**Pharmaceutical chemistry I**

**Lecture №3**

**Organic medicine substances. Aliphatic compounds.**

**Halocarbons, alcohols and their ethers. Aldehydes, carboxylic acids, and preparations of their derivatives.**

**Carbohydrates.**

Halocarbons are formed when one or some atoms of hydrogen ina hydrocarbon molecule are substituted by halogens.

The general stage in analysis of these compounds is determination of halogen.

For this purpose Beilstein’s test is usually used. To confirm halogen by analytical reactions it is necessary to transfer it into an ionized state. During mineralization the simple inorganic substances are formed.

This class of compounds includes such substances as chloroform, iodoform, ethylene chloride and halothane.

**Chloroform**

**(Chloroformium), Ph. Eur.**

**CHC13**

Trichloromethane

**Preparation.** Electrolysis of sodium chloride in the presence of alcohol or acetone:





**Properties.** A colourless, transparent, heavy and mobile volatile liquid with the characteristic odour and a sweet taste. It is mixed in all proportions with an anhydrous ethanol, ether and petrol, essential and fatty oils, immiscible with glycerol.

During storage can be oxidized.



To avoid the oxidation ethanol (0.6—1 %) used as a preservative is added:



**Identification.** Physical constants are the boiling point and density. According to the Pharmacopoeia it is necessary to make quantification of ethanol:



S=3/2. The indicator is starch.

Purity. Free chlorine:

CI2+ 2KI I2 + 2KCI

***Aldehydes:***



**Usage**. External medicine for massages in neuralgia. In poisonings with arsine, for laboratory works as a preservative.

**Storage.** In well-stoppered orange glass bottles, in cool place.

**Iodoform**

**(Iodoformium)**

**CHI**3

*Triiodomethane*

**Preparation**



**Properties.** A yellow pow'der with the specific odour. It melts at first, and then decomposes with educing of violet steams of iodine. Volatile already at the room temperature, distillated with water vapour. Solutions of the substance are quickly decomposed under action of light and air with educing of iodine.

**Identification.** When heating a violet steams of iodine are educed:



**Assay.** Argentometry (the Volhard method). The substance is dissolved in the water-alcohol mixture, heated with silver nitrate solution in the presence of nitric acid. The excess of silver nitrate is titrate with ammonia thiocyanate using ferric-ammonia sulphate solution an indicator *(s=* 1/3).



Carry out a blank titration.

**Usage.** Antiseptic. Use externally as a powder, ointments, past for treatment of wounds and ulcers.

**Storage.** In well-closed containers, protected from light.

**Ethyl Chloride  
(Aethylii chloridum)**

**C2H5C1**

**Preparation.** 1. Chlorination of ethane:

**C2H6 + CI2 C2H5CI + HCI**

2. Hydrochloration of ethylene:

**CH2=CH2 + HC1 CH3CH2C1**

**Properties.** A colourless, very volatile liquid. Catches fire easily. It burns with a green flame. The boiling temperature is 12 °C.

**Identification.** When heating with alkali:

C2H5C1 + KOH C2H5OH + KC1

carry out reactions of alcohol:

**C2H3OH + 4I2 + 6KOH CHI3 + 5KI + HCOOK + 5H20**

***yellow***

and reactions of chlorides.

The quality is confirmed by physical constants — the boiling point and density.

**Purity.** Impurity of ethanol is determined by iodoform test *(see* above).

**Usage.** For short-term narcosis or local anaesthesia due to cooling of tissues.

**Storage.** In ampules, or in bottles with special stoppers, in cool and protected from light action place.

**Halothane**

**(Phthorotanum),'Ph. Eur.**

**CF3—CHClBr**

(RS)-2-Bromo-2-chloro-1,1,1 – trifluoroethane

**Preparation**

F3C-CH2C1 + Br2 F3C— CHClBr + HBr

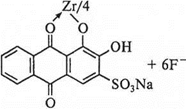
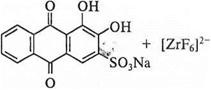
**Properties.** A clear, colourless, mobile, heavy, non-flammable liquid, slightly soluble in water, miscible with ethanol, with ether and with trichloroethylene.

