



**MINISTRY OF HEALTH OF UKRAINE
NATIONAL UNIVERSITY OF PHARMACY
Faculty for Foreign Citizens' Education
Department of Medicinal Chemistry**

TOXICOLOGICAL CHEMISTRY

(the name of educational component)

**WORK PROGRAM
of educational component**

training for Master
(Higher Educational Level Name)

in specialty 226 Pharmacy, industrial pharmacy
(Code and Specialty Name)

field of knowledge « 22 Public Health
(Code and Knowledge Field Name)

of educational program Pharmacy
(Educational Program Name)

in specialization(s) 226.01 Pharmacy
(name of specialization, if available)

The work program of the educational component **Toxicological chemistry** in specialty 226 Pharmacy, industrial pharmacy educational program **Pharmacy** in specialization(s)_____for applicants for higher education 4 year of study.

EDUCATIONAL COURSE TEAM:

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Work program has been considered and approved at the Department meeting of Medicinal Chemistry

Record from «23» August 2023 № 1

Head of the Department



(sig.)

prof.

Lina PEREKHODA

(first name LAST NAME)

Work program has been approved at the meeting of the Methodical Commission of of the chemical disciplines

Record from «5» September 2023 № 1

Head of Specialized Committee



(sig.)

prof. Viktoriia GEORGIYANTS

(first name LAST NAME)

1. The Description of the the educational component

Language of the study: English

Status of the educational component: Toxicological Chemistry is an optional discipline. It is professionally oriented, complex discipline in the system of higher pharmaceutical education. The discipline forms the basis of expert thinking, promotes the development of skills in the field of Forensic and Clinical Toxicology (the Forensic-Toxicological Laboratory of Bureau of forensic-medical examinations, the Emergency Centre for acutely poisoned patients, the Industrial Sanitary Laboratory which performs industrial and ecological supervision, the Toxicological Laboratory for Diagnostics of drug abuse and alcoholism). The discipline gives the methodical basis for preparation of pharmacists specializing in the fields of biopharmacy, farmaco- and toxicokinetics, clinical pharmacy. Without the knowledge of the poisonous substance metabolism, mechanism of toxicity, methods of determination of toxicants in biological samples it is impossible to search for safe biologically active substances, medicines for effective specific antidote therapy, to carry out toxicological diagnostics of fatal poisonings.

Prerequisites for studying the educational component: Toxicological Chemistry is based on the study of physical and chemical properties of inorganic and organic substances (courses of Inorganic, Organic and Analytical chemistry), biochemical processes occurring in the body (the course of Biochemistry), structure of organs, body systems and their disorders (courses of Anatomy, Physiology, Pathology and Pharmacology) and integrates with these disciplines.

The subject of educational component study «Toxicological Chemistry» is definition of a complex of toxicometric parameters characterizing the degree of toxicity and the risk of poisoning; study of mechanisms of toxicity of medicinal substances (toxicodynamics); study of medicinal substance distribution in a body, biotransformation and excretion of drugs (toxicokinetics); the theoretical and practical aspects of isolation, identification, quantitative determination of poisonous substances in various samples in the case of forensic and clinical toxicology studies.

Information content of the educational component. 4 ECTS credit 120 hours are assigned to the study of the educational component.

2. Objectives and tasks of the educational component

The purpose of teaching the educational component «Toxicological Chemistry» is to master the abilities for estimation of the safety of potent medicinal substances, the skills for performing the forensic toxicological examinations and the studies in the field of clinical toxicology.

The main tasks of the educational component «Toxicological Chemistry» is to provide the student with a set of knowledge about the causal relationship between the fact of the action of drugs and the development of toxic effects; to provide the basic knowledge of application, toxicity, chemical structure and physicochemical properties, toxicodynamics and toxicokinetics, isolation from the biological samples and analysis (detection with an appropriate screening procedure, identification and quantitative determination with the help of chemical and physicochemical methods) of the specific groups of toxicants: Heavy metal compounds, Volatile toxic substances, Pesticides (organophosphorus, chlorinated pesticides, carbamates, pyrethrins, organic mercurial compounds), Drugs (salicylates, barbiturates, pirazolones, acetaminophen, cannabinoids, 1,4-benzodiazepines, phenothiazines, derivatives of *p*-aminobenzoic acid, alkaloids, synthetic opioids and phenylalkylamines); basic normative documents which regulate the forensic toxicological and clinical toxicological examinations; to master the skills in sample preparation, methods of poisonous substance isolation from biological fluids and biological material, identification and quantitative determination by chemical and physicochemical methods; teaching to work independently with educational and special literature at the decision of the professional tasks related to the forensic-toxicological analysis and express-diagnostics of the acute poisoning; teaching to document the results of forensic-toxicological examination (processing rules of the laboratory workbook, act of forensic-toxicological examination).

3. Competence and planned educational outcomes

Educational component «Medical and Analytical Toxicology» ensures the acquisition of applicants for higher education the following competences:

Integral:

Ability to solve typical and complex specialized tasks and critically comprehend and solve practical problems in the professional pharmaceutical and/or research and innovation activity using provisions, theories and methods of the fundamental, chemical, technological, biomedical, socio-

economic science; integrate knowledge and solve complex issues, formulate judgments in the presence of incomplete or limited information, clearly and unambiguously to convey their conclusions and use their knowledge, reasonably substantiating them, to professional and non-professional audience.

Soft- skills / General competences (GC):

GC 11. Ability to assess and ensure the quality of performed work.

