MINISTRY OF HEALTH OF UKRAINE
BOGOMOLETS NATIONAL MEDICAL UNIVERSITY

WORK BOOK

FOR STUDENTS' INDEPENDENT WORK

(auditory and outside the auditorium)

Discipline of choice "Toxicological and forensic chemistry"

Field of knowledge 22 Health care

Specialty 226 "Pharmacy, industrial pharmacy"

Specialization 226.01 "Pharmacy"

Form of study Day

Department of medicinal chemistry and toxicology

Approved at the meeting of the department on "30" August 2024, protocol No. 14

Head of the Department of medicinal chemistry and toxicology
Doctor of Medicine, Professor Nizhenkovska I.V.

Considered and approved:

on the meeting of cycle methodical commission of specialty 226 "Pharmacy, industrial pharmacy" dated August 30, 2024, protocol No. 1

INTRODUCTION

Workbook for students' independent classroom and outside the auditorium work of 4th course of the specialty 226 "Pharmacy, industrial pharmacy" from the elective component "Toxicological and forensic chemistry" - a structured methodical development, containing the basic information for the successful assimilation of the educational material of each topic of the discipline and preparation for practical classes.

The main purpose of using a workbook is optimization and increasing the effectiveness of students' educational and cognitive activities by mastering methods of independent acquisition, active assimilation and application of knowledge about methods of isolation, qualitative detection and quantitative determination of toxic substances and their metabolites in objects of biological and of other origin, properties of poisonous and potent substances, their behavior in the body and cadaveric material, general principles of assessment toxicity of poisonous substances taking into account their physical and chemical properties, ways of penetration into the body, features of toxicokinetics and toxicodynamics, classification of poisons and poisonings.

Features of the proposed tasks. The proposed tasks for classroom and extracurricular work are aimed at the development of abstract thinking, analysis and synthesis, the ability to work in a team and the formation of the ability to apply knowledge in practical situations.

The order of tasks for independent work

Tasks for independent out-of-class training must be completed before conducting a practical lesson on this topic.

Tasks for classroom independent work are completed during a practical lesson.

During independent work, the student must write down his answers to the assigned tasks in the workbook.

Evaluation criteria

When evaluating the performance of independent work, preference is given to standardized control methods: tests and structured written tasks.

Excellent grade "5" - student gives at least 90% correct answers to standardized test tasks, answers written tasks without errors.

Good grade "4" - the student gives at least 75% correct answers to standardized test tasks, has minor errors in the answers to written tasks.

Satisfactory grade "3" - student gives at least 60% correct answers to standardized test tasks, has significant errors in answers to written tasks.

Unsatisfactory grade "2" - student gives less than 60% correct answers to standardized test tasks, has gross errors in answers to written tasks or does not give answers to them.

Rules for keeping a workbook: consistent, written and neat.

Mandatory observance of academic integrity by students, namely:

 independent performance of all types of work, tasks, forms of control provided for by the work program of this educational discipline;

 references to sources of information in the case of using ideas, developments, statements, information;

 compliance with the legislation on copyright and related rights;

 provision of reliable information about the results of one's own educational (scientific, creative) activities, used research methods and sources of information.

Topic N 1. Engineering of safety during the working at the laboratory of chemical-toxicological analysis. Theoretical base of toxicological and forensic chemistry and chemical-toxicological analysis. External examination of the objects of investigation, preliminary tests of the objects of investigation, draw up of the forensic-toxicological investigation's plan.

Purpose: the ability to implement the main stages of work in the laboratory of chemical and toxicological analysis: external inspection of research objects, preliminary tests of the research object and drawing up a forensic toxicological research plan.

The student must:

 know the basic concepts, strategy and tactics of chemical and toxicological analysis, theoretical foundations of toxicological and forensic chemistry;

 be able to propose a forensic toxicological research plan;

 evaluate the results of the external inspection of research objects, preliminary tests of the object;

 know the methods of purification and analysis of chemical substances,

 interpret the results of the analysis.

Basic concepts of the topic:

Term, parameter, characteristic	*Definition*
Toxicological and Forensic Chemistry	studies the methods of research in biological material of poisonous substances that caused the death of a person, as well as various physical evidence (means of murder, money, valuables, clothes - everything that is used during the investigation of the case)
Chemical and toxicological analysis	a set of scientifically based methods used in practice for the selection (isolation), detection and quantitative determination of toxic substances
Laboratory express analysis acute intoxications	examines the methods of researching poisonous substances in biological fluids (blood, urine, saliva, sweat secretions) of living people with the aim of providing assistance to the doctor in their rescue
Analysis residual quantities of pesticides	studies methods of researching poisonous substances in water, land, and food in order to prevent diseases and deaths of people
Sanitary and chemical analysis	pays attention to the methods of research of poisonous substances in the air of factories and enterprises in order to prevent occupational diseases of people
Objects	biological fluids (urine, blood plasma, saliva, sweat),

forensic toxicological analysis are:	cadaver material, food remains, medicines, household items, pesticides, technical fluids, food additives, cosmetics and other
Evidence	objects that are sent by judicial and investigative bodies to the laboratory for forensic toxicological examination
Foreign substances or xenobiotics	substances that can disrupt normal cellular processes, cause poisoning and death
Exergonic reactions (processes)	reactions accompanied by the release of chemical energy necessary for the functioning of living organisms
Endergonic reactions (processes)	reactions that require energy expenditure for their progress; these are enzymatic reactions of synthesis and reduction
Anabolism	formation as a result of metabolism of more complex molecules with the use of body energy
Catabolism	disintegration of the molecules of the original substance into separate parts (detoxification of the body)

Recommended literature:

Basic

1.Welchinska E.V. Toxicological and forensic chemistry (Criminal analysis). Poisonous substances and their biotransformation: textbook / E.V. Welchinska. — K.: PE Lopatina O.O., ISBN 978-617-7533-02-2, 2017. — p. 4-16. http://ir.librarynmu.com/handle/123456789/9123

2.Materials of Lecturers. The department of medicinal chemistry and toxicology of pharmaceutical faculty of Bogomolets NMU. https://www.youtube.com/@user-yj2fn5mz3x/

Auxiliary

1. Caio H. P. Rodrigues, Lívia S. Mariotto, Aline T. Bruni. Acute, chronic, and *post-mortem* toxicity: a review focused on three different classes of new psychoactive substances. *Forensic Toxicology*. V. 41,187–212 (2023).

2. Marine Deville & Corinne Charlier. Cannabidiol in urine is not a proof of CBD consumption—lesson learned from urine sample analysis in routine caseworks**.** *Forensic Toxicology*. V. 41,213–220 (2023)**.**

3. Kelly Francisco da Cunha, Karina Diniz Oliveira, Jose Luiz Costa. Green analytical toxicology method for determination of synthetic cathinones in oral fluid samples by microextraction by packed sorbent and liquid chromatography–tandem mass spectrometry**.** *Forensic Toxicology*. (2023)**.**

Informational resources

European Pharmacopoeia online - pheur.edqm.eu

The British Pharmacopoeia 2021 - www.pharmacopoeia.com

The British Pharmacopoeia 2020. London.2020: I-1298. www.webofpharma.com

Pharmacopoea USP. www.usp.org.

Website of the Department of Medicinal Chemistry and Toxicology of O.O. Bogomolets

http://nmu.ua/zagalni-vidomosti/kafedri/kafedra-farmatsevtycheskoj-byologycheskoj-ytoksykologycheskoj-hymyy/

Distance learning platform LIKAR_NMU

https://likar.nmu.kiev.ua/

Official website of the Ministry of Health of Ukraine

https://moz.gov.ua/

International Journal of Medical Toxicology and Forensic Medicine **(IJMTFM).** https://journals.sbmu.ac.ir/ijmtfm

Journal of Synthetic Organic Chemistry, Japan. http://www.ssocj.jp/indexenglish.

Journal of Organic Chemistry, USA. https://doi.org/10.1021/acs.joc.0c02255.

Synthetic Communications. Great Britain. http://www.tandfonline.com/page/terms-and-conditions
pubmed.ncbi.nlm.nih.gov

www.cochrane.org

Questions for theoretical study:

1. Toxicological and forensic chemistry, its content, tasks, main sections of toxicological and forensic chemistry (forensic-toxicological and chemical-toxicological analysis), its connection with toxicology and other medical-biological, pharmaceutical, fundamental disciplines.
2. Forensic - toxicological and chemical-toxicological laboratories, their tasks, organization of work, legal bases of activity.
3. Peculiarities of chemical and toxicological analysis. General and targeted chemical and toxicological analysis.
4. Fields of use of methods of chemical and toxicological analysis.
5. Procedure and documentation of forensic toxicological (chemical-toxicological) examinations.
6. Preliminary tests (screening studies) in chemical-toxicological analysis and their role in drawing up a plan of chemical-toxicological analysis.
7. Definition of the terms "poisoning" and "poison".

8. General principles of classification of poisons: according to chemical structure, purpose of use (production purpose), degree of toxicity (hygienic), type of toxic action (toxicological), selective toxicity, according to the method of isolation from objects of biological origin.
9. Classification of poisoning by the cause of occurrence (accidental, intentional), by the conditions (place) of development (domestic, industrial, medical). Division of intentional poisoning into criminal and suicidal. Classification of poisoning according to the clinical principle (acute, chronic, subacute poisoning); by ways of penetration into the body; nosological classification.
10. Metabolism (biotransformation) of poisons in the human body. I and II phases of metabolism.
11. Lethal synthesis.
12. Objects of chemical and toxicological research, their characteristics, preservation methods.
13. Rules for selection, transportation, acceptance of biological material for forensic chemical examination. Sample storage procedure.
14. Peculiarities of the analysis of certain types of biological material depending on their nature, state, chemical properties of poisonous substances.
15. General principles of interpretation of forensic chemical research results.
16. General characteristics of the methods used to detect and quantify poisons in chemical-toxicological analysis (chemical, physico-chemical, biochemical, pharmacological). Their comparative characteristics (sensitivity, specificity).

Tasks for independent processing of the topic:

Test tasks

Choose and justify the correct answer.

1. The specific smell of biological material (stomach and its contents) may indicate the presence of a certain poisonous substance. Name the poisonous substance, after poisoning with which the smell of bitter almonds is felt:

A. hydrocyanic acid

B. phenol

C. alcohol

D. acetic acid

2. The color of the stomach contents may indicate the presence of certain poisonous substances. Specify the color of the stomach contents, which is observed in picric acid poisoning:

A. purple

B. white

C. black

D. yellow

3. Green coloration of stomach contents is observed in case of "metallic" otta poisoning. Name the poison:

A. Cuprum and its compounds

B. Lead and its compounds

C. phenol

D. triethyl lead

4. The olive-black color of urine indicates poisoning with what poison?

A. phenol

B. alcohol

C. chloroform

D. acetone

5. Detection of ammonia and hydrogen sulfide in biological material is carried out with the help of indicator papers. What indicator paper is used to confirm the presence of ammonia?

A. phenolphthalein

B. moistened with a solution of lead acetate

C. moistened with an alkaline solution of copper sulfate

D. red litmus, moistened with water

Enter in the cells ☐ the letters that indicate the correct answers to the test questions:

1-☐ 2-☐ 3-☐ 4-☐ 5-☐

Written assignments

Task 1. Determination of the pH of the stomach contents in a glass using indicator papers: universal, phenolphthalein and litmus. In what range will the pH value be, if the biological material contains acetic acid? Which paper will change color? In what range will the pH value be, if the biological material contains sodium hydroxide? Which piece of paper will change color (Fig. 1)?

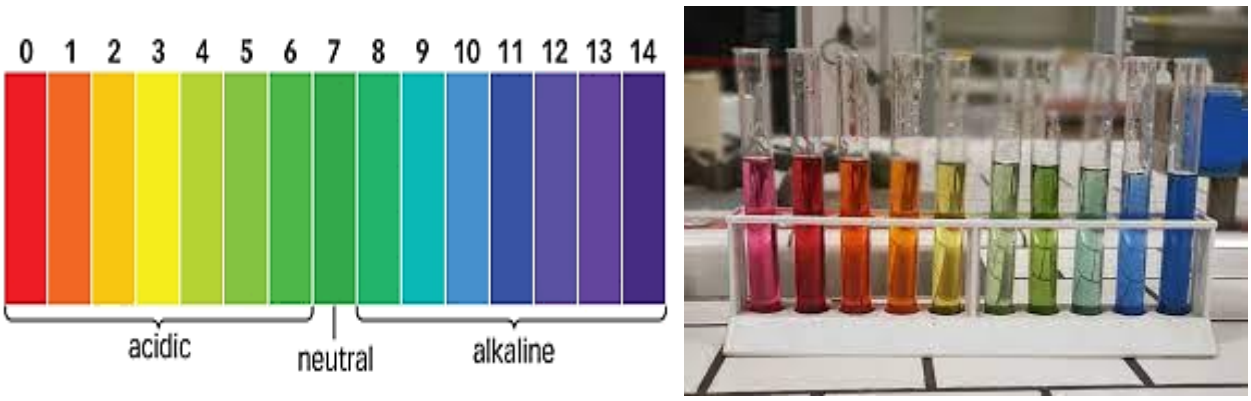

Figure 1.

The answer and its justification

Auditory collective work:

Task 1. After phenol poisoning, the color of the victim's urine changed. Enter the number of the glass with the urine of the poisoned person (Fig. 2).

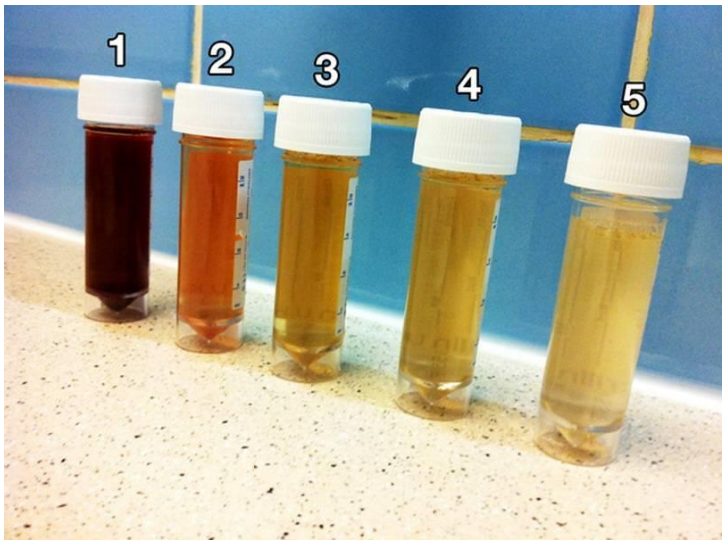

Figure 2.

The answer and its justification

Task 2. What objects, other than those shown in Figure 3, are physical evidence?

Figure 3.

The answer and its justification

Auditory independent work (supervised by the teacher):

Task 1. Which of the specified substances are xenobiotics: medicines, drugs, vitamins, pesticides, mineral fertilizers, fats, detergents, radionuclides, synthetic dyes, proteins. Add your examples to the list of xenobiotics.

The answer and its justification

An example of a task with an answer standard: Explain the processes of catabolism and anabolism.

Answer standard

Metabolism includes three stages: the entry of substances into the body, their intra-tissue exchange and the release of final products from the body. Food is digested in the gastrointestinal tract.

During digestion, polymers (proteins, polysaccharides, etc.) are hydrolyzed into monomers, which are absorbed into the blood and included in the intermediate exchange. Intracellular metabolism has two directions: catabolism and anabolism.

Catabolism is the process of breaking down organic molecules into final products. The main final products of the transformation of organic substances in animals and humans are CO_2, H_2O and urea.

Catabolism reactions are accompanied by the release of energy (exergonic reactions).

Anabolism combines biosynthetic processes in which simple building blocks are joined into complex macromolecules needed by the body. Anabolic reactions use energy released during catabolism (endergonic reactions). Metabolism combines anabolic and catabolic processes and ensures life processes in body cells.

The methodical development was made by: professor of the department, doctor of pharm. sc. Welchinska O.V.

Topic N 2. Toxicological characteristic of the group of substances isolated from biological material by water extraction of objects which investigated (mineral acids, alkalies and their salts). Peculiarities of isolation from biological material, identification and quantitative determination of sulfuric and nitric acids, nitrates and nitrites.

Purpose: the ability to operate with the basic concepts of the topic and to implement the main stages of chemical and toxicological analysis of poisonous substances, which are isolated from biological material by infusing the studied objects with water: mineral acids, alkalis and their salts; isolation from biological material and detection and quantitative determination of sulfuric acid, nitric acid, nitrates, nitrites.

The student must:

 to know the basic concepts, strategy and tactics of chemical and toxicological analysis of a group of poisonous substances that are isolated from biological material by infusing the studied objects with water (mineral acids, alkalis and their salts);

 be able to propose a forensic toxicological research plan;

 know the methods of isolating poisonous substances, which are isolated from biological material by infusing the studied objects with water (mineral acids, alkalis and their salts);

 evaluate the results of organoleptic control of research objects, preliminary tests;

 know the methods of analysis of poisonous substances that are isolated from biological material by infusing the studied objects with water (mineral acids, alkalis and their salts);

 interpret the results of the analysis.

Basic concepts of the topic:

Term, parameter, characteristic	*Definition*
Chemical and toxicological analysis	a set of scientifically based methods used in practice for the selection (isolation), detection and quantitative determination of toxic substances
Mineral acids: *sulfuric (sulphuric) acid* *nitric (nitric) acid* *hydrochloric (chloric) acid*	H_2SO_4 HNO_3 HCl

Alkalis and Ammonia (ammonia): *sodium hydroxide (caustic soda)* *potassium hydroxide* *ammonium hydroxide* *ammonia (ammonia)*	**$NaOH$** **KOH** **NH_4OH** **NH_3**
Salts of alkali metals: *nitrites* *nitrates*	**$NaNO_2$, KNO_2** **$NaNO_3$, KNO_3**
Griess reagent	a mixture of sulfanilic acid and α-naphthylamine in acetic acid

Recommended literature:

Basic

1.Welchinska E.V. Toxicological and forensic chemistry (Criminal analysis). Poisonous substances and their biotransformation: textbook / E.V. Welchinska. — K.: PE Lopatina O.O., ISBN 978-617-7533-02-2, 2017. — p. 320-330. http://ir.librarynmu.com/handle/123456789/9123

2.Materials of Lecturers. The department of medicinal chemistry and toxicology of pharmaceutical faculty of Bogomolets NMU. https://www.youtube.com/@user-yj2fn5mz3x/

Auxiliary

1.Caio H. P. Rodrigues, Lívia S. Mariotto, Aline T. Bruni. Acute, chronic, and post-mortem toxicity: a review focused on three different classes of new psychoactive substances. Forensic Toxicology. V. 41,187–212 (2023).

2. "Toxicology Overview". *American Chemical Society*. Retrieved 10 May 2020.

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Journal of Synthetic Organic Chemistry, Japan. http://www.ssocj.jp/indexenglish.

Journal of Organic Chemistry, USA. https://doi.org/10.1021/acs.joc.0c02255.

Synthetic Communications. Great Britain. http://www.tandfonline.com/page/terms-and-conditions
pubmed.ncbi.nlm.nih.gov

www.cochrane.org

Questions for theoretical study:

1. Mineral acids: sulfuric (sulphate) acid. Detection, isolation and metabolism.

2. Mineral acids: nitric (nitric) acid. Detection, isolation and metabolism.

3. Mineral acids: hydrochloric (chloric) acid. Detection, isolation and metabolism.

4. Alkalis: sodium hydroxide (caustic soda). Detection, isolation and metabolism.

5. Alkalis: potassium hydroxide. Detection, isolation and metabolism.

6. Alkalis and ammonia (ammonia): ammonium hydroxide, ammonia (ammonia). Detection, isolation and metabolism.

7. Salts of alkali metals: nitrites. Detection, isolation and metabolism.

8. Salts of alkali metals: nitrates. Detection, isolation and metabolism.

Tasks for independent processing of the topic:

Test tasks

Choose and justify the correct answer.

1. Specify the poisonous substance that is isolated from the biological analysis during the chemical-toxicological analysis by infusing the investigated objects with water:

A. hydrocyanic acid

B. sulfuric acid

C. acetone

D. acetic acid

2. For the qualitative detection of nitrates, a reaction with the alkaloid alkaloid reagent is used, as a result of which a red color is formed. Enter the name of the alkaloid:

A. brucin

B. morphine

C. nicotine

D. anabasin

3. In order to confirm poisoning with sulfuric acid, a reaction with copper flakes in the dialysate is used during the isolation of this poison from biological material. Recovery of sulfuric acid occurs. Name the compound that is formed:

A. sulfuric acid anhydride

B. sulphitic acid

C. hydrogen sulfide

D. Sulfur

4. Nitrites are detected by a reaction resulting in the formation of an azo dye. Name the acid used in this reaction:

A. sulfanilova

B. nitrate

C. acetate

D. sulfate

5. Hydrochloric acid is detected with a reagent that is a Silver salt. Name the reagent:

A. argentum nitrate

B. argentum phosphate

C. argentum sulfate

D. argentum iodide

Enter in the cells ☐ the letters that indicate the correct answers to the test questions:

1-☐ 2-☐ 3-☐ 4-☐ 5-☐

Written assignments

Task 1. Figure 1 shows a diagram of the metabolism of mineral acids. Describe metabolic reactions. Name the metabolites:

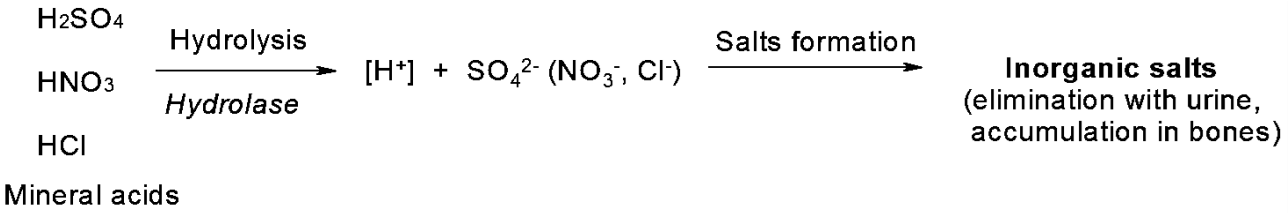


Figure 1.

The answer and its justification

Auditory collective work:

Task 1. Figure 2 shows schemes of chemical reactions. Explain for what purpose these reactions are used. Are there color changes?

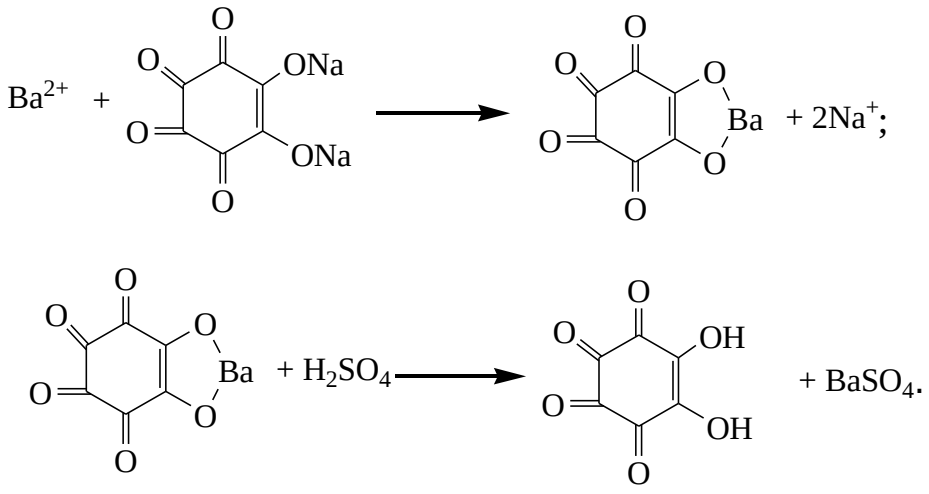


Figure 2.

The answer and its justification

Task 2. When studying which poisonous substance, the following chemical transformation takes place? What color should be formed in the case of a positive result of the reaction?