It contains 0.01 % of thymol as a stabiliser.

**Identification.** 1. The IR-spectrum.

2. To the substance add 2-methyl-2-propanol in a test-tube. Add copper edetate solution, concentrated ammonia and the mixture of strong hydrogen peroxide solution and water (solution u a blank at the same time (solution b). Prepare a blank at the same time (solution). Place both tubes in a water-bath, cool, and then add glacial acetic acid. To the each of solution add the mixture of freshly prepared alizarin solution and zirconyl nitrate solution. Solution (a) is yellow and solution (b) is red.

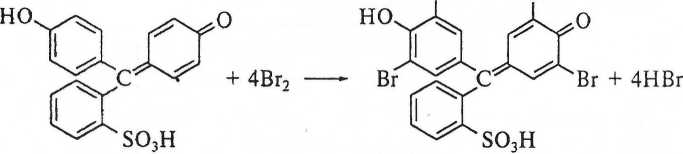
The fluorides obtained decompose the complex of alizarin with zirconium (in the examined test the red colouring becomes yellow; in the blank test the red colouring remains):

To 1 mL of each of solutions add buffer solution pH = 5.2, phenol red solution and chloramine solution. Solution (a) is bluish-violet and solution (b) is yellow.

At pH = 5.2 phenol red has a yellow colouring. In the presence of bromides and under action of chloramine it becomes bromothymol blue, which has a bluish-violet colouring:

Br Br



To 2 mL of each of solutions add sulphuric acid, acetone and po­tassium bromate solution. Warm the tubes in a water-bath, cool and add nitric acid and silver nitrate solution. Solution (a) is opalescent and a white precipitate is formed after a few minutes; solution (b) remains clear.

Bromides are oxidised to free bromine by interaction with potassi­um bromate:

5Br ¯ + BrOj3¯ + 6H+ 3Br2 + 3H20

and then they are deleted as pentabromoacetone:

CH3COCH3 + 5Br2 CBr3COCHBr2J + HBr

chlorides in the solution are detected with silver nitrate solution:

**Cl¯ + Ag+ AgCl**

**Purity.** The content of thymol is determined by gas-chromato­graphy.

**Usage.** General anaesthetic.

**Storage.** Store in an airtight container, protected from light, at the temperature of 25 °C. The choice of material for the container is made taking into account the particular reactivity of halothane with certain metals. In the end of each 6 months of storage the substance is re­xamined.

\* \* \*

***Alcohols*** are organic compounds with the general formula R—OH. They are classified as primary, secondary or tertiary according to the kind of carbon containing the —OH group.

Alcohols are enough inert chemically; they have weak-acid pro­perties, inclined to oxidation and enter into reactions of substitution (for example, esterification).

The main pharmacological action of low-molecular alcohols is influence on the central nervous system. High-molecular alcohols (more than 16 atoms of carbon) practically do not influence on the organism.

The simplest representatives are ethanol and glycerol.

**Ethanol**

**(Spiritus aethylicus), Ph. Eur.  
CH3-CH2OH**

**Preparation**





Alcohol fermentation of starch.

During manufacture of alcohol such side products as pyruvic acid, acetaldehyde, glycerol, and fusel oil can be obtained. For purifying ethyl alcohol must be distilled.

**Properties.** A colourless, clear, volatile, flammable liquid, hygro­scopic. Miscible with water and with methylene chloride. It bums with a blue, smokeless flame. The boiling point is 78 °C.

**Identification.** 1. Relative density (0.805—0.812).

1. The IR-spectrum.
2. Mix the substance with the solution of potassium permanganate and dilute sulphuric acid. Cover immediately with a filter paper mois­tened with a freshly prepared solution containing of sodium nitroprusside and piperazine hydrate in water.

5 C2H5OH + 2KMn04 + 3H2S04



In a few minutes an intense blue colour appears on the paper and becomes paler in 10—15 min.