Hard-skills / Professional (special) competences (PC):

PC 6. Ability to identify medications, xenobiotics, toxins and their metabolites in body fluids and tissues, to conduct chemical and toxicological tests to diagnose acute poisoning, drug and alcohol intoxication.

PC 15. Ability to organize and participate in the production of medications in the context of pharmaceutical companies, including the selection and justification of the technological process, equipment in accordance with the requirements of Good Manufacturing Practice (GMP) with the appropriate development and design of the necessary documentation. Determine the stability of medications.

PC 20. Ability to develop methods for quality control of medications, including active pharmaceutical ingredients, medicinal plant raw materials and excipients using physical, chemical, physicochemical, biological, microbiological, pharmacotechnological and pharmacoorganoleptic control methods.

Integrative final program learning outcomes (PLO), the formation of which is facilitated by the educational component:

PLO 16. To determine the influence of factors influencing the processes of absorption, distribution, deposition, metabolism and excretion of the drug and due to the condition, features of the human body and physico-chemical properties of medications.

PLO 17. To use clinical, laboratory and instrumental research data to monitor the efficacy and safety of medicines.

PLO 18. To select biological objects of analysis, to carry out the definition of xenobiotics and their metabolites in biological environments and to estimate the received results taking into account their distribution in an organism.

As a result of studying the educational component, the applicant for higher education will be *know*:

- toxicological characteristics of traditional and new drugs, relationship between mechanism of action and possible toxic effects of drugs;
- manifestations of drug toxic effects, symptoms of overdose, methods of their prevention and the principles of treatment;
- subject, tasks and main sections of analytical toxicology, the field of its application;
- theoretical bases of methods for isolation poisonous substances from the biological samples, their identification and quantitative determination by chemical and physicochemical methods; basic normative documents which regulate the forensic-toxicological and chemical- toxicological analysis;

be able to:

- predict the effects of drug interactions when combining medicines, a medicine and components of food, a medicine and alcohol;
- to search for information on the safe use of medicines in modern reference books, scientific and professional periodicals;
- provide a comparative characteristic of drugs for safety indicators;
- analyze data from educational and special literature in solving the professional tasks related to forensic and toxicological analysis;
- isolate the poisonous substances and their metabolites from the biological samples (isolation, purification, concentration);
- detect, identify and quantify the poisons isolated by means of chemical, biochemical and physicochemical methods;
- document the results of forensic-toxicological examination.

possess:

- methods of using the basic concepts and laws of chemistry, the results of independent search, analysis and synthesis of information from various information sources for the solution of applied problems;
- technologies of independent activity and self-control, generalization and systematization of information obtained as a result of scientific research, for solving typical tasks of professional activity.

4. The educational component structure

Names of content modules and topics	The amount of hours			
	full time study			
	the whole amount	including		
1		lab	self-study	
<i>1</i>	2	3	4	5
Content module 1. Biochemical and analytical aspects of toxicology of heavy metals, volatile poisons, nitrites and nitrates				
Topic 1. The subject of toxicological chemistry. Definition of basic concepts and terms of biochemical toxicology and analytical toxicology.	7	1	2	4
Topic 2. Biochemical and analytical aspects of heavy metal toxicology. Sample preparation of the biological samples by mineralization. Detection of lead, barium, manganese, chromium in the mineralizate by the fractional method.	7	1	2	4
Topic 3. Detection of silver, copper, zinc, bismuth, thallium, antimony, arsenic in the mineralizate by the fractional method.	8	-	4	4
Topic 4. Inorganic mercury compounds. Human exposure and health effects. Analytical aspects. Sample preparation. Detection of mercury in the destructate by the fractional method. Quantitative determination of heavy metals in biological samples.	8	-	4	4
Topic 5. Toxicology of toxic gases: hydrogen cyanide, formaldehyde, carbon (II) oxide. Sample preparation when examining biological samples for the presence of volatile poisons. Detection of cyanide and formaldehyde in the distillates by a chemical method.	9	1	4	4
Topic 6. Biochemical and analytical aspects of toxicology of organic solvents and some cauterizing substances. Examination of body fluids for the presence of alcohols by gas-liquid chromatography.	8	-	4	4
Topic 7. Biochemical and analytical aspects of nitrite, nitrate toxicology.	6	-	2	4
<i>Final test of CM 1 assimilation.</i>	7		2	5
The whole amount of hours for the content module 1	60	3	24	33
Content module 2. Biochemical and analytical aspects of toxicology of drugs and pesticides				
Topic 8. Toxicological aspects of opioid analgesics and hypnotics application. Methods of sample preparation in chemical-toxicological analysis of drugs.	9	1	4	4
Topic 9. Toxicological aspects of non-opioid analgesics and non-steroidal anti-inflammatory drugs application. Toxicological screening of drugs with thin layer chromatography.	8	1	4	3
Topic 10. Examination of the acid chloroform extract for derivatives of barbituric and salicylic acids, pyrazolone, purine.	7	-	4	3
Topic 11. Examination of the basic chloroform extract for alkaloids.	7	-	4	3
Topic 12. Toxicological aspects of neuroleptics, tranquilizers and local anesthetics application. Examination of the basic chloroform extract for derivatives of 1,4 benzodiazepine, phenothiazine, <i>p</i> -aminobenzoic acid.	8	1	4	3
Topic 13. Quantitative determination of drugs in the extracts. Examination of body fluids for drugs in acute intoxications.	7	-	4	3

Topic 14. Biochemical and analytical aspects of pesticide toxicology.	7	-	4	3
<i>Final test of CM 2 assimilation</i>	7	-	2	5
The whole amount of hours for the content module 2	60	3	30	27
Semester credit	-	-	-	-
<i>The whole amount of hours for the course</i>	120	6	54	60

5. Contents of the educational component

Content module 1. Biochemical and analytical aspects of heavy metals and metalloids, organic solvents, cauterizing agents and toxic gaseous substances

Topic 1. The subject of toxicological chemistry. Definition of basic concepts and terms of biochemical toxicology and analytical toxicology.