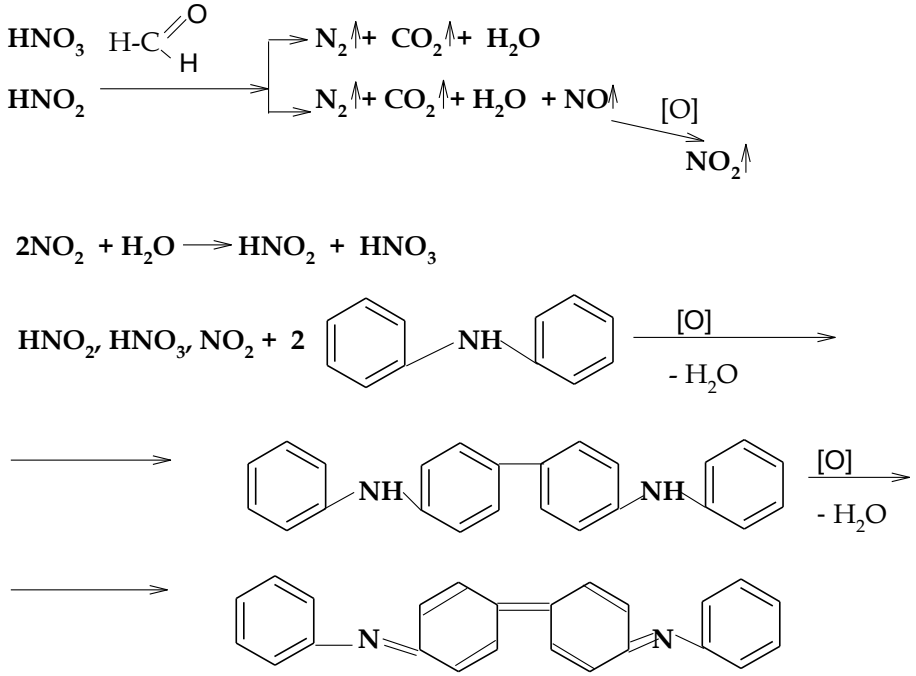


Figure 3.

The answer and its justification

Auditory independent work (supervised by the teacher):

Task 1. Reactions for the qualitative detection of nitrites (nitrite ions).

Reaction with sulfanilic acid and β-naphthol: after acidification of dialysate containing nitrites and addition of sulfanilic acid (I), diazonium salt (II) is formed. During the interaction of a diazonium salt with an alkaline solution of β-naphthol (III), an azo dye (IV) is formed.

Write a diagram of the described reaction.

The answer and its justification

An example of a task with an answer standard: to detect which poison is the Griess reaction used? Describe the reaction. Write the reaction scheme.

Answer standard

The Griess reaction is based on the interaction of nitrites with the Griess reagent (a mixture of sulfanilic acid and α-naphthylamine in acetic acid) (Fig. 4):

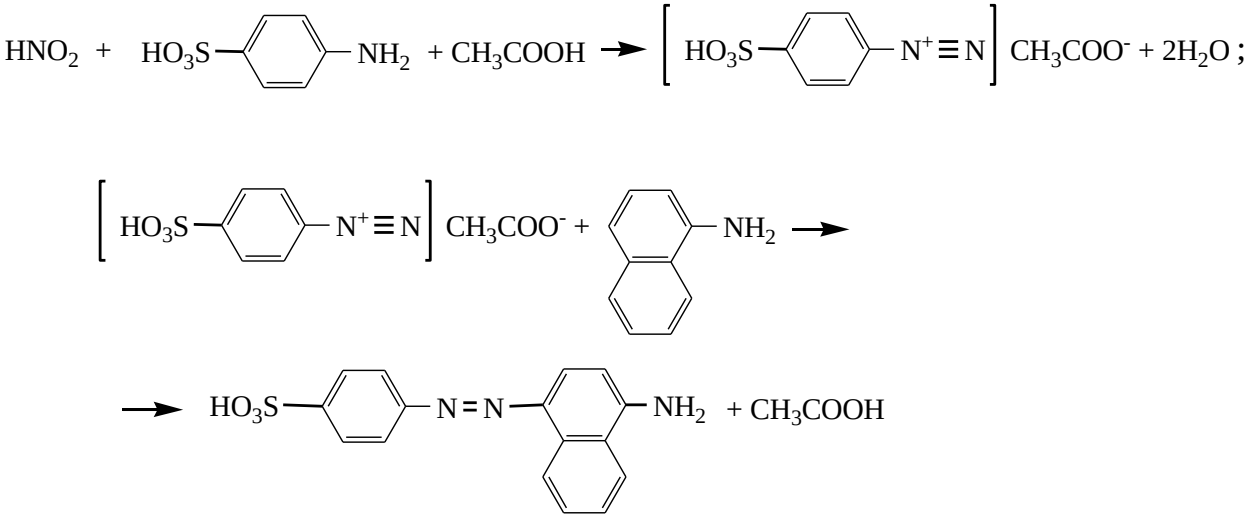


Figure 4

In the presence of nitrites, a red color appears immediately or after some time. Nitrates do not give this reaction.

The methodical development was made by: professor of the department, doctor of pharm. sc. Welchinska O.V.

Topic N 3. A group of poisonous substances isolated from biological material by steam distillation ("volatile" poisons): hydrocyanic acid and cyanides, alkyl halides, aliphatic alcohols, aldehydes, ketones, phenols, carboxylic acids, alkyl halides, phenols, aniline. Quantitative analysis of volatile substances. Control work № 1.

Purpose: the ability to operate with the basic concepts of the topic and to implement the main stages of chemical and toxicological analysis of poisonous substances that are isolated from biological material by distillation with water vapor ("volatile" poisons): hydrocyanic acid and cyanides, alkyl halides, aliphatic alcohols, aldehydes, ketones (acetone), phenols, carboxylic acids (acetic acid).

The student must:

 know the basic concepts, strategy and tactics of chemical-toxicological analysis of a group of poisonous substances isolated from biological material by steam distillation ("volatile" poisons);

 be able to propose a forensic toxicological research plan;

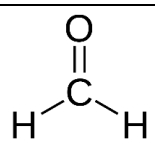
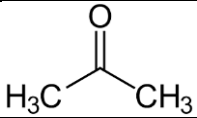
 know the methods of isolating poisonous substances, which are isolated from biological material from biological material by steam distillation ("volatile" poisons);

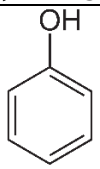
 evaluate the results of organoleptic control of distillates, preliminary tests;

 know the methods of analysis of poisonous substances that are isolated from biological material by steam distillation ("volatile" poisons);

 interpret the results of the analysis.

Basic concepts of the topic:

Term, parameter, characteristic	*Definition*
Hydrocyanic acid and its salts	HCN, KCN, NaCN
Alkyl halides	$CHCl_3$ – chloroform CCl_4 – carbon tetrachloride CF_3-CBrHCl – halothane CCl_3-C(O)H x H_2O – chloralhydrate CH_2Cl-CH_2Cl – dichloroethane
Formaldehyde	
Acetone	

Aliphatic alcohols	CH_3OH, C_2H_5OH, $(CH_3)_2CH\text{-}CH_2CH_2OH$
Phenol	
Acetic acid	CH_3COOH

Recommended literature:

Basic

1.Welchinska E.V. Toxicological and forensic chemistry (Criminal analysis). Poisonous substances and their biotransformation: textbook / E.V. Welchinska. — K.: PE Lopatina O.O., ISBN 978-617-7533-02-2, 2017. — p. 48-81. http://ir.librarynmu.com/handle/123456789/9123

2.Materials of Lecturers. The department of medicinal chemistry and toxicology of pharmaceutical faculty of Bogomolets NMU. https://www.youtube.com/@user-yj2fn5mz3x/

Auxiliary

1. "Isocyanic acid". National Institute of Standards and Technology (U.S. Department of Commerce). Retrieved 2023-04-20.

2. Scott, Kevin A.; Cox, Philip B.; Njardarson, Jon T. (2022-05-26). "Phenols in Pharmaceuticals: Analysis of a Recurring Motif". *Journal of Medicinal Chemistry*. **65** (10): 7044–7072. doi:10.1021/acs.jmedchem.2c00223. ISSN 0022-2623. PMID 35533692. S2CID 248667453.

Informational resources

European Pharmacopoeia online - pheur.edqm.eu

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Journal of Organic Chemistry, USA. https://doi.org/10.1021/acs.joc.0c02255.

Synthetic Communications. Great Britain. http://www.tandfonline.com/page/terms-and-conditions
pubmed.ncbi.nlm.nih.gov

www.cochrane.org

Questions for theoretical study:

1. A group of substances that are isolated by distillation ("volatile" poisons). General characteristics of the group. Physico-chemical properties, structure and effect on the body. The cause and frequency of poisoning. Features of combined poisoning. The significance of the results of chemical and toxicological analysis for the diagnosis of poisoning by "volatile" poisons.
2. Means of detoxification of the body in case of poisoning with "volatile" poisons.
3. Methods of isolating "volatile" poisons from biological material, food products, and environmental objects: steam distillation, dry air distillation.
4. Methods of purification and concentration of "volatile" poisons in distillates. Schematic diagram of the study of biological material for "volatile" poisons during general and targeted analysis using a combination of methods.
5. Individual representatives of the group of "volatile" poisons: hydrocyanic acid, aliphatic monoatomic alcohols (C1-C5), alkyl halides (chloroform, chloral hydrate, carbon tetrachloride), aldehydes (formaldehyde), acetone, phenol and its derivatives, acetic acid.
6. Hydrocyanic acid and its derivatives. Physico-chemical properties, application, toxic effect on the body. The main patterns of behavior in the body and corpse. Antidotes. Features of isolation from corpse organs and biological fluids, detection reactions and methods of quantitative determination. Assessment of their sensitivity and specificity. Assessment of forensic chemical analysis results.
7. Aliphatic monoatomic alcohols (C1-C5 alkanols). Physico-chemical properties, applications, mechanisms of toxic action on the body. The main patterns of behavior in the body and corpse. Features of isolation. Metabolism. Dichloroethane.
8. Formation of ethanol in the body during diseases. The value of the relative ratio of ethanol in urine and blood for the diagnosis of alcoholic coma.
9. Alkyl halides. Physico-chemical properties of chloroform, carbon

tetrachloride, chloral hydrate. Application, toxic effect on the body. Basic patterns of behavior in the body. Features of isolation from corpse organs and biological fluids.

10. Phenol and its derivatives (picric acid, picramic acid). Toxicological value. Detection methods.
11. Tetraethyllead (TES).
12. Fujiwara's reaction in the detection of chlorine-containing compounds: chloroform, carbon tetrachloride, chloral hydrate. Write reaction schemes. Specify a specific color.
13. Preliminary test for chloral hydrate in urine. Write reaction schemes. Specify a specific color.
14. Chlorine cleavage reaction in the detection of chlorine-containing compounds: chloroform, carbon tetrachloride, chloral hydrate. Write reaction schemes. Specify a specific color.
15. Reaction with resorcinol in the detection of chlorine-containing compounds: chloroform, carbon tetrachloride, chloral hydrate. Write reaction schemes. Specify a specific color.
16. Reaction with Fehling's reagent in the detection of chlorine-containing compounds. What compounds are opened by this reaction? Write reaction schemes. Specify a specific color.
17. Polyhydric alcohols (ethylene glycol). Physico-chemical properties, application, toxic effect on the body. The main patterns of behavior in the body and corpse. Features of isolation from biological objects.
18. Aldehydes (formaldehyde, acetaldehyde), monoatomic phenols (phenol, cresols), acetone, acetic acid. Physico-chemical properties, application, mechanisms of toxic action on the body.
19. Features of isolation of monoatomic phenols and acetic acid from objects of analysis.
20. Chemical reactions for the detection of formaldehyde, phenol, acetone, acetic acid. Assessment of their sensitivity and specificity.
21. Methods of quantitative determination of formaldehyde, phenol, acetic acid, acetone.
22. Detection of formaldehyde and acetaldehyde by the microdiffusion method in blood and urine.

Tasks for independent processing of the topic:

Test tasks

Choose and justify the correct answer.

1. Name the "volatile" poison whose metabolite is methanoic (formic) acid:

A. methanol

B. acetaldehyde

C. phenol

D. acetone

2. Which of the "volatile" poisons gives a positive reaction with Tollens' reagent (the reaction of the formation of a "silver mirror")?

A. formaldehyde

B. acetic acid

C. phenol

D. chloroform

3. Specify a specific reaction for the qualitative detection of hydrocyanic acid:

A. formation of "benzidine blue"

B. reaction with picric acid

C. formation of ferrum rhodanide

D. formation of "Berlin blue"

4. Specify the phase I metabolite of phenol:

A. hydroquinone

B. nitrobenzene

C. benzoic acid

D. benzaldehyde

5. To carry out a targeted chemical and toxicological analysis of urine for the presence of methanol or ethanol, a preliminary test is performed. What reaction is performed?

A. iodoform test

B. "copper mirror" formation reaction

C. oxidation with potassium dichromate in sulfuric acid

D. formation of ethyl benzoate

6. What method is used to isolate "volatile" poisons?

A. steam distillation method

B. mineralization method

C. method of infusion

D. dialysis method

7. Which of these compounds belongs to the class of "volatile" poisons?

A. phenol

B. arsine

C. ekgonin

D. phenacetin

8. Hydrocyanic acid is driven off during distillation with steam. How should the distillate be collected?

A. collecting the distillate in a cooled receiver

B. collecting the distillate in a receiver with sodium hydroxide solution

C. collecting the distillate in a receiver with chloroform

D. collecting the distillate in a cooled receiver

9. When poisoned with this "volatile" poison, the victim's urine acquires an olive-black color. Name the "volatile" poison:

A. formaldehyde

B. acetone

C. hydrocyanic acid

D. phenol

10. Which of the following reagents are used to detect acetone in the distillate?

A. furfural

B. bromine water

C. lanthanum nitrate

D. Fehling's reagent

Enter in the cells ☐ the letters that indicate the correct answers to the test questions:

1-☐ 2-☐ 3-☐ 4-☐ 5-☐

Written assignments

Task 1. Figure 1 shows the scheme of chemical transformations. Explain the scheme. What transformations are taking place? Do these chemical reactions belong to qualitative detection reactions?

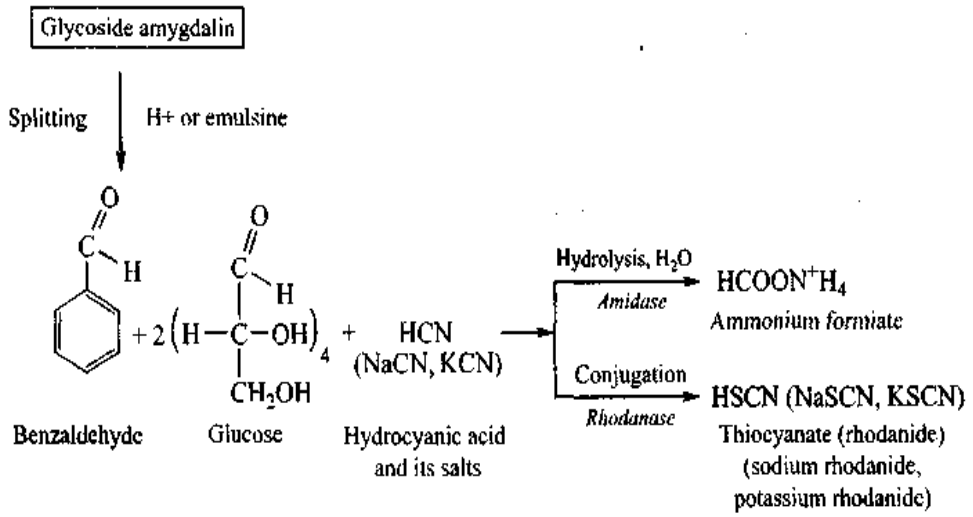

Figure 1.

The answer and its justification

Task 2. Figure 2 shows the scheme of chemical transformations. Explain the scheme. What transformations are taking place? Do these chemical reactions belong to qualitative detection reactions?

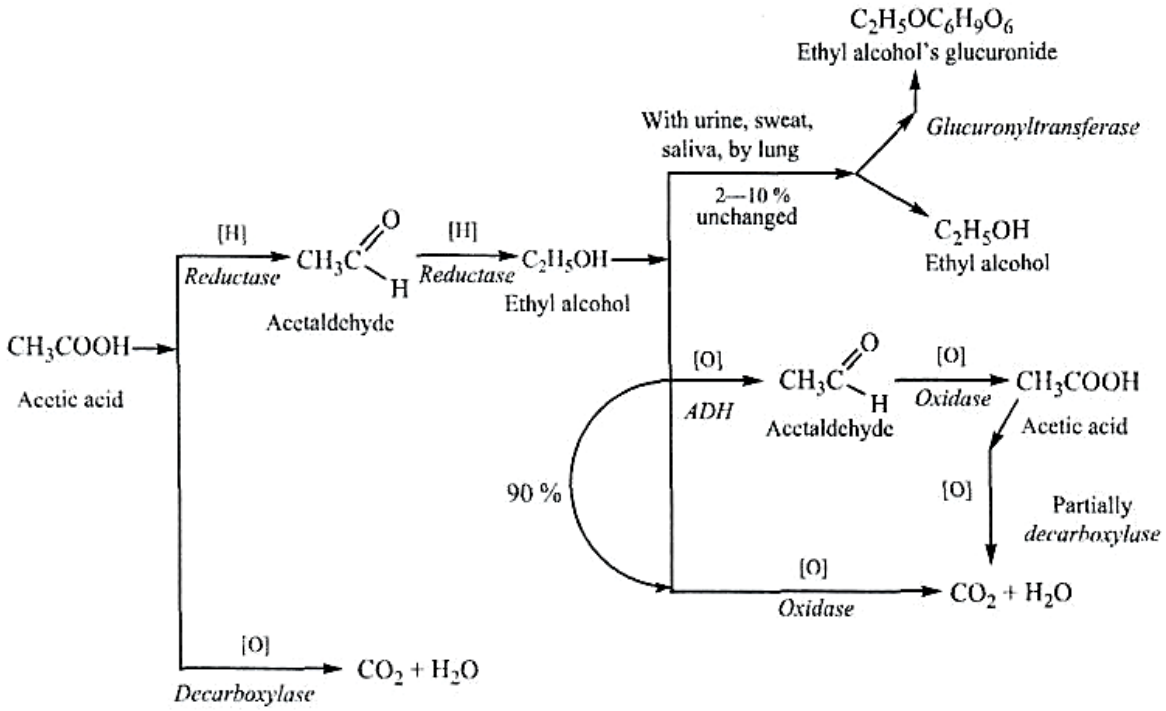

Figure 2.

The answer and its justification

Auditory collective work:

Task 1. Formaldehyde is detected in distillate No. 2. Perform reactions with chromotropic acid, with methyl violet, with Fehling's reagent. Write the schemes of the indicated reactions. What is observed with a positive reaction result: color, sediment, specific smell?

The answer and its justification

Task 2. Figure 3 shows the schemes of qualitative detection reactions in ethanol distillate. Describe the reactions. Enter their name. Which of the indicated reactions is the most sensitive?

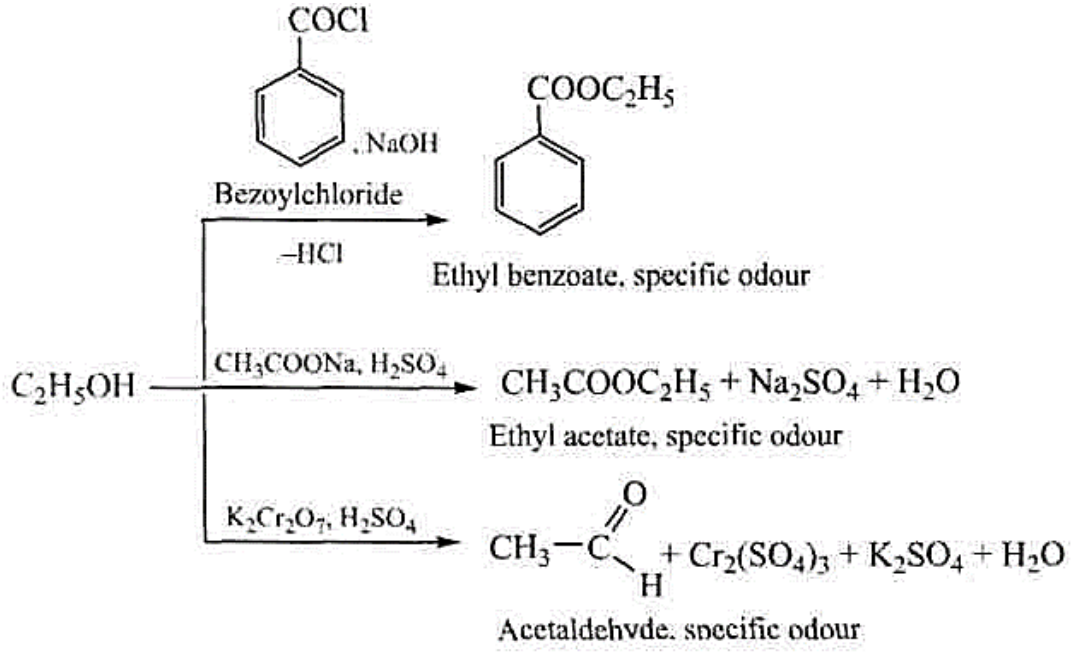

Figure 3.

The answer and its justification

Task 3. Acetic acid is detected in distillate No. 3. Perform reactions with ferrum (III) chloride, lanthanum with nitrate and iodine, formation of indigo. Write the schemes of the indicated reactions. What is observed with a positive reaction result: color, sediment, specific smell?

The answer and its justification

Task 4. Figure 4 shows the reaction schemes. Describe these reactions. What reagents are used in reactions and for what purpose are they carried out?

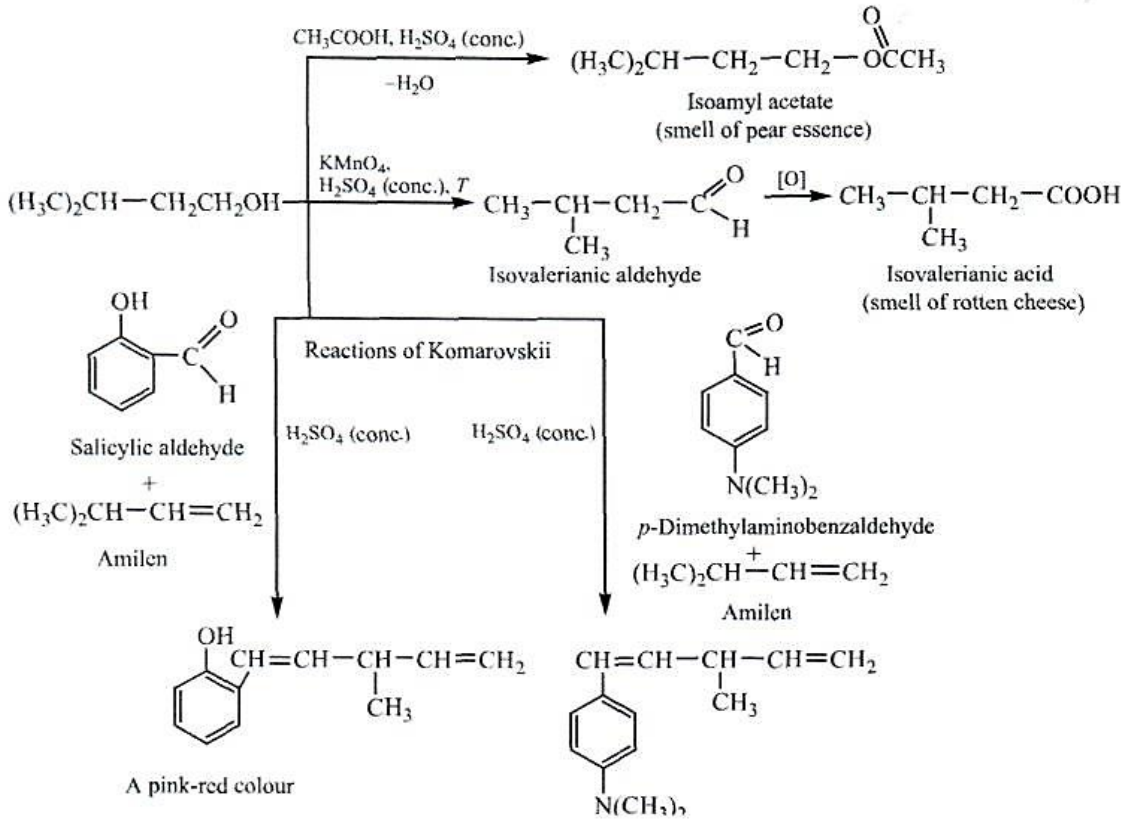

Figure 4.

The answer and its justification

Auditory independent work (supervised by the teacher):

Task 1. Figure 5 shows the scheme of the metabolism of ethyl alcohol. Methyl alcohol undergoes similar metabolic transformations. Write a diagram of the metabolic transformations of methyl alcohol.