1. To the substance add water and dilute sodium hydroxide solu­tion, then slowly add 0.05 M iodine. A yellow precipitate is formed within 30 min (iodoform test):

C2H5OH + 4I2 + 6KOH CHI3 + 5KI + HCOOK + 5H20

Purity. Volatile impurities are determined by the gas-chromatogra­phy method.

Assay. According to the Pharmacopoeia no assay is proposed.

**Non-Pharmacopoeial method***— dichromatometry:*

3C2H5OH + 2K2Cr207 +I6HNO3

***excess***

4Cr(N03)3 + 3CH3COOH + 4KN03 + 11H20

K2Cr207 + 6KI + 14HN03 8KNO3 + 2Cr(N03)3 + 3I2 + 7H20

I2 + 2Na2S203 2NaI + Na2S406

s = 3/2. The indicator is starch.

Usage. The external antiseptic and irritant substance for massages and compresses. It is manufactured as 95, 90, 70 and 40 % aqueous solutions.

Storage. In well-closed containers, protected from light.

Glycerol

(Glycerinum), Ph. Eur.



**Preparation.** By saponification of fats:



**Properties.** A syrupy liquid, unctuous to the touch, colourless or almost colourless, clear, very hygroscopic. Miscible with water and with alcohol, slightly soluble in acetone, practically insoluble in fatty oils and in essential oils.

**Identification.** 1. The refractive index (1.470—1.475).

1. The IR-spectrum.
2. The reaction with nitric acid and potassium dichromate solution. A blue colouring ring develops at the interface of the liquids within 10 min, the blue colour does not diffuse into the lower layer.
3. Heat the substance with potassium hydrogen sulphate in an evapo­rating dish. Vapours are evolved, they blacken filter paper impreg­nated with alkaline potassium tetraiodomercurate solution:



**Assay.** 1. Indirect alkalimetry method. Mix the substance with water. Add sulphuric acid and sodium periodate. Allow to stand protected from light for 15 min. Add the solution of ethylene glycol and allow to stand protected from light for 20 min. Using phenolphthalein as an indicator, titrate with 0.1 M sodium hydroxide; *s—* 1. Carry out a blank titration.



1. The formic acid educed is titrated with sodium hydroxide so­lution:

**HCOOH + 2NaOH HCOONa + H20**

1. Acetylation:



After destruction of acetic anhydride the solution analyzed is neu­tralized with an alkali (the indicator is phenolphthalein) and boiled with the sodium hydroxide solution:



The excess of the alkali is titrated with hydrochloric acid; *s =* 1/3.

NaOH + HC1 NaCl + H20

1. Back dichromatometry; *s* = 3/7.



The excess of potassium dichromate is titrated

with FeS04•(NH4)2S04 • 6H20:

K2Cr207 + 6Fe(NH4)2(S04)2 + 7H2S04

Cr2(S04)3 + 3Fe2(S04)3 + K2S04 + 6(NH4)2S04 + 7H20

**Usage.** It is a base for ointments and solutions. Anhydrous glycerol can cause burns.

**Storage.** In an airtight container.

***Aldehydes*** are compounds, which contain the aldehyde (carbonyl) group. Aldehydes have a strong reactive ability. They can get into reactions of oxidation (sometimes reduction), addition, and polyme­risation.

This chemical class of substances includes formaldehyde, hexamine and chloral hydrate.

**MEDICINAL SUBSTANCES DERIVATIVES OF ALDEHYDES**

**Formaldehyde Solution 35 %**

**(35 *%* Solutio Formaldehydi), Ph. Eur.**



**Preparation.** 1. Oxidation of methyl alcohol:



2. Oxidation of methane *(the Medvedev method):*



**Properties.** A clear, colourless liquid, miscible with water and with alcohol. It may be cloudy after storage.

Methyl alcohol is added as a stabiliser (to 15 %) to avoid parafor­maldehyde formation.

**Identification.** 1. The reaction with chromotropic acid in the presence of sulphuric acid. A violet-blue or violet-red colour develops within 5 min:





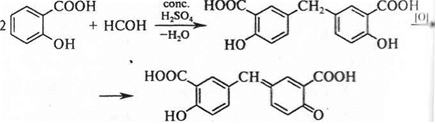
2. The reaction with phenyl hydrazine hydrochloride and potassium ferricyanide solution in the presence of hydrochloric acid. An intense red colour is formed.

