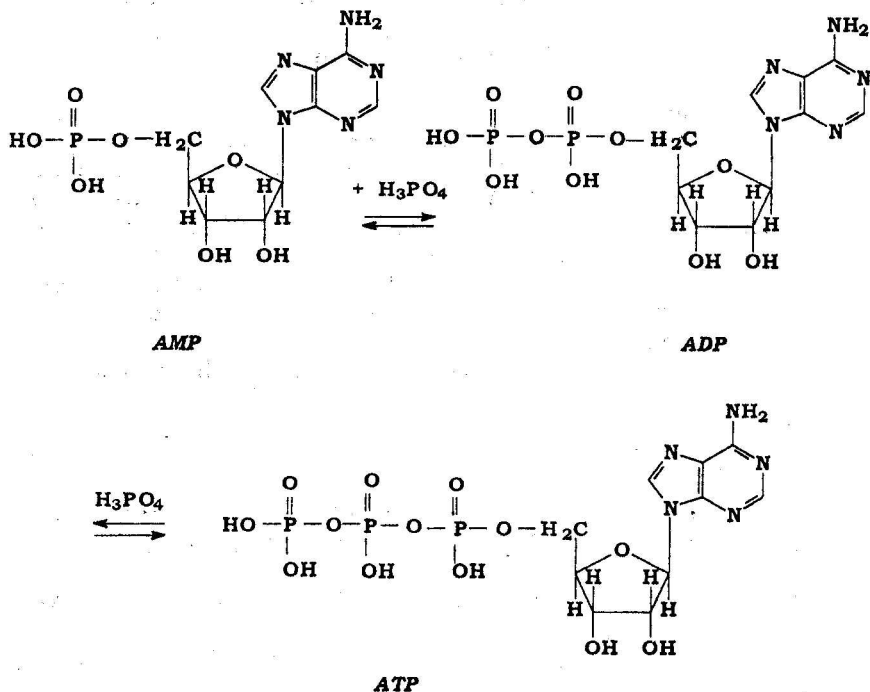
**Translation** is the process by which RNA uses the information to build proteins.

## Nucleotidephosphats. Nucleotidic coenzymes.

In all tissues of organisms are meet free mono-, di-, and triphosphats of nucleosides. Especially large are known adenosine-5'-monophosphate (AMP), adenosine-5'-diphosphate (ADP) and adenosine-5'-triphosphate (ATP). Diphosphate group keeps one, but triphosphate group two anhydric bonds, called *macroergic bond*, because at their splitting is given off a big value of energy.

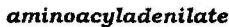
Especially important is adenosinetriphosphate acid (ATP), which participates in the phosphorilates reactions, in reactions of synthesis of nucleic acids and proteins.

### **The scheme of transformation of AMP in ADP in ATP.**

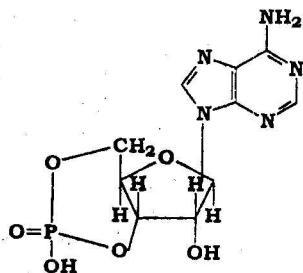


Adenosine-5'-triphosphate (ATP) is formed from adenosine 5'-diphosphate by oxidative phosphorylation in coupled mitochondria, by photophorylation in plants, and by substrate-level phosphorylation. Reactions in which it participates are often driven in the direction leading to hydrolysis of ATP. The chemical energy so

On the first step of this process takes place the activation of aminoacids with yield aminoacyladenilate, than activated aminoacid reacts with corresponding t-RNA.

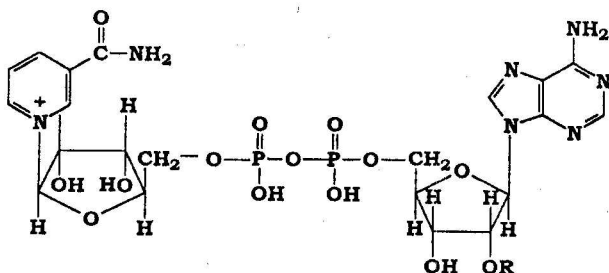


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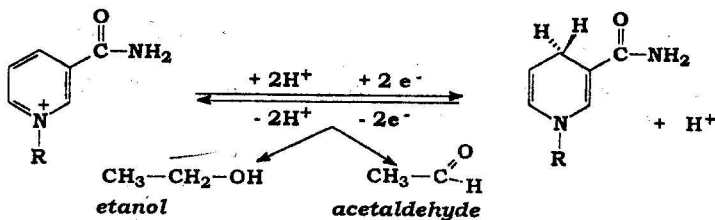
3', 5' AMPcyc