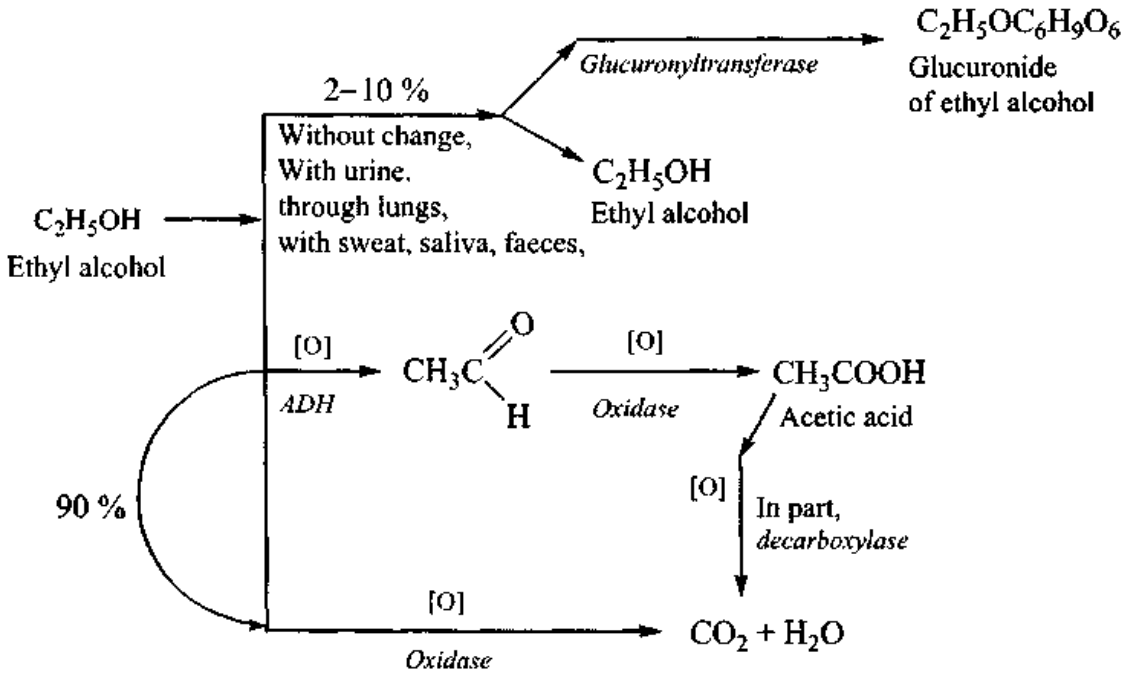

Figure 5.

The answer and its justification

Task 2. Figure 6 shows the reaction schemes for the qualitative detection of alkyl halides. These reactions are not used to detect which alkyl halides?

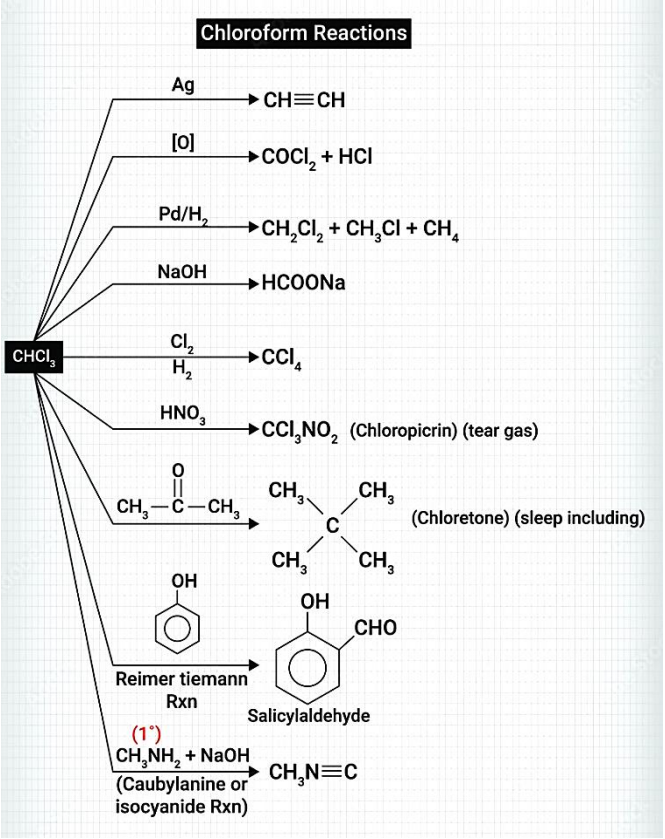

Figure 6.

An example of a task with an answer standard:

The method of distillation (distillation) with water vapor is a method of isolating "volatile" poisons.

Answer standard

Reagents for distillation: 10% solution of oxalic acid - for acidification of the contents of the distillation flask before distillation, 5% solution of sodium hydroxide - for subsequent distillation from alkalized biological objects; 2% sodium hydroxide solution – for collecting the first distillate fraction from an acidified medium (hydrocyanic acid); 0.1% solution of hydrochloric acid - for collecting fractions from an alkaline environment.

Scheme of the device for distillation with water vapor: 1 – steam generator, 2 – distillation flask, 3 – Liebig refrigerator, 4 – alonge, 5 – receiving flask (Fig. 7):

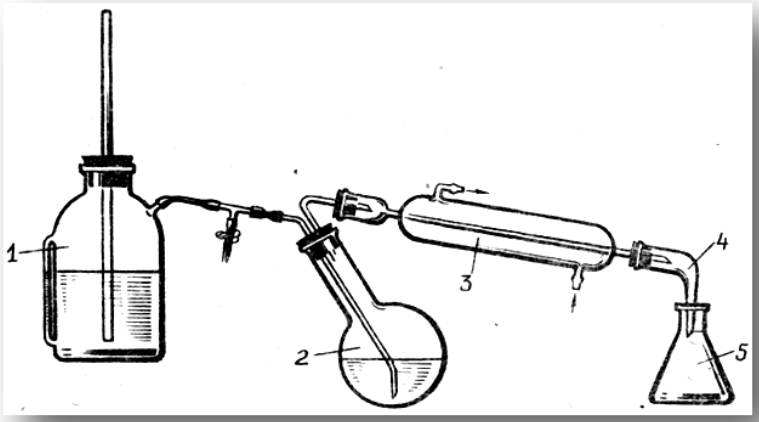

Figure 7.

Water is poured into the steam generator and heated to boiling. 20-100 g of crushed biological material is added to a distillation flask and mixed with water. The volume of the mixture should be no more than 1/3 of the volume of the flask, acidify the mixture with a 10% solution of tartaric or oxalic acid to pH 2-3. The distillation procedure is carried out. The first fraction of the distillate (3 ml) is collected in a receiver with 2 ml of 5% sodium hydroxide solution for precipitation of hydrocyanic acid. Clean receiving flasks are used to collect the following fractions of 25 ml each.

Qualitative reactions for the detection of phenol.

Answer standard

Phenol and its derivatives are detected in distillate No. 3: reaction with bromine water: in the presence of phenol in the solution, a yellowish-white precipitate of tribromophenol is formed; the reaction is given by cresols, aniline, some other aromatic amines; reaction with ferrum (III) chloride: in the presence of phenol, a purple or blue-violet color appears, which disappears when water, alcohol, and acids are added; the reaction is given by cresols, oxypyridines, oxyquinoline, substances with hydroxy groups; the formation of indophenol: the appearance of a dirty purple color indicates the presence of phenol in the sample; Lieberman's reaction (fig.8):

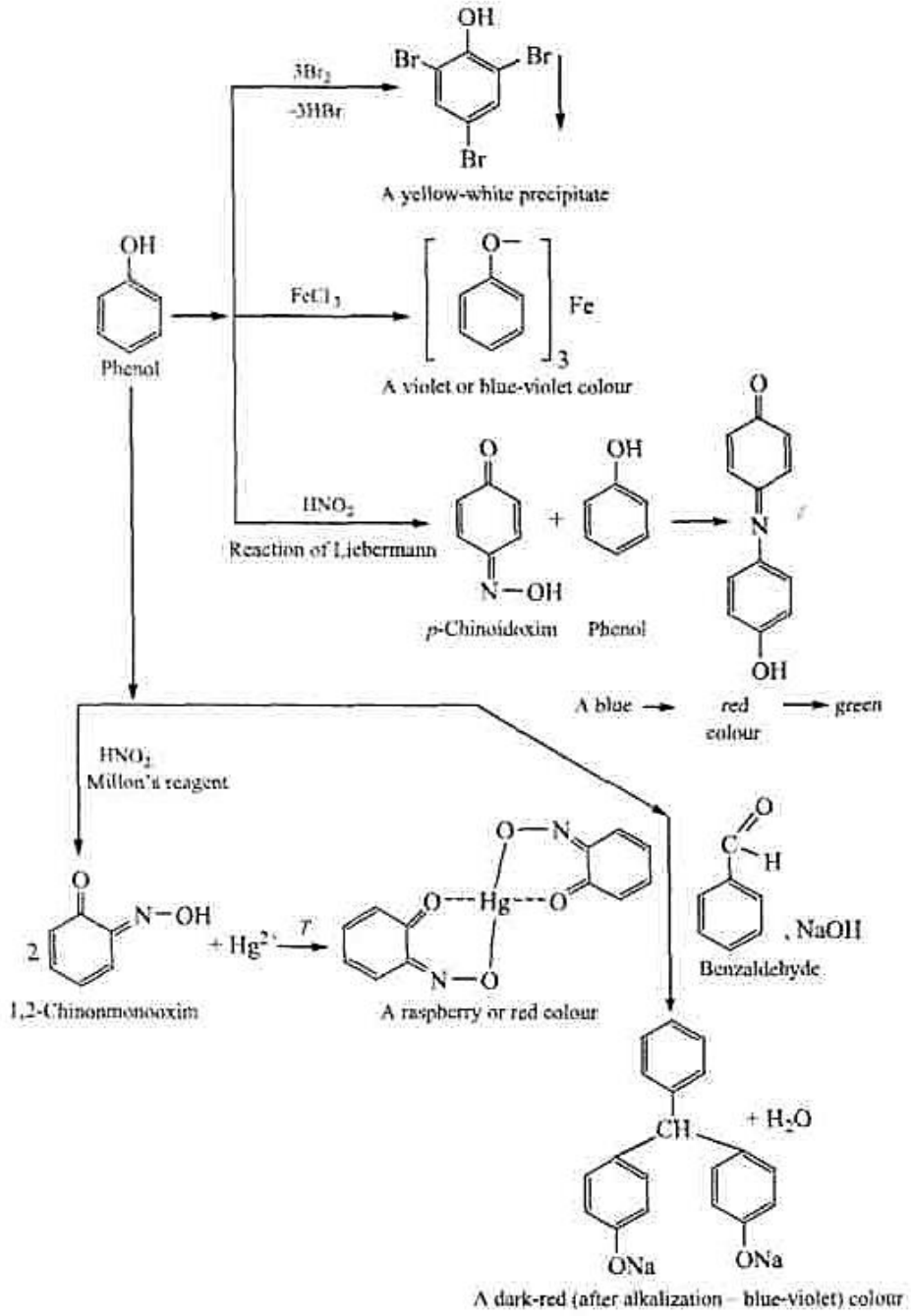

Figure 8.

Control work No. 1 - on questions of topics 1-3.

List of questions for control work No. 1.

1. Procedure and documentation of forensic toxicological (chemical-toxicological) examinations.

2. Preliminary tests (screening studies) in chemical-toxicological analysis and their role in drawing up a plan of chemical-toxicological analysis.

3. Definition of the terms "poisoning" and "poison".

4. General principles of classification of poisons: according to chemical structure, purpose of use (production purpose), degree of toxicity (hygienic), type of toxic effect (toxicological), selective toxicity, according to the method of isolation from objects of biological origin.

5. Classification of poisoning by the cause of occurrence (accidental, intentional), by the conditions (place) of development (domestic, industrial, medical). Division of intentional poisoning into criminal and suicidal. Classification of poisoning according to the clinical principle (acute, chronic, subacute poisoning); by ways of penetration into the body; nosological classification.

6. Metabolism (biotransformation) of poisons in the human body. I and II phases of metabolism.

7. Lethal synthesis.

8. Objects of chemical and toxicological research, their characteristics, preservation methods.

9. Rules for selection, transportation, acceptance of biological material for forensic chemical examination. Sample storage procedure.

10. Peculiarities of analysis of certain types of biological material depending on their nature, state, chemical properties of poisonous substances.

11. General principles of interpretation of forensic chemical research results.

12. General characteristics of the methods used to detect and quantify poisons in chemical-toxicological analysis (chemical, physical-chemical, biochemical, pharmacological). Their comparative characteristics (sensitivity, specificity).

13. Mineral acids: sulfuric (sulphate) acid. Detection, isolation and metabolism.

14. Mineral acids: nitric (nitric) acid. Detection, isolation and metabolism.

15. Mineral acids: hydrochloric (chloric) acid. Detection, isolation and metabolism.

16. Alkalis: sodium hydroxide (caustic soda). Detection, isolation and metabolism.

17. Alkalis: potassium hydroxide. Detection, isolation and metabolism.

18. Alkalis and ammonia (ammonia): ammonium hydroxide, ammonia (ammonia). Detection, isolation and metabolism.

19. Alkali metal salts: nitrites. Detection, isolation and metabolism.

20. Salts of alkali metals: nitrates. Detection, isolation and metabolism.

21. A group of substances isolated by distillation ("volatile" poisons). General characteristics of the group. Physico-chemical properties, structure and effect on the body.

22. Methods of isolating "volatile" poisons from biological material, food products and environmental objects: steam distillation.

23. Methods of distillate analysis: chemical and gas-liquid chromatography (GC).

24. Types of chemical reactions used in the analysis, assessment of their sensitivity and specificity.

25. Preparation of biological material for steam distillation. Selection of methods and conditions of distillation.

26. Schematic diagram of the study of biological material for "volatile" poisons during general and targeted analysis using a combination of methods.

27. Individual representatives of the group of "volatile" poisons: hydrocyanic acid, aliphatic monoatomic alcohols (C1-C5), ethylene glycol, alkyl halides (chloroform, chloral hydrate, carbon tetrachloride, 1,2-dichloroethane), aldehydes (formaldehyde, acetaldehyde), acetone, phenol , cresols, acetic acid.

28. Hydrocyanic acid and its derivatives. Physico-chemical properties, application, toxic effect on the body. The main patterns of behavior in the body and corpse. Antidotes. Features of isolation from corpse organs and biological fluids, detection reactions and methods of quantitative determination. Assessment of their sensitivity and specificity. Assessment of forensic chemical analysis results.

29. Aliphatic monoatomic alcohols (C1-C5). Physico-chemical properties, applications, mechanisms of toxic action on the body. The main patterns of behavior in the body and corpse. Features of isolation. Chemical reactions to alcohols. Evaluation of their sensitivity and specificity. Detection of alcohols in urine, blood, distillates by GC method.

30. Formation of ethanol in the body during diseases. The value of the relative ratio of ethanol in urine and blood for the diagnosis of alcoholic coma. First aid for alcohol poisoning and means of detoxification of the body.

31. Polyhydric alcohols (ethylene glycol). Physico-chemical properties, application, toxic effect on the body. The main patterns of behavior in the body and corpse. Features of isolation from biological objects.

32. Alkyl halides. Physico-chemical properties of chloroform, carbon tetrachloride, 1,2-dichloroethane, chloral hydrate. Application, toxic effect on the body. Basic patterns of behavior in the body. Features of isolation from corpse organs and biological fluids. Chemical reactions for detection of alkyl halides, evaluation of their sensitivity and specificity.

33. Aldehydes (formaldehyde, acetaldehyde), monoatomic phenols (phenol, cresols), acetone, acetic acid. Physico-chemical properties, applications, mechanisms of toxic action on the body.

34. Features of isolation of monoatomic phenols and acetic acid from objects of analysis.

35. Chemical reactions for the detection of formaldehyde, phenol, acetone, acetic acid. Evaluation of their sensitivity and specificity.

36. Methods of quantitative determination of formaldehyde, phenol, acetic acid, acetone.

37. Detection of formaldehyde and acetaldehyde by the microdiffusion method in blood and urine.

The methodical development was made by: professor of the department, doctor of pharm. sc. Welchinska O.V.

Topic N 4. Toxicological characteristic of the group of substances isolated from biological material by mineralization («metallic» poisons). Denitration. Examination of the compound of Barium, Lead, Manganese, Chromium, Silver, Copper and Zinc.

Purpose: the ability to operate with the basic concepts of the topic and to implement the main stages of chemical-toxicological analysis of poisonous substances that are isolated from biological material by mineralization ("metallic" poisons): compounds of Barium, Lead, Manganese, Chromium, Argentum, Cuprum and Zinc.

The student must:

 to know the basic concepts, strategy and tactics of chemical and toxicological analysis of a group of poisonous substances that are isolated from biological material by mineralization ("metallic" poisons);

 be able to propose a forensic toxicological research plan;

 know the methods of isolating poisonous substances that are isolated from biological material from biological material by mineralization ("metallic" poisons);

 evaluate the results of organoleptic control of minerals, preliminary tests;

 know methods of analysis of poisonous substances that are isolated from biological material by mineralization ("metallic" poisons);

 interpret the results of the analysis.

Basic concepts of the topic:

Term, parameter, characteristic	*Definition*
Mineralization	oxidation (burning) of organic matter, which is the object of research, with the aim of destroying complexes of metals with proteins, after which the "metallic" poisons pass into the solution in an ionic state
Denitration	the process of freeing the mineral from nitric, nitrite, nitrosyl sulfate acids and nitrogen oxides, as they are oxidizers that prevent the further detection of "metallic" poisons
Ion masking	the process of eliminating the influence of extraneous ions contained in a complex mixture on the detection of the studied ions
Unmasking of ions	the process of releasing previously masked ions from masking reagents
Toxic compounds of	hydroxide, carbonate, chloride, nitrate and chlorate

Barium	
Toxic compounds of Lead	arsenate, chromate, acetate, carbonate, chloride, nitrate, as well as an organometallic compound — tetraethyl lead (TEL)
Toxic compounds of Manganese	oxide, potassium permanganate, salts: phosphide, sulfate, di- and trihalides, nitrate, nitride, carbide, silicide and salts of manganese acid
Toxic compounds of Chromium	chromates and dichromates
Toxic compounds of Silver	nitrate (lapis), kolargol, protargol, argyrol; preparations for photography; hair dyes: silver nitrate and ammonia solution of argentum chloride; silver in the form of dust in places where silver ore is processed
Toxic compounds of Cuprum	Copper compounds combined with Arsenic compounds (Paris or Schweinfurt green Cu(CH3COO)2•3Cu(AsO2)2), salts: sulfate, citrate, carbonate, acetate; oxide
Toxic compounds of Zinc	metallic Zinc (dishes), dust

Recommended literature:

Basic

1.Welchinska E.V. Toxicological and forensic chemistry (Criminal analysis). Poisonous substances and their biotransformation: textbook / E.V. Welchinska. — K.: PE Lopatina O.O., ISBN 978-617-7533-02-2, 2017. — p. 85-122. http://ir.librarynmu.com/handle/123456789/9123

2.Materials of Lecturers. The department of medicinal chemistry and toxicology of pharmaceutical faculty of Bogomolets NMU. https://www.youtube.com/@user-yj2fn5mz3x/

Auxiliary

1.Prohaska, Thomas; Irrgeher, Johanna; Benefield, Jacqueline; Böhlke, John K.; Chesson, Lesley A.; Coplen, Tyler B.; Ding, Tiping; Dunn, Philip J. H.; Gröning, Manfred; Holden, Norman E.; Meijer, Harro A. J. (4 May 2022). "Standard atomic weights of the elements 2021 (IUPAC Technical Report)". Pure and Applied Chemistry. doi:10.1515/pac-2019-0603. ISSN 1365-3075.

2."IIT Kharagpur Study Finds 20% of India Has High Arsenic Levels in Groundwater". The Wire. PTI. 11 February 2021. Retrieved 23 May 2023.

Informational resources

European Pharmacopoeia online - pheur.edqm.eu

The British Pharmacopoeia 2021 - www.pharmacopoeia.com

The British Pharmacopoeia 2020. London.2020: I-1298. www.webofpharma.com

Pharmacopoea USP. www.usp.org.

Website of the Department of Medicinal Chemistry and Toxicology of O.O. Bogomolets

http://nmu.ua/zagalni-vidomosti/kafedri/kafedra-farmatsevtycheskoj-byologycheskoj-y-toksykologycheskoj-hymyy/

Distance learning platform LIKAR_NMU

https://likar.nmu.kiev.ua/

Official website of the Ministry of Health of Ukraine

https://moz.gov.ua/

International Journal of Medical Toxicology and Forensic Medicine **(IJMTFM).** https://journals.sbmu.ac.ir/ijmtfm

Journal of Synthetic Organic Chemistry, Japan. http://www.ssocj.jp/indexenglish.

Journal of Organic Chemistry, USA. https://doi.org/10.1021/acs.joc.0c02255.

Synthetic Communications. Great Britain. http://www.tandfonline.com/page/terms-and-conditions
pubmed.ncbi.nlm.nih.gov

www.cochrane.org

Questions for theoretical study:

1. General characteristics of the group (compounds of barium, lead, manganese, chromium, argentum, copper, cadmium, stibium, arsenic, bismuth, zinc, thallium, and mercury). Field of application, toxicological significance. Qualitative detection and quantitative determination of "metallic" poisons.

2. Characteristics of modern general and separate methods of mineralization. The choice of the mineralization method depends on the nature of the object and the studied "metallic" poison.

3. Denitration of mineralizate and its preparation for research.

4. Fractional research method. Theoretical provisions. Selection of research objects.

5. Scheme of the fractional method of analysis (according to O.M. Krylova).

6. Characteristics of reagents used in the fractional method for masking interfering

ions, isolation and analysis of "metallic" poisons.

7. General characteristics of methods of quantitative determination of "metallic" poisons in fractional analysis. The choice of method depends on the content of the poison. Possible errors during the analysis.

8. Lead compounds (plumbum). Toxicological significance, methods of qualitative and quantitative analysis in biological material.

9. Barium compounds. Toxicological significance, methods of qualitative and quantitative analysis in biological material.

10. Manganese (manganese) compounds. Toxicological significance, methods of qualitative and quantitative analysis in biological material.

11. Copper (copper) compounds. Toxicological significance, methods of qualitative and quantitative analysis in biological material.

12. Compounds of silver (argentum). Toxicological significance, methods of qualitative and quantitative analysis in biological material.

13. Chromium compounds. Toxicological significance, methods of qualitative and quantitative analysis in biological material.

14. Zinc compounds. Toxicological significance, methods of qualitative and quantitative analysis in biological material.

Tasks for independent processing of the topic:

Test tasks

Choose and justify the correct answer.

1. Mineralization of biological material is carried out in several stages. What is the name of the first stage of mineralization?

A. destruction

B. ashing

C. denitration

D. oxidation

2. What is the name of the method of isolating "metallic" poisons?

A. mineralization

B. extraction

C. distillation

D. dialysis

3. During mineralization, a white precipitate forms in the mineralization. The white sediment indicates the presence of which "metallic" poison?

A. Thallium compounds

B. Zinc compounds

C. compounds of Argentum

D. Lead compounds

4. Which of the Barium compounds is not toxic to the human body?

A. Barium sulfate

B. Barium hydroxide

C. Barium chloride

D. Barium nitrate

5. The mineralization contains a precipitate of barium sulfate and lead sulfate. You can separate these salts using:

A. solution of ammonium acetate

B. sodium hydroxide solution

C. nitric acid solution

D. ethyl alcohol solution

Enter in the cells ☐ the letters that indicate the correct answers to the test questions:

1-☐ 2-☐ 3-☐ 4-☐ 5-☐

Written assignments

Task 1. Figure 1 shows the scheme of chemical transformations. Explain the scheme. What transformations are taking place? Do these chemical reactions belong to qualitative detection reactions?

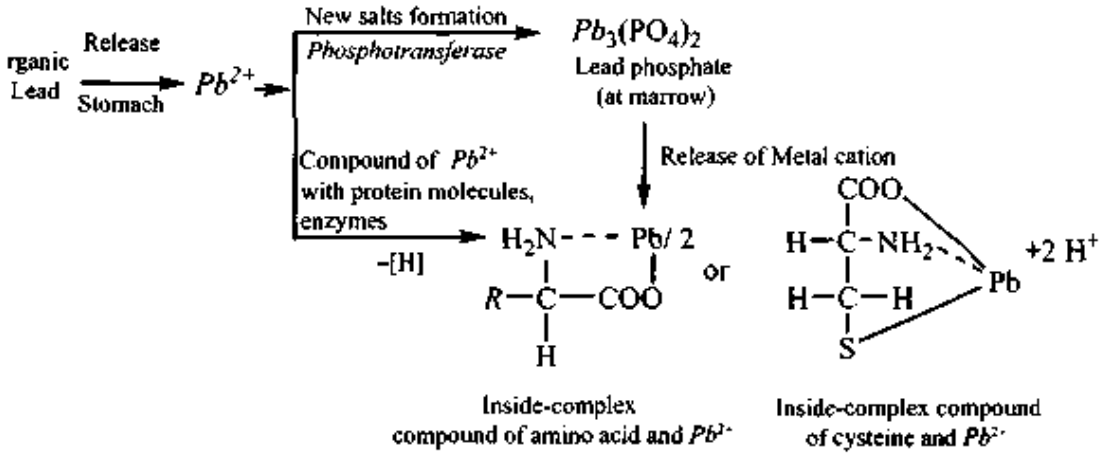

Figure 1.