To the substance add silver-nitrate solution and dilute ammonia until slightly alkaline. Heat on a water-bath —a grey precipitate or a silver mirror is formed:



Methanol (from 9 to 15 %) is determined by the gas-chromatography method (internal standard is ethanol Rl).

***The non-Pharmacopoeal reaction*** is with salicylic acid in the presence of concentrated sulphuric acid (a red colour):



Some authors propose such structure as:



**Purity. Acidity** is caused by the formed formic acid:



It is detected with phenolphthalein solution.

***Methanol*** is determined by gas chromatography.

**Assay.** 1. Iodometry; ***s=***1. To the solution of the substance add sodium hydroxide solution, iodine and dilute sulphuric acid. Titrate with sodium thiosulphate using starch solution as an indicator.



Sodium hydroxide solution is added because HI in the acidic me­dium can reduce formic acid to formaldehyde.







1. Oxidation with hydrogen peroxide in the alkaline medium; ***s*** = 1:



1. Titration with the sodium sulphite (for quantification of formal­dehyde in the “Formidron“); ***s—*** 1:





1. Refractometry.

**Usage.** Used in the treatment of warts and as an antiseptic, dis infectant and deodorant; in preservation of anatomical specimens.

***Formalin is a protoplasmatic poison!***

**Storage.** In well-closed containers, protected from light, at the temperature of 15 to 25 °C.

**Methenamine**

**(Hexamethylentetraminum), Ph. Eur.**



**Preparation.** Mix the solutions of formaldehyde and ammonia.





Summary:



**Properties.** A white, crystalline powder or colourless crystals, freely soluble in water, soluble in alcohol and in methylene chloride.

**Identification.** 1. The IR-spectrum.

1. To the solution of the substance add sulphuric acid and imme­diately heat to boiling. Allow to cool, then to the solution add water and the acetylacetone reagent. Heat for 5 min. An intense yellow co­lour develops.
2. To the solution of the substance add dilute sulphuric acid and immediately heat to boiling. The solution gives the reaction of ammo­nium salt and salts of volatile bases.



NH4)2S04 + 2NaOH  Na2S04 + 2NH4OH



Dissolve the substance in water and acidify with dilute hydrochlo­ric acid. Add potassium iodobismuthate solution. An orange precipi­tate is formed immediately.

4. With silver nitrate solution — a white precipitate appears:



**Assay.** 1. Dissolve the substance in methanol. Titrate with 0.1 M per­chloric acid determining the end-point potentiometrically; *s =* 1.

(CH2)6N4 + HC104 (CH2)6N4 • HC104

1. Acid-base titration. The indicator is methyl red solution; s = 1/2:



1. Acidimetry (with the mixed an indicator — methyl orange and methyl blue); *s=* 1:



1. Iodine monochloride method (iodchlorimetry). Back titration; the indicator is starch solution; *s* = 1/2:



5. Argentometry by the Volhard method. Back titration; the excess of silver nitrate is titrated with ammonia thiocyanate using ferric-am­monia sulphate as an indicator; *s =* 2/3:



AgN03 + NH4SCN AgSCN + NH4NO3

NH4SCN + Fe(NH4)(S04)2 Fe(SCN)3 + 2(NH4)2S04

**Usage.** Hexamine is used as a urinary antiseptic. It is used in poisonings by salts of heavy metals as antidote.

**Storage.** In well-stoppered bottles, protected from light.

**Chloral Hydrate  
(Chloralum hydratum)**



**2,2,2-Trichloroethane-1,1-diol**

**Preparation**





**trichloroacetic**

**aldehyde**

**Properties.** Transparent, colourless crystals, very soluble in water, freely soluble in alcohol and in ether.

Under the action of the light it slowly decomposes (oxidation):



**Identification. 1.** Add dilute sodium hydroxide solution — the mixturebecomes cloudy and when heated gives off an odour of chloroform:



2. To the solution of the substance add sodium sulphide solution - a yellow colour develops, it becomes reddish-brown quickly. While standing for a short time a red precipitate may be formed.