Coenzyme **nicotinamide - adenine dinucleotide** (NAD<sup>+</sup>) or **nicotinamide - adenine dinucleotide phosphate** (NADP<sup>+</sup>).



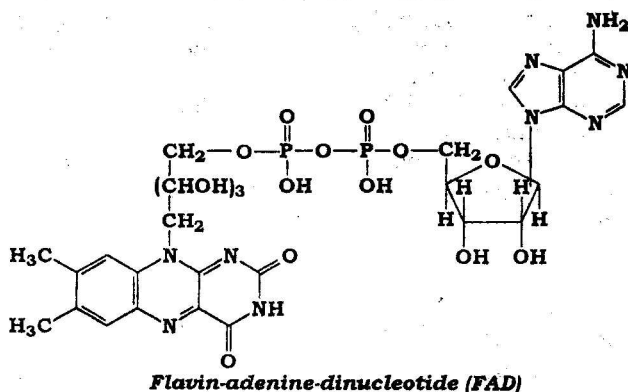
NADP<sup>+</sup> (R=PO<sub>3</sub>H<sub>3</sub>)

They are the specific coenzyme in numerous oxidoreductase enzyme reactions. In these reactions it stereospecifically accepts a hydrogen atom in position 4 of pyridine ring, plus an electron, to form nicotinamide adenine dinucleotide (reduced): NADH + H<sup>+</sup>, or NADPH + H<sup>+</sup>.

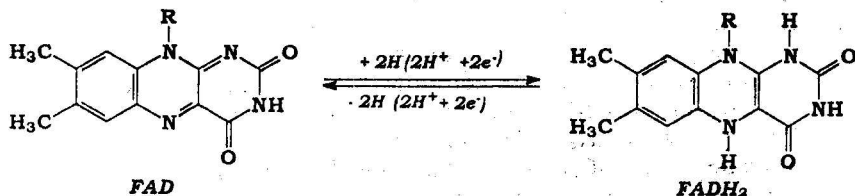


They are atypical dinucleotides containing a phosphoric anhydride linkages between the component mononucleotide units, i.e. between nicotinamide mononucleotide and adenilic acid.

Other important coenzyme flavin-adenine dinucleotide (FAD), it is the active form of riboflavin (vitamine B<sub>2</sub>).



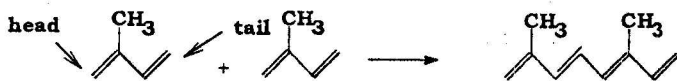
It forms the coenzyme or the prosthetic group of various flavoprotein oxidoreductase enzymes:



## ISOPRENoids. STERoids.

Although the lower alkenes do not exist like this in nature, other alkenes occur widely in a variety of complex forms. A large number of natural products are built from isoprene units. One important class of these natural products is the terpenes, which are sometimes called isoprenoid compounds because their carbon skeletons are multiples of the  $C_5$  isopren unit, the general formulas are  $(C_5H_8)_n$ , where  $n=2,3,4,6,8$ . This unit appears in most natural substances in a regular head-to-tail sequence.

The widespread occurrence of this structural unit has led to the isoprene rule, which states that the most probable structure of the terpene is that which allows its carbon skeleton to be divisible into isoprene units.



In some cases isoprene units are tail-to-tail arrangement, such as in  $\beta$ -carotene.

Terpenes are divided on number of isoprene units and on carbon chain structure.