The answer and its justification

Auditory collective work:

Task 1. Barium cations are detected in the filtrate. Perform reactions with sodium rhodizonate, with potassium permanganate, with potassium dichromate. Write the schemes of the indicated reactions. What is observed with a positive reaction result?

The answer and its justification

Task 2. Figure 2 shows schemes of qualitative reactions for the detection of Manganese cations. Describe the reactions. Which of the reactions are specific?

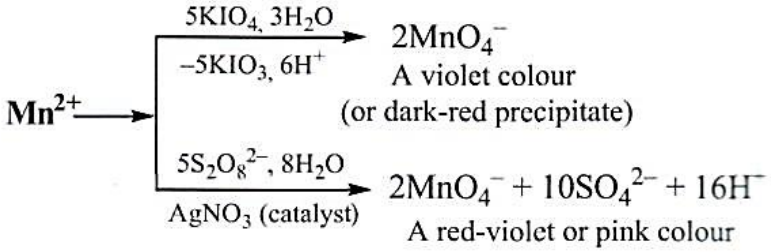

Figure 2.

The answer and its justification

Auditory independent work (supervised by the teacher):

Task 1. Figure 3 shows schemes of qualitative reactions for the detection of Copper cations. Describe the reactions. Which of the reactions are specific, sensitive and confirmatory? Which of the reactions refers to the previous reaction?

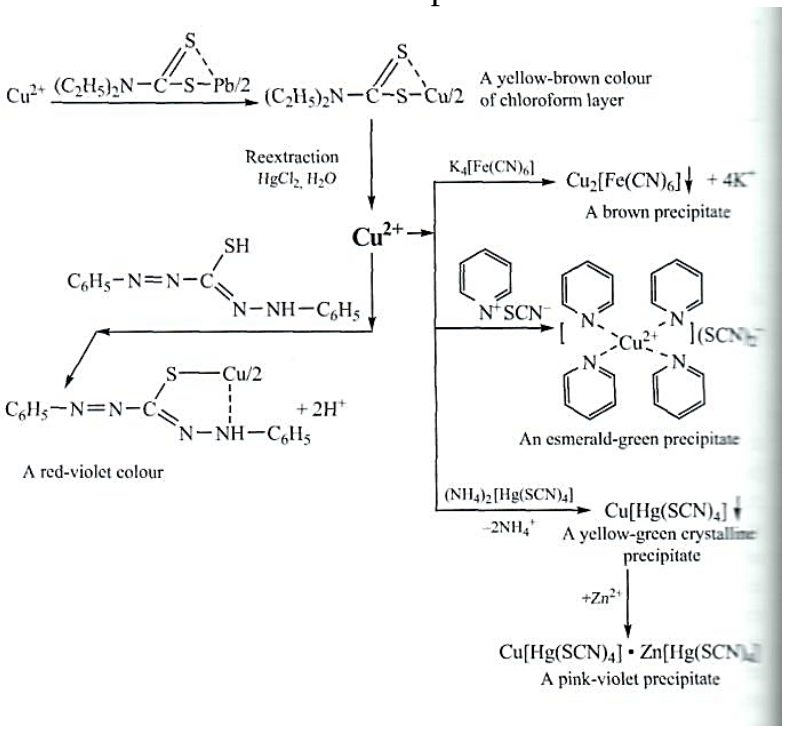

Figure 3.

An example of a task with an answer standard:

Research of the sediment of mineralizate.

Answer standard

Denitrated mineralizate is a transparent substance with a white precipitate, which is separated from the liquid phase by filtration and washed with a 5% solution of sulfuric acid. The resulting sediment is used to study it for the presence of lead, barium and strontium. The liquid phase of the mineral is examined for the presence of all other cations. Detection of cations in the liquid phase of the mineralization begins with the performance of preliminary tests, the results of which make it possible to significantly shorten the analysis time and reduce reagent costs. The study of barium and lead cations begins with the separation of the precipitate of their sulfates (Fig. 4).

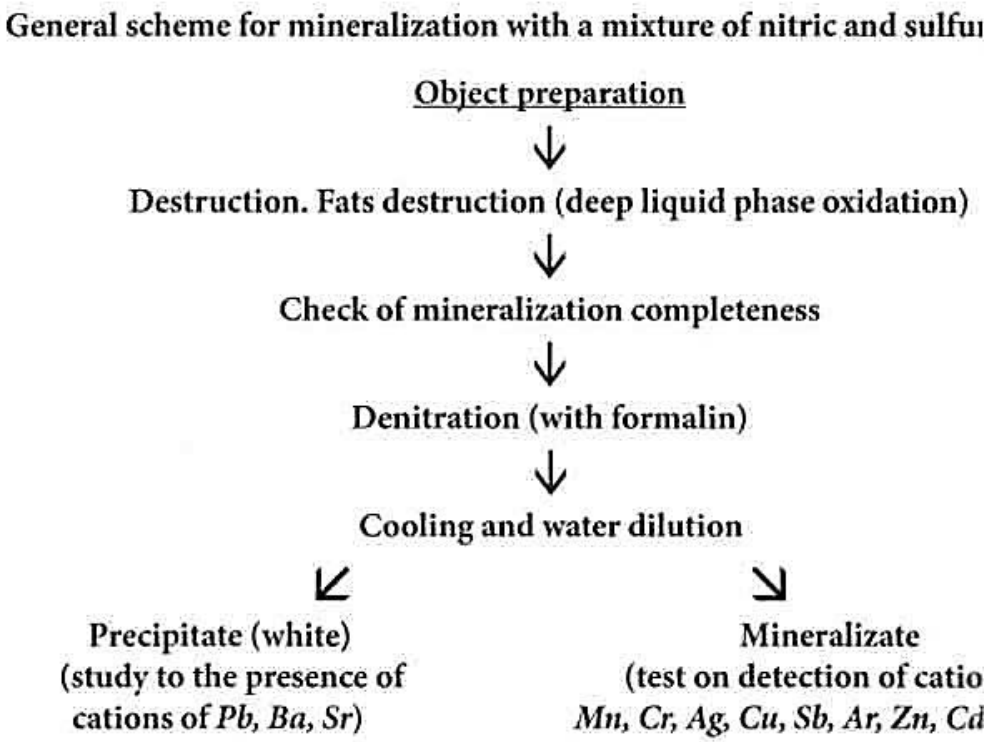

Figure 4.

After separation of barium and lead cations, their analysis is carried out in the filtrate (Lead cations) and in the sediment (Barium cations).

The methodical development was made by: professor of the department, doctor of pharm. sc. Welchinska O.V.

Topic N 5. Research of the liquid part of the mineralizate for the presence and content of Cadmium, Thallium, Bismuth, Antimony and Arsenic. Isolation of Mercury from biological material and its study in the destructate. Control work № 2.

Purpose: the ability to operate with the basic concepts of the topic and to implement the main stages of chemical and toxicological analysis of poisonous substances that are isolated from biological material by mineralization ("metallic" poisons): Cadmium, Thallium, Bismuth, Stybium, Arsenic, Mercury compounds.

The student must:

- ✓ to know the basic concepts, strategy and tactics of chemical and toxicological analysis of a group of poisonous substances that are isolated from biological material by mineralization ("metallic" poisons);
- ✓ be able to propose a forensic toxicological research plan;
- ✓ know the methods of isolating poisonous substances that are isolated from biological material from biological material by mineralization ("metallic" poisons);
- ✓ evaluate the results of organoleptic control of minerals, preliminary tests;
- ✓ know methods of analysis of poisonous substances that are isolated from biological material by mineralization ("metallic" poisons);
- ✓ interpret the results of the analysis.

Basic concepts of the topic:

Term, parameter, characteristic	*Definition*
Mineralization	oxidation (burning) of organic matter, which is the object of research, with the aim of destroying complexes of metals with proteins, after which the "metallic" poisons pass into the solution in an ionic state
Denitration	the process of freeing the mineral from nitric, nitrite, nitrosyl sulfate acids and nitrogen oxides, as they are oxidizers that prevent the further detection of "metallic" poisons
Ion masking	the process of eliminating the influence of extraneous ions contained in a complex mixture on the detection of the studied ions
Unmasking of ions	the process of releasing previously masked ions from masking reagents
Toxic compounds of Cadmium	arsenite, phosphide, carbonate, sulfide, sulfate, chloride, bromide, iodide, nitrate, acetate
Toxic compounds of	oxide, halides, sulfate, acetate, hydroxide

Thallium	
Toxic compounds of Bicmuth	potassium bismuthate, bismuth oxide, sulfate, sulfide, basic nitrate, salicylate
Toxic compounds of Antimony	stibiopotassium salt of tartaric acid, or "vomit stone" — [(SbO)•KC4H4O6], stibium-sodium tartrate; chemotherapeutic drugs based on Stibium organic compounds; stibium oxalate and lactate
Toxic compounds of Arsenic	"white arsenic" (arsenic acid anhydride As2O3), arsenites, arsenates, arsenic (III) chloride, arsine (AsH3), combat poisons (lewisite, adamsite)
Toxic compounds of Mercury	metallic Mercury, its vapor, organomercury pesticides, inorganic salts of Mercury; mercury monochloride (HgCl, calomel), dichloride (HgCl2, sulema), oxycyanide, amino chloride and oxide are used in medicine

Recommended literature:

Basic

1. Welchinska E.V. Toxicological and forensic chemistry (Criminal analysis). Poisonous substances and their biotransformation: textbook / E.V. Welchinska. — K.: PE Lopatina O.O., ISBN 978-617-7533-02-2, 2017. — p. 85-122. http://ir.librarynmu.com/handle/123456789/9123

2.Materials of Lecturers. The department of medicinal chemistry and toxicology of pharmaceutical faculty of Bogomolets NMU. https://www.youtube.com/@user-yj2fn5mz3x/

Auxiliary

1. Prohaska, Thomas; Irrgeher, Johanna; Benefield, Jacqueline; Böhlke, John K.; Chesson, Lesley A.; Coplen, Tyler B.; Ding, Tiping; Dunn, Philip J. H.; Gröning, Manfred; Holden, Norman E.; Meijer, Harro A. J. (4 May 2022). "Standard atomic weights of the elements 2021 (IUPAC Technical Report)". *Pure and Applied Chemistry*. doi:10.1515/pac-2019-0603. ISSN 1365-3075.

2. Henry Arnaud, Celia (April 26, 2022). "Structure of Pepto-Bismol active ingredient solved". *Chemical & Engineering News*. 100 (44): 34–35. doi:10.1021/cen-10044-cover6. ISSN 0009-2347. S2CID 254899845. Retrieved 15 April 2023.

Information resources

European Pharmacopoeia online - pheur.edqm.eu

The British Pharmacopoeia 2021 - www.pharmacopoeia.com

The British Pharmacopoeia 2020. London.2020: I-1298. www.webofpharma.com

Pharmacopoea USP. www.usp.org.

Website of the Department of Medicinal Chemistry and Toxicology of O.O. Bogomolets

http://nmu.ua/zagalni-vidomosti/kafedri/kafedra-farmatsevtycheskoj-byologycheskoj-y-toksykologycheskoj-hymyy/

Distance learning platform LIKAR_NMU

https://likar.nmu.kiev.ua/

Official website of the Ministry of Health of Ukraine

https://moz.gov.ua/

International Journal of Medical Toxicology and Forensic Medicine **(IJMTFM).** https://journals.sbmu.ac.ir/ijmtfm

Journal of Synthetic Organic Chemistry, Japan. http://www.ssocj.jp/indexenglish.

Journal of Organic Chemistry, USA. https://doi.org/10.1021/acs.joc.0c02255.

Synthetic Communications. Great Britain. http://www.tandfonline.com/page/terms-and-conditions
pubmed.ncbi.nlm.nih.gov

www.cochrane.org

Questions for theoretical study:

1. General characteristics of the group (compounds of Barium, Lead, Manganese, Chromium, Argentum, Copper, Cadmium, Stibium, Arsenic, Bismuth, Zinc, Thallium, and Mercury). Field of application, toxicological significance. Qualitative detection and quantitative determination of "metallic" poisons.

2. Characteristics of modern general and separate methods of mineralization. The choice of the mineralization method depends on the nature of the object and the studied "metallic" poison.

3. Denitration of mineralizate and its preparation for research.

4. Bismuth compounds. Toxicological significance, methods of qualitative and quantitative analysis in biological material.

5. Cadmium compounds. Toxicological significance, methods of qualitative and quantitative analysis in biological material.

6. Arsenic compounds. Toxicological significance, methods of qualitative and quantitative analysis in biological material.

7. Stibium compounds. Toxicological significance, methods of qualitative and quantitative analysis in biological material.

8. Compounds of Thallium. Toxicological significance, methods of qualitative and quantitative analysis in biological material.

9. A group of substances that are isolated from biological material by mineralization ("metallic" poisons). General characteristics of the group: compounds of Cadmium, Stibium, Arsenic. Scheme of metabolism.

10. Destructive mineralization of biological material.
11. Denitration of mineralizate when isolating mercury compounds.
12. Compounds of Mercury. Toxicological significance, methods of qualitative and quantitative analysis in biological material.

Tasks for independent processing of the topic:

Test tasks

Choose and justify the correct answer.

1. Which of the reactions for the detection of Bismuth ions in the mineral is a preliminary reaction?

A. with thiourea

B. with sodium diethyldithiocarbamate

C. with brucine and potassium bromide

D. with cesium chloride and potassium iodide

2. In the case of targeted analysis of Arsenic compounds, a preliminary test is first conducted. What is her name?

A. Sanger-Black test

B. Marsh test

C. reaction with dithizone

D. reaction with diethyldithiocarbamate

3. What reagent must be used to check the completeness of denitration?

A. diphenylamine

B. formaldehyde

C. urea

D. glycerin

4. Arsenic satellite compound is often present in biological material. What is her name?

A. Barium

B. Thalium

C. Bismuth

D. Antimony

5. When carrying out the Marsh test to detect arsenic, an "arsenic mirror" is formed. What color is the "arsenic mirror"?

A. black

B. yellow

C. silver

D. brownish gray

6. What type of reaction is the reaction with dithizone for the detection of mercury cations?

A. previous, non-specific

B. specific

C. confirming

D. insensitive

7. Which of the reagents is used for qualitative detection of Mercury cations?

A. iodine suspension

B. suspension of cuprum iodine (II)

C. suspension of barium iodine (I)

D. copper iodine suspension (I)

8. What color is formed in the reaction with dithizone during the qualitative detection of mercury cations?

A. orange-yellow

B. purple

C. red

D. blue

9. What reagent is used in the denitration of a mineral that contains mercury cations?

A. formalin

B. formaldehyde

C. methanol

D. urea

10. What is the name of the method of isolating mercury compounds from biological material?

A. destructive mineralization

B. mineralization

C. distillation

D. dialysis

Enter in the cells ☐ the letters that indicate the correct answers to the test questions:

1-☐ 2-☐ 3-☐ 4-☐ 5-☐

Written assignments

Task 1. Figure 1 shows the scheme of chemical transformations. Explain the scheme. What transformations are taking place? Do these chemical reactions belong to qualitative detection reactions?

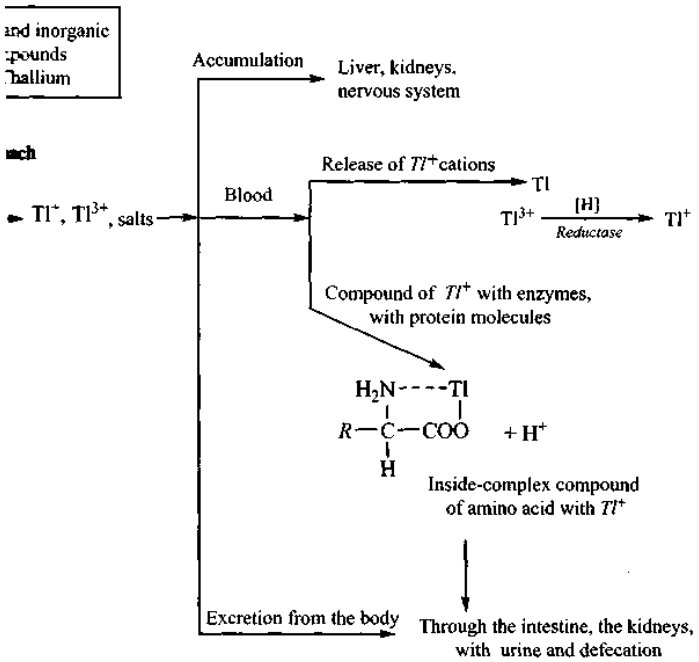

Figure 1.

The answer and its justification

Task 2. Figure 2 shows the scheme of chemical transformations. Explain the scheme. What transformations are taking place? Do these chemical reactions belong to qualitative detection reactions?

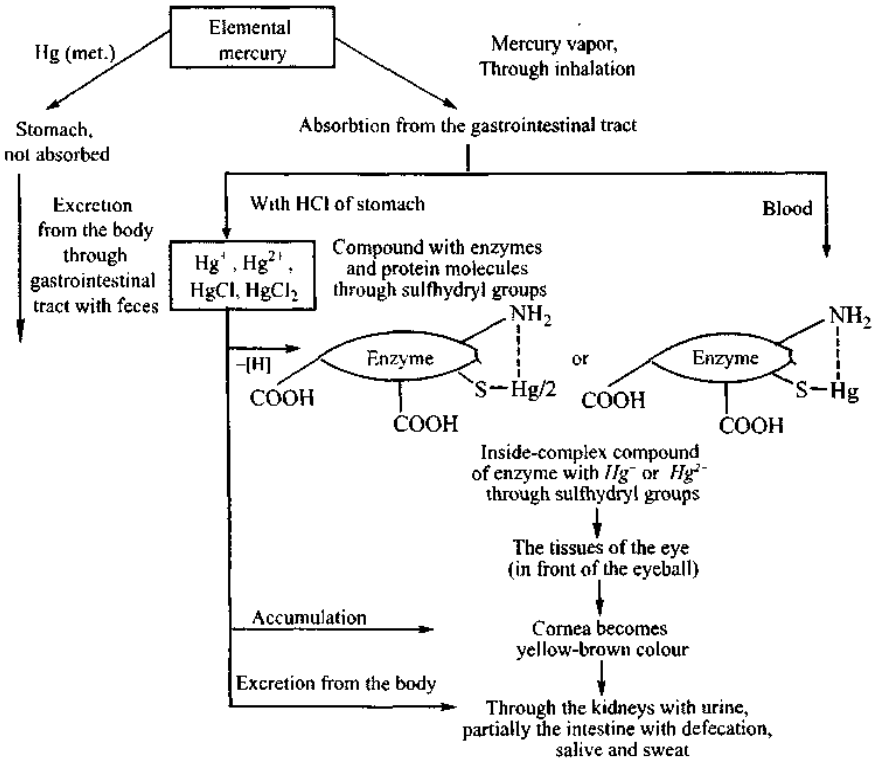

Figure 2.

The answer and its justification

Auditory collective work:

Task 1. Antimony cations are detected in the filtrate. Perform reactions with malachite green, with sodium thiosulfate. Write the schemes of the indicated reactions. What is observed with a positive reaction result?

The answer and its justification

Task 2. Figure 3 shows schemes of qualitative reactions for the detection of Thallium cations. Describe the reactions. Which of the reactions are specific?

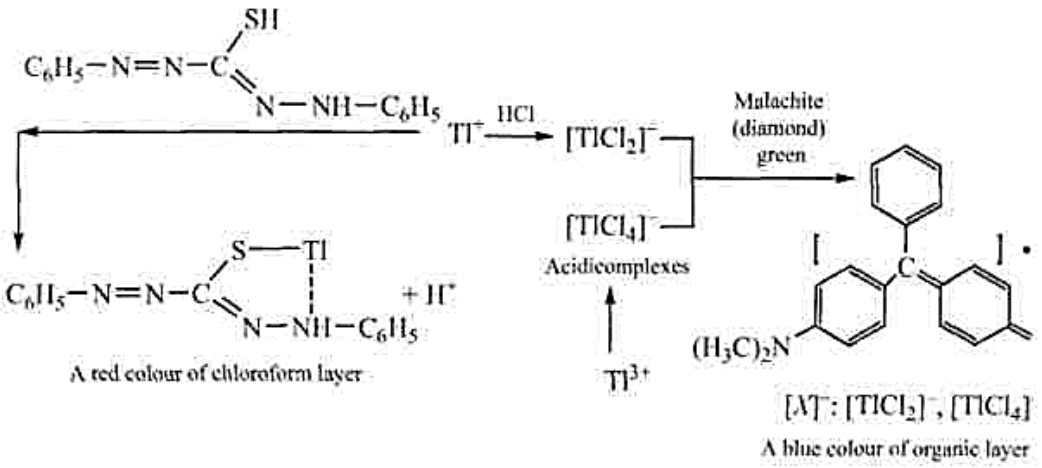

Figure 3.

The answer and its justification

Task 3. Mercury cations are detected in the filtrate. Perform a preliminary reaction with dithizone. Write the reaction scheme. What is observed with a positive result of the reaction?

The answer and its justification

Task 4. Figure 4 shows schemes of qualitative reactions for the detection of mercury cations. Describe the reactions. Which of the reactions are specific?

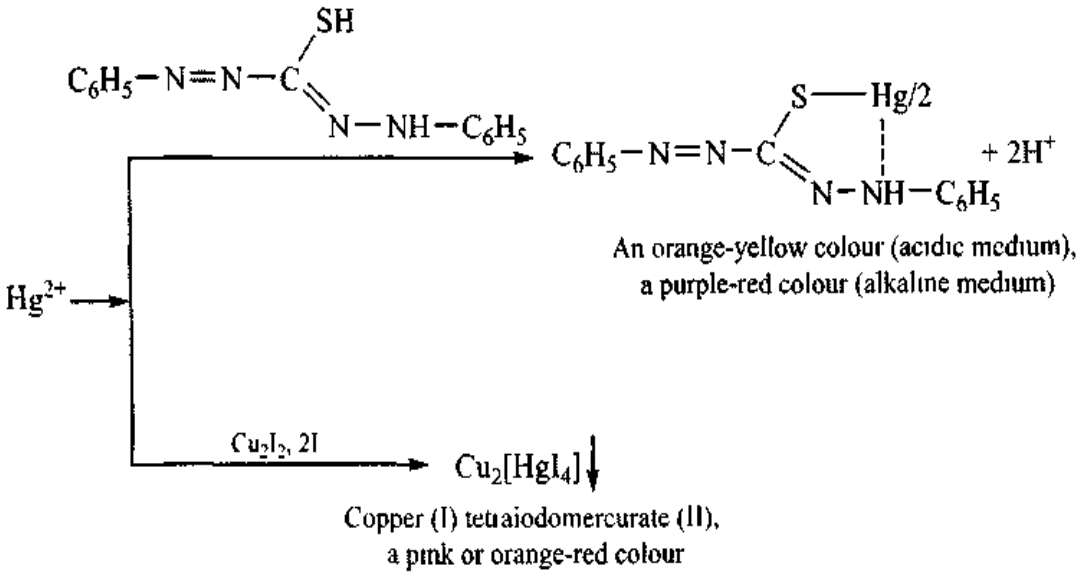

Figure 4.

The answer and its justification

Auditory independent work (supervised by the teacher):

Task 1. Figure 5 shows schemes of qualitative reactions for the detection of Arsenic cations. Describe the reactions. Which of the reactions are specific, sensitive and confirmatory?