***The non-Pharmacopoeial reaction*** — with silver ammonia-nitrate solution:



**Purity.** Chloral alcoholate is the intermediate product of synthesis; it is detected with sodium hydroxide solution when adding iodine (io­doform test).

CCl3CH(OH)OC2H5 + NaOH CHC13 + HCOONa + C2HsOH

C2H5OH + 4I2 + 6NaOH CHI3| + 5NaI + HCOONa + 5H20

**Assay.** 1. Dissolve the substance in water and add sodium hydrox­ide solution, titrate with sulphuric acid using phenolphthalein as an indicator.

Titrate the neutralised solution with silver nitrate using potassium chromate solution as an indicator; s=1.

CC13CH(0H)2 + NaOH CHC13 + HCOONa + H20

**excess**

2NaOH + H2S04 Na2S04 + 2H20

CHC13 + 4NaOH - 3NaCl + HCOONa + 2H20

The sodium chloride educed is titrated with silver nitrate solution:

NaCl +AgN03 AgCl +NaN03

AgN03 + K2Cr04 Ag2Cr04 + 2KN03

Volume of a titrant = [(VNaOH - Vh2S04) – V AgNO3 ]

1. Iodometry (the indicator is starch); s=1.

2CC13CH(0H)2 + 2I2 + 3Na2C03

2CCl3COONa + 4NaI + 3H20 + 3C02t

1. The fcid-base titration, the indicator is phenolphthalein solu­tion. Carry out a blank titration; s=1.

CC13CH(0H)2 + NaOH CHC13 + HCOONa + H20

**excess**

NaOH + HC1 NaCl + H20

**Usage.** Hypnotic.

**Storage.** In an airtight container.

**DERIVATIVES OF CARBOXYLIC ACIDS**

Carboxylic acids have the carboxyl group —COOH in their mole­cules.

General properties of these substances are ability to react with al­kali, to form precipitates with the salts of heavy metals, to get into reactions of esterification with alcohols, etc.

In the free state these substances are not used in medicine because of their irritant action. In the most causes their salts such as potassium acetate, calcium lactate, calcium gluconate, sodium citrate, etc. are used.

**Potassium Acetate  
(Kalii acetas), Ph. Eur.**

**CH3COOK**

**Preparation.** Neutralisation of acetic acid with potassium carbonate:

2CH3COOH + K2C03 2CH3COOK + H20 + C02

**Properties.** A white, crystalline powder or colourless crystals, de­liquescent, very sdluble in water, freely soluble in alcohol.

**Identification**. 1. Reactions of an acetate-ion:

1. reaction of ester forming with ethanol (a specific fruity odour):

2CH3COOK + 2C2H5OH + cone. H2S04

2CH3COOC2H5 + K2S04 + 2H30

1. interaction with ferric salts. A brown-red colour is produced:

9CH3COOK + 3FeCl3 + 2H20

2CH,COOH + [Fe3(OH)2(CH3COO)6]+CH3COO- + 9KC1

1. it gives the reaction of acetyl:

La3+ + 3CH3COO¯ + 2H20 La(0H)2CH3C00 + 2CH3COOH

***blue***

2. Reactions of K+:

1. the reaction with tartaric acid:

Kn+ + H2C4H406 KHC4H406 + H+

1. the reaction with sodium cobaltinitrite:

2K+ + Na- + [Co(N02)6]3¯ K2Na[Co(N02)6]

1. colouration of the flame (a violet colour).

**Assay.** 1. Non-aqueous titration. Dissolve the substance in anhyd­rous acetic acid. Add naphtholbenzein solution. Titrate with 0.1 M per­chloric acid. Carry out a blank titration; 5=1.

CH3COOK + CH3COOH (CH3COOKH)+ CH3COO¯

HC104 + CH3COOH (CH3COOH2)+ • C104¯

(CH3COOKH)+ • CH3COO¯ + (CH3COOH2)+ • C104¯ KC104 + 3CH3COOH

Summary:

CH3COOK + HC104 CH3COOH + KC104

2. Acidimetry (in liquid medicines). The indicator is tropeolin-00;

s= 1.