The content toxicological chemistry and its sections. Definition of the terms "poisoning" and "poison". General principles of classifications of poisons: by the chemical structure, by the usage by the toxicity rate (hygienical), by the nonorgan directed toxicity (toxicological), by the target organ toxicity, by the methods of isolation from biological material.

Classification of poisonings by the origin, by the features of clinical development (acute, chronic, subacute poisonings), by the routes of administration an organism; nosological classification. Drug abuse.

Fundamental concepts of General Toxicology: Toxicodynamics, Toxicokinetics. Types of toxic effects. Types of doses. Routes of administration, absorption, distribution, metabolism and excretion of toxicants in the body. The first and the second metabolism phases. Lethal synthesis.

Analytical Toxicology, the subject and basic assignments (Analytical Forensic Toxicology, Analytical Clinical Toxicology, Environmental Toxicology). History of development of Analytical Toxicology. Forensic science services and forensic toxicology testing. Special features of chemicotoxicological analysis. The kinds of samples for toxicological examinations, their method of preservation. Specimen collection, sending, reception and storage. Order of performance and documentation of forensic-toxicological examinations. Analytical testing scheme design. Specimen testing, external examination and preliminary tests. General principles of interpretation of results of forensic-toxicological examinations

Topic 2. Biochemical and analytical aspects of heavy metal toxicology. Sample preparation of the biological samples by mineralization. Detection of lead, barium, manganese, chromium in the mineralizate by the fractional method.

General description of the group. Usage and toxicity of heavy metal compounds. Causes of intoxications. Decontamination at acute intoxications. Antidote therapy at poisonings by heavy metals.

Theoretical basic of the necessity of the biological material mineralization at toxicological examination for «metallic» poisons. Description of the modern general and special mineralization methods. Choice of the method depending on the properties of the sample and «metallic» poison being detected. Denitration of mineralizate.

Fractional method of the mineralizate analysis. Theoretical base. The scheme of the fractional method of mineralizate analysis (by Krylova). Description of reagents used in the fractional method for masking the interfering ions, separation and detection of «metallic» poisons. Detection of lead, barium, manganese, chromium in the mineralizate by the fractional method.

Topic 3. Detection of silver, copper, zinc, bismuth, thallium, antimony, arsenic in the mineralizate by the fractional method.

Detection of silver, copper, zinc, bismuth, thallium, antimony, arsenic in the mineralizate by the fractional method. Characteristic of the organic reagents used in the fractional method for detection of «metallic» poisons..

Physical-chemical methods used for identification of «metallic» poisons: atom-absorption spectrophotometry (AAS), atom-emission spectrophotometry (AES), X-ray fluorescence method, ICP-AES and ICP-MS.

Topic 4. Inorganic mercury compounds. Human exposure and health effects. Analytical aspects. Sample preparation. Detection of mercury in the destructate by the fractional method. Quantitative determination of heavy metals in biological samples.

Physical and chemical properties of mercury and its inorganic compounds, usage, toxicity, accumulation in the body, causes of intoxications. Special isolation method of inorganic mercury compounds from the biological material. Detection of mercury in the destructure by the fractional method.

Methods of quantitative analysis of «metallic» poisons the mineralizate. Physical-chemical methods used for quantitative determination of «metallic» poisons: spectrophotometry in visible region of the spectrum and photolorimetry, atomic spectroscopy.

Topic 5. Toxicology of toxic gases: hydrogen cyanide, formaldehyde, carbon (II) oxide. Sample preparation when examining biological samples for the presence of volatile poisons. Detection of cyanide and formaldehyde in the distillates by a chemical method.

General description of hydrocyanide and cyanides, formaldehyde. Physical and chemical properties, usage and toxicity. Causes of intoxications. Decontamination at acute intoxications. Antidote therapy at poisonings by cyanides.

Methods of isolation of «volatile» poisons from the biological samples. Steam distillation, dry distillation. Analysis of the distillate by the chemical method. Types of chemical reactions, used the analysis, estimation of their sensitiveness and specificity. Detection of cyanide and formaldehyde in the distillates by a chemical method.

Charcoal gas (carbon monoxide). Toxicological significance, physical and chemical properties, toxicity, analysis of blood for presence of charcoal gas by chemical and spectrophotometry methods.

Hydrogen sulphide. Physical and chemical properties, toxicity, reasons of poisonings, detection of hydrogen sulphide in biological samples.

Topic 6. Biochemical and analytical aspects of toxicology of organic solvents and some cauterizing substances. Examination of body fluids for the presence of alcohols by gas-liquid chromatography

General description of chlorinated hydrocarbons (chloroform, tetrachloromethane, dichloroethane, chloral hydrate). Physical and chemical properties, usage and toxicity. Causes of intoxications. Decontamination at acute intoxications. Detection of chlorinated hydrocarbons in the distillates by a chemical method.