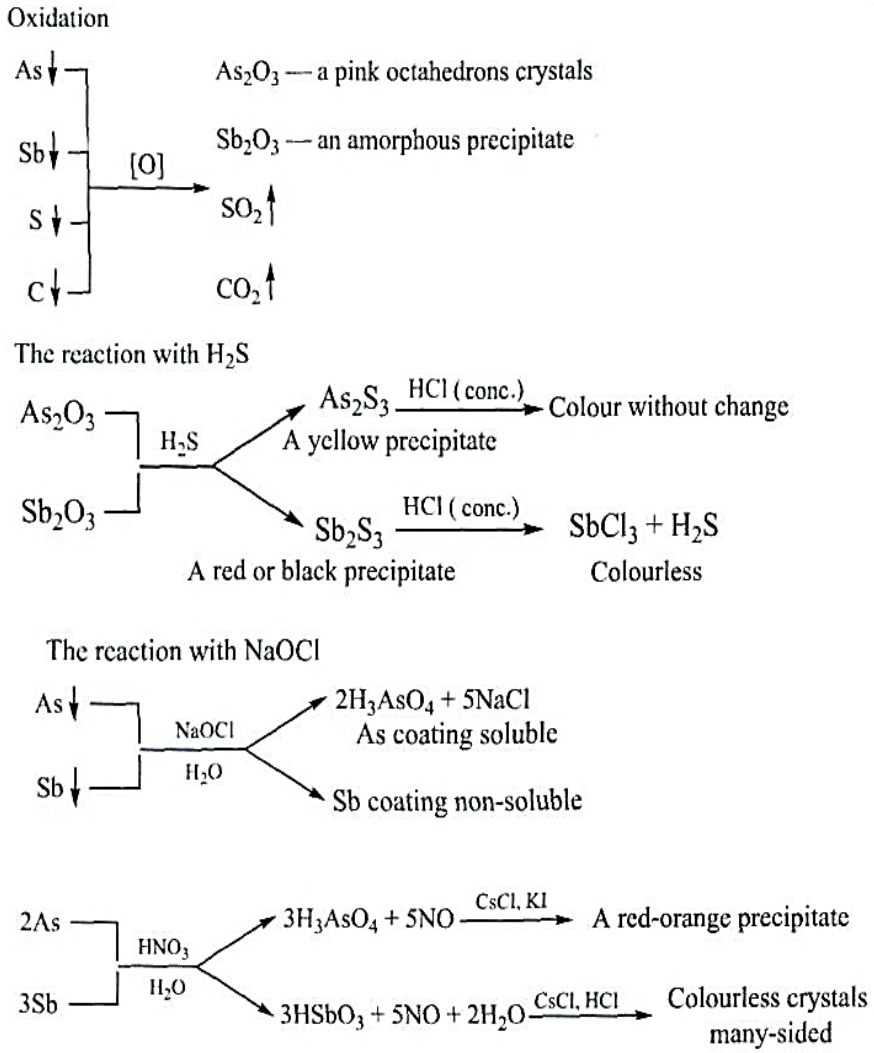

Figure 5.

Task 2. Describe the toxicological significance of mercury compounds. Name the symptoms of poisoning.

The answer and its justification

An example of a task with an answer standard:

Deposits of what compounds can form in the renewable tube of the Marsh device? How are deposits of various compounds located in a renewable tube?

Answer standard

COATINGS	POSITION OF COATINGS
As↓ «Arsenic mirror», a brown-grey colour with metallic luster	At narrow part of reductive tube, on the place of its heating
Sb↓ A dull-black colour	Up to both sides of the place of reductive tube heating, Antimony is less volatile
Se↓ A grey colour	Reductive tube
S↓ A yellow-brown colour	Reductive tube
C↓ A black colour	Reductive tube

How does metallic Mercury (Mercury) and its vapor affect the human body?

Answer standard

Metallic mercury and its vapor enter the body orally or by inhalation. In the case of acute mercury vapor poisoning, a person has symptoms: fever, shortness of breath, metallic taste in the mouth. With chronic intoxication, a classic triad of symptoms occurs: tremor, gingivitis, erythrism (insomnia, memory loss, impotence, emotional

lability, pathological shyness, depression). Mercury vapor in the human body is easily adsorbed by protein molecules, the protective functions of which decrease.
It is believed that Mercury accumulates in the tissues of the eyes (in the front part of the eyeball), as a result of which the yellow-brown color of the cornea appears. This symptom is considered a sign of mercury exposure, but not mercury poisoning. Metallic mercury is not adsorbed from the digestive tract, so poisonings occur rarely. Practically all metallic mercury in such cases (often mercury from a thermometer) is excreted from the body with feces.

Control work No. 2 - on questions of topics 4, 5.

List of questions for control work No. 2.

1. General characteristics of the group (compounds of Barium, Lead, Manganese, Chromium, Argentum, Cuprum, Cadmium, Stybium, Arsenic, Bismuth, Zinc, Thallium and Mercury). Field of application, toxicological significance. Qualitative detection and quantitative determination of "metallic" poisons.
2. Characteristics of modern general and separate methods of mineralization. The choice of the mineralization method depends on the nature of the object and the studied "metallic" poison.
3. Denitration of mineralizate and its preparation for research.
4. Fractional research method. Theoretical provisions. Selection of research objects.
5. Scheme of the fractional method of analysis (according to O.M. Krylova).
6. Characteristics of reagents used in the fractional method for masking interfering ions, isolation and analysis of "metallic" poisons.
7. General characteristics of methods of quantitative determination of "metallic" poisons in fractional analysis. The choice of method depends on the content of the poison. Possible errors during the analysis.
8. Lead compounds. Toxicological significance, methods of qualitative and quantitative analysis in biological material.
9. Barium compounds. Toxicological significance, methods of qualitative and quantitative analysis in biological material.
10. Manganese compounds. Toxicological significance, methods of qualitative and quantitative analysis in biological material.
11. Copper compounds. Toxicological significance, methods of qualitative and quantitative analysis in biological material.
12. Argentum compounds. Toxicological significance, methods of qualitative and quantitative analysis in biological material.
13. Chromium compounds. Toxicological significance, methods of qualitative and quantitative analysis in biological material.

14. Zinc compounds. Toxicological significance, methods of qualitative and quantitative analysis in biological material.
15. Cadmium compounds. Toxicological significance, methods of qualitative and quantitative analysis in biological material.
16. Thallium compounds. Toxicological significance, methods of qualitative and quantitative analysis in biological material.
17. Bismuth compounds. Toxicological significance, methods of qualitative and quantitative analysis in biological material.
18. Compounds of Stybius. Toxicological significance, methods of qualitative and quantitative analysis in biological material.
19. Compounds of Arsen. Toxicological significance, methods of qualitative and quantitative analysis in biological material.
20. Destructive mineralization of biological material.
21. Denitration of mineralizate when isolating mercury compounds.
22. Compounds of Mercury. Toxicological significance, methods of qualitative and quantitative analysis in biological material.

The methodical development was made by: professor of the department, doctor of pharm. sc. Welchinska O.V.

Topic N 6. Group of toxic substances which are isolated from the biological material with acidified water or with acidified ethanol (drugs or "medicinal" poisons). Research of model "acid" chloroform extracts the presence of pyrazolone derivatives, xanthine derivatives (methylated derivatives of purine), derivatives of barbituric acid and salicylic acid.

Purpose: the ability to operate with the basic concepts of the topic and to implement the main stages of chemical-toxicological analysis of poisonous substances isolated from biological material by extraction with acidified water or acidified ethanol ("medicinal" poisons): pyrazolone derivatives, xanthine (methylated purine derivatives), barbituric acid and salicylic acid.

The student must:

 to know the basic concepts, strategy and tactics of chemical-toxicological analysis of a group of poisonous substances isolated from biological material by extraction with acidified water or acidified ethanol ("medicinal" poisons);

 be able to propose a forensic toxicological research plan;

 know the methods of isolating poisonous substances, which are isolated from biological material by extraction with acidified water or acidified ethanol ("medicinal" poisons);

 evaluate the results of organoleptic control of extracts, preliminary tests;

 know the methods of analysis of poisonous substances that are isolated from biological material by extraction with acidified water or acidified ethanol ("medicinal" poisons);

 interpret the results of the analysis.

Basic concepts of the topic:

Term, parameter, characteristic	*Definition*
Extraction	the process of extracting one or more components from solutions or solids using selective solvents (extractants)
Pyrazolone derivatives	antipyrine (1-phenyl-2,3-dimethyl-pyrazolone-5), analgin (1-phenyl-2,3-dimethyl-4-N-methylaminopyrazolone-5-4-N-methanesulfonate sodium), butadione (1,2-diphenyl-4-butylpyrazolidine-dione-3, 5)
Derivatives of barbituric acid	barbital, phenobarbital (luminal), barbamil, etaminal sodium, hexenal (evipan)
Derivatives of xanthine (purine)	caffeine (1,3,7-trimethylxanthine), theobromine (3,7-dimethylxanthine), theophylline (1,3-dimethylxanthine)
Derivatives of salicylic	salicylic acid (o-oxybenzoic acid), aspirin (acetylsalicylic

acid	acid), sodium salicylate, methyl salicylate, salicylamide

Recommended literature:

Basic

1. Welchinska E.V. Toxicological and forensic chemistry (Criminal analysis). Poisonous substances and their biotransformation: textbook / E.V. Welchinska. — K.: PE Lopatina O.O., ISBN 978-617-7533-02-2, 2017. — p. 128-209. http://ir.librarynmu.com/handle/123456789/9123

2.Materials of Lecturers. The department of medicinal chemistry and toxicology of pharmaceutical faculty of Bogomolets NMU. https://www.youtube.com/@user-yj2fn5mz3x/

Auxiliary

1. Singh, Omender; Juneja, Deven (2019). *Principles and Practice of Critical Care Toxicology*. Jaypee Brothers Medical Publishers Pvt. Limited. ISBN 978-93-5270-674-7. For barbiturate overdose, urinary alkalinization with sodium bicarbonate may be beneficial. The optimum urinary pH which needs to be achieved is >7.5 and urine output should be more than 2 mL/kg/min.

2.Suddock, Jolee T.; Cain, Matthew D. (2020), "Barbiturate Toxicity", *StatPearls*, Treasure Island (FL): StatPearls Publishing, PMID 29763050, retrieved 5 August 2020.

Information resources

European Pharmacopoeia online - pheur.edqm.eu

The British Pharmacopoeia 2021 - www.pharmacopoeia.com

The British Pharmacopoeia 2020. London.2020: I-1298. www.webofpharma.com

Pharmacopoea USP. www.usp.org.

Website of the Department of Medicinal Chemistry and Toxicology of O.O. Bogomolets

http://nmu.ua/zagalni-vidomosti/kafedri/kafedra-farmatsevtycheskoj-byologycheskoj-y-toksykologycheskoj-hymyy/

Distance learning platform LIKAR_NMU

https://likar.nmu.kiev.ua/

Official website of the Ministry of Health of Ukraine

https://moz.gov.ua/

International Journal of Medical Toxicology and Forensic Medicine **(IJMTFM).** https://journals.sbmu.ac.ir/ijmtfm

Journal of Synthetic Organic Chemistry, Japan. http://www.ssocj.jp/indexenglish.

Journal of Organic Chemistry, USA. https://doi.org/10.1021/acs.joc.0c02255.

Synthetic Communications. Great Britain. http://www.tandfonline.com/page/terms-and-conditions
pubmed.ncbi.nlm.nih.gov

www.cochrane.org

Questions for theoretical study:

1. A group of substances that are isolated by extraction with polar solvents. General characteristics of the group. Physico-chemical properties, structure and effect on the body of poisonous and potent substances of organic nature.

2. Preliminary preparation of the object, the nature of the solvent, the pH of the solution, the nature of the acid, the degree of ionization, methods of protein precipitation. Characteristics of solvents that are most often used for isolation. Modern general and personal methods of isolation with polar solvents (acidified alcohol, acidified water) V.P. Kramarenka, Valova, V.I. Popova.

3. Methods of cleaning hoods from biological material from accompanying impurities. The choice of method depends on the condition, type and method of isolating poison from biological material.

4. Features of the metabolism of salicylic acid derivatives (aspirin, sodium salicylate, methyl salicylate, salicylamide).

5. Toxic concentrations of salicylates in blood serum.

6. Peculiarities of the metabolism of barbituric acid derivatives: barbamil, barbital, phenobarbital, sodium ethaminal, benzonal, hexenal.

7. Microcrystalloscopic reactions to barbiturates. What reagents are used to perform these reactions. Characteristics of final products.

8. Murexide test for barbiturates. What exactly barbiturates give this reaction? Schemes of reactions. Which barbiturates do not give this reaction? Does this reaction belong to the express analysis?

9. Peculiarities of the metabolism of p-aminophenol derivatives (phenacetin, paracetamol).

10. Paracetamol is formed as a result of the dealkylation reaction during the metabolism of the drug ...?

11. Peculiarities of the metabolism of pyrazolone derivatives (analgin, antipyrine,

amidopyrine, butadione).

12. Peculiarities of the metabolism of purine derivatives (caffeine, theophylline, theobromine).

13. Methods of qualitative detection and quantitative determination of caffeine.

14. Methods of qualitative detection and quantitative determination of theobromine.

15. Methods of qualitative detection and quantitative determination of theophylline.

Tasks for independent processing of the topic:

Test tasks

Choose and justify the correct answer.

1. Previous reactions to the detection of barbiturates in urine include the reaction:
   A. Cobalt acetate and lithium hydroxide
   B. Cobalt sulfate
   C. Cobalt chloride and sodium hydroxide
   D. Cobalt bromide and potassium hydroxide
2. Fatal poisoning with a pyrazolone derivative occurred. To isolate a pyrazolone derivative from biological material, use:
   A. water extraction with acidification with oxalic acid
   B. extraction with alkaline water
   C. ethanol extraction
   D. chloroform extraction
3. What acid is used to acidify biological material in the method of O.O. Vasilieva?
   A. sulfate
   B. phosphate
   C. nitrate
   D. oxalate
4. Name an alkaloid that can be isolated from biological material with acidification or alkalization:
   A. caffeine
   B. quinine
   C. codeine
   D. atropine
5. What reaction is used to distinguish between theophylline and theobromine, since only theophylline undergoes this reaction?
   A. reaction with diazotized sulfanilic acid
   B. reaction with hydrogen peroxide
   C. reaction with Dragendorff's reagent
   D. reaction with potassium chlorate

Enter in the cells ☐ the letters that indicate the correct answers to the test questions:

1-☐ 2-☐ 3-☐ 4-☐ 5-☐

Written assignments

Task 1. Figure 1 shows the scheme of chemical transformations. Explain the scheme. What transformations are taking place? Do these chemical reactions belong to qualitative detection reactions?

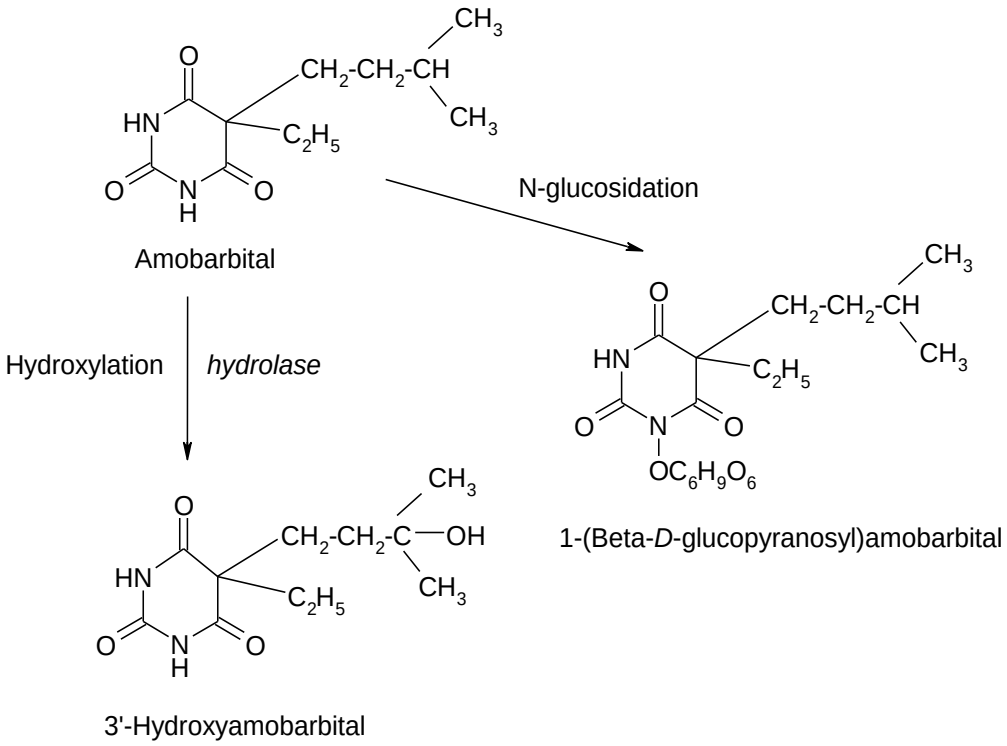

Figure 1.

The answer and its justification

Auditory collective work:

Task 1. Barbiturates are detected with the help of reagents - Cobalt salts. For example, a preliminary test for barbiturates in urine (Fig. 2):

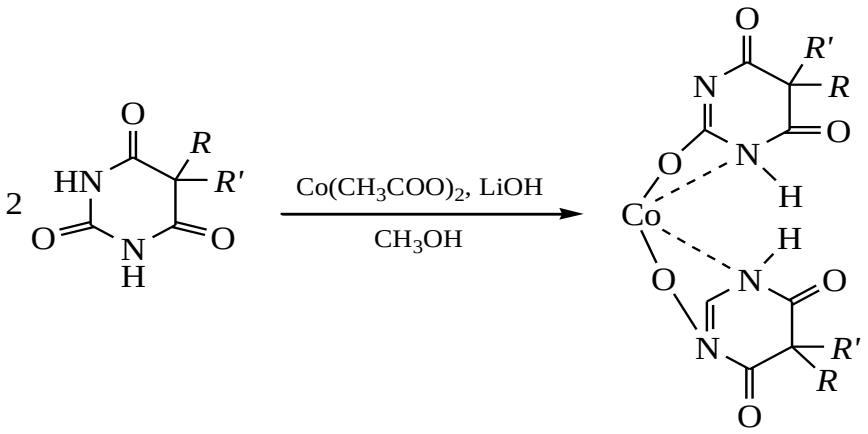

Figure 2.

What other reactions for the detection of barbiturates are used with reagents that contain Cobalt? Write the reaction schemes.

The answer and its justification

Task 2. Figure 3 shows the formula of the reaction product, which is performed for the qualitative detection of barbiturates. Write a diagram of this reaction. What color occurs with a positive result of this reaction?

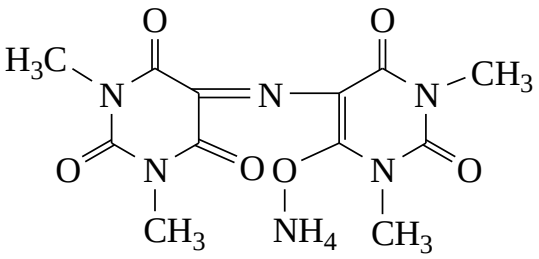

Figure 3.

The answer and its justification

Auditory independent work (supervised by the teacher):

Task 1. Describe the methods of isolating "medical" poisons from biological material O.O. Vasylieva and Stas-Otto. What are the differences between the methods?

The answer and its justification

An example of a task with an answer standard:
Qualitative detection of salicylic acid by reaction with ferrum (III) chloride.

Answer standard

Coloration reaction: reaction with ferrum (III) chloride — colored complexes are formed: blue-violet (pH 1,8-2,5), red-brown (4-8), yellow (8-11) (fig.4):

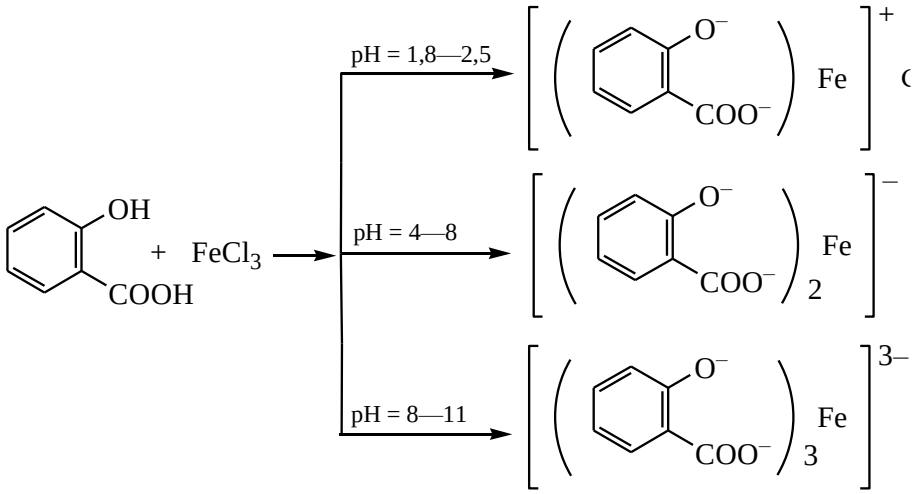

Figure 4.

The methodical development was made by: professor of the department, doctor of pharm. sc. Welchinska O.V.

Topic N 7. Research of model "alkaline" chloroform extracts for the presence of tropane derivatives (atropine, scopolamine, cocaine), quinoline derivatives, isoquinoline (narcotine, narceine, papaverine, morphine, codeine, ethylmorphine, heroin), acyclic alkaloids (ephedrine, pseudoephedrine) according to with the help of color, precipitation and microcrystallographic reactions.

Purpose: the ability to operate with the basic concepts of the topic and to implement the main stages of chemical and toxicological analysis of poisonous substances isolated from biological material by extraction from alkalized chloroform extracts ("medical" poisons): tropane derivatives (atropine, scopolamine, cocaine), quinoline derivatives (quinine, quinidine, quinosol), isoquinoline (narcotine, narceine, papaverine, morphine, codeine, ethylmorphine, heroin), acyclic alkaloids (ephedrine, pseudoephedrine).

The student must:

 to know the basic concepts, strategy and tactics of chemical-toxicological analysis of a group of poisonous substances isolated from biological material by extraction from alkalized chloroform extracts ("medical" poisons);

 be able to propose a forensic toxicological research plan;

 know the methods of isolating poisonous substances that are isolated from biological material by extraction from alkalized chloroform extracts ("medicinal" poisons);

 evaluate the results of organoleptic control of extracts, preliminary tests;

 know methods of analysis of poisonous substances isolated from biological material by extraction from alkalized chloroform extracts ("medicinal" poisons);

 interpret the results of the analysis.

Basic concepts of the topic:

Term, parameter, characteristic	*Definition*
Extraction	the process of extracting one or more components from solutions or solids using selective solvents (extractants)
Derivatives of tropane	atropine (8-methyl-8-azabicyclo-[3.2.1]-octane), hyoscyamine — a stereoisomer of atropine, scopolamine (scopine ester of (–)-tropic acid), cocaine (methyl ester of benzoylecgonine)
Derivatives of quinoline	quinine ((6´-methoxyquinolyl-4´)-(5-vinylquinuclidyl-2)-carbinol), quinidine (dextrorotatory isomer (at the C9 atom) of quinine)
Isoquinoline derivatives	morphine (3,6-α-dihydroxy-4,5-α-epoxy-17-methyl-7-morphinene), codeine (monomethyl ether of phenolic hydroxyl 3,6-α-dihydroxy-4,5-α-epoxy- 17-methyl-7-

	morphine), papaverine (6,7-dimethoxy-1-(3',4''-dimethoxybenzyl) isoquinoline), narcotine (gnoscapine, phthalidiisoquinoline)
Acyclic alkaloids	ephedrine (1-phenyl-2-methylamino-1-propanol, exists in erythro-form, racemic mixture (+), pseudoephedrine (1-phenyl-2-methylamino-1-propanol, exists in threo-form, racemic mixture (+))
Synthetic derivatives of morphine	heroin (diamorphine, acetomorphine, diacetylmorphine hydrochloride)

Recommended literature:

Basic

1. Welchinska E.V. Toxicological and forensic chemistry (Criminal analysis). Poisonous substances and their biotransformation: textbook / E.V. Welchinska. — K.: PE Lopatina O.O., ISBN 978-617-7533-02-2, 2017. — p. 157-214. http://ir.librarynmu.com/handle/123456789/9123

2.Materials of Lecturers. The department of medicinal chemistry and toxicology of pharmaceutical faculty of Bogomolets NMU. https://www.youtube.com/@user-yj2fn5mz3x/

Auxiliary

1.Gresnigt, Femke M.J.; Gubbels, Nanda P.; Riezebos, Robert K. (2021-01-01). "The current practice for cocaine-associated chest pain in the Netherlands". *Toxicology Reports*. **8**:23–27. doi:10.1016/j.toxrep.2020.12.011. ISSN 2214-7500. PMC 7770504. PMID 33384944.

2.*"AusPAR: Atropine sulfate monohydrate". Therapeutic Goods Administration (TGA). 31 May 2022. Archived from the original on 31 May 2022*. Retrieved *12 June* 2022.

3.Jump up to: *"Atropine sulfate". dailymed.nlm.nih.gov. U.S. National Library of Medicine. Archived from the original on 26 July 2020*. Retrieved *30 October* 2019.