CH3COOK + HC1 CH3COOH + KC1

Usage. Used in solutions for dialysis.

Storage. In well-closed containers, protected from moisture.

**Calcium Lactate  
(Calcii lactas), Ph. Eur.**



**Preparation.** Fermentation of sugary materials (molasses, glucose) by pure cultures of lactic acid bacteria in the presence of calcium carbonate.

CaCO3

**C**6**H**12**0**6 **—-** 2 **CH**3**CHCOOH**

OH

(CH3CH(OH)COO)2Ca + C02 + H20

**Properties.** A white or almost white, crystalline or granular pow­der, slightly efflorescent, soluble in water, freely soluble in boiling wa­ter, very soluble in alcohol.

The substance exhibits the optical isomerism.

**Identification. 1**. The reaction of lactate-ion.

Dissolve the substance in water R. Add bromine water R and dilute sulphuric acid R. Heat on a water-bath until the colour is discharged, stirring occasionally with a glass rod. Add ammonium sulphate R and mix. Add sodium nitroprusside R solution in dilute sulphuric acid R. Still without mixing add the concentrated ammonia R. Allow to stand for 30 min. A dark green ring appears at the junction of the two liquids.

2. Reactions of Ca2+.

***The non-Pharmacopoeial reaction*** - with potassium permanganat solution gets colourless with forming of acetaldehyde (the characteris­tic fruity odour).



**Assay.** Complexometry (the indicator is calconcarboxylic acid). Direct titration in the presence of concentrated sodium hydroxide solution. Calculate on an anhydrous substance; *s=1.*









**Usage.** It is the source of Ca2+-ions. An antiallergic medicine, it is also used in poisonings with salts of heavy metals like an antidote.

**Storage.** In a well-closed container.

**Calcium Gluconate**

**(Calcii gluconas), Ph. Eur.**



***Calcium D-gluconate monohydrate***

**Preparation.** Electrochemical oxidation of glucose in the presence of calcium carbonate and bromine:



**Properties.** A white, crystalline or granular powder, sparingly solu­ble in water, freely soluble in boiling water.

**Identification.** 1. The thin-layer chromatography.

2. Reactions of Ca2+ .

***The non-Pharmacopoeial reaction*:** with FeCl3 solution. A light-green colouring develops (the reaction of gluconate-ion).

**Purity.** Sucrose and reducing sugars are determined with cupri- tartaric solution (Fehling reagent). No red precipitate is formed.

**Assay.** Complexonometry *(see* Calcium Lactate).

**Usage.** Used in treatment of calcium deficiency.

**Storage.** In well-closed containers.

**Sodium Citrate  
(Natrii citras), Ph. Eur.**



Trisodium 2-hydroxypropane-1,2,3-tricarboxylate

Calculations in the assay are made with reference to the anhydrous substance.

**Preparation**



**Properties.** A white, crystalline powder or white, granular crystals, slightly deliquescent in the moist air, freely soluble inwater, practically insoluble in alcohol.

**Identification.** 1. The reaction of citrates. Dissolve the substance in water R. Add sulphuric acid R and potassium permanganate solution R. Warm until the colour of the permanganate is discharged. Add sodium nitroprusside R solution in dilute sulphuric acid R and 4 g of sulphamic acid.R. Make alkaline with concentrated ammonia R. added dropwise until all the sulphamic acid has dissolved. Addition of an excess of concentrated ammonia R produces a violet colour turning to violet-blue:



2. Reactions of Na+.

***Non-Pharmacopoeial reactions:*** a) forming of pentabromacetone:



b) when heating a white precipitate develops, it dissolves when cooling:



Purity. Oxalates. Dissolve the substance in water, add hydrochloric acid and granulated zinc. Heat ona water-bath. Add phenylhydrazine hydrochloride and boil. Cool rapidly, add hydrochloric acid and potassium ferricyanide solution.

Any pink colour in the solution is not more intense than that in the standard.