By the number of isoprene units terpenes are divided into the following groups

Monoterpenes -  $(C_5H_8)_2$ , containing two isoprene units

Sesquiterpenes -  $(C_5H_8)_3$ , containing three isoprene units

Diterpenes -  $(C_5H_8)_4$ , containing four isoprene units

Triterpenes -  $(C_5H_8)_6$ , containing six isoprene units

Tetroterpenes -  $(C_5H_8)_8$ , containing eight isoprene units

By carbon chain structure terpenes are divided into acyclic, monocyclic, bicyclic.

### Mono- and bicyclic terpenes

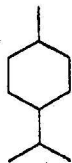
At monocyclic terpenes attributes limonene (1-methyl-4-isopropenylcyclohexane-1). Limonene enters in composition of lemon's oil and oils of other plants.

Another monocyclic terpene is menthol - the base part of mint. Menthol is applied as antiseptic in medicine.

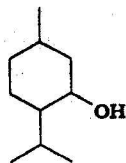




**Limonene**

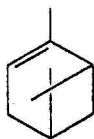


**Menthane**

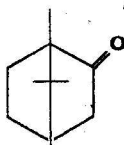


**Menthol**

$\alpha$ -pinene (chief constituent of turpentine from pine tree sap) and camphor (used in medicine and industry, obtained from the bark of the Formosan camphor tree or by synthesis from pinene) attract to diterpenes.



**$\alpha$ -pinene**

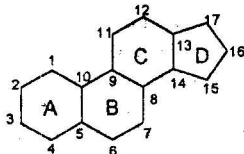


**camphor**

The sesquiterpene farnesol is the precursor of the triterpene squalene, which is itself the precursor in the biosynthesis of the important steroidal alcohol cholesterol. The diterpene vitamin A is apparently in the body by the oxidation of the central double bond of the tetraterpene  $\beta$ -carotene, the yellow coloring matter of carrots.

### **The steroids. Sterane**

The steroids are a family of compounds widely distributed in animals. Common to the structure of all compounds of this class is tetracyclic framework composed of the phenanthrene nucleus to which is fused at the 1,2-positions a cyclopentene ring.



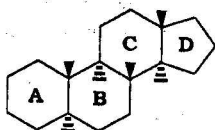
**The steroid ring system (sterane)**

The rings in the steroid molecule usually are not aromatic but often contain one or more isolated double bonds. The total structure of one steroid differs from that of another, usually by a variation in the number and type of functional groups. To the family of steroids

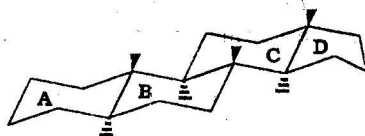
with this common ring system belong the sterols, the sex hormones, the bile acids, and other biologically important materials.

Cyclohexane rings A, B and C entered in sterane's system existence in the more profitable easy-chair (arm-chair) conformation and can unite by cis- or trans-type.

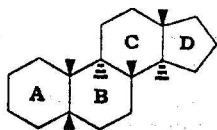
All the steroids are divided in two rows: 5 $\alpha$ -row (A/B trans unit) and 5 $\beta$ -row (A/B-cis-unit) in dependence of the type unite. The rest of rings B, C, D in most cases join by type trans- and rarely by type cis for C and D



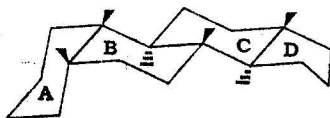
**configuration**  
5 $\alpha$ -sterane



**conformation**  
A/B, B/C, C/D - type trans



**configuration**  
5 $\beta$ -sterane

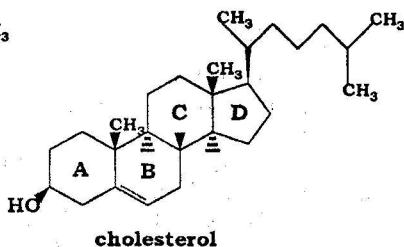
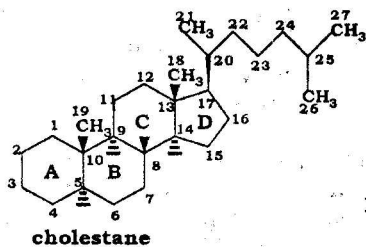