Information resources

European Pharmacopoeia online - pheur.edqm.eu

The British Pharmacopoeia 2021 - www.pharmacopoeia.com

The British Pharmacopoeia 2020. London.2020: I-1298. www.webofpharma.com

Pharmacopoea USP. www.usp.org.

Website of the Department of Medicinal Chemistry and Toxicology of O.O. Bogomolets

http://nmu.ua/zagalni-vidomosti/kafedri/kafedra-farmatsevtycheskoj-byologycheskoj-y-toksykologycheskoj-hymyy/

Distance learning platform LIKAR_NMU

https://likar.nmu.kiev.ua/

Official website of the Ministry of Health of Ukraine

https://moz.gov.ua/

International Journal of Medical Toxicology and Forensic Medicine **(IJMTFM).** https://journals.sbmu.ac.ir/ijmtfm

Journal of Synthetic Organic Chemistry, Japan. http://www.ssocj.jp/indexenglish.

Journal of Organic Chemistry, USA. https://doi.org/10.1021/acs.joc.0c02255.

Synthetic Communications. Great Britain. http://www.tandfonline.com/page/terms-and-conditions
pubmed.ncbi.nlm.nih.gov

www.cochrane.org

Questions for theoretical study:

1.Peculiarities of the metabolism of tropane derivatives (atropine, scopolamine, cocaine, ecgonine).

2. When poisoned by which alkaloid of the tropane group, a drug addict develops a complex of symptoms called "crack dance"?

3. Peculiarities of the metabolism of quinoline derivatives (quinine, quinidine).

4. Oxyquinine and dioxyquinine are metabolites of quinine, which are formed by the oxidation of which cycle of the quinine molecule?

5. What metabolite is formed during the oxidation of the quinuclidine cycle of the quinine molecule?

6. Thaleiochin reaction. What compound is it used to detect? Does it refer to express analysis? Write a diagram.

7. Detection of quinine in urine (or blood plasma). Methodology of this experiment. What is this reaction called and why did it get that name?

8. Methods of qualitative detection and quantitative determination of atropine.

9. Methods of qualitative detection and quantitative determination of cocaine.

10. Methods of qualitative detection and quantitative determination of quinine.

11.Peculiarities of the metabolism of isoquinoline derivatives (morphine).

12.Peculiarities of the metabolism of isoquinoline derivatives (codeine).

13.Peculiarities of the metabolism of isoquinoline derivatives (papaverine).

14.Peculiarities of the metabolism of isoquinoline derivatives (narcotine).

15.Peculiarities of the metabolism of isoquinoline derivatives (heroin).

16.Qulitative and qnantitative analysis of morphine.

17.Qulitative and qnantitative analysis of codeine.

18.Qulitative and qnantitative analysis of papaverine.

19.Qulitative and qnantitative analysis of narcotine.

20.Qulitative and qnantitative analysis of heroin.

21.Qulitative and qnantitative analysis of ephedrine.

22.Qulitative and qnantitative analysis of pseudoephedrine.

Tasks for independent processing of the topic:

Test tasks

Choose and justify the correct answer.

1. Name the metabolite of atropine:

A. tropic acid

B. benzoic acid

C. benzaldehyde

D. benzene

2. With which reagent does atropine give a microcrystalline reaction?

A. Reinecke salt

B. Dragendorff's reagent

C. potassium permanganate

D. Marcy's reagent

3. What is the name of the coloring reaction, in which atropine and scopolamine enter, with the formation of a purple colored product?

A. Vitaly-Morena

B. with cobalt rhodanide

C. with resorcinol

D. with benzaldehyde

4. Name the alkaloid that reacts with the formation of benzoin-ethyl ester:

A. cocaine

B. quinine

C. codeine

D. atropine

5. What is the name of the reaction of quinine, as a result of which a product of emerald-green color is formed?

A. taleiohinna

B. erythrochinna

C. fluorescence

D. Vitaly-Morena

6. Name the metabolite of morphine:

A. oxydimorphine

B. benzoic acid

C. benzaldehyde

D. benzene

7. With which reagent does codeine give a microcrystalline reaction?

A. Reinecke salt

B. Dragendorff's reagent

C. potassium permanganate

D. Bouchard's reagent

8. What is the name of the reaction reagent with which papaverine forms crystals in the form of clusters of thin plates in the shape of a cube?

A. cadmium chloride

B. cobalt rhodanide

C. resorcinol

D. benzaldehyde

9. Name the alkaloid that forms the normorphine metabolite:

A. morphine

B. quinine

C. codeine

D. atropine

10. What alkaloid enters into the reaction of formation of "Berlin blue"?

A. papaverine

B. narcotic

C. ephedrine

D. morphine

Enter in the cells ☐ the letters that indicate the correct answers to the test questions:

1-☐ 2-☐ 3-☐ 4-☐ 5-☐

Written assignments

Task 1. Figure 1 shows the scheme of chemical transformations. Explain the scheme. What transformations are taking place? Do these chemical reactions belong to qualitative detection reactions?

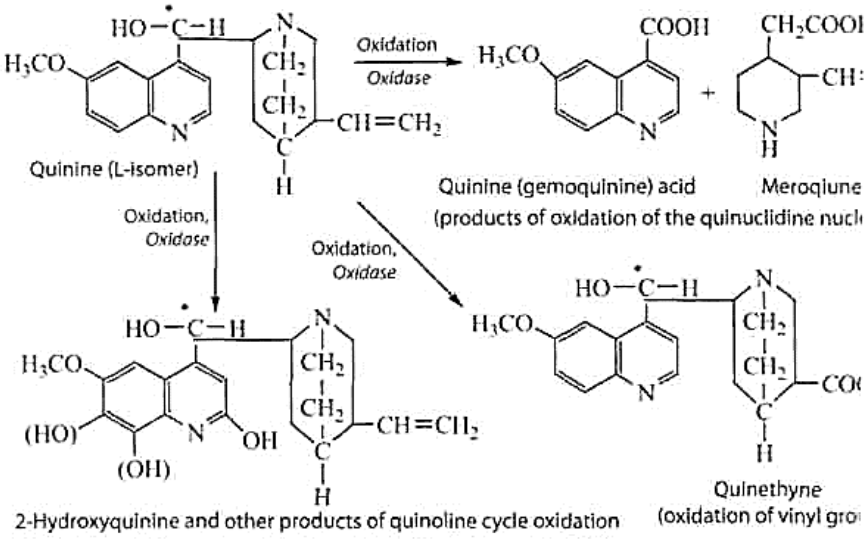

Figure 1.

The answer and its justification

Task 2. Figure 2 shows the scheme of chemical transformations. Explain the scheme. What transformations are taking place? Do these chemical reactions belong to qualitative detection reactions?

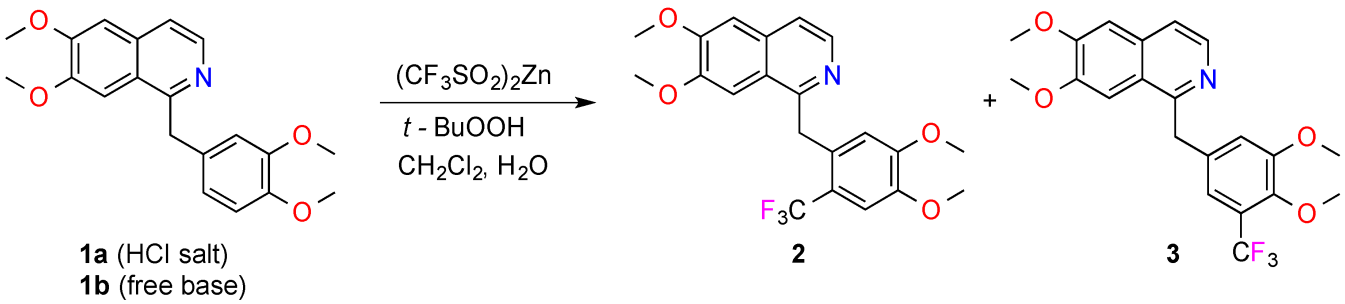

Figure 2.

The answer and its justification

Auditory collective work:

Task 1. Figure 3 shows the scheme of the second stage of the qualitative reaction of atropine. Name the reaction. Write the scheme of the first step of the reaction.

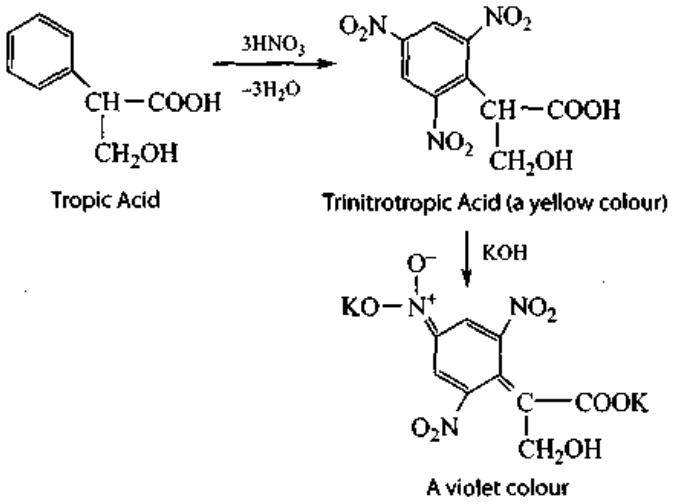

Figure 3.

The answer and its justification

Task 2. Toxicological value of atropine. What are the symptoms of atropine poisoning?

The answer and its justification

Task 3. Figure 4 shows the scheme of the second stage of the qualitative reaction of ephedrine. Name the reaction. Write the scheme of the first step of the reaction.

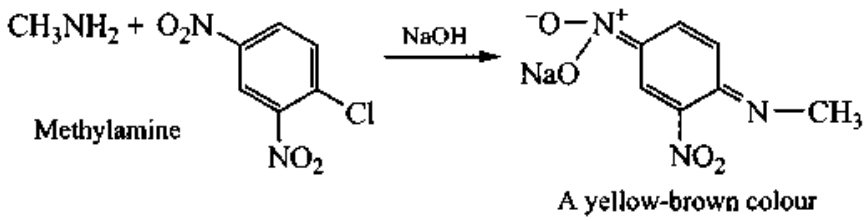

Figure 4.

The answer and its justification

Task 4. Toxicological value of morphine. What are the symptoms of morphine poisoning?

The answer and its justification

Auditory independent work (supervised by the teacher):

Task 1. Describe the reactions of scopolamine metabolism (Fig. 5). What chemical transformations occur with scopolamine?

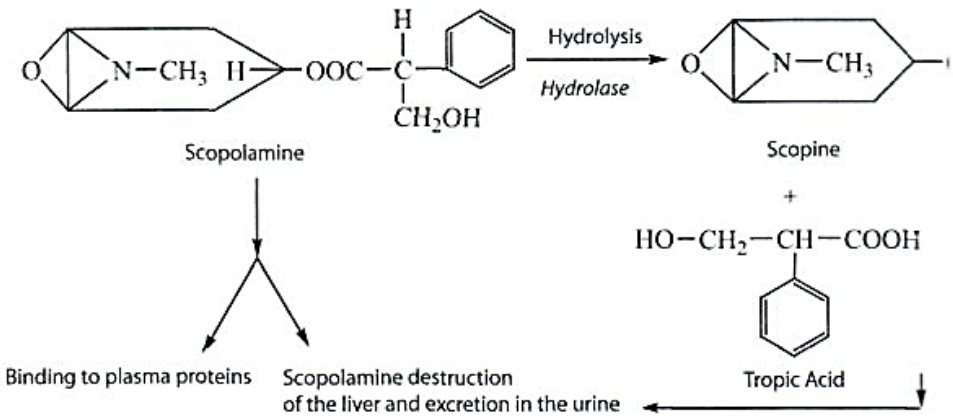

Figure 5.

Task 2. Describe the reactions of drug metabolism (Fig. 6). What chemical transformations occur with narcotine?

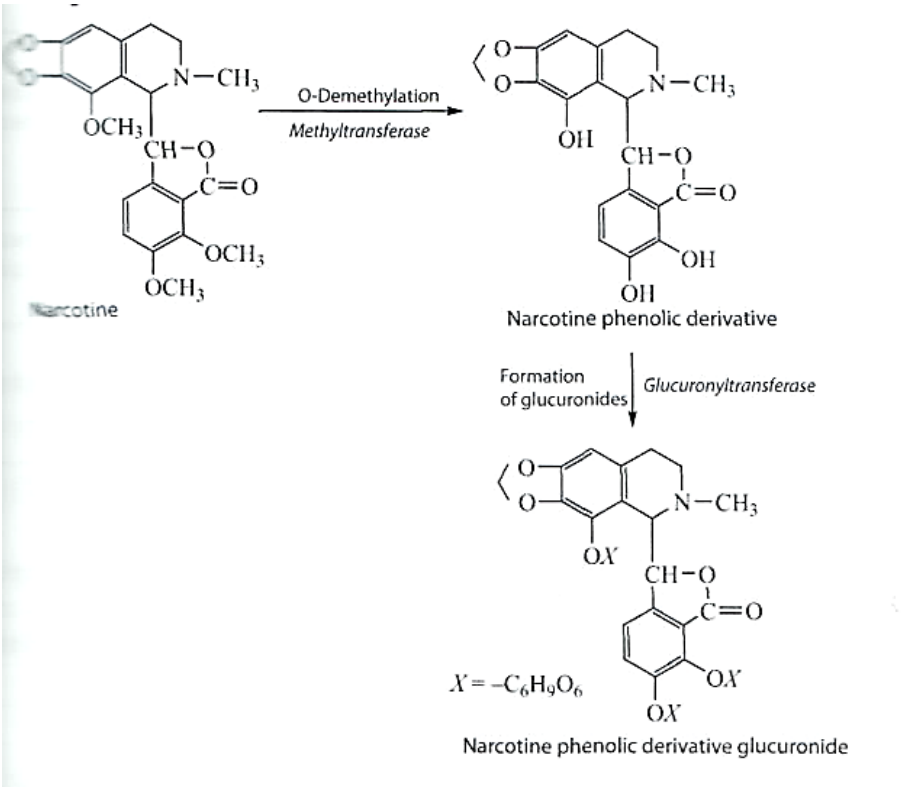

Figure 6.

The answer and its justification

An example of a task with an answer standard:
Microcrystallographic reaction to cocaine.

Answer standard

One of the vivid examples of microcrystallographic reactions is the reaction of the formation of ***cocaine permanganate*** in the form of crystals: purple rectangular and square plates and growths from them (Fig. 7):

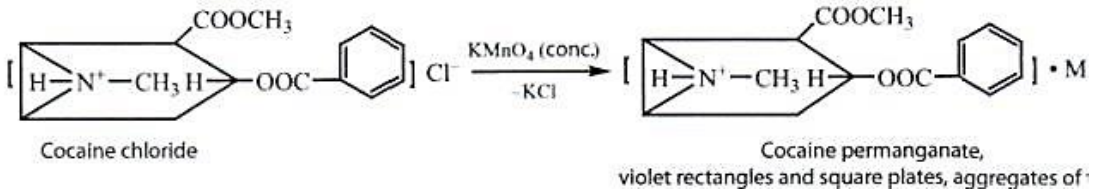

Figure 7.

Metabolism of pseudoephedrine.

Answer standard

Pseudoephedrine is resistant to the effects of monoamine oxidase and is excreted in a significant amount (more than 90%) with urine within 24 hours. Less than 1% of pseudoephedrine is metabolized in the liver, and its molecules undergo N-demethylation with the formation of norpseudoephedrine (cathine) (Fig. 8):

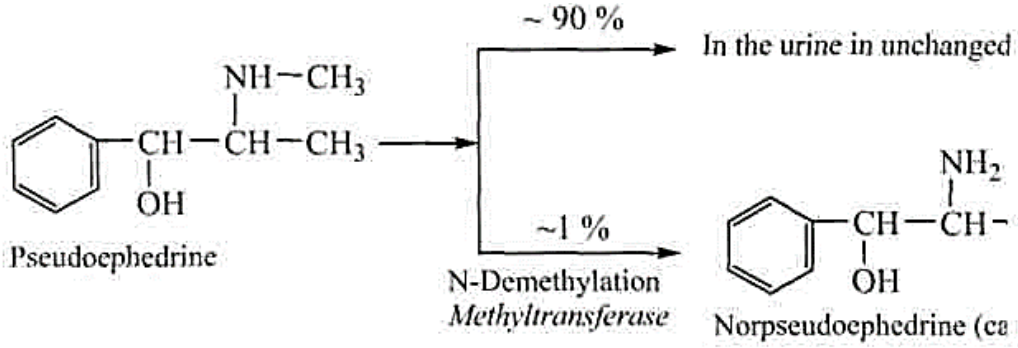

Figure 8.

The methodical development was made by: professor of the department, doctor of pharm. sc. Welchinska O.V.

Topic N 8. Research of model "alkaline" chloroform extracts for the presence of phenothiazine derivatives, 1,4-benzodiazepine derivatives, p-aminobenzoic acid derivatives, oxypiperidine derivatives, 2-substituted propionic acid derivatives (ibuprofen), imidazoline derivatives (clofelin); poisons of natural origin (plants, mushrooms, animals and insects). Express analysis. Control work № 3.

Purpose: the ability to operate with the basic concepts of the topic and to implement the main stages of the chemical-toxicological analysis of poisonous substances isolated from biological material by extraction from alkalized chloroform extracts ("medicinal" poisons): derivatives of phenothiazine, 1,4-benzodiazepine, p-aminobenzoic acid, oxypiperidine, 2-substituted propionic acid (ibuprofen), imidazoline (clofelin); poisons of natural origin (plants, mushrooms, animals and insects).

The student must:

 to know the basic concepts, strategy and tactics of chemical-toxicological analysis of a group of poisonous substances isolated from biological material by extraction from alkalized chloroform extracts ("medical" poisons);

 be able to propose a forensic toxicological research plan;

 know the methods of isolating poisonous substances that are isolated from biological material by extraction from alkalized chloroform extracts ("medicinal" poisons);

 evaluate the results of organoleptic control of extracts, preliminary tests;

 know methods of analysis of poisonous substances isolated from biological material by extraction from alkalized chloroform extracts ("medicinal" poisons);

 know methods of analysis of poisons of natural origin (plants, mushrooms, animals and insects);

 interpret the results of the analysis.

Basic concepts of the topic:

Term, parameter, characteristic	*Definition*
Extraction	the process of extracting one or more components from solutions or solids using selective solvents (extractants)
Phenothiazine derivatives	aminazine (2-chloro-10-(3-dimethylaminopropyl)-phenothiazine hydrochloride), diprazine (10-(2-dimethylaminopropyl)-phenothiazine hydrochloride), tisercin (2-methoxy-10-(3-dimethylamino-2-

	methylpropyl)-phenothiazine hydrochloride)
Derivatives of 1,4-benzodiazepine	chlordiazepoxide (7-chloro-2-methylamino-5-phenyl-3H-1,4-benzodiazepine chloride), diazepam (7-chloro-1,2-dihydro-1-methyl-2-oxo-5-phenyl-3H-1,4-benzodiazepine), nitrazepam (1,2-dihydro-7-nitro-2-oxo-5- phenyl-3H-1,4-benzodiazepine), oxazepam (7-chloro-1,2-dihydro-3-hydroxy-2-oxo-5-phenyl-3H-1,4-benzodiazepine)
Derivatives p-aminobenzoic acid (PABA)	novocaine (β-diethylaminoethyl ester of p-aminobenzoic acid hydrochloride), dicaine (β-dimethylaminoethyl ester of p-butylaminobenzoic acid hydrochloride), novocainamide (β-diethylaminoethylamide of p-aminobenzoic acid hydrochloride)
Oxypiperidine derivatives	promedol (1,2,5-trimethyl-4-phenyl-4-propionyloxy-piperidine hydrochloride), Prosidol (1-(2-ethoxyethyl)-4-phenyl-4-propionyl-oxypiperidine hydrochloride)
Derivatives of 2-substituted propionic acid (ibuprofen)	ibuprofen ((+)-2-(4-isobutylphenyl)-propionic acid)
Imidazoline derivatives (Clofelin, clonidine)	Clophelin, clonidine (2-(2,6-dichlorophenylamino)-imidazoline hydrochloride)

Tetrodotoxin	one of the strongest known natural toxins, contained in the liver of some fugu fish (*Fugu niphobles, Fugu ocellatus)*, the skin of frogs (*genus Atelopus*), eggs of the California newt (*Taricha torosa*), mollusks (*Charonia saulinae, Babylonia japonica*)
Batrachotoxin	found in the skin glands of amphibians — tree climbers (*genus Phyllobates*), has a strong cardiotoxic effect, and also has a paralytic effect on the respiratory muscles
Pumiliotoxins (A, B and C)	found in the skin glands of other representatives of amphibian tree climbers (*Dendrobates pumilio and Dendrobates Auratus)*; the biological effect of pumiliotoxins consists in the violation of coordination of movements, the appearance of convulsions, partial paralysis of the limbs
Bufotoxins	cardiotonic steroids contained in the skin secretion of common toads (*Bufo vulgaris*)

	
Fugu niphobles	*Taricha torosa*
	
genus Phyllobates	*Bufo vulgaris*

Recommended literature:

Basic

1.Welchinska E.V. Toxicological and forensic chemistry (Criminal analysis). Poisonous substances and their biotransformation: textbook / E.V. Welchinska. — K.: PE Lopatina O.O., ISBN 978-617-7533-02-2, 2017. — p. 256-283. http://ir.librarynmu.com/handle/123456789/9123

2.Materials of Lecturers. The department of medicinal chemistry and toxicology of pharmaceutical faculty of Bogomolets NMU. https://www.youtube.com/@user-yj2fn5mz3x/

Auxiliary

1. Caio H. P. Rodrigues, Lívia S. Mariotto, Aline T. Bruni. Acute, chronic, and *post-mortem* toxicity: a review focused on three different classes of new psychoactive substances. *Forensic Toxicology*. V. 41,187–212 (2023).

2. Kelly Francisco da Cunha, Karina Diniz Oliveira, Jose Luiz Costa. Green analytical toxicology method for determination of synthetic cathinones in oral fluid samples by microextraction by packed sorbent and liquid chromatography–tandem mass spectrometry**.** *Forensic Toxicology*. (2023)**.**

3. Islam MB, Islam MI, Nath N, Emran TB, Rahman MR, Sharma R, Matin MM. Recent Advances in Pyridine Scaffold: Focus on Chemistry, Synthesis, and Antibacterial Activities. Biomed Res Int. 2023 May 18; 2023: 9967591. doi: 10.1155/2023/9967591. PMID: 37250749; PMCID: PMC10212683.

Informational resources

European Pharmacopoeia online - pheur.edqm.eu

The British Pharmacopoeia 2021 - www.pharmacopoeia.com

The British Pharmacopoeia 2020. London.2020: I-1298. www.webofpharma.com

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Distance learning platform LIKAR_NMU

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Official website of the Ministry of Health of Ukraine

https://moz.gov.ua/

International Journal of Medical Toxicology and Forensic Medicine **(IJMTFM).** https://journals.sbmu.ac.ir/ijmtfm

Journal of Synthetic Organic Chemistry, Japan. http://www.ssocj.jp/indexenglish.

Journal of Organic Chemistry, USA. https://doi.org/10.1021/acs.joc.0c02255.

Synthetic Communications. Great Britain. http://www.tandfonline.com/page/terms-and-conditions
pubmed.ncbi.nlm.nih.gov

www.cochrane.org

Questions for theoretical study:

1.Physical-chemical properties, chemical structure, application, toxicological characteristics, causes of poisoning, mechanisms of toxic action, toxicodynamics and toxicokinetics (pathways of entry into the body, metabolism, distribution, excretion) and methods of analysis of medicinal substances.

2. Synthetic medicinal substances: phenothiazine derivatives (aminazine, diprazine,

etmosine, levomepromazine, thioridazine); 1,4-benzodiazepine derivatives (chlordiazepoxide, diazepam, oxazepam, mezapam, phenazepam, nitrazepam, clonazepam).

3. Synthetic medicinal substances: p-aminobenzoic acid derivatives (novocaine, novocaineamide).

4. Synthetic medicinal substances: derivatives of oxypiperidine (Promedol, Prosidol).

5. Synthetic medicinal substances: derivatives of 2-substituted propionic acid (ibuprofen), imidazoline derivatives (clonidine).

6. Physical-chemical methods of research of medicinal substances: chromatography in thin layers of sorbent (TLH), high-performance liquid chromatography (HPLC) and gas-liquid chromatography (HLC).

7. TLC-screening as a preliminary stage of identification in undirected chemical-toxicological analysis. Group developers in TLC.