Assay. 1. Non-aqueous titration. Titrate with perchloric acid in the medium of anhydrous acetic acid, the indicator is naphtholbenzein; s=1/3.



2. Ion-exchange ehromatography:



Citric acid is neutralized with an alkali; s=1/3.



3.Back argentometry by the Volhard method; s=1/3:



Usage. It is used for containing of the blood.

Storage. Store in an air-tight container.

**Sodium Hydrogen Citrate**

**(Natrii hydrocitras pro injectionibus)**



*Disodium hydrogen 2-hydroxypropane-1,2,3-tricarboxylate sesquihydrate*

**Identification, assay, usage** and **storage** - *see* Sodium Citrate.

**MEDICINAL SUBSTANCES FROM GROUP OF CARBOHYDRATES**

Carbohydrates are organic compounds, consisting of carbon, hyd­rogen and oxygen. Most carbohydrates have the general formula C4(H20)4.

The fundamental compound of the carbohydrate group is monosac- caride or simple sugar. Such molecules are polyhvdroxy-aldehydes or polyhydroxy-ketones, and are the primary oxidation products of polyhydric alcohols.

Classification: 1) by the number of carbon atoms — tetroses, pen­toses, hexoses, etc.;

1. by the basic functional group — aldoses and ketoses;
2. by the number of atoms in a cycle (for cyclic structures) — furanoses and pyranoses;
3. by the number of monosaccharide units — simple (monosac­charides), oligosaccharides (2—10 monosaccharides) and polysaccha­rides (more than 10 monosaccharides).

Glucose is the main representative of monosaccharides and is widely distributed in nature. D-Glucose, like many sugars, exhibits a phe­nomenon known as “mutarotation". Sugars exist in solution as a mix­ture of two ring forms of glucoses in equilibrium with a comparatively small proportion of the open-chain or aldehyde form and p-glucofuranoses: α-D-(+)-glucopyranose (α-D-glucose) the specific rotation near + 119°; β-D-(+)-glucopyranose (β-D-glucose) is near +19°. The mixture of different tautomery forms of D-glucose appears as the result of mutual transformations, containing of β-D-(+)-glucopvranose, 36 % α-D-(+)-glucopyranose and le one percent of acyclic form and α- and β-glucofuranoses. S rotation of this mixture is +51.5 —+53°. The change is known as “mutarotation” and is catalysed by acids, and even more by alkalis.



α-*D*-(+)-glucopyranose *D*-aldohexose β -D-(+)-glucopyranose

(*D*-glucose) (β -*D*-glucose)

(α-*D-*glucose) open-chain form

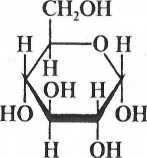
-36% -63%



-D-(+)-glucofuranose β-D-(+)-glucofuranose

~1%

Glucose

(Glucosum), Ph. Eur.

(+)-*D*-glucopyranose

Properties. A white, crystalline powder, with a sweet taste, soluble in water, sparingly soluble in alcohol.

Preparation. It is a product of hydrolysis of many common disaccarides, and also of starch and cellulose. For medical purposes glucose is obtained by the hydrolysis of potato or corn starch in the presence of mineral acids:



**Identification.** 1. Specific optical rotation is at +52.5 to +53.3°.

1. Thin-layer chromatography.
2. With cupri-tartaric solution after heating a red precipitate is formed:





**Non-Pharmacopoeial reactions:** a) with ammonia silver nitrate so­lution (the reaction of silver mirror):



b) with phenylhydrazine — a yellow appears and the smell of the ammonia is educed:





c)with mineral acids when heating glucose forms oxymethyl furfurol:



Oxymethyl furfurol is volatile compound; it interacts with aniline or procaine, inflicted on a filtration paper, which covers a test tube. The result is a yellow colour. Then the furan cycle opens up with formation of polymethine dye (a raspberry-violet colour). The sup­posed mechanism of this reaction is:



**Assay. *Non-Pharmacopodal methods:*** 1. Back iodometry; *s=l.*

Carry out a blank.