General description of alcohols (methanol, ethanol, isopentanol, ethylene glycol) and ketones (acetone). Physical and chemical properties, usage and toxicity. Causes of intoxications. Decontamination at acute intoxications. Antidote therapy at poisonings by methanol and ethylene glycol. Detection of methanol, ethanol, isopentanol, ethylene glycol and acetone in the distillates by a chemical method.

Analytical diagnostics of the alcoholic intoxication. Procedure for conducting, selection and storage of samples, determination of ethanol in the biological fluids by the GLC method, sample preparation with the use of the vapor phase analysis method and its modification - the alkyl nitrite method. Stages of ethanol poisoning according to its concentration in the blood and clinical manifestations of intoxication. The concept of the national levels of blood alcohol concentration for the drivers (BAC). Methods for detecting ethanol in exhaled air (indicator tubes Mochova-Shynkarenko, portable devices with an electrochemical detector, in which ethanol is oxidized to acetaldehyde (alcoholmeters), ethanol-IR analyzers and their evaluation by specificity. Features of postmortem ethanol redistribution.

Physical and chemical properties of monoatomic phenols (phenol, crezols), carboxylic acids (acetic acid). Usage and toxicity. Causes of intoxications. Decontamination at acute intoxications. Detection of phenol and acetic acid in the distillates by a chemical method.

Usage, toxicity of nitric, sulphuric, hydrochloric acids, alkalis (hydroxides of sodium, potassium, ammonium, calcium). Special features of isolation of acids, alkalis, from the samples of biological origin. Methods of purification, usage of dialysis and osmosis phenomena for this purpose. Methods of detection of acids, alkalis, and their quantitative determination.

Topic 7. Biochemical and analytical aspects of nitrite, nitrate toxicology.

Salts of nitrate and nitrogenous acids (nitrate, nitrite). Use in the national economy and medicine. Causes of poisoning, biotransformation in the body. The mechanism of toxic action of nitrites. Antidote therapy at poisonings by nitrite. Isolation of nitrite and nitrate from the samples of biological origin. Detection of nitrate, nitrite and their quantitative determination.

Content module 2. Biochemical and analytical aspects of toxicology of drugs and pesticides.

Topic 8. Toxicological aspects of opioid analgesics and hypnotics application. Methods of sample preparation in chemical-toxicological analysis of drugs.

Toxicology of narcotic analgesics of natural and semi-synthetic origin (morphine, codeine, omponon, ethylmorphine), synthetic origin (fentanyl, tramadol, buprenorphine, butorphanol). Toxicodynamics and toxicokinetics of NA. The range of therapeutic and toxic doses for NA. The targets of NA toxic action are - GIT, CVS, CNS, respiratory system. Acute poisoning by narcotic analgetics. A concept about drug addiction, morphinism, abstinence syndrome. Basic mechanisms of NA toxic effects development. Properties of NA, which influence on their toxicity. Factors which influence on NA toxicity. Specific forms of NA toxicity. Algorithm of the first aid in case of NA poisoning. Specific antidotes of Morphinum are Naloxonum and Naltrexonum. A role of a pharmacist in prevention of NA toxic effects.

Toxicological features of hypnotic medicines: derivatives of barbituric acid, benzodiazepine. Specific toxicity of barbiturates. Range of therapeutic and toxic doses.

Modern general and special methods of drug isolation from the biological material, their advantages and disadvantages, comparative estimation, the main stages.

Methods of purification and separation of toxic substances from endogenous admixtures (proteins, fats, lipids etc.): back extraction, solid phase extraction (SPhE), Thin Layer Chromatography (TLC), gel-cromatography, electrophoresis, dialysis and electro-dialysis, sublimation, etc. Choice of purification method depending on state of the sample and method of isolation of the substance being detected. Methods of concentration of the substances analysed in the extracts: liquid- liquid extraction (LLE), SPhE, evaporation and etc.

Topic 9. Toxicological aspects of non-opioid analgesics and non-steroidal anti-inflammatory drugs application. Toxicological screening of drugs with thin layer chromatography.

Toxicology of non-opioid analgesics of various groups: with peripheral action (metamizol sodium), with a central component of action (paracetamol). Biotransformation of paracetamol and formation of toxic metabolite *N*-acetyl benzo quinone imine. Decontamination at acute intoxications and antidote therapy at poisonings by metamizol sodium and paracetamol. Toxic phenomena, which take place at paracetamol application for children and adults.

The general scheme of drug determination in the biological material. Detection with an appropriate screening procedure (TLC-screening and immunochromatographic tests), identification and quantitative determination with the help of chemical and physicochemical methods.

Chemical methods of drug detection. Types of reactions used: colour, sedimentary and microcrystaloscopic reactions, technique of their performing, sensitiveness and specificity of the reactions.

Topic 10. Examination of the acid chloroform extract for derivatives of barbituric and salicylic acids, pyrazolone, purine.

Chemical methods of drug detection. Types of reactions used: colour, sedimentary and microcrystaloscopic reactions, technique of their performing, sensitiveness and specificity of the reactions. Detection and identification of barbiturates, salicylates, pyrazolones and purines in the acid chloroform extract.

Derivatives of salicylic acid, pyrazolone (analgin, antipyrine). Chemical-toxicological analysis of «acid» chloroform extract for acidic, neutral and weak-basic substances. Special methods of barbiturate isolation (methods of V.I. Popova, Valov) at the directed forensic-toxicological examination. Chemical reactions (sedimentary and microcrystaloscopic reactions, colour tests), UV-spectrophotometry (features of light absorption of barbiturates in UV-region of spectrum, bathochromic shift), GLC and HPLC at identification of particular groups of drugs. Quantitative determination with the help of physicochemical methods.