**conformation**  
A/B-cis, B/C, C/D - type trans join

### **Cholesterol. Ergosterol. Vitamine D**

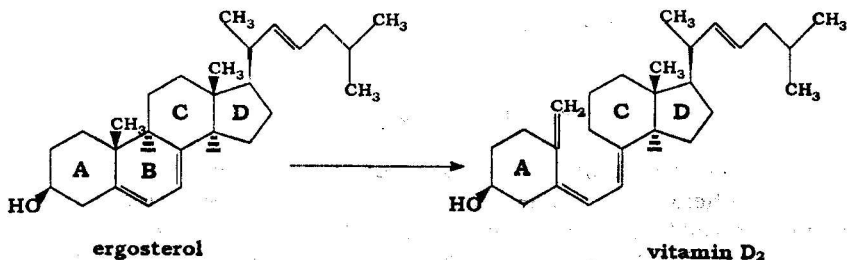
An ancestor of the sterid's group is cholesterolane, containing 27 carbon atoms. Cholestane present 10,13 - dimethyl - 17 - izooctansterane.

The sterols are solid alcohol's that posses a hydroxyl group in position 3 a double bond between carbon 5 and 6, a side chain of carbon 17, and methyl groups joined to ring carbons numbered 10 and 13. The sterols are divided in zoosterane, phytosteranes and microsteranes. Cholesterol, C<sub>27</sub>H<sub>46</sub>O, one of the most widely distributed sterols, is found in almost all animal tissue but is particularly abundant in the brain, the spinal cord, gallstones. Cholesterol is the starting material for the formation of the bile acids, steroid hormones and vitamin D. Deposition of cholesterol or its derivatives in the flow of blood, causes high blood pressure, and leads to some forms of cardiovascular disease. The structure of cholesterol is shown with asymmetric carbon atoms by asterisks.



### **Ergosterol**

Although cholesterol is found only in animals, a large number of closely related compounds known as phytosterols are found in plants. One of these, ergosterol,  $C_{28}H_{44}O$ , is produced by yeast. Ergosterol is of particular interest because, when irradiated, it yields calciferol, vitamin  $D_2$ .



Vitamin D is sometimes referred to as the "antirachitic" vitamin. It is related to the proper deposition of calcium phosphate and controls the normal development of the teeth and bones.

### **Fat-soluble Vitamins**

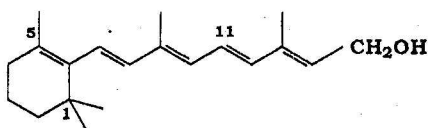
The fat-soluble vitamins are those soluble in fats and fat solvents. Included in this classification are vitamins A, D, E, and K. The role of vitamins as food accessories usually is considered in relation to nutritional deficiencies. It should be pointed out that doses of the fat-soluble vitamins, when given far in excess of normal requirements also could have toxic effects. Vitamin poisoning occurred in a number of arctic explorers, who became seriously ill often eating polar bear liver.

Poisoning by water-soluble vitamins is not possible because any amounts not required are voided from the body in urine.

Vitamin A may be obtained from the coloring matter of many green and yellow vegetables. Vitamin A, as such is not found in plants, only  $\beta$ -carotene, its precursor or provitamin. Other sources of vitamin A are fish-liver oil, the livers of other animals, eggs, butter, and cheese.

Vitamin A, or retinol, is oxidized in the body to the aldehyde 11-cis-retinal, which combines with a protein called opsin to produce a light-sensitive substance rhodopsin. Rhodopsin is located in the retina and, upon absorption of the radiation within the visible range, causes an isomerisation of cis-retinal to trans form.

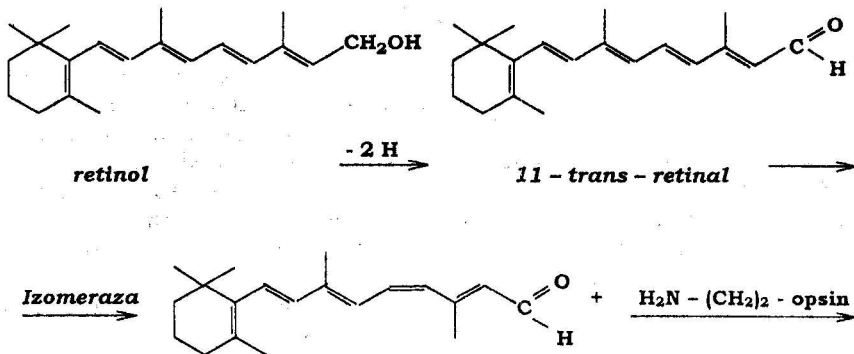
A deficiency of vitamin A causes night blindness and an inability to see in dim light. Another disease of the eye known as xerophthalmia, in which the tear glands cease to function, results from a lack of vitamin A.