I2 + 2NaOH Nal + NaOI + H20



Nal + NaOI + H2S04 Na2S04 + I2 + H20  
 I2 + 2Na2S203 2NaI + Na2S406

1. Refractometry (for solutions for injections).
2. Polarimetry.

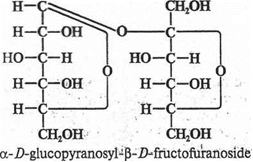
**Usage.** Diseases of the heart, in shock, collapse, as a source of the nutrition.

**Storage.** In well closed containers.

**Sucrose**

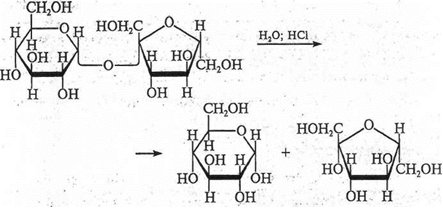
**(Saccharum), Ph. Eur.**





The configurational formula shows how the a-D-glucopyranose unit (on the left) and the p-D-fructofuranose unit (on the right) are joined by oxygen through the carbonyl-carbon atoms of each. Sucrose cannot react therefore in an opan-chaiii aldose or ketose form, and this ex­plains why it has no reducing properties. The furanose ring does not survive hydrolysis, since this process results in the conversion of suc­rose into D-glucose and D-fructose in their normal (pyranose) forms.

*Invert sugar.* Hot, dilute acids hydroliyse sucrose to a mixture of equal parts of D-glucose and D-fructose:



Since D-fructose rotates the plane of polarization of polarized light to the left (—) to a greater extent than D-glucose does to the right (+), the mixture of sugars produced is slightly laevo-rotatory (40°). The original sucrose was dextrarotatory (the specific rotation of suc­rose solution before the hydrolysis: [a] =+66.3 ...+67.0°). Hence, during the hydrolysis, the optical rotation of the solution has under­gone an inversion or change from dextro- to laevo. As a result of hydrolysis is the mixture of:

****

The mixture of sugars is called invert sugar:



Sucrose belongs to the oligosaccharides. It is usually obtained from the sugar-cane or sugar-beet.

**Properties.** A white, crystalline powder or lustrous, dry, colourless or white crystals, very soluble in water, slightly soluble in alcohol, practically insoluble in ethanol.

**Identification.** 1. Infrared absorption spectrophotometry.

1. Thin-layer chromatography.
2. With copper sulphate solution and freshly prepared dilute sodi­um hydroxide solution the solution is blue and clear and remains so after boiling. To the hot solution add dilute hydrochloric acid, boil and add dilute sodium hydroxide solution — an orange precipitate is formed immediately.

***Non-Pharmacopoeial reactions:*** a) the reaction with cobalt nitrate in the alkaline medium — a violet colour appears;

b) in medicinal forms it is identified by the reaction with resorcinol: when heating in the presence of hydrochloric acid a red colour appears.

**Assay.** Refractometry; polarimetry.

**Usage.** For preparation of syrups and as additive matter in medic­inal forms.

**Storage.** In well closed containers.

**Lactose Anhydrous Milk Sugar**

**(Lactosum anhydricum), Ph. Eur. (Saccharum lactis)**



*Lactose is O-β-D-galactopyranosyl-1(14)-β-D-glucopyranose*

*or*

*a mixture of O-β-D-galactopyranosyl-1(14)-α-D-glucopyranose*

*and O-β-D-galactopyranosyl-1(14)-α-D-glucopyranose*

**Properties.** A white or almost white, crystalline powder, freely but slowly soluble in water, practically insoluble in alcohol.

**Identication. 1.** Infrared absorption spectrophotometry.

1. Thin-layer chromatography.
2. With ammonia at heating a red colour develops.
3. Solution of lactose restores cupri-tartaric reagent.

***Specific optical rotation.*** Dissolve the substance in water, heat to 50 °C, add dilute ammonia. In 30 min the specific optica! rotation is +54.4 to +55.9°, calculated with reference to the anhydrom sar- stance.

**Assay.** *See*Glucose.

**Usage.** Additive matter.

**Storage.** In well closed containers.