Topic 11. Examination of the basic chloroform extract for alkaloids.

Alkaloids derivatives of pyridine and piperidine (nicotine, anabasine, pachycarpine); tropane (atropine, scopolamine, cocaine); quinoline (quinine, quinidine); isoquinoline (morphine, codeine); opiates and synthetic analogues of morphine (papaverine, ethylmorphine, heroin, promedol, fentanyl); acyclic alkaloids (ephedrine, efedron), indole (strychnine, brucine, rezerpine). Usage in medicine, causes of poisoning (opiate abuse), epidemiology of poisonings. Drug addiction. Physical and chemical properties, chemical structure (classification by the structure of heterocycle), basic laws of behaviour in an organism (routes of administration, distribution, excreting, metabolism), toxicity. Chemical-toxicological analysis of the «basic» chloroform extract for alkaloids. Special method of alkaloid isolation by V.Ph. Kramarenko. TLC-screening of «basic» chloroform extract. Chemical reactions (sedimentary and microcrystalloscopic reactions, colour tests), UV-spectrophotometry (features of light absorption of barbiturates in UV-region of spectrum, bathochromic shift), GLC and HPLC at identification of particular groups of drugs. Quantitative determination with the help of physicochemical methods.

Topic 12. Toxicological aspects of neuroleptics, tranquilizers and local anesthetics application. Examination of the basic chloroform extract for derivatives of 1,4 benzodiazepine, phenothiazine, p-aminobenzoic acid.

Toxicological aspects of tranquilizers: 1,4-benzodiazepines and antipsychotic drugs (neuroleptics): phenothiasines. Toxicodynamics, connection between the mechanism of action of antipsychotic medicines and development of toxic displays. Help during intoxication by antipsychotic medicines. Toxicological features of tranquilizers, the derivatives of benzodiazepine. The factors which influence on toxicity of tranquilizers. The first aid during intoxication by tranquilizers. Epidemiology of poisonings. Chemical-toxicological analysis of «basic» chloroform extract for the synthetic basic drugs. Special isolation methods for 1,4-benzodiazepines (method by B.N. Izotov), phenothiasines (methods by E.N. Salomatin). TLC-screening, location reagents. Detection and identification by means of the sedimentary and colour reactions, UV-spectrophotometry, GLC and HPLC.

Toxicology of local anesthetics, the derivatives of p-aminobenzoyl acid. Toxicodynamics and toxicokinetics of local anesthetics. Range of therapeutic and toxic doses. Features of local anesthetics influence on CNS, CVS, allergy development. Basic factors which influence on toxicity of local anesthetics. Specific forms of toxicity of local anesthetics. Prevention of toxicity development and the first aid in case of poisoning by local anesthetics. Chemical-toxicological analysis of procaine.

Topic 13. Quantitative determination of drugs in the extracts. Examination of body fluids for drugs in acute intoxications.

Methods of quantitative determination of drugs used in toxicological analysis: spectral (spectrophotometry in visible-, UV-region of spectrum, MS, densitometry) and chromatographic methods (HPLC, GLC), immunoassays.

Special features of express-analysis at acute poisonings: samples (biological fluids), direction of the analysis, requirements to sensitiveness and specificity for the analytical methods used, isolation of drugs from the biological fluids: LLE, SPHE. Detection in the biological fluids of particular groups of drugs (salicylates, p-amino phenol derivatives (paracetamol), quinine, phenothiasines, barbiturates, opiates) by means of chemical reactions. Application of immunoassays (radioimmunoassays and enzyme immunoassays) for determination of drugs in the biological fluids.

Topic 14. Biochemical and analytical aspects of pesticide toxicology.

General description of pesticides. Usage in the national economy. Negative sides of the usage of pesticides for an environment and man. Problem of remaining amounts of pesticides. Facilities of prophylaxis of pesticide poisonings. Classifications of pesticides by usage, toxicity, chemical structure. Organophosphorus pesticides. Structure, physical and chemical properties of chlorophos, dihalophos, carbophos, metaphos. Causes of poisoning by organophosphorus, stage of poisoning PhOS. Routes of administration in an organism. Basic laws of behavior in an organism and corpse. Samples for toxicological analysis for organophosphorus pesticides. Methods of isolation from the corpse organs, biological fluids, food stuffs. Choice of the extractant depending on the state, nature of the sample and poison. Purification methods of the extracts from the biological admixtures. Methods of the analysis of extracts for organophosphorus pesticides: chemical, biochemical, chromatography (gas-liquid and thin-

layer chromatography). The methods of organophosphorus pesticides quantitation (photometric by phosphorus, biochemical method, GLC).

Chlorinated pesticides, derivatives of carbamine acid, pyrethrins, derivatives of phenol. Chemical structure and physical and chemical properties of hexachlorocyclohexane, heptachlor, carbyryl, permethrin, cypermethrin, toxicity, clinical presentation of the poisoning. Basic the laws of behaviour in an organism and corpe. Samples for toxicological analysis. Methods of isolation from the biological samples. Methods of identification and quantitative determination with the help of chemical and physicochemical methods.

Carbamates. Chemical structure, physicochemical properties, general rules of behaviour in a body, chemicotoxicological analysis.