8. Peculiarities of the metabolism of phenothiazine derivatives (aminazine, diprazine, tizercin).

9. Peculiarities of the metabolism of p-aminobenzoic acid (PABA) derivatives (novocaine, dicaine, novocaineamide).

10. Features of the metabolism of 1,4-benzodiazepine derivatives (chlordiazepoxide, diazepam, oxazepam, nitrazepam).

11. Peculiarities of the metabolism of synthetic derivatives of 2-substituted propionic acid (ibuprofen).

12. What symptoms of poisoning appear in a person with an overdose of ibuprofen?

13. Peculiarities of the metabolism of synthetic derivatives of imidazoline (clofelin).

14. Methods of qualitative detection and quantitative determination of ibuprofen.

15. Methods of qualitative detection and quantitative determination of nitrazepam.

16. Methods of qualitative detection and quantitative determination of diazepam.

17. Methods of qualitative detection and quantitative determination of oxazepam.

18. Methods of qualitative detection and quantitative determination of aminazine.

19. Methods of qualitative detection and quantitative determination of clofelin.

20.Methods of qualitative detection and quantitative determination of chlordiazepoxide.

21. Methods of qualitative detection and quantitative determination of diprazine.

22. Methods of qualitative detection and quantitative determination of tizercin.

23.Characterization and analysis of poisons of natural origin.

24. Plant poisons (phytotoxins) - ricin, dithyline, nicotine, strychnine, scopolamine, etc.

25. Poisons of animal origin (zootoxins) - tetrodotoxin.

26. Poisons of cap mushrooms and their classification.

27. Mechanisms of toxic action and clinical symptoms of poisoning when using poisonous mushrooms (pale toadstool, red fly agaric, false boletus, false morels) and conditionally edible mushrooms (morels, morels, porcini mushrooms, champignons, champignons).

28. Methods of isolation from objects of research and chemical-toxicological analysis of cap mushroom poisons.

29.Diagnosis, emergency care, antidote and symptomatic therapy for mushroom poisoning.

30.Poisons of natural origin that require special methods of isolation from research objects: toxins of lower fungi or fungal poisons (mycotoxins), algae toxins (algotoxins) and microbial toxins.

Tasks for independent processing of the topic:

Test tasks

Choose and justify the correct answer.

1. Name the metabolite of novocaine:

A. diethylaminoethanol

B. benzoic acid

C. benzaldehyde

D. benzene

2. With which reagent does dicain give a microcrystalline reaction?

A. Vitaly-Morena

B. Mayer's reagent

C. potassium permanganate

D. Bouchard's reagent

3. What is the name of the reaction reagent with which aminazine forms a red color?

A. ferrum (III) chloride

B. cobalt acetate

C. resorcinol

D. bromine water

4. Which of the 1,4-benzodiazepine derivatives during metabolism forms a metabolite - lactam?

A. Chlordiazepoxide

B. diazepam

C. nitrazepam

D. oxazepam

5. What color does chlordiazepoxide form in the Vitali-Moren reaction?

A. yellow

B. red

C. blue

D. brown

6. Tetrodotoxin is a derivative of which compound?

A. pyridine

B. quinolone

C. phenanthrenisoquinoline

D. 2-iminoperhydroquinazoline

7. Which zootoxin is a structural analogue of tetrodotoxin?

A. chirikitotoxin

B. batrachotoxin

C. pumiliotoxin

D. bufotoxin

8. Which reagent is used to detect zootoxins - pyridine derivatives?

A. ferrum (III) chloride

B. cobalt acetate

C. α-naphthol

D. formaldehyde in concentrated sulfuric acid

9. By chemical structure, bufotoxins belong to:

A. steroids

B. piperidine derivatives

C. pyridine derivatives

D. pyrimidine derivatives

10. Metabolites of tetrodotoxin have not been identified, but the molecule contains free functional groups that can be detected. Name the functional groups:

A. hydroxy

B. carboxy

C. keto

D. amino

Enter in the cells ☐ the letters that indicate the correct answers to the test questions:

1-☐ 2-☐ 3-☐ 4-☐ 5-☐

Written assignments

Task 1. Figure 1 shows the scheme of chemical transformations. Explain the scheme. What transformations are taking place? Do these chemical reactions belong to qualitative detection reactions?

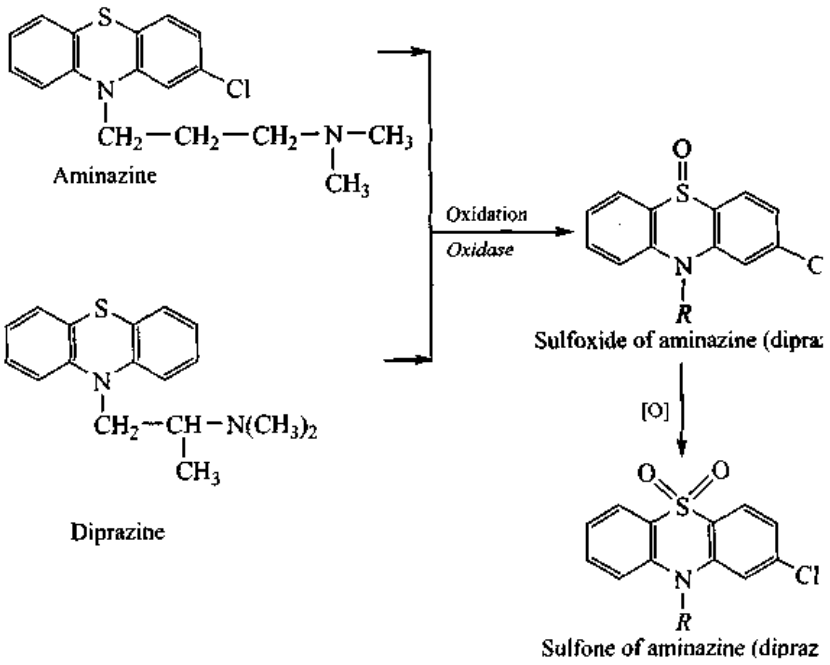


Figure 1.

The answer and its justification

Task 2. Figure 2 shows the scheme of chemical transformations. Explain the scheme. What transformations are taking place? Do these chemical reactions belong to qualitative detection reactions?

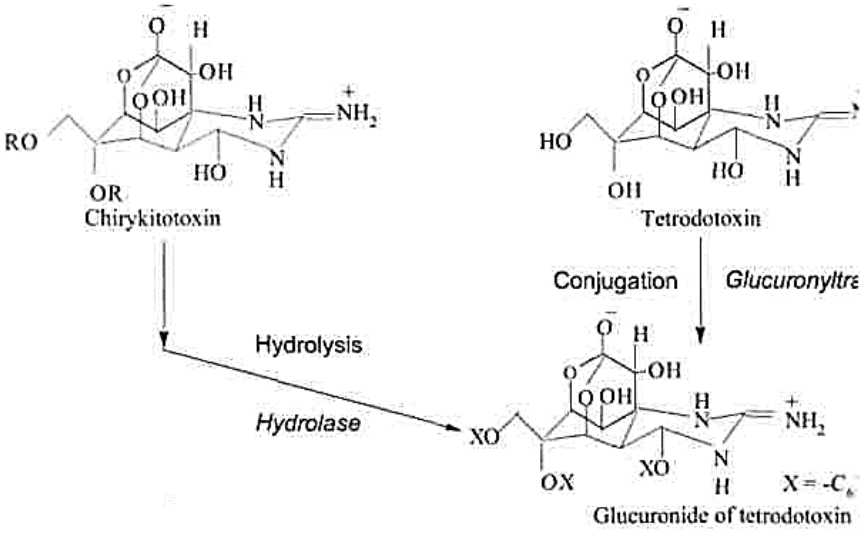


Figure 2.

The answer and its justification

Auditory collective work:

Task 1. Figure 3 shows a diagram of the qualitative reaction of novocaine. Name the products of the reaction.

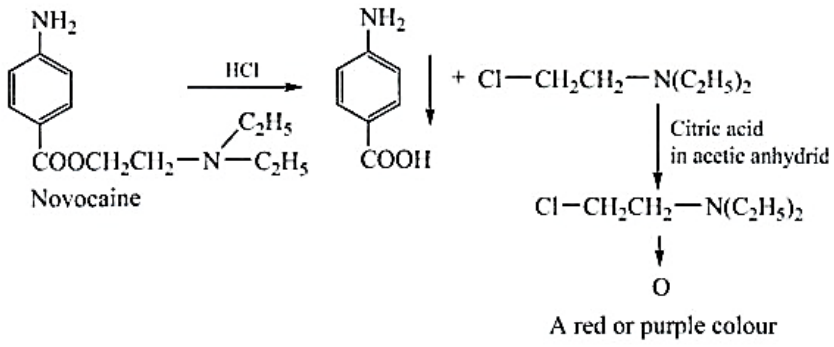


Figure 3.

The answer and its justification

Task 2. Toxicological value of promedol. What are the symptoms of promedol poisoning?

The answer and its justification

Task 3. Figure 4 shows the general chemical formula of pumiliooxins (A, B C). According to which functional groups can their qualitative detection be carried out?

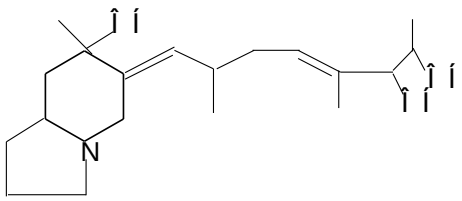


Figure 4.

The answer and its justification

Task 4. Toxicological value of tetrodotoxin. What are the symptoms of tetrodotoxin poisoning?

The answer and its justification

Auditory independent work (supervised by the teacher):

Task 1. Figure 5 shows a scheme of the qualitative reaction to the detection of promedol. Write diagrams of other qualitative reactions that are performed to detect promedol.

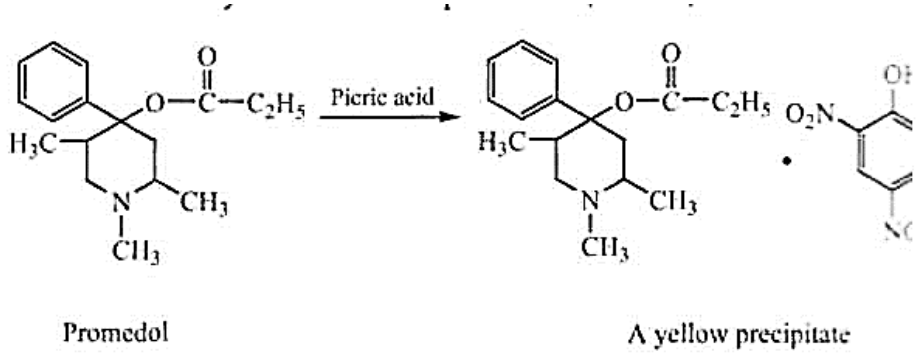
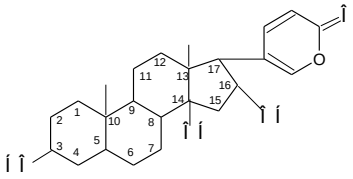


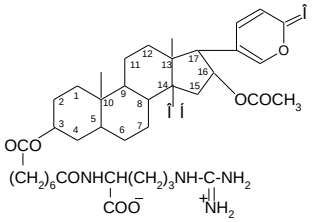
Figure 5.

The answer and its justification

Task 2. Figures 6 and 7 show the chemical formulas of bufotoxins. Analyze their chemical structures. What is the difference in the chemical structures of zootoxins?



Bufodienolide bufogenin (bufotalin)
Figure 6.



Bufotoxin
Figure 7.

The answer and its justification

An example of a task with an answer standard:

Metabolism of promedol.

Answer standard

Oxypiperidine derivatives as substances of a basic nature are absorbed mainly in the intestines, actively bind to proteins, which determines their ability to accumulate in the body. The drugs are localized in the brain, liver, and kidneys. They are excreted by the kidneys, they are found in the urine mainly in the form of metabolites. Metabolism of oxypiperidine derivatives takes place in the following directions: 1) N-demethylation; 2) oxidation (hydroxylation) of the aromatic fragment; 3) hydrolysis at the site of the ester group; 4) formation of conjugates with glucuronic acid or sulfates (Fig. 8):

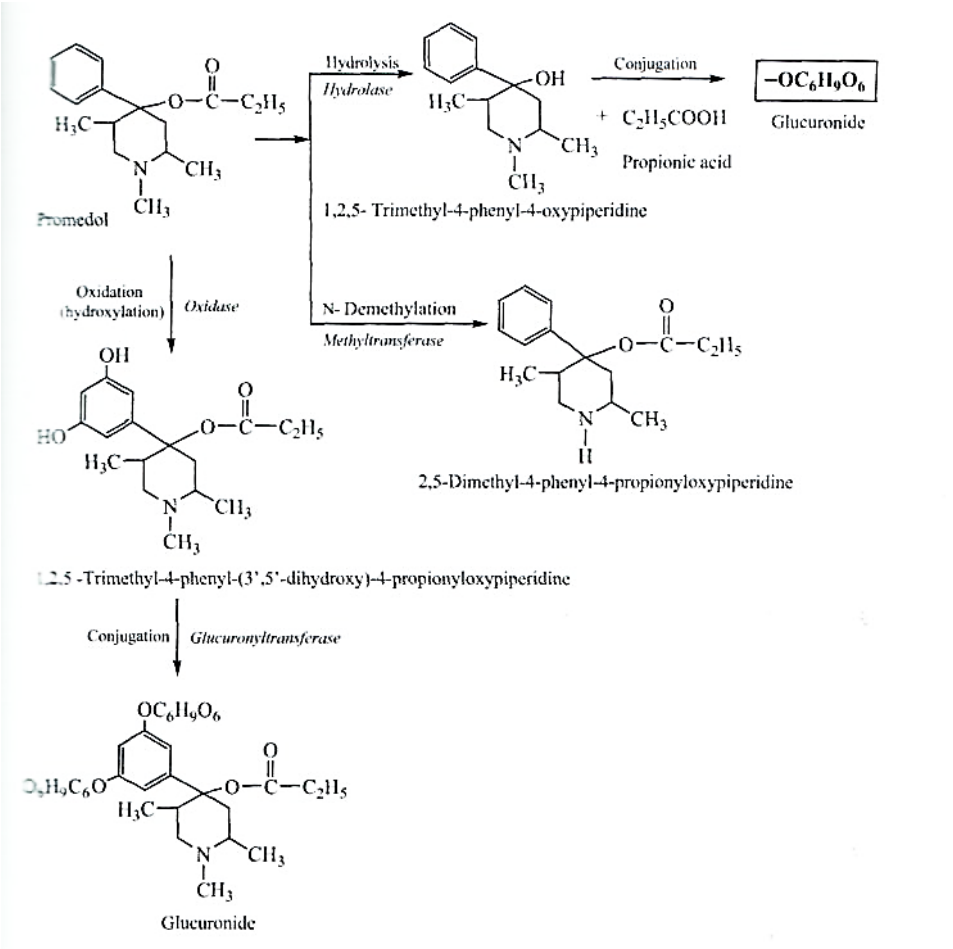


Figure 8.

An example of a task with an answer standard:

Toxicological value of tetrodotoxin.

Answer standard

Tetrodotoxin is one of the strongest known natural toxins, it is contained in the liver of some fugu fish (Fugu niphobles, Fugu ocellatus), the skin of frogs (*genus*

Atelopus), eggs of the California newt (*Taricha torosa*), molluscs (*Charonia saulinae, Babylonia japonica*). According to its chemical structure, tetrodotoxin is a derivative of 2-iminoperhydroquinazoline. It is a colorless crystalline substance that darkens at 220°C with decomposition without melting. The value of [a]25D is -8.6° in dilute acetic acid. It quickly decomposes when boiled in strongly acidic aqueous solutions (pH <2). The biological effect of tetrodotoxin resembles the neurotoxic effect of alkaloids of the curare group, causing paralysis of the respiratory muscles or the respiratory center. The tetrodotoxin molecule blocks the permeability of the membranes of neurons of the nervous system to Na+ ions, which almost instantly interrupts the nerve impulse. It is believed that this is due to the existence of a guanidine fragment in the quinazoline fragment of the tetrodotoxin molecule. The lethal dose for humans is approximately 0.01 mg/kg.

Control work No. 3 - on questions of topics 6-8.

List of questions for control work No. 3.

1. A group of substances that are isolated by extraction with polar solvents. General characteristics of the group. Physico-chemical properties, structure and effect on the body of poisonous and potent substances of organic nature.

2. Characteristics of the solvents most often used for isolation. Modern general and personal isolation methods with polar solvents (acidified alcohol, acidified water) V.P. Kramarenko, P.V. Valova, V.I. Popova

3. Methods of cleaning hoods from biological material from accompanying impurities. The choice of method depends on the condition, type and method of isolating poison from biological material.

4. Features of the metabolism of salicylic acid derivatives (aspirin, sodium salicylate, methyl salicylate, salicylamide).

5. Toxicological significance of salicylates.

6. Peculiarities of the metabolism of barbituric acid derivatives: barbamil, barbital, phenobarbital, sodium ethaminal, benzonal, hexenal.

7. Microcrystalloscopic reactions to barbiturates. What reagents are used to perform these reactions. Characteristics of final products.

8. Murexide test for barbiturates. What exactly barbiturates give this reaction? Schemes of reactions. Which barbiturates do not cause this reaction? Does this reaction belong to the express analysis?

9. Peculiarities of the metabolism of pyrazolone derivatives (analgin, antipyrine, butadione).

10. Peculiarities of the metabolism of purine derivatives (caffeine, theophylline, theobromine).

11. Methods of qualitative detection and quantitative determination of caffeine.

12. Methods of qualitative detection and quantitative determination of theobromine.

13. Methods of qualitative detection and quantitative determination of theophylline.

14. Peculiarities of the metabolism of tropane derivatives (atropine, scopolamine, cocaine, ecgonine).

15. When poisoned by which alkaloid of the tropane group, a drug addict develops a complex of symptoms called "crack dance"?

16. Peculiarities of the metabolism of quinoline derivatives (quinine, quinidine).

17. Oxyquinine and dioxyquinine are metabolites of quinine, which are formed by the oxidation of which cycle of the quinine molecule?

18. What metabolite is formed during the oxidation of the quinuclidine cycle of the quinine molecule?

19. Thaleiochin reaction. What compound is it used to detect? Does it refer to express analysis? Write a diagram.

20. Detection of quinine in urine (or blood plasma). Methodology of this experiment. What is this reaction called and why did it get that name?

21. Methods of qualitative detection and quantitative determination of atropine.

22. Methods of qualitative detection and quantitative determination of cocaine.

23. Methods of qualitative detection and quantitative determination of quinine.

24. Peculiarities of the metabolism of isoquinoline derivatives (morphine, codeine, papaverine).

25. Peculiarities of the metabolism of ephedrine and pseudoephedrine.

26. Peculiarities of heroin metabolism.

27. Methods of qualitative detection and quantitative determination of morphine.

28. Methods of qualitative detection and quantitative determination of codeine.

29. Methods of qualitative detection and quantitative determination of papaverine.

30. Methods of qualitative detection and quantitative determination of narcotics.

31. Methods of qualitative detection and quantitative determination of heroin.

32. Methods of qualitative detection and quantitative determination of ephedrine.

33. Methods of qualitative detection and quantitative determination of pseudoephedrine.

34.Toxicological characteristics of synthetic medicinal substances: phenothiazine derivatives (aminazine, diprazine, etmosine, levomepromazine, thioridazine).

35.Toxicological characteristics of synthetic medicinal substances: 1,4-benzodiazepine derivatives (chlordiazepoxide, diazepam, oxazepam, mezapam, phenazepam, nitrazepam, clonazepam).

36.Toxicological characteristics of synthetic medicinal substances: derivatives of p-aminobenzoic acid (novocaine, novocaineamide).

37.Toxicological characteristics of synthetic medicinal substances: oxypiperidine derivatives (promedol, prosidol).

38.Toxicological characteristics of synthetic medicinal substances: derivatives of 2-substituted propionic acid (ibuprofen).

39.Toxicological characteristics of synthetic medicinal substances: imidazoline derivatives (clofelin).

40.Peculiarities of the metabolism of phenothiazine derivatives (aminazine, diprazine, tizercin).

41.Peculiarities of the metabolism of p-aminobenzoic acid (*PABA*) derivatives (novocaine, dicaine, novocaineamide).

42.Peculiarities of the metabolism of 1,4-benzodiazepine derivatives (chlordiazepoxide, diazepam, oxazepam, nitrazepam).

43.Peculiarities of the metabolism of synthetic derivatives of 2-substituted propionic acid (ibuprofen).

44.Peculiarities of the metabolism of synthetic derivatives of imidazoline (clofelin).

45.Methods of qualitative detection and quantitative determination of tizercin.

46.Methods of qualitative detection and quantitative determination of ibuprofen.

47.Methods of qualitative detection and quantitative determination of nitrazepam.

48.Methods of qualitative detection and quantitative determination of diazepam.

49.Methods of qualitative detection and quantitative determination of oxazepam.

50.Methods of qualitative detection and quantitative determination of aminazine.

51.Methods of qualitative detection and quantitative determination of clofelin.

52.Methods of qualitative detection and quantitative determination of chlordiazepoxide.

53.Methods of qualitative detection and quantitative determination of diprazine.

54. Plant poisons (phytotoxins) - nicotine. Toxicological value, metabolism, methods of analysis.

55. Plant poisons (phytotoxins) - strychnine. Toxicological value, metabolism, methods of analysis.

56. Plant poisons (phytotoxins) - scopolamine. Toxicological value, metabolism, methods of analysis.

57. Plant poisons (phytotoxins) - cocaine. Toxicological value, metabolism, methods of analysis.

58. Plant poisons (phytotoxins) - aconitine. Toxicological value, metabolism, methods of analysis.

59. Plant poisons (phytotoxins) - quinine. Toxicological value, metabolism, methods of analysis.

60. Tetrodotoxin. Toxicological significance, methods of analysis.

61. Bufotoxins. Toxicological significance, methods of analysis.

62. Pumiliotoxins (A, B, C). Toxicological value, methods of analysis.

The methodical development was made by: professor of the department, doctor of pharm. sc. Welchinska O.V.

Topic N 9. Toxicological characteristics, methods of isolation and analysis of organophosphorus pesticides. Toxicological characteristics of "carbon monoxide" gas. Methods of detecting carboxyhemoglobin and carboxymyoglobin. Control work № 4.

Purpose: the ability to operate with the basic concepts of the topic and the implementation of the main stages of chemical and toxicological analysis of poisonous substances - organophosphorus pesticides, "carbon monoxide" gas.

The student must:

 to know the basic concepts, strategy and tactics of chemical and toxicological analysis of a group of poisonous substances - organophosphorus pesticides, "carbon monoxide" gas;

 to be able to propose a forensic toxicological research plan;

 to know the methods of isolation of poisonous substances - organophosphorus pesticides, "carbon monoxide" gas;

 evaluate the results of organoleptic control of extracts, preliminary tests;

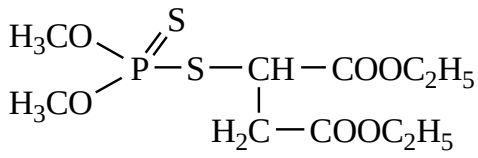
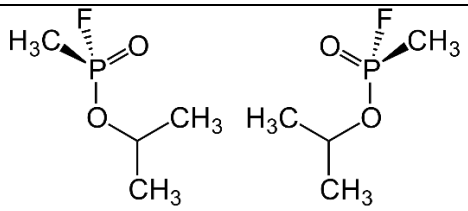
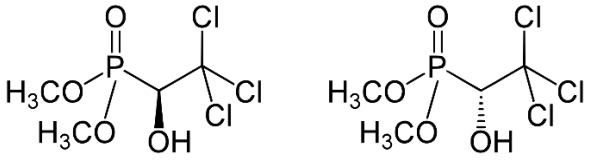
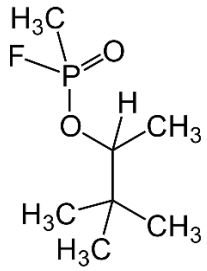
 to know methods of analysis of poisonous substances - organophosphorus pesticides, "carbon monoxide" gas;

 interpret the results of the analysis.