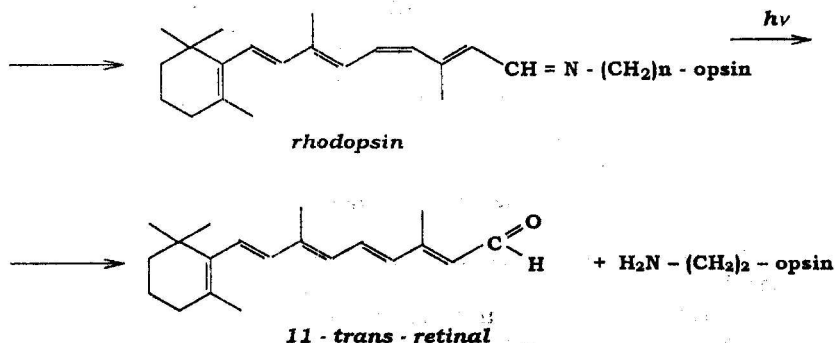
### The chemistry of vision

Vision, the most remarkable of our senses, is a complex chemical phenomenon. The human eye is roughly spherical with an opening in the front to admit light. The molecules responsible for vision are attached to the tops of the rods and cones. We will consider here the function of one of them, rhodopsin.

Rhodopsin has two parts: protein portion called opsin, and a small aldehyde portion called retinal. The structure of retinal has two isomers: trans and cis.



**11 - cis retinal**



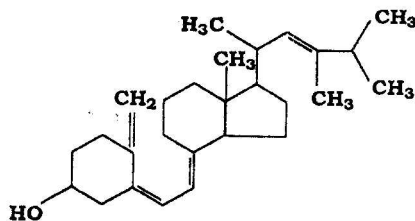
**Fig. Mechanism of retinal transformation**

It is interesting to note that vit A, a substance known to aid vision, especially night vision, has the same structure as retinal except that the terminal aldehyde group is replaced by an - OH group to give an alcohol. In the cis- form retinal is bound to opsin. When rhodopsin absorbs light, the retinal is isomerized to all - trans form, which separates from the opsin.

When the two portions separate, the natural reddish - purple color of rhodopsin is lost. The cell to which rhodopsin is attached becomes excited. This receptor cell then excites other cells and sends a message to the brain.

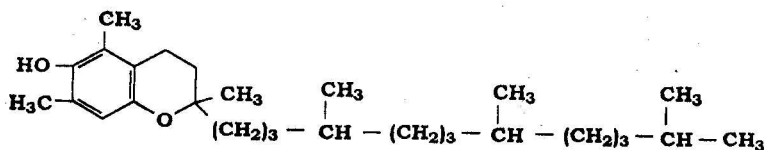
After the activation of rhodopsin and the separation of the trans form of retinal, the retinal returns to the 11 - cis form and reconnects to opsin. This process is relatively slow. Color discrimination is possible because cone cells occur in three groups: those receptive to blue light, to green and yellow - red light.

Vitamin D is sometimes referred to as the "antirachitic" vitamin. It is related to the proper deposition of calcium phosphate and controls the normal development of the teeth and bones. There are more than ten compounds that have antirachitic properties and are designated D<sub>1</sub>, D<sub>2</sub>, D<sub>3</sub> etc. Vitamin D from fish oils is D<sub>3</sub>, while that produced by irradiation of the skin with ultraviolet or sunlight is D<sub>2</sub>. Vitamin D<sub>2</sub> is known as calciferol and is derived from ergosterol.