Pyrethrins. Chemical structure, physicochemical properties, general rules of behaviour in a body, chemicotoxicological analysis.

Organic mercural pesticides (ethylmercury phosphate, ethylmercury chloride) physical and chemical properties. Usage and toxicity. Rotes of administration in an organism, distribution, metabolism and excretion. Methods of isolation from biological samples. Methods of detection and identification by native compound and by mercury (II). Estimation of the analysis results.

Antidotes at pesticide intoxications.

Semester module supervision

6. Topics of lectures

No.	Name of topic	Hours
1.	Introduction into Toxicological chemistry. Definition of basic concepts and terms of biochemical toxicology and analytical toxicology.	1
2.	Biochemical and analytical aspects of heavy metal toxicology.	1
3.	Toxicology of toxic gases, organic solvents and some cauterizing agents	1
4.	Chemical-toxicological analysis of volatile poisons.	1
5.	Toxicological aspects of application of opioid and non-opioid analgesics, non-steroidal anti-inflammatory drugs, neuroleptics, tranquilizers and hypnotics.	1
6	Sample preparation when examining biological samples for the presence of drugs. Toxicological screening of drugs with thin layer chromatography.	1
The whole amount of hours		6

7. Topics of seminars

(not provided)

8. Topics of practical lessons

(not provided)

9. Topics of laboratorial lessons

No.	Name of topic	Hours
1	Introduction into toxicological chemistry. Definition of basic concepts and terms of biochemical toxicology and analytical toxicology. Biochemical and analytical aspects of heavy metal toxicology. Sample preparation of the biological samples by mineralization. Detection of lead, barium, manganese, chromium in the mineralizate by the fractional method.	4
2	Detection of silver, copper, zinc, bismuth, thallium, antimony, arsenic in the mineralizate by the fractional method.	4
3	Inorganic mercury compounds. Human exposure and health effects. Analytical aspects. Sample preparation. Detection of mercury in the destructate by the fractional method.	4

	Quantitative determination of heavy metals in biological samples.	
4	Toxicology of toxic gases: hydrogen cyanide, formaldehyde, carbon (II) oxide. Sample preparation when examining biological samples for the presence of volatile poisons. Detection of cyanide and formaldehyde in the distillates by a chemical method.	4
5	Biochemical and analytical aspects of toxicology of organic solvents and some cauterizing substances. Examination of body fluids for the presence of alcohols by gas-liquid chromatography.	4
6	Biochemical and analytical aspects of nitrite, nitrate toxicology. <i>Final test of CM 1 assimilation.</i>	4
7	Toxicological aspects of opioid analgesics and hypnotics application. Methods of sample preparation in chemical-toxicological analysis of drugs.	4
8	Toxicological aspects of non-opioid analgesics and non-steroidal anti-inflammatory drugs application. Toxicological screening of drugs with thin layer chromatography.	4
9	Examination of the acid chloroform extract for derivatives of barbituric and salicylic acids, pyrazolone, purine.	4
10	Examination of the basic chloroform extract for alkaloids	4
11	Toxicological aspects of neuroleptics, tranquilizers and local anesthetics application. Examination of the basic chloroform extract for derivatives of 1,4 benzodiazepine, phenothiazine, <i>p</i> -aminobenzoic acid.	4
12	Quantitative determination of drugs in the extracts. Examination of body fluids for drugs in acute intoxications.	4
13	Biochemical and analytical aspects of pesticide toxicology. <i>Final test of CM 2 assimilation.</i>	4
14	Semester credit: "Toxicological Chemistry"	2
The whole amount of hours		54

10. Self-study work

No.	Topics	Hours
1	The subject of toxicological chemistry. Definition of basic concepts and terms of biochemical toxicology and analytical toxicology.	4
2	Biochemical and analytical aspects of heavy metal toxicology. Sample preparation of the biological samples by mineralization. Detection of lead, barium, manganese, chromium in the mineralizate by the fractional method.	4
3	Detection of silver, copper, zinc, bismuth, thallium, antimony, arsenic in the mineralizate by the fractional method.	4
4	Inorganic mercury compounds. Human exposure and health effects. Analytical aspects. Sample preparation. Detection of mercury in the destructate by the fractional method. Quantitative determination of heavy metals in biological samples.	4
5	Toxicology of toxic gases: hydrogen cyanide, formaldehyde, carbon (II) oxide. Sample preparation when examining biological samples for the presence of volatile poisons. Detection of cyanide and formaldehyde in the distillates by a chemical method.	4
6	Biochemical and analytical aspects of toxicology of organic solvents and some cauterizing substances. Examination of body fluids for the presence of alcohols by gas-liquid chromatography.	4
7	Biochemical and analytical aspects of nitrite, nitrate toxicology.	4
8	Preparation for final test of CM 1 assimilation	5
9	Toxicological aspects of opioid analgesics and hypnotics application. Methods of sample preparation in chemical-toxicological analysis of drugs.	4
10	Toxicological aspects of non-opioid analgesics and non-steroidal anti-inflammatory drugs application. Toxicological screening of drugs with thin layer chromatography.	3

11	Examination of the acid chloroform extract for derivatives of barbituric and salicylic acids, pyrazolone, purine.	3
12	Examination of the basic chloroform extract for alkaloids.	3
13	Toxicological aspects of neuroleptics, tranquilizers and local anesthetics application. Examination of the basic chloroform extract for derivatives of 1,4 benzodiazepine, phenothiazine, <i>p</i> -aminobenzoic acid.	3
14	Quantitative determination of drugs in the extracts. Examination of body fluids for drugs in acute intoxications.	3
15	Biochemical and analytical aspects of pesticide toxicology.	3
16	Preparation for final test of CM 2 assimilation	5
The whole amount of hours		60