Basic concepts of the topic:

Term, parameter, characteristic	*Definition*

Pesticides	chemical means of combating harmful or unwanted microorganisms, plants and animals
Fungicides	means of combating fungi
Insecticides	means of controlling insects
Bactericides	means of combating bacteria
Molluscicides	means of fighting snails and slugs
Hormonal insecticides and chemosterilizers	interfere with normal development and reproduction
Desiccants	plants are dried
PhOC (PhOS)	organophosphorus compounds that are esters of phosphate acids: phosphate, pyrophosphate, thiophosphate, dithiophosphate, phosphonic
CO	"chargoal" gas, carbon (II) oxide

 Carbophos (derivative of dithiophosphoric acid)	 Sarin, *GB* (isopropyl ester of methylfluorophosphonic acid)
 Chlorophos (derivative of phosphonic acid)	 Soman, *GD* (pinacolone ester of methylfluorophosphonic acid)

Recommended literature:

Basic

1. Welchinska E.V. Toxicological and forensic chemistry (Criminal analysis). Poisonous substances and their biotransformation: textbook / E.V. Welchinska. — K.:

PE Lopatina O.O., ISBN 978-617-7533-02-2, 2017. — p. 293-317.
http://ir.librarynmu.com/handle/123456789/9123

2.Materials of Lecturers. The department of medicinal chemistry and toxicology of pharmaceutical faculty of Bogomolets NMU. https://www.youtube.com/@user-yj2fn5mz3x/

Auxiliary

1. *"About Pesticide Registration". Environmental Protection Agency. Jan 25, 2023. Retrieved 2023-12-13.*

2. Jump up to:*"Approval of active substances". European Commission. Retrieved 2023-12-13.*

Informational resources

European Pharmacopoeia online - pheur.edqm.eu

The British Pharmacopoeia 2021 - www.pharmacopoeia.com

The British Pharmacopoeia 2020. London.2020: I-1298. www.webofpharma.com

Pharmacopoea USP. www.usp.org.

Website of the Department of Medicinal Chemistry and Toxicology of O.O. Bogomolets

http://nmu.ua/zagalni-vidomosti/kafedri/kafedra-farmatsevtycheskoj-byologycheskoj-y-toksykologycheskoj-hymyy/

Distance learning platform LIKAR_NMU

https://likar.nmu.kiev.ua/

Official website of the Ministry of Health of Ukraine

https://moz.gov.ua/

International Journal of Medical Toxicology and Forensic Medicine **(IJMTFM).** https://journals.sbmu.ac.ir/ijmtfm

Journal of Synthetic Organic Chemistry, Japan. http://www.ssocj.jp/indexenglish.

Journal of Organic Chemistry, USA. https://doi.org/10.1021/acs.joc.0c02255.

Synthetic Communications. Great Britain. http://www.tandfonline.com/page/terms-and-conditions
pubmed.ncbi.nlm.nih.gov

www.cochrane.org

Questions for theoretical study:

1. Classification of pesticides by direction of application, toxicity, form of use, chemical structure. Classification of insecticides.

2. Objects of chemical and toxicological analysis for PhOS. Methods of separation of PhOS from corpse organs, biological fluids, food products. The choice of the extractant depends on the condition, the nature of the research object and the poison.

3. Selection of the method of cleaning hoods containing PhOS, depending on the nature and amount of substances.

4. Chemical methods of PhOS analysis in extracts from biological material. Detection by functional-active groups and hydrolysis products. Assessment of analysis results.

5. Detection and identification of PhOS in extracts from biological material by TLC, GC and HPLC methods. Assessment of analysis results.

6. Methods of quantitative determination of PhOS (photocolorimetric, photometric by phosphorus, planimetric, enzymatic, GLC method) and their comparative assessment.

7. Ways and means of prevention of pesticide poisoning. Methods and methods of providing first aid in case of pesticide poisoning of various groups. Antidote therapy for PhOS poisoning.

8. A group of poisonous substances that are determined directly in biological material — carbon monoxide (CO).

9. Physico-chemical properties, toxicological characteristics, mechanism of toxic action.

10. Acute poisoning and classification of carbon monoxide poisoning by degree of severity.

11. Detection of carboxyhemoglobin and carboxymyoglobin by chemical, spectroscopic and spectrophotometric methods.

12. Quantitative determination of carboxyhemoglobin and carboxymyoglobin by spectrophotometric and spectroscopic methods.

13. Methods of natural and artificial detoxification of the body in acute carbon monoxide poisoning.

Tasks for independent processing of the topic:

Test tasks

Choose and justify the correct answer.

1. For what purpose are fungicides used?

A. to combat fungi

B. to control nematodes

C. for borotua with bacteria

D. to control algae

2. What acid is chlorophos a derivative of?

A. phosphonate

B. phosphate

C. thiophosphate

D. dithiophosphate

3. Chlorophos is detected by reaction with o-tolidine. What color occurs with a positive result of this reaction?

A. orange

B. pink

C. yellow

D. purple

4. What is the name of the metabolite of parathion?

A. paraoxan

B. phenol

C. nitrophenol

D. benzene

5. As a result of which pesticide detection reaction is "molybdenum blue" formed?

A. reaction with ammonium molybdate

B. hydroperoxide test

C. with acetone

D. with p-tolidine

Enter in the cells ☐ the letters that indicate the correct answers to the test questions:

1-☐ 2-☐ 3-☐ 4-☐ 5-☐

Written assignments

Task 1. Figure 1 shows the scheme of chemical transformations. Explain the scheme. What transformations are taking place? Do these chemical reactions belong to qualitative detection reactions?

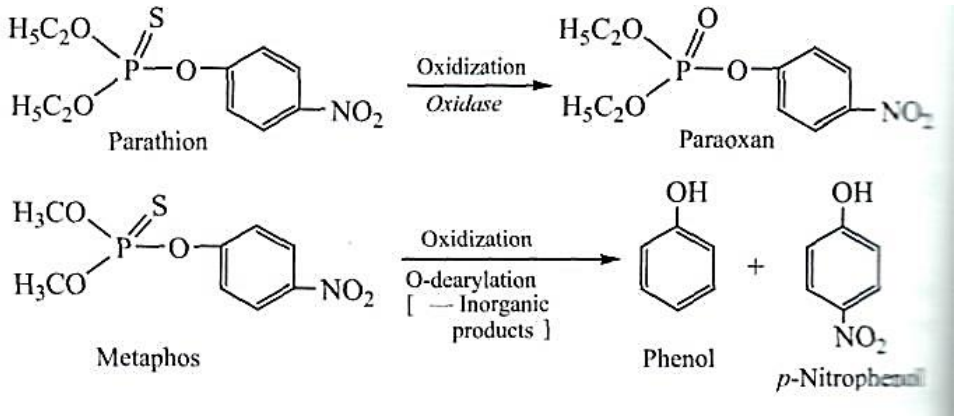


Figure 1.

The answer and its justification

Auditory collective work:

Task 1. Figure 2 shows a diagram of the qualitative response to PhS. Name the reaction. What reagents are used for this reaction?

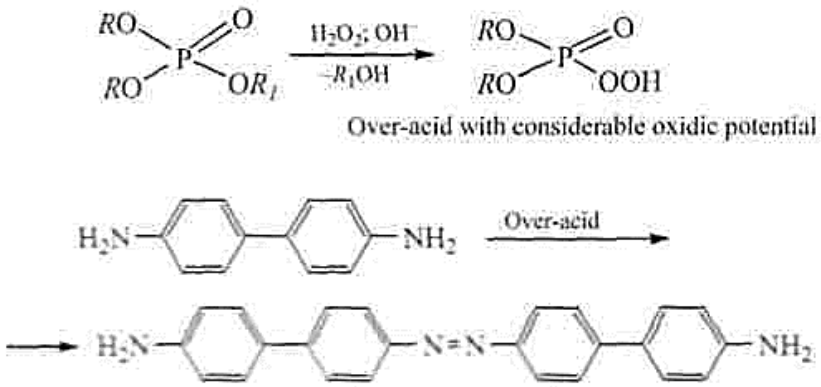


Figure 2.

The answer and its justification

Task 2. Toxicological value of Sarin. What are the symptoms of Sarin poisoning?

The answer and its justification

Auditory independent work (supervised by the teacher):

Task 1. Figures 3 and 4 show reaction schemes that are used to analyze carbon monoxide poisoning. Name the reactions.

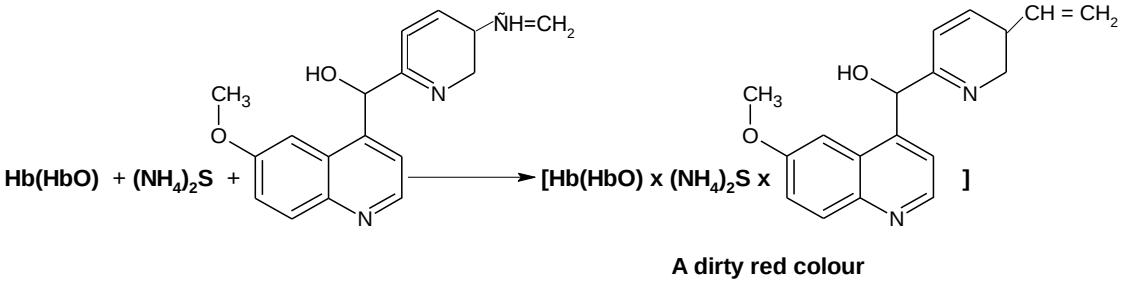


Figure 3.

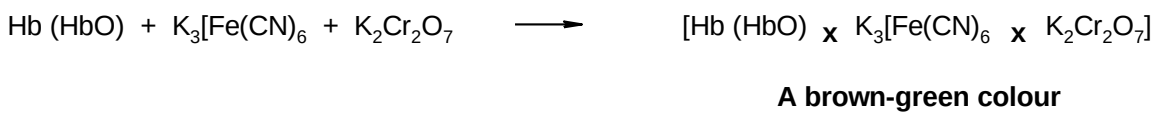


Figure 4.

The answer and its justification

An example of a task with an answer standard:

Hemoglobin compounds in blood and muscles.

Answer standard

Compounds of hemoglobin Symbols

Blood

Desoxyhemoglobin (free hemoglobin)	Hb
Oxyhemoglobin (compound of hemoglobin with O_2)	HbO
Carboxyhemoglobin (compound of hemoglobin with CO)	HbCO
Methemoglobin (not bound to CO)	HbMt
Muscles	
Desoxymyoglobin (free myoglobin)	HbM
Oxymyoglobin (compound of myoglobin with O_2)	HbOM
Carboxymyoglobin (compound of myoglobin with CO)	HbCOM

Control work No. 4 - on questions of topic 9.

List of questions for control work No. 4.

1. Classification of pesticides by direction of application, toxicity, form of use, chemical structure. Classification of insecticides.

2. Objects of chemical and toxicological analysis for PhS. Methods of separation of PhS from corpse organs, biological fluids, food products. The choice of the extractant depends on the condition, the nature of the research object and the poison.

3. Selection of the method of cleaning hoods containing PhS, depending on the nature and amount of substances.

4. Chemical methods of PhS analysis in extracts from biological material. Detection by functional-active groups and hydrolysis products. Assessment of analysis results.

5. Detection and identification of PhS in extracts from biological material by TLC, GC and HPLC methods. Assessment of analysis results.

6. Methods of quantitative determination of PhS (photocolorimetric, photometric by phosphorus, planimetric, enzymatic, GLC method) and their comparative evaluation.

7. Ways and means of prevention of pesticide poisoning. Methods and methods of providing first aid in case of pesticide poisoning of various groups. Antidote therapy for PhS poisoning.

8. A group of poisonous substances that are determined directly in biological material — carbon monoxide (CO).

9. Physico-chemical properties, toxicological characteristics, mechanism of toxic effect of CO.

10. Acute poisoning and classification of carbon monoxide poisoning by degree of severity.

11. Detection of carboxyhemoglobin and carboxymyoglobin by chemical, spectroscopic and spectrophotometric methods.

12. Quantitative determination of carboxyhemoglobin and carboxymyoglobin by spectrophotometric and spectroscopic methods.

13. Methods of natural and artificial detoxification of the body in acute carbon monoxide poisoning.

14. Reaction with sodium hydroxide (Hoppe-Zeyler test).

15. Reaction with ammonium sulfide (Salkovsky-Katayama test).

16. Reaction with quinine and ammonium sulfide (Khoroshkevich-Marx test).

17. Reaction with potassium hexacyanoferrate (III) (Burger's test).

18. Reaction with potassium hexacyanoferrate (III) and potassium dichromate (Sidorov's test).

19. Reaction with potassium hexacyanoferrate (III) and acetic acid (Wetzel's test).

20. Reaction with tannin (Kunkel-Wetzel test).

21. Reaction with formaldehyde (Libman test).

22. Reaction with lead acetate (Rubner's test).

23. Reaction with cuprum sulfate (Zalessky test).

The methodical development was made by: professor of the department, doctor of pharm. sc. Welchinska O.V.

Topic N 10. Combat poisonous substances. Classification. Toxicological value. Peculiarities of chemical and toxicological analysis. *Differential control.*

Purpose: the ability to operate with the basic concepts of the topic regarding the main stages of the chemical and toxicological analysis of combat poisonous substances.

The student must:

 to know the basic concepts, strategy and tactics of chemical and toxicological analysis of combat poisonous substances;

 to be able to propose a forensic toxicological research plan;

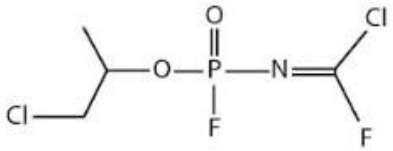
 to know the methods of isolation of combat poisonous substances;

 to know the methods of analysis of combat toxic substances.

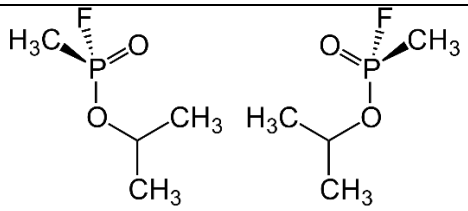
Basic concepts of the topic:

Term, parameter, characteristic	*Definition*
CPS	Combat Poisonous Substances

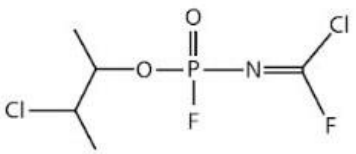
CWA	Chemical Warfar Agents
Nerve-paralytic combat poisons, organophosphorus poisons (PhOP)	nerve gases are in a liquid state at room temperature
Series G	is the first and oldest in the family of nerve agents: GA (tabun), GB (sarin), GD (zoman), GF (cyclosarin)
Series V	is the second family of nerve agents: VE, VG, VM, VR and VX
Chemical weapons	a type of weapon of mass destruction, which is based on the toxic properties of chemical substances, where the main components are poisonous substances
Vesicants	chemicals that cause blistering (vesicles) and include mustards, including Sulfur mustard and Nitrogen mustard
Systemic asphyxiants	is a type of chemical substance used in chemical warfare, cause suffocation (asphyxia)
CWA with nerve-paralytic effect	are chemicals used in chemical warfare that act directly on nerve synapses, usually by increasing the activity of acetylcholine
CWA generally poisonous	act when victims inhale their vapors; damage by hydrocyanic acid may also occur if it enters the gastrointestinal tract in the form of liquid or salts (hydrocyanic acid, cyanide)
CWA of psychochemical action	psychoactive substances that are used in combat to damage enemy personnel, causing temporary incapacitation (LSD, bufotenin, psilocin, mescaline)

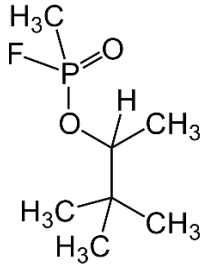


Novichok -5 (A-232)

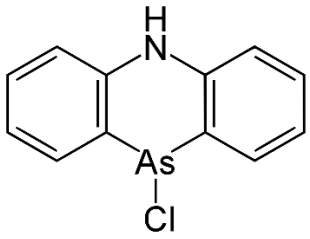
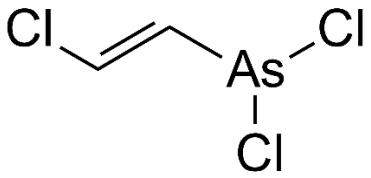


Sarin, *GB*
(isopropyl ester of methylfluorophosphonic acid)





Soman, *GD*

Novichok-7 (A-234)	(pinacolone ester of methylfluorophosphonic acid)
 Adamsite (diphenylaminechloroarsine)	 Lewisite (L, [E-2-Chloroethen-1—yl]arsonous dichloride)

Recommended literature:

Basic

1.Welchinska E.V. Toxicological and forensic chemistry (Criminal analysis). Poisonous substances and their biotransformation: textbook / E.V. Welchinska. — K.: PE Lopatina O.O., ISBN 978-617-7533-02-2, 2017. — p. 293-317. http://ir.librarynmu.com/handle/123456789/9123

2.Materials of Lecturers. The department of medicinal chemistry and toxicology of pharmaceutical faculty of Bogomolets NMU. https://www.youtube.com/@user-yj2fn5mz3x/

Auxiliary

1. Caio H. P. Rodrigues, Lívia S. Mariotto, Aline T. Bruni. Acute, chronic, and *post-mortem* toxicity: a review focused on three different classes of new psychoactive substances. *Forensic Toxicology*. V. 41,187–212 (2023).

2. Marine Deville & Corinne Charlier. Cannabidiol in urine is not a proof of CBD consumption—lesson learned from urine sample analysis in routine caseworks**.** *Forensic Toxicology*. V. 41,213–220 (2023)**.**

3. Keunhong Jeong, Junwon Choi. Theoretical study on the toxicity of 'Novichok' agent candidates // Royal Society Open Science. — 2019. — Т. 6, вип. 8 (7 серпня). — DOI:10.1098/rsos.190414.

*4.*Steindl, David; Boehmerle, Wolfgang; Körner, Roland; Praeger, Damaris; Haug, Marcel; Nee, Jens; Schreiber, Adrian; Scheibe, Franziska; Demin, Katharina; Jacoby, Philipp; Tauber, Rudolf (22 грудня 2020). Novichok nerve agent poisoning. The Lancet. *doi:10.1016/s0140-6736(20)32644-1. ISSN 0140-6736. Архів оригіналу за 23 січня 2021.*

5."Nerve Agent Treatment – Autoinjector Instructions – CHEMM". chemm.nlm.nih.gov. Retrieved 27 July 2020.

6."NERVE AGENTS". 3 September 2018. Archived from the original on 3 September 2018. Retrieved 27 July 2020.

Informational resources

European Pharmacopoeia online - pheur.edqm.eu

The British Pharmacopoeia 2021 - www.pharmacopoeia.com

The British Pharmacopoeia 2020. London.2020: I-1298. www.webofpharma.com

Pharmacopoea USP. www.usp.org.

Website of the Department of Medicinal Chemistry and Toxicology of O.O. Bogomolets

http://nmu.ua/zagalni-vidomosti/kafedri/kafedra-farmatsevtycheskoj-byologycheskoj-y-toksykologycheskoj-hymyy/

Distance learning platform LIKAR_NMU

https://likar.nmu.kiev.ua/

Official website of the Ministry of Health of Ukraine

https://moz.gov.ua/

International Journal of Medical Toxicology and Forensic Medicine **(IJMTFM).** https://journals.sbmu.ac.ir/ijmtfm

Journal of Synthetic Organic Chemistry, Japan. http://www.ssocj.jp/indexenglish.

Journal of Organic Chemistry, USA. https://doi.org/10.1021/acs.joc.0c02255.

Synthetic Communications. Great Britain. http://www.tandfonline.com/page/terms-and-conditions
pubmed.ncbi.nlm.nih.gov

www.cochrane.org

Questions for theoretical study:

1. Classifications of toxic warfare agents (CWA).

2. Give the chemical formulas of the representatives of the "nerve paralytic agents (PhOS)" series: V, G, A: Zarin, Zoman, Tabun, Vi-gaz. Name the functional groups in the molecules of these compounds. On what reactions is the functional analysis of these compounds based?

3. What methods are used to determine Phosphorus in the molecules of

representatives of the "nerve-paralytic agents (PhOS)" group?

4. Give the chemical formulas of representatives of the "irritants" group: Chlorpicrin, 1-chloroacetophenone, etc. Name the functional groups in the molecules of these compounds. On what reactions is the functional analysis of these compounds based?

5. What methods are used to determine halogens in molecules of representatives of the "irritants" group?

6. Give the chemical formulas of representatives of the "vesicants" group: Mustard (H, HD), Lewisite (L), Methyldichloroarsine (MD), Phosgene-oxime (CX), etc. Name the functional groups in the molecules of these compounds. On what reactions is the functional analysis of these compounds based?

7. What methods are used to determine Sulfur and Arsenic in the molecules of representatives of the "vesicants" group?

9. Lewisite. Peculiarities of chemical structure, toxicological significance and methods of analysis.

10. Mustard (mustard gas). Peculiarities of chemical structure, toxicological significance and methods of analysis.

11. Adamsite. Peculiarities of chemical structure, toxicological significance and methods of analysis.

12. Cyanides. Peculiarities of chemical structure, toxicological significance and methods of analysis.

13. Asphyxiating CWA: phosgene, diphosgene. Peculiarities of chemical structure, toxicological significance and methods of analysis.

14. Organomercury CWA. Peculiarities of chemical structure, toxicological significance and methods of analysis.

15. Ricin. Peculiarities of chemical structure, toxicological significance and methods of analysis.

16. Chlorocyan. Peculiarities of chemical structure, toxicological significance and methods of analysis.

17. Qualitative reactions to Chlorine.

18. Qualitative reactions to Mercury.

Tasks for independent processing of the topic:

Test tasks

Choose and justify the correct answer.

1. To which class of chemicals does CWA "Novichok" belong?

A. carbonimidic phosphorus halides

B. phosphorus-containing heterocycles

C. phosphorus-containing arenes

D. phosphorus-containing acetylenes

2. Sarin is an ether of which acid?

A. phosphonate

B. phosphate

C. thiophosphate

D. dithiophosphate

3. Zoman is a pinacolinic ether of methylfluorophosphonate acid. Name the alkyl radical that is contained in the structure of the molecule.

A. pinacolil

B. ethyl

C. ethenyl

D. propyl

4. Which of the CWA refers to irritants?

A. cyanide

B. sarin

C. soman

D. CS

5. Mustard belongs to the class of vesicants. What is the negative effect of vesicants on the human body?

A. formation of blisters (vesicles)

B. cause asphyxiation

C. cause yellowing of the skin

D. lead to a state of coma

Enter in the cells ☐ the letters that indicate the correct answers to the test questions:

1-☐ 2-☐ 3-☐ 4-☐ 5-☐

Written assignments

Task 1. Figure 1 shows the chemical formula of CWA (in the form of two isomers). Name the trivial name of BOR if its chemical names are: cyanophosphate acid ethyl ester dimethylamide, N,N-dimethylamide-O-ethylcyanophosphate?

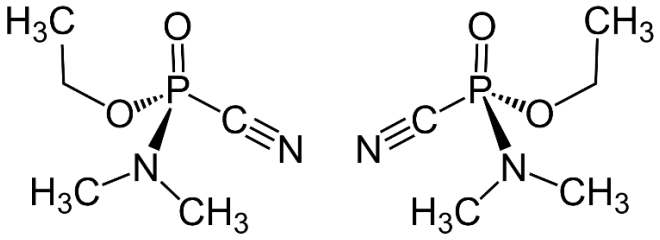


Figure 1.

The answer and its justification

Auditory collective work:

Task 1. Figure 2 shows the synthesis scheme of organophosphorus BOR - zoman. The same synthesis scheme as for sarin is suitable for zoman. Name the original compounds that, as a result of the interaction, form a zoman molecule.

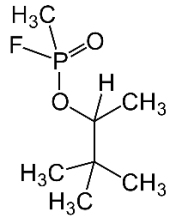
$CH_3P(O)F_2 + CH_3CH(OH)C(CH_3) \rightarrow$ 

Figure 2.

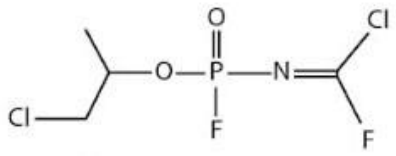
The answer and its justification

Task 2. Toxicological significance of Soman. What are the symptoms of Soman poisoning?

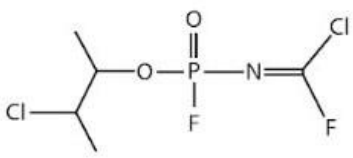
The answer and its justification

Auditory independent work (supervised by the teacher):

Task 1. Figures 3 and 4 show the chemical formulas of the A-232 and A-234 combat poison "Novichok". Name the differences in the chemical formulas of related molecules.



Novichok -5 (A-232)
Figure 3.



Novichok-7 (A-234)
Figure 4.

The answer and its justification

An example of a task with an answer standard:
Classification of CWA according to the physiological effect on the body.

Answer standard

According to the physiological classification, combat poisonous substances are divided into:

1. Nerve-paralytic (organophosphorus compounds): sarin, zoman, tabun, VX;

2. General poisons: hydrocyanic acid, chlorocyanine, ricin;

3. Suffocating: phosgene, diphosgene;

4. Skin abscesses: mustard gas, nitrogen mustard gas, Lewisite;

5. Incapacitants (non-lethal action)

The methodical development was made by: professor of the department, doctor of pharm. sc. Welchinska O.V.