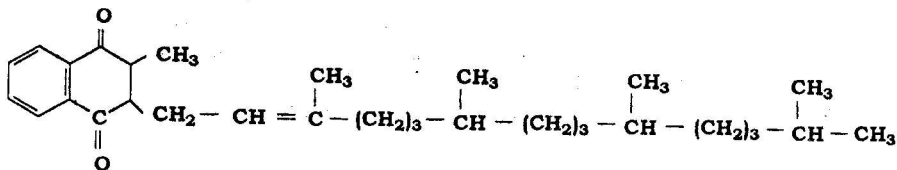
*Calciferol (vitamin D<sub>2</sub>)*

Vitamin E, sometimes called the fertility factor, is related to the proper functioning of the reproductive system. Vitamin E is found in the nonsaponifiable fraction of vegetable oils such as corn-germ oil, cottonseed oils, wheat-germ oil and peanut oil. It also occurs in green leafy vegetables. As in the case of A and D vitamins, there also is more than one form of vitamin E. Four different structures called tocopherols have vitamin E activity. There are designated  $\alpha$ -,  $\beta$ -,  $\gamma$ -,  $\delta$ -tocopherols. The structure of  $\alpha$ -tocopherol, the most potent, is shown below



Vitamin E is also used as an antioxidant for the prevention of oxidative rancidity in vegetable oils.

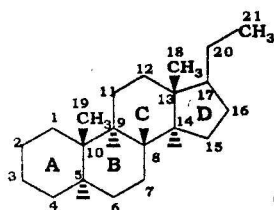
Vitamin K is the antihemorrhagic factor related to the blood clotting mechanism. This vitamin is important especially from surgical standpoint. There are at least two K vitamins. Vitamin K<sub>1</sub> is obtained from the alfalfa leaf; vitamin K<sub>2</sub> is produced by bacterial action in the intestinal canal. The structure of K<sub>1</sub> is shown below.



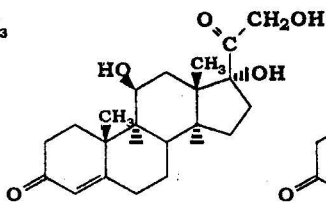
## Steroids Hormones. Adrenal steroids. Sex hormones.

The structure of adrenal steroids based of pregnane structure (10,13-dimethyl 17 - ethylsterane)

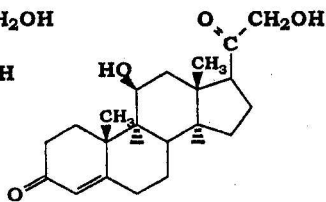
The main representatives of the adrenal cortex hormones are hydrocortizone and corticosterone. These hormones are the antagonists of insulin and increase the concentration of glucose in blood. These compounds have been used with beneficial results in the treatment of inflammatory and allergic diseases. The structures of hydrocortizone and corticosterone are shown.



**pregnane**



**hydrocortizone**

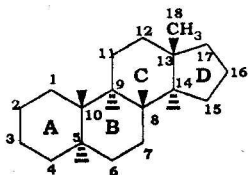


**corticosterone**

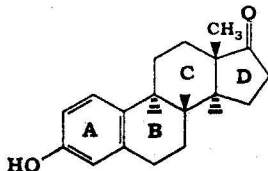
## Sex hormones

The male and female sex hormones are structurally related steroids responsible for the development of sex characteristics and sexual processes in animals. Sex hormones are produced in the gonads (ovaries and testes) when other gonadotropic hormones stimulate the latter. The female sex hormones are involved in the menstrual cycle, the changes in the uterus, and preparation for and maintenance of pregnancy.

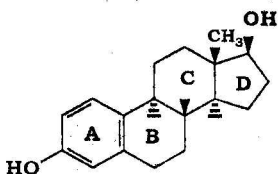
The structures and names of the principal female sex hormones are shown below.