Tasks for self-study work

1. Modern practical assignments of Analytical Toxicology: Therapeutic Drug Monitoring, Environmental Toxicology, Food Toxicology, Occupational Toxicology.
2. Methods of natural and artificial decontamination at acute poisonings. Antidote therapy.
3. Usage of heavy metal compounds in industry, agriculture and medicine.
4. The chemical equations of the reactions used to detect heavy metal cations, arsenic and antimony compounds in the mineralizate by fractional method.
5. Theoretical bases of titrimetric methods of quantitative analysis (complexometry, iodometry, dichromatometry, rhodanometry).
6. Theoretical bases of photolorimetric method of quantitative analysis.
7. The chemical equations of the reactions of silver, copper, zinc, bismuth, cadmium, thallium, antimony, arsenic mercury compound detection by the fractional method.
8. Theoretical bases of titrimetric methods of quantitative analysis (complexometry, iodometry, dichromatometry, rhodanometry).
9. Spectral methods of quantitative determination of heavy metal compounds: atomic emission analysis, mass spectrometry with inductively coupled plasma, atomic, X-ray fluorescence, photometric analysis.
10. Application of organic solvents (halogenated hydrocarbons, alcohols), cyanides, formaldehyde, phenol, acetic acid in industry, agriculture and medicine.
11. Theoretical bases of the steam distillation method.
12. Microdiffusion and dry-air distillation in isolation of volatile substances from the biological samples.
13. Chemical-toxicological analysis of ethylene glycol and tetraethyl lead.
14. The chemical equations of the reactions used for detection of volatile substances in the distillate.
15. Theoretical basis of qualitative and quantitative analysis of chemical substances by gas-liquid chromatography. Advantages and disadvantages of the GHG method in the analysis of volatile substances (relative to the chemical method and GC), assessment of the method for sensitivity and specificity. The value of the GHG method for forensic toxicological analysis of volatile substances.
16. Charcoal gas (carbon monoxide). Toxicological significance, physical and chemical properties, toxicity, analysis of blood for presence of charcoal gas by chemical and spectrophotometry methods.
17. Hydrogen sulphide. Physical and chemical properties, toxicity, reasons of poisonings, detection of hydrogen sulphide in biological samples.
18. Nitric acid. Mechanism of toxic action. Chemical-toxicological analysis of nitric acid.
19. Hydrochloric acid. mechanism of toxic action. Chemical-toxicological analysis of hydrochloric acid.
20. Toxicity and treatment of nitrate and nitrite poisonings. Antidote therapy.
21. Chemical-toxicological analysis of nitrates and nitrites.
22. Alkalis. Mechanism of toxic action. Chemical-toxicological analysis of caustic alkalis (sodium hydroxide, potassium hydroxide) and ammonia.

23. Physical basis of the dialysis method.
24. Toxicological characteristics of NSAIDs of phenylpropionic and phenylacetic acid derivatives (ibuprofen, diclofenac sodium).
25. Toxicological characteristic of NSAIDs of pyrazolone derivatives (phenylbutazone) and indolacetic acid (indomethacin).
26. Toxicology of sedative medicines (bromides). Methods of treating acute poisoning with these drugs.
27. Toxicology of analeptics (strychnine). Targets of toxic action on CNS, CVS and other organs and systems. Help in case of analeptics poisoning. Toxicodynamics. Prevention of poisoning and first aid during intoxication by this medicine.
28. Toxicology of psychostimulants (amphetamines, caffeine). Targets of toxic action on CNS, CVS and other organs and systems. Help in case of psychostimulant poisoning. Psychostimulants and their toxicodynamics. Prevention of poisoning and first aid during intoxication by these medicines.
29. Toxicology of psychotomimetics (cocaine). Targets of toxic action on CNS, CVS and other organs and systems. Help in case of cocaine poisoning. Toxicodynamics. Prevention of poisoning and first aid during intoxication by this substance.
30. Toxicology of local anesthetics, the derivatives of p-aminobenzoyl acid (benzocaine, procaine hydrochloride, lidocaine, cocaine hydrochloride). Toxicodynamics and toxicokinetics of local anesthetics. Prevention of poisoning and first aid during intoxication by these medicines.
31. Sulphuric acid. Mechanism of toxic action. Chemical-toxicological analysis of sulphuric acid.
32. Physicochemical property of drugs (solubility, ionization constant, lipophilicity).
33. Theoretical bases of liquid-liquid extraction.
34. Theoretical bases of salting out, gel-chromatography, sublimation, electrophoresis.
35. Usage in medicine and toxicity of salicylates, barbiturates, pyrazolones-5.
36. Physico-chemical properties of barbiturates.
37. The chemical equations of the reactions used in chemical-toxicological analysis of salicylates, barbiturates, derivatives of purine and pyrazolone-5.
38. Chemical-toxicological analysis of p-aminophenol derivatives (paracetamol).
39. Toxicity, special symptoms of intoxication, first aid and detoxification in poisoning by alkaloids of various chemical groups.
40. Chemical-toxicological analysis of opium alkaloids: narcotine, papaverine, semi-synthetic opiates - heroin, as well as opium components – meconic acid, meconin.
41. The chemical equations of reactions used in the chemical equations for detection of alkaloids of the specified groups.
42. Drug addiction – social problem of society. Give definitions of terms "narcotic substance", "psychoactive substance", "drug addiction".
43. Toxicity, specific symptoms of intoxication, first aid and detoxification measures in poisonings with 1,4-benzodiazepine, phenothiazine, p-aminobenzoic acid derivatives.
44. The chemical toxicological significance and methods of toxicological screening of some narcotic, psychotropic and potent medicinal substances (synthetic opioids, amphetamines, dimedrol, clonidine, amitriptyline).
45. Quantitative determination of drugs in the extracts from the biological material.
46. Methods of clinical diagnosis of acute poisonings.
47. The main directions of laboratory express analysis of acute intoxication. The role of analytical diagnostics in the express analysis of acute intoxications.
48. Use of immunochemical and immunochromatographic screening, TLC-screening, HPLC and GLC screening) for analytical diagnostics of acute poisoning.
49. Usage of pesticides in agriculture, industry and medicine.
50. Theoretical bases of Thin Layer Chromatography method.
51. Toxicity, clinical presentation, antidote therapy in the poisoning of acetyl choline inhibitors.