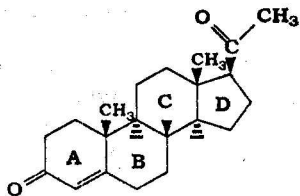
**estrane (13-methylsterane)**



**estrone**



**estradiol**  
(3,17 dihydroxi - estratrien -1,3,5(10))

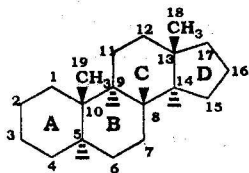


**progesterone**  
(pregnene-4diol-3,20)

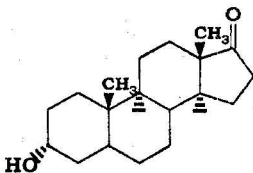
Oral contraceptives that have been developed contain synthetic compounds structurally similar to progesterone and estradiol but modified chemically to permit easier assimilation into the blood stream. These synthetic agents, when taken orally, suppress ovulation and mimic pregnancy

### Androgens (male sex hormones)

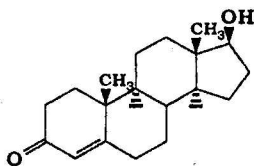
The male sex hormones, called androgens, except for the absence of an aromatic ring, are very similar in structure to the female hormones. The male sex hormones control the development of the male genital tract and the secondary male characteristics - e.g., beard, voice. The structures of the principal male sex hormones are shown below.



**androstane**



**androsterone**

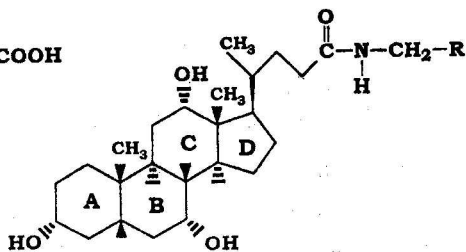
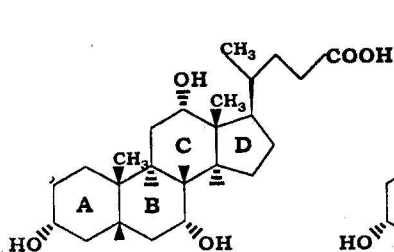
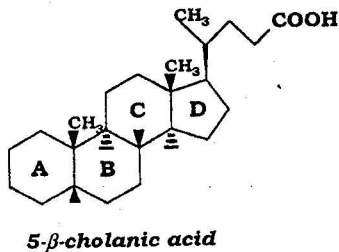
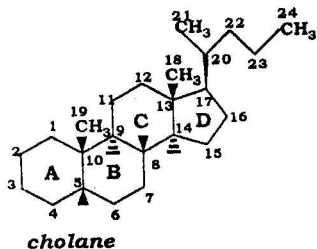


**testosterone**

### The bile acids

Cholesterol is metabolized to the bile acids. These powerful emulsifying agents flow from the liver into the bile duct and the small intestine. Later a large fraction is reabsorbed in the duodenum and is returned to the liver for reuse. Formation of bile acids involves the removal of the double bond of cholesterol, inversion at C-3 to give a 3 $\alpha$ -hydroxyl group followed by hydroxylation and  $\beta$ -oxidation of the side chain. The structures of the principal bile acids are

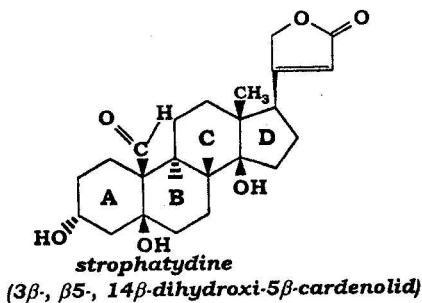
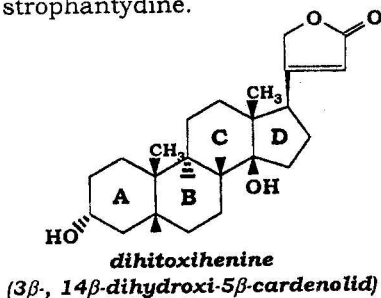




### Heart's glycozides. Aglycones of heart's glycozides: dihitoxihenine and strophatyndine

The most importance in medicine among plant's glycozides has heart's glycosides. These substances excite heart activity and represent a valuable drug for medicine.

The active compounds in heart's glycosides are aglycone (henin). These aglycones are presented bellow dinitoxyhenine and strophatyndine.



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