11. Criteria and evaluation order of educational outcomes

Evaluation system of the educational component: The results of the semester supervision in the form of a semester credit are evaluated on a 100-point, non-differentiated scale ("passed", "failed") and on the ECTS scale.

Progress supervision: oral survey, writing test tasks, solving situational problems.

Supervision of content modules: preparation of test tasks, solution of situational problems.

Semester exam: not provided)

Semester control form: semester credit.

Conditions for admission to the supervision of content modules: For admission to the supervision of content module 1 and 2, it is necessary to have a minimum number of points for the topics (classes) of content module 1 and 2.

Conditions for admission to semester supervision: A current rating of more than 60 points, absence of missed laboratory classes, fulfillment of all requirements stipulated in the work program of the educational component.

Grading Scheme for progress supervision

Modules required points Content modules				Semester credit	Total
Content module 1		Content module 2		-	100
T1-T7	Final test of CM 1 assimilation	T8-T13	Final test of CM 2 assimilation		
16-28	12-20	20-32	12-20		

The academic activities during the laboratorial lessons

Lab lesson N	Points	Criteria
P.L. N 1-13	max (5; 4; 3)	Are given to the such student who performed practical work deals with the description of the toxicological characteristics of particular groups of medicine in detail and correctly, answered for homework questions and filled a laboratory journal.
	min (3; 1)	Are given to the such student who performed practical work deals with the description of the toxicological characteristics of particular groups of medicine correctly, filled a laboratory journal, but answered for homework questions with significant mistakes or incorrectly.

Non-differentiated scale	Scale ECTS	Rating estimation, points
passed	A-fine	90-100
passed	B-very well	82-89
passed	C-well	74-81
passed	D-satisfactorily	64-73
passed	E-sufficiently (satisfies minimum criteria)	60-63
failed	FX- unsatisfactory	35-59
failed	F- unsatisfactory (necessary additional work)	1-34

Rating estimations as **FX**, **F** are proposed to the students is not passed the discipline module after completion of its learning.

Rating estimation as **FX** is proposed to the students obtained the least of points as a result of current control, but not passed the final module control. Such students have a right to retaking of the module control by the schedule ratified by dean's office.

Rating estimation **F** is proposed to the students, attended all audience classes of the discipline, but they did not obtain the enough amount of points as a result of current control and they are not admitted to the final module control. This category of students has a right to the repeated study of the module.

12. Forms of progress and semester supervision of academic achievements

Semester control is carried out in the form of a semester credit.

13. Methodological support

1. Educational program of the educational component.
2. Work program of the educational component.
3. Textbook on toxicological chemistry with analytical toxicology.
4. Lecture course.
5. Methodological manual for teachers and self-studying of students.
6. Workbook for laboratory lessons.
7. List of theoretical questions for final control.
8. Collection of multiple choice questions.
9. Variants for final control.

14. Reading suggestions

The main reading suggestions

1. Karpushina S.A. Toxicological Chemistry with Analytical Toxicology : Textbook for students of higher education institutions / S. A. Karpushyna, S. V. Baiurka. Kharkiv : NUPh, 2021. — 352 p.
2. Karpushyna S. A. Collection of Multiple Choice Questions on Toxicological Chemistry with answers and explanations / S. A. Karpushyna, K.Yu. Netiosova, S.V. Baiurka – Kh.: NUPh Publishing, 2018. – 92 p.

Supplementary reading suggestions

1. Baselt C. R. Disposition of Toxic Drugs and Chemicals in Man / Randall C. Baselt. – [9-th ed.]. – Seal Beach, California : Biomedical Publications, 2011. – 1900 p.
2. Clarke's analysis of drugs and poisons in pharmaceuticals, body fluids and postmortem material: 4-th edition / A. C. Moffat; M.D. Osselton; B. Widdop [et al.]. – London, Chicago: Pharmaceutical Press, 2011. – 2736 p.

15. Electronic resources including the Internet

1. <https://www.ncbi.nlm.nih.gov/pmc/>
2. <https://apps.who.int/iris/handle/10665/42020>
3. <https://www.unodc.org/unodc/en/scientists/guidance-for-the-validation-of-analytical-methodology-and-calibration-of-equipment.html>
4. http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/-Quality/Q2_R1/Step4/Q2_R1__Guideline.pdf.